

# CD Spectroscopic Study on the Molecular Recognition of Chiral Salen-Metal Complexes<sup>†</sup>

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The molecular recognition behavior of the chiral salen-metal complexes towards guest molecules, such as imidazole derivatives and amino-acid ester, was systematically investigated by means of circular dichroism (CD) spectra. The coordination numbers of the host-guest complexes as well as the recognition capability of the salen-metal complexes were explained by character and intensity analyses of the CD spectra.

**Keywords** chiral salen complex, circular dichroism spectrum, molecular recognition

## Introduction

The steric configuration of biological molecules and consequent effects *in vivo* attract much attention, since different space structures may result in fairly different physiological actions. The CD spectrum is a powerful method for the study on conformation, configuration and three-dimensional structure of organic and biological macromolecules, because the circular dichroism of optically active compounds can provide valuable information about their conformation, absolute configuration and reaction mechanism. The asymmetric environment has an influence on the energy level transition of the chromophore group in the organic molecules, which is the origin of circular dichroism Cotton effects. The Cotton effects can be generated by (a) the inherent chiral chromophores, (b) distortion of the symmetric chromophores in the chiral environment, and (c) the interaction among non-bonding dipoles.<sup>1</sup> The steric configuration and conformation may be determined by CD Cotton effects, and even weak Cotton effects blanketed by strong absorption can be distinguished because of the high resolution and sensitivity of CD spectra. The CD spectrum has been widely applied instead of optical rotatory dispersion (ORD) in the study of chiral compounds. The metal complexes with salen ligands, *i. e.*, the quadridentate Schiff base ligands, are promising hosts for chiral molecular recognition because of its simple preparation, low cost and structural variety.<sup>2</sup> The

syntheses of a series of (salen)Cu complexes<sup>3</sup> and the [(salen)Mn<sup>III</sup>]<sup>+</sup> complex<sup>4</sup> were previously reported by Tanaka and Gravert, respectively. A series of water-soluble (salen)Ni complexes was synthesized and their molecular recognition towards DNA molecules was investigated by Muller *et al* in 1999.<sup>5</sup> The boric acid substituted chiral salen compound (salen)Co<sup>III</sup>Br was proved to be an excellent host for the enantiomer recognition of oligosaccharides, such as mannitose and talose.<sup>6</sup> We have investigated the molecular recognition of salen metal complexes towards imidazole derivatives<sup>7a,7b</sup> and amino-acid guests<sup>7c</sup> by a spectrophotometric titration method. Here we report the CD spectroscopic study of the molecular recognition process of the salen-metal complexes.

## Experimental

### Instruments and reagents

All reagents were commercial products. The solvents were purified according to literature,<sup>8</sup> while the ligand was recrystallized before use. The chiral (salen)Fe<sup>III</sup>Cl and (salen)Co<sup>II</sup> complexes were synthesized through the reported procedure.<sup>9</sup> The <sup>1</sup>H NMR spectra were recorded on a Bruker AC-P300 spectrometer. The UV-Vis and CD spectra were determined on a Beckman DU-8B spectrometer and a JASCO715 spectropolarimeter, respectively. Elemental analysis was performed on a Yanaco CHN Corder MT-3 analyzer.

The ligand was examined by its <sup>1</sup>H NMR spectrum, while the salen complexes were characterized by elemental analysis and UV-Vis spectra. The structure of (salen)Fe<sup>III</sup>-Cl complex is shown in Fig. 1a as an example.

### CD spectra determination

The molecular recognition of (salen)Fe<sup>III</sup>Cl complex with imidazole (Im), 1-methylimidazole (1-MeIm), 2-

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methylimidazole (2-MeIm) and clotrimazole (GMZ) (Fig. 1b), as well as that of (salen)Co<sup>II</sup> complex with amino-acid esters was investigated by CD spectroscopic titration method at  $(15\text{--}30) \pm 0.1$  °C. Each CH<sub>2</sub>Cl<sub>2</sub> solution containing  $1.0 \times 10^{-5}$  mol/dm<sup>3</sup> of a chiral salen metal complex and a guest, of which the concentration is 20–1000 times of the host, was let to stand to approach its equilibrium before the CD detection. Investigation on the recognition systems of (salen)Co<sup>II</sup> complex and amino-acid esters was accomplished by recording the CD spectra of the CH<sub>2</sub>Cl<sub>2</sub> solution of (salen)Co<sup>II</sup> complex together with *D*-amino-acid esters and their enantiomers, *L*-amino-acid esters, respectively.

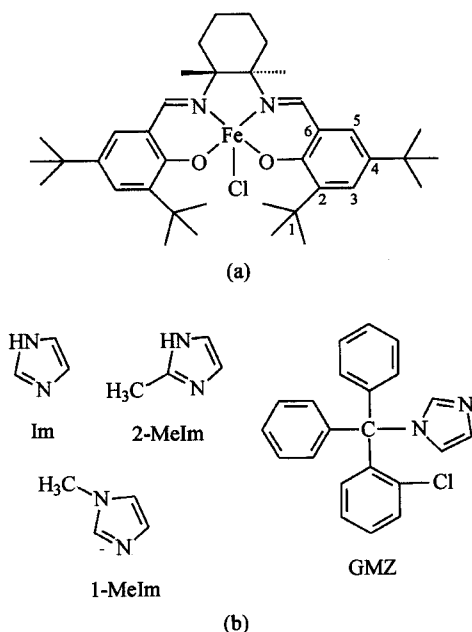


Fig. 1 Structure of (a) chiral (salen)Fe<sup>III</sup> complex and (b) Im, 1-MeIm, 2-MeIm, GMZ.

## Results and discussion

### Molecular recognition between (salen)Fe<sup>III</sup>Cl and imidazole and its derivatives

Our previous study<sup>7a,7b</sup> has proved that for the molecular recognition of chiral salen metal complexes, the axial coordination number of the host-guest complexes of imidazole, 1-methylimidazole and 2-methylimidazole is two, while that of clotrimazole is one. In addition, the sequence of coordination constant is  $K(\text{Im}) > K(2\text{-MeIm}) > K(1\text{-MeIm}) > K(\text{GMZ})$ . The differences of the coordination number and constant can be intuitively seen in the CD spectra of the recognition systems.

#### (1) Effect of coordination number

The CD spectra of the recognition system of (salen)Fe<sup>III</sup>Cl and imidazole are shown in Fig. 2. Free (salen)Fe<sup>III</sup>Cl host displays its negative Cotton effects at 280 and 375 nm, and positive Cotton effect at 320 nm. During the formation of host-guest complex, the absorption of the host

complex decreases, while a new signal at 300 nm forms gradually. The decrease of the intensity of the absorption band at *ca.* 320 nm indicates that larger guest concentration results in the decrease of the number of pentacoordinated conformations. When the concentration of the guest reaches a certain value, the hexacoordinated complex appears, as seen from the CD spectra, *i. e.*, the reversion of the sign of the Cotton effects occurs.<sup>10</sup>

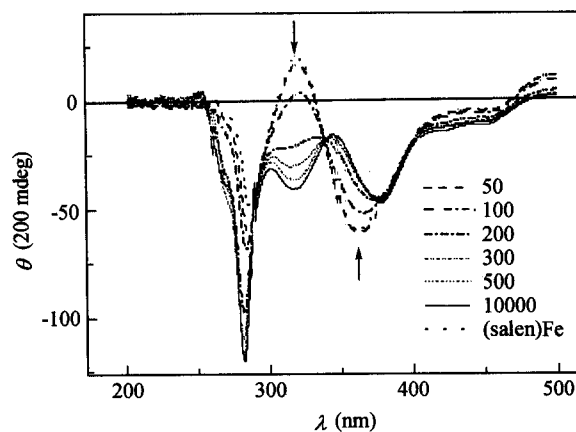


Fig. 2 CD spectra of the recognition system of (salen)Fe<sup>III</sup>Cl and imidazole.

In a relatively low concentration of imidazole, the salen complex is still in a pentacoordinated fashion, however, two species are possible, namely the host complex (salen)FeCl and the (salen)FeIm, which is generated by the substitution of imidazole for the chlorine atom. The absorption of the host (salen)FeCl is subtracted from the CD curves as a background to illustrate the formation of the new species with imidazole ligand as shown in Fig. 3 [(salen)FeCl line did not subtract background in Fig. 3]. As seen in Fig. 3, in a low concentration of imidazole, the CD spectra are nearly straight lines, and it is suggested that no host-guest complex is formed. When the concentration of imidazole ligand increases, the host-guest complex gradually occurs.

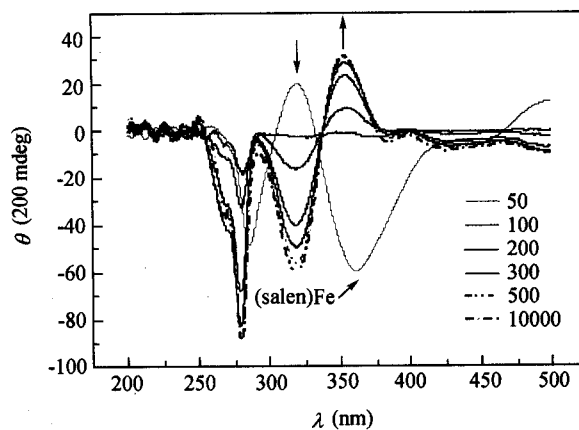


Fig. 3 CD spectra of (salen)Fe<sup>III</sup>-imidazole system with background correction.

As shown in Fig. 4, the recognition system of (salen)Fe<sup>III</sup>Cl complex and 2-MeIm has similar behavior to that of (salen)Fe<sup>III</sup>Cl and imidazole. The Cotton effect of the host complex at 320 nm decreases along with the increase of the guest concentration, while a new Cotton effect splitting band appears at *ca.* 425 nm, which indicates that the new chromophore is induced by the formation of the hexacoordinated complex.

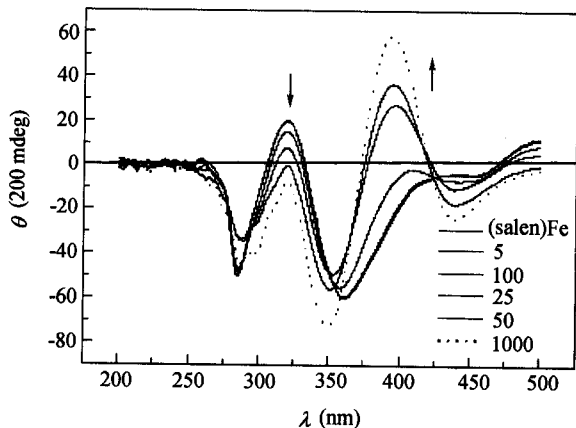


Fig. 4 CD spectra of the recognition system of (salen)Fe<sup>III</sup>Cl and 2-MeIm.

Fig. 5 is the CD spectra of the same system with background correction, which are similar to that of the imidazole system. Only when the guest concentration is large enough, can the guest molecules be completely coordinated. In addition, the Cotton effect at *ca.* 325 nm has split into two new bands to some extent at 280 nm and 380 nm as seen in Fig. 5.

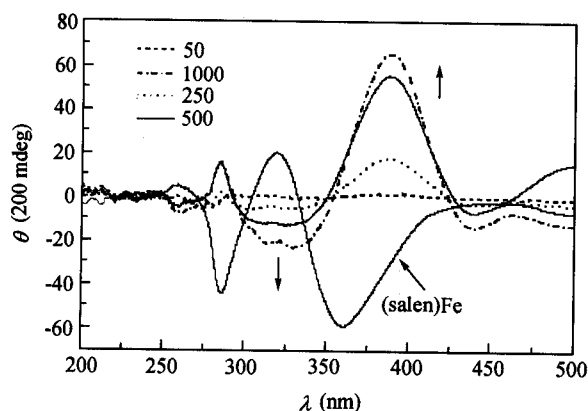


Fig. 5 CD spectra of (salen)Fe<sup>III</sup>-2-MeIm system with background correction.

The CD spectra of the recognition system of (salen)-Fe<sup>III</sup>Cl and 1-MeIm are shown in Figs. 6 and 7. The similar reversion of Cotton effect signs can be seen in Fig. 6. Interestingly, remarkable difference occurs in Fig. 7 when the guest concentration increases, and it is suggested that large conformation changes with increase of the concentration. The Cotton effects of the host lie at *ca.* 375, 320

and 280 nm. The 280 nm band splits in the system with a low guest concentration. When the guest concentration rises to a certain value, the band split at 280 nm disappears to form a complete positive Cotton effect, while the sign of the band at 370 and 320 nm reverses. The difference between the recognition process of 1-MeIm and 2-MeIm is probably caused by their different coordination capabilities. The coordination constant of 1-MeIm is less than that of 2-MeIm. The hexacoordinated complex with both chlorine and 1-MeIm ligand might first form in a low 1-MeIm concentration, and 1-MeIm would substitute the chlorine to form (salen)Fe<sup>III</sup>-(1-MeIm)<sub>2</sub> at a 1-MeIm concentration large enough.

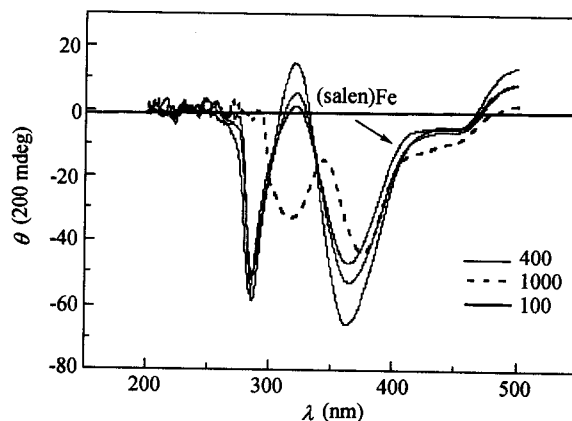


Fig. 6 CD spectra of the recognition system of (salen)Fe<sup>III</sup>Cl and 1-MeIm.

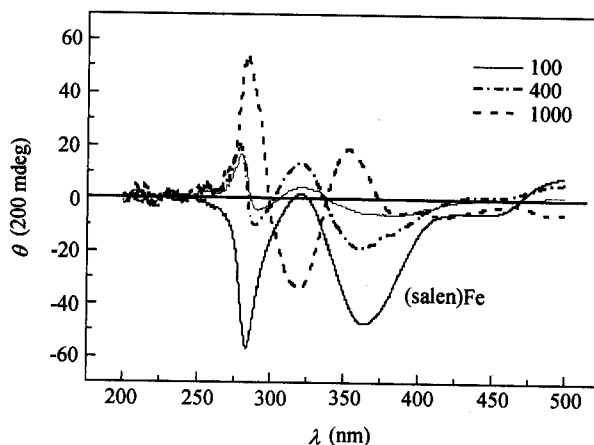


Fig. 7 CD spectra of (salen)Fe<sup>III</sup>-1-MeIm system with background correction.

The CD spectra of the recognition process of (salen)-Fe<sup>III</sup>Cl and clotrimazole are shown in Fig. 8, in which the dashed line is treated with host background correction. Similar intensity decrease of Cotton bands a and b can be observed in Fig. 8, and the coordination saturates when the guest concentration reaches over 400 times of the host concentration. This is due to the weak coordination ability of clotrimazole and its coordination number is only one.<sup>7a,7b</sup> The host-guest complex formed has the hexacoor-

minated structure with one clotrimazole ligand and one chlorine ligand.

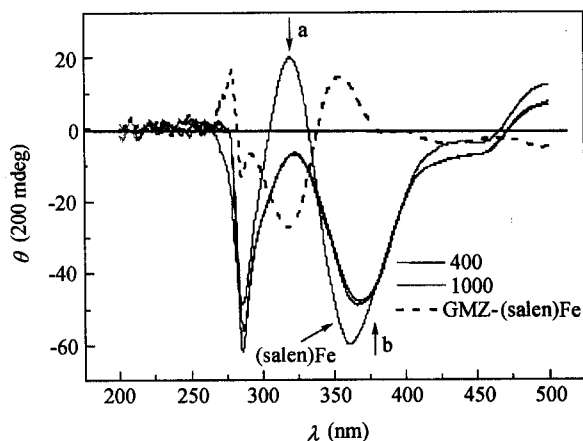


Fig. 8 CD spectra of the recognition system of  $(salen)Fe^{III}Cl$  and clotrimazole.

(2) Different recognition capabilities of  $(salen)Fe^{III}Cl$  towards different guests

The CD spectra of the equilibrated systems of  $(salen)Fe^{III}Cl$  and imidazole derivatives with the same guest concentrations (400 times of that of the host) are illustrated in Fig. 9.

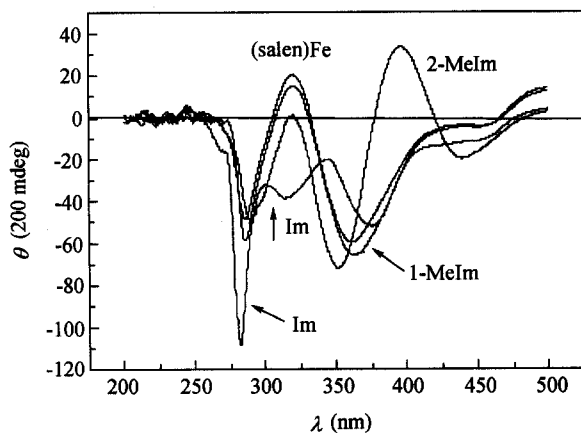


Fig. 9 CD spectra of the recognition systems of  $(salen)Fe^{III}Cl$  and different guests.

As seen in Fig. 9, different guests in the same concentration present different recognition capabilities. For imidazole and 2-MeIm, the CD spectra show evident Cotton effects of the host-guest complex, however, from the CD spectrum of 1-MeIm system it is suggested that the main component of the mixture is still the pentacoordinated complex. In addition, the absorption bands of different systems at *ca.* 320 nm possess similar character but different intensity, which may be considered to represent the nature of the host-guest coordinating. The relative intensity of this absorption band to that of the host attributes to the intensity of host-guest interaction.<sup>11</sup> The relative intensity

of the absorption bands of recognition systems at *ca.* 320 nm, together with the corresponding coordination constants determined by thermodynamic method, are compiled in Table 1.

Table 1 Relation between the CD bands at *ca.* 320 nm and the coordination constant

	Guest		
	Im	2-MeIm	1-MeIm
Relative intensity of the CD absorption band	57	19	4.4
Coordination constant	$7.76 \times 10^4$	$2.43 \times 10^4$	$1.56 \times 10^4$

As seen in Table 1, the intensity sequence of the CD bands well coincides with the sequence of the corresponding coordination constant, and it is suggested that CD spectroscopic method can characterize the strength of the host-guest interaction.

The molecular recognition between  $(salen)Co^{II}$  and amino acid esters

The CD spectrum of the recognition system of  $(salen)Co^{II}$  and *D*-alanine methyl ester and that of  $(salen)Co^{II}$  and *L*-alanine methyl ester are shown in Fig. 10.

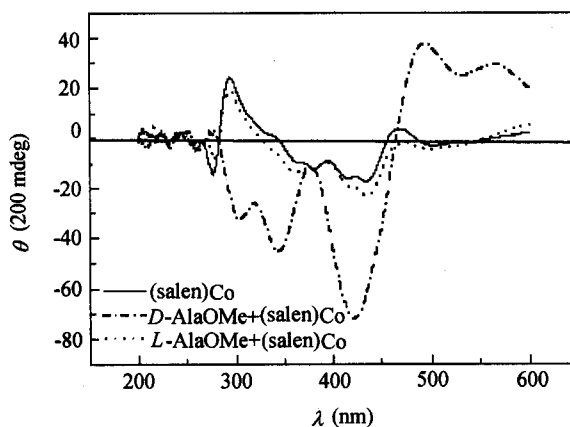


Fig. 10 CD spectra of the recognition systems of  $(salen)Co^{II}$  and *D*- and *L*-alanine methyl esters.

As seen in Fig. 10, the alanine esters cause apparent changes of the CD spectra of the  $(salen)Co^{II}$  host. In addition, the guests with different configurations, *i. e.*, *D*-alanine ester and *L*-alanine ester, yield significantly different host-guest interaction, which is suggested by the different CD spectra of the two recognition systems. The system of  $(salen)Co^{II}$  and *L*-alanine ester displays a CD spectrum that is almost the same as that of the  $(salen)Co^{II}$  host. On the contrary, the CD spectrum of the system of  $(salen)Co^{II}$  and *D*-alanine ester displays remarkable Cotton effects above 450 nm as well as other strong Cotton effects, which are largely different from that of the host. The

difference between the CD spectra indicates a high recognition selectivity of (salen)Co<sup>II</sup> towards *D*- and *L*-alanine esters, which coincides with the coordination constant data determined by UV-Vis titration.<sup>7b</sup> In addition, (salen)Co<sup>II</sup> complex was also found to have noticeable enantiomer recognition towards the methyl esters of leucine, serine and tyrosine.

## Conclusion

The study on the CD spectroscopy of the system shows that the pentacoordinated complex is formed first in the molecular recognition process of the chiral (salen)Fe<sup>III</sup>Cl towards imidazole and its derivatives, then the hexacoordinated complex. The sequence of the relative intensity of the CD bands well coincides with the sequence of the corresponding coordination constant data determined by UV-Vis titration. The CD spectra of the system of (salen)Co<sup>II</sup> and *D*-alanine ester displays remarkable Cotton effects compared to that of *L*-alanine ester. It indicates a high recognition selectivity of (salen)Co<sup>II</sup> towards *D*- and *L*-alanine ester which coincides with the coordination constant data.

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