Non-covalent Interactions in Metal Complexes. II.[1] Induction of Asymmetry in Cobalt(III) Complexes with Amino Acid-Schiff Bases. Importance of CH···π-Interaction in Determining Configuration of Complexes

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Cobalt(III) complexes, $[Co(l\text{-mop=aa})_2]^-$ and $[Co(cop=aa)_2]^-$ (aa=ala$^-$, val$^-$, leu$^-$, phe$^-$), where $H_2(l\text{-mop=aa})$ and $H_2(cop=aa)$ denote amino acid–Schiff bases of *l*-menthyl 3-(*o*-hydroxybenzoyl)propionate and cholesteryl 3-(*o*-hydroxybenzoyl)propionate, respectively, were prepared in solution. The intensity of the CD peak induced at 520 nm changes with the solvent used for preparation of the complex, decreasing in the order: ethanol, methanol, dimethyl sulfoxide, *N,N*-dimethylformamide and acetonitrile. Since the order corresponds to the increasing order of the CH..π-interaction between the solvent and benzene, it seems that the CH..π-interaction between the chiral group and the aromatic nucleus in the ligand plays an important role in determining the configuration of the complexes.

Asymmetric transformation of racemic amino acids into an optical isomer by the use of metal complexes is important in amino acid industry and of interest in connection with the model of transamination reaction in the biological system. Amino acid coordinated to an optically active cobalt(III) complex is epimerized in alkaline solution, whereby D- or L-amino acid is produced in excess in equilibrium.[2,3] Activation of the hydrogen at the α-carbon of amino acid coordinated to a metal is attained only under high pH conditions. On the other hand, when an amino acid is incorporated into the ligand system of a complex by Schiff base formation, the hydrogen at the α-carbon atom is easily labilized in the physiological pH range, an optical amino acid being isomerized.[4-6] This is thought to be a racemase model in the biological system. If a complex with amino acid–Schiff base is formed in an asymmetric environment, DL-amino acids might be transformed into an optical isomer. This type of reaction should operate in the transamination reaction of vitamine B_6.[7] However, only a few studies have been reported on asymmetric transformation of racemic amino acid into an optical isomer by the use of Schiff base complex.[1,8,9]

It was found that in the cobalt(III) complexes, $[Co(l\text{-mop=aa})_2]^-$ (Fig. 1a), with the Schiff base obtained from *l*-menthyl 3-(*o*-hydroxybenzoyl)propionate and DL-amino acid, asymmetry around the metal is induced and DL-amino acids are partially transformed into an optical isomer.[1] The *l*-menthyl group on the side chain exerts a vicinal effect but not a Pfeiffer effect on determining the configuration of the complex, since the group no longer affects the asymmetry induction when it is detached from the ligand. However, the origin of the vicinal effect has not been clarified yet. We intended to elucidate how the *l*-menthylg roup causes the asymmetry around the metal. For this purpose new cobalt(III) complexes, $[Co(cop=aa)_2]^-$, with the amino acid–Schiff bases of cholesteryl 3-(*o*-hydroxybenzoyl)propionate were also prepared in solutions (Fig. 1b) and the effect of the cholesteryl group on the asymmetry induction was examined.

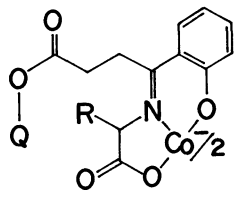

Fig. 1.
(a) Q=*l*-menthyl
(b) Q=cholesteryl

Experimental

Preparation. 3-(*o*-Hydroxybenzoyl)propionic acid was synthesized by the method of Fieser *et al.*[10] Synthesis of *l*-menthyl 3-(*o*-hydroxybenzoyl)propionate (H(*l*-mop)) was described in the preceding paper.[1]

Cholesteryl 3-(o-Hydroxybenzoyl)propionate (Hcop). 3-(*o*-Hydroxybenzoyl)propionic acid (7.2 g) and cholesterol (14.3 g) were dissolved in benzene (100 cm^3). To this was added a drop of concd sulfuric acid and the mixture was refluxed for 48 h. During the course of this reaction, water formed by esterification was eliminated as a benzene azeotrope. The solvent was evaporated and the pale brown precipitate obtained was recrystallized twice from a ethanol–benzene mixture to give colorless needles melting at 160—161 °C.

Found: C, 79.30; H, 9.81%. Calcd for $C_{37}H_{52}O_4$: C, 78.96; H, 9.67%.

Cobalt(III) Complexes. Preparation of the solutions of $[Co(l\text{-mop=aa})_2]^-$ is as follows. Racemic amino acid (5×10^{-4} mol), H(*l*-mop) (5×10^{-4} mol), cobalt(II) acetate tetrahydrate (2.5×10^{-4} mol) and triethylamine (*ca.* 60 mg) were placed in a 50 cm^3 volumemetric flask and the volume was adjusted with a solvent (ethanol, methanol, dimethyl sulfoxide, *N,N*-dimethylformamide, or acetonitrile). Synthesis of $[Co(cop=aa)_2]^-$ is nearly the same as that of $[Co(l\text{-mop=aa})_2]^-$ except for using a 1: 1 mixture of a solvent and carbon tetrachloride, because of low solubility of Hcop in ethanol and so on. Clear red solutions were obtained after 2 or 3 d.

Measurements. Electronic spectra and circular dichroism spectra were measured with a Shimazu multipurpose spectrophotometer Model MSP-5000 and a JASCO ORD/CD optical dispersion recorder, respectively. NMR spectra were measured with a Hitachi NMR spectrophotometer Model R-20-B in carbon tetrachloride and in benzene using tetramethylsilane as an internal standard.

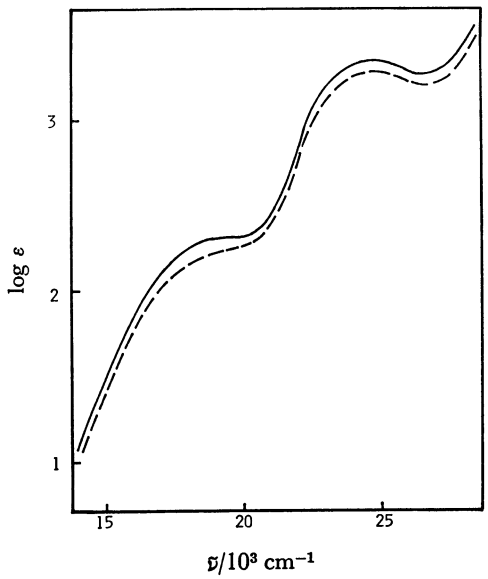

Fig. 2. Electronic spectra of (——) $[Co(l\text{-mop=ala})_2]^-$ (in methanol) and (– – –) $[Co(cop=ala)_2]^-$ (in methanol–carbon tetrachloride).

Results and Discussion

Electronic spectra of $[Co(l\text{-mop=aa})_2]^-$ and $[Co(cop=aa)_2]^-$ are similar to each other. Typical examples are shown in Fig. 2. Two absorption bands appeared near 19000 and 24500 cm^{-1}, whose extinction coefficients gradually increased and converged after 120 h to *ca.* 200 and 1500 $mol^{-1}\,dm^3\,cm^{-1}$, respectively. The frequencies and the extinction coefficients of these bands are almost independent of the amino acid and the solvent used for preparation of the complex. Although we were not successful in isolating the complexes, it seems reasonable to formulate the complexes as $[Co(l\text{-mop=aa})_2]^-$ and $[Co(cop=aa)_2]^-$.

CD spectra of $[Co(l\text{-mop=ala})_2]^-$ prepared in methanol and $[Co(cop=ala)_2]^-$ prepared in methanol–carbon tetrachloride (1 : 1) are given in Figs. 3 and 4,

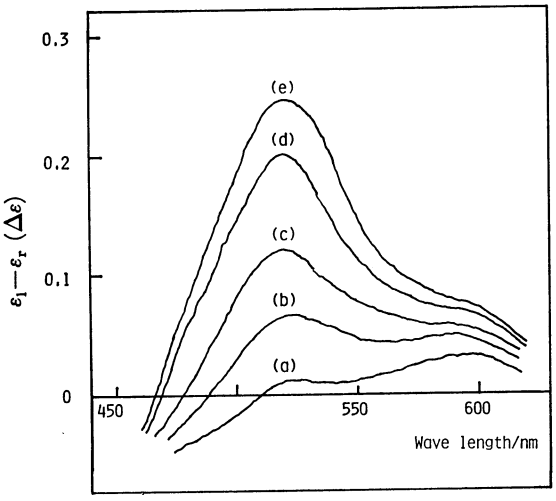

Fig. 3. CD spectra of $[Co(l\text{-mop=ala})_2]^-$ (in methanol) at various reaction times.
(a) 20, (b) 43, (c) 63, (d) 113, and (e) 230 h.

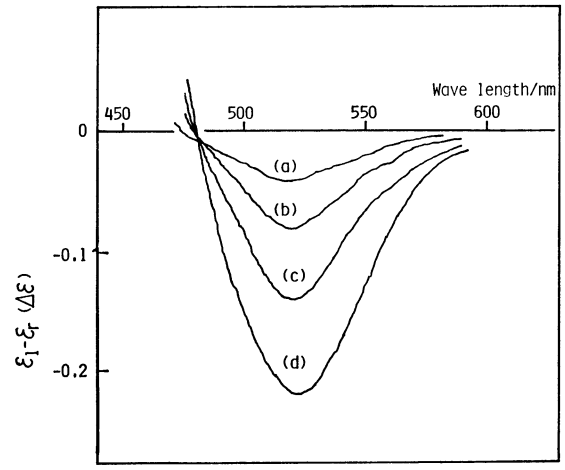

Fig. 4. CD spectra of $[Co(cop=ala)_2]^-$ (in methanol–carbon tetrachloride) at various reaction times.
(a) 20, (b) 60, (c) 120, and (d) 240 h.

respectively. In the spectrum of $[Co(l\text{-mop=ala})_2]^-$ a positive CD peak appeared near 520 nm, whose intensity gradually increased and converged after *ca.* 240 h. Similar CD spectra were observed for $[Co(l\text{-mop=val})_2]^-$ and $[Co(l\text{-mop=leu})_2]^-$. On the other hand, a negative CD peak was induced in $[Co(cop=ala)_2]^-$. A negative CD peak was also induced in $[Co(cop=val)_2]^-$ and $[Co(cop=leu)_2]^-$ prepared in methanol–carbon tetrachloride. It is likely that the cholesteryl group exerts an opposite vicinal effect to the *l*-menthyl group. Appearance of the CD band in the visible region indicates that an asymmetry around the metal is induced. We presumed that *l*-mop=aa^{2-} facially coordinates to the cobalt(III) ion form the view of Burrows and Bailar, Jr.,[11] that the *fac*-form is more stable than the *mer*-form. Belokon *et al.*[12] determined the structure of an optically active form (*Λ*(*SS*)) of potassium bis[*N*-(3-methylsalicylidene)threoninato]-cobaltate(III) and showed that the Schiff base meridionally coordinates to the metal. $[Co(l\text{-mop=aa})_2]^-$ and $[Co(cop=aa)_2]^-$ are thus presumed to also possess a *mer*-configuration. One set of optical isomers (*Δ* and *Λ*) is considered for these complexes. It seems that an isomer showing a positive CD peak at 520 nm is formed in excess for $[Co(l\text{-mop=aa})_2]^-$, while an isomer showing a negative CD peak at 520 nm for $[Co(cop=aa)_2]^-$, owing to the effect of the chiral group on the side chain.

On the basis of the Dreiding model, it is unlikely that the chiral group in the present complexes exerts any steric hindrance to the complex formation. In fact, no CD peak was detected for the copper(II) and the nickel(II) complexes with H_2(*l*-mop=aa) and H_2(cop=aa). A hydrophobic interaction between the chiral group and the group attached to the α-carbon of the amino acid can not be the main effect, since the CD peak was induced in $[Co(l\text{-mop=gly})_2]^-$.[1] Thus, it is most probable that some non-covalent interaction between the chiral group and some part of the molecule or an asymmetric packing effect of the chiral group in the cavity of the molecule[13] causes the asymmetry around the metal.

Table 1. Intensities ($\Delta\varepsilon$) of CD band induced at 520 nm

	EtOH	MeOH	DMSO	DMF	AN
$[Co(l\text{-mop=ala})_2]^-$	0.40	0.24	0.14	0.12	0
$[Co(l\text{-mop=val})_2]^-$	0.21	0.20	0.06	0.05	0
$[Co(l\text{-mop=leu})_2]^-$	0.24	0.18	0.09	0.07	0
$[Co(l\text{-mop=phe})^2]^-$	0	0	0	0	0
$[Co(cop=ala)_2]^-$	−0.22	−0.11	0	0	0
$[Co(cop=val)_2]^-$	−0.04	−0.03	0	0	0
$[Co(cop=leu)_2]^-$	−0.03	−0.02	0	0	0
$[Co(cop=phe)_2]^-$	0	0	0	0	0

$[Co(cop=aa)_2]^-$ was prepared in a 1:1 mixture of a solvent and carbon tetrachloride. EtOH=ethanol, MeOH=methanol, DMSO=dimethyl sulfoxide, DMF=*N,N*-dimethylformamide, and AN=acetonitrile.

In order to elucidate the CD induction in the complexes, the complexes were prepared in various solvents (1:1 mixture of a solvent and CCl_4 in the case of $[Co(cop=aa)_2]^-$) and their CD spectra were compared. Despite the resemblance of absorption spectra of the complexes, the CD spectrum depends a great deal on the solvent used for preparation of the complex. CD intensities induced at 520 nm are summarized in Table 1. We see that the CD intensity of $[Co(l\text{-mop=aa})_2]^-$ except for $[Co(l\text{-mop=phe})_2]^-$ decreases in the order ethanol, methanol, dimethyl sulfoxide, *N,N*-dimethylformamide. No CD peak was induced in acetonitrile. On the other hand, the absolute CD intensity of $[Co(cop=aa)_2]^-$ except for $[Co(cop=phe)_2]^-$ decreases in the order: ethanol and methanol. No CD peak was induced in dimethyl sulfoxide, *N,N*-dimethylformamide and acetonitrile. Thus, the order of solvents in inducing the asymmetry around the metal is as follows: ethanol>methanol>dimethyl sulfoxide>*N,N*-dimethylformamide>acetonitrile. The solvent dependence of CD intensity indicates that the vicinal effect of the chiral group is greatly affected by the character of solvent. However, the order mentioned above can not be correlated with any property of solvent such as dielectric constant or dipole moment. From the fact that no CD induction takes place in $[Co(l\text{-mop=phe})_2]^-$ and $[Co(cop=phe)_2]^-$ even in ethanol, we presume that a certain interaction operates between the chiral group and the aromatic nucleus of the ligand. For the sake of confirmation, proton NMR spectra of ethanol, methanol, dimethyl sulfoxide, *N,N*-dimethylformamide and acetonitrile were measured in carbon tetrachloride and in benzene, and the chemical shifts of methyl proton were compared. The results are given in Table 2. Proton NMR signals are always observed at higher field in benzene as compared with in carbon tetrachloride. This can be interpreted in terms of the CH..π-interaction[14] between the methyl proton and benzene. As a measure of the CH..π-interaction we adopted the difference in methyl proton chemical shift between in carbon tetrachloride and in benzene ($\Delta\delta=\delta(CCl_4)-\delta(Bz)$). The small $\Delta\delta$ values of ethanol and methanol indicate that these molecules weakly interact with the aromatic nucleus. The $\Delta\delta$ values of dimethyl sulfoxide, *N,N*-dimethylformamide and acetonitrile are considerably large, indicating a strong CH..π-interaction with the aromatic nucleus. When we adopt the mean of the $\Delta\delta$ values for two inequivalent methyl groups of *N,N*-dimethylformamide, the increasing order in $\Delta\delta$ value (increasing order of the CH..π-interaction) of solvents is as follows: ethanol<methanol<dimethyl sulfoxide<*N,N*-dimethylformamide<acetonitrile. The decreasing order of the induced CD intensity agrees with the increasing order of the CH..π-interaction of solvents utilized for preparation of the complexes. A typical example of this correlation is given for $[Co(l\text{-mop=val})_2]^-$ in Fig. 5. It is likely that the chiral group at the side chain interacts with the aromatic nucleus of the ligand in ethanol or methanol, the CH..π-interaction causing the asymmetry of the configuration of the complex. On the other hand, in dimethyl sulfoxide, *N,N*-dimethylformamide or acetonitrile the CH..π-interaction between the solvent and the aromatic ring of the ligand is strong enough to supress the CH..π-interaction between the chiral group and the aromatic nucleus. $[Co(l\text{-mop=ala})_2]^-$ prepared in a chloroform–methanol (8:2) mixture showed a weak CD peak ($\Delta\varepsilon=0.113$) as compared with the complex prepared in methanol. This can be attributed to the fact that the CH..π-interaction between chloroform and benzene is so strong ($\Delta\delta=1.0$) as to reduce the CH..π-interaction between the chiral group and the aromatic nucleus of the ligand. The CD intensity induced in $[Co(cop=aa)_2]^-$ is much weaker than that induced in $[Co(l\text{-mop=aa})_2]^-$. It seems that the cholesteryl group is

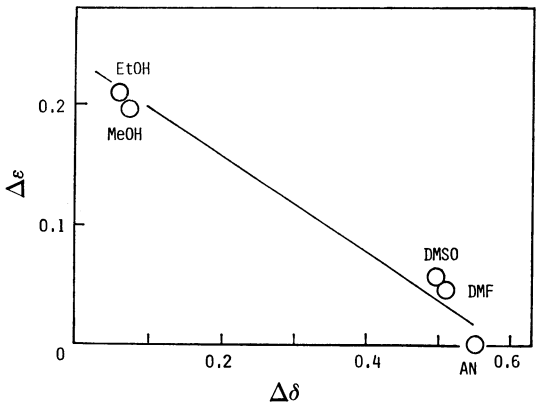

Fig. 5. Correlation between induced CD intensity ($\Delta\varepsilon$) and CH···π-interaction ($\Delta\delta$) of solvents used for preparation of $[Co(l\text{-mop=val})_2]^-$.

Table 2. Chemical shifts (ppm) of methyl proton of solvents in benzene and in carbon tetrachloride

	$\delta(CCl_4)$	δ(Bz)	$\Delta\delta$[a]
EtOH	1.20	1.14	0.06
MeOH	3.36	3.29	0.07
DMSO	2.52	2.02	0.50
DMF	2.96 2.82	2.51 2.25	0.51[b]
AN	1.96	1.41	0.55

a) $\Delta\delta=\delta(CCl_4)-\delta(Bz)$. b) Average value.

less effective than the *l*-menthyl group for introducing the asymmetry around the metal. So far we can not explain why no asymmetry was induced in $[Co(l\text{-}mop{=}phe)_2]^-$ and $[Co(cop{=}phe)_2]^-$. However, it is likely that the chiral group interacts with the phenylalanine nucleus rather than the phenolic nucleus, the interaction exerting no marked effect on asymmetry induction around the metal ions.

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