Stereoselective Interaction of Chiral Metal Complexes in Solution as Studied by Chromatography. I. Modes of Chiral Discrimination and Optical Resolution of Anion Complexes

Katsuhiko Miyoshi, Yukio Sakamoto, Atsuko Ohguni, and Hayami Yoneda*
Department of Chemistry, Faculty of Science, Hiroshima University, Higashi-senda-machi, Naka-ku, Hiroshima 730

(Received March 1, 1985)

Chromatographic resolution of some anion complexes, $[Co(ox)_2(en)]^-$, C_1- and C_2-*cis*(*N*)-$[Co(ox)(gly)_2]^-$, $[Co(ox)_2(gly)]^{2-}$, and $[Co(ox)_2(acac)]^{2-}$ (ox=oxalate ion, en=ethylenediamine, gly=glycinate ion, and acac=acetylacetonate ion), was attempted on an ion-exchange column using as chiral selectors several optically active cation complexes such as $[Co(en)_3]^{3+}$, $[Co(sep)]^{3+}$, $[Co(pn)_3]^{3+}$, $[Co(chxn)_3]^{3+}$, $[Co(acac)(en)_2]^{2+}$, and $[Co(gly)(en)_2]^{2+}$ (sep=1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]icosane, pn=propylenediamine, and chxn=*trans*-1,2-cyclohexanediamine). The elution orders and degrees of optical resolution attained were interpreted on the basis that chiral discrimination is effected along either the C_3 (or pseudo C_3) axis or the C_2 (or pseudo C_2) axis of the respective complexes; the cation complex faces the anion complex with its N–H protons hydrogen-bonded to the coordinated oxygen atoms of the anion complex along the (pseudo) C_3 or C_2 axis. Plausible association models were proposed, which indicate that homochiral (*i.e.*, *Δ*-*Δ* or *Λ*-*Λ*) and heterochiral (*i.e.*, *Δ*-*Λ* or *Λ*-*Δ*) combinations are favored when the cation complex directs its C_3 and C_2 axes to the anion complex, respectively, regardless of which axis (C_3 or C_2) of the anion complex is directed to the cation complex. Most of the experimental data are consistently explained within the framework of the association models proposed.

Several attempts have been made to resolve metal complex anions into optical isomers by chromatography.[1] However, only few examples are known in which optically active metal complex cations are utilized as chiral selectors, and thus the mechanism of chiral discrimination between complex cation and anion in solution has not yet been elucidated clearly. For example, Tatehata *et al.*[2] have succeeded in complete resolution of $[Co(ox)_2(gly)]^{2-}$ (ox=oxalate dianion and gly=glycinate anion) on the DEAE-Sephadex A-25 column with *Λ*-$[Co(en)_3]^{3+}$ cation (en=ethylenediamine) employed as an eluent, the *Δ* anion complex being eluted faster. They proposed an association model for a favorable pair, *Λ*-$[Co(en)_3]^{3+}$-*Δ*-$[Co(ox)_2(gly)]^{2-}$, in which *Λ*-$[Co(en)_3]^{3+}$ faces the anion complex along its C_3 axis (C_3 access) with its three N–H protons triply hydrogen-bonded to the three oxygen atoms of different chelate rings of $[Co(ox)_2(gly)]^{2-}$. This model well explains fairly strong association between the two complex ions (association constant K_A=480 $mol^{-1}dm^3$ at μ=0.01),[2] but it is not clearly demonstrated why the *Δ* anion complex associates more favorably with *Λ*-$[Co(en)_3]^{3+}$ than the antipode does. Furthermore, this model fails to account for the fact that the reversed elution order is obtained for $[Co(ox)_2(gly)]^{2-}$ when the eluent used is *Λ*-$[Co(d\text{-}chxn)_3]^{3+}$ (*d*-chxn=(1*S*,2*S*)-1,2-cyclohexanediamine) which can also direct the C_3 axis like *Λ*-$[Co(en)_3]^{3+}$ to the anion complex, as seen later in Table 1.

Subsequently, Sakaguchi *et al.*[3] attempted to elucidate the discrimination mechanism more generally by employing as chiral selectors various cation complexes which had some structural characteristics restricting their possible interaction modes. A similar allowance was made for the selection of anion complexes to be examined. Some of the results they obtained are listed in Table 1. Based on these elution orders (*i.e.*, favorable pairs), they assumed that favorable pairs are formed between those chiral cation and anion complexes which have the same handedness of chelate rings when viewed along the axis that each complex directs to the counterpart complex upon association. However, it is not easily accepted that the overlapping of chelate rings rather than the interionic hydrogen bonding takes a major part in chiral discrimination between these amine complexes and oxalato or amino acidato complexes. In fact, the mechanism they proposed leads to a somewhat strange assertion that $[Co(en)_3]^{3+}$ always "uses" its C_2 axis to recognize the chirality of the anion complexes. In addition, the elution orders of $[Co(ox)_2(en)]^-$ obtained with *Δ*-$[Co(sep)]^{3+}$ (sep=1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]icosane) and *Δ*-$[Co(l\text{-}chxn)_3]^{3+}$ (*l*-chxn=(1*R*,2*R*)-1,2-cyclohexanediamine) are opposite to those predicted by their proposal.

Table 1. Enantiomers of some anion complexes which form favorable pairs with Δ cation complexes

	Δ-$[Co(en)_3]^{3+}$	*Δ*-$[Co(sep)]^{3+}$	*Δ*-$[Co(l\text{-}chxn)_3]^{3+}$
$[Co(edta)]^-$	*Λ*	*Λ*	*Δ*
$[Co(ox)_2(en)]^-$	*Δ*	*Λ*[a]	*Δ*[a]
$[Co(ox)_2(gly)]^{2-}$	*Λ*	*Λ*	*Δ*
$[Cr(mal)_3]^{3-}$	*Λ*	*Λ*	*Δ*
fac-$[Co(\beta\text{-}ala)_3]$	*Δ*[a]	*Λ*	*Δ*

edta=ethylenediaminetetraacetate ion and mal=malonate ion.

a) Erroneously determined in Ref. 3 and thus corrected here.

As presented above, no satisfactory explanation has been so far afforded for the elution orders (or favorable pairs formed between chiral complex cations and anions) determined by chromatography. It is a main purpose of the present study to elucidate the detailed mechanism by which chiral discrimination is effected between these complex cations and anions bearing a hydrogen-bonding ability.

Experimental

Preparation of Metal Complexes. Appropriate salts of Δ isomers of $[Co(en)_3]^{3+}$, $[Co(sep)]^{3+}$, $[Co(sen)]^{3+}$ (sen=1,1,1-tris(((2-aminoethyl)amino)methyl)ethane), $[Co(l\text{-}chxn)_3]^{3+}$, $[Co(l\text{-}pn)_3]^{3+}$, (*l*-pn=(*R*)-propylenediamine), $[Co(gly)(en)_2]^{2+}$, $[Co(acac)(en)_2]^{2+}$, and *cis*-$[Co(NO_2)_2(en)_2]^+$ were available from the previous works[3,4] and/or were prepared by well-established methods. $[Co(sar)(en)_2]^{2+}$[5] (sar=sarcosinate anion), $[Co(\beta\text{-}ala)(en)_2]^{2+}$[6] (β-ala=β-alaninate anion), and $[Co(N,N'\text{-}Me_2\text{-}en)(en)_2]^{3+}$[7] (*N,N'*-Me$_2$-en=*N,N'*-dimethylethylenediamine) were also prepared as racemates of appropriate salts by the literature methods. Racemic $[Co(gly)(N,N'\text{-}Me_2\text{-}en)(en)]^{2+}$ and $[Co(\beta\text{-}ala)(N,N'\text{-}Me_2\text{-}en)(en)]^{2+}$ were newly prepared as perchlorate salts by allowing $[Co(Cl)(gly)(OH_2)(en)]Cl$[8] and $[Co(Cl)_2(\beta\text{-}ala)(en)]$,[9] respectively, to react with an equivalent amount of *N,N'*-Me$_2$-en in dimethyl sulfoxide at 60 °C for 5 h. The precipitates which formed upon addition of acetone were purified and converted to perchlorate salts by ion-exchange chromatography. Found: C, 19.73; H, 5.09; N, 14.31%. Calcd for $[Co(gly)(N,N'\text{-}Me_2\text{-}en)(en)](ClO_4)_2$=$C_8H_{24}N_5O_{10}Cl_2Co$: C, 20.01; H, 5.04; N, 14.59%. Found: C, 21.60; H, 5.24; N, 13.93%. Calcd for $[Co(\beta\text{-}ala)(N,N'\text{-}Me_2\text{-}en)(en)](ClO_4)_2$=$C_9H_{26}N_5O_{10}Cl_2Co$: C, 21.87; H, 5.30; N, 14.17%.

Following anion complexes were also available from the previous work[3] and/or were prepared as described in the literature; $[Co(ox)_2(en)]^-$, $[Co(ox)_2(gly)]^{2-}$,[10] $[Co(ox)_2(acac)]^{2-}$,[10] and C$_1$- and C$_2$-*cis(N)*-$[Co(ox)(gly)_2]^-$.[11] They were found all chromatographically pure. The first two complexes were resolved by conventional methods.[10,12]

The absolute configuration has been assigned to most of the above complexes; the Δ isomers have a negative main CD component at the first d-d transition region except for $[Co(sep)]^{3+}$[13] and $[Co(sen)]^{3+}$,[14] the Δ isomers of which have a positive component.

Chromatographic Experiments. Two types of experiments were carried out in essentially the same manner as in the previous work[3] to determine the enantiomers of anion complexes which associate favorably with various types of Δ cation complexes.

Type (a) Experiment: The SP-Sephadex C-25 resin saturated with a Δ complex cation was packed in a glass column (12 mm i.d. ×170 mm). At the end of the column was placed a small amount of the resin (Na$^+$ form) to adsorb the complex cation eluted slightly during the chromatographic run. A racemic complex anion (0.3 cm^3 in 30 mmol dm^{-3}) was loaded on the top of the column and was eluted with 30% aqueous ethanol solution. The elution rate was regulated at 0.3 cm min^{-1} with a peristaltic pump. The eluate was fractionally collected, and absorption and circular dichroism spectra of each fraction (2 cm^3) were recorded on a Shimadzu UV-240 spectrophotometer and a Jasco J-40CS spectropolarimeter, respectively at ambient temperatures. The elution curves were obtained in this way when necessary, but the degree of resolution was generally so low that only the elution orders were determined for the most cases. Care was taken to ensure that the elution order was determined by the chirality of the complex cation in the resin, but not of the resin matrix.[15] It is the late-eluted enantiomer that interacts favorably with the Δ cation complex in the resin. Similar experiments were carried out for some racemic cation complexes on the QAE-Sephadex A-25 column saturated with an optically active $[Co(ox)_2(en)]^-$ or $[Co(ox)_2(gly)]^{2-}$ ion.

Type (b) Experiment: The same procedures as before[3,16] were applied to measure the retention volumes of some anion complexes. A racemic anion complex (20 µl in 0.1 mol dm^{-3}) was loaded with a syringe on the top of the IEX-520-SIL (anion-exchange resin) column and was eluted with an aqueous solution containing a Δ cation complex as a chloride salt in 10 mmol dm^{-3}. The column size was 4 mm i.d. ×150 mm and the elution rate was regulated at 0.5 cm^3 min^{-1} with a Jasco BIP-1 pump for HPLC. The eluate was guided to a flow cell to detect the anion complex at an appropriate wavelength with a Shimadzu UV-140 spectrophotometer. The retention volumes thus recorded were found to be reproducible to within at least ±0.1 cm^3. When necessary, two enantiomers of the anion complex were chromatographed separately to estimate respective retention volumes V_R.

Results and Discussion

In Table 2 are summarized enantiomers of anion

TABLE 2. ENANTIOMERS OF ANION COMPLEXES WHICH FORM FAVORABLE PAIRS WITH Δ CATION COMPLEXES

	C$_2^-$		C$_3^-$	C$_2^-$+C$_3^-$	
	$[Co(ox)_2(en)]^-$	C$_2$-*cis(N)*-$[Co(ox)(gly)_2]^-$	C$_1$-*cis(N)*-$[Co(ox)(gly)_2]^-$	$[Co(ox)_2(gly)]^{2-}$	$[Co(ox)_2(acac)]^{2-}$
C$_2^+$					
Δ-$[Co(sep)]^{3+}$	$\Lambda^{a,b)}$	Λ	Λ	$\Lambda^{a)}$	Λ
Δ-$[Co(acac)(en)_2]^{2+}$	$\Lambda^{c)}$	Λ	Λ	$\Lambda^{c)}$	$\Lambda^{c)}$
Δ-*cis*-$[Co(NO_2)_2(en)_2]^+$	$\Lambda^{d)}$	Λ	Λ	$\Lambda^{d)}$	Λ
C$_3^+$					
Δ-$[Co(l\text{-}chxn)_3]^{3+}$	$\Delta^{a,b)}$	Δ	Δ	$\Delta^{a)}$	Δ
Δ-$[Co(l\text{-}pn)_3]^{3+}$	Λ	Λ	Δ	Δ	Δ
C$_2^+$+C$_3^+$					
Δ-$[Co(en)_3]^{3+}$	$\Delta^{a,c,e)}$	$\Delta^{e,f)}$	$\Lambda^{f)}$	$\Lambda^{a,g)}$	$\Lambda^{c)}$
Δ-$[Co(gly)(en)_2]^{2+}$	$\Delta^{c,e)}$	$\Lambda^{e)}$	Λ	$\Lambda^{c)}$	$\Lambda^{c)}$
Δ-$[Co(sen)]^{3+}$	Λ	Λ	Λ	Λ	Λ

a) Also reported in Ref. 3. b) Erroneously determined in Ref. 3. c) Also reported in Ref. 17. d) Also reported in Ref. 19. e) Very low resolution attained. f) Also reported in Ref. 18. g) Ref. 2.

complexes which are eluted later in the type (a) experiment with Δ cation complexes employed as chiral selectors. Thus, it is these enantiomers that form favorable pairs with the Δ cation complexes. Some of the favorable pairs listed in Table 2 have been already reported by Tatehata *et al.*[17,18] and Sakaguchi *et al.*[3] Most of their results are reproduced by our present study, but those for $[\mathrm{Co(ox)_2(en)}]^-$ obtained with Δ-$[\mathrm{Co(sep)}]^{3+}$ and Δ-$[\mathrm{Co}(l\text{-chxn})_3]^{3+}$ are at variance with the present results. Then, the elution order was determined repeatedly for $[\mathrm{Co(ox)_2(en)}]^-$ with a longer column, leading to the conclusion that the two elution orders (or favorable pairs) were erroneously determined by Sakaguchi *et al.*

Structural Characteristics of Complexes. The cation complexes used as chiral selectors in the present study are Δ-$[\mathrm{Co(en)_3}]^{3+}$, Δ-$[\mathrm{Co(sep)}]^{3+}$, Δ-$[\mathrm{Co(sen)}]^{3+}$, Δ-$[\mathrm{Co}(l\text{-chxn})_3]^{3+}$, Δ-$[\mathrm{Co}(l\text{-pn})_3]^{3+}$ (a mixture of *fac*-$\mathrm{lel_3}$ and *mer*-$\mathrm{lel_3}$ isomers), Δ-$[\mathrm{Co(acac)(en)_2}]^{2+}$, Δ-$[\mathrm{Co(gly)(en)_2}]^{2+}$, and Δ-*cis*-$[\mathrm{Co(NO_2)_2(en)_2}]^+$. It is likely that interionic hydrogen bonds play a major role in association of these amine complex cations with complex anions such as $[\mathrm{Co(ox)_2(en)}]^-$, $[\mathrm{Co(ox)_2(gly)}]^{2-}$, and $[\mathrm{Co(ox)_2(acac)}]^{2-}$. If inter-chelate repulsion is taken into account, hydrogen bonds are intimately formed between amino protons of the cation complex and coordinated oxygen atoms of the anion complex along either the (pseudo) C_3 or the (pseudo) C_2 axis of the respective complexes. That is, we assume that chiral discrimination between these complex cations and anions is effected along either the C_3 or the C_2 axis.

$[\mathrm{Co(sep)}]^{3+}$ is covalently capped along both sides of the C_3 axis.[13] Thus, this complex can form hydrogen bonds to the anion complex only along its C_2 axis. Then, we say that $[\mathrm{Co(sep)}]^{3+}$ belongs to the C_2^+ group complex and "uses" the C_2 axis only in association with the anion complex (C_2^+ access). $[\mathrm{Co(acac)(en)_2}]^{2+}$ and *cis*-$[\mathrm{Co(NO_2)_2(en)_2}]^+$ are also classified as the C_2^+ group, since they are expected to approach the anion complex along their C_2 axis from the side of their en rings so as to avoid the electrostatic repulsion between the negatively charged acac or $\mathrm{NO_2}$ groups and the negative charge on the complex anion. On the other hand, $[\mathrm{Co}(l\text{-chxn})_3]^{3+}$ and $[\mathrm{Co}(l\text{-pn})_3]^{3+}$ are regarded as the C_3^+ group complex, since they are expected to direct the (pseudo) C_3 axis to the anion complex (C_3^+ access) owing to the presence of chxn or $\mathrm{CH_3}$ groups on the chelate rings which will block the C_2^+ access. It is easily accepted that both C_2^+ and C_3^+ accesses are possible for $[\mathrm{Co(en)_3}]^{3+}$ and $[\mathrm{Co(gly)(en)_2}]^{2+}$, which thus belong to the (C_2^++ C_3^+) group. $[\mathrm{Co(sen)}]^{3+}$ is also regarded as the (C_2^++C_3^+) group complex, since it is capped covalently along one side of the C_3 axis, but the other side is available for hydrogen bonds to the anion complex.[14]

The anion complexes are also classified into three groups on the basis of the axis which they "use" in association with the cation complexes. For these anion complexes, charge localization on chelate rings is taken into account to determine the site and the direction of ion association.[3] Thus, $[\mathrm{Co(ox)_2(en)}]^-$ and C_2-*cis(N)*-$[\mathrm{Co(ox)(gly)_2}]^-$ belong to the C_2^- group complex, while C_1-*cis(N)*-$[\mathrm{Co(ox)(gly)_2}]^-$ belongs to the C_3^- group, since three oxygen atoms are disposed triangularly along the pseudo C_3 axis in the last complex. $[\mathrm{Co(ox)_2(gly)}]^{2-}$ as well as $[\mathrm{Co(ox)_2(acac)}]^{2-}$ is, on the other hand, regarded as the (C_2^-+C_3^-) group if the coordinated oxygen atoms of the acac ligand are available for the hydrogen-bonding interaction with amine complex cations.

Analysis of Favorable Pairs. As is evident in Tables 1 and 2, a typical C_2^+ group cation, Δ-$[\mathrm{Co(sep)}]^{3+}$ forms favorable pairs always with the Λ anion complexes, whereas a typical C_3^+ group cation, Δ-$[\mathrm{Co}(l\text{-chxn})_3]^{3+}$ does always with the Δ anion complexes. In other words, homochiral (*i.e.*, Δ-Δ or Λ-Λ) and heterochiral (*i.e.*, Δ-Λ or Λ-Δ) combinations are favored when the cation complex "uses" the C_3 and C_2 axes, respectively, regardless of which axis (C_3 or C_2) of the anion complex is directed to the cation complex. In fact, both Δ-$[\mathrm{Co(acac)(en)_2}]^{2+}$ and Δ-*cis*-$[\mathrm{Co(NO_2)_2(en)_2}]^+$ which belong to the C_2^+ group form favorable pairs with the Λ anion complexes.[19] Δ-$[\mathrm{Co}(l\text{-pn})_3]^{3+}$ which has been tentatively classified as the C_3^+ group, however, favors unexpectedly a heterochiral combination (Δ-Λ) with the C_2^- group anions such as $[\mathrm{Co(ox)_2(en)}]^-$ and C_2-*cis(N)*-$[\mathrm{Co(ox)(gly)_2}]^-$. This is probably because the C_2^+ access of $[\mathrm{Co}(l\text{-pn})_3]^{3+}$ can not be fully blocked by the $\mathrm{CH_3}$ groups on the pn chelates.

For the (C_2^++C_3^+) group cations, a heterochiral (Δ-Λ) combination is certainly favored in the interaction with the C_3^- and (C_2^-+C_3^-) group anions, but the favorable pairs with the C_2^- group anions are not amenable to generalization. It should be noted here

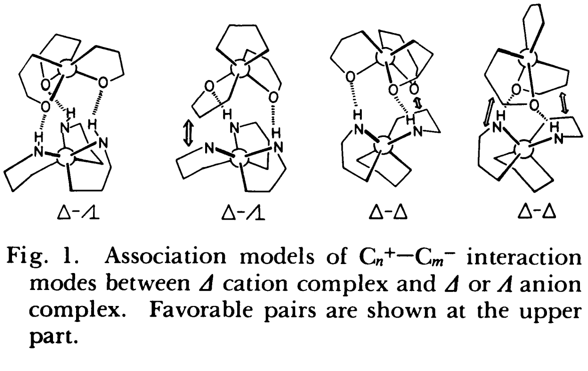

Fig. 1. Association models of C_n^+—C_m^- interaction modes between Δ cation complex and Δ or Λ anion complex. Favorable pairs are shown at the upper part.

that the degrees of resolution attained with Δ-$[Co(en)_3]^{3+}$ and Δ-$[Co(gly)(en)_2]^{2+}$ are very low, particularly for the C_2^- group anions. This implies that the $(C_2^+ + C_3^+)$ group cations use both of the C_2 and C_3 axes in association with the anion complexes; they favor a heterochiral combination in the C_2^+ access, while they favor a homochiral one in the C_3^+ access, overall discrimination efficiency being thereby low. By contrast, $[Co(sen)]^{3+}$ always favors a heterochiral combination, though it has been classified above as the $(C_2^+ + C_3^+)$ group cation.

Association Models. We now propose association models which explain consistently all the experimental data given in Table 2. In constructing the models, two acceptable assumptions were made; hydrogen-bonding interaction prevails between complex cation and anion, and these hydrogen bonds are formed intimately along either the (pseudo) C_3 or the (pseudo) C_2 axis of the respective complexes. All the possible interaction modes (C_3^+—C_3^-, C_3^+—C_2^-, C_2^+—C_3^-, and C_2^+—C_2^-) are depicted in Fig. 1, where C_n^+—C_m^- refers to the interaction in which complex cation and anion "use" the C_n and C_m axes, respectively on association. Each complex is assumed here to have five-membered bidentate chelates such as en, gly, or ox. Favorable pairs are drawn at the upper part, and the anion complex is located above the Δ cation complex in each pair where interionic hydrogen bonds are shown by dotted lines.

In the C_2^+—C_3^- and C_2^+—C_2^- interaction modes, favorable pairs are heterochiral (*Δ-Λ* or *Λ-Δ*), since inter-chelate repulsion is anticipated for the homochiral pair, as indicated by arrows. On the other hand, a favorable pair is homochiral (*Δ-Δ* or *Λ-Λ*) in the C_3^+—C_2^- mode because of the presence of similar interchelate repulsion in the heterochiral pair. In the C_3^+—C_3^- mode, such repulsion is not anticipated for either pair. However, the strength of the interionic hydrogen bond may be different between the two diastereomeric pairs; it depends greatly on the spacial disposition of the interacting atoms (H and O). A close examination of the two pairs in the C_3^+—C_3^- mode reveals that lone pair electrons on the O atoms of the anion complex are more favorably disposed in the homochiral pair for the hydrogen bonding with axial N-H protons of the cation complex than in the heterochiral pair, when the cation complex assumes the lel_3 conformation. Thus, a favorable pair is also homochiral in the C_3^+—C_3^- mode.

Tatehata *et al.*[2] supposed, on the contrary, that a favorable pair was heterochiral in the C_3^+—C_3^- mode, since they assumed that both $[Co(en)_3]^{3+}$ and $[Co(ox)_2(gly)]^{2-}$ use the (pseudo) C_3 axis in association. If so, favorable pairs formed with Δ-$[Co(l\text{-chxn})_3]^{3+}$ could not be accounted for, as discussed in Introduction. It should be pointed out here that discrimination efficiency may be very low in the C_3^+—C_3^- mode for conformationally labile complexes such as $[Co(en)_3]^{3+}$ and $[Co(gly)(en)_2]^{2+}$, since only a small difference in the strength of the interionic hydrogen bond is expected between the two diastereomeric pairs if the cation complex is conformationally labile.

In this way, the association models proposed here demonstrate that homochiral and heterochiral combinations are favored when the cation complex "uses" the C_3 and C_2 axes, respectively, in conformity with the experimental data listed in Table 2.

Now, if the above generalization is accepted as valid, favorable pairs formed with the $(C_2^+ + C_3^+)$ group cations are analyzed in more detail. For $[Co(en)_3]^{3+}$, for example, all of the four modes, C_3^+—C_3^-, C_3^+—C_2^-, C_2^+—C_3^-, and C_2^+—C_2^- are possible in the interaction with the $(C_3^- + C_2^-)$ group anions such as $[Co(ox)_2(gly)]^{2-}$ or $[Co(ox)_2(acac)]^{2-}$. The former two modes favor a homochiral combination, while the latter two favor a heterochiral one. The C_3^+—C_3^- mode is likely to contribute appreciably to the overall interaction between $[Co(en)_3]^{3+}$ and $[Co(ox)_2(gly)]^{2-}$ or $[Co(ox)_2(acac)]^{2-}$, but discrimination efficiency of this mode is low owing to the conformational lability of $[Co(en)_3]^{3+}$. Thus, the resulting favorable pair is eventually determined by the C_2^+ access which favors a heterochiral combination; the contribution due to the C_2^+—C_3^- and C_2^+—C_2^- modes surpasses that due to the C_3^+—C_3^- and C_3^+—C_2^- modes. Similarly, the C_2^+—C_3^- mode predominates over the C_3^+—C_3^- mode in the discriminating interaction of $[Co(en)_3]^{3+}$ with the C_3^- group anion like C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$.

With the C_2^- group complex anion, the C_3^+—C_2^- and C_2^+—C_2^- modes contribute to chiral discrimination. It is not obvious in Fig. 1 which mode contributes more effectively. As a result, overall discrimination efficiency should be extremely low; the former mode barely predominates over the latter, a homochiral pair being eventually favored slightly over a heterochiral pair. The results obtained for $[Co(gly)(en)_2]^{2+}$ are analyzed similarly, though the C_2^+—C_2^- mode seems to predominate accidentally over the C_3^+—C_2^- mode in the interaction with C_2-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_2^-).

$[Co(sen)]^{3+}$ which also belongs to the $(C_2^+ + C_3^+)$ group, however, always favors a heterochiral combination. This suggests that $[Co(sen)]^{3+}$ uses the C_2 axis more frequently than the C_3 axis,[4] probably because this complex is covalently capped along one side of the C_3 axis, while both of the two sides are available for hydrogen bonding in $[Co(en)_3]^{3+}$ which behaves as a typical $(C_2^+ + C_3^+)$ group cation. In short, $[Co(sen)]^{3+}$ behaves as if it were a prototype of the C_2^+ group cation.

Effect of N-*Methylation on Chiral Discrimination.* In order to account for the favorable pairs formed with $[Co(en)_3]^{3+}$ or $[Co(gly)(en)_2]^{2+}$, we have made an assumption that both of the C_3^+ and C_2^+ accesses are

Table 3. Enantiomers of complex cations which form favorable pairs with Λ-[Co(ox)$_2$(en)]$^-$ and Λ-[Co(ox)$_2$(gly)]$^{2-}$

	C$_2^-$ Λ-[Co(ox)$_2$(en)]$^-$	C$_2^-$+C$_3^-$ Λ-[Co(ox)$_2$(gly)]$^{2-}$
[Co(en)$_3$]$^{3+}$	Λ[b)]	Δ
[Co(N,N'-Me$_2$-en)(en)$_2$]$^{3+}$[a)]	Λ(RR)[b,c)]	Δ(SS)[c)]
[Co(gly)(en)$_2$]$^{2+}$	Λ[b)]	Δ
[Co(β-ala)(en)$_2$]$^{2+}$	Λ[b)]	Δ
[Co(sar)(en)$_2$]$^{2+}$[a)]	Λ(R)[b,c)]	Δ(S)[c)]
[Co(gly)(N,N'-Me$_2$-en)(en)]$^{2+}$[a)]	Δ(SS)[c)]	Δ(SS)[c)]
[Co(β-ala)(N,N'-Me$_2$-en)(en)]$^{2+}$[a)]	Δ(SS)[c)]	Δ(SS)[c)]

a) Isomers having CH$_3$ group(s) parallel to the pseudo C$_3$ axis. b) Very low resolution. c) R and S in the parentheses donote the configurations around the N atoms coordinated to Co(III).

involved in the interaction of these cation complexes. Then, if either of the two accesses is prohibited, say, by N-methylation of amino groups of the en or gly ligand, the discrimination mechanism would be drastically affected. With this expectation in mind, N-methyl derivatives of [Co(en)$_3$]$^{3+}$, [Co(gly)(en)$_2$]$^{2+}$, and [Co(β-ala)(en)$_2$]$^{2+}$ were chromatographed on the QAE-Sephadex column saturated with Λ-[Co(ox)$_2$(en)]$^-$ or Λ-[Co(ox)$_2$(gly)]$^{2-}$ ion. The late-eluted enantiomers, *i.e.*, those forming favorable pairs with these Λ anion complexes are listed in Table 3.

With Λ-[Co(ox)$_2$(en)]$^-$ ion (C$_2^-$), both of the C$_3^+$—C$_2^-$ and C$_2^+$—C$_2^-$ modes are possible for [Co(en)$_3$]$^{3+}$, [Co(gly)(en)$_2$]$^{2+}$, and [Co(β-ala)(en)$_2$]$^{2+}$. Since the former mode barely predominates over the latter, favorable pairs are homochiral, and the degrees of resolution are very low, as discussed earlier. For [Co(N,N'-Me$_2$-en)(en)$_2$]$^{3+}$ and [Co(sar)(en)$_2$]$^{2+}$ which have CH$_3$ group (s) parallel to the pseudo C$_3$ axis,[20)] favorable pairs with [Co(ox)$_2$(en)]$^-$ are still homochiral, suggesting that the C$_3^+$ access is not prohibited in these N-methylated complexes. In other words, only two NH$_2$ groups are involved in the C$_3^+$—C$_2^-$ mode (see Fig. 1), and the amino group of gly or β-ala is not effectively utilized in the C$_3^+$—C$_2^-$ mode.

On the contrary, [Co(gly)(N,N'-Me$_2$-en)(en)]$^{2+}$ and [Co(β-ala)(N,N'-Me$_2$-en)(en)]$^{2+}$ favor a heterochiral combination with [Co(ox)$_2$(en)]$^-$ and discrimination efficiency exhibited is not so low. This indicates that the CH$_3$ group located parallel to the pseudo C$_3$ axis renders the C$_3^+$ access impossible in these complexes, provided that the CH$_3$ group is present on the amino group of en but not of gly or β-ala. Thus, favorable pairs of the two cation complexes with [Co(ox)$_2$(en)]$^-$ are governed by the C$_2^+$—C$_2^-$ mode which survives and favors a heterochiral combination, and thus the degree of resolution attained should not be so low.

With Λ-[Co(ox)$_2$(gly)]$^{2-}$ (C$_2^-$+C$_3^-$), all of the four modes are possible for [Co(en)$_3$]$^{3+}$, [Co(gly)(en)$_2$]$^{2+}$, and [Co(β-ala)(en)$_2$]$^{2+}$. Since the contribution of the C$_3^+$—C$_3^-$ mode to chiral discrimination is negligible for these conformationally labile complexes, favorable pairs are governed by the C$_2^+$ access which favors a heterochiral combination. Then, even if the C$_3^+$—C$_3^-$ and C$_3^+$—C$_2^-$ modes are prohibited by N-methylation favorable pairs remain heterochiral. Instead, discrimination efficiency should be improved. In fact, the degree of resolution is found to be higher for [Co(gly)(N,N'-Me$_2$-en)(en)]$^{2+}$ and [Co(β-ala)(N,N'-Me$_2$-en)(en)]$^{2+}$ than for [Co(gly)(en)$_2$]$^{2+}$ and [Co(β-

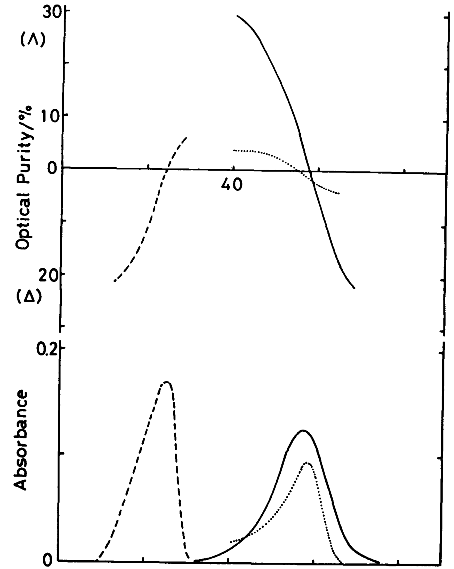

Fig. 2. Elution curves and plots of optical purity obtained for [Co(ox)$_2$(en)]$^-$ with Δ-[Co(sep)]$^{3+}$ (---), Δ-[Co(l-chxn)$_3$]$^{3+}$ (——), and Δ-[Co(en)$_3$]$^{3+}$ (···) employed as chiral selectors.

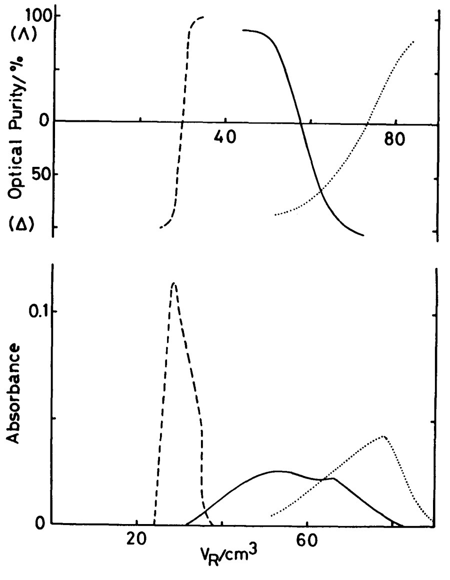

Fig. 3. Elution curves and plots of optical purity obtained for C$_1$-cis(N)-[Co(ox)(gly)$_2$]$^-$ with Δ-[Co(sep)]$^{3+}$ (---), Δ-[Co(l-chxn)$_3$]$^{3+}$ (——), and Δ-[Co(en)$_3$]$^{3+}$ (····) employed as chiral selectors.

ala)(en)$_2$]$^{2+}$, respectively. In this way, our assumption that both of the C_3^+ and C_2^+ accesses are involved in the (C_2^++C_3^+) group cation complexes, is verified experimentally.

Elution Curves. In Figs. 2 and 3 are shown the elution curves of $[Co(ox)_2(en)]^-$ (C_2^-) and C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_3^-), respectively, obtained by the type (a) experiment with Δ-$[Co(sep)]^{3+}$ (C_2^+), Δ-[Co(*l*-chxn)$_3$]$^{3+}$ (C_3^+), and Δ-$[Co(en)_3]^{3+}$ (C_2^++C_3^+) ions as chiral selectors. Also plotted is the optical purity of each fraction of the eluate as a function of a retention volume V_R. It is seen that fairly good resolution is attained for both anion complexes with Δ-$[Co(sep)]^{3+}$ and Δ-[Co(*l*-chxn)$_3$]$^{3+}$, for which only the C_2^+ and C_3^+ accesses are possible, respectively. A comparison between Figs. 2 and 3 indicates that better resolution is attained for C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_3^-) than for $[Co(ox)_2(en)]^-$ (C_2^-) with both cation complexes. This observation suggests that the C_2^+—C_3^- mode contributes more effectively to chiral discrimination than the C_2^+—C_2^- mode, and the C_3^+—C_3^- mode does than the C_3^+—C_2^- mode, provided that the C_3^+—C_3^- mode is of conformationally rigid complexes.

On the other hand, $[Co(en)_3]^{3+}$ certainly serves as a moderately good chiral selector for C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_3^-), but it hardly discriminates the chirality of $[Co(ox)_2(en)]^-$ (C_2^-); the C_3^+—C_3^- mode is negligible as compared with the C_2^+—C_3^- mode for the former C_3^- complex, while the C_3^+—C_2^- and C_2^+—C_2^- modes contribute almost equally but oppositely to chiral discrimination for the latter C_2^- complex. Similarly, $[Co(en)_3]^{3+}$ is expected not to serve as a good selector for another C_2^- anion complex, C_2-*cis(N)*-$[Co(ox)(gly)_2]^-$.[18] The finding that the degree of resolution attained for C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_3^-) with $[Co(en)_3]^{3+}$ is comparable to that attained with $[Co(sep)]^{3+}$ or [Co(*l*-chxn)$_3$]$^{3+}$, is consistent with the above assertion that discrimination efficiency is comparatively high in the C_2^+—C_3^- mode. If the C_3^+—C_2^- mode as well as the C_3^+—C_3^- mode of conformationally labile $[Co(en)_3]^{3+}$ is not effective, as mentioned above, $[Co(en)_3]^{3+}$ is expected to serve as a moderately effective selector for the (C_2^-+C_3^-) and particularly for the C_3^- group anions; the contribution of the C_2^+ access overwhelmingly surpasses that of the C_3^+ access in the discriminating interaction of conformationally labile $[Co(en)_3]^{3+}$ with these anion complexes. In fact, Tatehata *et al.*[18] have found that several anion complexes which we can classify as the C_3^- or (C_2^-+C_3^-) group anions, are completely resolved by usual ion-exchange chromatography with $[Co(en)_3]^{3+}$ employed as an eluent, though on a somewhat longer column.

In Figs. 4 and 5 are shown similar elution curves obtained by the type (a) experiment with Δ-$[Co(gly)(en)_2]^{2+}$(C_2^++C_3^+) and Δ-$[Co(acac)(en)_2]^{2+}$ (C_2^+) cations as chiral selectors. It is confirmed that $[Co(gly)(en)_2]^{2+}$ discriminates the chirality of $[Co(ox)_2(en)]^-$ (C_2^-) to a much lesser extent than $[Co(acac)(en)_2]^{2+}$ which uses the C_2 axis only and thus is expected to serve as a good selector. In fact, even $[Co(en)_3]^{3+}$ is less effective than $[Co(acac)(en)_2]^{2+}$ (Fig. 2). On the other hand, when the anion complex uses the C_3 axis only like C_1-*cis(N)*-$[Co(ox)(gly)_2]^-$ (C_3^-), the degree of resolution attained with $[Co(gly)(en)_2]^{2+}$ is almost comparable to that obtained with $[Co(acac)(en)_2]^{2+}$. This is again because the C_2^+—C_3^- mode is effective, but the C_3^+—C_3^- mode of conformationally labile $[Co(gly)(en)_2]^{2+}$ does not contribute appreciably

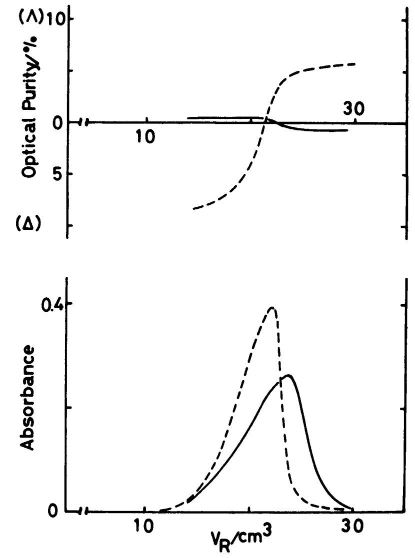

Fig. 4. Elution curves and plots of optical purity obtained for $[Co(ox)_2(en)]^-$ with Δ-$[Co(acac)(en)_2]^{2+}$ (---) and Δ-$[Co(gly)(en)_2]^{2+}$ (——) employed as chiral selectors.

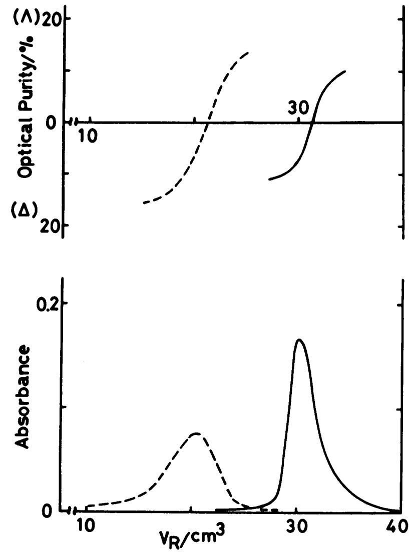

Fig. 5. Elution curves and plots of optical purity obtained for C_1-*cis*(*N*)-$[Co(ox)(gly)_2]^-$ with Δ-$[Co(acac)(en)_2]^{2+}$ (----) and Δ-$[Co(gly)(en)_2]^{2+}$ (——) employed as chiral selectors.

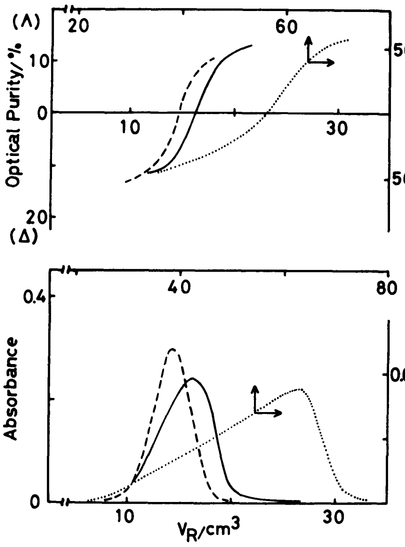

Fig. 6. Elution curves and plots of optical purity obtained for $[\mathrm{Co(ox)_2(gly)}]^{2-}$ with Δ-$[\mathrm{Co(acac)(en)_2}]^{2+}$ (----), Δ-$[\mathrm{Co(gly)(en)_2}]^{2+}$ (——), and Δ-$[\mathrm{Co(en)_3}]^{3+}$ (····) employed as chiral selectors.

to chiral discrimination, as discussed above. It is notable that $[\mathrm{Co(gly)(en)_2}]^{2+}$ gives a greater retention volume V_R to C_1-*cis(N)*-$[\mathrm{Co(ox)(gly)_2}]^-$ (C_3^-) than does $[\mathrm{Co(acac)(en)_2}]^{2+}$ (C_2^+). This suggests that the C_3^+—C_3^- mode of $[\mathrm{Co(gly)(en)_2}]^{2+}$ contributes appreciably to the overall interaction with the C_3^- anion complex.

Figure 6 shows the elution curves of $[\mathrm{Co(ox)_2(gly)}]^{2-}$ obtained similarly with Δ-$[\mathrm{Co(en)_3}]^{3+}$, Δ-$[\mathrm{Co(gly)(en)_2}]^{2+}$, and Δ-$[\mathrm{Co(acac)(en)_2}]^{2+}$ employed as a chiral selector. It is evident there that $[\mathrm{Co(gly)(en)_2}]^{2+}$ is as effective as $[\mathrm{Co(acac)(en)_2}]^{2+}$ in chiral discrimination of a typical (C_2^-+C_3^-) group anion, $[\mathrm{Co(ox)_2(gly)}]^{2-}$, as expected. It is probably the difference in electric charge on the selectors that is responsible for generally lower optical resolution attained with $[\mathrm{Co(gly)(en)_2}]^{2+}$ and $[\mathrm{Co(acac)(en)_2}]^{2+}$ than with $[\mathrm{Co(en)_3}]^{3+}$. The retention volumes V_R of $[\mathrm{Co(ox)_2(gly)}]^{2-}$ obtained with these bivalent complexes are actually much smaller than that obtained with $[\mathrm{Co(en)_3}]^{3+}$. By the same reason, univalent *cis*-$[\mathrm{Co(NO_2)_2(en)_2}]^+$ does not serve as a good selector, though it uses the C_2 axis exclusively.

It is worthy of note here that some experimental results relevant to our present study have been reported. Miyoshi *et al.*[21] have found that Λ-*cis*-$[\mathrm{Co(X)(Y)(en)_2}]^{n+}$-type complexes (X and/or Y=anion ligand) displace the chiral equilibrium of $[\mathrm{Cr(ox)_3}]^{3-}$ in favor of its Δ enantiomer in dioxane–water mixtures. They have claimed that this phenomenon is successfully utilized to assign the absolute configuration to *cis*-$[\mathrm{M(X)(Y)(diamine)_2}]^{n+}$-type complexes. Since these complexes are prototypes of the C_2^+ group cations, they should always favor a heterochiral combination, as is actually the case. Another experimental result to be noted is that the Δ enantiomer is enriched when a racemic mixture of tris(2,6-pyridinedicarboxylato)terbium(III) is mixed with Λ-$[\mathrm{Cr(en)_3}]^{3+}$ in dioxane–water mixtures.[22] Since the lanthanoid complex has an approximate D_3 symmetry and is regarded as the (C_2^-+C_3^-) group anion, all of the four interaction modes are possible. However, the contribution of the C_3^+—C_3^- mode is expected to be small because of the conformational lability of $[\mathrm{Cr(en)_3}]^{3+}$. Consequently, the favorable pair should be heterochiral, as explained repeatedly.

TABLE 4. RETENTION VOLUMES V_R AND SEPARATION FACTORS α OF $[\mathrm{Co(ox)_2(gly)}]^{2-}$ OBTAINED BY HPLC

eluent	V_R/cm^3		α
	Λ	Δ	
Δ-$[\mathrm{Co(sep)}]\mathrm{Cl_3}$	19.2	24.0	1.25
Δ-$[\mathrm{Co(}l\text{-}\mathrm{chxn)_3}]\mathrm{Cl_3}$	15.2	11.9	1.28
Δ-$[\mathrm{Co(en)_3}]\mathrm{Cl_3}$	13.7[a]	14.3[a]	1.04

a) Determined by eluting resolved enantiomers separately.

Optical Resolution by HPLC. The above-mentioned discussions lead us to conclude that highly charged cation complexes which use the C_3 axis only and are conformationally rigid or which use the C_2 axis only, can recognize the chirality of anion complexes effectively, while those which use the two axes simultaneously do not in general serve as a good selector. However, the type (a) experiment is inherently not suitable for the practical resolution of anion complexes, since so-called ion-exclusion effect due to the negatively charged functional groups in the resin tends to diminish the chance of the anion complex to interact with the chiral cationic selector adsorbed in the resin.[23] In fact, very small retention volumes are obtained for all the anion complexes in the type (a) experiments. Then, we attempted to resolve $[\mathrm{Co(ox)_2(gly)}]^{2-}$ by usual ion-exchange chromatography (type (b) experiment) with three cation complexes, Δ-$[\mathrm{Co(sep)}]^{3+}$ (C_2^+), Δ-$[\mathrm{Co(}l\text{-}\mathrm{chxn)_3}]^{3+}$ (C_3^+), and Δ-$[\mathrm{Co(en)_3}]^{3+}$ (C_2^++C_3^+) used as a chiral eluent. The retention volumes V_R and separation factors α obtained are given in Table 4.

The V_R values tell us that $[\mathrm{Co(en)_3}]^{3+}$ and $[\mathrm{Co(chxn)_3}]^{3+}$ which can use the C_3 axis bear a greater elution ability for $[\mathrm{Co(ox)_2(gly)}]^{2-}$ than does $[\mathrm{Co(sep)}]^{3+}$ which uses the C_2 axis only. That is, the C_3^+ access contributes to the overall interaction with the anion complex to a greater extent than the C_2^+ access. This seems to hold also for the interaction with C_1-*cis(N)*-$[\mathrm{Co(ox)(gly)_2}]^-$ (Fig. 3) and $[\mathrm{Co(ox)_2(en)}]^-$ (Fig. 2). On the other hand, a much higher α value is obtained with Δ-$[\mathrm{Co(sep)}]^{3+}$ (α=1.25) which uses the C_2 axis only and with Δ-$[\mathrm{Co(}l\text{-}\mathrm{chxn)_3}]^{3+}$ (α=1.28) which uses the C_3 axis only than with Δ-$[\mathrm{Co(en)_3}]^{3+}$ (α=1.04) which uses both of the C_3 and C_2 axes. This observation is in perfect agreement with what is predicted by our association models shown in Fig. 1. Tatehata *et* *al.*,[2] nevertheless, succeeded in complete resolution of $[Co(ox)_2(gly)]^{2-}$ with chiral $[Co(en)_3]^{3+}$ employed as an eluent on a very long column (1300 mm long) of the DEAE-Sephadex A-25 resin and the α value is estimated to be *ca.* 1.08 from the elution curves. Therefore, if optically active $[Co(sep)]^{3+}$ or $[Co(chxn)_3]^{3+}$ is used in place of $[Co(en)_3]^{3+}$, much more efficient resolution of this anion complex should be achieved.

References

1) H. Yoneda, *J. Chromatogr.*, **313**, 59 (1984).

2) A. Tatehata, M. Iiyoshi, and K. Kotsuji, *J. Am. Chem. Soc.*, **103**, 7391 (1981).

3) U. Sakaguchi, I. Yamamoto, S. Izumoto, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **56**, 153 (1983).

4) U. Sakaguchi, A. Tsuge, and H. Yoneda, *Inorg. Chem.*, **22**, 1630, 3745 (1983).

5) M. Fujita, Y. Yoshikawa, and H. Yamatera, *Bull. Chem. Soc. Jpn.*, **50**, 3209 (1977).

6) M. Kojima, H. Takayanagi, and J. Fujita, *Bull. Chem. Soc. Jpn.*, **50**, 1891 (1977).

7) J. A. Hearson, S. F. Mason, and R. H. Seal, *J. Chem. Soc., Dalton Trans.*, **1977**, 1026.

8) N. Matsuoka, J. Hidaka, and Y. Shimura, *Bull. Chem. Soc. Jpn.*, **39**, 1257 (1966).

9) This complex was prepared by the same procedures as applied to the preparation of $[Co(gly)(Cl)(OH_2)(en)]Cl$ using β-ala in place of gly.

10) F. P. Dwyer, I. K. Reid, and A. M. Sargeson, *Aust. J. Chem.*, **18**, 1919 (1965).

11) N. Matsuoka, J. Hidaka, and Y. Shimura, *Bull. Chem. Soc. Jpn.*, **40**, 1868 (1967); *Inorg. Chem.*, **9**, 719 (1970).

12) J. H. Worrell, *Inorg. Chem.*, **10**, 870 (1971).

13) I. I. Creaser, J. MacB. Harrowfield, A. J. Herlt, A. M. Sargeson, J. Springborg, R. J. Geue, and M. R. Snow, *J. Am. Chem. Soc.*, **99**, 3181 (1977).

14) J. E. Sarneski and F. L. Urbach, *J. Am. Chem. Soc.*, **93**, 884 (1971); H. Okazaki, U. Sakaguchi, and H. Yoneda, *Inorg. Chem.*, **22**, 1539 (1983).

15) Y. Yoshikawa and K. Yamasaki, *Coord. Chem. Rev.*, **28**, 205 (1979).

16) K. Miyoshi, M. Natsubori, N. Dohmoto, S. Izumoto, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **58**, 1529 (1985).

17) A. Tatehata, Y. Ejima, and K. Kotsuji, 29th Symposium on Coordination Chemistry, Hamamatsu, October, 1979, Abstr. No. 1B01.

18) A. Tatehata, K. Andoh, M. Fujita, and Y. Asaba, 33rd Symposium on Coordination Chemistry, Osaka, October, 1983, Abstr. No. 1PA13.

19) A. Tatehata, H. Fukui, M. Iiyoshi, and K. Kotsuji, 37th National Meeting of the Chemical Society of Japan, Tokyo, April, 1978, Abstr. No. 4J14.

20) Several diastereomers are possible in each of these *N*-methylated complexes. In the present study, however, a racemic mixture of the most stable isomers is used; $\Lambda(R)$ (or $\Lambda(RR)$) and $\Delta(S)$ (or $\Delta(SS)$) isomers which have CH_3 group(s) parallel to the pseudo C_3 axes.

21) K. Miyoshi, Y. Matsumoto, and H. Yoneda, *Inorg. Chem.*, **20**, 1057 (1981); K. Miyoshi, K. Watanabe, Y. Toda, and H. Yoneda, *Bull. Chem. Soc. Jpn.*, **56**, 3845 (1983).

22) J. S. Madaras and H. G. Brittain, *Inorg. Chem.*, **19**, 3841 (1980); F. Yan, R. A. Copeland, and H. G. Brittain, *Inorg. Chem.*, **21**, 1180 (1982).

23) In this respect, the type (a) experiment should be applied to the resolution of electrically neutral complexes such as *mer*- and *fac*-$[Co(\beta\text{-ala})_3]$ (see, for example, S. Yamazaki and H. Yoneda, *Inorg. Nucl. Chem. Lett.*, **15**, 195 (1979) and T. Yukimoto and H. Yoneda, *J. Chromatogr.*, **210**, 477 (1981)). Chromatographic resolution of these neutral complexes is now in progress with chiral metal complexes employed as selectors, and the results will be reported soon as Part II of this series.