# Chiral Recognition in Ion Pairing of an Optically Active Tris(ethylenediamine)cobalt(III) Cation and Application to Chromatographic Resolution of Metal Complex Anions

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A series of cobalt(III) complex anions have been completely resolved by column chromatography on a DEAE-Sephadex A-25 column using $\Lambda$-$[Co(en)_3]Cl_3\cdot H_2O$ (en = ethylenediamine) as an eluting agent. By this method the $\Delta$-complex anions are always eluted faster than the $\Lambda$-complex anions. In order to explain this elution order, the diastereomeric ion-pair formation constants for $[Co(en)_3]^{3+}$–*cis*(N)-$[Co(ida)_2]^-$ (ida = iminodiacetate) and $[Co(en)_3]^{3+}$–$[Co(edta)]^-$ (edta = ethylenediaminetetra-acetate) systems have been determined by the conductance method. The results were consistent with those of the elution order: the ion-pair formation constants of the faster-eluted $\Delta$-complex anions with $\Lambda$-$[Co(en)_3]^{3+}$ ion were significantly larger than those of the $\Lambda$-complex anions with the same cation for both the above systems. The favourable ion-pair mode of the complex anions with $\Lambda$-$[Co(en)_3]^{3+}$ is discussed on the basis of the hydrogen bonds between the co-ordinated oxygen atoms of the complex anions and the N–H protons of the complex cation. By taking advantage of the ability of the $\Lambda$-$[Co(en)_3]^{3+}$ cation to discriminate the chirality of complex anions, a chromatographic resolution method using $\Lambda$-$[Co(en)_3]Cl_3\cdot H_2O$ as eluting agent is proposed for various metal complex anions.

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A number of metal complex cations have been resolved by chromatographic methods.[1] However, few studies of the complete chromatographic resolution of complex anions have been reported because of the lack of effective eluting agents. Recently, we have reported that when $\Lambda$-$(+)_{589}$-$[Co(en)_3]Cl_3\cdot H_2O$ (en = ethylenediamine) in 30% ethanolic solution is used as the eluting agent, $[Co(ox)_2(glyO)]^{2-}$ [ox = oxalate(2–), glyO = glycinate(1–)] can be resolved by column chromatography on DEAE-Sephadex A-25.[2] The determination of the diastereomeric ion-pair formation constants between optically active $[Co(en)_3]^{3+}$ and $[Co(ox)_2(glyO)]^{2-}$ led to a good understanding of the chromatographic behaviour; the conductance method was shown to be effective for this purpose. Interionic hydrogen bonds have been supposed to play an important role in the formation of the stereoselective ion-pair between the two complex ions. In order to ascertain the mode of the stereoselective interactions, it is important to establish the relation between the capacity of the $[Co(en)_3]^{3+}$ ion for chiral discrimination and the structural characteristics of the complex anions. The object of the present study is to obtain an insight into the diastereomeric ion-pair formation in which optically active $[Co(en)_3]^{3+}$ participates, and then to extend the chromatographic resolution to many other complex anions.

## Experimental

*Preparation of the Complexes.*—Sodium or potassium salts of anionic complexes used in the chromatographic studies were prepared by literature methods: $[Co(ox)_2L]^{2-}$,[3] $[Co(mal)_2L]^{2-}$,[3] $C_1$ *cis*(N)-$[Co(ox)L_2]^-$,[4] β-*cis*-$[Co(ox)(edda)]^-$,[5] $[Co(edta)]^-$,[6] and *cis*(N)-$[Co(ida)_2]^-$.[7,†] The eluting agent $\Lambda$-$[Co(en)_3]Cl_3\cdot H_2O$ was prepared by a partial asymmetric synthesis of Dwyer and co-workers[8] in order to obtain almost exclusively the Λ isomer of the $[Co(en)_3]^{3+}$ cation. The optically active complexes for the conductance measurements, $\Lambda$-$(-)_{546}$- and $\Delta$-$(+)_{546}$-$K[Co(edta)]\cdot 2H_2O$,[9a] and $\Lambda$-$(+)_{589}$- and $\Delta$-$(-)_{589}$-$[Co(en)_3]I_3\cdot H_2O$,[10] were prepared by well established methods. The optical rotations of these complexes obtained in the present study were in good agreement with those reported in the literature.[9b,10]

The optical resolution of *cis*(N)-$[Co(ida)_2]^-$ was carried out by a modification of the literature method.[11] The complex $\Lambda$-$[Co(ox)(en)_2]Br\cdot H_2O$ (7.3 g), resolved according to the method of Douglas and co-workers,[9] was converted to the acetate by mixing with suspended anion exchanger (Dowex 1-X8) in the acetate form. After the removal of the anion exchanger by filtration, *cis*(N)-$K[Co(ida)_2]\cdot 2.5H_2O$ (3.8 g) was dissolved in the filtrate (120 $cm^3$), warmed at 60 °C, and ethanol (50 $cm^3$) was added. The mixture was kept in a refrigerator overnight to precipitate the diastereomer. The precipitates gave a mixture containing $\Lambda$-$[Co(ox)(en)_2]^+$–$\Delta$-*cis*(N)-$[Co(ida)_2]^-$ and a small portion of $\Lambda$-$[Co(ox)(en)_2]$–$^+\Lambda$-*cis*(N)-$[Co(ida)_2]^-$; the optical purity was increased by washing the mixture several times with aqueous 30% ethanol. Recrystallization of the diastereomer from water by the addition of ethanol was repeated until a constant value of the optical rotation was reached. The final value for the pure diastereomer, $\Lambda$-$[Co(ox)(en)_2]^+$–$\Delta$-*cis*(N)-$[Co(ida)_2]^-$, was $\alpha(H_2O, 546\ nm) = +1\,860°$. The solution of the diastereomer dissolved in water was passed through an SP-Sephadex C-25 ($K^+$ form) column [inside diameter (i.d.) 2.5 × 20 cm] to adsorb $\Lambda$-$[Co(ox)(en)_2]^+$ cation and the eluate was evaporated to 100 $cm^3$ at $<30$ °C under reduced pressure. The solution was cooled in ice with continued stirring, and ethanol was added dropwise. The product thus obtained, consisting of brilliant fine crystals, was recrystallized twice for the conductivity measurements; $\alpha(H_2O, 546\ nm) = +2\,520°$ (Found: C, 25.4; H, 3.10; N, 7.45. Calc. for $C_8H_{12}CoKN_2O_9$: C, 25.4; H, 3.20; N, 7.40%).

*Chromatographic Experiments.*— The racemic anionic complex (20—40 mg) dissolved in an appropriate aqueous ethanolic solution (30 or 40%, 10 $cm^3$) was placed on the top of a column (i.d. 1.8 × 130—148 cm) of DEAE-Sephadex A-25 and was

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† Abbreviations: mal = malonate(2–), edda = ethylenediamine-*NN'*-diacetate(2–), edta = ethylenediamine-*NNN'N'*-tetra-acetate(4–), ida = iminodiacetate(2–); and L = glycinate(1–) (glyO) or β-alaninate(1–) (alaO).

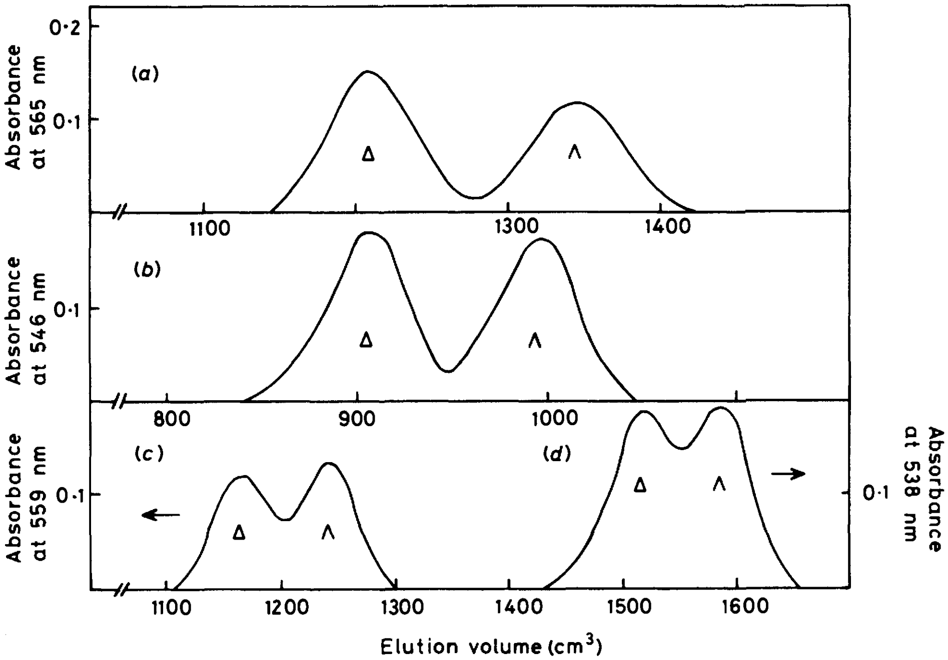

**Figure 1.** Elution curves of $[Co(ox)_2(alaO)]^{2-}$ (*a*), $C_1$ *cis*(N)-$[Co(ox)(glyO)_2]^-$ (*b*), *cis*(N)-$[Co(ida)_2]^-$ (*c*), and $[Co(edta)]^-$ (*d*) by column chromatography (DEAE-Sephadex A-25) using an ethanolic solution of Λ-$[Co(en)_3]Cl_3{\cdot}H_2O$ as an eluant. The concentration and ethanol content of the eluant, and the column length used for each complex anion are given in Table 1

eluted with 0.04—0.1 mol dm$^{-3}$ Λ-$[Co(en)_3]Cl_3{\cdot}H_2O$ in aqeuous 30 or 40% ethanolic solution. The elution rate was 0.3—0.4 cm$^3$ min$^{-1}$. During elution the anionic complex was completely separated into two enantiomers. In all cases in the present study, the Δ enantiomer of the complex anion was eluted before the Λ enantiomer. In order to obtain the elution curve, the absorbance of each fraction (3—5 cm$^3$) collected was measured at the maximum wavelength of the first absorption band of the complex anion using the eluant as reference solution. To make sure of complete resolution, the initial fractions of the first band and the final fractions of the second band were collected and were passed separately through a DEAE-Sephadex short column (i.d. 1.8 × 20 cm) after dilution with a large quantity of water to adsorb the enantiomer of the anionic complex. The adsorbed complex anion was eluted with 0.5 mol dm$^{-3}$ NaI or KI and was obtained as the sodium or potassium salt by concentration using an evaporator and addition of ethanol. The optical rotations of the anionic complexes thus obtained demonstrated that complexes contained in the first and second bands were enantiomeric pairs and were completely resolved.

*Conductivity Measurements.*—The determination of ion-pair formation constants between chiral complexes was carried out according to the procedure of Katayama and Tamamushi,[12] in which the deviation of the measured conductivity of electrolyte mixtures from additivity was attributed to the ion-pair formation.

The conductivities of the mixtures prepared by mixing the solutions of constant ionic strength of a complex cation and complex anion at various volume fractions were measured at 25 ± 0.01 °C with a conductometer (Yanagimoto MY-7) with a Wheatstone bridge at a frequency of 800 Hz. Two conductance cells, of cell constants 0.4379 and 0.4291 cm$^{-1}$, were used. Aqueous solutions of complex cations {Λ- and Δ-$[Co(en)_3]I_3{\cdot}H_2O$} and complex anions {Δ-*cis*(N)-$K[Co(ida)_2]{\cdot}H_2O$ and Λ- and Δ-$K[Co(edta)]{\cdot}2H_2O$} of ionic strength $I = 0.01$ or 0.05 mol dm$^{-3}$ were carefully prepared using 'conductivity water' (prepared by passing distilled water through mixed-bed ion exchange resin prior to use and with a specific conductivity $< 7 \times 10^{-7}$ ohm$^{-1}$ cm$^{-1}$ at 25 °C). The following four cases of combination between chiral complexes were studied. Case 1: Λ-$[Co(en)_3]I_3{\cdot}H_2O$–Δ-*cis*(N)-$K[Co(ida)_2]{\cdot}H_2O$ and Δ-$[Co(en)_3]I_3{\cdot}H_2O$–Δ-*cis*(N)-$K[Co(ida)_2]{\cdot}H_2O$ at $I = 0.01$ mol dm$^{-3}$, abbreviated as Λ–Δ and Δ–Δ pairs in the $[Co(en)_3]^{3+}$–*cis*(N)-$[Co(ida)_2]^-$ system, respectively. Case 2: Λ-$[Co(en)_3]I_3{\cdot}H_2O$–Δ-$K[Co(edta)]{\cdot}2H_2O$ and Δ-$[Co(en)_3]I_3{\cdot}H_2O$–Δ-$K[Co(edta)]{\cdot}2H_2O$ at $I = 0.01$ mol dm$^{-3}$, Λ–Δ and Δ–Δ pairs in the $[Co(en)_3]^{3+}$–$[Co(edta)]^-$ system. Case 3: Λ–Δ and Λ–Λ pairs in the $[Co(en)_3]^{3+}$–$[Co(edta)]^-$ system at $I = 0.01$ mol dm$^{-3}$. Case 4: Λ–Δ and Δ–Δ pairs in the $[Co(en)_3]^{3+}$–$[Co(edta)]^-$ system at $I = 0.05$ mol dm$^{-3}$. The deviations, $\Delta\kappa$/ohm$^{-1}$ cm$^{-1}$, of the conductance from additivity were observed as a function of volume fraction, $x$, of the cation complex for the diastereomeric pairs in each case.

Absorption spectra and optical rotations were obtained in aqueous solution at room temperature with a Shimadzu MPS-50L recording spectrophotometer and a Union automatic polarimeter PM-101, respectively. Absorbances of the eluates were measured with a JASCO UVIDEC-320 spectrophotometer.

## Results and Discussion

Typical chromatograms of $[Co(ox)_2(alaO)]^{2-}$, $C_1$ *cis*(N)-$[Co(ox)(glyO)_2]^-$, *cis*(N)-$[Co(ida)_2]^-$, and $[Co(edta)]^-$ are shown in Figure 1. The results for the anionic complexes resolved by column chromatography in the present study are summarized in Table 1. The column length, the concentration of eluant, and amounts of ethanol contained in the eluant were varied depending upon the charge on the complex anion and the ease of resolution.

It can be noted from Table 1 that for anionic complexes of the same charge, the retention volume of complexes having a six-membered chelate ring is smaller than that of the corresponding

**Table 1.** Resolution of complex anions by column chromatography (DEAE-Sephadex A-25) using $\Lambda$-$[Co(en)_3]Cl_3{\cdot}H_2O$ as eluting agent

| Complex anion | [Eluant][a]/ mol dm$^{-3}$ | Ethanol content of the eluant (v/v %) | Diameter × length of the column (cm) | Retention volume[b] (cm$^3$) | Separation factor, $\alpha$ |
|---|---|---|---|---|---|
| $[Co(ox)_2(glyO)]^{2-}$ | 0.1 | 30 | 1.8 × 130 | 1 705 ($\Delta$)<br>1 845 ($\Lambda$) | 1.08 |
| $[Co(ox)_2(alaO)]^{2-}$ | 0.1 | 30 | 1.8 × 130 | 1 210 ($\Delta$)<br>1 343 ($\Lambda$) | 1.11 |
| $[Co(mal)_2(glyO)]^{2-}$ | 0.1 | 30 | 1.8 × 130 | 850 ($\Delta$)<br>908 ($\Lambda$) | 1.07 |
| $[Co(mal)_2(alaO)]^{2-}$ | 0.1 | 30 | 1.8 × 130 | 627 ($\Delta$)<br>660 ($\Lambda$) | 1.05 |
| $C_1$ *cis*(N)-$[Co(ox)(glyO)_2]^-$ | 0.05 | 30 | 1.8 × 145 | 910 ($\Delta$)<br>994 ($\Lambda$) | 1.09 |
| $C_1$ *cis*(N)-$[Co(ox)(alaO)_2]^-$ | 0.05 | 30 | 1.8 × 145 | 507 ($\Delta$)<br>562 ($\Lambda$) | 1.11 |
| $\beta$-*cis*-$[Co(ox)(edda)]^-$ | 0.05 | 30 | 1.8 × 145 | 937 ($\Delta$)<br>1 011 ($\Lambda$) | 1.08 |
| *cis*(N)-$[Co(ida)_2]^-$ | 0.04 | 40 | 1.8 × 148 | 1 169 ($\Delta$)<br>1 236 ($\Lambda$) | 1.06 |
| $[Co(edta)]^-$ | 0.04 | 40 | 1.8 × 148 | 1 518 ($\Delta$)<br>1 582 ($\Lambda$) | 1.04 |

[a] $\Lambda$-$[Co(en)_3]Cl_3{\cdot}H_2O$. [b] Upper value is for first band, lower for second band.

complexes having a five-membered chelate ring, as seen for the malonato and oxalato complexes as well as the β-alaninato and glycinato complexes. Thus, $[Co(mal)_2(alaO)]^{2-}$, with three six-membered chelate rings, shows the smallest retention volume of all the complexes of the type $[CoL'_2L]$ (L′ = ox or mal, L = glyO or alaO) and a similar tendency is also seen for the complexes of the type $C_1$ *cis*(N)-$[Co(ox)L_2]^-$ (L = glyO or alaO). This result is understandable in terms of the bulkiness of the anionic complex; that is, the complex with the more bulky six-membered chelate ring is eluted earlier because of the lower charge density of the anionic complex, as reported for the elution order of cationic complexes such as $[CoL'(en)_2]^+$ (L′ = mal or ox) and $[Co(ox)L_2]^+$ [L = en or tn (trimethylenediamine)].[13]

In addition, the retention volume may also be correlated to the number of chelate rings contained in an anionic complex. For example, the retention volume of $C_1$ *cis*(N)-$[Co(ox)(glyO)_2]^-$ (with three chelate rings) is slightly smaller than that of β-*cis*-$[Co(ox)(edda)]^-$ (four chelate rings); that of *cis*-(N)-$[Co(ida)_2]^-$ (four chelate rings) is smaller than that of $[Co(edta)]^-$ (five chelate rings). This may be partly related to the difference in the ease of formation of the ion pair with the complex cation. The existence of a chelate ring in a complex anion largely prevents access to a complex cation from the direction of the chelate ring. Therefore, it appears reasonable that the complexes with more chelate rings are eluted later because the charge of the ion-pairing species is lowered less due to the decrease in ion-pair formation. In fact, consistent with the results of the conductance experiments (see later), it was observed that the ion-pair formation constant of *cis*(N)-$[Co(ida)_2]^-$ with $[Co(en)_3]^{3+}$ was larger than that of $[Co(edta)]^-$ with $[Co(en)_3]^{3+}$.

The extent of separation of each enantiomeric pair is shown by means of a separation factor, α, which is given by the value of the retention volume of the second-eluted enantiomer divided by that of the first-eluted enantiomer. The separation of the enantiomers was improved with the addition of an appropriate amount of ethanol. The effect of ethanol can be explained not only as its dehydrating effect from the solvation sphere of the ion-pairing species,[14] but also its effect of lowering the dielectric constant of the medium. As seen in Table 1, the first isomer of the anionic complexes eluted with $\Lambda$-$[Co(en)_3]Cl_3$ as eluant always has $\Delta$ configuration, indicating that the $\Delta$ enantiomer of all the anionic complexes in the present study forms the favourable ion pair with $\Lambda$-$[Co(en)_3]^{3+}$. As shown previously for the $[Co(en)_3]^{3+}$-$[Co(ox)_2(glyO)]^{2-}$ system, the differential diastereomeric interactions were found to be observable by conductance measurements.[2] Thus, the diastereomeric ion-pair formation constants between optically active $[Co(en)_3]^{3+}$ and $[Co(ox)_2(glyO)]^{2-}$ have been shown to have a ratio $[K(\Lambda\text{-}\Delta)/K(\Delta\text{-}\Delta)]$ of 1.04—1.17.

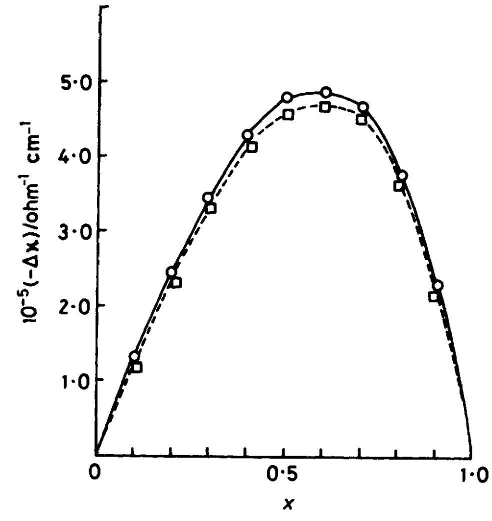

**Figure 2.** The deviations of the measured conductivity ($-\Delta\kappa$/ohm$^{-1}$ cm$^{-1}$) from additivity as a function of the volume fraction, $x$, of $\Lambda$-$[Co(en)_3]I_3{\cdot}H_2O$ for the $\Lambda$-$\Delta$ (○) and the $\Delta$-$\Delta$ (□) pairs in the $[Co(en)_3]^{3+}$-*cis*(N)-$[Co(ida)_2]^-$ system at $I$ = 0.01 mol dm$^{-3}$

Once again in order to rationalize the present chromatographic results, *cis*(N)-$[Co(ida)_2]^-$ and $[Co(edta)]^-$ were used for the conductance measurements. Figure 2 shows the deviations, $\Delta\kappa$, of the measured conductivity from additivity as a function of the volume fraction, $x$, of $\Lambda$-$[Co(en)_3]I_3{\cdot}H_2O$ for the $\Lambda$–$\Delta$ and $\Delta$–$\Delta$ pairs in the $[Co(en)_3]^{3+}$-*cis*(N)-$[Co(ida)_2]^-$ system. The $\Delta\kappa$ value for the mixture, consisting of a solution of $[Co(en)_3]I_3{\cdot}H_2O$ (concentration $c_M$ mol dm$^{-3}$) and a solution of *cis*(N)-$K[Co(ida)_2]^-$ (concentration $c_B$ mol dm$^{-3}$) at volume fractions of $x$ and $1 - x$, respectively, is given by equation (1); $\kappa$ is the specific conductivity of the mixture and $\Lambda_m$ is the molar conductivity of the species specified in parentheses

$$10^3\Delta\kappa = 10^3\kappa - c_M x\Lambda_m(\mathrm{MI_3}) - c_B(1 - x)\Lambda_m(\mathrm{KB}) \quad (1)$$

$\{M = [Co(en)_3]^{3+}$, $B = cis(N)\text{-}[Co(ida)_2]^-\}$ at an ionic strength of 0.01 mol dm$^{-3}$. If a 1:1 ion pair, $M^{3+}\text{-}B^-$, is assumed, $\Delta\kappa$ can be related to the molar concentration of the

$$[M^{3+}\text{-}B^-] = 10^3\Delta\kappa/\alpha \quad (2)$$

$$\alpha = 2\lambda(M^{3+}\text{-}B^-) - 3\lambda(M^{3+}) - \lambda(B^-) \quad (3)$$

ion pair $M^{3+}\text{-}B^-$ by equations (2) and (3), where $\lambda$ is the ionic equivalent conductance at an ionic strength of 0.01 mol dm$^{-3}$ of $M^{3+}\text{-}B^-$, $M^{3+}$, and $B^-$, respectively.

The ion-pair formation constants, $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$ dm$^3$ mol$^{-1}$, of $M^{3+}\text{-}B^-$ were obtained by analyzing the $\Delta\kappa$ values for $\Lambda$-$\Delta$ and $\Delta$-$\Delta$ pairs according to the literature procedure.[12] As seen in Figure 2, the $|\Delta\kappa|$ values of the $\Lambda$-$\Delta$ pair for every volume fraction, $x$, were always larger than the corresponding values of the $\Delta$-$\Delta$ pair and the $|\Delta\kappa|$ value reached a maximum at $x$ = 0.5—0.7 in both pairs. The calculated $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$ values and the ratio (discrimination factor), $K(\Lambda\text{-}\Delta)/K(\Delta\text{-}\Delta)$, for the $[Co(en)_3]^{3+}\text{-}cis(N)\text{-}[Co(ida)_2]^-$ system are given in Table 2. The values for $x$ = 0.1 and 0.9, which involve very dilute solutions of one of the component complexes, were precluded because of the possible large experimental errors involved. Although the slight dependence of the volume fraction of the ion-pair formation constants was seen for both pairs, for each volume fraction the value of $K(\Lambda\text{-}\Delta)$ was invariably larger than that of $K(\Delta\text{-}\Delta)$ and the discrimination factor calculated for every volume fraction was 1.05 ± 0.02 (see footnote *a* in Table 2). Taking into account the correlation coefficient ($\rho$) between $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$, the ratio and the standard deviation, calculated by using the average and the standard deviation of the ion-pair formation constants (see footnote *b* in Table 2), was the same as the value obtained above, indicating that there is considerable correlation between $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$ (Table 2). The discrimination factor is small but the diastereomeric effect is enhanced by the chromatographic process and must be of fundamental significance in the chromatographic resolution.

**Table 2.** Ion-pair formation constants and discrimination factors in the $[Co(en)_3]^{3+}\text{-}cis(N)\text{-}[Co(ida)_2]^-$ system as studied by conductance ($I$ = 0.01 mol dm$^{-3}$, at 25 °C)

| Volume fraction, $x$ | Ion-pair formation constants/dm$^3$ mol$^{-1}$ $K(\Lambda\text{-}\Delta)$ | $K(\Delta\text{-}\Delta)$ | Discrimination factor, $K(\Lambda\text{-}\Delta)/K(\Delta\text{-}\Delta)$ |
|---|---|---|---|
| 0.2 | 188 | 183 | 1.03 |
| 0.3 | 191 | 183 | 1.04 |
| 0.4 | 194 | 184 | 1.05 |
| 0.5 | 193 | 179 | 1.08 |
| 0.6 | 185 | 173 | 1.07 |
| 0.7 | 187 | 179 | 1.04 |
| 0.8 | 179 | 175 | 1.02 |
| | 188 ± 5[a] | 179 ± 4[a] | 1.05 ± 0.02[a]<br>(1.05 ± 0.02)[b] |

[a] Average and standard deviation. [b] Ratio and standard deviation calculated by using the average and the standard deviation ($\delta K$) of the ion-pair formation constants as given below, where $\rho$ (value used 0.726) is the correlation coefficient between $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$.

$$s = \frac{K(\Lambda\text{-}\Delta)}{K(\Delta\text{-}\Delta)} \times \sqrt{\left(\frac{\delta K(\Lambda\text{-}\Delta)}{K(\Lambda\text{-}\Delta)}\right)^2 + \left(\frac{\delta K(\Delta\text{-}\Delta)}{K(\Delta\text{-}\Delta)}\right)^2 - 2\rho\left(\frac{\delta K(\Lambda\text{-}\Delta)}{K(\Lambda\text{-}\Delta)}\right)\left(\frac{\delta K(\Delta\text{-}\Delta)}{K(\Delta\text{-}\Delta)}\right)}$$

In Table 3 the results for the diastereomeric pairs of cases 1—4 are summarized. To make sure that a small and significant difference between the ion-pair formation constants of a particular set of diastereomeric pairs is also reproducible for another set, the experiments for cases 2 and 3 were carried out at the same ionic strength. The values of $K(\Lambda\text{-}\Delta)$ and $K(\Delta\text{-}\Delta)$ for both enantiomers of $[Co(en)_3]^{3+}$ with $\Delta\text{-}[Co(edta)]^-$ were confirmed to be very close to those of $K(\Lambda\text{-}\Delta)$ and $K(\Lambda\text{-}\Lambda)$ for $\Lambda\text{-}[Co(en)_3]^{3+}$ with both enantiomers of $[Co(edta)]^-$, respectively (Table 3). The discrimination factor, at $I$ = 0.05 mol dm$^{-3}$, of the $[Co(en)_3]^{3+}\text{-}[Co(edta)]^-$ system (case 4) is considerably larger than that at $I$ = 0.01 mol dm$^{-3}$.

In order to examine the validity of $K$ values at $I$ = 0.05 mol dm$^{-3}$, the $K$ values at $I$ = 0.01 mol dm$^{-3}$ were extrapolated to $I$ = 0.05 mol dm$^{-3}$ by employing the extended Debye-Hückel equation for activity coefficients with the distance of closest approach of the ions, $a$ = 4 Å.[15] The values extrapolated to $I$ = 0.05 mol dm$^{-3}$, $K(\Lambda\text{-}\Delta)$ = 70 and $K(\Delta\text{-}\Delta)$ = 66, were more than twice as large as those obtained by experiment [$K(\Lambda\text{-}\Delta)$ = 34.4 and $K(\Delta\text{-}\Delta)$ = 29.2]. The smaller experimental values of $K$ at $I$ = 0.05 mol dm$^{-3}$ may be attributed to the ion-pair formation of $[Co(en)_3]^{3+}$ ion with $I^-$ ion due to increase in the concentration of solutions. The electrostatic field of the $[Co(en)_3]^{3+}$ ion is reduced by ion-pair formation with the $I^-$ ion, and the electrostatic interaction between $[Co(en)_3]^{3+}$ and $[Co(edta)]^-$ is weakened. Consequently, the non-electrostatic interaction is relatively enhanced and becomes more effective for chiral discrimination. This can be considered to lead to the

**Table 3.** Summary of ion-pair formation constants and discrimination factors for the diastereomeric pairs of cases 1—4 in the conductance measurements

| Case | System | $I$/mol dm$^{-3}$ | Diastereomeric pair | Ion-pair formation constant,[a] $K$/dm$^3$ mol$^{-1}$ | Discrimination factor |
|---|---|---|---|---|---|
| 1 | $[Co(en)_3]^{3+}\text{-}cis(N)\text{-}[Co(ida)_2]^-$ | 0.01 | Λ-Δ | 188 ± 5 | 1.05 ± 0.02[b] |
| | | | Δ-Δ | 179 ± 4 | (1.05 ± 0.02)[c] |
| 2 | $[Co(en)_3]^{3+}\text{-}[Co(edta)]^-$ | 0.01 | Λ-Δ | 125 ± 5 | 1.05 ± 0.03[b] |
| | | | Δ-Δ | 119 ± 5 | (1.05 ± 0.03)[c] |
| 3 | $[Co(en)_3]^{3+}\text{-}[Co(edta)]^-$ | 0.01 | Λ-Δ | 124 ± 6 | 1.06 ± 0.03[b] |
| | | | Λ-Λ | 117 ± 4 | (1.06 ± 0.03)[c] |
| 4 | $[Co(en)_3]^{3+}\text{-}[Co(edta)]^-$ | 0.05 | Λ-Δ | 34.4 ± 4.6 | 1.19 ± 0.10[b] |
| | | | Δ-Δ | 29.2 ± 5.0 | (1.18 ± 0.08)[c] |

[a] Average and standard deviation of the ion-pair formation constants at volume fraction $x$ = 0.2—0.8. [b] Average and standard deviation of the discrimination factors calculated for all volume fractions. [c] Ratio and standard deviation evaluated from the average and the standard deviation of the ion-pair formation constants, as shown in footnote *b* of Table 2.

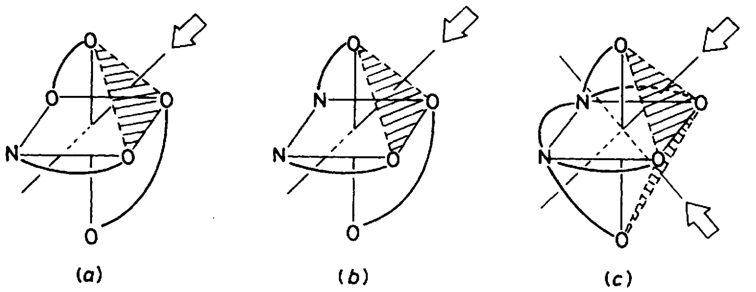

**Figure 3.** Schematic structures of the anionic complexes resolved by the present chromatographic method: $[CoL'_2L]^{2-}$ (*a*), $C_1$ *cis*(N)-$[Co(ox)L_2]^-$ (*b*), and $[Co(edta)]^-$ (*c*), (L′ = ox or mal, L = glyO or alaO)

large discrimination factor at $I = 0.05$ mol dm$^{-3}$; a similar increase of discrimination factor in the presence of excess anions used for adjustment of ionic strength was also reported for the ion-pair formation of $[Co(en)_3]^{3+}$ with L-tartrate ion.[16]

As expected already from the retention volume of *cis*-(N)-$[Co(ida)_2]^-$ being smaller than that of $[Co(edta)]^-$, the ion-pair formation constants of *cis*(N)-$[Co(ida)_2]^-$ with $[Co(en)_3]^{3+}$ were larger than those of $[Co(edta)]^-$ with the same cation because of the existence of more chelate rings in $[Co(edta)]^-$ than in *cis*(N)-$[Co(ida)_2]^-$. However, the discrimination factors of both anionic complexes were almost equal (Table 3), indicating that a common structural characteristic of the two anionic complexes affects the chiral discrimination: the ethylenediamine-like chelate ring moiety of $[Co(edta)]^-$ is not important but the anionic oxygen atoms in the latter complex are important in the chiral discrimination.

The schematic structures of the complex anions resolved by the present chromatographic method are shown in Figure 3. As an important and common characteristic of these complex anions, there exist one or two triangular faces composed of three anionic co-ordinated carboxyl oxygen atoms, where we chose the triangular face in such a way that no chelate ring is involved in it, as shown by the shaded parts in Figure 3.

The presence of the chelate ring in the triangular face prevents approach of a complex cation from the direction perpendicular to the triangular face because of the steric hindrance between chelate ligands. The importance of the triangular face in the complex anion is supported by the fact that only the $C_1$ *cis*(N) isomer of three geometrical isomers, *trans*(N), $C_2$ *cis*(N), and $C_1$ *cis*(N), of $[Co(ox)L_2]^-$ (L = glyO or alaO) and only the β-*cis* isomer of two, α-*cis* and β-*cis*, of $[Co(ox)(edda)]^-$ have such a triangular face and can be resolved by the present type of chromatography. The complex cation will approach from the 'anionic side' of the complex anion along its pseudo-$C_3$ axis by electrostatic interaction, as shown by the arrows in Figure 3.

The $[Co(en)_3]^{3+}$ cation also has two triangular faces composed of three axial N–H protons, nearly parallel to the $C_3$ axis of the cation, which are available for hydrogen bonding with three oxygen atoms of the complex anion. Thus, the $[Co(en)_3]^{3+}$ cation and the complex anion will approach each other along the collinear cationic $C_3$ axis and the anionic pseudo-$C_3$ axis in such a way that the 'cationic side' of the complex cation faces the 'anionic side' of the complex anion and the hydrogen bonds can be triply formed between three N–H protons of $[Co(en)_3]^{3+}$ and three co-ordinated oxygen atoms of the complex anion. In that case, the direction of the lone-pair electrons of the three oxygen atoms may determine which enantiomer of the cation forms the favourable ion pair with the anion. Taking into account the $sp^2$ hybrid orbital of the co-ordinated oxygen atoms in the carboxyl group, the molecular model reveals that the directions of the lone-pair electrons of the three oxygen atoms in a Δ-complex anion are more favourable for the formation of a triple hydrogen bond with three N–H protons of Λ-$[Co(en)_3]^{3+}$ than with those of Δ-$[Co(en)_3]^{3+}$. Such a strong hydrogen bonding may be similar to that shown for the interactions between $[Co(en)_3]^{3+}$ and $PO_4^{3-}$, in the crystal[17] as well as in solution.[18]

Thus, the chromatographic behaviour interpreted as due to the formation of the favourable ion pair, Λ-$[Co(en)_3]^{3+}$–Δ-complex anion, is consistent with the results of the discrimination factor in the ion pairing of the Λ-$[Co(en)_3]^{3+}$ cation studied by conductance experiments (Tables 1 and 3).

Dwyer *et al.*[6] reported on the resolution of $[Co(edta)]^-$ using Λ-$[Co(en)_3]Cl_3$ as a precipitating agent. The less soluble diastereomer was obtained as Λ-$[Co(en)_3]$–Δ-$[Co(edta)]_2Cl\cdot 4H_2O$ by adding alcohol. It is noteworthy that the preference of the Λ–Δ combination in the formation of the crystal is the same as that in ion-pair formation in solution. This may be the first example in which the difference in the ion-pair formation constants was clearly demonstrated for the diastereomeric complex cation–complex anion pairs capable of resolution by the solubility method, although it is known in a system comprising $[Co(en)_3]^{3+}$ and an optically active organic anion such as L-tartrate.[19]

It is presumed that Λ-$[Co(en)_3]^{3+}$ discriminates the chirality of $[Co(edta)]^-$ to form the favourable ion pair prior to the occurrence of the crystal of the less soluble diastereomer, and then precipitates the less soluble diastereomer involving the ion pair. However, in the case of some complex anions, which cannot be resolved by the fractional crystallization method based on diastereomer solubility, by taking advantage of the ability of Λ-$[Co(en)_3]^{3+}$ to discriminate the chirality of complex anions, application of the chromatographic technique is very useful for optical resolution. In such a case, Λ-$[Co(en)_3]Cl_3\cdot H_2O$ can serve as a highly promising eluting agent for the chromatographic resolution of the complex anions. It is of great advantage that Λ-$[Co(en)_3]^{3+}$ ion has a tendency to form easily the ion pair with various complex anions because of a highly charged cation. Moreover, Λ-$[Co(en)_3]Cl_3\cdot H_2O$ is cheap to make and does not racemize readily, the preparation is easy and well established. Therefore, the present resolution method using column chromatography with Λ-$[Co(en)_3]Cl_3\cdot H_2O$ as an eluting agent can be extensively applied to many complex anions.

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