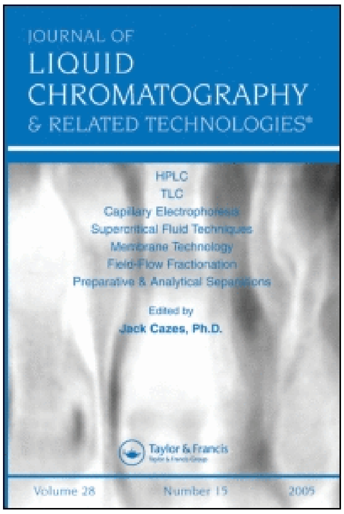

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Stereochemical Aspects of Optical Resolution of Octahedral Metal Chelates by Liquid Chromatography

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STEREOCHEMICAL ASPECTS OF OPTICAL RESOLUTION OF OCTAHEDRAL METAL CHELATES BY LIQUID CHROMATOGRAPHY

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INTRODUCTION

Discrimination of enantiomers of octahedral metal complexes should be done in a mechanism different from that of organic compounds having a tetrahedral asymmetric center. In this respect, the elucidation of the mechanism of optical resolution by chromatography has been one of the most fascinating subjects in coordination chemistry. Since metal complexes usually exist as ions, they are charged on ion-exchange resin and eluted into enantiomers with the eluent containing suitable chiral ions(resolving agent). While so many chiral metal complexes can be resolved into enantiomers by way of diastereomeric crystals, comparatively few examples of complete resolution by chromatographic techniques have been reported. This is because there are only two resolving agents, d-tartrate and antimony d-tartrate, which are conveniently used for chromatographic separation(1). Here I will describe the outline of works which were done in my laboratory to clarify the mechanism of chromatographic resolution of metal chelates.

OPTICAL RESOLUTION BY d-TARTRATE

Resolution of $[Co(en)_3]^{3+}$ (en = $NH_2CH_2CH_2NH_2$)

Since $[Co(en)_3]^{3+}$ is the fundamental chiral complexes, attempts to separate it into enatiomers by chromatography were made before all other racemic complexes. We succeeded in complete resolution by means of paper electrophoresis(2) as well as silica gel thin layer chromatography(3) using an aqueous solution of sodium d-tartrate containing aluminum ion. This success proved to be a lucky one which can not be applied to any other complexes. On the other hand, Yoshikawa and Yamasaki(4) succeeded in complete resolution of the same complex through SE-Sephadex ion-exchange column using an aqueous solution of sodium d-tartrate(abbreviated as d-tart hereafter) as eluent. With this success as a starting point, chromatographic separations of various isomers (geometric, conformational and optical) were attempted by many coordination chemists. However, the mechanism of optical resolution had not been elucidated before we attempted.

Crystal Structures of Diastereomers Containing $[M(en)_3]^{3+}$ and d-Tart^{2-}

As a part of the structural study of optical resolution, we have determined the crystal structures of the following three kinds of diastereomers.

Λ-$[Co(en)_3]$ Br d-tart$\cdot 5H_2O$ (5)
Li Λ-$[Cr(en)_3]$(d-tart)$_2\cdot 3H_2O$ (6)
H Λ-$[Co(en)_3]$(d-tart)$_2\cdot 3H_2O$ (7)

As a result, a unique face-to-face intimate ion-pair structure of Λ-$[M(en)_3]^{3+}$ and d-tart^{2-} was found in all three crystals. These three crystals are different in chemical formula, cell dimension and space group symmetry, yet they have a unique ion-pair structure in common. This suggests that the origin of the discrimination by d-tart lies in this face-to-face ion-pair structure. Figure 1 shows the ion-pair structure viewed down along

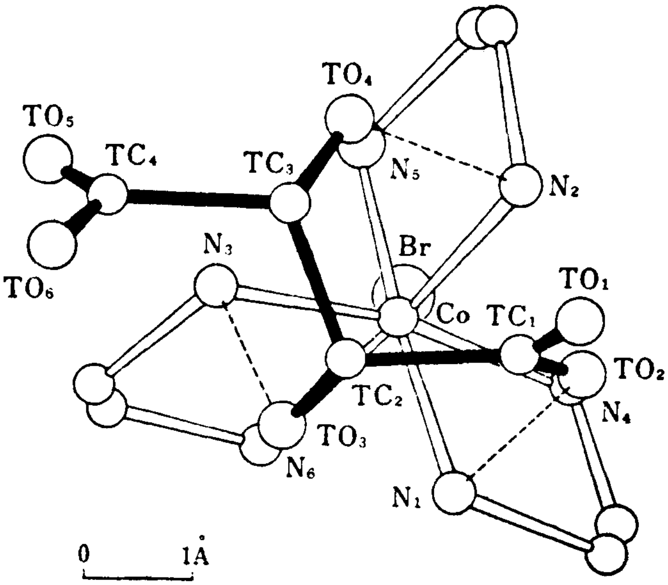


Figure 1. The ion-pair structure between Λ-$[Co(en)_3]^{3+}$ and d-tart, viewed along the threefold axis of the complex cation.

the threefold axis of the complex. Here four carbon atoms of d-tart make a plane which is perpendicular to the threefold axis of the complex, and four oxygen atoms are projecting toward the complex and are facing the triangular facet formed by three NH_2 groups of the complex. Since this ion-pair structure is preserved in different crystals, it is presumed to be stable and to exist even in solution. In other words, d-tart associates with Λ-$[M(en)_3]^{3+}$ to form the intimate ion-pair, while d-tart can not form such an intimate ion-pair with Δ-$[M(en)_3]^{3+}$. Thus, d-tart associates more with the Λ than with the Δ and discriminates the Λ from the Δ even in solution. In fact, the association constant K_Λ is larger than K_Δ(8) (vide infra).

$$\Lambda\text{-complex} + \text{d-tart} \rightleftarrows \Lambda\text{-d ion-pair}$$

$$K_\Lambda = \frac{[\Lambda\text{-d ion-pair}]}{[\Lambda\text{-complex}][\text{d-tart}]}$$

$$\Delta\text{-complex} + \text{d-tart} \rightleftarrows \Delta\text{-d ion-pair}$$

$$K_\Delta = \frac{[\Delta\text{-d ion-pair}]}{[\Delta\text{-complex}][\text{d-tart}]}$$

Nature of the Discrimination by d-Tart

From the above discussion, it has become clear that the origin of the discrimination of $[Co(en)_3]^{3+}$ lies in the unique face-to-face association with d-tart. However, why such an association enables the discrimination is still in question. To clarify this point, it is neccessary to compare both structures of the Λ-d and Δ-d ion-pairs. However, since Δ-$[Co(en)_3]^{3+}$ and d-tart do not form crystals, the Δ-d ion-pair structure can not be obtained from crystal structure determination. Therefore, there is no other way than to presume the Δ-d ion-pair structure, based on the real structure of the Λ-d ion-pair. To grasp the chracteristic feature of the Λ-d ion-pair structure, it is reasonable to pick up and to observe only the parts of associating ions that are facing to each other. Since the part of the complex which has a direct relation to association is its upper half, we have only to consider its upper half, that is, the shoulders of three en chelate rings. On the other hand, since d-tart associates with the complex with its four oxygen atoms, it is enough to consider the configuration of these four oxygen atoms. By superimposing these two parts, we get Fig. 2(a). Here four large circles drawn by broken lines represent the effective atomic radii of oxygen atoms. As is clearly seen in this figure, these four oxygen circles are placed in the opening formed by three chelate rings. Thus, the intimate ion-pair structure can be understood. In contrast to this, if we replace the Λ with the Δ as shown in Fig. 2(b), such an intimate superimposition is not feasible. In Fig. 2(b), three oxygen circles are placed in the opening between three chelate rings, but the fourth one comes onto the shoulder of the chelate ring, so that the Δ-d combination does not make the intimate structure like Fig. 2(a). In other words, the discrimination by d-tart is performed by four oxygen atoms, that is, by three oxygen atoms which hydrogen-bond to the three NH groups of the complex and by the fourth

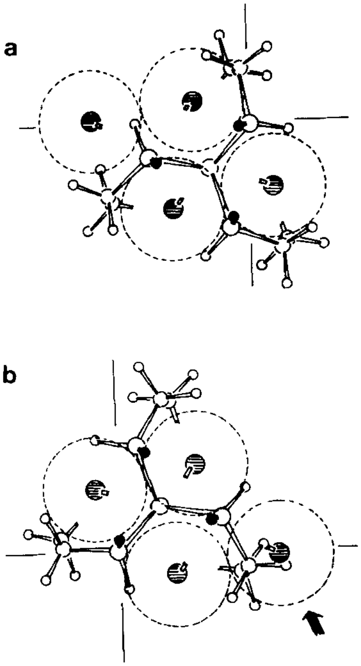


Figure 2. A schematic presentation of the mode of association between d-tart and $[Co(en)_3]^{3+}$.

(a) The compact fit between d-tart and Λ-complex.

(b) The non-compact fit between d-tart and Δ-complex.

oxygen atom which does not pertain to the hydrogen-bond to the NH group.

Complete Resolution of fac-[Co(β-ala)$_3$] (11)

As stated in the preceding sections, only the upper half of the complex is involved in the discrimination of enantiomers by d-tart. Therefore, d-tart should resolve not only $[Co(en)_3]^{3+}$ but also any complexes having three NH_2 groups in a triangular facet of their octahedral coordination. In fact, complete resolution by d-tart is reported for $[Co(AA)(en)_2]^{2+}$ (AA represents glycinate(9), β-alaninate(9), ethanolamine(10) and thioethanolamine(10)). If this idea is valid, we can expect a complete resolution of a neutral complex, fac-[Co(β-ala)$_3$] (See Fig. 3). Although this complex is electrically neutral, its three NH_2 groups are disposed in a triangular facet, and its three COO^- groups are situated in another triangular facet, so that a fairly large dipole moment is expected. Thus, the complex should be adsorbed fairly strongly on an ion-exchange resin and associate with d-tart also fairly strongly. This expectation was completely fulfilled as shown in Fig. 4. The complex is completely resolved through the Na form of CM-Sephadex ion-exchanger using ethanol-water mixed solution of Na_2d-tart. If we use the solution of NaCl or Na_2SO_4, instead of the solution of Na_2d-tart, the elution curve becomes one peak.

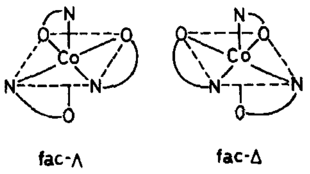


Figure 3. Two enantiomers of fac-[Co(β-ala)$_3$]

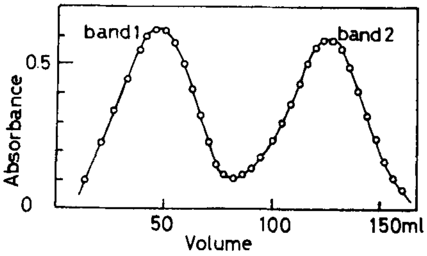


Figure 4. Elution curve of fac-[Co(ß-ala)$_3$].

Therefore, the optical resolution is presumed to be effected by d-tart and not by the chirality of the Sephadex skeleton.

Application of the Threefold-Axis Association Model to More Complicated Systems (12)

The validity of the stereoselective association along the threefold or quasi-threefold axis of the complex is supported by the following data. We determined the association constants of four isomers of [Co(phe)(en)$_2$]$^{2+}$ (phe represents D- or L-phenylalaninate), Λ-(L-phe), Δ-(L-phe), Λ-(D-phe) and Δ-(D-phe), with d-tart and attributed the difference in association constants to the difference in the magnitude of steric repulsion between the phenyl group of phynylalaninate ligand and d-tart. Figure 5 shows the schematic representations of these four isomers. Here, A and B are enantiomers. C and D are also enantiomers. But (A,B) and (C,D) are diastereomers. As is seen in these figures, the phenyl group in C and D is directed along the quasi-threefold axis of the complex and prevents the approach of d-tart to the complex. In contrast, the phenyl group in A and B is directed away from the quasi-threefold axis and does not prevent the approach of d-tart. Thus, the association constants with d-tart are smaller in C and D, and

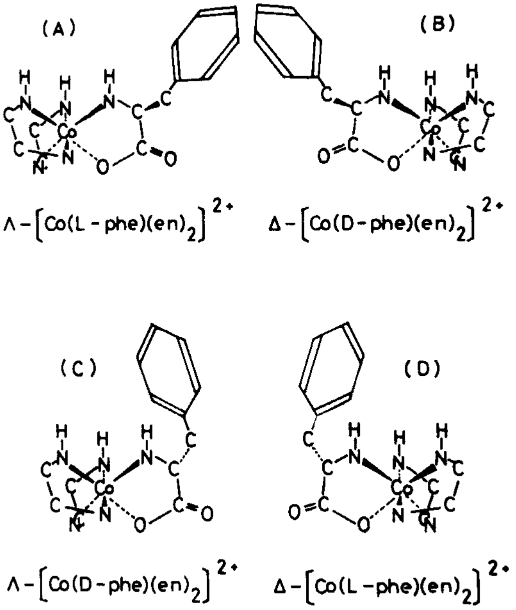


Figure 5. Molecular models for the phenylalaninato complexes.

larger in A and B. The association constants in A and B are nearly equal to those in $[Co(gly)(en)_2]^{2+}$ for which almost no steric repulsion toward the oncoming d-tart is expected. In addition, as expected from the figures, if d-tart approaches along the quasi-threefold axis and associates with the complex, the association constants show the smaller difference between the enantiomers, and larger difference between the diastereomers. The situation is clearly reflected on the chromatogram through the SP-Sephadex column with d-tart solution as eluent (See Fig. 6).

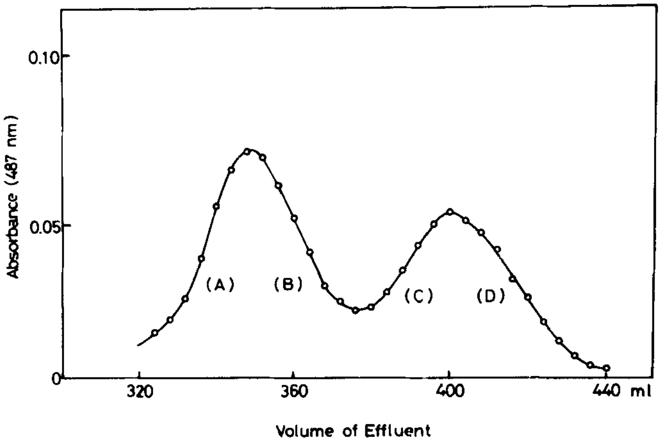


Figure 6. Elution curve of $[Co(DL\text{-}phe)(en)_2]I_2$ (20 mg) with d-tartrate (0.15 M) (resin SP-Sephadex, column 1.1 × 70 cm): A, Λ-$[Co(L\text{-}phe)(en)_2]^{2+}$; B, Δ-$[Co(D\text{-}phe)(en)_2]^{2+}$; C, Λ-$[Co(D\text{-}phe)(en)_2]^{2+}$; D, Δ-$[Co(L\text{-}phe)(en)_2]^{2+}$.

OPTICAL RESOLUTION BY ANTIMONY d-TARTRATE

Proposed Association Model for Sb d-Tart (13)

Antimony d-tartrate is a divalent anion having a dimeric structure as shown in Fig. 7 (abbreviated hereafter as Sb d-tart). We found that the association constant of Sb d-tart with $[Co(en)_3]^{3+}$ is greater than that of d-tart, and that K_Λ/K_Δ (the ratio of the association constant of a resolving agent with the Λ complex to that with the Δ complex) is considerably greater for Sb d-tart than for d-tart(8)(See Table 1). The separation factor α (14) of $[Co(en)_3]^{3+}$ obtained by ion-exchange chromatography (SP-Sephadex C-25) with 0.1M K_2Sb d-tart is greater than that with 0.1M Na_2d-tart: 1.42 for the former and 1.21 for the latter(8). From these data it is concluded that Sb d-tart is the better resolving agent than d-tart for $[Co(en)_3]^{3+}$, and this has been generally found to hold

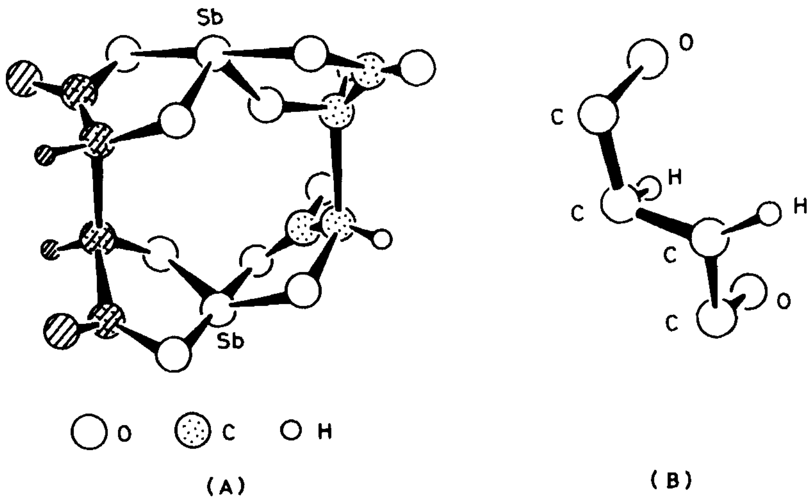


Figure 7. Structure of $[Sb_2(d\text{-}tart)_2]^{2-}$.

(A) Overall structure.

(B) Hatched atoms in (A), as viewed from the center of the ion.

TABLE 1

Association Constants at 25°C (μ=0.1)

	nm	d-tart	Sb-tart
Λ-$[Co(en)_3]^{3+}$	430	13.0±0.1	46.6±0.7
	455	13.6±0.2	47.3±0.6
Δ-$[Co(en)_3]^{3+}$	430	10.5±0.4	25.6±0.9
	455	11.7±0.4	26.8±0.6
K_Λ/K_Δ (average)		1.2	1.8

for other complexes. Sb d-tart has resolved more types of complexes than d-tart. These facts seem to indicate that the mode of association of Sb d-tart is different from that of d-tart.

Here Sb d-tart is presumed to approach the complex from the direction other than along the threefold axis and to discriminate the chirality of the complex. Thus, let us take $[Co(en)_3]^{3+}$ as the representative of tris-chelate complexes and consider how different the Λ and Δ configurations look, when viewed in the direction other than along the threefold axis. As is seen in Fig. 8, the Λ and Δ configurations are characterised by the mode of coordination of three en ligands and, at the same time, by the shape of the opening between three chelate rings. The opening between three chelate rings in the Λ configuration has a shape "L", and is called the "L-shaped chan-

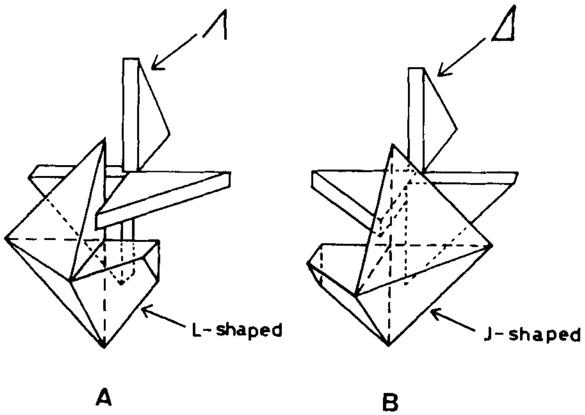


Figure 8. Schematic presentation of the Λ-$[Co(en)_3]^{3+}$... L-shaped counter-ion pair (A), and the Δ-$[Co(en)_3]^{3+}$... J-shaped counter-ion pair (B). The L(J)-shaped counter-ion fits well the L(J)-shaped channel(s) of $\Lambda(\Delta)$-$[Co(en)_3]^{3+}$.

nel". In contrast, the opening between three chelate rings in the Δ configurations has a shape reverse to the "L-shaped channel, and is called the "J-shaped channel". The Λ complex has only L-shaped channels, and the Δ complex has only J-shaped channels. The counter ion which fits the L-shaped channel does not fit the J-shaped channel. Such a counter ion should work as a resolving agent. Sb d-tart should have the part that can fit the L-shaped channel. In fact, the tart bridging the two Sb atoms corresponds to this part as shown in Fig. 9.

Λ-$[Co(en)_3]^{3+}$ has six L-shaped channels. Any other complexes having such L-shaped channels should be resolved by chromatography with Sb d-tart. Here, a complex which

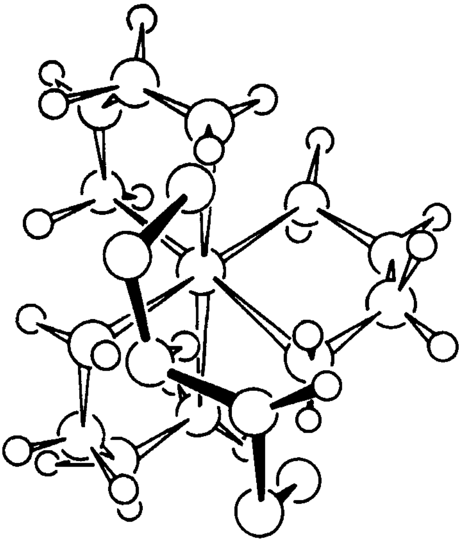


Figure 9. Stereoselective association model of $[Sb_2(d\text{-}tart)_2]^{2-}$ with one of the L-shaped channels of Λ-$[Co(en)_3]^{3+}$.

has more number of such channels should be more efficiently resolved with Sb d-tart, and the separation factor should be larger. To see whether this association model for Sb d-tart is valid, we prepared a series of complexes which satisfy the following conditions and chromatographed them through SP-Sephadex column with Sb d-tart as eluent and obtained the retention volumes and separation factors of enantiomers. The conditions which the complex should meet are

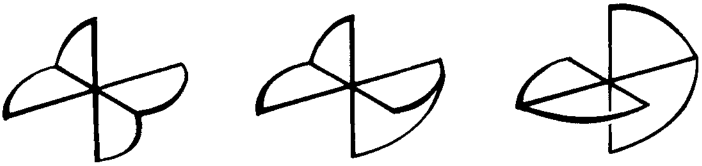
1) They should have the same charge, i.e., 3+. The charge should not be localized.

2) They should have the same number (four) of en bridges, so that the affinity toward the resin should be equal.

3) They differ only in the number of L-shaped channels.

The complexes examined are shown in Fig. 10. $[Co(en)_3]^{3+}$ was also studied, because it is the fundamental chiral chelate and has the largest number(six) of L-shaped channels. The result is shown in Table 2. In this table

α-$[Co(trien)(en)]^{3+}$ β-$[Co(trien)(en)]^{3+}$



s-fac-$[Co(dien)_2]^{3+}$ u-fac-$[Co(dien)_2]^{3+}$ mer-$[Co(dien)_2]^{3+}$

Figure 10. The five complexes examined, including geometric isomers.

TABLE 2

Adjusted Retention Volumes and Separation Factors

L, J=The number of L- and J-shaped channels in the first eluted enantiomer. Vol(I)=retention volume of the first band eluted with $K_2[Sb_2(d\text{-}tart)_2]$. Vol(II)=retention volume of the second band eluted with $K_2[Sb_2(d\text{-}tart)_2]$. Vol(III)=retention volume of the band eluted with KCl. Diff=Vol(II)-Vol(I). α=Separation factor.

complexes	L,J	Vol(I) (ml)	Vol(II) (ml)	Vol(III) (ml)	Diff	α
(A) $[Co(en)_3]^{3+}$	6,0	200.1	289.3	113.9	89.2	1.45
(B) α-$[Co(trien)(en)]^{3+}$	4,0	199.1	272.6	1.4.3	73.5	1.37
(C) β-$[Co(trien)(en)]^{3+}$	3,0	214.5	275.0	106.7	60.5	1.28
(D) u-fac-$[Co(dien)_2]^{3+}$	2,0	236.4	283.7	110.4	47.3	1.20
(E) s-fac-$[Co(dien)_2]^{3+}$	2,2	238.9	---	104.8	---	---
(F) mer-$[Co(dien)_2]^{3+}$	0,0	265.2	(298.8)*	108.6	(33.6)	(1.13)

* Estimated, because of a partial resolution.

L-J represents the number of L- and J-shaped channels of the first eluted enantiomers. Vol(I) and (II) represent the adjusted retention volumes of the first and the second eluted enantiomers, respectively. Separation factor is the ratio of Vol(II)/Vol(I). As is seen in this table, the separation factors for complexes (A), (B), (C) and (D) are 1.45, 1.37, 1.28 and 1.20 respectively. These figures correspond nicely to the number of L-shaped channels of the first eluted Λ enantiomer. Complex (E) is not chiral and is not resolved into enantiomers, but its adjusted retention volume is equal to Vol(I) of complex (D) and shows the behavior of the two L-shaped channels. Further, it is noteworthy that Vol(II) values of complexes (B), (C) and (D) are considered to be nearly equal, which corresponds to the zero number of L-shaped channels.

In conclusion, as far as these data concern, the association model for Sb d-tart that we imagined at the outset proved to be valid.

Resolution of cis-[Co(N_3)$_2$(en)$_2$]$^+$ (15)

Since the Λ form of cis-[CoX_2(en)$_2$]$^+$ has also L-shaped channels, the complex should be separated into enantiomers through the ion-exchange column using antimony d-tartrate aqueous solution as eluent. Thus, an attempt was made to chromatograph cis-[CoX_2(en)$_2$]$^+$ (X=NO_2^-, NCS^- and N_3^-) using antimony d-tartrate aqueous solution as eluent. Figure 11 shows the elution curves of these

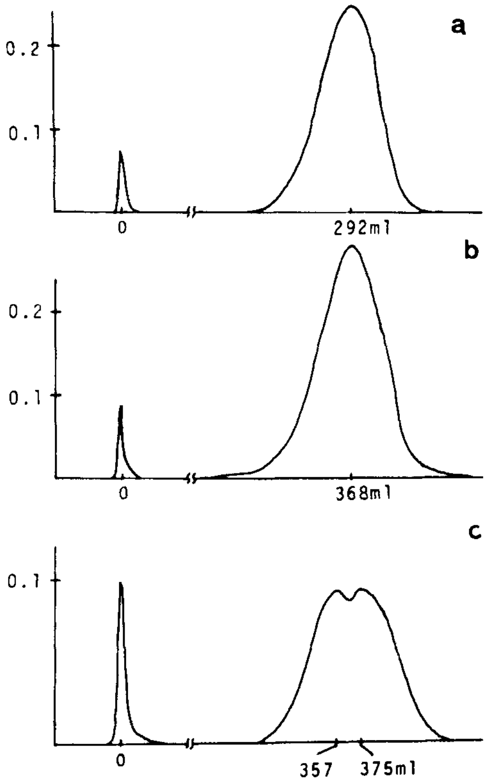


Figure 11. Chromatograms of cis-[Co(X)$_2$(en)$_2$]$^+$: (a) X=NCS. (b) X=NO_2. (c) X=N_3. Packing, SP-Sephadex C-25; flow rate, 0.5-0.7 ml/min; column, 98×1.1 cm glass bore; eluent, 0.05 M K_2[Sb_2(d-tart)$_2$] aqueous solution.

three complexes eluted with 0.05M $K_2(Sb\ d\text{-}tart)_2$ aqueous solution. The elution curves of dirhodanato and dinitro complexes consist of a single peak. The fractions of the front and the rear of the peak showed almost no CD peak. This indicates that optical resolution is not achieved practically for dirhodanato and dinitro complexes. However, the elution peak of diazido complex shows a slight splitting as shown in Fig. 11(c), and the fractions corresponding to these split peaks showed the CD spectra of opposite signs. Therefore, it can be said that optical resolution is achieved to a considerable extent for cis-$[Co(N_3)_2(en)_2]^+$.

Here it must be explained why only the diazido complex is resolved and why the dirhodanato and dinitro complexes are not resolved by the same chromatographic procedure. If we assume that the discrimination of Λ and Δ by Sb d-tart is done with its fitting to the L-shaped channel of the Λ, Sb d-tart should approach to the complex in the directions indicated by thin arrows in Fig. 12(a). However, the L-shaped channel in cis-$[CoX_2(en)_2]^+$ is adjacent to the anionic ligand X^-, so that the oncoming Sb d-tart anion will feel electrostatic repulsion from X^-, which makes the possibility of the approach in this direction very small. Thus, it is understandable that most of cis-$[CoX_2(en)_2]^+$ can not be resolved by ion-exchange chromatography. However, since cis-$[Co(N_3)_2(en)_2]^+$ is fairly well resolved by Sb d-tart, the ion association using the L-shaped channel should occur to a considerable extent as shown with a bit broader arrows in Fig. 12(c). This may be possible because the negative charge of N_3^- is diluted through three nitrogen atoms as suggested in the following resonance scheme so that the electrostatic repulsion against the approaching Sb d-tart is lowered.

$$Co-\overset{-}{N}-\overset{+}{N}\equiv N \qquad\qquad Co-N=\overset{+}{N}=\overset{-}{N}$$

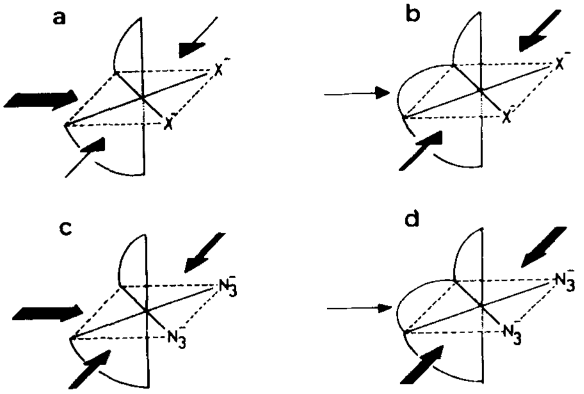


Figure 12. Access of $[Sb_2(d\text{-}tart)_2]^{2-}$ toward cis-$[Co(X)_2(N)_4]^+$; (a) cis-$[Co(X)_2(en)_2]^+$; (b) cis-α-$[Co(X)_2trien]^+$ (X= NCS and NO_2); (c) cis-$[Co(N_3)_2(en)_2]^+$; (d) cis-α-$[Co(N_3)_2trien]^+$.

If this interpretation is valid, more efficient optical resolution should be achieved for cis-α-$[Co(N_3)_2(trien)]^+$ (trien = $NH_2CH_2CH_2NHCH_2CH_2NHCH_2CH_2NH_2$) in which the bridging ethylene group between two en prevents the approach of Sb d-tart in this direction (a thin arrow in Fig. 12(d)) and drifts the anion to associate the complex using the L-shaped channel as shown with broad arrows in Fig. 12(d). This expectation was fulfilled. The splitting of the elution peak became more marked for cis-α-$[Co(N_3)_2(trien)]^+$ as shown in Fig. 13(c). The situation should be quite similar for cis-α-$[Co(NO_2)_2(trien)]^+$ and cis-α-$[Co(NCS)_2(trien)]^+$. In these complexes, although the elution curves still remained as a single peak, the front and the rear of the peak showed the CD spectra of opposite signs. Thus, the partial resolution is definitely achieved in these two cases.

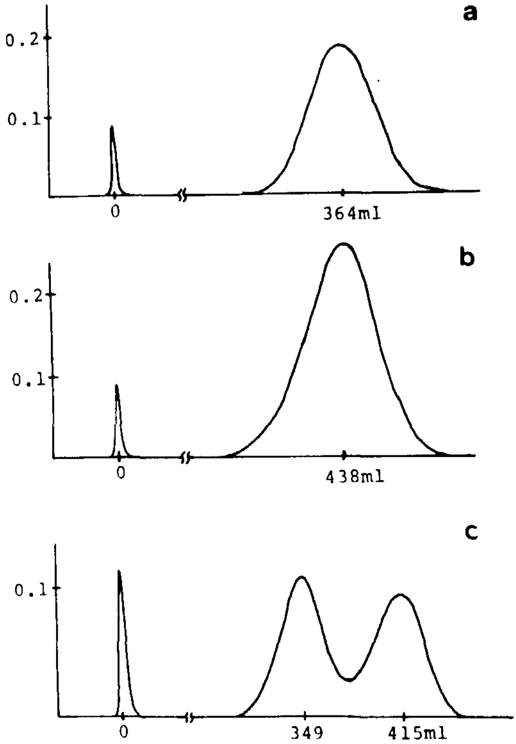


Figure 13. Chromatograms of cis-α-$[Co(X)_2trien]^+$. Condition for elution as in Fig. 11.

Resolution of fac-$[Co(\alpha\text{-}AA)_n(\beta\text{-}AA)_{3-n}]$ (16)

Since facial and meridional tris(aminoacidato) chelates have L-shaped channels, they are expected to be resolved into enantiomers with Sb d-tart as eluent. In order to see the detailed feature of the mechanism of optical resolution, we prepared a series of tris(aminoacidato) mixed chelates of the formula, fac-$[Co(\alpha\text{-}AA)_n(\beta\text{-}AA)_{3-n}]$, and measured the retention volume of each isomer when eluted with 0.1M Na_2Sb d-tart as well as Na_2d-tart, and calculated the separation factor of each enantiomeric pairs. The results given in Figs. 14 and 15 can be summarized as follows.

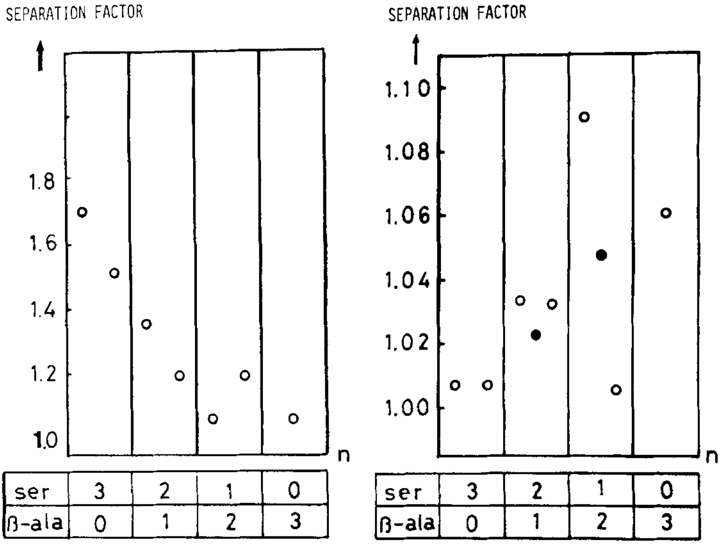


Figure 14 and 15. Separation factor of fac-trisaminoacidato-cobalt(III) complex. Eluent: 0.1 M Na_2tart solution(14). 0.1 M $Na_2[Sb_2(d\text{-}tart)_2]$ solution(15); o, serine complex; o, glycine complex.

1) When eluted with d-tart, the separation factor is the largest for fac-$[Co(\beta\text{-}ala)_3]$. With successive substitution of six-membered chelate rings with five-membered rings, it decreases and finally in fac-$[Co(L\text{-}ser)_3]$ and $[Co(D\text{-}ser)_3]$ pairs, the separation factor is the smallest, 1.007. This means that no resolution takes place for fac-$[Co(\alpha\text{-}AA)_3]$ which has no NH bonds directed along the threefold axis of the complex.

2) When eluted with Sb d-tart, a quite reverse trend is observed as is shown in Fig. 15. The separation factor is the largest, 1.702, for $[Co(\alpha\text{-}AA)_3]$ and decreases by replacement with six-membered AA.

These findings suggest that the mechanism of optical resolution is quite different between for d-tart and for Sb d-tart.

Resolution of mer-[Co(β-ala)$_3$] (17)

Meridional isomers of tris(aminoacidato) chelates have also L-shaped channels (Fig. 16), and is expected to be resolved into enantiomers with Sb d-tart. In fact, mer-[Co(β-ala)$_3$] dissolved in Na$_2$Sb d-tart solution shows the induced CD spectrum in the d-d absorption region, which suggests that Sb d-tart does discriminate the Λ and Δ in solution. Thus, Sb d-tart was loaded on the Q.A.E. Sephadex anion-exchanger, through which the complex was eluted with distilled water. With this procedure, the complex was completely separated into enantiomers. The separation factor was 1.18 (2×76 cm column, flow rate= 0.06 ml/min). The separation factor was improved further with 50% ethanol-water (α=1.34)(See Fig. 17). The larger separation factor in the case of ethanol-water was attributed to the dehydration effect of ethanol which facilitates the complex and Sb d-tart to make a close contact.

CONCLUSION

I have shown, though in a limited space, several examples wherein complete resolution of metal complexes has been achieved by liquid chromatographic techniques.

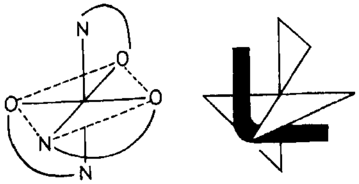


Figure 16. Λ-mer-[Co(β-ala)$_3$] and its L-shaped channel.

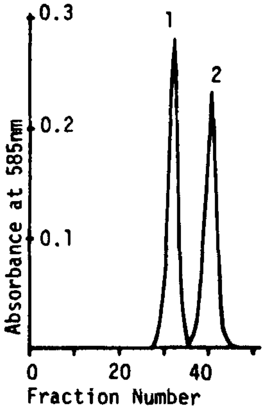


Figure 17. Elution curve of mer-[Co(β-ala)$_3$]
(eluent: 50% ethanol-water mixed solvent)

As we go through and scrutinize the mechanism of resolution, it has become clearer that the gist lies in a "cozy fit" between the resolving agent and the complex to be resolved. This is surely quite natural, and so it is also apparent that any selection of resolving agent without stereochemical considerations will not necessarily lead to complete resolution.

REFERENCES AND NOTES

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14. The separation factor is the ratio of the adjusted retention volume of the second band to that of the first band, and is a measure of the degree of separation. The greater the separation factor the better two bands are separated, and no separation results when it is unity.

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