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Chromatographic Study of Optical Resolution. XIV.[1] Optical Resolution of Amine Complex Cations of the Type $[Co(N)_6]^{3+}$ by Reversed-Phase Ion-Pair Chromatography Using Bis(*μ*-*d*-tartrato)diantimonate(III) and Arsenic Analog as an Ion-Pairing Reagent

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Reversed-phase ion-pair chromatography (RPIPC) was applied to the optical resolution of amine complex cations of the type $[Co(N)_6]^{3+}$ using either bis(*μ*-*d*-tartrato)diantimonate(III) ion, $[Sb_2(d\text{-tart})_2]^{2-}$ or its arsenic analog, $[As_2(d\text{-tart})_2]^{2-}$ as an ion-pairing reagent. With either reagent, efficient optical resolution was attained for $[Co(en)_3]^{3+}$, $[Co(tn)_3]^{3+}$, $[Co(sen)]^{3+}$, $[Co(sep)]^{3+}$, and $[Co(diNOsar)]^{3+}$ (en=ethylenediamine, tn=trimethylenediamine, sen=1,1,1-tris[[(2-aminoethyl)amino]methyl]ethane, sep=1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]icosane, and diNOsar=1,8-dinitro-3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane). Dependence of retention volumes and separation factors of these complexes on the concentration and the counterion of the ion-pairing reagents was examined with Na^+, Me_4N^+, and Et_4N^+ employed as counterions. Experimental results were discussed with reference to those obtained by means of normal-phase ion-exchange chromatography (NPIEC) using the same eluents. It was concluded that $[As_2(d\text{-tart})_2]^{2-}$ serves as a more effective eluent in both RPIPC and NPIEC than $[Sb_2(d\text{-tart})_2]^{2-}$, and that RPIPC is a much more useful tool for the optical resolution of the $[Co(N)_6]^{3+}$-type complex cations than NPIEC.

In a previous work,[2] optical resolution of some *cis*(N)-$[Co(O)_4(N)_2]^-$-type complex anions was accomplished by means of reversed-phase ion-pair chromatography (abbreviated as RPIPC hereafter) using cinchona alkaloid cations as an ion-pairing reagent. In the present study, optical resolution of some amine complex cations of the type $[Co(N)_6]^{3+}$ was attempted by the same technique. The key factor here is to find out a suitable chiral anion capable of functioning as an ion-pairing reagent. The two chiral anions, *d*-tartrate ($d\text{-tart}^{2-}$) and bis(*μ*-*d*-tartrato)diantimonate(III) ($[Sb_2(d\text{-tart})_2]^{2-}$) ions have been successfully utilized as a chiral eluent to resolve a variety of complex cations by normal-phase ion-exchange chromatography[3] (abbreviated as NPIEC). The former anion is found to be too hydrophilic to be distributed to the stationary phase composed of linear-chain alkyl moieties in RPIPC. The latter anion, $[Sb_2(d\text{-tart})_2]^{2-}$ does not contain any alkyl chains nor aromatic rings and it carries a high electric charge compared with commonly used ion-pairing reagents such as tetraalkylammonium and alkanesulfonate ions. However, it is regarded as rather hydrophobic, since its charged groups are all coordinated to Sb(III) ions and it is fairly large in size. Therefore, this chiral anion is expected to serve as a potential ion-pairing reagent in RPIPC.[4a] $[As_2(d\text{-tart})_2]^{2-}$ ion, an As analog of $[Sb_2(d\text{-tart})_2]^{2-}$, has seen limited use as a chiral eluent, since it is not commercially available. Thus, it seems attractive to compare the two anions with respect to their ability as an eluent in chromatography.

In RPIPC, structural characteristics of ion-pairing reagents have been examined in detail, since they have a profound influence on the retention volumes as well as on the separation factors.[4] By contrast, the functions of the counterions M^+ of the ion-pairing reagents have been hardly taken into consideration. In the present study, however, the electric charge of the tervalent complex cation is not completely neutralized in the 1:1 association with $[Sb_2(d\text{-tart})_2]^{2-}$, and thus the complex cation is distributed to the stationary phase probably in the form of $M[Co(N)_6]][Sb_2(d\text{-tart})_2]_2$ rather than $[Co(N)_6]_2[Sb_2(d\text{-tart})_2]_3$ if the counterion M^+ is more hydrophobic than $[Sb_2(d\text{-tart})_2]^{2-}$. Consequently, a hydrophobic counterion M^+ is expected to promote cooperatively the retention of the complex cation to a considerable extent, since $[Sb_2(d\text{-tart})_2]^{2-}$ is less hydrophobic than usual ion-pairing reagents.

Experimental

Materials. The $[Co(N)_6]^{3+}$-type complexes used were $[Co(en)_3]^{3+}$,[5] $[Co(tn)_3]^{3+}$,[6] $[Co(sen)]^{3+}$,[7] $[Co(sep)]^{3+}$,[8] *lel*$_3$-$[Co(chxn)_3]^{3+}$,[9] and $[Co(diNOsar)]^{3+}$[10] (en=ethylenediamine, tn=trimethylenediamine, sen=1,1,1-tris[[(2-aminoethyl)-amino]methyl]ethane, sep=1,3,6,8,10,13,16,19-octaazabicyclo-[6.6.6]icosane, chxn=*trans*-1,2-cyclohexanediamine, and diNOsar=1,8-dinitro-3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane). For comparison, $[Co(gly)(en)_2]^{2+}$[11] was also used (gly=glycinate anion). Figure 1 illustrates schematic structures of some of these complexes, which were prepared as chloride salts by the literature methods. Absolute configurations have been already assigned to all of them.

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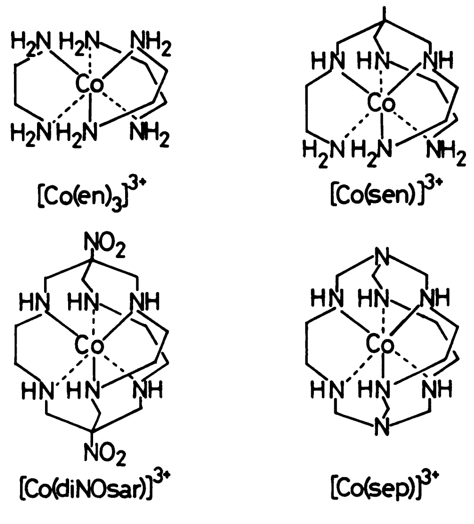

Fig. 1. Structures of Δ-enantiomers of the [Co(N)$_6$]$^{3+}$-type complexes investigated in the present study.

K[Co(edta)]·2H_2O (edta=ethylenediaminetetraacetate anion), used as a marker for the void volume measurement, was prepared by a well-established method.[12]

Following salts of [Sb_2(*d*-tart)$_2$]$^{2-}$ or [As_2(*d*-tart)$_2$]$^{2-}$ were used as ion-pairing reagents; Na_2[Sb_2(*d*-tart)$_2$]·5H_2O, K_2[Sb_2(*d*-tart)$_2$]·3H_2O, (NH_4)$_2$[Sb_2(*d*-tart)$_2$]·3H_2O, (Me_4N)$_2$[Sb_2(*d*-tart)$_2$]·3.5H_2O, (Et_4N)$_2$[Sb_2(*d*-tart)$_2$]·1.5H_2O, and Na_2[As_2(*d*-tart)$_2$]·5H_2O. The potassium salt was obtained commercially and was used without purification. The sodium salt was prepared by the literature method.[3b)] The ammonium salt was similarly prepared using ammonium hydrogen *d*-tartrate in place of sodium hydrogen *d*-tartrate. Found: C, 15.43; H, 2.94; N, 4.40%. Calcd for $C_8H_{12}N_2O_{12}Sb_2\cdot3H_2O$: C, 15.35; H, 2.91; N, 4.48%. The tetramethylammonium and tetraethylammonium salts were prepared in a following way. An equivalent amount of antimony(III) oxide was added to an aqueous solution of *d*-tartaric acid. After heating just to the boiling point, an equivalent amount of aqueous MOH (M^+=Me_4N^+ or Et_4N^+) was carefully added dropwise with stirring. The suspension was concentrated and undissolved substances were filtered off. The filtrate was evaporated to dryness to obtain a glassy material. Its purity was checked by elemental analysis. Found: C, 25.69; H, 4.71; N, 3.70%. Calcd for $C_{16}H_{28}N_2O_{12}Sb_2\cdot3.5H_2O$: C, 25.72; H, 4.73; N, 3.75%. Found: C, 34.89; H, 5.65; N, 3.37%. Calcd for $C_{24}H_{44}N_2O_{12}Sb_2\cdot1.5H_2O$: C, 35.01; H, 5.77; N, 3.40%. Na_2[As_2(*d*-tart)$_2$]·5H_2O was easily prepared according to well-established procedures[13)] followed by recrystallization from water. Found: C, 16.47; H, 2.42%. Calcd for $C_8H_4As_2Na_2O_{12}\cdot5H_2O$: C, 16.62; H, 2.45%.

The column packings used in the present study were TSK gel ODS-120A (Toyo Soda Manufacturing Co., Ltd.), which carries linear-chain alkyl moieties (octadecyl groups) covalently bonded to the surface of silica gel (for RPIPC), and TSK gel SP-2SW (Toyo Soda Manufacturing Co., Ltd.), which carries sulfopropyl groups covalently bonded to the surface of silica gel (for NPIEC).

Chromatographic Experiments. A stainless steel column (4×300 mm) packed with TSK gel ODS-120A or a similar column (7.5×75 mm) packed with TSK gel SP-2SW was equilibrated with an aqueous eluent solution. A mixture of 20 μl of an aqueous solution of a racemic complex (0.1 mol dm^{-3}) with 10 μl of an aqueous solution of a marker (0.01 mol dm^{-3}), was injected by a syringe on the top of the column and was eluted at an elution rate of 0.25 cm^3 min^{-1}. The effluents were fractionally collected and their absorption and circular dichroism (CD) spectra were measured to obtain elution curves and to determine elution orders. The chromatographic apparatus used here consisted of a JASCO BIP-1 pump for HPLC, a JASCO variable loop injector VL-613, and a Shimadzu UV-140 double beam spectrophotometer. The CD spectra were recorded on a JASCO J-40CS recording spectropolarimeter.

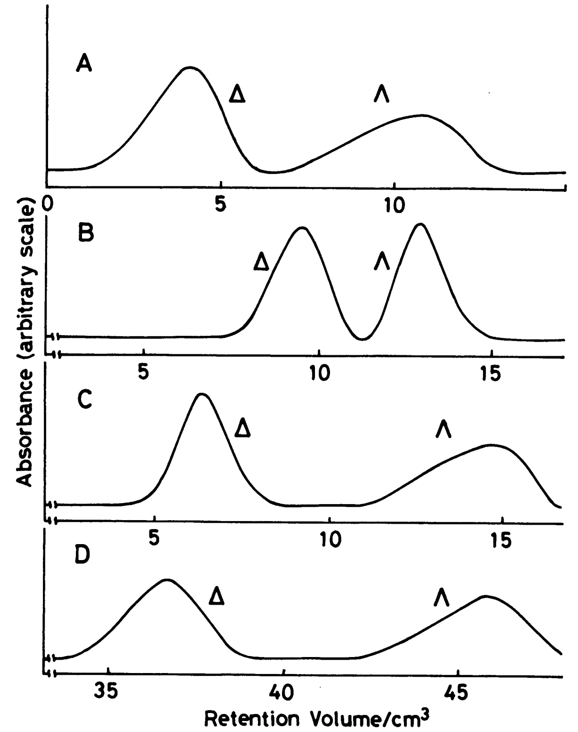

Fig. 2. Elution curves of [Co(en)$_3$]$^{3+}$ (A), [Co(tn)$_3$]$^{3+}$ (B), [Co(sen)]$^{3+}$ (C), and [Co(sep)]$^{3+}$ (D) obtained by RPIPC. Eluent: aqueous K_2[Sb_2(*d*-tart)$_2$] (0.1 mol dm^{-3}).

Results and Discussion

Reversed-Phase Ion-Pair Chromatography (RPIPC). Typical elution curves obtained for the [Co(N)$_6$]$^{3+}$-type complexes with K_2[Sb_2(*d*-tart)$_2$] employed as an eluent in RPIPC are shown in Fig. 2. Though the curves are rather broad, base-line resolution is assured for each complex. It is noteworthy that complete resolution is accomplished easily even for [Co(tn)$_3$]$^{3+}$, complete resolution of which has been barely attained with resort to time-consuming recycling chromatography.[14)] Experimental data obtained with M_2[Sb_2(*d*-tart)$_2$] (M^+=Na^+, K^+, NH_4^+, Me_4N^+, and Et_4N^+) used

Table 1. Effect of Counterion M^+ on Retention Volume V_R and Separation Factor α Obtained by RPIPC with Aqueous M_2 $[Sb_2(d\text{-tart})_2]$(0.1 mol dm^{-3})

	$M^+=Na^+$		K^+		NH_4^+		Me_4N^+		Et_4N^+	
	V_R[a)]/cm^3	α	V_R[a)]/cm^3	α	V_R[a)]/cm^3	α	V_R[a)]/cm^3	α	V_R[a)]/cm^3	α
$[Co(en)_3]^{3+}$	10.95	2.03	11.05	2.63	12.63	2.99	23.18	3.84	12.15	4.76
$[Co(tn)_3]^{3+}$	7.15	1.32	12.73	1.33	10.75	1.34	13.38	1.39	4.98	1.52
$[Co(sen)]^{3+}$	11.60	2.04	15.03	2.39	13.70	2.95	21.40	3.43	12.03	4.25
$[Co(sep)]^{3+}$	28.00	1.27	46.03	1.25	37.40	1.25	48.53	1.29	14.55	1.36

a) Retention volume of the later-eluted Λ-enantiomer.

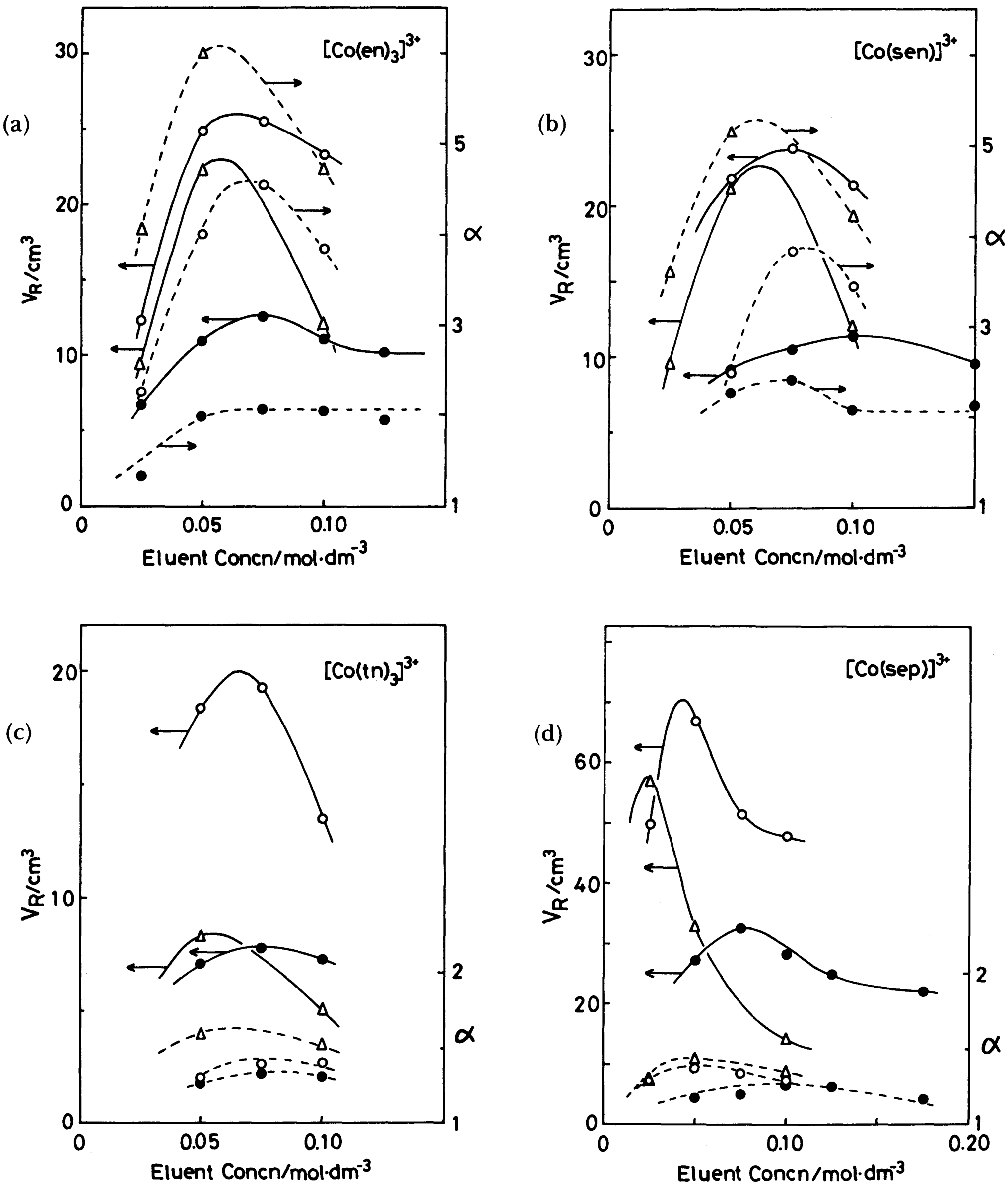

Fig. 3. Plots of retention volumes V_R (——) of the later-eluted enantiomer and of separation factors α (------) obtained by RPIPC against the eluent concentration. Eluent: $Na_2[Sb_2(d\text{-tart})_2]$ (●), $(Me_4N)_2[Sb_2(d\text{-tart})_2]$ (○), and $(Et_4N)_2[Sb_2(d\text{-tart})_2]$ (Δ).

as an ion-pairing reagent are summarized in Table 1.[15] For all the complexes, the Λ-enantiomers are eluted later. This means that $[Sb_2(d\text{-tart})_2]^{2-}$ gets associated more readily with the Λ- than with the Δ-enantiomer, in keeping with the association constants estimated for these complex cations with $[Sb_2(d\text{-tart})_2]^{2-}$ in aqueous solution.[16] Furthermore, this observation does not contradict with the elution orders predicted from the chiral discrimination mechanism established earlier between $[Sb_2(d\text{-tart})_2]^{2-}$ and $[Co(N)_6]^{3+}$-type complexes.[17] One different elution order is noted between RPIPC and NPIEC. The complex cation, $[Co(tn)_3]^{3+}$, when eluted from either an SP-Sephadex C-25 or Dowex 50W-X2 cation-exchange column with aqueous $Na_2[Sb_2(d\text{-tart})_2]$, was partially resolved with the Δ-enantiomer eluted slightly faster unlike other $[Co(N)_6]^{3+}$-type complexes.[18] This suggests that $[Sb_2(d\text{-tart})_2]^{2-}$ favors the Δ- over the Λ-enantiomer for $[Co(tn)_3]^{3+}$ in NPIEC. In RPIPC, on the contrary, $[Sb_2(d\text{-tart})_2]^{2-}$ always exhibits a greater affinity toward the Λ-enantiomer for all the complexes including $[Co(tn)_3]^{3+}$. The anomalous behavior of $[Co(tn)_3]^{3+}$ will be discussed later.

Data in Table 1 reveal that different counterions M^+ of $[Sb_2(d\text{-tart})_2]^{2-}$ give different retention volumes V_R and separation factors α for each $[Co(N)_6]^{3+}$-type complex. In general, the larger the size of M^+, i.e., the more hydrophobic nature M^+ bears, the greater the retention volume of each complex. However, when M^+ is as large as Et_4N^+, the retention volume starts to decrease. Then, in Figs. 3-a to 3-d are plotted the V_R and α values of $[Co(en)_3]^{3+}$, $[Co(sen)]^{3+}$, $[Co(tn)_3]^{3+}$, and $[Co(sep)]^{3+}$, in this order, as a function of the concentration of ion-pairing reagents with $M^+=Na^+$, Me_4N^+, and Et_4N^+. For each complex, V_R shows a clear maximum with $M^+=Me_4N^+$ and Et_4N^+, the latter exhibiting it at lower eluent concentrations and the former giving a higher maximum at least in the concentration range covered. On the contrary, the V_R curve with $M^+=Na^+$ shows a less clear maximum. Appearance of such maxima in V_R may be explained as follows. Since Me_4N^+ and Et_4N^+ are much more hydrophobic than Na^+, they are more easily distributed together with $[Sb_2(d\text{-tart})_2]^{2-}$ to the stationary phase composed of linear-chain alkyl moieties,[19] generating more cation-exchange sites on the stationary phase.[4b] This will lead to remarkably increased retention volumes. On the other hand, the effect of expelling the complex cation already distributed to the stationary phase by the counterion M^+ present in the moving phase, viz., the exclusion effect of M^+, becomes more and more dominant with increasing concentration of the eluent and with increasing hydrophobic nature of M^+. Thus, a maximum in V_R appears at a lower eluent concentration for $M^+=Et_4N^+$ than for $M^+=Me_4N^+$, since the former counterion is more hydrophobic and thus has a greater exclusion effect. A lower maximum in V_R observed for the former is similarly interpreted, and the absence of a clear V_R maximum for $M^+=Na^+$ may be due to its hydrophilic nature which leads to a small retention volume and to a weak exclusion effect. These interpretations are indirectly supported by the observation that $[Co(sep)]^{3+}$, regarded as the most hydrophobic of the four complexes, exhibits the V_R maxima at the lowest eluent concentrations, and that it always gives greater retention volumes than $[Co(en)_3]^{3+}$ regardless of the kind of M^+.[20]

Let us next look into the separation factors α obtained by RPIPC. It is seen in Table 1 and Fig. 2 that fairly high separation factors are obtained to such an extent that complete resolution is attained with ease for each complex. In a previous study, for example, optical resolution of $[Co(en)_3]^{3+}$ resulted in a separation factor of 1.45[21] on an SP-Sephadex C-25 column with an aqueous $K_2[Sb_2(d\text{-tart})_2]$ solution (0.1 mol dm^{-3}) employed as an eluent. The α value of 2.63 obtained in the present RPIPC under a similar set of conditions (Table 1) demonstrates a remarkable improvement in the resolution efficiency. As noted above, $[Co(tn)_3]^{3+}$ can also be resolved completely with a separation factor of 1.33 under the same conditions as above, though NPIEC gives a separation factor of 1.00 for this complex, as seen later in Table 3.

It is noticeable in Fig. 3 that surprisingly high α values are obtained for $[Co(en)_3]^{3+}$, $[Co(sen)]^{3+}$, and $[Co(tn)_3]^{3+}$,[22] particularly when their retention volumes are increased with Me_4N^+ or Et_4N^+. On the contrary, $[Co(sep)]^{3+}$ gives an almost constant separation factor even if its retention volume is increased appreciably. Structural characteristics of these complexes (Fig. 1) indicate that the former three complexes allow the hydrogen-bonding association of $[Sb_2(d\text{-tart})_2]^{2-}$ from the direction of the C_3 axis (C_3 association) or the C_2 axis (C_2 association), while only the C_2 association is allowed for $[Co(sep)]^{3+}$ because it has alkyl caps along the C_3 axis. These characteristics seem to be responsible for the chromatographic behavior mentioned above, which will be discussed more closely in the last section.

Now, a comparison is made between $[Sb_2(d\text{-tart})_2]^{2-}$ and its As analog, $[As_2(d\text{-tart})_2]^{2-}$ with respect to their ability as an ion-pairing reagent in RPIEC. Table 2 compares the experimental data obtained with the two ion-pairing reagents. It is evident that first, $[As_2(d\text{-tart})_2]^{2-}$ gives much greater retention volumes than $[Sb_2(d\text{-tart})_2]^{2-}$ for all the complexes, second, the former gives correspondingly somewhat higher separation factors, and finally, the Λ-enantiomers are eluted later with either of the two eluents. These results lead us to conclude that $[As_2(d\text{-tart})_2]^{2-}$ interacts more strongly with these amine complex cations of the type $[Co(N)_6]^{3+}$ than does $[Sb_2(d\text{-tart})_2]^{2-}$ and thus can be

Table 2. Comparison of Retention Volumes V_R and Separation Factors α Obtained by RPIPC with $Na_2[As_2(d\text{-tart})_2]$ and with $Na_2[Sb_2(d\text{-tart})_2]$ (0.1 mol dm^{-3})

	$[As_2(d\text{-tart})_2]^{2-}$		$[Sb_2(d\text{-tart})_2]^{2-}$	
	V_R[a]/cm^3	α	V_R[a]/cm^3	α
$[Co(en)_3]^{3+}$	61.25	3.33	10.95	2.03
$[Co(tn)_3]^{3+}$	61.35	1.30	7.15	1.32
$[Co(sen)]^{3+}$	60.75	3.25	11.60	2.04
$[Co(sep)]^{3+}$	101.43	1.37	28.00	1.27
$[Co(diNOsar)]^{3+}$	52.30	1.84	14.33	1.70

a) Retention volumes of the later-eluted Λ-enantiomer.

Table 3. Comparison of Retention Volumes V_R and Separation Factors α Obtained by NPIEC with $Na_2[As_2(d\text{-tart})_2]$ and with $Na_2[Sb_2(d\text{-tart})_2]$ (0.075 mol dm^{-3})

	$[As_2(d\text{-tart})_2]^{2-}$		$[Sb_2(d\text{-tart})_2]^{2-}$	
	V_R[a]/cm^3	α	V_R[a]/cm^3	α
$[Co(en)_3]^{3+}$	41.4	1.23	62.0	1.32[d]
$[Co(tn)_3]^{3+}$	56.6	1.00[b]	104.0[c]	1.00[b]
$[Co(sen)]^{3+}$	46.2	1.28	60.0	1.39[d]
$[Co(sep)]^{3+}$	27.6	1.41	65.2	1.31[d]
$[Co(diNOsar)]^{3+}$	···	···	40.2	1.83[d]

a) Retention volumes of the faster-eluted Λ-enantiomer. b) Single elution curve observed. c) The Δ-enantiomer is eluted faster. d) Data taken from Ref. 17b.

used more preferably as an ion-pairing reagent for the optical resolution of these complex cations in RPIPC, and that the chiral discrimination mechanisms are essentially the same for the two ion-pairing reagents.

$[Co(diNOsar)]^{3+}$ behaves somewhat anomalously in that it gives smaller V_R values and considerably greater α values than the analogous cage complex, $[Co(sep)]^{3+}$ with either ion-pairing reagent (Table 2). Highly efficient optical resolution attained for $[Co(diNOsar)]^{3+}$ has been already interpreted in terms of the severe steric repulsion expected stereoselectively between the nitro group of the Δ-enantiomer and the distal carboxylato group of $[Sb_2(d\text{-tart})_2]^{2-}$.[17b] The smaller retention volumes obtained for this complex may be attributed to the presence of the polar nitro groups which render this complex less hydrophobic than the parent complex $[Co(sep)]^{3+}$.[23]

Normal-Phase Ion-Exchange Chromatography (NPIEC). For the purpose of elucidating why $[As_2(d\text{-tart})_2]^{2-}$ gives greater V_R values than $[Sb_2(d\text{-tart})_2]^{2-}$ in RPIPC, NPIEC was applied to the optical resolution of the $[Co(N)_6]^{3+}$-type complexes with the two chiral anions employed as an eluent. The results are listed in Table 3. For each of these complexes, $[As_2(d\text{-tart})_2]^{2-}$ and $[Sb_2(d\text{-tart})_2]^{2-}$ give comparable separation factors, but the former gives smaller retention volumes, indicative of the stronger affinity of the former anion for these complexes. This is in complete conformity with the results obtained by RPIPC. In other words, $[As_2(d\text{-tart})_2]^{2-}$ has inherently a stronger association tendency toward these complexes than $[Sb_2(d\text{-tart})_2]^{2-}$.

An X-ray crystallographic analysis has revealed that $[As_2(d\text{-tart})_2]^{2-}$ is somewhat smaller in size than $[Sb_2(d\text{-tart})_2]^{2-}$. If the two oxygen atoms coordinated to the same Sb or As atom, i.e., the alcoholic oxygen atom of one *d*-tartrate moiety and the carboxylic oxygen atom of the other *d*-tartrate moiety are used for the double hydrogen bonding to the two axial NH protons of the complex directed along either the C_3 or the C_2 axis, as assumed before,[17] the matching of the O–O and H–H distances is of prime importance to the interaction. The O–O distance actually estimated is 2.561 Å[24] for $[As_2(d\text{-tart})_2]^{2-}$ and 2.692 Å[25] for $[Sb_2(d\text{-tart})_2]^{2-}$. The H–H distance of $[Co(en)_3]^{3+}$ is 2.283 and 2.270 Å for the C_3 and C_2 axial protons, respectively.[26] It will then follow that $[As_2(d\text{-tart})_2]^{2-}$ is more susceptible to intimate hydrogen bonds to $[Co(en)_3]^{3+}$ and other related complexes than $[Sb_2(d\text{-tart})_2]^{2-}$ is. In this way, smaller and greater V_R values obtained with $[As_2(d\text{-tart})_2]^{2-}$ in NPIEC and RPIPC, respectively, are interpreted reasonably within the framework of the C_3 and C_2 association modes proposed previously.[17]

Comparison between RPIPC and NPIEC. A comparison of the experimental results obtained between RPIPC and NPIEC (Tables 2 and 3) reveals very interesting facts as follows. For such complexes as $[Co(en)_3]^{3+}$, $[Co(sen)]^{3+}$, and $[Co(tn)_3]^{3+}$ for which both of the C_3 and C_2 association modes are possible, the application of RPIPC leads to a remarkable improvement in the separation factor. For example, $[Co(tn)_3]^{3+}$ gives a single elution curve in NPIEC, while base-line resolution is attained for this complex in RPIPC. By contrast, no such drastic improvement is detected for $[Co(sep)]^{3+}$, $[Co(diNOsar)]^{3+}$, and *lel*$_3$-$[Co(chxn)_3]^{3+}$ (chxn=*trans*-1,2-cyclohexanediamine) (Table 4)[27] for which only the C_2 or the C_3 association mode is possible owing to the presence of alkyl caps along the C_3 axis or bulky substituents along the C_2 axis (Fig. 1).

Several reasons are conceivable why RPIPC offers highly improved resolution efficiency for the former three complexes. The sample retention in NPIEC depends on the sample-ion-exchange resin interaction which is not related to chiral discrimination as well as on the sample-resolving reagent interaction, and the contribution of the former is unfortunately dominant generally in NPIEC. For example, for *lel*$_3$-$[Co(chxn)_3]^{3+}$ having presumably a very strong affinity for the resin, the α value is as high as 1.09 (Table 4). In other words, NPIEC appears unable to take full advantage of the chiral discrimination ability of the resolving reagent. On the other hand, the sample

Table 4. Comparison of Retention Volumes V_R and Separation Factors α Obtained with $Na_2[Sb_2(d\text{-tart})_2]$ by NPIEC and by RPIPC

	NPIEC			RPIPC		
	Eluent concn / mol dm^{-3}	V_R[a)] / cm^3	α	Eluent concn / mol dm^{-3}	V_R[b)] / cm^3	α
$[Co(en)_3]^{3+}$	0.1	10.2	1.35	0.175	9.98	2.09
$[Co(en)_3]^{3+}$	0.075	62.0	1.32	0.075	12.63	2.06
lel$_3$-$[Co(chxn)_3]^{3+}$	0.1	55.4	1.09	0.175	82.5	1.31
$[Co(gly)(en)_2]^{2+}$	0.075	10.6	1.21	0.075	1.85	1.42

a) Retention volume of the faster-eluted Λ-enantiomer. b) Retention volume of the later-eluted Λ-enantiomer.

retention in RPIPC is governed mainly by the sample-resolving reagent interaction which is directly associated with chiral discrimination. Consequently, RPIPC has a general possibility to afford a higher separation factor than NPIEC for a particular sample. However, it is hard to accept that the improvement in α detected in the present study has been brought about simply by the above-mentioned reason, because α is greatly improved only for those complexes which adopt both the C_3 and the C_2 modes.

The chiral discrimination mechanism of $[Sb_2(d\text{-tart})_2]^{2-}$ proposed previously can be summarized as follows.[17)] $[Sb_2(d\text{-tart})_2]^{2-}$ comes into interaction with the complex cation from the direction of either the C_3 or the C_2 axis to form hydrogen bonds to the axial NH protons directed along the C_3 or the C_2 axis, respectively. When the C_3 association mode is adopted, the chiral anion favors the Λ- over the Δ-enantiomer, whereas the Δ-enantiomer is favored in the C_2 association mode.[28)] As a result, the chiral discrimination efficiency is in general low for those complexes which can adopt both association modes. A typical example is provided by $[Co(tn)_3]^{3+}$ for which so low resolution is attained in NPIEC that its elution order is reversed even when the eluent employed is changed from $[Sb_2(d\text{-tart})_2]^{2-}$ to $[As_2(d\text{-tart})_2]^{2-}$ (Table 3). This means that the elution order of $[Co(tn)_3]^{3+}$ is determined by a delicate balance of the two comparable association modes prevailing in NPIEC. However, in the stationary phase of RPIPC where the effective dielectric constant is probably very low, the second-step association forming an ion triplet $[Co(N)_6][Sb_2(d\text{-tart})_2]_2^-$, the electric charge of which is finally neutralized by the counterion M^+,[19)] will take place, because the tervalent charge of the complex cation is not completely neutralized in the ion pair $[Co(N)_6][Sb_2(d\text{-tart})_2]^+$ formed in the first-step association. In the ion triplet where the electrostatic repulsion is inevitable between the two anions, the C_3 association mode should be much more favored than in the ion pair, since the electrostatic repulsion is the least when the two anions approach the complex cation along the C_3 axis from the opposite side. Consequently, the relative fraction of the C_3 mode will be increased and thus the discrimination efficiency will be greatly improved, when RPIPC is applied to the tervalent complex cations for which both of the C_3 and C_2 modes are possible. In fact, the α value of the divalent complex $[Co(gly)(en)_2]^{2+}$ for which the two modes are similarly possible, is not appreciably improved in RPIPC (Table 4). This is because the electric charge of $[Co(gly)(en)_2]^{2+}$ has been completely neutralized in the first-step association and thus the ion triplet is not formed even in RPIPC.

It should be noted here that the α value of $[Co(sen)]^{3+}$ is greatly improved in RPIPC, though both of the two ion-pairing anions cannot adopt the C_3 mode in the ion triplet $[Co(sen)][Sb_2(d\text{-tart})_2]_2^-$ owing to the steric demand of $[Co(sen)]^{3+}$ (Fig. 1). It is certain that the C_3 mode favors the Λ-enantiomer, while the C_2 mode favors the Δ-enantiomer for $[Co(sen)]^{3+}$ like for $[Co(en)_3]^{3+}$, as far as the first-step association is concerned.[17)] In the ion triplet of $[Co(sen)]^{3+}$, however, both the C_3 and the C_2 modes favor the Λ-enantiomer, since the chiral ion-pairing anion adopting the C_2 mode is disposed so as to escape the electrostatic repulsion from the other ion-pairing anion adopting the C_3 mode, imposing a severe steric repulsion stereoselectively on the alkyl cap of the Δ-enantiomer.[17b)] As a result, an improved α value is also expected for $[Co(sen)]^{3+}$ in RPIPC, though one chiral anion adopts the C_3 mode and the other anion adopts the C_2 mode in the ion triplet $[Co(sen)][Sb_2(d\text{-tart})_2]_2^-$.

For those complexes which adopt either the C_3 or the C_2 mode only, on the other hand, no appreciable improvement in α is expected,[27)] since the relative fraction of the C_3 or the C_2 mode adopted by them is always unity even if the ion triplet is formed in RPIPC. The above interpretations are highly speculative, but they seem quite attractive.

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20) Greater retention volumes obtained for $[Co(sep)]^{3+}$ than for $[Co(en)_3]^{3+}$ are attributed not only to the greater hydrophobic nature of the former complex, but also to its greater hydrogen-bonding ability to the ion-pairing reagent. See, Refs. 16 and 23.

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28) Why the C_2 association mode favors the Λ-enantiomer but not the Δ-enantiomer for the cage complexes, has been discussed in detail in Ref. 17b.