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Inversion of the Retention Volume Order of Enantiomers Caused by the Concentration of Eluent[1)]

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The retention volumes of enantiomers of several complex anions on the IEX 220 anion-exchange resin, when eluted by an aqueous solution of Δ-$[Co(en)_3]^{3+}$, Δ-$[Co(sep)]^{3+}$, or Δ-$[Co(l\text{-}chxn)_3]^{3+}$, have been measured as a function of the eluent concentration, where en=ethylenediamine, sep=1,3,6,8,10,13,16,19-octaazabicyclo-[6.6.6]eicosane, and *l*-chxn=(−)-*trans*-1,2-cyclohexanediamine. The order of retention volumes of enantiomers of some complex anions has been found to be inverted by the concentration of the eluents. The mechanism of the inversion has been discussed.

Optical resolution of metal complex ions has been effected frequently by ion-exchange chromatography.[2)] Usually, the complex ion is adsorbed on an achiral ion-exchange resin and eluted by an aqueous solution of some optically active substance (resolving agent). In this type of experiment, it would appear rather reasonable to assume that the faster-eluted enantiomer should be the one which forms the favorable diastereomeric pair with the resolving agent in the eluent. Though such is often the case indeed, such an assumption does not necessarily hold true because of the two fundamental processes involved in the chromatographic separation; adsorption of complex ions to the resin in the stationary phase and ion-pairing of complex ions with the resolving agent in the mobile phase. Thus, critical examination is needed to establish which of these two processes governs the chromatographic optical resolution.

In this work, we have measured the retention volumes of enantiomers of several complex anions when eluted by an aqueous solution of Δ-$[Co(en)_3]^{3+}$, Δ-$[Co(sep)]^{3+}$, or Δ-$[Co(l\text{-}chxn)_3]^{3+}$, as a function of the eluent concentration, where en=ethylenediamine, sep=1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]eicosane, and *l*-chxn=(−)-*trans*-1,2-cyclohexanediamine. It has been found that the order of retention volumes of enantiomers of some complex anions is inverted by the concentration of the eluents. The implications of this result have been discussed from the viewpoints of the above two processes and the mode of chiral discrimination between complex ions.

Experimental

All the metal complexes used in this work were available from previous works.[3,4)]

The resin used was the IEX 220 (Toyo Soda Manufacturing Co., Ltd.), which is based on a styrene-divinylbenzene copolymer and carries the tetraalkylammonium group as the functional group. A column (50×4 mm) of the IEX 220 anion-exchange resin was equilibrated with an eluent, which was an aqueous solution of an optically active cationic complex. An aqueous solution containing one enantiomer of an anionic complex and bis(glycinato)copper(II), which was used as a marker for void volume measurement, was injected by a syringe on top of the column and eluted at an elution rate of 0.3 cm^3/min. The concentration of the cationic complex in eluents was varied from 4×10^{-3} to 60×10^{-3} mol dm^{-3}. The adjusted retention volumes were obtained from the elution curves as in the previous studies.[3,4)] The retention volumes were found to be reproducible to within 0.05%.

Results

In this work, one enantiomer of an anionic complex was adsorbed on an anion-exchange resin and eluted by an aqueous solution containing a Δ complex cation. The adjusted retention volumes obtained in this way are summarized in Table 1. The most noteworthy feature in Table 1 is the inversion of the order of retention volumes of some enantiomers caused by the concentration of the eluents. For example, in the combination of Δ-$[Co(sep)]Cl_3\cdots[Co(mal)_2(en)]^-$ (mal=malonate dianion), the faster-eluted enantiomer at lower eluent concentrations is Λ, whereas it is Δ at an eluent concentration higher than 15×10^{-3} mol dm^{-3}. Likewise, Δ-$[Co(edta)]^-$ (edta=ethylenediaminetetraacetate) is eluted faster by the 4×10^{-3} mol dm^{-3} solution of Δ-$[Co(sep)]Cl_3$, while Λ-$[Co(edta)]^-$ is eluted faster by the eluent of higher concentrations or by an eluent containing Δ-$[Co(sep)]Br_3$. A similar inversion takes place for other combinations. Further, the bromide salts are more effective in inverting the retention volume orders than the chloride salts, in that lower concentrations of bromides yielded similar results obtained for higher concentrations of chlorides.

Discussion

Recently, we have studied the mode of chiral discrimination between optically active complex ions in solution.[3)] It was proposed there that (i) chiral discrimination is effected along the C_2 axis of Δ-$[Co(en)_3]^{3+}$ and Δ-$[Co(sep)]^{3+}$, while it is effected along the C_3 axis of Δ-$[Co(l\text{-}chxn)_3]^{3+}$, (ii) the chirality of $[Co(edta)]^-$ or $[Co(tdta)]^-$ (tdta=1,4-butanediamine-*N,N,N′,N′*-tetraacetate) is recognized by a complex cation along their pseudo C_3 axes, whereas the chirality of $[Co(mal)_2(en)]^-$ or $[Co(ox)_2(en)]^-$ (ox=oxalate) is recognized along their C_2 axes, and (iii) favorable ion pairs are formed in the combinations for which the handedness of chelate rings of both ions, when oriented along the above axes, is the same.[3)] The handedness of a Δ complex ion can be specified as either $P(C_3)$ (right-handed propeller) when viewed along the C_3 axis, or $M(C_2)$ (left-handed propeller) when viewed along the C_2 axis.[5)] For example, the

TABLE 1. THE ADJUSTED RETENTION VOLUMES (cm^3) OBTAINED ON A COLUMN (50×4 mm) OF THE IEX 220 RESIN (ANION-EXCHANGER)
The elution rate was 0.3 cm^3/min.

Eluent	Concn[a]	Sample							
		K[Co(edta)]		K[Co(tdta)]		Na[Co(ox)$_2$(en)]		Na[Co(mal)$_2$(en)]	
		Δ	Λ	Δ	Λ	Δ	Λ	Δ	Λ
Δ-[Co(en)$_3$]Cl$_3$	4	19.33	18.60	16.70	16.31	11.78	11.89	2.952	2.871
	15	4.436	4.380	3.879	3.625	3.213	3.270	0.903	0.922
Δ-[Co(sep)]Cl$_3$	4	17.29	17.81	16.58	19.66	11.02	10.82	3.230	3.131
	8	9.234	8.952	8.043	8.367	6.450	6.447	1.945	1.802
	15	4.565	4.391	4.353	3.936	3.461	3.335	0.979	0.999
Δ-[Co(sep)]Br$_3$	4	9.834	9.675	9.768	9.711	6.898	6.612	2.121	2.143
	8	5.400	5.280	5.940	5.580	3.115	3.120	1.590	1.680
Δ-[Co(l-chxn)$_3$]Cl$_3$	4	13.89	14.66	8.769	10.24	10.97	11.22	3.038	3.014
	15	3.321	3.941	1.724	2.117	3.088	3.461	1.020	0.980
	30					1.920	2.130		
	60					1.200	1.200		
Δ-[Co(l-chxn)$_3$]Br$_3$	4	9.480	10.470	6.750	7.830	6.750	6.330	3.030	2.880

a) The eluent concentration is in 10^{-3} mol dm^{-3}.

favorable pair is M(C$_2$)–M(pseudo C$_3$) for Δ-[Co(sep)]$^{3+}$···Λ-[Co(edta)]$^-$, where the former chirality notation refers to the cation and the latter one to the anion. Likewise, the favorable pairs are P(C$_3$)–P(pseudo C$_3$) for Δ-[Co(l-chxn)$_3$]$^{3+}$···Δ-[Co(edta)]$^-$, M(C$_2$)–M(C$_2$) for Δ-[Co(sep)]$^{3+}$···Δ-[Co(ox)$_2$(en)]$^-$, and P(C$_3$)–P(C$_2$) for Δ-[Co(l-chxn)$_3$]$^{3+}$···Λ-[Co(ox)$_2$(en)]$^-$. The ions [Co(en)$_3$]$^{3+}$, [Co(tdta)]$^-$, and [Co(mal)$_2$(en)]$^-$ can be considered in the same way as for [Co(sep)]$^{3+}$, [Co(edta)]$^-$, and [Co(ox)$_2$(en)]$^-$, respectively.

The inversion of the retention volume order of enantiomers obtained in this work may be explained by combining the above ideas with the two fundamental processes in ion-exchange chromatographic experiments. The origin of the inversion of the combination Δ-[Co(sep)]$^{3+}$···[Co(mal)$_2$(en)]$^-$ will be considered as an example. In this work, one enantiomer of an anionic complex was adsorbed on the anion-exchange resin and eluted by an aqueous solution containing a Δ complex cation. The [Co(mal)$_2$(en)]$^-$ ion will be adsorbed to the resin functional group along its C$_2$ axis *via* two oxygen atoms of coordinated malonates. At higher eluent concentrations, the elution is governed by ion-pairing in the mobile phase rather than in the stationary phase. This is because the chloride or bromide ions in the eluent replace the [Co(mal)$_2$(en)]$^-$ ions adsorbed on the resin and the concentration of [Co(mal)$_2$(en)]$^-$ in the mobile phase is thus enhanced. As a result, the enantiomer that associates more favorably with Δ-[Co(sep)]$^{3+}$ in the mobile phase is eluted faster and shows a smaller retention volume than its enantiomorph. The favorable combination is therefore Δ–Δ or M(C$_2$)–M(C$_2$), as stated previously, and this situation is illustrated in Fig. 1(a).

At lower eluent concentrations, the elution is governed by adsorption of a complex anion to the resin functional group, which means that chiral discrimination is effected through ion-pairing of the Δ cation with the [Co(mal)$_2$(en)]$^-$ ion adsorbed to the resin, *i.e.*, chiral discrimination is effected in the stationary phase. Recall that the [Co(mal)$_2$(en)]$^-$ anion is bound to the resin along its C$_2$ axis, leaving only the pseudo C$_3$ axis for the ion-pairing direction for the Δ cation. Thus, the Δ-[Co(sep)]$^{3+}$ cation will be forced to associate with [Co(mal)$_2$(en)]$^-$ along the anion's pseudo C$_3$ axis. This situation is illustrated in Fig. 1(b). It should be noted here that the handedness of chelate rings of the complex anion is inverted depending upon the direction of watching the anion;[5] Δ-[Co(mal)$_2$(en)]$^-$ is left-handed or M(pseudo C$_3$) when watched along the pseudo C$_3$ axis, while it is right-handed or P(C$_2$) when watched along the C$_2$ axis. Since Δ-[Co(sep)]$^{3+}$ has the M(C$_2$) chirality and is discriminated along its C$_2$ axis, and since the enan-

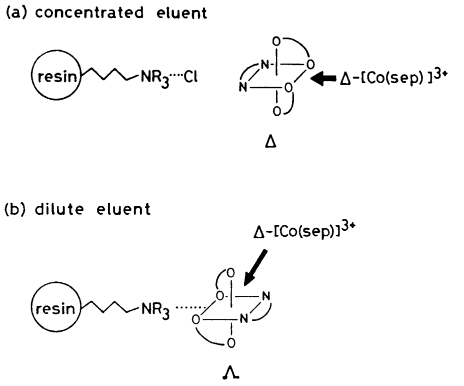

Fig. 1. An illustration of the ion-pairing equilibrium in stationary and mobile phases. The enantiomer depicted for [Co(mal)$_2$(en)]$^-$ is the one which forms the favorable pair with Δ-[Co(sep)]$^{3+}$. The cation discriminates the chirality of the anion along (a) the anion's C$_2$ axis and (b) the anion's pseudo C$_3$ axis.

tiomer of the anion that associates more favorably with the M(C_2) cation should have the same M chirality, the preferred enantiomer is either M(C_2) or M(pseudo C_3). As depicted in Fig. 1(b), the $[Co(mal)_2(en)]^-$ anion is now assumed to be discriminated along its pseudo C_3 axis. Thus, the M(pseudo C_3) enantiomer (the Δ enantiomer) is preferred and the favorable pair at lower eluent concentration is Δ-$[Co(sep)]^{3+}\cdots$Δ-$[Co(mal)_2(en)]^-$. Namely, at higher eluent concentrations, the anion is discriminated along its C_2 axis in the mobile phase, whereas at lower eluent concentrations, the anion has to be discriminated along its pseudo C_3 axis in the stationary phase. This may be responsible for the observed inversion. The results for the other combinations may be explained similarly.

The above reasoning seems to gain some support from the results obtained by using the bromide salts instead of the chloride salts. The bromide anion is known to be adsorbed to anion-exchange resins more strongly or selectively than the chloride ion.[6] Thus, compared with the chloride ion, the bromide ion will enhance the effective concentration of a complex anion in the mobile phase, which will in turn enhance the ion-pairing with a Δ cation in the mobile phase. This will make the situation similar to that depicted in Fig. 1(a). Namely, the bromide ion is more effective in driving the dynamic equilibrium to the side of elution-governing. This may be the reason for the bromides being more effective in inverting the retention volume orders.

In Table 1, it is also noted that $[Co(mal)_2(en)]^-$ shows much smaller retention volumes than the other anions for all the eluents. This suggests either that this complex anion associates very strongly with the Δ cations in the mobile phase, or that $[Co(mal)_2(en)]^-$ is adsorbed very weakly to the resin. But the former possibility seems to be unlikely, because even at lower Δ-$[Co(sep)]Cl_3$ concentrations, where the elution is adsorption-governed as explained above, this anion exhibits much smaller retention volumes than the other complex anions. Thus, $[Co(mal)_2(en)]^-$ may be adsorbed to the resin more weakly than $[Co(edta)]^-$, $[Co(tdta)]^-$, and $[Co(ox)_2(en)]^-$ owing possibly to greater hydration of $[Co(mal)_2(en)]^-$. An indication that $[Co(mal)_2(en)]^-$ is hydrated to a greater extent than $[Co(edta)]^-$ has been obtained recently by conductance measurements.[7]

Conclusion

The inversion of the retention volume orders of enantiomers reflects that ion-pairing is highly directional both in mobile and stationary phases and a cation recognizes an inverted chirality of an anion when the cation approaches the anion along different directions.

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