calculation indicated virtually no barrier.[13] Thus, in the present piperidine case the structure, static solid-state [113]Cd NMR, and potential energy calculations are in complete agreement.

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Kinetic Optical Resolution of Metal Complexes through a Stereoselective Adsorption and Inhibition Mechanism Caused by Chiral Additives

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Four kinds of conglomerates, $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$, $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl·4H$_2$O, $\Delta\Lambda$-[Co(ox)(en)$_2$]Br·H$_2$O, and $\Delta\Lambda$-[Co-(NO$_2$)$_2$(en)$_2$]Cl (aet = 2-aminoethanethiolate(1–), ox = oxalate(2–), and en = ethylenediamine), were kinetically resolved by crystallization in the presence of chiral additives Δ'- (or Λ'-) [Co(AB)(en)$_2$]X$_n$ (AB = two unidentate ligands or one bidentate ligand). The resolution mechanism is best explained in terms of stereoselective adsorption of the chiral additive at the crystal surfaces of one enantiomer of the same absolute configuration as the chiral additive and a drastic decrease of the growth rate of these crystals, as proposed by Addadi et al. Three characteristic aspects of this mechanism, i.e. preferential crystallization of the opposite enantiomer, stereoselective adsorption of the chiral additive, and a morphological change in the crystals of one enantiomer having the same absolute configuration as the chiral additive, were all observed in the present systems. Detailed study of the system $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl (substrate)–Λ'-[Co(gly)(en)$_2$]Cl$_2$ (chiral additive; gly = glycinate(1–)) revealed that this kind of resolution takes place repeatedly, with alternative crystallization of Δ- and Λ-[Co(ox)(en)$_2$]Cl·4H$_2$O. The relationship between the enantiomeric excess and the crystal yield of the partially resolved substrate and the role of the chiral additive are discussed on the basis of the measurement of the solubilities in the supernatant solution. The above kinetic resolution was also found to be applicable to some substrates of racemic compound.

Introduction

Many resolution methods for metal complexes are known, such as diastereomer formation and column chromatography. Most of these methods are based on the electrostatic attraction between the complex ion and the oppositely charged ion of the resolving agent. However, as a special method of optical resolution, it has been reported that a certain chiral additive, which has the same kind of charge as the substrate,[1] can behave as an efficient resolving agent. For example, Werner reported the resolution of $\Delta\Lambda$-[Co(NO$_2$)$_2$(en)$_2$]Cl using Λ-[Co(ox)(en)$_2$]Cl as a chiral additive.[2] Broomhead resolved $\Delta\Lambda$-[Co(ox)(en)$_2$]CH$_3$CO$_2$ with a mixture of Λ-[Co(en)$_3$](CH$_3$CO$_2$)$_3$ + KBr to give a 40% yield of Δ-[Co(ox)(en)$_2$]Br.[3] It has been suggested that hydrogen bonding[3] and configurational activity[4] are responsible for these phenomena, but no mechanistic investigation has been performed thus far.

We were interested in the recent investigations by Addadi et al., who reported the optical resolution of organic conglomerates with the assistance of "tailor-made impurities".[5] The mechanism is based on stereoselective adsorption of a chiral additive and inhibition of crystal growth, as shown in Figure 1. In the absence of a Λ'-chiral additive that is stereochemically similar to one enantiomer (Λ) of the conglomerate substrate, the two crystallization rates k_Δ and k_Λ are equal.[6] In the presence of a Λ'-chiral additive, however, it is adsorbed on the Λ-crystals and inhibits their crystal growth, leading to $k_\Delta > k_\Lambda$. Therefore, the enantiomer crystallized in excess first has the absolute configuration opposite to that of the chiral additive ("rule of reversal"), and the affected enantiomer, Λ, should be found in the second crop of crystals. This mechanism can account for the experimental results of Werner and Broomhead.[7]

We report here a systematic investigation of a kinetic resolution of metal complexes due to chiral additives. Both the substrates and the chiral additives used in this paper belong to the same complex type of [Co(AB)(en)$_2$]X$_n$ (AB = two unidentate ligands or one bidentate ligand). Several combinations of the substrates and the chiral additives were found to show high resolution percentages. A detailed study in the system $\Delta\Lambda$-[Co(ox)(en)$_2$]-Cl–Λ'-[Co(gly)(en)$_2$]Cl$_2$ (CA)[8] revealed that the resolution process occurs time after time and apparent supersaturation of the Λ-substrate increases with concentration of the chiral additive. It was found that this resolution is applicable not only to conglomerates but also to some racemic compounds.

Experimental Section

Preparation of Metal Complexes. The following cobalt(III) complexes used in this study were prepared and/or resolved according to methods described in the literature and were converted into the desired salts by using QAE-Sephadex A-25: $\Delta\Lambda$-, Δ-, and Λ-[Co(aet)(en)$_2$](ClO$_4$)$_2$;[9]

(1) The terminology of chiral substances is based on that given in: Jacques, J.; Collet, A.; Wilen, S. H. "Enantiomers, Racemates and Resolutions"; Wiley: New York, 1981. *Substrate* denotes the racemic complex to be optically resolved. *Racemate* is an equimolar mixture of two enantiomers whose physical state is unspecified or unknown. *Conglomerate* (or *Racemic mixture*) is a mechanical mixture of crystals of the two pure enantiomers and is formed as a result of a spontaneous resolution. *Racemic compound* is a homogeneous solid in which two enantiomers are present in equal quantities in a well-defined arrangement within the crystal lattice.
(2) Werner, A. *Chem. Ber.* **1914,** *47,* 2171.
(3) Broomhead, J. A. *Nature (London),* **1966,** *211,* 742.
(4) Dwyer, F. P.; Gyarfas, E. C.; Dwyer, M. F. O. *Nature (London),* **1951,** *167,* 1036.
(5) Addadi, L.; van Mil, J.; Lahav, M. *J. Am. Chem. Soc.* **1981,** *103,* 1249. Addadi, L.; Weinstein, S.; Gati, E.; Weissbuch, I.; Lahav, M. *J. Am. Chem. Soc.* **1982,** *104,* 4610.

(6) Greek letters Δ (or Λ) and Δ' (or Λ') represent the absolute configurations of substrates and chiral additives, respectively.
(7) Werner reported that Λ-[Co(NO$_2$)$_2$(en)$_2$]Cl is deposited by the addition of Λ'-[Co(ox)(en)$_2$]Cl,[1] but the opposite Δ-configuration was confirmed to appear as the first crystals by our reinvestigation.
(8) CA denotes a chiral additive.
(9) (a) Nosco, D. L.; Deutsch, E. *Inorg. Synth.* **1982,** *21,* 19. (b) Yamanari, K.; Hidaka, J.; Shimura, Y. *Bull Chem. Soc. Jpn.* **1977,** *50,* 2299. (c) Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1983,** *56,* 2283.

Table I. Resolution of $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$ in the Presence of Chiral Additives[a,c]

		amt	ee, config (yield)	
expt	CA	of CA[b]	1st crop	2nd crop
1	Δ'-[Co(maa)(en)$_2$]ClO$_4$	1.6	15%, Λ (29%)	72%, Δ (10%)
2	Δ'-[Co(maa)(en)$_2$]ClO$_4$	1.9	39%, Λ (23%)	33%, Δ (31%)
3	Δ'-[Co(maa)(en)$_2$]ClO$_4$	2.1	37%, Λ (16%)	
4	Δ'-[Co(maa)(en)$_2$]ClO$_4$	3.9	16%, Λ (39%)	17%, Δ (30%)
5	Δ'-[Co(maa)(en)$_2$]ClO$_4$	4.7	15%, Λ (26%)	7%, Δ (31%)
6	Δ'-[Co(maa)(en)$_2$]ClO$_4$	7.8	79%, Λ (17%)	92%, Δ (10%)
7	Δ'-[Co(maa)(en)$_2$]ClO$_4$	9.5	42%, Λ (21%)	18%, Δ (14%)
8	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	1.6	3%, Δ (41%)	2%, Λ (30%)
9	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	1.9	13%, Δ (17%)	
10	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	1.9	62%, Δ (10%)	
11	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	2.1	11%, Δ (22%)	
12	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	2.1	18%, Δ (16%)	
13	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	3.9	7%, Δ (37%)	11%, Λ (16%)
14	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	4.7	21%, Δ (29%)	20%, Λ (21%)
15	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	9.5	8%, Δ (34%)	100%, Λ (2%)
16	Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$	1.9	25%, Λ (14%)	
17	Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$	2.1	24%, Λ (16%)	
18	Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$	2.1	9%, Λ (24%)	

[a] Crystallization was performed by allowing the solution to stand at room temperature for 1–3 days. [b] In mg of CA/100 mg of $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$. [c] Key: ee, enantiomeric excess; CA, chiral additive.

Table II. Efficient Systems on Kinetic Resolution of Conglomerates[a,c]

|		amt	ee, config (yield)	
S	CA	of CA[b]	1st crop	2nd crop
[Co(aet)(en)$_2$](ClO$_4$)$_2$	Δ'-[Co(maa)(en)$_2$]ClO$_4$	1.9	39%, Λ (23%)	33%, Δ (31%)
	Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$	1.9	62%, Δ (10%)	
	Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$	1.9	25%, Λ (14%)	
[Co(ox)(en)$_2$]Cl·4H$_2$O	Λ'-[Co(gly)(en)$_2$]Cl$_2$·H$_2$O	4.0	73%, Δ (13%)	51%, Λ (21%)
[Co(NO$_2$)$_2$(en)$_2$]Cl	Λ'-[Co(ox)(en)$_2$]Cl·H$_2$O	2.2	3%, Δ (17%)	
	Λ'-[Co(en)$_3$]Cl$_3$·H$_2$O	5.5	1%, Δ (12%)	
[Co(ox)(en)$_2$]Br·H$_2$O	Δ'-[Co(CO$_3$)(en)$_2$]Br	4.0	13%, Λ (16%)	10%, Δ (42%)

[a] Each resolution was repeated more than five times by allowing the solution to stand at room temperature for 1–3 days. The enantiomeric excess is the highest under the given conditions. [b] In mg of CA/100 mg of S. [c] Key: S, substrate; CA, chiral additive; ee, enantiomeric excess.
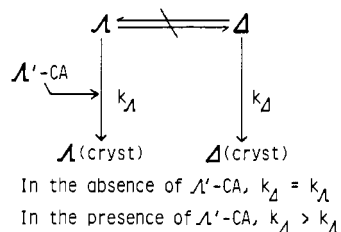
Figure 1. Optical resolution scheme due to the selective adsorption and inhibition mechanism, where Δ (or Λ) and Λ' denote the absolute configurations of one enantiomer of a conglomerate and a chiral additive, respectively, and k_Δ and k_Λ the rates of crystallization of enantiomers of the conglomerate.

$\Delta\Lambda$-, Δ-, and Λ-[Co(ox)(en)$_2$]X (X = ClO$_4$, Cl, Br);[10] $\Delta\Lambda$-, Δ-, and Λ-[Co(maa)(en)$_2$]X (X = ClO$_4$, Cl);[11] Δ-[Co(pyt)$_2$(R-pn)]ClO$_4$;[12] Δ-[Co(dtc)$_2$(R-pn)]ClO$_4$;[13] $\Delta\Lambda$-, Δ-, and Λ-[Co(NO$_2$)$_2$(en)$_2$]X (X = Cl, I);[14] $\Delta\Lambda$-, Δ-, and Λ-[Co(CO$_3$)(en)$_2$]X (X = Cl, Br);[15] $\Delta\Lambda$-, Δ-, and Λ-[Co(gly)(en)$_2$]X$_2$ (X = ClO$_4$, Cl, I);[16] $\Delta\Lambda$-[Co(L-ala)(en)$_2$]Cl$_2$;[17] Λ-[Co(pyt)(en)$_2$](ClO$_4$)$_2$;[12] Δ-[Co(dtc)(en)$_2$](ClO$_4$)$_2$;[13] $\Delta\Lambda$-, Δ-, and Λ-[Co(en)$_3$]X$_3$ (X = ClO$_4$, Cl, I),[18] where aet, en, ox, maa, pyt, R-pn, dtc,

(10) Dwyer, F. P.; Reid, I. K.; Garvan, F. L. *J. Am. Chem. Soc.* **1961**, *83*, 1285. Yamanari, K.; Igaki, M.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3007.
(11) Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1596.
(12) Kita, M.; Yamanari, K.; Shimura, Y. *Chem. Lett.* **1984**, 297.
(13) Kita, M.; Yamanari, K.; Shimura, Y., paper presented at the 33rd Symposium on the Coordination Chemistry of Japan, Osaka, Japan, 1983; see Abstract No. 2A13.
(14) Springborg, J.; Schaffer, C. E. *Inorg. Synth.* **1973**, *14*, 72. Dwyer, F. P.; Garvan, F. L. *Inorg. Synth.* **1960**, *6*, 195.
(15) Springborg, J.; Schaffer, C. E. *Inorg. Synth.* **1973**, *14*, 64. Dwyer, F. P.; Sargeson, A. M.; Reid, I. K. *J. Am. Chem. Soc.* **1963**, *85*, 1215.
(16) Meisenheimer, J.; Angermann, L.; Holsten, H. *Justus Liebigs Ann. Chem.* **1924**, *438*, 217. Kaki, S.; Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 769.
(17) Liu, C. T.; Douglas, B. E. *Inorg. Chem.* **1964**, *3*, 1356.
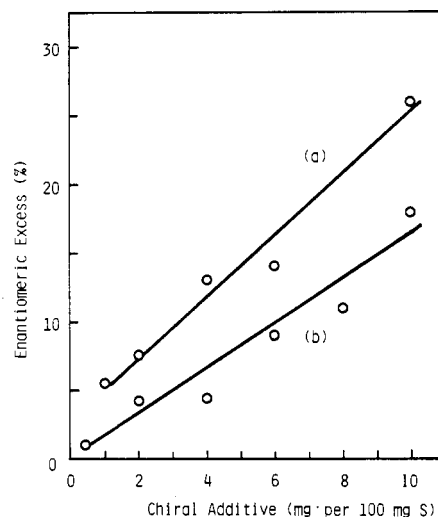
Figure 2. Concentration effect of chiral additive on enantiomeric excess of substrate: (a) $\Delta\Lambda$-[Co(ox)(en)$_2$]Br–Δ'-[Co(CO$_3$)(en)$_2$]Br (CA); (b) $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl–Λ'-[Co(gly)(en)$_2$]Cl$_2$ (CA).

gly, and L-ala stand for 2-aminoethanethiolate(1–), ethylenediamine, oxalate(2–), mercaptoacetate(2–), 2-pyridinethiolate(1–), (R)-propylenediamine, N,N-dimethyldithiocarbamate(1–), glycinate(1–), and L-alaninate(1–) ligands.

Resolution of Metal Complexes with the Assistance of Chiral Additives. The general procedure is as follows. A racemic substrate and a small amount of a chiral additive are dissolved in an appropriate amount of water. In each experiment, the same counterion is used for the substrate

(18) Werner, A. *Chem. Ber.* **1912**, *45*, 121. Broomhead, J. A.; Dwyer, F. P.; Hogarth, J. W. *Inorg. Synth.* **1960**, *6*, 186. Fuyuhiro, A.; Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3577.

Table III. Selective Adsorption of Chiral Additives[e]

S	CA	amt of CA[a]	adsorption quant	Λ/Δ
Λ-[Co(ox)(en)₂]Cl·4H₂O	Δ'Λ'-[Co(maa)(en)₂]Cl·H₂O	13	no	
	Δ'Λ'-[Co(maa)(en)₂]Cl·H₂O	71	no	
	Δ'Λ'-[Co(NO₂)₂(en)₂]Cl	71	no	
	Δ'Λ'-[Co(CO₃)(en)₂]Cl	13	no	
	Δ'Λ'-[Co(CO₃)(en)₂]Cl	71	no	
	Δ'Λ'-[Co(gly)(en)₂]Cl₂·H₂O	50	0.35%	6.1
	Δ'Λ'-[Co(gly)(en)₂]Cl₂·H₂O	71	0.80%	6.1
	Δ'Λ'-[Co(L-ala)(en)₂]Cl₂	23	no	
	Δ'Λ'-[Co(L-ala)(en)₂]Cl₂	70	no	
	Δ'Λ'-[Co(en)₃]Cl₃·3H₂O	13	no	
	Δ'Λ'-[Co(en)₃]Cl₃·3H₂O	98	no	
Λ-[Co(aet)(en)₂](ClO₄)₂	Δ'Λ'-[Co(maa)(en)₂]ClO₄	3.9	0.36%	1.9
	Δ'Λ'-[Co(gly)(en)₂](ClO₄)₂·2H₂O	70	no	
	Δ'Λ'-[Co(pyt)(en)₂](ClO₄)₂	5.0	0.014%	2.0
	Δ'Λ'-[Co(en)₃](ClO₄)₃	70	no	
Λ-[Co(NO₂)₂(en)₂]Cl	Δ'Λ'-[Co(gly)(en)₂]Cl₂·H₂O	68	no	
	Δ'Λ'-[Co(en)₃]Cl₃·3H₂O	97	no	
Λ-[Co(ox)(en)₂]Br·H₂O	Δ'Λ'-[Co(CO₃)(en)₂]Br	11	0.25%	1.7
ΔΛ-[Co(gly)(en)₂]Cl₂·H₂O[b]	Δ'-[Co(ox)(en)₂]Cl·H₂O	1.1	0.20%, 0.69%[c]	
Λ-[Co(maa)(en)₂]ClO₄	Δ'Λ'-[Co(aet)(en)₂](ClO₄)₂	60	0.94%[d]	

[a] In mg of CA/100 mg of S. [b] Note that this pair is only exceptional concerning the explanation in the Experimental Section. [c] These correspond to the values for the first and the second crop, respectively. [d] The Λ-substrate completely racemized before crystallization. [e] Key: S, substrate; CA, chiral additive.

Table IV. Optical Resolution of Racemic Compounds[b]

| S	CA	amt of CA[a]	ee, confign (yield)
[Co(NO₂)₂(en)₂]I	Δ'-[Co(gly)(en)₂]I₂	4.0	0.4%, Λ (12%)
	Λ'-[Co(en)₃]I₃·H₂O	4.0	0.2%, Δ (13%)
[Co(CO₃)(en)₂]Cl	Δ'-[Co(ox)(en)₂]Cl·H₂O	1.4	0
	Λ'-[Co(maa)(en)₂]Cl·0.5H₂O	2.8	0
	Λ'-[Co(NO₂)₂(en)₂]Cl	2.8	0
	Λ'-[Co(gly)(en)₂]Cl₂·H₂O	2.8	0
	Λ'-[Co(en)₃]Cl₃·H₂O	2.8	0
[Co(maa)(en)₂]ClO₄	Λ'-[Co(aet)(en)₂](ClO₄)₂	43	2.8%, Δ (13%)
[Co(gly)(en)₂]Cl₂·H₂O	Δ'-[Co(ox)(en)₂]Cl·H₂O	1.0	0.2%, Λ (15%)

[a] mg of CA/100 mg of S. [b] Key: S, substrate; CA, chiral additive; ee, enantiomeric excess.
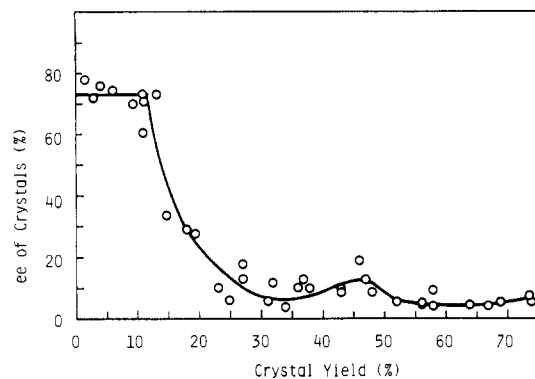
Figure 3. Plots of enantiomeric excess against crystal yield in the system ΔΛ-[Co(ox)(en)₂]Cl–Δ'-[Co(gly)(en)₂]Cl₂ (CA; 4% concentration).

and the chiral additive. The amount of the additive is chosen on the basis of its solubility in water. The mixed solution is kept standing at room temperature. After partial crystallization of the substrate, the solution is decanted and the crystals are dried on filter paper. These crystals are dissolved in water again, and the crystal yield and enantiomeric excess are determined by the absorption and circular dichroism (CD) spectra of the solution. A second crop can be collected from the mother liquor. Each resolution experiment was repeated at least five times under identical conditions. In the case of conglomerates, the following systems were examined: eight chiral additives, Δ'-[Co(ox)(en)₂]ClO₄, Δ'-[Co-(maa)(en)₂]ClO₄, Δ'-[Co(pyt)₂(R-pn)]ClO₄, Δ'-[Co(dtc)₂(R-pn)]ClO₄, Δ'-[Co(gly)(en)₂](ClO₄)₂·2H₂O, Λ'-[Co(pyt)(en)₂](ClO₄)₂, Δ'-[Co-(dtc)(en)₂](ClO₄)₂, and Δ'-[Co(en)₃](ClO₄)₃ for ΔΛ-[Co(aet)(en)₂]-(ClO₄)₂; five chiral additives, Δ'-[Co(CO₃)(en)₂]Cl, Δ'-[Co(maa)-(en)₂]Cl·0.5H₂O, Λ'-[Co(NO₂)₂(en)₂]Cl, Λ'-[Co(gly)(en)₂]Cl₂·H₂O, and Λ'-[Co(en)₃]Cl₃·H₂O for ΔΛ-[Co(ox)(en)₂]Cl·4H₂O; four chiral addi-
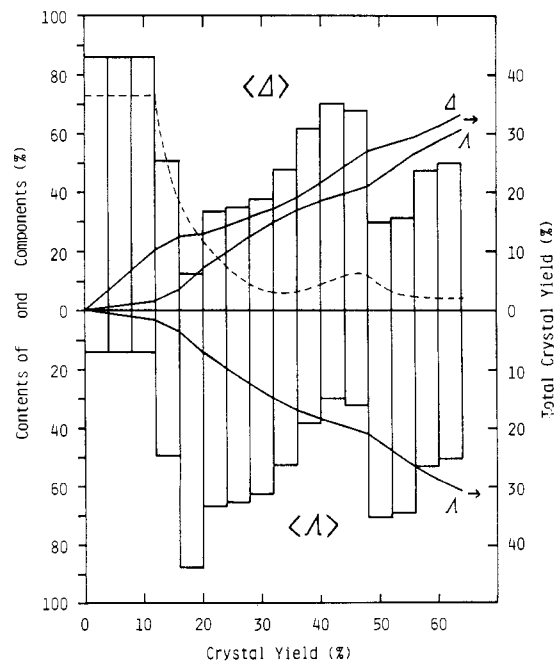
Figure 4. Fractionated representation of the resolution curve (dotted curve) in the system ΔΛ-[Co(ox)(en)₂]Cl–Δ'-[Co(gly)(en)₂]Cl₂: bar graph, contents of the Δ- and Λ-enantiomers (%) at every 4% yield of the substrate; folded curve, total crystal yield (%) of the Δ- or Λ-enantiomer.

tives, Δ'-[Co(maa)(en)₂]Cl·0.5H₂O, Δ'-[Co(ox)(en)₂]Cl·H₂O, Δ'-[Co-(gly)(en)₂]Cl₂·H₂O, and Δ'-[Co(en)₃]Cl₃·H₂O for ΔΛ-[Co(NO₂)₂-
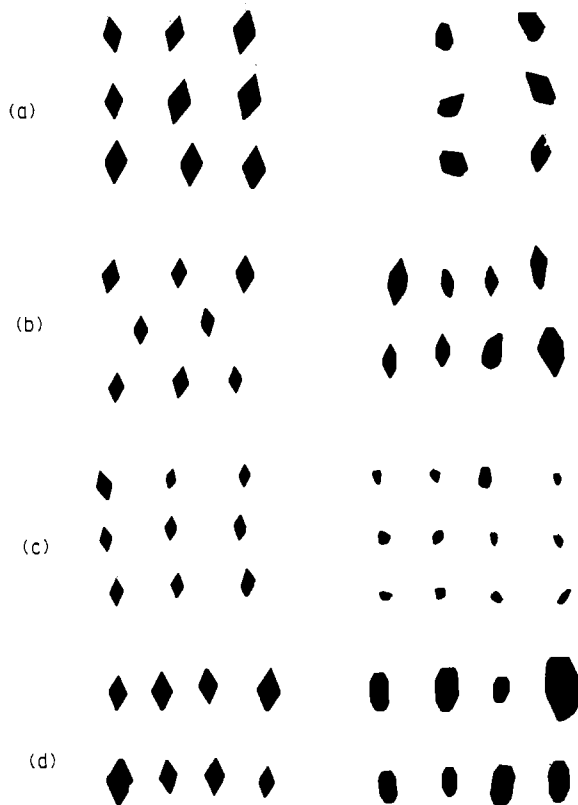
Figure 5. Crystal morphologies of Δ- (left) and Λ- (right) enantiomers of [Co(ox)(en)₂]Cl·4H₂O in the presence of Λ'-chiral additives: (a) Λ'-[Co(maa)(en)₂]Cl·0.5H₂O; (b) Λ'-[Co(NO₂)₂(en)₂]Cl; (c) Λ'-[Co-(gly)(en)₂]Cl₂·H₂O; (d) Λ'-[Co(en)₃]Cl₃·H₂O.

Figure 6. Plots of the concentration of Λ'-[Co(gly)(en)₂]Cl₂ (a), supersaturation degrees of Δ- and Λ-[Co(ox)(en)₂]Cl (b), and enantiomeric excess of the solution (c) against the amount of the residual substrate in solution in the system ΔΛ-[Co(ox)(en)₂]Cl–Λ'-[Co(gly)(en)₂]Cl₂ (CA). The ordinate curvature of supersaturation degree in part b is due to the common-ion effect of a chiral additive.

(en)₂]Cl; Δ'-[Co(CO₃)(en)₂]Br for ΔΛ-[Co(ox)(en)₂]Br·H₂O. The results are tabulated in Tables I and II. The systems containing racemic compounds are shown in Table IV.

The concentration effect of the chiral additive was examined for the two systems ΔΛ-[Co(ox)(en)₂]Br–Δ'-[Co(CO₃)(en)₂]Br (CA) and ΔΛ-[Co(ox)(en)₂]Cl–Δ'-[Co(gly)(en)₂]Cl₂ (CA). The results are shown in Figure 2. The influence of crystal yield on enantiomeric excess was studied in detail for the system ΔΛ-[Co(ox)(en)₂]Cl–Δ'-[Co(gly)(en)₂]-Cl₂ (CA). These data are shown in Figures 3 and 4.

Selective Adsorption of Chiral Additive in Crystals of Substrate. This experiment was carried out to check whether a chiral additive is actually adsorbed into substrate crystals or not. The general procedure is as follows. An aqueous solution containing Δ- (or Λ-) substrate and Δ'Λ'-chiral additive is kept standing at room temperature. After partial crystallization by spontaneous concentration, the solution is decanted and the crystals are washed with a small amount of water two or three times and then dried on filter paper. These crystals are dissolved in water again. The solution is poured onto a column of SP-Sephadex C-25 (Na⁺ form, o.d. 4 × 5 cm) and eluted with 0.2 mol dm⁻³ NaCl to separate the chiral additive from the Δ- (or Λ-) substrate. If the chiral additive is present, its amount and enantiomeric excess are determined by absorption and CD spectra. The results are shown in Table III. The separation of two complexes with an identical charge, e.g. [Co(ox)(en)₂]⁺–[Co-(NO₂)₂(en)₂]⁺ or [Co(ox)(en)₂]⁺–[Co(CO₃)(en)₂]⁺, necessitated a long column of SP-Sephadex C-25 (o.d. 4 × 20 cm) and an optically active elution agent, K₂[Sb₂(d-C₄H₂O₆)₂]·3H₂O.

Morphological Change of Δ- and Λ-[Co(ox)(en)₂]Cl·4H₂O Crystals. The optically active complex Δ- (or Λ-) [Co(ox)(en)₂]Cl·4H₂O crystallizes in a rhombic form from an aqueous solution at room temperature.[19] The same crystallization experiments were carried out in the presence of one of the chiral additives, Λ'-[Co(maa)(en)₂]Cl·0.5H₂O, Λ'-[Co-(NO₂)₂(en)₂]Cl, Λ'-[Co(en)₃]Cl₃·H₂O, or Λ'-[Co(gly)(en)₂]Cl₂·H₂O. The results are shown in Figure 5. The crystal morphology of Λ-[Co-(ox)(en)₂]Cl·4H₂O is modified in every case, but that of Δ-[Co(ox)-(en)₂]Cl·4H₂O is not.

Solubility Measurement in the System ΔΛ-[Co(ox)(en)₂]Cl–Λ'-[Co-(gly)(en)₂]Cl₂ (CA). The above kinetic resolution may be based on the

mechanism that a chiral additive is adsorbed at the crystal surfaces of one enantiomer and retards the crystal growth. This means that the solubility of enantiomer with the same absolute configuration as the chiral additive becomes higher than that of the other enantiomer in the presence of the chiral additive. Therefore, we determined the solubilities of Δ- and Λ-[Co(ox)(en)₂]Cl in the system ΔΛ-[Co(ox)(en)₂]Cl–Λ'-[Co(gly)(en)₂]Cl₂ (CA), which are available to clarify the role of the chiral additive. Here, note that the solubilities are those in the solution of the actual kinetic resolution process and not of the equilibrium condition. They were derived by subtracting the quantity of the deposited crystals from that of the initial substrate because the solution contains the additional species Λ'-[Co(gly)(en)₂]Cl₂.

A mixture of 1.5 g of ΔΛ-[Co(ox)(en)₂]Cl·H₂O and 0.06 g of Λ'-[Co(gly)(en)₂]Cl₂·H₂O is placed in a crystallizing dish of weight W_d and an appropriate amount of water is added to them. The mixed solution is kept standing at 24 °C. After the substrate [Co(ox)(en)₂]Cl·4H₂O partially crystallized by spontaneous concentration, the total weight W_t is measured. If the crystals deposited are composed of $w_Δ{}^c$ g of Δ- and $w_Λ{}^c$ g of Λ-substrate of the anhydrous salt (the numerical value of which can be obtained by the absorption and CD spectral measurements), the residual substrate in the solution is $(0.7079 - w_Δ{}^c)$ g of Δ- and $(0.7079 - w_Λ{}^c)$ g of Λ-substrate, because 1.5 g of ΔΛ-[Co(ox)(en)₂]Cl·H₂O contains 0.7079 g of the Δ- and 0.7079 g of the Λ-substrate of the anhydrous salt. At this stage, the weight of water in the solution can be calculated by the equation $w_{H_2O}{}^s = W_t - W_d - (0.7079 - w_Δ{}^c) - (0.7079 - w_Λ{}^c) - 0.0568 - 0.192(w_Δ{}^c + w_Λ{}^c)$, where the last two terms denote the weight of the anhydrous salt in Λ'-[Co(gly)(en)₂]Cl₂·H₂O and the weight of water incorporated into the crystals of [Co(ox)(en)₂]Cl·4H₂O, respectively. Thus, the solubilities of the Δ- and Λ-substrates in 100 g of H₂O, $S_Δ$ and $S_Λ$, can be obtained. In this experiment, the amount of chiral additive occluded into the crystals of [Co(ox)(en)₂]Cl·4H₂O is negligible. The degree of apparent supersaturation is calculated by the equation $σ_Δ$ (or $σ_Λ$) = $100([S_Δ$ (or $S_Λ$) $- (S_{ΔΛ}/2)]/(S_{ΔΛ}/2))$, where $S_{ΔΛ}$ denotes the equilibrium solubility of ΔΛ-[Co(ox)(en)₂]Cl·4H₂O at 24 °C. Figure 6 shows the data, which are corrected for the common-ion effect of the chloride ion in Λ'-[Co(gly)(en)₂]Cl₂.

Measurement. The solubilities in water were determined according to the previously reported method.[20,21] The solid phases were identified by elemental analysis and absorption and CD spectra. The absorbances were measured with a Hitachi 330 spectrophotometer and the CD spectra

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(19) The crystals of [Co(ox)(en)₂]Cl·4H₂O effloresce completely after 2 h in the air to give monohydrate.

(20) Yamanari, K.; Hidaka, J.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3724.

(21) Shimura, Y.; Tsutsui, K. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 145.

with a JASCO MOE-1 spectropolarimeter.

Results and Discussion

Optical Resolution of Conglomerates. The kinetic resolutions of four kinds of conglomerates, $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$, $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl·4H$_2$O, $\Delta\Lambda$-[Co(NO$_2$)$_2$(en)$_2$]Cl, and $\Delta\Lambda$-[Co(ox)(en)$_2$]Br·H$_2$O, were performed in the presence of a variety of chiral additives. In the case of $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$, eight resolved complexes, Δ'-[Co(ox)(en)$_2$]ClO$_4$, Δ'-[Co(maa)(en)$_2$]-ClO$_4$, Δ'-[Co(pyt)$_2$(R-pn)]ClO$_4$, Δ'-[Co(dtc)$_2$(R-pn)]ClO$_4$, Δ'-[Co(gly)(en)$_2$](ClO$_4$)$_2$·2H$_2$O, Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$, Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$, and Δ'-[Co(en)$_3$](ClO$_4$)$_3$, were examined as the chiral additives. Of these complexes, only three chiral additives, Δ'-[Co(maa)(en)$_2$]ClO$_4$, Δ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$, and Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$, are effective and give the relatively high enantiomeric excess as shown in Table I. It should be noted that the absolute configuration of the first crop is always opposite to that of the chiral additive in every experiment. On the other hand, the second crop shows the same absolute configuration as the chiral additive. This is responsible for the unbalanced enantiomeric composition in the solution. Namely, one enantiomer having the same absolute configuration as the chiral additive will be enriched in the supernatant solution owing to the crystallization of the other enantiomer, and then will crystallize as a second crop.

Similar resolution experiments were repeated for the other systems. The results are summarized in Table II. In these systems, the first crystals always show configuration opposite to that of the chiral additive. This is in good agreement with the expectation deduced from the stereoselective adsorption and inhibition mechanism. But it should be also noted that the effective systems are very limited; for example, in the case of $\Delta\Lambda$-[Co(ox)(en)$_2$]-Cl·4H$_2$O, five chiral additives were examined and only Δ'-[Co(gly)(en)$_2$]Cl$_2$·H$_2$O is efficient. These facts indicate that only some of the many possible sets of substrates and chiral additives have a strong enough interaction to exhibit the "rule of reversal".

The enantiomeric excesses in Table I are especially high in the systems with low crystal yields, e.g. 62% Δ for 10% yield and 100% Λ for 2% yield in $\Delta\Lambda$-[Co(aet)(en)$_2$](ClO$_4$)$_2$–Δ'-[Co(pyt)-(en)$_2$](ClO$_4$)$_2$ (CA). It is difficult to estimate the concentration effect of the chiral additive among the systems of different crystal yields. Figure 2 shows the plots of the resolution percentages against the quantities of the chiral additive. The crystal yields in each system are almost identical, that is ca. 17% and ca. 32% for $\Delta\Lambda$-[Co(ox)(en)$_2$]Br–Δ'-[Co(CO$_3$)(en)$_2$]Br (CA) and $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl–Δ'-[Co(gly)(en)$_2$]Cl$_2$ (CA), respectively. The resolution percentage clearly increases in proportion to the quantity of the chiral additive. Such results are consistent with the selective adsorption and inhibition mechanism, because the adsorption of the chiral additive is expected to increase in proportion to its concentration.

Influence of Crystal Yield on Enantiomeric Excess. Figure 3 shows the plots of enantiomeric excesses vs. crystal yields in the system $\Delta\Lambda$-[Co(ox)(en$_2$)]Cl–Δ'-[Co(gly)(en)$_2$]Cl$_2$ (CA). It indicates the clear correlation between enantiomeric excess and crystal yield. The enantiomeric excess is almost constant at 0–13% of crystal yield, it decreases gradually at 13–32%, and increases again at 35–46%. Therefore, to achieve efficient resolution, the first crystal yield should be kept below ca. 15%. In the kinetic resolution of organic conglomerates, the remarkable lowering of enantiomeric excess is observed when the crystal yield is beyond 20%.[5]

The constant enantiomeric excess during the first crystallization is very interesting, and may be related to the ratio Λ'/Δ' = 6.1 found in the adsorption experiment described below. The ratio means that 86% and 14% of Λ'-[Co(gly)(en)$_2$]Cl$_2$·H$_2$O will be adsorbed on the crystals of Λ- and Δ-[Co(ox)(en)$_2$]Cl·4H$_2$O, respectively. If the crystal growth is inhibited in proportion to the adsorption amount, the first crystals of [Co(ox)(en)$_2$]Cl·4H$_2$O should be composed of 86% of the Δ-enantiomer and 14% of the Λ-enantiomer, that is, it shows ca. 72% Δ in enantiomeric excess.

The above resolution curve was fractionated at every 4% yield of the substrate in Figure 4. Since the total crystal yield of Δ-[Co(ox)(en)$_2$]Cl is always higher than that of the Λ-enantiomer,

the first crystals precipitated are Δ-rich irrespective of the crystal yield. On the other hand, the Λ-rich crystals can be obtained by the subsequent crystallization. The bar graph shows the content of the Δ- or Λ-[Co(ox)(en)$_2$]Cl at every crop. This clearly indicates that the Δ-rich substrate crystallizes at 0–~12% of crystal yield, and then the Λ-rich substrate begins to deposit at ~16–~32%. Therefore, the Λ-rich crystals will be obtained by using the latter crystal region. The second process of the alternative crystallization is also observed: the Δ-rich crystals deposit at ~36–~48% of crystal yield, and then the Λ-rich crystals deposit at ~48–~56%. Further observation of this process is difficult owing to the increase of experimental errors, but such a process will be repeated.

Selective Adsorption of Chiral Additives. Table III shows the results of selective adsorption of chiral additives. In the case of [Co(ox)(en)$_2$]Cl·4H$_2$O, the adsorption was confirmed only for [Co(gly)(en)$_2$]Cl$_2$·H$_2$O. The adsorbate quantity increases with the concentration of [Co(gly)(en)$_2$]Cl$_2$, but the ratio Λ'/Δ' is constant in both the experiments. Substitution of L-alaninate for the glycinate ligand led to no observation of adsorption. In the case of [Co(aet)(en)$_2$](ClO$_4$)$_2$, selective adsorption was found for two chiral additives, [Co(maa)(en)$_2$]ClO$_4$ and [Co(pyt)(en)$_2$]-(ClO$_4$)$_2$, though the concentrations of the chiral additives are relatively low because of their low solubilities. The adsorption was also found for Λ-[Co(ox)(en)$_2$]Br–$\Delta'\Lambda'$-[Co(CO$_3$)(en)$_2$]Br (CA). However, no adsorption was observed for the corresponding chloride pair, Λ-[Co(ox)(en)$_2$]Cl–$\Delta'\Lambda'$-[Co(CO$_3$)(en)$_2$]Cl (CA). This means that the adsorption depends upon the total interaction of the substrate and the chiral additive, including counterions.

The results of adsorption experiments correlate completely with those of resolutions; that is, in the system where selective adsorption of the chiral additive was found, a high enantiomeric excess was observed without exception. Thus, these results give direct verification of the selective adsorption and inhibition mechanism. The degree of adsorption (0.014%–0.94%) is somewhat lower than the value found for organic compounds (0.5%–3%).[5]

Morphological Change. Selective adsorption of a chiral additive on some of the crystal faces of the substrate changes the relative growth rates of faces, and then causes an overall morphological change of the enantiomorph where absorption took place, whereas the antipode is almost unmodified.[22] About 30 organic compounds, such as asparagine, threonine, and ammonium hydrogen tartrate have been tested by Addadi et al.[5] They found that these compounds follow the above rule without exception. In the present study, the enantiomers Δ- and Λ-[Co(ox)(en)$_2$]Cl·4H$_2$O, which usually becomes a rhombic form at room temperature, were crystallized in the presence of four kinds of the chiral additives, Δ'-[Co(maa)(en)$_2$]Cl·0.5H$_2$O, Δ'-[Co(NO$_2$)$_2$(en)$_2$]Cl, Δ'-[Co(gly)(en)$_2$]Cl$_2$·H$_2$O, and Δ'-[Co(en)$_3$]Cl$_3$·H$_2$O. These results are shown in Figure 5. The enantiomer of the Δ-configuration crystallizes in the same rhombic form as the pure substrate, whereas the crystals of the Λ-configuration are modified to different extents depending upon the kinds of chiral additives. It is noteworth that three chiral additives Δ'-[Co(maa)(en)$_2$]Cl·0.5H$_2$O, Δ'-[Co(NO$_2$)$_2$(en)$_2$]Cl, and Δ'-[Co(en)$_3$]Cl$_3$·H$_2$O, which are not effective in both the kinetic resolution and the adsorption experiments, show the same morphological change. These facts mean that the sensitivity to the chiral additive is higher in the experiment of morphological change than in that of kinetic resolution or selective adsorption. Such a striking morphological effect will be applicable to the assignment of absolute configurations of metal complexes, as is shown for organic compounds.[5,22,23]

Kinetic Resolution Mechanism. As described above, some essential aspects, preferential crystallization of one enantiomer, stereoselective adsorption of a chiral additive, and a morphological

(22) Addadi, L.; Gati, E.; Lahav, M. *J. Am. Chem. Soc.* **1981**, *103*, 1251.
(23) Berkovitch-Yellin, Z.; Addadi, L.; Idelson, M.; Leiserowitz, L.; Lahav, M. *Nature (London)* **1982**, *296*, 27. Weissbuch, I.; Addadi, L.; Berkovitch-Yellin, Z.; Gati, E.; Weinstein, S.; Lahav, L.; Leiserowitz, L. *J. Am. Chem. Soc.* **1983**, *105*, 6615.
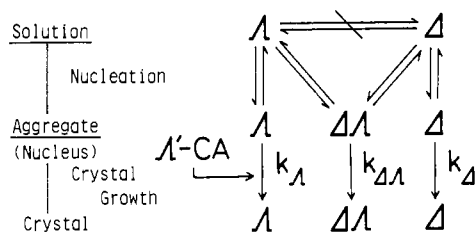
Figure 7. Proposed resolution mechanism of racemic compounds. In the presence of a Λ'-chiral additive, three kinds of aggregates, $\Delta\Lambda$, Δ, and Λ, will all be formed in solution through a reversible process. The aggregates of the Λ-enantiomer cannot develop because of the crystal growth inhibition, whereas the aggregates of the racemic compound ($\Delta\Lambda$) and the Δ-enantiomer will develop and deposit as crystals. The crystallization rates are $k_{\Delta\Lambda} \gg k_{\Delta} > k_{\Lambda}$. Thus, the first crystals will be composed of a large amount of the racemic compound and a small amount of the Δ-enantiomer.

change of the other enantiomer, are all observed in the present systems. These results confirm that the mechanism of the present kinetic resolution is due to the stereoselective adsorption of a chiral additive on the crystal surfaces of one enantiomer of the same absolute configuration as a chiral additive and a drastic decrease of the growth rate of these crystals, as proposed by Addadi et al.[5]

For the further understanding of the resolution process, the solubilities of Δ- and Λ-[Co(ox)(en)$_2$]Cl, S_Δ and S_Λ, in the system $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl–Λ'-[Co(gly)(en)$_2$]Cl$_2$ (CA) were determined at 24 °C. The results are shown in Figure 6 against the amount of the residual substrate in solution: curve a shows the concentration change of the chiral additive Λ'-[Co(gly)(en)$_2$]Cl$_2$, plot b the change of apparent supersaturation degree of the Δ- (or Λ-) substrate (which is defined as σ_Δ (or σ_Λ) $= 100([S_\Delta$ (or S_Λ) $- (S_{\Delta\Lambda}/2)]/(S_{\Delta\Lambda}/2))$ where $S_{\Delta\Lambda}$ denotes the equilibrium solubility of $\Delta\Lambda$-[Co(ox)(en)$_2$]Cl·H$_2$O at 24 °C), and curve c the enantiomeric excess change of the solution.

The concentration of the chiral additive increases monotonously with the spontaneous evaporation of water, because the occlusion of the chiral additive into the substrate crystals can be ignored. The degree of apparent supersaturation of Δ-[Co(ox)(en)$_2$]Cl, σ_Δ, decreases initially because of crystal deposition and becomes the lowest near ca. 80% of the residual substrate in solution, which corresponds to deposition of the ca. 20% crystals. Then, σ_Δ increases in proportion to the concentration of the chiral additive. The degree of apparent supersaturation of Λ-[Co(ox)(en)$_2$]Cl, σ_Λ, shows a temporarily rapid decrease at ca. 65% and ca. 50% on the abscissa owing to the crystallization of the Λ-rich substrate. However, except for these regions, σ_Λ increases in proportion to the concentration of the chiral additive. In particular, σ_Λ is always higher than σ_Δ all over the regions measured. This means that the Λ-enantiomer of [Co(ox)(en)$_2$]Cl is more soluble than the Δ-enantiomer in the presence of Λ'-[Co(gly)(en)$_2$]Cl$_2$. It is also noteworthy that there is no special critical value with respect to the degree of supersaturation of the substrate.

The curve of the enantiomeric excess of the solution against the amount of the residual substrate in solution (Figure 6c) was derived from the full line in Figure 6b. The enantiomeric excess of the solution becomes a maximum near the two regions of ca. 82% and ca. 55% on the abscissa. These maximum values (ca. 8%) are fairly constant and seem to be critical, because the crystallization of the Λ-rich substrate occurs whenever the enantiomeric excess of the solution becomes close to the value. The role of the chiral additive is considered to inhibit the crystal growth of one enantiomer with the same absolute configuration as it and to maintain as high a degree of supersaturation in solution as possible.

Resolution of Racemic Compounds due to Chiral Additives. The kinetic resolution was applied for some racemic compounds. Table IV shows the resolution of the racemic compounds. The complex [Co(NO$_2$)$_2$(en)$_2$]I is successfully resolved by several kinds of chiral additives. However, the racemic compound [Co(CO$_3$)(en)$_2$]Cl is not resolved by any chiral additives. The complexes [Co(maa)(en)$_2$]ClO$_4$ and [Co(gly)(en)$_2$]Cl$_2$·H$_2$O[24] are partially resolved by Λ'-[Co(aet)(en)$_2$](ClO$_4$)$_2$ and Δ'-[Co(ox)(en)$_2$]Cl, respectively. It is important that adsorption of the chiral additive into the crystals of the substrate is confirmed for these two systems, [Co(maa)(en)$_2$]ClO$_4$–[Co(aet)(en)$_2$](ClO$_4$)$_2$ (CA) and [Co(gly)(en)$_2$]Cl$_2$–[Co(ox)(en)$_2$]Cl (CA) as shown in Table III. In all cases of successful resolution, the first crystals show the opposite absolute configuration to the chiral additive. The "rule of reversal" holds for the systems containing racemic compounds.

A model for kinetic resolution process of a racemic compound ($\Delta\Lambda$), which consists of two steps of nucleation and crystal growth, is proposed in Figure 7. In the nucleation step, small aggregates of several substrate ions will be formed through a reversible process.[25] These aggregates involve not only the thermodynamically stable racemic compound ($\Delta\Lambda$) but also the unstable enantiomers (Δ and Λ) under such a nonequilibrium condition. In a system where a Λ'-chiral additive is efficiently adsorbed on the crystal surfaces of the Λ-substrate, the aggregates of the Λ-enantiomer cannot develop and this species will have a greater tendency to remain in solution, as described above. On the other hand, the aggregates of the racemic compound and the Δ-enantiomer will develop as nuclei and then grow to crystals by spontaneous evaporation of the solution. The order of the three crystallization rates will be $k_{\Delta\Lambda} \gg k_\Delta > k_\Lambda$. The first crystals obtained in this way are composed of a large amount of the racemic compound and a small amount of the Δ-enantiomer, that is, being partially resolved. Thus, the kinetic resolution due to a chiral additive is applicable to the systems having the strong interaction between a substrate and a chiral additive, whether the substrate is a conglomerate or a racemic compound.

Safety Notes. Perchlorate salts of metal complexes with organic ligands are potentially explosive. In general, when noncoordinating agents are required, every attempt should be made to substitute anions such as the fluoro sulfonates for the perchlorates. If a perchlorate must be used, only small amounts of material should be prepared and this should be handled with great caution. [Cf.: *J. Chem. Educ.* **1978**, *55*, A355. *Chem. Eng. News* **1983**, *61* (Dec 5), 4; **1963**, *41* (July 8), 47.]

Registry No. [Co(aet)(en)$_2$](ClO$_4$)$_2$, 40330-50-5; Λ-[Co(aet)-(en)$_2$](ClO$_4$)$_2$, 64726-53-0; [Co(ox)(en)$_2$]Cl, 17439-00-8; [Co(ox)-(en)$_2$]Br, 15713-71-0; Λ'-[Co(ox)(en)$_2$]Cl, 31716-15-1; Λ-[Co(ox)-(en)$_2$]Br, 31126-56-4; Δ'-[Co(ox)(en)$_2$]Cl, 62598-17-8; [Co(NO$_2$)$_2$-(en)$_2$]Cl, 15079-78-4; Λ-[Co(NO$_2$)$_2$(en)$_2$]Cl, 28190-75-2; [Co(NO$_2$)$_2$-(en)$_2$]I, 51321-45-0; Δ'-[Co(maa)(en)$_2$]ClO$_4$, 91741-56-9; Λ-[Co-(maa)(en)$_2$]ClO$_4$, 91741-58-1; [Co(maa)(en)$_2$]ClO$_4$, 26743-67-9; Λ'-[Co(pyt)(en)$_2$](ClO$_4$)$_2$, 99267-46-6; [Co(pyt)(en)$_2$](ClO$_4$)$_2$, 84946-61-2; Δ'-[Co(dtc)(en)$_2$](ClO$_4$)$_2$, 89688-11-9; Λ'-[Co(gly)(en)$_2$]Cl$_2$, 54003-28-0; [Co(gly)(en)$_2$]Cl$_2$, 14408-57-2; Δ'-[Co(gly)(en)$_2$]I$_2$, 99267-47-7; Λ'-[Co(en)$_3$]Cl$_3$, 23778-88-3; Λ'-[Co(en)$_3$]I$_3$, 19456-53-2; Δ'-[Co(CO$_3$)-(en)$_2$]Br, 51321-42-7; [Co(CO$_3$)(en)$_2$]Br, 31055-39-7; [Co(CO$_3$)(en)$_2$]-Cl, 15842-50-9.

(24) Solubility data in g/100 g of H$_2$O at 25 °C: $S_{\Delta\Lambda} = 1.16$ and $S_\Delta = 3.51$ for $\Delta\Lambda$- and Δ-[Co(maa)(en)$_2$]ClO$_4$, respectively; $S_{\Delta\Lambda} = 36.0$ and $S_\Delta = 115$ for $\Delta\Lambda$- and Δ-[Co(gly)(en)$_2$]Cl$_2$, respectively.

(25) Jacques, J.; Collet, A.; Wilen, S. H. "Enantiomers, Racemates, and Resolutions"; Wiley: New York, 1981; p 237.