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The Base-Catalyzed Isomerization of the Bis(ethylenediamine-*N*-acetato)cobalt(III) Complex

Hiroshi Kawaguchi,* Ryuichi Niiyama, Tomoharu Ama, and Takaji Yasui
Department of Chemistry, Faculty of Science, Kochi University, Akebono-cho, Kochi 780

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The isomerization reaction among six geometrical isomers of $[Co(edma)_2]^+$, which were all resolved into optically active isomers except for the achiral C_i-trans(O) isomer, has been studied in a basic aqueous solution. It has been found that the reaction is stereoselective and that the main reaction schemes may be described as follows: (1) $\Lambda\Delta\Lambda$(S,S)-C_2-trans(O) $\rightleftharpoons$ $\Delta\Lambda\Delta$(R*,S)-C_1-cis(O) $\rightleftharpoons$ $\Delta\Lambda$(R,R)-cis(O)trans(NH) $\rightleftharpoons$ meso(R,S)-C_i-trans(O)$\rightarrow$$\Lambda\Delta\Lambda$(R,R)[or $\Delta\Lambda\Delta$(S,S)]-cis(O)trans(NH_2) and (2) meso(R,S)-C_i-trans(O)$\leftarrow$$(+)^{CD}_{504}$-mer$\rightarrow$$\Lambda\Delta\Lambda$(S,S)-$C_2$-trans(O). In each of the isomerization steps of (1), the inversion occurs at one of two secondary-N centers of the coordinated edma ligands. The rate of deuteration at the secondary-NH was also measured for all geometrical isomers; a linear relationship between the rates of the deuteration and isomerization was found. It was suggested that the isomerization of the $[Co(edma)_2]^+$ system proceeded through the deprotonated five-coordinated intermediates formed by Co–O bond-rupture in the conjugate-base forms.

Numerous data of intramolecular rearrangement (isomerization and inversion) reactions have been reported, and two major pathways of twist and bond-rupture mechanisms have been proposed.[1,2] Complexes with multidentate ligands[3,4] can be used for mechanistic studies of rearrangement reactions, because (1) the coupled chelate rings restrict the number of different possible interconversions and (2) such molecules possess more distinguishable points of reference by which the paths of specific rearrangements can be traced. Recently it has been found that an interesting rearrangement (inversion-isomerization) occurs in the chiral complexes containing multidentate ligands.[5–7] Also, in the substitution reactions of the chiral complexes containing tetradentate ligands, some examples of inversion-isomerization have been reported.[8–10] Examples concerning structure-reactivity patterns in octahedral complexes have been reviewed by House[11] and by Radanovic.[12]

The bis(ethylenediamine-*N*-acetato)cobalt(III) ion, $[Co(edma)_2]^+$, provides six geometrical isomers, as is shown in Fig. 1. When the edma ligand coordinates to a cobalt(III) ion, the secondary nitrogen (–C–NH–C–) becomes asymmetric (R or S). Although each isomer of $[Co(edma)_2]^+$ may be expected to provide several diastereomers, some of them (except for the mer isomer, E-3) do not exist because of structural restrictions. The possible configurations[13] for the geometrical isomers containing facially coordinated edma are listed in Table 1. In previous papers,[14,15] we reported the preparation and characterization of the six geometrical isomers and also the determination of the absolute configurations of the chiral isomers, except for the mer isomer (E-3).

Recently we have found that the isomers of $[Co(edma)_2]^+$ isomerized to other one with inversion at one of the secondary nitrogen (sec-N) centers of the coordinated edma ligands.[16] In this paper the details of these isomerization reactions will be reported. The deuteration reactions at the sec-N centers will also be described.

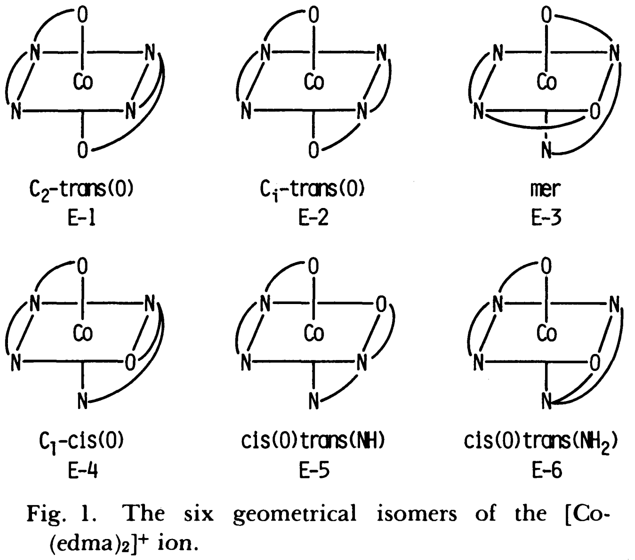


Fig. 1. The six geometrical isomers of the $[Co(edma)_2]^+$ ion.

Experimental

Complexes. The complexes examined here were prepared and resolved according to the methods described in our previous papers.[14,15] They are $(+)^{CD}_{543}$-C_2-*trans*(O)-

Table 1. Possible Configurations and CD Signs of the $[Co(edma)_2]^+$ Ion

Isomer	Possible configuration and CD sign	
E-1	$(-)^{CD}_{543}$-$\Delta\Lambda\Delta$(*R*,*R*)	$(+)^{CD}_{543}$-$\Lambda\Delta\Lambda$(*S*,*S*)
E-2	(*R*,*S*) (achiral isomer)	
E-4	$(+)^{CD}_{534}$-$\Lambda\Delta\Lambda$(*S**,*R*)	$(-)^{CD}_{534}$-$\Delta\Lambda\Delta$(*R**,*S*)
E-5	$(-)^{CD}_{521}$-Δ(GG)Λ(EE)(*R*,*R*)	$(+)^{CD}_{521}$-Λ(GG)Δ(EE)(*S*,*S*)
E-6	$(-)^{CD}_{509}$-$\Lambda\Delta\Lambda$(*R**,*R**)	$(+)^{CD}_{509}$-$\Delta\Lambda\Delta$(*S**,*S**)

R or *S*: Chirality around the asymmetric nitrogen. *R** or *S**: Chirality around the asymmetric nitrogen being present at the position trans to ligating oxygen atom. G and E represent the glycinate-ring and ethylenediamine-ring of the edma ligand respectively.

[Co(edma)$_2$]Cl·2H$_2$O (E-1), C_i-*trans*(O)-[Co(edma)$_2$]Cl·2H$_2$O (E-2), $(+)^{CD}_{504}$-*mer*-[Co(edma)$_2$]Br (E-3), $(-)^{CD}_{534}$-C$_1$-*cis*(O)-[Co(edma)$_2$]Cl·2H$_2$O (E-4), $(-)^{CD}_{521}$-*cis*(O)*trans*(NH)-[Co(edma)$_2$]Br (E-5), $(-)^{CD}_{509}$-*cis*(O)*trans*(NH$_2$)-[Co(edma)$_2$]Cl·1.5H$_2$O (E-6).

Spectral Change in the Isomerization Reaction Solution. The time-course changes in the absorption and CD spectra of each isomer in a basic aqueous solution were followed by the use of a Hitachi 557 spectrophotometer and a JASCO J-22 spectropolarimeter. All the chemicals used were of a reagent grade, and the deionized water was degassed before use. The reaction was started by stirring a buffer solution into the complex solution in a reaction vessel kept in a thermostat. About 3 cm^3 of the reaction solution was then quickly transferred into the cell with a stopper in order to record the absorption and CD spectra. The following conditions were set: Complex concentration, 2.68 or 4.66×10^{-3} M (M=mol dm^{-3}); pH, 10.24—10.37 (Na$_2$CO$_3$-NaHCO$_3$ buffer); temperature, 40.1 or 30.1 °C.

Isomerization. $(-)^{CD}_{534}$-E-4 Isomer: This isomer (0.150 g) was dissolved in 200 cm^3 of water in a reaction vessel kept in a thermostated bath at 40.0 °C. The reaction was started by stirring 300 cm^3 of a buffer solution [Na$_2$CO$_3$(0.1165 M)–NaHCO$_3$(0.03887 M)] previously kept at 40.0 °C into the reaction vessel. The temperature and the pH of the reaction solution were checked with a thermister thermometer (Takara D221) and a pH meter (Toa TSC-10A) respectively. During the experiment (160 h), the reaction solution was kept at 40.0±0.1 °C, with the pH 10.35±0.02.

At prescribed time intervals, a constant volume (40.0 or 30.0 cm^3) of the reaction solution was taken out and acidified to pH 6 in order to stop the reaction. The acidified solution was poured onto an SP-Sephadex C-25 column (3.0 cm×60 cm, Na$^+$ form). The adsorbed band was developed with a 0.2 M NaCl aqueous solution and separated into two bands, el-1 and el-2 in order of elution. The el-1 eluate contained $(+)^{CD}_{543}$-E-1 (major) and E-2 (minor), while the el-2 eluate contained $(-)^{CD}_{534}$-E-4 and $(-)^{CD}_{521}$-E-5. Each of the el-1 and el-2 eluates was concentrated to a constant volume (10.0 or 5.0 cm^3) and used for the measurements of the absorption and CD spectra. From the binary-curve analysis of the absorption spectrum of the concentrated el-1 eluate (on the basis of the known absorption data of authentic E-1 and E-2), the amounts of E-1 and E-2 formed were calculated. The optical purity of $(+)^{CD}_{543}$-E-1 in the el-1 eluate was obtained from the CD intensity of the el-1 eluate and the concentration of E-1 estimated from the absorption data. The amounts and optical purities of $(-)^{CD}_{534}$-E-4 and $(-)^{CD}_{521}$-E-5 were also estimated from the binary-curve analyses of the absorption and CD spectra of the el-2 eluate. In these curve-analyses, the spectral data at 20—25 points in the visible region were used; the analyses were carried out on an NEC PC-9801F computer using the least-squares method.

The isomerization reactions of the other isomers were carried out by a procedure similar to that used for $(+)^{CD}_{534}$-E-4. The reaction conditions were the same as those in the case of $(+)^{CD}_{534}$-E-4.

Deuteration. The deuteration reactions were carried out for the six geometrical isomers of the [Co(edma)$_2$]$^+$ complex in a DCl(0.096 M)–D$_2$O solution and followed with a ^{1}H NMR spectrometer (JEOL MH-100). The solutions were 0.15—0.25 M in complex concentration. The reactions were started by dissolving the complex in DCl–D$_2$O solution in a thermostat at 80 °C. About 0.5 cm^3 aliquots of the reaction solutions were rapidly quenched in an ice bath, and then the ^{1}H NMR spectra were measured.

Results and Discussion

The Absorption and CD Spectral Changes in a Basic Aqueous Solution. $(-)^{CD}_{534}$-E-4 Isomer: Figure 2 shows the changes in the absorption and CD spectra of $(-)^{CD}_{534}$-E-4 in a basic solution (pH 10.37) at 40.1 °C. The absorption maximum in the 1st d–d band region shifts gradually to a longer wavelength (from 502 to 525 nm), and the final spectral pattern is similar to that of E-1 (λ_{max} 530 nm). The initial isosbestic points at 527 and 450 nm, which are lost at longer times, are close to the cross points (522 and 449 nm) between the absorption curve of the E-1 and that of E-4. On the other hand, the CD spectrum of $(-)^{CD}_{534}$-E-4 in a basic aqueous solution changes drastically, as is shown in Fig. 2; that is, the CD patterns in the 1st band region are almost inverted with the passage of time. In the initial stage of the reaction, isoextinct points are observed at 497 and 400 nm, which are near in position to the cross points (494 and 399 nm) between the CD curve of $(+)^{CD}_{543}$-E-1 and that of $(-)^{CD}_{534}$-E-4. Further, the final CD curve in Fig. 2 resembles that of

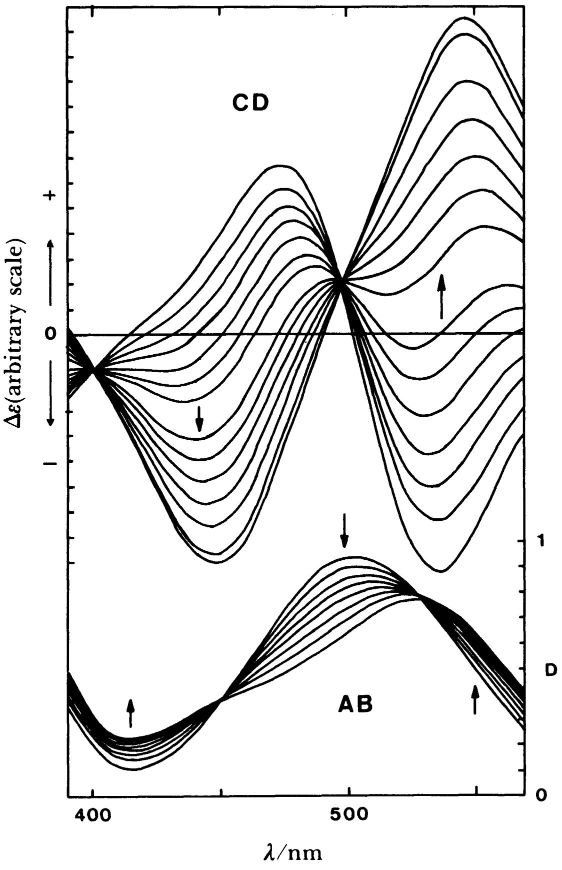


Fig. 2. The absorption (AB) and CD spectral changes of $(-)^{CD}_{534}$-E-4 in a basic aqueous solution (pH 10.37) at 40.1 °C. The final AB and CD curves were recorded after 95 h.

$(+)^{\mathrm{CD}}_{543}$-E-1. These results indicate that optically active $(+)^{\mathrm{CD}}_{543}$-E-1 was formed in a considerable amount from $(-)^{\mathrm{CD}}_{534}$-E-4. No minor products in this reaction were identified by the present experimental procedure.

$(+)^{\mathrm{CD}}_{521}$-E-5 and Other Isomers: Figure 3 shows the absorption and CD spectral changes (till 61 days) of $(+)^{\mathrm{CD}}_{521}$-E-5, which were measured under the same conditions as those used for $(-)^{\mathrm{CD}}_{534}$-E-4. The change in the absorption curve, in which the absorption maximum shifts to the lower energy side (from 478 to 516 nm), suggests that the trans(O) type isomers are formed in considerable concentrations at the final equilibrium stage of the reaction. It is apparent from the CD spectral change that optically active products are formed. However, the products could not be identified on the basis of those CD data.

The same measurements were performed for other isomers of $[\mathrm{Co(edma)_2}]^+$. These absorption and CD spectral changes were complicated, indicating that some kinds of isomers were formed in the reactions. The spectral changes in the basic aqueous solutions were relatively faster in E-4, E-3, and E-6 than in the others.

The Identification and Quantification of the Isomerization Reaction Products. The band adsorbed on an SP-Sephadex C-25 column, which contains six geometrical isomers of $[\mathrm{Co(edma)_2}]^+$ (E-1—E-6), separated into 3 bands—el-1 (E-1 and E-2), el-2 (E-3, E-4, and E-5), and el-3 (E-6) in order of elution, when developed with 0.2 M NaCl as the eluent. In order to estimate the amounts of the starting material and products in the isomerization reaction solution at an arbitrary time, this chromatographic separation technique was used. Constant volumes of the reaction solution were taken out from the reaction vessel at prescribed time intervals. The solution was acidified to pH 6 to stop the reaction and then poured onto an SP-Sephadex column. The adsorbed band was separated into 3 bands (el-1, el-2, and el-3) by development with 0.2 M NaCl. The eluate from each band was concentrated to a constant volume, and the absorption spectra of the concentrated solution were measured. The amount of the E-6 isomer was estimated from the absorption data of the el-3 eluate. This el-3 band was detected only in a case of the isomerization reaction used E-6 as the starting material. The amounts of E-1 and E-2 were estimated from the binary-curve analysis of the absorption spectrum of the concentrated el-1 solution. If the three isomers of E-3, E-4, and E-5 are present in the reaction solution, all these isomers should be included in the el-2 solution. In the preliminary isomerization reaction of each isomer (except for the E-3 isomer), the ^{1}H NMR spectrum of the residue obtained from the el-2 eluate was measured to check the formation of E-3 on the basis of the difference in the glycinate-ring $-\mathrm{CH_2}-$ signal pattern of E-3 from those of the others.[14,15] In the cases of the isomers except E-3, the formation of E-3 was not detected throughout the isomerization reaction. Therefore, the absorption curve of the el-2 solution was analyzed as the curve of a mixture of E-4 and E-5. While in the isomerization reaction using E-3 as a starting material, the absorption spectrum of the el-2 eluate was identical to that of pure E-3, indicating no formation of either E-4 or E-5. (However, at longer reaction times, the absorption and CD curves of the el-2 eluate was better fitted by those of a mixture of E-3 and a very small amount of E-4.)

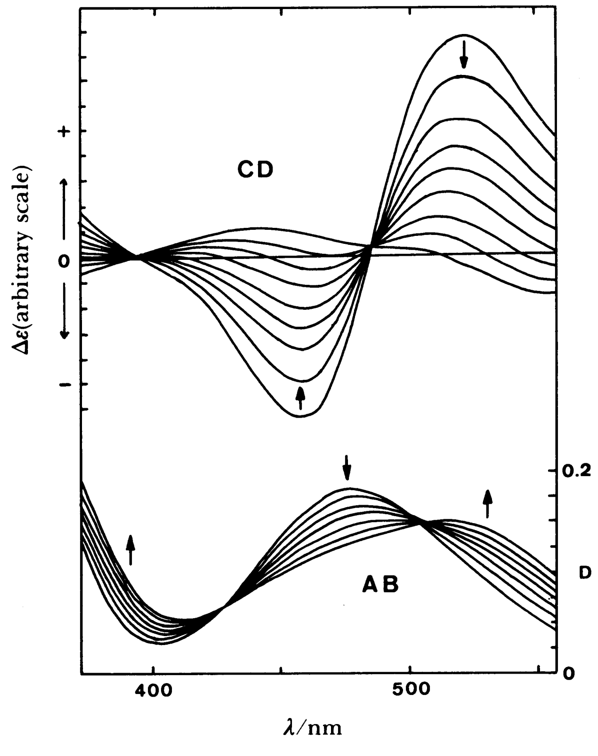


Fig. 3. The absorption (AB) and CD spectral changes of $(+)^{\mathrm{CD}}_{521}$-E-5 in a basic aqueous solution (pH 10.25) at 40.1 °C. The final AB and CD curves were recorded after 61 days.

When the optically active isomers were used as starting materials (except for achiral E-2), the CD spectra of the el-1—el-3 eluates were also measured. The CD spectra of the el-1 and el-3 solutions are due to the optical activities of E-1 and E-6 respectively. From the binary-curve analyses of the CD and absorption spectra of the el-2 solution, the optical purities of E-4 and E-5 were estimated.

In a weak acidic or neutral solution at room temperature, the isomerization of each isomer was not observed, at least not for several days. Therefore, the progress of the isomerization reaction during such procedures as chromatographic separation and concentration under reduced pressure should be negligible. In this experiment, the solutions (el-1—el-3) used for the measurements of the absorption and CD spectra contained a considerable amount of NaCl. As the absorption and CD spectra, especially the CD spectrum, of the [Co(edma)$_2$]$^+$ complex are affected by the amount of coexisting NaCl, the absorption and CD data of the isomers of [Co(edma)$_2$]$^+$, which were obtained in an NaCl aqueous solution, were used for the absorption and CD curve analyses of the el-1—el-3 eluates.

Base-Catalyzed Isomerization Reaction. (−)$^{CD}_{534}$-E-4 Isomer: The isomerization reaction of (−)$^{CD}_{534}$-E-4 was carried out in a carbonate buffer solution (pH 10.35) at 40.0 °C. Figure 4 shows the concentration changes in (−)$^{CD}_{534}$-E-4 and the reaction products. A part of the numerical data (five data points) are listed in Table 2, together with the enantiomer excess percentage of each product. In the isomerization reaction of E-4 over a period of 150 h, three products — E-1 (major), E-5, and E-2 — were formed. The formation of E-2 was not detected during the first ca. 50 h; after that time, its amount increased very slowly. The E-2 isomer is likely to be produced from the E-5 or E-1 isomer. Therefore, the reaction paths in this isomerization may be expected to be as follows:

$$\text{E-4} \longrightarrow \text{E-5} \xrightarrow{?} \text{E-2}$$
$$\text{E-4} \longrightarrow \text{E-1} \xrightarrow{?} \text{E-2}$$

Throughout the reaction (150 h), no racemization of the starting material occurred: The recovered (−)$^{CD}_{534}$-E-4 retained 100% optical purity. As is shown in Table 2, (+)$^{CD}_{543}$-E-1 and (−)$^{CD}_{521}$-E-5, which were formed from (−)$^{CD}_{534}$-E-4 in a basic aqueous solution, showed optical purities of ca. 100% and ca. 60% respectively: These two isomerization paths are thus stereoselective.

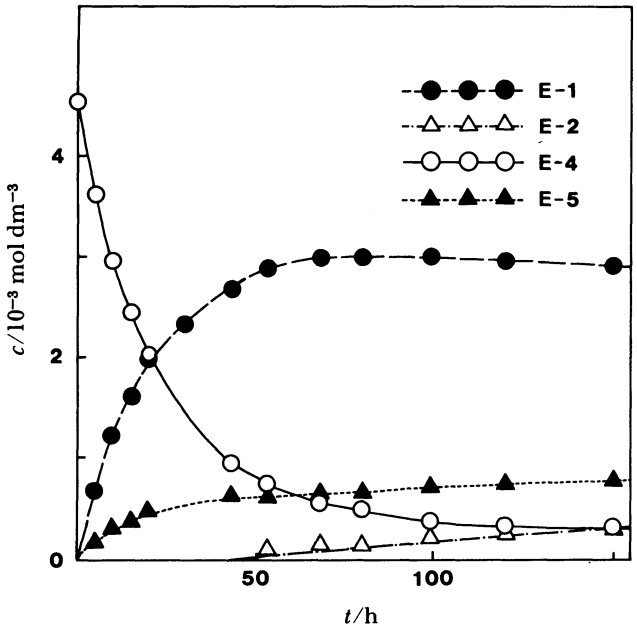


Fig. 4. The isomerization reaction of (−)$^{CD}_{534}$-E-4 in a basic aqueous solution (pH 10.35) at 40.0 °C.

(+)$^{CD}_{543}$-E-1 Isomer: In the isomerization reaction using (+)$^{CD}_{543}$-E-1 as the starting material, E-4 was formed first (Fig. 5 and Table 2). The amount of E-4

Table 2. The Concentration Changes and Optical Purities of the Starting Materials and Products in the Isomerization Reaction (40.0 °C, pH 10.35)

(i) (+)$^{CD}_{543}$-E-1

t/h	Concn/10^{-3} mol dm^{-3} (optical purity/%) (+)$^{CD}_{543}$-E-1	E-2	(−)$^{CD}_{534}$-E-4	(−)-$^{CD}_{521}$-E-5
10	4.41 (100)		0.16 (90)	
25	4.20 (100)		0.32 (80)	0.10 (20)
50	3.99 (100)	0.08	0.41 (80)	0.24 (20)
100	3.67 (100)	0.20	0.43 (80)	0.34 (20)
150	3.48 (100)	0.24	0.41 (80)	0.45 (20)

(ii) E-2

t/h	Concn/10^{-3} mol dm^{-3} E-1	E-2	E-5
10		4.46	0.08
34		4.53	0.26
66		4.31	0.38
100		4.15	0.48
150	0.07	3.97	0.57

(iii) (+)$^{CD}_{504}$-E-3

t/h	Concn/10^{-3} mol dm^{-3} (optical purity/%) (+)$^{CD}_{543}$-E-1	E-2	(+)$^{CD}_{504}$-E-3
3	0.06 (100)	0.05	4.49 (95)
6	0.13 (100)	0.11	4.32 (95)
26	0.53 (100)	0.49	3.46 (90)
53	0.93 (100)	0.92	2.72 (90)

(iv) (−)$^{CD}_{534}$-E-4

t/h	Concn/10^{-3} mol dm^{-3} (optical purity/%) (+)$^{CD}_{543}$-E-1	E-2	(−)$^{CD}_{534}$-E-4	(−)$^{CD}_{521}$-E-5
10	1.22 (100)		2.96 (100)	0.31 (60)
20	1.96 (100)		2.02 (100)	0.48 (60)
43	2.69 (100)		0.95 (100)	0.63 (60)
68	2.99 (100)	0.15	0.56 (100)	0.65 (60)
99	3.01 (100)	0.21	0.38 (100)	0.71 (60)

(v) (−)$^{CD}_{521}$-E-5

t/h	Concn/10^{-3} mol dm^{-3} (optical purity/%) (+)$^{CD}_{543}$-E-1	E-2	(−)$^{CD}_{534}$-E-4*	(−)$^{CD}_{521}$-E-5
30		0.05	0.12	4.37 (100)
68	0.23 (80)	0.11	0.12	4.13 (100)
100	0.35 (80)	0.17	0.12	3.96 (100)
164	0.59 (80)	0.26	0.13	3.66 (100)

* The optical purity is unreliable.

(vi) (−)$^{CD}_{509}$-E-6

t/h	Concn/10^{-3} mol dm^{-3} (optical purity/%) E-2	E-5	(−)$^{CD}_{509}$-E-6
0.5	0.20		4.45 (100)
2	0.87	0.17	3.37 (100)
5	1.89	0.27	2.15 (100)
9	2.84	0.34	1.10 (100)
18	3.70	0.42	0.32 (100)

increased until ca. 50 h, but after that it was almost constant throughout the reaction examined here (150 h). The formation of E-5 was first observed ca. 20 h after the start of the reaction. The amount of E-5 increased with the passage of time and exceeded the amount of E-4 after ca. 140 h. The formation of E-2, in a very small amount, was observed later than that of E-5. From the results of the isomerization reactions of both E-1 and E-4, the following reaction path may be presumed:

$$\text{E-1} \longrightarrow \text{E-4} \longrightarrow \text{E-5} \longrightarrow \text{E-2}$$

As is shown in Table 2, $(-)^{\mathrm{CD}}_{534}$-E-4, which was obtained by the isomerization reaction of $(+)^{\mathrm{CD}}_{543}$-E-1, retained an optical purity of 80—90%, showing a high stereoselectivity in the E-1→E-4 change. On the other hand, the $(-)^{\mathrm{CD}}_{521}$-E-5 produced in the same reaction retained an optical purity of only ca. 20%. This value is a little lower than the value to be expected from the presumed reaction path of $(+)^{\mathrm{CD}}_{543}$-E-1→$(-)^{\mathrm{CD}}_{534}$-E-4→$(-)^{\mathrm{CD}}_{521}$-E-5, because pure $(+)^{\mathrm{CD}}_{543}$-E-1 produced $(-)^{\mathrm{CD}}_{534}$-E-4 with an optical purity of 80—90% and pure $(-)^{\mathrm{CD}}_{534}$-E-4 produced $(-)^{\mathrm{CD}}_{521}$-E-5 with an optical purity of ca. 60%. However, the successive reactions of $(+)^{\mathrm{CD}}_{543}$-E-1→$(-)^{\mathrm{CD}}_{534}$-E-4→$(-)^{\mathrm{CD}}_{521}$-E-5 can also be supported by the following consideration. The absolute configurations of $(+)^{\mathrm{CD}}_{543}$-E-1 and $(-)^{\mathrm{CD}}_{521}$-E-5 are ΛΔΛ(S,S) and Δ(GG)Λ(EE)(R,R) respectively, as is shown in Table 1. If E-5 is formed directly from E-1, the inversions at the two asymmetric N centers must occur simultaneously. However, such inversions are very difficult judging from the consideration using molecular models. (If a direct $(+)^{\mathrm{CD}}_{543}$-E-1→$(+)^{\mathrm{CD}}_{521}$-E-5 change with a retention of the sec-N configuration by twist mechanism is slightly involved, the optical purity of $(-)^{\mathrm{CD}}_{521}$-E-5 may be lowered.) The isomerization of E-1 was slower than that of E-4.

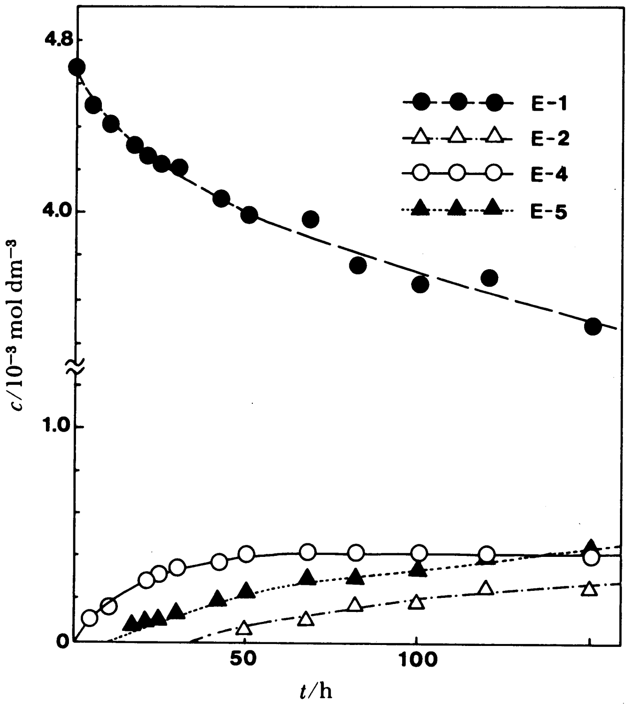


Fig. 5. The isomerization reaction of $(+)^{\mathrm{CD}}_{543}$-E-1 in a basic aqueous solution (pH 10.35) at 40.0 °C.

$(-)^{\mathrm{CD}}_{521}$-E-5 Isomer: The isomerization of $(-)^{\mathrm{CD}}_{521}$-E-5 was also slow under the conditions of pH 10.35 and 40.0 °C. In this reaction, the formations of E-4 and E-2 first occurred, and then E-1 was formed. Early in the reaction (10—20 h) the amounts of the products were in the order of E-4>E-2>E-1. After ca. 30 h, the concentration of E-4 reached its maximum and thereafter did not increase, while the concentrations of E-1 and E-2 increased with the passage of time (Table 2), E-1 (after ca. 40 h) and E-2 (after ca. 70 h) exceeding E-4 in the amount formed. Thus, the following reaction paths may be presumed by considering the reaction paths of E-4:

$$\text{E-5} \longrightarrow \text{E-4} \longrightarrow \text{E-1}$$
$$\text{E-5} \longrightarrow \text{E-2}$$

We could not calculate the optical purity of the E-4 produced in the isomerization reaction of $(-)^{\mathrm{CD}}_{521}$-E-5, because too little of it was formed for us to estimate the optical purity from the curve analyses of the absorption and CD spectra of the el-2 eluate [a mixture of E-5 (major) and E-4 (minor)]. The E-1 isomer obtained by the isomerization of $(-)^{\mathrm{CD}}_{521}$-E-5 was of the $(+)^{\mathrm{CD}}_{543}$ form, with an optical purity of ca. 80% (Table 2). Judging from the results of the isomerization of $(-)^{\mathrm{CD}}_{534}$-E-4, the isomerization reaction of $(-)^{\mathrm{CD}}_{521}$-E-5 can be expected to produce $(-)^{\mathrm{CD}}_{534}$-E-4 selectively. This reaction path is the reverse of the isomerization path of $(+)^{\mathrm{CD}}_{543}$-E-1 (E-1→E-4→E-5).

E-2 and $(-)^{\mathrm{CD}}_{509}$-E-6 Isomers: The isomerization reaction of achiral E-2 is slow, and the major product is E-5, as is shown in Table 2. At longer times (>ca. 100 h), a small amount of E-1 was formed. (After 215 h, the E-1 constitutes ca. 30% of the reaction products.) It is thought that the E-1 is formed by the path of E-2→E-5→E-4→E-1. However, the formation of E-4 could not be observed. This is probably because the E-4→E-1 change is faster than the E-5→E-4 change.

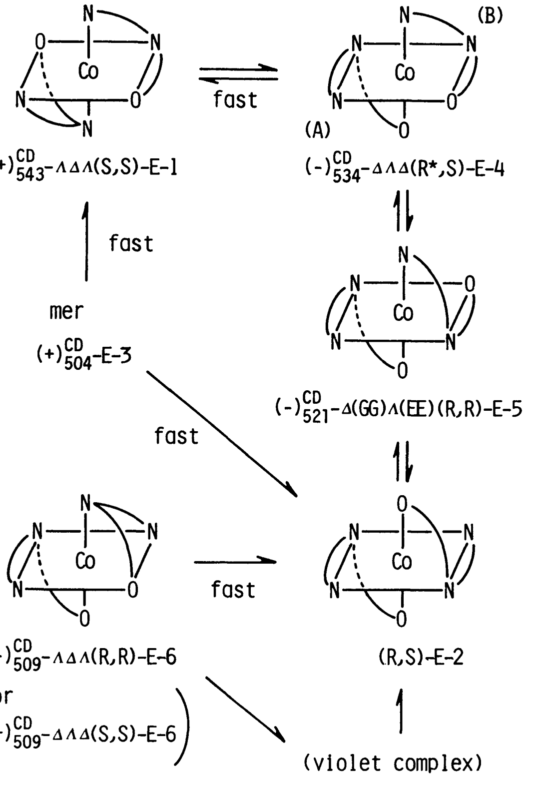
The isomerization of $(-)^{\mathrm{CD}}_{509}$-E-6 is the fastest among the reactions of this series (Table 2). The half-lives (with regard to the decrease in E-6) is ca. 4—5 h under the conditions of pH 10.35 and 40.0 °C. The isomerization reaction of $(-)^{\mathrm{CD}}_{509}$-E-6 produced E-2 (major), E-5, and by-products. The E-5 formed in this reaction was racemate; this fact is favorable to the reaction path of E-6→E-2(achiral)→E-5. However, the observed formation rate of E-5 is a little faster than that to be expected from the path of E-6→E-2→E-5, where the E-2→E-5 change is very slow. Another reaction path passing through an achiral intermediate (or transition state) may, therefore, be thought to exist.

In the initial stage of the isomerization reaction of (−)$^{CD}_{509}$-E-6, a violet by-product was formed in a small amount. The amount of the violet by-product, which was a noncharged and optically active complex, was maximal ca. 3 h after the reaction start, and thereafter it gradually decreased. The violet complex could not be isolated, because it was unstable and was formed in only a small amount. During the concentration of the solution containing the violet complex under reduced pressure at 40 °C, the complex changed to E-2. In the isomerization reaction of E-6, the decomposition product, which was a species with a charge of more than +2, was observed after ca. 7 h; its amount increased slowly with the passage of time. The isomerization studies of E-6 and E-3 (to be discussed in the next section) were not sufficient, for the preparation of these isomers was very difficult.

(+)$^{CD}_{504}$-E-3 Isomer: The isomerization reaction of (+)$^{CD}_{504}$-E-3 was followed over a period of 53 h under the conditions of pH 10.35 and 40.0 °C. E-3 is thought to be thermodynamically less stable because of its meridional chelate form; however, the isomerization rate was slower than that of E-4 or E-6 (Table 2). The products were (+)$^{CD}_{543}$-E-1, with an optical purity of ca. 100%, and E-2; the formation ratio of these two isomers was ca. 1:1. The racemization of (+)$^{CD}_{504}$-E-3 was almost negligible throughout the reaction. The other products were in the limit of the accuracy of the experimental method. (However, it was presumed that a small amount of (−)$^{CD}_{534}$-E-4 was formed through the path of E-3→E-1→E-4 at longer times.) The E-3 ion provides six possible diastereomers, arising from three chiral centers (cobalt and two sec-N of coordinated two edma ligands): $\Lambda(C_2)$(R,R), $\Lambda(C_2)$-(R,S), and $\Lambda(C_2)$(S,S) and the $\Delta(C_2)$ series.[17] Judging from the racemization rate of *mer*-[Co(edma)(dien)],[18] it is presumed that the inversion of the sec-N configuration in E-3 occurs rapidly under the present reaction conditions; that is, the equilibration of the RR⇄RS⇄SS is rapidly attained. Therefore, the configuration at the cobalt center in E-3 is the main factor in determining the configuration of the E-1 formed, even though the shift of the RR⇄RS⇄SS equilibrium must also be taken into consideration. As the absolute configuration of the isolated (+)$^{CD}_{504}$- or (−)$^{CD}_{504}$-E-3 has not yet been determined, the reaction scheme of E-3 can not be discussed in detail. However, the formation of E-2 excludes the possibility of a twist mechanism for the isomerization of E-3.

The Main Isomerization Paths of the [Co(edma)$_2$]$^+$ Series. From the isomerization data examined here, the main paths of the isomerization of the [Co(edma)$_2$]$^+$ series are represented in Scheme 1.
(The "fast" in the scheme indicates qualitatively the relative rate of each path.) This isomerization scheme is different from that of the [Co(ida)$_2$]$^-$ system,[4] in which the isomerization proceeds through the mer isomer. In the present scheme, it is noteworthy that the inversion at one of two sec-N centers in [Co(edma)$_2$]$^+$ occurs in each isomerization step, except for the E-3→E-1 and E-3→E-2 changes. These experimental results can not be explained by the twist mechanism. The reasons are as follows: In all the isomers containing facially coordinated edma ligands (1) the twisting about the pseudo-C_3 axis passing through the triangle faces of the chelated edma ligands does not result in the inversion at the asymmetric sec-N of the edma ligand and (2) the possible twistings about other pseudo-C_3 axes provide E-3 (mer). (In the *fac*-[Co(edma)$_2$]$^+$ isomers, some of the twisting about the pseudo-C_3 axes is not possible because of the limits of the ligating manner of the linear terdentate edma ligand.) Thus, the isomerization reaction of the [Co(edma)$_2$]$^+$ series should be explained by the Co–O bond-rupture mechanism. (Recently, Baraniak et al. have revealed that the Co–O bond fission occurs in the [Co(β-ala)(en)$_2$]$^+$ ion under alkaline conditions.[19])

When the coordination sites of the O and sec-N atoms of one edma ligand in the *fac*-[Co(edma)$_2$]$^+$ ion are exchanged for one another, the isomerization of the complex and the inversion at the sec-N center occur simultaneously. Such an exchange in *ΛΔΛ*(*S*,*S*)-E-1 leads to *ΔΛΔ*(*R**,*S*)-E-4, corresponding to the (+)$^{CD}_{543}$-E-1→(−)$^{CD}_{534}$-E-4 change in Scheme 1. As E-4 is



Scheme 1.

the C_1 symmetry, the two edma ligands [(A) and (B) in Scheme 1] of E-4 are not equivalent: The sec-N of the (A) edma is in the trans position to the O atom of another edma ligand, while the sec-N of the (B) edma is in the trans position to the terminal N atom of the (A) edma ligand. The exchange of the coordination sites of the ligating sec-N and O atoms in the (A) edma ligand leads to the $(-)^{CD}_{534}$-E-4→$(+)^{CD}_{543}$-E-1 change, while the similar exchange in the (B) edma ligand leads to the $(-)^{CD}_{534}$-E-4→$(-)^{CD}_{521}$-E-5 change. Similarly, the exchange between the coordination sites of the sec-N and O atoms in one edma ligand of the $[Co(edma)_2]^+$ ion is found in the isomerization steps of $(-)^{CD}_{509}$[or $(+)^{CD}_{509}$]-E-6→E-2 and $(-)^{CD}_{521}$-E-5→$(-)^{CD}_{534}$-E-4 (Scheme 1). In the slow isomerization step of E-2⇄$(-)^{CD}_{521}$[or $(+)^{CD}_{521}$]-E-5, an exchange between the coordination sites of the terminal-N and O atoms in one edma ligand can be found. This exchange also results in the inversion at the asymmetric sec-N center.

Deuteration of the sec-NH Proton. The H–D exchange reaction of the two sec-NH protons in $[Co(edma)_2]^+$ was carried out in DCl–D_2O at 80 °C. In the ^1H NMR spectra for all isomers of $[Co(edma)_2]^+$, the two protons of the glycinate-ring (G-ring) $-CH_2-$ of the edma ligand are not equivalent, and the resulting AB system is further coupled to the proton on the adjacent sec-N atom to give an eight-line ABX spectrum. The kinetic data for the *fac*-$[Co(edma)_2]^+$ isomers were obtained by following the collapse of the ABX signal to an AB signal as the sec-NH protons exchange with D^+. The E-4 isomer has two kinds of sec-NH protons depending on the geometrical situation: Sec-NH of (A) and (B) edma in Scheme 1. The signals due to the G-ring $-CH_2-$ of (A) and (B) edma have been assigned in our previous paper.[15] However, this method was not suitable for the H–D exchange reaction of E-3, because the ABX spectrum was observed in a narrow chemical shift region. The rate data of the H–D exchange for E-3 was calculated from the decrease in the sec-NH peak area relative to the total G-ring $-CH_2-$ peak area. The H–D exchange results are collected in Table 3. The rate of the H–D exchange is fast in E-6 and in one of the edma ligands [(A) edma in Scheme 1] of E-4. These sec-NH lie in the position trans to the ligating oxygen atom (trans(O)-sec-NH). In E-3, the H–D exchange rate of sec-NH, which lies in the position trans to the ligating nitrogen atom (trans(N)-sec-NH), is comparable to those of the trans(N)-sec-NH in the fac isomers (Table 3). These results indicate that the H–D exchange rate of sec-NH is affected by the nature of the atom ligating in the trans coordination site rather than by the chelation form of the edma ligand (mer or fac).

Table 3. The H-D Exchange Rates of the Sec-NH Protons of the $[Co(edma)_2]^+$ Ion at 80 °C

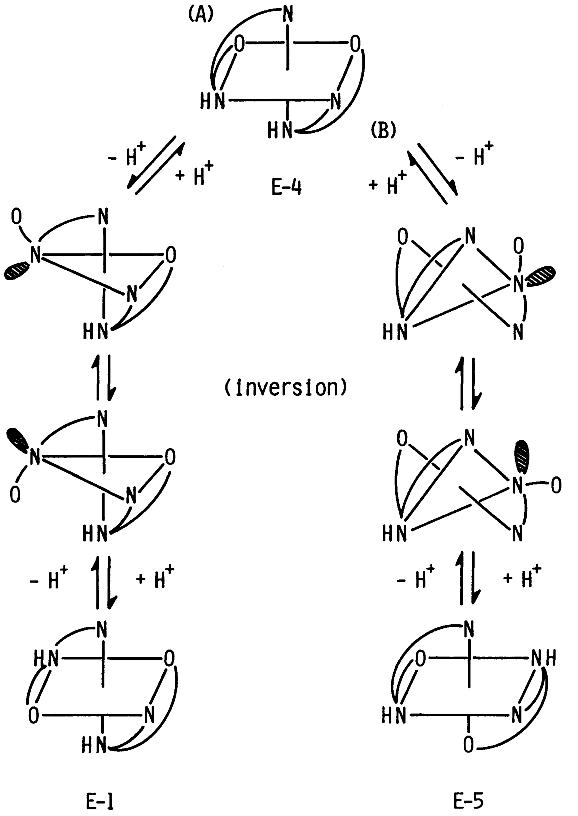
Isomer	$\frac{k'}{10^{-3}\,s^{-1}}$	Isomer	$\frac{k'}{10^{-3}\,s^{-1}}$	Isomer	$\frac{k'}{10^{-3}\,s^{-1}}$
E-1	0.048	E-2	0.050	E-3	0.17
E-4 (A)	1.2	E-5	0.075	E-6	1.4
(B)	0.18				

(A): The position trans to the ligating O atom.
(B): The position trans to the ligating N atom.
Solvent: DCl(0.096 M)-D_2O.

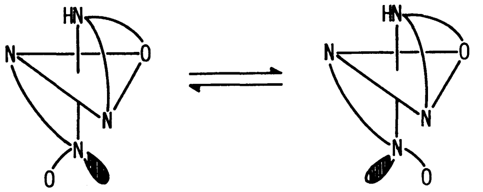
In Scheme 1, each isomerization step (except for E-3→E-1 and E-3→E-2) is shown to be accompanying the inversion at one of two asymmetric sec-N centers. In the slow isomerization paths, such as the E-4⇄E-5 change, the inversion occurs at the trans(N)-sec-N center, accompanied by a slow H–D exchange of the trans(N)-sec-NH proton. On the other hand, in the fast isomerization paths, such as E-4→E-1 and E-6→E-2, the inversion occurs at the trans(O)-sec-N center, accompanied by the fast H–D exchange of the trans(O)-sec-NH proton; a linear relationship can been seen between the rates of the isomerization and the H–D exchange. The isomerization reaction of the $[Co(edma)_2]^+$ complex is base-catalyzed and probably involves a conjugate base intermediate. Even though the $[Co(edma)_2]^+$ complex has more than one potentially acidic amine protons, the reactive conjugate base intermediate should be produced by the deprotonation at the secondary amine, for that deprotonation is essential for the inversion of the configuration about the sec-N center. (In this case, the isomerization rate constant (k_{obsd}) is represented, by using the pre-equilibrium constant (K_{CB}) and the isomerization rate constant of the conjugate base (k_0), as $k_{obsd}=K_{CB}k_0$.) If the H–D exchange rate is taken as a criterion for the degree of the deprotonation of the sec-NH proton (acidity),[20] it is probable that the acidity of the sec-NH is reflected in the difference in the isomerization rate for this series of complexes.

All the experimental data for the reactions of the $[Co(edma)_2]^+$ series are most satisfactorily accommodated by the proposal of transient five-coordinated intermediates formed by Co–O bond rupture. In the Co–O bond-ruptured state, the inversion at the sec-N of "bidentate edma" can be expected to occur easily under the present experimental conditions (40 °C, pH 10.35), judging from the inversion data of the cobalt(III) complexes containing *N*-methylethylenediamine or sarcosine as a ligand.[21–24] For the isomerization of E-4, the mechanism shown in Scheme 2 may be proposed. A similar reaction scheme may be presumed for the other isomerization process in Scheme 1. However, the postulated intermediate in the E-2⇄E-5 path may be pictured as Scheme 3, because, in this isomerization, an exchange between the coordination sites of the terminal-N and O atoms in one edma ligand occurs.

For E-3, which contains meridionaly coordinated edma, the rate of the H–D exchange at the sec-N



Scheme 2.



Scheme 3.

position is relatively slow, but the rate of the isomerization is relatively fast compared with those of the fac isomers (Tables 2 and 3); the result found for E-3 is different from those obtained in the fac isomers, in which "linear relationships" between the rates of the H–D exchange and isomerization reactions are observed. This may be attributed to the fact that the mer structure of an coordinated edma is thermodynamically less stable as a result of the strain on its mer chelate ring form. This unstability may be one of the reasons for the relatively rapid isomerization of E-3.

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