April, 1990] Bull. Chem. Soc. Jpn., 63, 1111—1114 (1990)

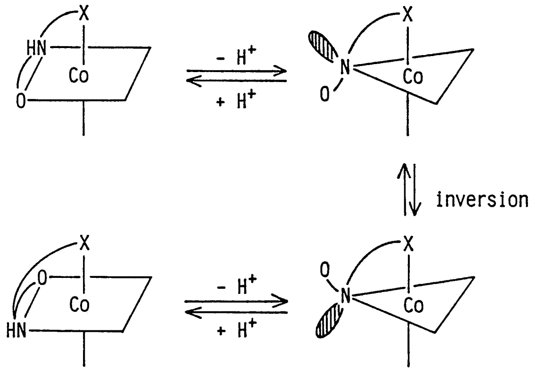
# Stereoselective Isomerization and Racemization of (*N*-Methyliminodiacetato)(ethylenediamine-*N*-acetato)cobalt(III), [Co(mida)(edma)], in a Basic Aqueous Solution

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

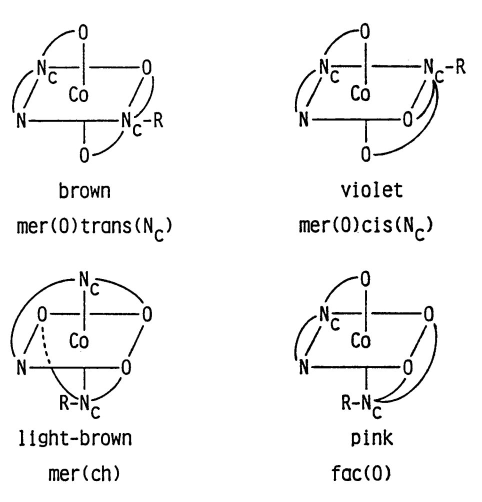
(Received September 13, 1989)

Isomerization reactions of four geometrical isomers (pink, violet, brown, and light-brown) of [Co(mida)(edma)] were studied in a basic aqueous solution. In a reaction of the $(-)^{\mathrm{CD}}_{565}$-pink isomer, two isomers of $(-)^{\mathrm{CD}}_{561}$-brown and racemic light-brown formed simultaneously. The light-brown isomer isomerized mainly to the brown isomer. In reactions of the $(+)^{\mathrm{CD}}_{572}$-violet and $(+)^{\mathrm{CD}}_{561}$-brown isomers, the formations of other isomers were not observed but the racemizations occurred. The racemization reaction of the $(+)^{\mathrm{CD}}_{572}$-violet isomer proceeded at a considerable rate. These reactions are discussed in connection with those for the [Co(ida)(edma)] system.

Previously, we studied the base-catalyzed isomerization reaction of the [Co(ida)(edma)] system (ida= iminodiacetate dianion: edma=ethylenediamine-*N*-acetate anion) and found that the reaction was stereoselective.[1] In order to interpret the stereoselectivity, we proposed a bond-rupture mechanism as shown in Scheme 1; the coordination sites were exchanged between the secondary nitrogen (sec-N) and carboxylato oxygen (O) atoms of the coordinated edma or ida ligand, and consequently, the asymmetry at the sec-N center was inverted in the case of the edma ligand.



Scheme 1.



brown
mer(O)trans(N$_C$)

violet
mer(O)cis(N$_C$)

light-brown
mer(ch)

pink
fac(O)

Fig. 1. Four geometrical, isomers of [Co(mida)(edma)] ($R=CH_3$) and [Co(ida)(edma)] (R=H). $N_c$ denotes a central nitrogen.

Table 1. Possible Configurations and CD Signs of [Co(mida) (edma)]

| Geometrical isomer | Possible configuration and CD sign | |
|---|---|---|
| *mer*(*O*)*trans*(*N*c)<br>(brown) | $(+)^{\mathrm{CD}}_{561}$-$\Lambda\Delta(S)$ | $(-)^{\mathrm{CD}}_{561}$-$\Delta\Lambda(R)$ |
| *mer*(*O*)*cis*(*N*c)<br>(violet) | $(+)^{\mathrm{CD}}_{572}$-$\Lambda\Delta\Lambda(S)$ | $(-)^{\mathrm{CD}}_{572}$-$\Delta\Lambda\Delta(R)$ |
| *fac*(*O*)<br>(pink) | $(-)^{\mathrm{CD}}_{565}$-$\Delta\Lambda\Delta(S)$ | $(+)^{\mathrm{CD}}_{565}$-$\Lambda\Delta\Lambda(R)$ |

*R* or *S* denotes the chirality around the asymmetric nitrogen.

If the mechanism described above is adequate, some of the reaction paths in the [Co(ida)(edma)] system should be excluded in the [Co(mida)(edma)] system (mida=*N*-methyliminodiacetate dianion); the inversion at the tertiary N center of the coordinated mida ligand is impossible. In this paper, we describe the isomerization reaction of the [Co(mida)(edma)] system, which is discussed on the basis of the previous study[1] on the related complexes. Four possible geometrical isomers of [Co(mida)(edma)] (Fig. 1) have been separated, and the absolute configurations of three isomers containing facially coordinated ligands have also been determined as shown in Table 1.[2]

## Experimental

**Complexes and Reagents.** The complexes examined here were prepared and optically resolved according to the method described in our previous paper.[2] They are $(+)^{\mathrm{CD}}_{561}$-*mer*(*O*)*trans*(*N*c)-[Co(mida)(edma)]·$H_2O$ (abbreviation: $(+)^{\mathrm{CD}}_{561}$-brown), $(+)^{\mathrm{CD}}_{572}$-*mer*(*O*)*cis*(*N*c)-[Co(mida)(edma)]·$H_2O$ (($(+)^{\mathrm{CD}}_{572}$-violet), $(-)^{\mathrm{CD}}_{565}$-*fac*(*O*)-[Co(mida)(edma)]·$2H_2O$ (($(-)^{\mathrm{CD}}_{565}$-pink), and *mer*(*ch*)-[Co(mida)(edma)]·$1.5H_2O$ (light-brown). All the chemicals used were of a reagent grade, and the deionized water was degassed before use.

**Isomerization. $(-)^{\mathrm{CD}}_{565}$-Pink Isomer:** The isomer (0.3158g) was dissolved in 160.0 cm$^3$ of water in a reaction vessel kept in a thermostated bath at 40.0 °C. The reaction was started by stirring 100.0 cm$^3$ of a buffer solution [$Na_2CO_3$(0.1102 g)-$NaHCO_3$(0.7863 g)/water(100.0 cm$^3$)] previously kept at 40.0 °C into the reaction vessel. The reaction conditions were as follows: Complex concentration, $3.4\times10^{-3}$ M (M=mol dm$^{-3}$); pH, 9.17±0.02; temperature, 40.0±0.1 °C. The temperature and pH of the reaction solution were checked with a thermistor thermometer (Takara D221) and a pH meter (Toa TSC-10A), respectively, throughout the kinetic run. At prescribed time intervals, a constant volume (40.0 cm$^3$) of the reaction solution was taken out and acidified to pH 5 with 1 M HCl in order to stop the reaction. The acidified solution was concentrated under reduced pressure at 35—40 °C and then chromatographed on a column (2.8 cm×40 cm) of SP-Sephadex C-25 ($K^+$ form) using water as an eluent. Two bands, el 1 (a mixture of the brown and light-brown isomers)[3] and el 2 (the pink isomer), were separated. (It was confirmed in a preliminary large scale experiment using a long column that the violet isomer was not formed from the pink isomer.) The two eluates were collected separately and concentrated to appropriate constant volumes. The amount and optical purity of each isomer were determined from absorption and CD data measured by a Hitachi 557 spectrophotometer and a JASCO J-22 spectropolarimeter, respectively. The amounts of the two isomers in el 1 were estimated from binary-curve analysis of the absorption spectrum. In this curve analysis, the spectral data at 20 points in the visible region were used; the analysis was carried out on an NEC PC-9801F computer using a least-squares method.

**$(+)^{\mathrm{CD}}_{572}$-Violet, $(+)^{\mathrm{CD}}_{561}$-Brown, and Light-Brown Isomers:** The isomerization reactions of the $(+)^{\mathrm{CD}}_{572}$-violet and $(+)^{\mathrm{CD}}_{561}$-brown isomers were attempted by a procedure similar to that used for the $(-)^{\mathrm{CD}}_{565}$-pink isomer. The reaction conditions were pH 10.31 (carbonate buffer) and 40.0 °C. As the light-brown isomer was isolated in only a small amount, the method described above could not be used for the reaction of this isomer. The light-brown isomer (0.0118 g) was dissolved in 10 cm$^3$ of a carbonate buffer solution (pH 10.35) at 40.0 °C, and then the absorption spectral change of the solution was followed using a thermostated cell. The absorption spectra obtained in suitable time intervals were analyzed as a binary system of the light-brown and brown isomers. In weak acidic and neutral solutions at room temperature, the absorption and CD spectral changes of all the isomers were very slow. Therefore, the progress of the isomerization and/or racemization reaction during such procedures as chromatographic separation and concentration under reduced pressure was ignored.

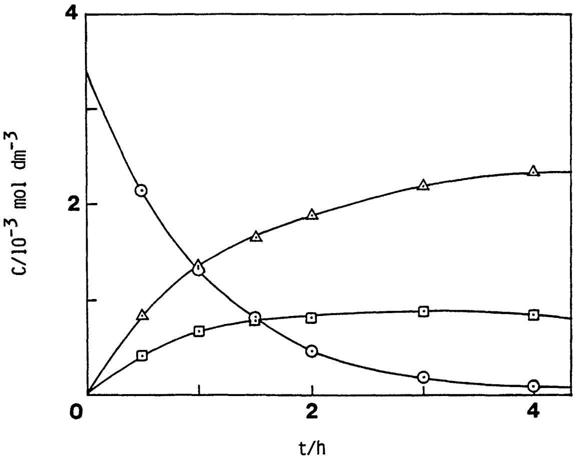


Fig. 2. The isomerization reaction of $(-)^{\mathrm{CD}}_{565}$-pink in a basic aqueous solution (pH 9.17) at 40.0 °C; pink (—○—), brown (—△—), and light-brown (—□—).

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

(i) $(-)^{\mathrm{CD}}_{565}$-Pink (pH 9.17)

| | Concn/10$^{-3}$ mol dm$^{-3}$ (optical purity/%) | | | | |
|---|---|---|---|---|---|
| | 0.5 h | 1 h | 1.5 h | 2 h | 4 h |
| $(-)^{\mathrm{CD}}_{565}$-Pink(*S*) | 2.14 | 1.32 | 0.82 | 0.46 | 0.08 |
| | (98) | (98) | (98) | (92) | (70) |
| $(-)^{\mathrm{CD}}_{561}$-Brown(*R*) | 0.82 | 1.36 | 1.63 | 1.88 | 2.33 |
| | (91) | (87) | (87) | (80) | (73) |
| Light-brown | 0.41 | 0.66 | 0.78 | 0.79 | 0.84 |

(ii) $(+)^{\mathrm{CD}}_{572}$-Violet (pH 10.31)

| | Concn/10$^{-3}$ mol dm$^{-3}$ (optical purity/%) | | | | |
|---|---|---|---|---|---|
| | 1.5 h | 3 h | 6 h | 12 h | 30 h |
| $(+)^{\mathrm{CD}}_{572}$-Violet(*S*) | 2.83 | 2.53 | 2.01 | 1.42 | 0.64 |
| | (52) | (28) | ( 9) | ( 1) | ( 0) |

(iii) $(+)^{\mathrm{CD}}_{561}$-Brown (pH 10.31)

| | Concn/10$^{-3}$ mol dm$^{-3}$ (optical purity/%) | | | |
|---|---|---|---|---|
| | 2 h | 10 h | 20 h | 80 h |
| $(+)^{\mathrm{CD}}_{561}$-Brown(*S*) | 3.31 | 3.29 | 3.25 | 2.86 |
| | (84) | (78) | (74) | (52) |

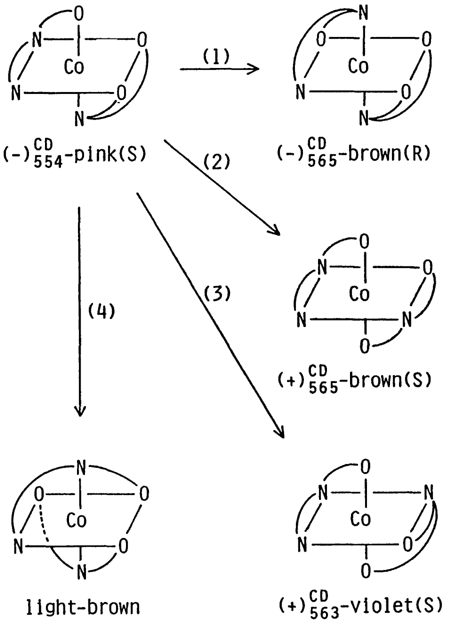
(vi) Light-brown (pH 10.35)

| | Concn/10$^{-3}$ mol dm$^{-3}$ | | | |
|---|---|---|---|---|
| | 1 h | 2 h | 3 h | 4 h |
| Light-brown | 2.68 | 2.07 | 1.75 | 1.43 |
| Brown | 0.72 | 1.33 | 1.65 | 1.95 |

## Results and Discussion

**Base-Catalyzed Isomerization Reaction. $(-)^{\mathrm{CD}}_{565}$-Pink Isomer:** The isomerization rate of the $(-)^{\mathrm{CD}}_{565}$-pink isomer was too fast under the conditions of pH 10.31 and 40.0 °C to follow by the present experimental method. Therefore, the pH was set at 9.17 for this isomer only. Figure 2 shows the concentration changes of the starting material and reaction products. The numerical data are listed in Table 2, together with the enantiomer excess percentage of each isomer. In this reaction, the optically active brown ($(-)^{\mathrm{CD}}_{561}$ form) and racemic light-brown isomers were formed simultaneously. Throughout the reaction, the violet isomer and by-products were not detected by the present experimental method. The $(-)^{\mathrm{CD}}_{565}$-pink isomer (starting material) decreased in amount with retention of the high optical purity. This fact indicates that virtually no racemization of the $(-)^{\mathrm{CD}}_{565}$-pink isomer occurs. The $(-)^{\mathrm{CD}}_{561}$-brown isomer formed from the $(-)^{\mathrm{CD}}_{565}$-pink isomer showed a high optical purity, indicating that the isomerization path of $(-)^{\mathrm{CD}}_{565}$-pink isomer→$(-)^{CD}_{561}$-brown isomer is highly stereoselective. The light-brown isomer formed in the reaction was a racemate. However, it is not clear whether the $(-)^{CD}_{565}$-pink→light-brown change is stereoselective or not. Even though the change is stereoselective, the optically active light-brown isomer formed from the $(-)^{CD}_{565}$-pink isomer is considered to racemize very rapidly under the present reaction conditions, judging from the racemization rates of *mer*-[Co(ida)(dien)]$^+$,[4] *mer*-[Co(edma)(dien)]$^{2+}$,[5] and *mer*-[Co(dien)$_2$]$^{3+}$.[6] The gradual decreases in optical purity of the $(-)^{CD}_{565}$-pink and $(-)^{CD}_{561}$-brown isomers with the passage of time may be attributed to the reverse paths from the racemic light-brown isomer to the pink and brown isomers.

In the isomerization reaction of the $(-)^{CD}_{565}$-pink isomer (*ΔΛΔ*(*S*)-*fac*(*O*)-[Co(mida)(edma)]), two isomers of $(-)^{CD}_{561}$-brown (*ΔΛ*(*R*)-*mer*(*O*)*trans*($N_c$)) and racemic light-brown (*mer*(*ch*)) were simultaneously formed. While, in the case of the [Co(ida)(edma)] system, the $(-)^{CD}_{554}$-pink isomer (*ΔΛΔ*(*S*)-*fac*(*O*)) isomerized to three isomers of $(+)^{CD}_{563}$-violet (*ΛΔΛ*(*S*)-*mer*(*O*)*cis*($N_c$)), $(+)^{CD}_{565}$-brown (*ΛΔ*(*S*)-*mer*(*O*)*trans*($N_c$)) with a low optical purity, and racemic light-brown (*mer*(*ch*)). The results for the $(-)^{CD}_{554}$-pink isomer of the ida complex have been explained by the simultaneous occurrence of four paths in Scheme 2:[2] The three paths, (1)—(3), are proposed by considering the mechanism of Scheme 1, and path (4) is proposed on the basis of the assumption that the reaction proceeds by a process similar to that for the [Co(ida)$_2$]$^-$ system, where the reaction scheme is *u-fac*⇄*mer*⇄*s-fac*.[7] If the isomerization reaction of the $(-)^{CD}_{565}$-pink isomer of the mida complex proceeds according to the same mechanisms as those for the ida complex, such paths as (2) and (3) in Scheme 2 would be excluded. These paths require the inversion at the tertiary N center of the mida ligand, but such inversion is impossible. Accordingly, the $(-)^{CD}_{565}$-pink isomer of the mida complex is expected to form the $(-)^{CD}_{561}$-brown and racemic light-brown isomers. The experimental results are well explained by the systems described above.

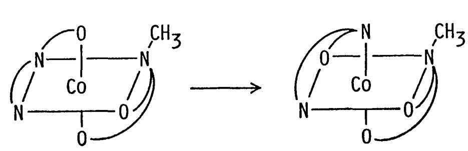


Scheme 2. Isomerization of the $(-)^{CD}_{554}$-pink isomer of [Co(ida)(edma)].

**$(+)^{CD}_{572}$-Violet, $(+)^{CD}_{561}$-Brown, and Light-Brown Isomers:** The reaction of the $(+)^{CD}_{572}$-violet isomer was followed over a period of 30 h under the conditions of pH 10.31 and 40.0 °C. When the acidified reaction solution was chromatographed on an SP-Sephadex column (K$^+$ form), the hydrolysis products were adsorbed on the top of the column, and only one band was eluted with water. The absorption and CD spectral patterns of the eluate were consistent with those of the $(+)^{CD}_{572}$-violet isomer; no other isomers were observed. Some of the data are listed in Table 2. The optical purity of the $(+)^{CD}_{572}$-violet isomer decreased more rapidly compared with the rate of its concentration decrease; the $(+)^{CD}_{572}$-violet isomer racemized at a considerable rate. This racemization indicates that the coordination site exchange occurred between the sec-N and O atoms of the edma ligand as shown in Scheme 3. In the case of the [Co(ida)(edma)] system, the $(+)^{CD}_{563}$-violet isomer isomerized to the $(+)^{CD}_{565}$-brown and $(-)^{CD}_{554}$-pink isomers in addition to the racemization of itself. This difference is also explained by the same idea as is used in the case of the $(-)^{CD}_{565}$-pink isomer.

The isomerization study of the $(+)^{CD}_{561}$-brown isomer was also attempted under the same conditions as used for the violet isomer. When the reaction solution was chromatographed on an SP-Sephadex column, only one band was eluted with water. This indicates that the pink and violet isomers were not formed. The absorption and CD spectral patterns of the eluate almost coincided with those of the starting $(+)^{CD}_{561}$-brown isomer. To make sure that no other isomers were formed from the brown isomer, the absorption curve of the eluate was analyzed as a curve of a mixture of the brown and light-brown isomers.[8] However, throughout the reaction, the amount of the light-brown isomer was less than 1% of that of the brown isomer, indicating that the formation of the light-brown isomer may be ignored. Some of the data are listed in Table 2.

The isomerization study of the light-brown isomer could not be carried out in the same manner as that for the other isomers, since the preparation of this isomer



Scheme 3.

was very difficult. Accordingly, the absorption spectral change of the light-brown isomer was followed under the conditions of pH 10.35 and 40.0 °C. The intensity of the absorption curve decreased with the passage of time, but the peak position of the 1st d-d band changed little. This spectral change suggests that the light-brown isomer mainly isomerizes to the brown isomer and that the pink and violet isomers may be formed in small amounts.[8)] The concentration changes of the light-brown and brown isomers were estimated from the binary-curve analysis of each absorption spectrum at the prescribed time. Some of the data are listed in Table 2.

The major reaction paths of the [Co(mida)(edma)] system are as follows: (1) $(-)^{\mathrm{CD}}_{565}$-pink isomer→$(-)^{\mathrm{CD}}_{561}$-brown isomer, (2) $(+)^{\mathrm{CD}}_{572}$-violet isomer⇄$(-)^{\mathrm{CD}}_{572}$-violet isomer, and (3) pink isomer→light-brown isomer→brown isomer. These paths are also explained by the mechanism proposed for the [Co(ida)(edma)] system; the coordination site exchange between the sec-N and O atoms in the terdentate ligand (Scheme 1) and the $[\mathrm{Co(ida)_2}]^-$ type process.[7)] The reaction due to the mechanism of Scheme 1 occurs easily only when the sec-N atom of the edma ligand is trans to the ligating O atom. The same tendency has been observed in the [Co(ida)(edma)][1)] and $[\mathrm{Co(edma)_2}]^+$[9)] systems. The [Co(mida)(edma)] system seems to be more labile than the [Co(ida)(edma)] system. This may be attributed to the electron donative effect of the $\mathrm{CH_3}$ group. A similar effect was observed in the reactions of the other Co(III) terdentate-ligand complexes.[4,7)]

## References

1) H. Kawaguchi, H. Miyamoto, T. Ama, and T. Yasui, *Bull. Chem. Soc. Jpn.*, **62**, 1065 (1989).

2) T. Ama, R. Niiyama, H. Kawaguchi, and T. Yasui, *Bull. Chem. Soc. Jpn.*, **60**, 119 (1987).

3) It was also confirmed from $^1$H NMR spectral data that el 1 contained brown and light-brown.

4) H. Kawaguchi, M. Shimizu, T. Ama, and T. Yasui, *Bull. Chem. Soc. Jpn.*, **62**, 753 (1989).

5) H. Kawaguchi, H. Fukaki, T. Ama, T. Yasui, K. Okamoto, and J. Hidaka, *Bull. Chem. Soc. Jpn.*, **61**, 2359 (1988).

6) G. H. Searle and F. R. Keene, *Inorg. Chem.*, **11**, 1006 (1972).

7) H. Kawaguchi, T. Ama, and T. Yasui, *Bull. Chem. Soc. Jpn.*, **57**, 2422 (1984).

8) The 1st d-d band peaks of brown and light-brown are close to each other. The 1st d-d band [$\lambda_{\max}$/nm (log $\varepsilon$)]: brown, 562 (sh), 492 (1.73); light-brown, 495 (2.30); violet, 550 (2.00), 476 (sh); pink, 529 (2.13).

9) H. Kawaguchi, R. Niiyama, T. Ama, and T. Yasui, *Bull. Chem. Soc. Jpn.*, **60**, 3953 (1987).