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Stereochemistry of the (Iminodiacetato or *N*-Methyliminodiacetato)-(ethylenediamine-*N*-acetato)cobalt(III) Complexes

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Four geometrical isomers of [Co(mida)(edma)] were prepared in the first time and their structures were determined on the basis of their visible and UV absorption spectral data. Three of the isomers were optically resolved by the use of a column containing QAE-Sephadex of the $Sb_2(d\text{-tart})_2^{2-}$ form. Absolute configurations of the facially chelated isomers of [Co(mida)(edma)] were determined by measuring the ^1H NMR spectra of the optically resolved isomers with an asymmetric carbon-containing edma (obtained from the stereospecifically deuterated $(-)^{\rm CD}_{543}$ C_2-*trans*(O)-$[Co(edma)_2]^{2+}$). Absolute configuations of the facially chelated isomers of [Co(ida)(edma)] were determined on the basis of their CD spectral data.

Either [Co(ida)(edma)] or [Co(mida)(edma)] (ida= iminodiacetato; edma=ethylenediamine-*N*-acetato; and mida=*N*-methyliminodiacetato) provides four geometrical isomers,[1] as shown in Fig. 1. In the present paper, chromatographic methods to separate and to resolve the isomers of [Co(ida)(edma)] and [Co(mida)-(edma)] which are uncharged complexes will be described.

The absolute configuration of the complex containing edma is closely related to the chirality of the asymmetric nitrogen arising from coordination of the ligand. The determination of the chirality of the asymmetric nitrogen make it possible to determine the absolute configuration of the edma chiral complex. On this basis, a ^1H NMR method to determine the absolute configurations of the isomers of $[Co(edma)_2]^+$ was reported in the previous paper.[2] In the present paper, we report on a modification of the method to determine the absolute configurations, which was applied to the isomers of [Co(mida)(edma)].

Experimental

Ligands. *N*-Methyliminodiacetic acid (H_2mida) and ethylenediamine-*N*-acetic acid (Hedma) were synthesized as described in the previous papers.[3—5]

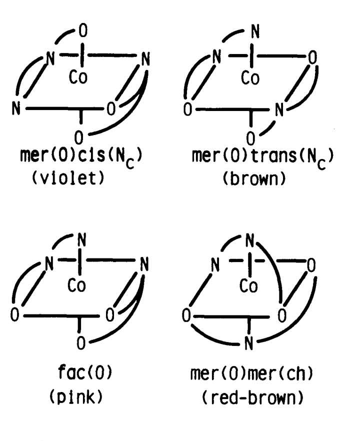

Fig. 1. The four geometrical isomers of [Co(ida)-(edma)] or [Co(mida)(edma)].

Preparation of the Complexes. Four Geometrical Isomers of the [Co(mida)(edma)] Complexes: A solution containing 2.4 g of $CoCl_2\cdot 6H_2O$, 1.5 g of *N*-methyliminodiacetic acid (H_2mida) and 2.3 g of ethylenediamine-*N*-acetic acid dihydrochloride dihydrate (Hedma·2HCl·$2H_2O$) in 100 cm^3 of water was adjusted to pH 5 with a 2 mol dm^{-3} NaOH solution. The pH being kept constant at 5, 24 g of PbO_2 was stirred into the solution in small portions at 30 °C. After 1 h, the insoluble materials were removed by filtration. A solution containing neutral complexes was obtained by passing the filtrate through a QAE-Sephadex (SO_4^{2-} form) column and then an SP-Sephadex (K^+ form) column (eluent: water). This solution was evaporated to about 10 cm^3 and poured onto an SP-Sephadex (K^+ form) column. A band adsorbed on the column was separated into three parts by recyclic development with water: the first was an overlapped band (brown and red-brown); the second a violet band; and the third a pink band. Crude violet crystals were obtained by addition of methanol to the concentrated solution of the second eluant. Crude pink crystals were obtained by the same method as for the violet crystals. The solution obtained from the first part was acidified with a few drops of acetic acid and then concentrated under reduced pressure. Methanol was added to the concentrated solution. Brown crystals (unresolved) were deposited and were filtered off. The filtrate was evaporated almost to dryness to remove methanol and diluted with a small amount of water. The solution was repeatedly developed on a QAE-Sephadex column ($Sb_2(d\text{-tart})_2^{2-}$ form; eluent: water), $(+)^{\rm CD}_{561}$-brown (resolved; trace amount), red-brown (unresolved), and $(-)^{\rm CD}_{561}$-brown band (resolved; trace amount) were separated (in the order of elution). The red-brown eluant (acidified with acetic acid) was concentrated under reduced pressure, and then acetone was added to the concentrated solution to obtain crude red-brown crystals. Each of the brown (unresolved), violet, and pink isomers was recrystallized from water by adding methanol and the red-brown isomer was next recrystallized from methanol by adding acetone. Yields of the isomers: the brown (unresolved), 420 mg; the violet, 650 mg; the red-brown, 10 mg; and the pink, 130 mg. Anal. Found for the brown isomer: C, 30.92; H, 5.64; N, 12.10%. Found for the red-brown isomer: C, 31.07; H, 5.46; N, 11.94%. Calcd for [Co(mida)(edma)]·$1.5H_2O$=$C_9H_{19}N_3O_{7.5}Co$: C, 31.05; H, 5.50; N, 12.07%. Found for the violet isomer: C, 31.74; H, 5.33; N, 12.31%. Calcd for [Co(mida)(edma)]·H_2O=$C_9H_{18}N_3O_7Co$: C, 31.87; H, 5.35;

N, 12.39%.

Four Geometrical Isomers of [Co(ida)(edma)]: These isomers were prepared according to the method reported in the previous paper.[1)]

Optical Resolution. Isomers of [Co(ida)(edma)]: The racemic brown isomer of [Co(ida)(edma)] (ca. 50 mg) was dissolved in a small amount of warm water. The solution was poured onto a QAE-Sephadex column ($Sb_2(d\text{-}tart)_2^{2-}$ form, 3.7 cm×70 cm) and the adsorbed band developed with water. Developing was repeated on the same column using a micropump until the adsorbed band completely separated into two bands (recycle-times: 2). The earlier eluted isomer was $(+)^{\mathrm{CD}}_{565}$ and the later eluted was $(-)^{\mathrm{CD}}_{565}$. Each eluting solution from the two bands was concentrated to a small volume under reduced pressure at 35—40 °C. A crude complex was obtained by adding methanol to the concentrated solution: it was recrystallized from water by addition of methanol. The violet isomer of [Co(ida)(edma)] was resolved by the same method as that described above (recycle-times: 4). The earlier eluted isomer was $(+)^{\mathrm{CD}}_{563}$ and the later eluted was $(-)^{\mathrm{CD}}_{563}$. Though the pink isomer was chromatographed by the same method as that described for the brown isomer, the adsorbed band of the isomer was not separated into two bands upon 40 recycle-times. However, the faster eluted part showed (−) CD sign at 554 nm and the later one did (+). Fine needle crystals were obtained by adding methanol to each of the concentrated solutions. Found for $(+)^{\mathrm{CD}}_{565}$ brown isomer: C 31.20; H, 4.55; N, 13.74%. Calcd for [Co(ida)(edma)]=$C_8H_{14}N_3O_6Co$: C, 31.28; H, 4.59; N, 13.68%. Found for $(+)^{\mathrm{CD}}_{563}$ violet isomer: C, 29.41; H, 5.05; N, 12.89%. Calcd for [Co(ida)(edma)]·H_2O: C, 29.55; H, 4.96; N, 12.92%.

Isomers of [Co(mida)(edma)]: The brown and pink isomers of [Co(mida)(edma)] were resolved by the same method as that used for [Co(ida)(edma)]. The recycle times to attain complete separation of the enantiomers of the brown isomers were 5 and those of the pink isomer were 8. The earlier eluted bands of the brown and pink isomers showed (+) CD sign at 561 nm and at 565 nm, respectively. The resolution of the violet isomer was incomplete on the chromatograph using a QAE-Sephadex column ($Sb_2(d\text{-}tart)_2^{2-}$ form). However, it separated into enantiomers by 15 times recyclic development on a Sephadex G-10 column. Found for $(+)^{\mathrm{CD}}_{561}$ brown isomer: C, 31.79; H, 5.51; N, 12.39%. Found for $(-)^{\mathrm{CD}}_{572}$ violet isomer: C, 31.84; H, 5.35; N, 12.34%. Calcd for [Co(mida)(edma)]·H_2O=$C_9H_{18}N_3O_7Co$: C, 31.87; H, 5.35; N, 12.39%. Found for $(+)^{\mathrm{CD}}_{565}$ pink isomer: C, 30.22; H, 5.70 N, 11.77%. Calcd for [Co(mida)(edma)]·$2H_2O$: C, 30.26; H, 5.64; N, 11.76%.

Determination of the Absolute Configuration of [Co(mida)(edma)]. A buffer solution (pH 10) was prepared by adding a suitable amount of 2 mol dm^{-3} DCl–D_2O to a solution containing 530 mg of Na_2CO_3 in 50 cm^3 of D_2O. About 1.0 g of $(-)^{\mathrm{CD}}_{543}$ ($\Delta\Lambda\Delta$(N_R,N_R)) C_2-*trans*(O)-$[Co(edma)_2]Cl\cdot 2H_2O$[2)] was dissolved into the buffer solution. The stereospecific deuteration reaction on the coordinating edma was allowed to proceed (40 °C, 25 min) and then stopped as described in the previous paper[1)] (being adjusted the pH of the solution to 5 by addition of 1 mol dm^{-3} HCl). The complex solution was mixed with 10 g of zinc powder to reduce the central cobalt(III) and the mixture was stirred for 5 min. After the excess of zinc was filtered off, 0.64 g of $CoCl_2\cdot 6H_2O$ and 0.79 g of H_2mida were added to the filtrate and then the pH of the solution was adjusted to 5 with 2 mol dm^{-3} NaOH solution. After 15 g of PbO_2 was added to the solution, the mixture was stirred for 30 min at room temperature and the reactant solution was filtered. The filtrate was treated on a column chromatograph as described for separation of the racemic isomers of [Co(mida)(edma)]. Each facially chelated isomer so obtained was resolved into enantiomeric isomers by the chromatographic method described in the previous section. The ^1H NMR spectra of these isomers are illustrated in Fig. 5.

Spectral Measurements. The visible and UV absorption and CD spectra were recorded on a Hitachi 557 spectrophotometer and a JASCO J-22 spectropolarimeter in aqueous solutions, respectively. ^1H NMR spectra were recorded on a JEOL MH-100 spectrometer using DSS as an internal standard in D_2O or 0.1 mol dm^{-3} DCl–D_2O solutions.

Results and Discussion

Structural Assignments for the Isomers of [Co(mida)(edma)]. Each of the [Co(ida)(edma)] and [Co(mida)(edma)] complexes provides four geometrical isomers, as shown in Fig. 1. The structural assignments for the geometrical isomers of the former complex have been reported in the previous paper:[1)] violet, *mer*(O)*cis*(N_c); brown, *mer*(O)*trans*(N_c); red-brown, *mer*(O)*mer*(ch); and pink, *fac*(O). The isomeric structures of the latter complex can be assigned by comparing their absorption spectra with those of the isomers of [Co(ida)(edma)]: violet, *mer*(O)*cis*(N_c); brown, *mer*(O)*trans*(N_c); red-brown, *mer*(O)*mer*(ch); and pink, *fac*(O) (Figs. 2 and 3). These assignments are also supported by the observation that the CD spectral behavior of an isomer of [Co(ida)(edma)] is similar to that of the corresponding isomer of [Co(mida)(edma)] (vide infra).

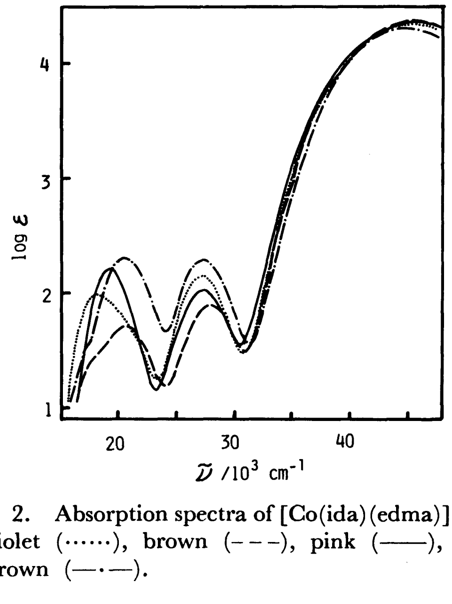

Fig. 2. Absorption spectra of [Co(ida)(edma)] in water: violet (······), brown (– – –), pink (——), and red-brown (—·—).

^{1}H NMR Spectra. Table 1 shows the ^{1}H NMR data of the glycinate methylene protons of the edma complexes. The ^{1}H NMR spectra of the isomers which contain facially coordinating edma were measured in 0.1 mol dm^{-3} DCl–D$_2$O and in D$_2$O. The glycinate-ring (G-ring) signal for each isomer was observed as four peaks (an AB quartet) in D$_2$O, but it appeared as eight peaks in DCl because of the $J_{\mathrm{H_a,H_b}}$, $J_{\mathrm{N\text{-}H,H_a}}$, and $J_{\mathrm{N\text{-}H,H_b}}$ couplings (Table 1). The $J_{\mathrm{N\text{-}H,H_b}}$ and $J_{\mathrm{N\text{-}H,H_a}}$ values are ca. 8 Hz's (for the peaks at lower field) and 1 Hz's (for those at higher field), respectively. On the basis of the Karplus equation,[6] the following assignments are possible: the dihedral angles of the proton resonating at higher field against the N–H proton ($\underline{\mathrm{H}}$-C-N-H) is about 90°, and the proton can be assigned to H$_a$ (inside; Fig. 4 (A)). The angle of the proton (which is assigned to H$_b$ (outside)) resonating at lower field is about 30°. Similar assignments for the G-ring methylene protons have been made for the isomers of $[\mathrm{Co(edma)_2}]^{2+}$[2] and for edda-Co(III) complexes.[7,8] When the N–H proton on the facially coordinating edma was deuterated, the signal of the G-ring methylene protons appeared as an AB quartet.

The G-ring methylene protons in the facially coordinating edma are known to be stereospecifically deuterated.[2,9–13] A new singlet appeared between the two higher-field peaks of the AB quartet, with intensity loss of the AB quartet. In other words, the deuteration rates are different between the two protons; the deuteration of the higher-field proton is much slower than that of the lower-field one. (The new singlet signal disappeared after a long period). Sudmeier and Occupati[9] found that the deuteration of the inside proton of the facial G-ring is slower than that of the outside proton for the edda-Co(III) complexes. The application of this to the present edma complexes leads to the conclusion that the two lower-field peaks of the AB quartet arise from the outside proton which is easily deuterated, while the two higher field peaks arise from the inside proton. These assignments are consistent with those made by the Karplus equation mentioned above.

Correlation between the Absolute Configuration Around the Cobalt Center and the Chirality of Asymmetric Nitrogen. When the edma ligand coor-

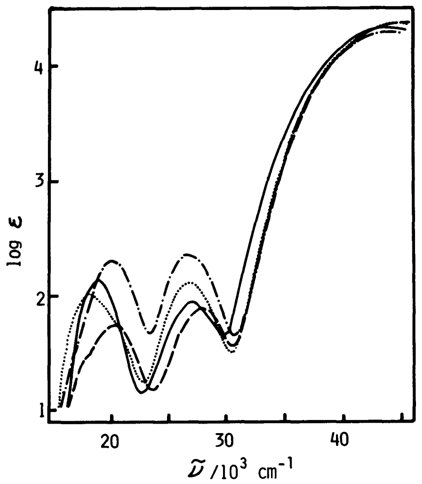

Fig. 3. Absorption spectra of [Co(mida)(edma)] in water: violet (······), brown (– – –), pink (——), and red-brown (—·—).

Table 1. ^{1}H NMR Data of the G-Ring Protons of edma in the [Co(mida)(edma)] Complexes

Geometrical Isomer	δ		$J_{\mathrm{H_a,H_b}}$ /Hz	$J_{\mathrm{N\text{-}H,H_a}}$ /Hz	$J_{\mathrm{N\text{-}H,H_b}}$ /Hz
	H$_a$	H$_b$			
mer(O)*cis*(N$_c$)	3.18	4.14	18	0	8
mer(O)*trans*(N$_c$)	3.40	4.22	18	0	8
fac(O)	3.15	4.00	18	2	9
mer(O)*mer*(ch)	3.84	3.84	—	7	9

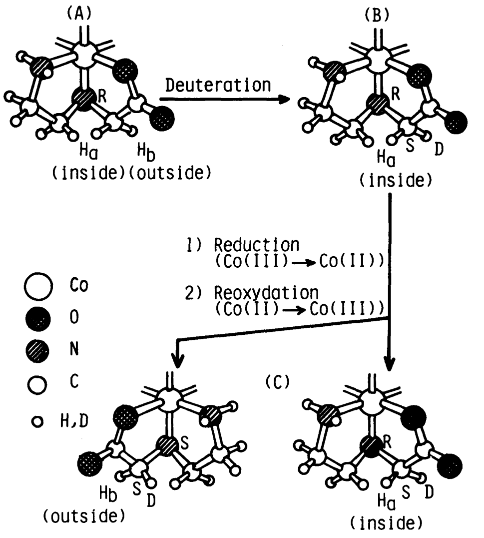

Fig. 4. Chemical environment of the facially coordinating edma. (A): undeuterated, (B): deuterated, and (C): reprepared by oxydizing the reduction product of (B) (See Experimental).

Table 2. Possible Configurations and CD Signs of [Co(mida)(edma)] Complexes Containing Facially Coordinating edma

Geometrical Isomer	Possible Configuration		CD sign
	around cobalt(III)	asymmetric nitrogen	
mer(O)*cis*(N$_c$)	$\Lambda\Delta\Lambda$	N$_\mathrm{S}$	$(+)^{\mathrm{CD}}_{572}$
(violet)	$\Delta\Lambda\Delta$	N$_\mathrm{R}$	$(-)^{\mathrm{CD}}_{572}$
mer(O)*trans*(N$_c$)	$\Delta\Lambda$	N$_\mathrm{S}$	$(+)^{\mathrm{CD}}_{561}$
(brown)	$\Lambda\Delta$	N$_\mathrm{R}$	$(-)^{\mathrm{CD}}_{561}$
fac(O)	$\Lambda\Delta\Lambda$	N$_\mathrm{R}$	$(+)^{\mathrm{CD}}_{565}$
(pink)	$\Delta\Lambda\Delta$	N$_\mathrm{S}$	$(-)^{\mathrm{CD}}_{565}$

dinates to a cobalt(III) ion in the facial form, the secondary nitrogen (C-N̲H-C) becomes an asymmetric center (Fig. 4).[2] Where a geometrical structure of the edma complex is given, the absolute configuration around the cobalt(III) is restricted by the chirality of the asymmetric nitrogen. For example, in the *fac*(O) isomer of [Co(mida)(edma)], if the asymmetric nitrogen has R chirality (N_R), the absolute configuration around the cobalt(III) is *ΛΔΛ*. The correlation between the configurations around cobalt(III) and the chirality of asymmetric nitrogen is shown in Table 2.

Determination of Absolute Configurations by ^{1}H NMR. An outline of the method to determine the absolute configurations is illustrated in Fig. 4. The $(-)^{CD}_{543}$ C_2-*trans*(O)-$[Co(edma)_2]^{2+}$ isomer, the structure of which was determined in the previous work, has the configuration *ΔΛΔ*(N_R,N_R).[2] One of the G-ring $-CH_2-$ protons in this complex is stereospecifically deuterated in basic D_2O. When the outside proton (H_b in Fig. 4 (A)) was deuterated, the methylene carbon becomes an asymmetric center with the S chirality (C_S) (Fig. 4 (B)). Using this edma which contains C_S (edma(C_S)), the isomers of [Co(mida)(edma(C_S))] were prepared and resolved as described in the experimental section. In that experimental procedure, the C_S chirality was retained but the N_R chirality was not retained (yielded a 1:1 mixture of N_R and N_S). It is noteworthy that, when the nitrogen atom of the facially coordinating edma(C_S) takes N_R chirality, the undeuterated proton (-CH̲D-) occupies an inside position (Fig. 4 (C)). (When edma(C_S) takes N_S chirality, the -CH̲D- proton occupies an outside position.) In $(+)^{CD}_{561}$ *mer*(O)*trans*(N_c)-[Co(mida)(edma(C_S))], the NMR signal of G-ring -CH̲D- in edma(C_S)

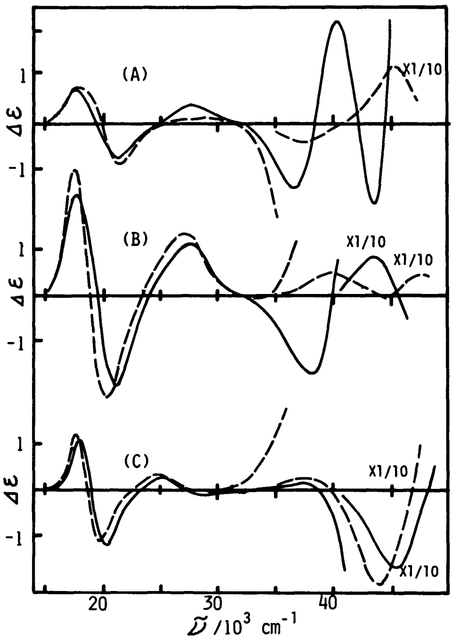

Fig. 6. CD spectra of the isomers of [Co(ida)(edma)] (——) and [Co(mida)(edma)] (– – –). (A) brown isomers of $(+)^{CD}_{565}$ [Co(ida)(edma)] and $(+)^{CD}_{561}$ [Co(mida)(edma)]; (B) violet isomers of $(+)^{CD}_{563}$ [Co(ida)(edma)] and $(+)^{CD}_{572}$ [Co(mida)(edma)]; and (C) pink isomers of $(+)^{CD}_{554}$ [Co(ida)(edma)] and $(+)^{CD}_{565}$ [Co(mida)(edma)].

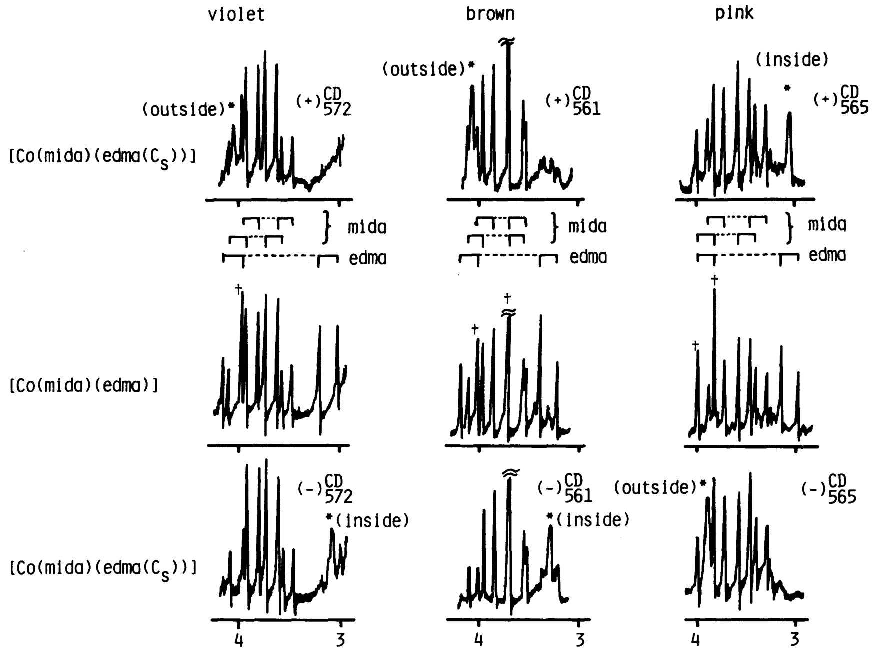

Fig. 5. ^{1}H NMR spectra of the optically active isomers of [Co(mida)(edma(C_S))] and those of the undeuterated isomers of [Co(mida)(edma)]. (Asterisked peaks: G-ring –CH̲D– of edma. Daggered peaks: Overlapped peaks.)

appeared at the chemical shift that corresponds to the outside proton ($\mathrm{H_b}$; lower field) (Fig. 5). Accordingly, the chirality of the asymmetric nitrogen is $\mathrm{N_S}$ in $(+)^{\mathrm{CD}}_{561}$ *mer*(O)*trans*($\mathrm{N_c}$)-[Co(mida)(edma($\mathrm{C_S}$))]. On the other hand, in $(-)^{\mathrm{CD}}_{561}$ *mer*(O)*trans*($\mathrm{N_c}$)-[Co(mida)(edma($\mathrm{C_S}$))] the signal of $-\mathrm{C\underline{H}D}-$ appeared at higher field (corresponding to the inside proton). This isomer should have $\mathrm{N_R}$ chirality. In a similar manner, the absolute configurations of three isomers of [Co(mida)(edma)] were determined. These are summarized in Table 2 and Fig. 5.

CD Spectra of the Complexes. The CD spectra of the complexes examined are illustrated in Fig. 6. The facially chelated isomers of [Co(ida)(edma)] show similar CD patterns in the first and second band regions to those of the corresponding isomers (with the same colors) of [Co(mida)(edma)] except that the CD bands of the violet and pink isomers of [Co(mida)(edma)] shift slightly to the lower energy side than those of the corresponding isomers of [Co(ida)(edma)]. No shift was observed in the CD bands of the brown isomer of [Co(mida)(edma)]. Since the violet and pink isomers belong to *cis*($\mathrm{N_c}$) type isomers (violet, *mer*(O)*cis*($\mathrm{N_c}$); pink, *fac*(O) (Fig. 1)), steric compression between the methyl group of mida and the ethylene or methylene groups of edma is large in these isomers. The shift to the lower energy side results from this compression. Such compression is not expected in the brown isomer (*trans*($\mathrm{N_c}$) type) of [Co(mida)(edma)].

The first absorption bands of the *fac*(O)-[Co($\mathrm{N_3}$)($\mathrm{O_3}$)] type complexes are sharp but those of *mer*(O)-[Co($\mathrm{N_3}$)($\mathrm{O_3}$)] are broad or not sharp with accompanying shoulder bands.[14,15] However, both isomers show two CD bands with opposite signs in the first absorption band region. This may be a general feature of the bis(terdentate)cobalt(III) type complex containing five membered chelate rings, even though the vicinal CD from the ligand may make the feature vague. The u-fac isomers of $[\mathrm{Co(ida)_2}]^-$[16] and $[\mathrm{Co(dien)_2}]^{3+}$[17] also show similar spectral patterns in the first absorption band region.

The $(+)^{\mathrm{CD}}_{572}$ $\Lambda\Delta\Lambda$ *mer*(O)*cis*($\mathrm{N_c}$)-[Co(mida)(edma)] gives two component CD bands with (+) and (−) signs at the lower and higher energy sides in the first absorption band region and the intensities (absolute values) are larger than those of $(+)^{\mathrm{CD}}_{565}$ *fac*(O)-[Co(mida)(edma)]. The low CD intensities of the *fac*(O) isomer may result from one of the following two reasons: (1) although the *fac*(O) isomer has $\Lambda\Delta\Lambda$ configuration the same as the *mer*(O)*cis*($\mathrm{N_c}$) isomer does, the $\mathrm{N_R}$ chirality of the coordinating edma in the *fac*(O) isomer is different from the $\mathrm{N_S}$ chirality in the *mer*(O)*cis*($\mathrm{N_c}$); (2) the split of the CD components in the first absorption band is smaller in the *fac*(O) isomer than in the *mer*(O)*cis*($\mathrm{N_c}$).

The CD intensities of $(+)^{\mathrm{CD}}_{561}$ *mer*(O)*trans*($\mathrm{N_c}$) are the smallest among three resolved isomers of [Co(mida)(edma)]. As this isomer has Δ and Λ-configurational ring pair, the CD contribution from the configurational effect is the smallest among three isomers and the vicinal CD from the $\mathrm{N_S}$ is dominant in this isomer.

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