Stereoselectivities in Mixed Ligand Complexes of Cobalt(III), with L-Asparagine as a Ligand

Hideto TAKENAKA and Muraji SHIBATA

Department of Chemistry, Faculty of Science, Kanazawa University, Kanazawa 920

(Received March 26, 1976)

The [Co(ox)(L-aspNH$_2$)(en)] complex as well as the [Co(L-aspNH$_2$)$_{3-n}$(L-asp)$_n$]$^{n-}$ complexes (n=1,2) have been prepared and separated into their diastereoisomers by means of column chromatography. The structures of the isomers thus isolated have been characterized by their absorption, CD, and PMR spectra. Stereoselectivity in the [Co(ox)(L-aspNH$_2$)(en)] complex has been found for the *fac*-Λ and *mer*-Λ isomers, and those in the [Co(L-aspNH$_2$)$_{3-n}$(L-asp)$_n$]$^{n-}$ complexes, for the *fac*-Λ and *mer*-Λ isomers. These results have provided proof of the stereoselective effect due to the chelated L-asparaginate ion.

Metal complexes containing optically active ligands frequently exhibit stereoselective effects upon the formation of their diastereoisomers. In order to study such stereoselective formation, we previously examined the mixed amino acidato cobalt(III) complexes containing the L- or D-aspartate ion (L- or D-asp) as the primary ligand.[1-3] More recently we examined the complex consisting of the L-aspartate ion, the oxalate ion, and ethylenediamine, [Co(ox)(L-Hasp)(en)], in order to obtain proof of the stereoselective effect due to the chelated optically active aspartate ion.[4]

In the present work L-asparagine (L-HaspNH$_2$) was chosen as the primary ligand; a mixed complex [Co(ox)(L-aspNH$_2$)(en)] has been prepared in order to study the stereoselective influence due to the chelated L-asparaginate ion. Furthermore, a series of complexes, [Co(L-aspNH$_2$)$_{3-n}$(L-Hasp)$_n$] (n=1,2) have been prepared in order to study their stereochemistry and stereoselectivities. Related complexes, [Co(L-aspNH$_2$)$_3$] and [Co(L-aspNH$_2$)$_2$(D-Hasp)] have also been investigated.

Experimental

Preparation. Oxalato(L-asparaginato)ethylenediaminecobalt(III), [Co(ox)(L-aspNH$_2$)(en)]: The diastereoisomers of this complex were obtained much as were those of the corresponding L-aspartato complex.[4] The separation of the diastereoisomers was carried out by the use of a column containing 200—400 mesh Dowex 50WX8 resin in the Na-form (5.0×40.0 cm). During elution with water, six bands of non-charged species descended; the first and fourth bands, formed in very poor yields, were not the desired species. The other four bands corresponded to four isomers of the desired complex and were labeled A-1—A-4 according to the order of elution. These bands were collected in fractions, and each fraction was concentrated to a small volume with a rotary evaporator at *ca.* 35 °C. The concentrated solution was then kept in a refrigerator for a few days in order to crystallize the desired isomers. Recrystallization was performed from warm water (*ca.* 50 °C).

Bis(L-asparaginato)-L-hydrogenaspartato and L-Asparaginatobis(L-hydrogenaspartato)cobalt(III), [Co(L-aspNH$_2$)$_{3-n}$(L-Hasp)$_n$] (n=1, 2): To a green solution of tricarbonatocobaltate(III), (Co(NO$_3$)$_2$·6H$_2$O, 5.82 g, 0.02 mol scale) prepared by the usual method,[5] we added L-asparagine monohydrate (6.0 g, 0.04 mol); the mixture was then stirred at 40 °C for 2 h. To this solution we added L-aspartic acid (3.4 g, 0.025 mol) and activated charcoal (2.0 g), after which the mixture was stirred at *ca.* 50 °C for 1 h. The charcoal and a small amount of precipitates were removed by filtration, and then perchloric acid (60%) was added in order to neutralize the filtrate (pH *ca.* 7.0), whereupon the precipitation of KClO$_4$ and the evolution of CO$_2$ took place. The resulting solution was iced for a while and then filtered two or three times. A quarter of the final filtrate was diluted to *ca.* 1 l with water and then charged on a column of Sephadex QAE-A25 in the Cl-form (3.0×120.0 cm). After washing with water, the gradient elution with aqueous solutions of CaCl$_2$ prepared in 0.01 M and 0.03 M was employed at the rate of *ca.* 0.5 ml/min. The twelve bands completely separated were labeled L-1—L-12 according to the order of elution. The four bands from L-9 to L-12 corresponded to the *mer*-Λ, *mer*-Λ, *fac*-Λ, and *fac*-Λ isomers of the *tris*(L-aspartato)cobaltate(III) complex respectively, which had already been characterized.[6] The L-3 and L-4 bands were very poor in yield and were not the desired ones. The other six bands (L-1, L-2 and L-5—L-8) were collected in fractions, and every fraction was concentrated to a small volume with a rotary evaporator at *ca.* 35 °C. When the L-1 and L-6 concentrates were acidified with aqueous HCl (pH *ca.* 1.0), crude hydrogen compounds were obtained (Compounds L-1 and L-6). After the removal of the L-1 compound, the filtrate, which exhibited a minus CD sign in the first absorption-band region, was passed through a column containing Dowex 50 WX8 resin in the H-form (3.0×20.0 cm). The effluent was evaporated to a small volume, and ethanol was added until silky precipitates appeared. The precipitates (labeled L-1′) were collected by centrifuging. Similarly, after the removal of the L-6 compound the filtrate was also passed through a resin column in the H-form, and the effluent in the earlier stage, which exhibited a minus CD sign, was collected (L-6′). However, we failed to isolate crystals from that fraction because of the extremely poor yield. The L-2, L-5, L-7, and L-8 concentrates were also passed through the resin columns in the H-form. Each effluent was evaporated to a small volume, and a small amount of ethanol was added to precipitate each hydrogen compound. The desired compounds were obtained from the L-2, L-7, and L-8 fractions, but no compound was isolated from the L-5 fraction because of its great solubility and because it was obtained in the poorest yield. Recrystallization of each crude compound was performed by dissolving it in water containing a small amount of NaOH, and by then acidifying it with aqueous perchloric acid, and by finally adding a small amount of ethanol. Of these complexes, the L-6 complex was again recrystallized from a solution of pH *ca.* 4.0 in order to remove another isomer which still contaminated it.

Bis(L-asparaginato)-D-hydrogenaspartatocobalt(III), [Co(L-aspNH$_2$)$_2$(D-Hasp)]: This complex was prepared using D-aspartic acid in place of L-aspartic acid according to the procedure described above. Six bands of univalent anionic species separated on a Sephadex column were collected in

fractions (D-1—D-6). The D-4 and D-6 fractions were very poor in yield and were not the desired complexes. However, from the D-6 fraction a novel complex, *fac(N)*-[Co(L-aspNH$_2$)(D-asp)] in which both the ligands act as terdentate, was isolated.[7] The other four fractions (D-1—D-3 and D-5) were concentrated with a rotary evaporator at *ca.* 35 °C. Each of the D-1 and D-5 concentrates was passed through a column of Dowex 50 WX8 resin in the H-form (3.0×20.0 cm). The effluent was evaporated to a small volume. To the D-1 concentrate, methanol was added to give crystals of the desired hydrogen compound (D-1). The filtrate, which exhibited a minus CD sign, was further evaporated almost to dryness to obtain the residue (D-1′). The D-5 concentrate was stored in a refrigerator for a few days to obtain the hydrogen compound (D-5). The concentrated D-2 and D-3 fractions were acidified with aqueous HCl. The D-2 was then stored in a refrigerator for a few days to obtain the hydrogen compound (D-2), while the D-3 fraction, when treated similarly, gave the hydrogen compound (D-3) after the addition of ethanol. The recrystallization of each hydrogen compound was performed by dissolving it in an aqueous NaOH solution, by acidifying it with aqueous perchloric acid, and by then cooling it. As for the D-1′ compound, recrystallization was performed by dissolving it in a warm mixture of methanol and water and by then adding ethanol when cold.

Tris(L-asparaginato)cobalt(III), [*Co(L-aspNH$_2$)$_3$*]: The method used for the isolation of the four isomers of the [Co(L-Hasp)$_3$][6] complex was employed; to a green solution of tricarbonatocobaltate(III) (0.02 mol scale) we added L-asparagine monohydrate (9.0 g, 0.06 mol), and the solution was stirred at 60 °C for 2 h. Then the solution was adjusted to pH *ca.* 4.0 with aqueous HCl and stirred for a few min. The solution was again adjusted to pH *ca.* 8.0 with an aqueous solution of NaOH and then stirred at *ca.* 70 °C for 2 h. The resulting solution was kept in a refrigerator for a day in order to precipitate one of the desired isomers (*mer-Λ*). After the isomer had been collected by filtration, the filtrate was adsorbed on a column containing Dowex 50 WX8 resin in the Na-form (7.0×15.0 cm); two bands corresponding to non-charged species were collected in one fraction by elution with water. The fraction was concentrated to a small volume, and the concentrate was charged on another column in the Na-form (5.0×30.0 cm); after a while, two separate bands appeared. The fast-descending band was confirmed to be the *mer-Λ* isomer, and the slow-descending one, to be the *fac-Λ* species. Each band was collected in a fraction and concentrated to crystallize the isomer. Recrystallization was performed from warm water except for the *mer-Λ* isomer. The recrystallization of the *mer-Λ* isomer was performed by dissolving it in 30% perchloric acid and by then diluting it with water. The last isomer, *fac-Λ*, could not be isolated because of its poor yield.

Formation Ratios of the Isomers. Although asparagine is hydrolyzed to aspartic acid under certain conditions,[8] the hydrolysis was negligible in the reactions used in the present work. To every reaction mixture mentioned in *Preparation*, activated charcoal was added in order to favor the formation of an equilibrium mixture of diastereoisomers. From the spectral data on the fractions obtained by chromatographic separation, the formation ratios of the isomers were evaluated. For some isomers not isolated as crystals, the ε and the $|\Delta\varepsilon|$ values were assumed to be the same as those for the corresponding geometrical isomers isolated as crystals.

Measurement. The absorption (AB) spectra were measured with a Hitachi 323 Recording Spectrophotometer. The circular dichroism (CD) spectra were recorded on a JASCO Model ORD/UV-5 spectrophotometer with a CD attachment. The proton magnetic resonance (PMR) spectra were recorded on a JEOL JNM-PS-100 NMR spectrometer at *ca.* 23 °C, using D_2O as the solvent. The values of the chemical shifts were referred to internal sodium d_4-trimethylsilylpropionate (TMSP). The pH values of the solutions were measured with a Hitachi-Horiba M-7E pH meter. Sodium carbonate was used to adjust the pH values.

Results and Discussion

Characterization of Isomers. The [Co(ox)(L-aspNH$_2$)(en)] Complex: No work has been reported on cobalt(III) complexes containing asparagine as ligands except for the *tris*(asparaginato) complex.[9] The results of the elemental analyses for the isolated complexes are summarized in Table 1. The AB and CD spectral data in the d-d transition region are also given in Table 1. The *mer* or *fac* structure of each isomer was determined from the AB spectrum. The *Λ* or *Δ* configuration of the diastereomers was determined from the sign of the main CD peak in the first absorption-band region.

The PMR spectra of the four isomers of the [Co(ox)-(L-aspNH$_2$)(en)] complex are shown in Fig. 1. Two protons of the CH$_2$ group and one proton of the CH group of L-aspNH$_2$ correspond to the AB and X portions respectively in an ABX system. The multiplet-like signals at 3.8—4.0 ppm are due to the CH moiety (X proton), and the separation width of the complicated signals is represented by the expression of $(J_{AX}+J_{BX})$.[10] Moreover, since the coupling constant of the vicinal protons, the J_{vic} value, depends on the dihedral angle,[11] the value of $(J_{AX}+J_{BX})/2$ gives information about the orientation of the side-chain of the chelated asparaginate ion, the X proton of the CH moiety being spatially fixed in the chelated state. The $(J_{AX}+J_{BX})/2$ values observed for the four isomers are: *mer-Δ*, 4.0 Hz; *mer-Λ*, 6.2 Hz; *fac-Λ*, 4.0 Hz; *fac-Δ*, 6.0 Hz. The corresponding value for the terdentate

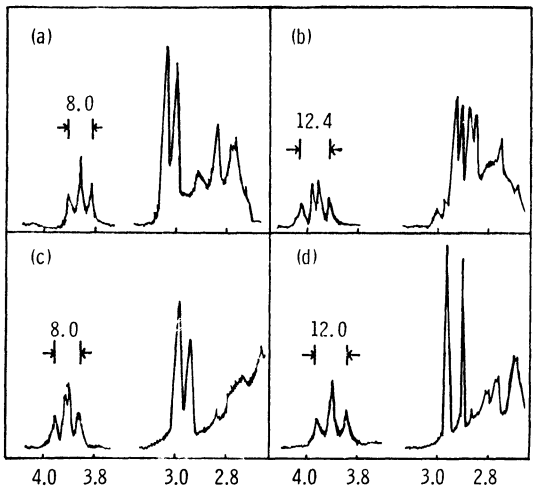

Fig. 1. PMR spectra of [Co(ox)(L-aspNH$_2$)(en)] in D_2O.
(a): *mer-Δ* Isomer, (b): *mer-Λ* isomer,
(c): *fac-Λ* isomer, (d): *fac-Δ* isomer.

TABLE 1. ELEMENTAL ANALYSES, ABSORPTION[a] AND CD[a] SPECTRAL DATA

Label	Complex	Elemental anal, %[b]			Band I		Band II		CD	
		C	H	N	$10^{-3}\tilde{\nu}_{max}$ cm^{-1}	ε_{max}	$10^{-3}\tilde{\nu}_{max}$ cm^{-1}	ε_{max}	$10^{-3}\tilde{\nu}_{max}$ cm^{-1}	$\Delta\varepsilon_{max}$
A-1	*mer*-*Λ*-[Co(ox)(L-aspNH$_2$)(en)]·H$_2$O	27.28 (26.96)	5.24 (4.81)	15.94 (15.73)	19.2	100	26.8	179	17.8 21.0	−2.07 −1.50
A-2	*mer*-*Λ*-[Co(ox)(L-aspNH$_2$)(en)]·H$_2$O	27.31 (26.96)	5.03 (4.81)	16.00 (15.73)	19.2	99	26.9	184	18.0 20.4	+1.97 +1.40
A-3	*fac*-*Λ*-[Co(ox)(L-aspNH$_2$)(en)]·2.5H$_2$O	25.31 (25.06)	5.41 (5.26)	14.50 (14.62)	19.2	152	27.2	170	18.9	+4.25
A-4	*fac*-*Λ*-[Co(ox)(L-aspNH$_2$)(en)]·0.5H$_2$O	27.98 (27.66)	4.84 (4.65)	15.83 (16.14)	19.2	149	27.0	162	19.0	−3.85
	mer-*Λ*-[Co(L-aspNH$_2$)$_3$]·1.5H$_2$O	29.86 (30.07)	5.35 (5.05)	18.06 (17.53)	18.5	106	26.8	159	18.8	+3.77
	mer-*Λ*-[Co(L-aspNH$_2$)$_3$]·3.5H$_2$O	28.06 (27.97)	5.87 (5.48)	15.98 (16.30)	18.4	110	26.7	166	18.6	−3.07
	fac-*Λ*-[Co(L-aspNH$_2$)$_3$]·2H$_2$O	29.47 (29.52)	5.62 (5.16)	17.31 (17.20)	19.3	204	26.7	154	19.1	−2.89
L-1	*mer*-*Λ*-[Co(L-aspNH$_2$)$_2$(L-Hasp)]·3H$_2$O	28.55 (28.41)	4.85 (5.17)	14.10 (13.81)	18.5	117	26.9	184	19.0	+3.41
L-1′	*mer*-*Λ*-[Co(L-aspNH$_2$)$_2$(L-Hasp)]·3H$_2$O	28.27 (28.41)	4.85 (5.17)	13.98 (13.81)	18.5	100	26.9	148	18.6	−2.10
L-2	*fac*-*Λ*-[Co(L-aspNH$_2$)$_2$(L-Hasp)]·2H$_2$O	30.30 (30.52)	4.32 (4.61)	11.66 (11.86)	19.4	197	26.7	165	19.3	−2.51
L-6	*mer*$_1$-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$]·2H$_2$O	29.49 (29.40)	4.27 (4.73)	11.75 (11.42)	18.5	109	27.0	165	19.3	+3.12
L-7	*mer*$_2$-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$]·4H$_2$O	26.95 (26.93)	5.46 (5.18)	10.67 (10.62)	18.5	113	27.0	179	19.3	+3.36
L-8	*fac*-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$]	31.43 (31.73)	4.18 (4.22)	12.70 (12.33)	19.4	201	26.8	154	19.2	−2.76
D-1	*mer*$_1$-*Λ*-[Co(L-aspNH$_2$)$_2$(D-Hasp)]·5H$_2$O	26.14 (26.53)	5.04 (5.57)	13.01 (12.89)	18.4	115	26.9	181	18.7	+3.11
D-1′	*mer*-*Λ*-[Co(L-aspNH$_2$)$_2$(D-Hasp)]·4.5H$_2$O	26.81 (26.97)	4.82 (5.47)	13.16 (13.11)	18.3	107	26.9	168	18.6	−2.68
D-2	*mer*$_2$-*Λ*-[Co(L-aspNH$_2$)$_2$(D-Hasp)]·2H$_2$O	29.52 (29.46)	5.53 (4.95)	14.22 (14.31)	18.5	107	26.7	154	18.8	+3.29
D-3	*fac*-*Λ*-[Co(L-aspNH$_2$)$_2$(D-Hasp)]·2.5H$_2$O	29.10 (28.91)	5.37 (5.06)	13.80 (14.06)	19.2	207	26.6	174	18.7	+2.74
D-5	*fac*-*Λ*-[Co(L-aspNH$_2$)$_2$(D-Hasp)]·2.5H$_2$O	28.93 (28.91)	5.47 (5.06)	13.77 (14.06)	19.2	207	26.6	186	18.7	−2.56

a) Measured in alkaline solutions except for *mer*-*Λ*-[Co(L-aspNH$_2$)$_3$], which was measured in 60% HClO$_4$. b) ( ): Calcd.

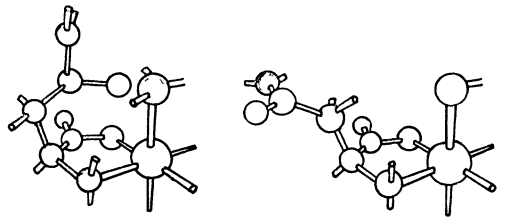

Fig. 2. Orientations of chelated L-aspNH$_2$ side-chain.

L-aspNH$_2$ ion in the [Co(L-aspNH$_2$)(D-asp)] complex is known to be 4.0 Hz.[7] This suggests that, in both the *mer*-*Δ* and *fac*-*Δ* isomers, the side-chain of the chelated L-aspNH$_2$ turns its *β*-acid amide group toward the apical site occupied by an NH$_2$ group of the chelated en, and that, in both the *mer*-*Δ* and *fac*-*Δ* isomers, the side-chain is far from the apical site occupied by an O group in the chelated $C_2O_4^{2-}$ ion (Fig. 2). Thus, these different orientations of the side-chain of chelated L-aspNH$_2$ are caused by the different inter-ligand interactions.

The [Co(L-aspNH$_2$)$_{3-n}$(L-Hasp)$_n$] Complexes: In a mixed tris-type complex with two kinds of amino acidate ion, three *mer* isomers can exist, each of them consisting of a pair of diastereomeric isomers: *cis*(*N*)-*cis*(*O*)-*Δ* and -*Λ*, *cis*(*N*)*trans*(*O*)-*Δ* and -*Λ*, and *trans*(*N*)-*cis*(*O*)-*Δ* and -*Λ*, according to the arrangements of two identical amino acidate ions. Previously, we characterized three isomers of *mer*-*Δ*-[Co(L-pro)(D-Hasp)$_2$] and one isomer of *mer*-*Λ*-[Co(L-pro)(L-Hasp)$_2$] on the basis of the PMR spectral data, the formation ratios, and an examination of the molecular models.[3] Yoneda *et al.*[12] characterized two isomers of *mer*-*Λ*-[Co(gly)$_2$(L-Hglu)][13] on the basis of a semiempirical consideration of the PMR spectrum.

Now, let us attempt to characterize two isomers of *mer*-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$] on the basis of the PMR spectra. When we pay attention to three methine protons, namely, one proton for the chelated L-aspNH$_2$ ion and two protons for the two chelated L-asp ions, the following four criteria help in the characterization of the *mer*-*Λ* isomers concerned:

1. When an $NH_2CH(R)COO^-$ ion is chelating through a five-membered ring, the methine proton (*α*-hydrogen) shows no chemical shift in the range of pH 6—9.[14]

2. The methine proton adjacent to the coordinated N atom resonates at a higher magnetic field when the O atom occupies the site *trans* to the N atom than when the N atom occupies the same site.[15]

3. When the methine groups of both the chelating L-aspNH$_2$ and L-asp are present in the same types of chemical and magnetical environments, the methine proton of the L-aspNH$_2$ always resonates in a field lower by 0.10—0.12 ppm than that of the L-asp. This was confirmed by comparing the PMR spectra of complexes of the same type (Table 2).

4. The $(J_{AX}+J_{BX})/2$ values of the chelated L-aspNH$_2$ and L-asp give information about the orientations of the side-chains of both ligands.[3,4,16]

We first assign the signals of the methine protons in the spectrum of the *mer*-*Λ*-[Co(L-Hasp)$_3$] complex on the basis of the above criteria; the spectrum and the structure are shown in Figs. 3 and 4 respectively. The signals of the methine protons appear at 3.55, 3.80, and 3.98 ppm. From the second criterion, the two protons at B and C in Fig. 4 are expected to resonate in lower fields than that at A. Thus, the signals at 3.55 ppm are assignable to the methine proton at the A position. From the fourth criterion, the signals centered at 3.80 ppm with the value of $(J_{AX}+J_{BX})/2=3.5$ Hz, and those at 3.98 ppm with the value of $(J_{AX}+J_{BX})/2=5.8$ Hz, are assignable to the methine protons situated in the B and C positions respectively. When the L-asp ion chelating at the A position in Fig. 4 is replaced by a L-aspNH$_2$ ion to give *mer*-*Λ*-*trans*(*N*)*cis*(*O*) geometry, the chemical shift of the methine proton of the chelated L-aspNH$_2$ can be expected to be *ca.* 3.65—3.67 ppm from the third criterion, and the

TABLE 2. PMR SPECTRAL DATA[a]

Complex	-CH (ppm)		-CH$_2$ (ppm)		$(J_{AX}+J_{BX})/2$ (Hz)		pD in D_2O soln
	aspNH$_2$	asp	aspNH$_2$	asp	aspNH$_2$	asp	
mer-*Δ*-[Co(ox)(L-aspNH$_2$)(en)]	3.86		3.04		4.0		5.0
mer-*Δ*-[Co(ox)(L-Hasp)(en)]		3.72		2.85		3.7	4.8
mer-*Λ*-[Co(ox)(L-aspNH$_2$)(en)]	3.98		2.90		6.2		6.4
mer-*Λ*-[Co(ox)(L-Hasp)(en)]		3.86		2.80		5.0	5.1
fac-*Δ*-[Co(ox)(L-aspNH$_2$)(en)]	3.90		2.96		4.0		6.5
fac-*Δ*-[Co(ox)(L-Hasp)(en)]		3.72		2.78		3.8	4.3
fac-*Δ*-[Co(ox)(L-aspNH$_2$)(en)]	3.94		2.90		6.0		5.2
fac-*Δ*-[Co(ox)(L-Hasp)(en)]		3.84		2.81		6.0	5.3
fac-*Δ*-[Co(L-aspNH$_2$)$_3$]	3.75		2.97		3.9		8.2[b]
fac-*Δ*-[Co(L-Hasp)$_3$]		3.61		2.78		3.9	9.0[b]
fac-*Δ*-[Co(L-aspNH$_2$)$_2$(L-Hasp)]	3.84 3.86		3.06 3.06		4.0 4.0		8.6[b]
		3.73		2.87		3.8	
fac-*Δ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$]	3.78		3.00		4.0		
		3.66 3.67		2.82 2.82		3.6 3.6	8.8[b]

a) Measured in D_2O. b) Adjusted with Na_2CO_3.

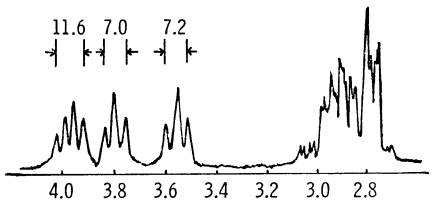

Fig. 3. PMR spectrum of *mer*-*Λ*-[Co(L-Hasp)$_3$] in D_2O (pD 9.1).

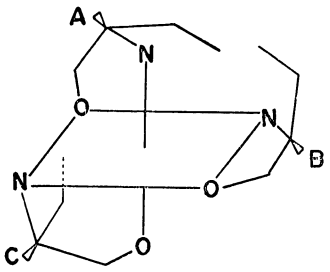

Fig. 4. Structure of *mer*-*Λ*-[Co(L-Hasp)$_3$].

chemical shifts of the two methine protons of the two chelated L-asp ions at the B and C positions can be expected to appear at *ca.* 3.80 ppm and *ca.* 3.98 ppm respectively from a comparison with the known signals for the *mer*-*Λ*-[Co(L-Hasp)$_3$] complex. By analogy, the chemical shifts of the methine protons of the chelating L-aspNH$_2$ and L-asp ions for the *mer*-*Λ*-[Co(L-aspNH$_2$)-(L-Hasp)$_2$] complex are expected to be *ca.* 3.55 ppm (L-asp at A), 3.90—3.92 ppm (L-aspNH$_2$ at B), and 3.80 ppm (L-asp at C) for the isomer of *cis*(*N*)*cis*(*O*) geometry, and *ca.* 3.55 ppm (L-asp at A), 3.80 ppm (L-asp at B), and 4.08—4.10 ppm (L-aspNH$_2$ at C) for the isomer of *cis*(*N*)*trans*(*O*) geometry. The spectra of the L-6 and L-7 isomers are partially shown in Fig. 5, as is that of the crude L-6 complex. From the values predicted above, the L-6 is identified as the *cis*(*N*)*cis*(*O*) isomer and the L-7, as the *trans*(*N*)*cis*(*O*) isomer. The crude L-6 complex shows a more complicated spectrum, indicating an overlapping of the signals arising from the *cis*(*N*)*cis*(*O*) isomer and contaminating *cis*(*N*)*trans*(*O*) isomer. The relative chemical shifts of methine protons for the present *mer*-*Λ* isomers and the *mer*-*Λ*-[Co(L-Hasp)$_3$] complex are illustrated in Fig. 6.

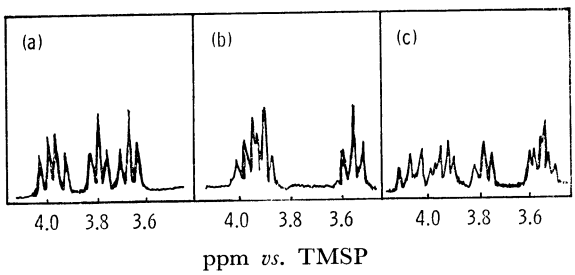

Fig. 5. PMR spectra of *mer*-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$] in D_2O.
(a): L-7 Crystals (pD 9.3), (b): L-6 crystals (pD 8.3), (c): crude L-6 crystals (pD 9.5).

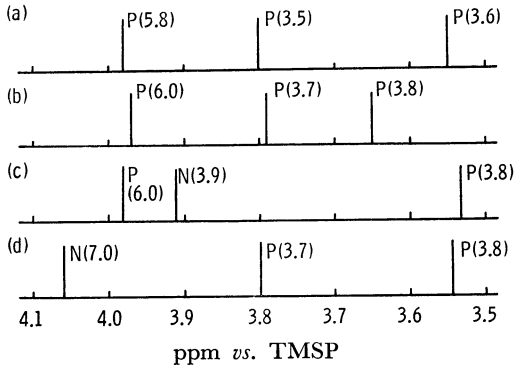

Fig. 6. Relative chemical shifts of methine protons in *mer*-*Λ*-[Co(L-aspNH$_2$)(L-Hasp)$_2$].
(a): Reference; *mer*-*Λ*-[Co(L-Hasp)$_3$], (b): *cis*(*O*)-*trans*(*N*), (c): *cis*(*O*)*cis*(*N*), (d): *cis*(*N*)*trans*(*O*).
P: L-Hasp, N: L-aspNH$_2$, ( ): $(J_{AX}+J_{BX})/2$, Hz.

Stereoselectivity. The [Co(ox)(L-aspNH$_2$)(en)] Complex: The percentage distribution of all the isomers for the [Co(ox)(L-aspNH$_2$)(en)] complex are given in Table 3, in which the values for related complexes[4] are also included for comparison. The percentage compositions of the diastereomeric pairs are summarized in Table 4. From Table 3 it is seen that the *mer*-(*Λ*+*Δ*) isomer existing in the present L-asparaginato complex and also those in the other complexes are more abundant than the *fac*(*Λ*+*Δ*) isomer, and that the abundances in the *mer* isomers are roughly 80%. Since the statistical weight of the L-amino acidate (L-am) ion upon chelation in such a reaction system is the same between the formation of the *mer* isomer and that of the *fac* isomer, the above fact suggests that the selective formation of the *mer* isomer in a [Co(ox)(L-am)(en)]-type complex takes place irrespective of the kind of L-am ligand. Table 4 shows that a significant stereoselectivity of over 70% is found in both the *mer*-*Δ* and *fac*-*Λ* isomers for the present L-aspNH$_2$ complex, while the selectivity for the L-asp complex is over 80%. The comparison of the stereoselectivities among the [Co(ox)(L-am)(en)]-type complexes suggests that the stereoselective formation of an isomer relates to the side-chain length and the existence of CO group in the side-chain of the chelated L-am ion. The marked stereoselectivity in the L-asp complex has been explained as a combined result of an interaction of the *β*-COO^- group in the chelated L-asp ion with an NH_2 group of the chelated en, which is favorable for the stereoselectivity, and an electrostatic repulsion of the *β*-COO^- with an O atom of the chelated $C_2O_4^{2-}$ ion, which is disadvantageous in the stereo-

Table 3. Percentage compositions of reaction mixtures

	mer-*Λ*	*mer*-*Δ*	*fac*-*Λ*	*fac*-*Δ*
[Co(ox)(L-aspNH$_2$)(en)]	62	19	14	5
[Co(ox)(L-Hasp)(en)][a)]	72	11	14	3
[Co(ox)(L-Hglu)(en)][a)]	48	32	11	9
[Co(ox)(L-leu)(en)][a)]	49	35	8	8
[Co(ox)(gly)(en)][a)]	42	42	8	8

a) Ref. 4.

TABLE 4. PERCENTAGE COMPOSITIONS OF DIASTEREOISOMERS

	[Co(ox)(L-aspNH$_2$)(en)]	[Co(ox)(L-Hasp)(en)][a)]	[Co(ox)(L-Hglu)(en)][a)]	[Co(ox)(L-leu)(en)][a)]	[Co(ox)(gly)(en)][a)]
mer-Λ	77	87	60	58	50
fac-Λ	74	82	55	51	50

a) Ref. 4.

selective formation.[4] For the stereoselectivity in the [Co(ox)(L-aspNH$_2$)(en)] complex, the following explanation can be offered; provided that the stereoselective formation of an isomer depends on the interaction of the CO group rather than on that of the NH$_2$ group of the free β-CONH$_2$ group with the adjacent group or donor atom in an apical position, for the *mer-Λ* or *fac-Λ* isomer, in which the apical position is occupied by an NH$_2$ group of the chelated en, the CO group tends to make a hydrogen bond with the NH$_2$ group to give favorable interaction. On the other hand, for the *mer-Λ* or *fac-Λ* isomer, in which the apical position is occupied by an O atom in the chelated $C_2O_4^{2-}$, the CO group tends to repel the O atom. This explanation is supported by the information about the orientation of the β-acid amide group mentioned before.

The [Co(L-aspNH$_2$)$_{3-n}$(L-asp)$_n$]$^{n-}$ Complexes: The results of the formation ratios through all the isomers of the [Co(L-aspNH$_2$)$_{3-n}$(L-asp)$_n$]$^{n-}$ complexes are given in Table 5. The minor component in each fraction in the chromatographic separations is evaluated as below 10% on the basis of the spectral data. The marked stereoselectivity was found in either the asparaginato complex (n=2) or the *bis*(asparaginato) complex (n=1); in either complex, the selective formation of the *Δ* isomer was found for the *fac* isomer, and that of the *Λ* isomer for the *mer* one. The stereoselectivities found in these complexes can be understood as the combined effects due to the two kinds of ligands. When a chelated L-asp ion is replaced by a D-asp ion to give the [Co(L-aspNH$_2$)$_2$(D-asp)]$^-$ complex, the formation ratio and the degree of the stereoselectivity are expected to vary from those of the [Co(L-aspNH$_2$)$_2$(L-asp)]$^-$ complex. Table 6 shows the results for the [Co(L-aspNH$_2$)$_2$(D-asp)]$^-$ complex. The fact that no appreciable selectivity is found in the [Co(L-aspNH$_2$)$_2$(D-asp)]$^-$ complex can be understood as the net result arising from the opposite stereoselective effects due to the chelated L-aspNH$_2$ and D-asp.

TABLE 5. FORMATION RATIOS AND STEREOSELECTIVITIES IN [Co(L-aspNH$_2$)$_{3-n}$(L-asp)$_n$]$^{n-}$ (n=1, 2, 3)

n	Label	Isomer	Ratio	Stereoselectivity	
1	L-1	*mer-Λ*	11.5	..... *mer-Λ*	82%
	L-1′	*mer-Δ*	2.5		
	L-2	*fac-Δ*	16.3	*fac-Δ*	~95%
2	L-5	*mer-Δ*	0.4		
	L-6	*mer-Λ*	13.0	..... *mer-Λ*	83%
	L-6′	*mer-Δ*	3.3		
	L-7	*mer-Λ*	5.1		
	L-8	*fac-Δ*	39.8	*fac-Δ*	~100%
3	L-9	*mer-Δ*	1.5	..... *mer-Λ*	66%
	L-10	*mer-Λ*	2.9		
	L-11	*fac-Λ*	0.2	..... *fac-Δ*	95%
	L-12	*fac-Δ*	3.5		

TABLE 6. FORMATION RATIOS AND STEREOSELECTIVITIES IN [Co(L-aspNH$_2$)$_2$(D-asp)]$^-$

Label	Isomer	Ratio	Stereoselectivity	
D-1	*mer-Λ*	21		
D-1′	*mer-Λ*	33	..... *mer-Λ*	58%
D-2	*mer-Λ*	21		
D-3	*fac-Λ*	7		
D-5	*fac-Δ*	18	..... *fac-Δ*	7%

References

1) K. Kawasaki, J. Yoshii, and M. Shibata, *Bull. Chem. Soc. Jpn.*, **43**, 819 (1970).
2) T. Matsuda, T. Okumoto, and M. Shibata, *Bull. Chem. Soc. Jpn.*, **45**, 802 (1972).
3) T. Matsuda and M. Shibata, *Bull. Chem. Soc. Jpn.*, **46**, 3104 (1973).
4) M. Takeuchi and M. Shibata, *Bull. Chem. Soc. Jpn.*, **47**, 2797 (1974).
5) M. Shibata, *Nippon Kagaku Zasshi*, **87**, 771 (1966).
6) M. Shibata, H. Nishikawa, and K. Hosaka, *Bull. Chem. Soc. Jpn.*, **40**, 236 (1967).
7) H. Takenaka and M. Shibata, *Chem. Lett.*, sumbitted for publication.
8) F. C. Steward and J. F. Tompson, *Nature*, **169**, 739 (1952).
9) P. Spacu, C. Gheorghice, M. Brezeanu, and S. Popescu, *Rev. Chim. Acad. Republ. Populaire Roum.*, **3**, 127 (1958).
10) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London (1965), p. 361.
11) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).
12) H. Yoneda, U. Sakaguchi, and Y. Nakashima, *Bull. Chem. Soc. Jpn.*, **48**, 209 (1975).
13) K. Kawasaki and M. Shibata, *Bull. Chem. Soc. Jpn.*, **45**, 3100 (1972).
14) I. Legg and J. Steele, *Inorg. Chem.*, **10**, 2177 (1971).
15) M. Watabe, K. Onuki, and S. Yoshikawa, *Bull. Chem. Soc. Jpn.*, **48**, 687 (1975).
16) H. Ishizuka, T. Yamamoto, Y. Arata, and S. Fujiwara, *Bull. Chem. Soc. Jpn.*, **46**, 468 (1973).