Stereochemistry and Circular Dichroism of Cobalt(III) Complexes with Quadridentate Nitrilotriacetate Analogues

By

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Contents

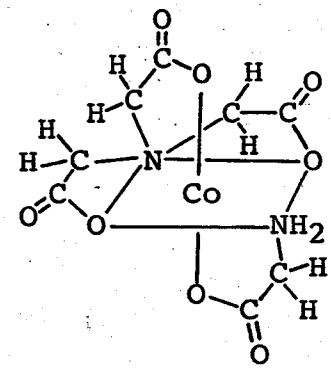
Introduction

The circular dichroism (CD) spectra in the region of the first and second d-d spin allowed absorption bands have been investigated for a large number of metal complexes, and have provided a powerful information, for example, for the stereochemistry and electronic structure of the metal complexes.[1-43] At present, however, there is no unifying theoretical model which explains the relationship between the CD spectra and structures of the complexes. In this circumstances, it is highly desired to prepare optically active complexes of a new type and to examine their CD behaviors.

In most of the optically active complexes so far studied, the optical activity is contributed from "configurational" effect due to a chiral distribution of two or more chelate rings around the central metal ion,[1-9] or from the configurational effect combined with "vicinal" effect due to optically active ligands.[10-24] In the latter case, it has been known for several cobalt(III) complexes that the configurational and vicinal contributions to the CD are separable and almost additive.[10-23] It seems, therefore, to be important to study the CD spectra of the complexes which have only the vicinal effect for elucidating the origin of optical activity in metal complexes. However, such a study has been made for the complexes of a limmited type, although several reports have been published so far,[24-43] and there remain some unresolved subjects with

respect to the CD contribution from the vicinal effect. In these circumstances, it is desirable to study the CD behavior of complexes of different types which have only the vicinal effect.

The trans(N)-(nitrilotriacetato)(glycinato)cobaltate-(III), trans(N)-[Co(nta)(gly)]$^-$, which is a parent complex of the complexes in this work, is optically inactive,



trans(N)-[Co(nta)(gly)]$^-$

because it has a plane of symmetry through coordinated oxygen and nitrogen atoms of gly ligand and a nitrogen atom of nta ligand. When one of the two methylene protons of gly is replaced by a methyl group, leading to trans-[Co-(nta)((R)- or (S)-ala)]$^-$ ((R)- or (S)-ala = (R)- or (S)-alaninate) complex, or one of six protons of nta ligand is replaced by a methyl group, leading to the trans(N)-[Co((R)- or (S)-alada)(gly)]$^-$ ((R)- or (S)-alada = (R)- or (S)-alaninate-N,N-diacetate) complex, the resultant complex contains an asymmetric carbon atom and is optically active. The optical activity of both complexes is contributed only from the vicinal effect due to the optically acitve ligand, (R)- or (S)-ala for the former complex and (R)- or (S)-alada for the latter one.

When one of the two coplanar N-acetate rings of nta in the parent nta complex is replaced by a N-propionate ring, leading to the trans(N)-[Co(β-alada)(gly)]$^-$ (β-alada = β-alaninate-N,N-diacetate), the resultant complex is optically active because of loss of the plane of symmetry in the original nta complex. The optical activity of this complex is not contributed from the "conventional" sources of chirality, configurational and vicinal effects, and is contributed from the effect which is named as "arrangement" in this work.

The optically active complexes in this work have the chiral structure where the two kinds of sources of chirality, vicinal and arrangement effects, are introduced in various manners to the parent nta complex or the corresponding cis(N) complex. For example, the optical activity of the trans(N)- or cis(N)-[Co((S)-alada)((S)-ala)]$^-$ complex is contributed from the vicinal effects due to the two different optically active ligands in the complex.

The nitrilotricarboxylato ligands except nta used to prepare the present complexes have nonidentical feet, as in (S)-alada and β-alada. When such a ligand coordinates to an octahedral cobalt(III) ion as quadridentate, several stereoisomers are possible with respect to the arrangement of the three feet of the ligand. Therefore, the present complexes are also interesting in connection with the stereochemistry of the stereoisomers.

In this work, the preparation and the separation of stereoisomers of the trans(N)- and cis(N)-(nitrilotri-

carboxylato)(aminocarboxylato)cobaltate(III) type complexes will be reported. The structural assignment of these stereoisomers will be made based on the electronic absorption and PMR spectra and stereochemical considerations. The CD spectra of the chiral complexes of which the optical activities are contributed from the vicinal and arrangement effects will be discussed. Furthermore, the absolute configuration of the chiral stereoisomers will be determined on the basis of the CD spectra.

Purpose of this work.

This work was conducted with the following purposes,

(a) To prepare new complexes of (nitrilotricarboxylato)-(aminocarboxylato)cobaltate(III) type,

(b) To study the CD contribution from the vicinal and arrangement effects,

(c) To determine the absolute configuration of the complex on the basis of the CD spectra,

(d) To explore the stereochemistry of the complexes with nitrilotricarboxylato ligands having nonidentical feet.

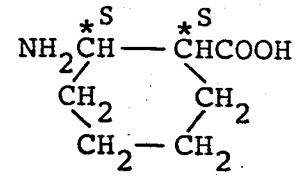
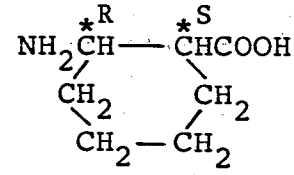
Abbreviations of ligands.

(a) Nitrilotricarboxylate ($N-O_3$ in general).

nta	nitrilotriacetic acid (H_3nta)	$N(CH_2COOH)_3$
(R)-or (S)-alada..	(R)- or (S)-alanine-N,N-diacetic acid ((R)- or (S)-H_3alada)	$N(CH_2COOH)_2(\overset{*}{C}H(CH_3)COOH)$
(R,S)-alaipa	(R,S)-alanine-N-iso-propionic-N-acetic acid ((R,S)-H_3alaipa)	$N(CH_2COOH)(\overset{*R}{C}H(CH_3)COOH)(\overset{*S}{C}H(CH_3)COOH)$
(S,S)-alaipa	(S,S)-alanine-N-iso-propionic-N-acetic acid ((S,S)-H_3alaipa)	$N(CH_2COOH)(\overset{*S}{C}H(CH_3)COOH)(\overset{*S}{C}H(CH_3)COOH)$
β-alada	β-alanine-N,N-diacetic acid (β-H_3alada)	$N(CH_2COOH)_2(CH_2CH_2COOH)$
(S)-alapa	(S)-alanine-N-propionic-N-acetic acid ((S)-H_3alapa)	$N(CH_2COOH)(CH_2CH_2COOH)(\overset{*}{C}H(CH_3)COOH)$

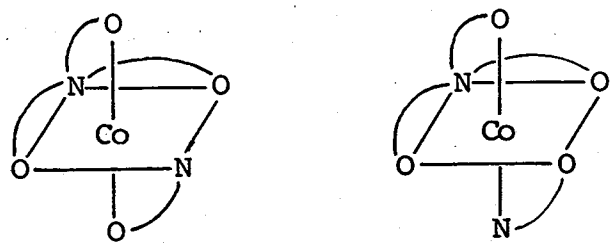
(b) Aminocarboxylate (am in general)

gly	glycine (Hgly)	NH_2CH_2COOH
(S)-ala	(S)-alanine ((S)-Hala)	$NH_2\overset{*}{C}H(CH_3)COOH$
(S)-val	(S)-valine ((S)-Hval)	$NH_2\overset{*}{C}H(CH(CH_3)_2)COOH$
(S)-ser	(S)-serine ((S)-Hser)	$NH_2\overset{*}{C}H(CH_2OH)COOH$
(S)-pro	(S)-proline ((S)-Hpro)	$NH(CH_2)_3\overset{*}{C}HCOOH$

(S)-sar	(S)-sarcosine ((S)-Hsar)	$NH(CH_3)CH_2COOH$
β-ala	β-alanine (β-Hala)	$NH_2CH_2CH_2COOH$
(R)-α-Me-β-ala ..	(R)-α-methyl-β-alanine ((R)-α-Me-β-Hala)	$NH_2CH_2\overset{*}{C}H(CH_3)COOH$
(S)-β-Me-β-ala ..	(S)-β-methyl-β-alanine ((S)-β-Me-β-Hala)	$NH_2\overset{*}{C}H(CH_3)CH_2COOH$
(S,S)-achc	(1S,2S)-trans-2-amino-cyclohexanecarboxvlic acid ((S,S)-Hachc)	
(S,R)-achc	(1S,2R)-cis-2-amino-cyclohexanecarboxylic acid ((S,R)-Hachc)	
γ-ambut	γ-aminobutylic acid (γ-Hambut)	$NH_2CH_2CH_2CH_2COOH$

A general consideration of stereoisomers of complexes.

In the (nitriolotricarboxylato)(aminocarboxylato)-cobaltate(III) type complexes, the nitrilotricarboxylato ligand occupies the four coordination sites of an octahedron by its three feet in the only way, remaining two sites cis to each other. The aminocarboxylato ligand coordinates to the remaining two sites in the two coordination ways, trans and cis, with respect to the two donor nitrogen atoms in the complex. Accordingly, two geometrical isomers, trans(N) and cis(N), are possible for each of the complexes of this type (Fig. 1).



trans(N) cis(N)

Fig. 1. Two possible geometrical isomers.

For the complex with nitrilotriacetate (nta) of which the feet are identical, only the trans(N) and cis(N) isomers are possible. On the other hand, for the complex with a nitrilotricarboxylato ligand which has nonidentical feet, additional stereoisomers (geometrical and/or optical) are possible with respect to the arrangement of the three feet. For example, when the ligand β-alaninate-N,N-diacetate (β-alada) spans four coordination sites by its

three feet, of which one makes a six-membered chelate ring and the other two five-membered rings, three kinds of structure are possible as shown in Fig. 2. Thus, the

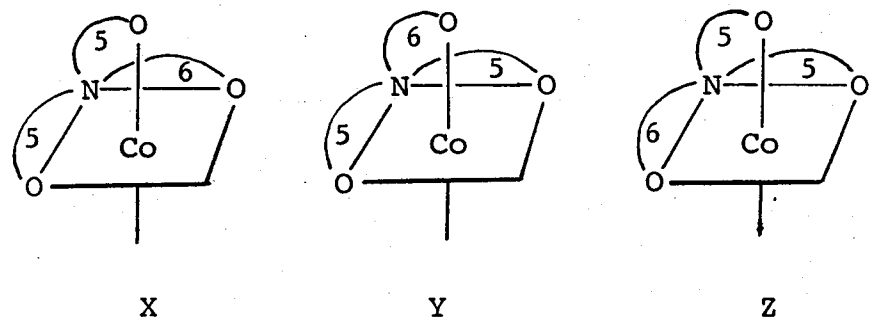


Fig. 2. Three possible structures of the coordinated β-alada.

isomers possible for the β-alada complexes with an amino-carboxylate are distinguishable from one another by use of two kinds of prefixes, that is, trans(N) or cis(N), and the designation (X,Y or Z)*1 of the three structures. In this work, such isomers with respect to the arrangement of the chelate rings of nitrilotricarboxylato ligand are named as "arrangement" isomer. The arrangement isomers possible for the present complexes are shown with their designations*1 in Table I.

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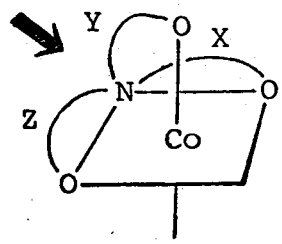
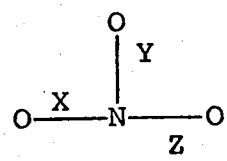
*1. A coordinated nitrilotricarboxylato ligand is observed along the arrow (I) and pictured schematically as in (II). Each chelate ring of the nitrilotricarboxylato ligands is shown by the following abbreviations, N—O, N-acetate ring, N—▼—O, N-iso-propionate ring (the symbol, ▼, represents the methyl group), and N—O, N-propionate ring.



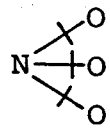
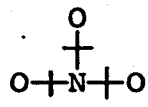
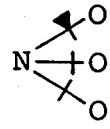
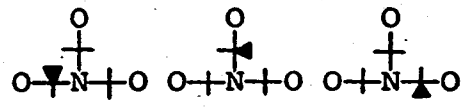
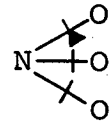
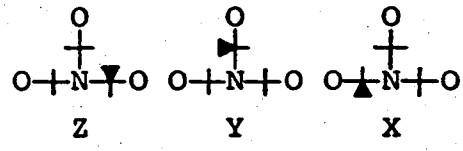
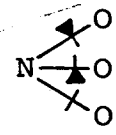
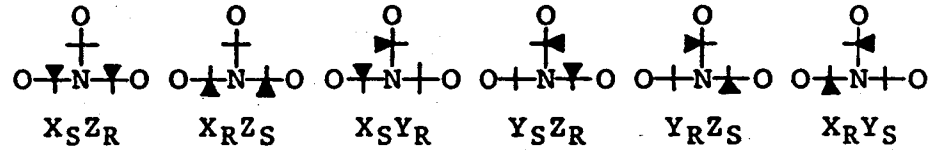
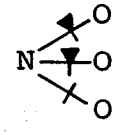
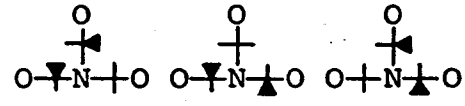
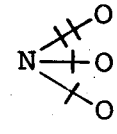
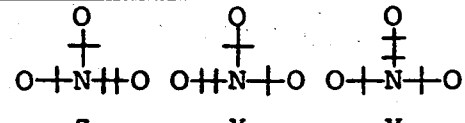
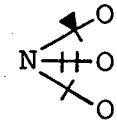
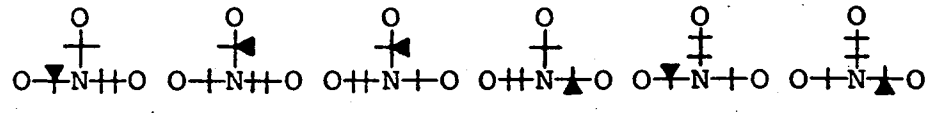
(I)



(II)

The designations of the arrangement isomers were made as follows. The three feet of nitrilotricarboxylato ligand are named by the symbols, X, Y and Z (I). The foot other than N-acetate ring is noted and the symbols corresponding to the noted foot or feet are used as the prefixes. If the distinction is impossible in this manner, the feet are distinguished by use of the following subscripts: "R or S" (absolute configuration of asymmetric carbon atom on the ring) and "6" (six-membered ring). Additional designation, u or s, is used for the β-alaninate-N,N-acetato (β-alada) complex. The u denotes unsymmetrical isomer with respect to the coordinated β-alada, while the s symmetrical isomer.

Table I. The possible arrangement isomers for the complexes[a)]

Ligand	Arrangement isomer
 nta	 X
 (S)-alada	 X Y Z
 (R)-alada	 Z Y X
 (R,S)-alaipa	 X_SZ_R X_RZ_S X_SY_R Y_SZ_R Y_RZ_S X_RY_S
 (S,S)-alaipa	 XY XZ YZ
 β-alada	 Z X (u) Y (s)
 (S)-alapa	 X_SZ_6 Y_SZ_6 Y_SX_6 Z_SX_6 X_SY_6 Z_SY_6

a) See footnote *1.

Chapter I. Experimental

I-1. Preparation of nitrilotricarboxylato ligands.

I-1-1. (R)- and (S)-Alanine-N,N-diacetic acid: (R)- and (S)-H_3alada.

(1) The ligand (S)-H_3alada was prepared by the following procedure. A solution of monochloroacetic acid (130 g, 1.1 mol) in 200 ml (0.8 mol) of 4N potassium hydroxide was added to a solution of (S)-alanine (44.5 g, 0.5 mol) in 125 ml (0.5 mol) of 4N potassium hydroxide. To the resulting solution 325 ml (1.3 mol) of 4N potassium hydroxide was added dropwise with vigorous stirring at 70-75° for 3 hr (at 90° for 20 min at the final stage of the reaction). The pH of the solution was maintained in the range of 9-11 during the reaction. After the reaction had been completed, the reaction mixture was acidified to pH 0.6 with concentrated hydrochloric acid and the solution was concentrated on a vacuum evaporator until an appropriate amount of granular crystals (potassium chloride) appeared. The crystals were removed by filtration, washed well with hot methanol and the combined filtrate and washings were concentrated again. After about 100 g of potassium chloride in total had been removed from the mixture by repeating this operation, the fine crystals began to crystallize out from the final filtrate. The solution was kept in a refrigerator overnight and the desired product deposited was filtered and washed well with cold water. The combined filtrate and washings were concentrated on a vacuum evaporator and the

potassium chloride deposited was removed by filtration. The desired product deposited from the filtrate was collected by filtration and washed with cold water and the combined filtrate and washings were concentrated again. After this operation was repeated several times, the desired product 112 g in total was obtained. The product was contaminated with a considerable amount of potassium chloride and recrystallized a few times from boiling water; yield 62.5 g (61 %); $[\alpha]_D^{21-25}$ -41.2°– -42.4° (c 4, water) in several experiments. Anal. Calcd for $C_7H_{11}NO_6$: C, 40.97; H, 5.41; N, 6.83 %. Found: C, 40.66; H, 5.42; N, 6.71 %.

The (R)-H_3alada ligand was prepared by the same procedure as that for (S)-H_3alada by use of (R)-alanine instead of (S)-alanine; $[\alpha]_D^{25}$ +41.4° (c 4.0, water). Anal. Found: C, 40.53, H, 5.24; N, 6.74 %.

(2) Recovery of (S)-H_3alada from X-trans(N)-K[Co((S)-alada)(gly)].

In order to examine the optical purity of the (S)- and (R)-H_3alada obtained in (1), optically pure (S)-H_3alada was recovered from the X-trans(N)-K[Co((S)-alada)(gly)]·3.5H_2O, which was confirmed to be optically pure (I-3-2-(2-b)). Into a solution of 2 g of the (S)-alada complex in dilute aqueous ammonium was bubbled hydrogen sulfide until the supernatant solution of the resulting mixture became to pale yellow. The cobalt sulfide precipitated was removed by filtration and the filtrate was concentrated to syrup. To the concentrate was added 3 ml of water and small amount of insoluble materials were removed by filtration. The

filtrate was poured into a column (17 × 50 mm) containing a cation-exchange resin (Dowex 50W-X8, 200-400 mesh, hydrogen form). Water was passed through the column and the eluates containing the desired acid were collected and concentrated to dryness. The desired acid deposited was recrystallized once from boiling water; yield 0.6 g; $[\alpha]_D^{23}$ -42.6° (c 4, water).

I-1-2. (S,S)- and (R,S)-Alanine-N-iso-propionic-N-acetic acid: (S,S)- and (R,S)-H_3alaipa.

(1) (S,S)- and (R,S)-Alanine-N-mono-iso-propionic acid.

A solution of α-chloropropionic acid (119 g, 1.1 mol) in 200 ml (1.2 mol) of 4N potassium hydroxide was added to a solution of (S)-alanine (89 g, 1.0 mol) in 250 ml (1.0 mol) of 4N potassium hydroxide. To the resulting solution 4N potassium hydroxide (325 ml, 1.3 mol) was added dropwise with vigorous stirring at 85-90° for 3 hr. The pH of of the solution was maintained in the 10-11 range during the reaction. The reaction mixture was acidified to pH 2.4 with concentrated hydrochloric acid. The contaminant potassium chloride was removed as much as possible from the solution by a similar procedure to that in the preparation of (S)-H_3alada (I-1-1-(1)). When the pH of the solution was adjusted to 2.0 with concentrated hydrochloric acid, the white crystals began to crystallized out. To the mixture was added a large amount of methanol and this was kept in a refrigerator overnight. The crystals deposited were filtered and washed well with cold water.

The product (60 g) obtained was a mixture of (S,S)- and (R,S)-alanine-N-mono-iso-propionic acid and contaminated with a small amount of potassium chloride. The combined filtrate and washings were concentrated on a vacuum evaporator and potassium chloride deposited as granular crystals was removed by filtration. An additional 32 g of the crude desired product was obtained from the filtrate. The combined product was recrystallized from boiling water; yield 74 g (46 %); $[a]_D$ + 6.2° (c 4, water). The PMR measurement showed that the product was a mixture of approximately equal amount of the (S,S)- and (R,S)-isomers. Anal. Calcd for $C_6H_{11}NO_4$: C, 44.71; H, 6.89; N, 8.69 %. Found: C, 44.68; H, 6.97; N, 8.63 %.

(2) (S,S)- and (R,S)-H_3alaipa.

A mixture of (S,S)- and (R,S)-alanine-N-mono-iso-propionic acid (56.3 g, 0.35 mol) obtained in (1) and monochloroacetic acid (38.7 g, 0.41 mol) were dissolved with stirring in 253 ml (1.01 mol) of 4N potassium hydroxide. To this solution 113 ml (0.45 mol) of 4N potassium hydroxide was added dropwise with vigorous stirring at 85-90° for 3 hr (at 95-98° for 30 min at the final stage of the reaction). The pH of the solution was maintained in the 11-11.5 range during the reaction. After the addition, the solution was acidified to pH 1.6 with concentrated hydrochloric acid. After a large amount of potassium chloride had been removed from the solution as in the preparation of (S)-H_3alada (I-1-1-(1)), 50 ml of water was added to the final syrupy

filtrate. The pH of the solution was adjusted to 1.0 with concentrated hydrochloric acid and the solution was kept in a refrigerator for a few hours. The first crop deposited as fine crystals was filtered and washed well with cold water. This product was the desired acid, which contaminated with a small amount of potassium chloride. The combined filtrate and washings were concentrated again and the potassium chloride deposited was removed by filtration. The several crops were obtained by repeating this operation. The crops (20 g) which contain mainly (S,S)-isomer (more than 90 %) were collected and recrystallized several times from boiling water until the optical rotation at 300 nm became constant; yield 14.8 g (19.3 % based on the mixture of (S,S)- and (R,S)-alanine-N-mono-iso-propionic acids used); $[\alpha]_D^{22}$ -57.1° (c 0.8, water). The crops (12.1 g) which contain mainly (R,S)-isomer (more than 90 %) were recrystallized from boiling water until the optical rotation at 300 nm became zero within experimental error; yield 10.8 g (14.1 %). The separation of isomers from the other crops (10.6 g) was not attempted. The proportion of the (S,S)- and (R,S)-isomers in a product can be approximately estimated on the basis of the characteristic peaks in the IR spectra: 688 cm^{-1} for (S,S)-isomer and 717 cm^{-1} for (R,S)-isomer. Anal. Calcd for $C_8H_{13}NO_6$: C, 43.83; H, 5.99; N, 6.39 %. Found: C, 43.99; H, 5.91; N, 6.39 % for (R,S)-H_3alaipa and C, 43.81; H, 6.05; N, 6.40 % for (S,S)-H_3alaipa.

I-1-3. β-Alanine-N,N-diacetic acid: β-H_3alada.

This was prepared from the β-alanine and monochloro-

acetic acid by the method of Thuchiya and co-workers.[55]

I-1-4. (S)-Alanine-N-propionic-N-acetic acid: (S)-H_3alapa.

(1) (S)-Alanine-N-monopropionic acid.

A solution of β-chloropropionic acid (58.7 g, 0.55 mol) in 100 ml (0.4 mol) of 4N potassium hydroxide was added to a solution of (S)-alanine (44.5 g, 0.5 mol) in 125 ml (0.5 mol) of 4N potassium hydroxide. To the resulting solution 163 ml (0.65 mol) of 4N potassium hydroxide was added dropwise with vigorous stirring at 75-80° for about 2 hr. The pH of the solution was maintained in the range of 9-10 during the reaction. The reaction mixture was acidified to pH 2.0 with concentrated hydrochloric acid and concentrated as far as possible on a vacuum evaporator. After an appropriate amount of water had been added to the residue in order to dissolve potassium chloride deposited as glanular crystals, the remaining fine crystals were collected by filtration and washed well with cold water; yield 55 g. The product was the desired acid, which was contaminated with a small amount of potassium chloride. This was recyrstallized from 90 ml of boiling water; yield 40.8 g (51 %) of prismatic crystals; $[\alpha]_D^{24}$ +4.7° (c 6, water) (lit,[56] $[\alpha]_D^{20}$ +3.2° (c 2.47, water)).

(2) (S)-H_3alapa.

(S)-Alanine-N-monopropionic acid (32.2 g, 0.2 mol) obtained in (1) and monochloroacetic acid (22,7 g, 0.24 mol) were dissolved with stirring in 140 ml (0.56 mol) of 4N

potassium hydroxide. To this solution 70 ml (0.56 mol) of 4N potassium hydroxide was added dropwise with vigorous stirring at 80-85° for 2.5 hr. The pH of the solution was maintained in the range 10-11 during the reaction. The reaction mixture was acidified to pH 1.4 with concentrated hyrochloric acid and concentrated as far as possible on a vacuum evaporator. To the concentrate a large amount of methanol was added and the mixture was stirred well at about 70°. A large amount of potassium chloride remained in solid was filtered and washed with hot methanol, and then the combined filtrate and washings were concentrated to syrup on a vacuum evaporator. To the concentrate was added 100 ml of water. The solution was poured into a column (35 x 800 mm) containing a cation-exchange resin (Dowex-X8, 200-400 mesh, hydrogen form) and water was passed through the column. The eluates containing the desired acid were collected and concentrated to dryness. The crystals (22 g) deposited were recrystallized from 35 ml of boiling water; yield 19 g (43 %); $[\alpha]_D^{25}$ -8.4° (c 4, water). Anal. Calcd for $C_8H_{13}NO_6$: C, 43.84; H, 5.89; N, 6.39 %. Found: C, 43.77; H, 6.04; N, 6.36 %.

I-2. Preparation of β-aminocarboxylato ligands.

I-2-1. (R)-α-Methyl-β-alanine: (R)-α-Me-β-Hala.

The racemic modification was prepared by Pollack's method[57] and resolved by the method of Kakimoto and Armstrong[58]; mp 192-194° (decomp); $[\alpha]_D^{19}$ -15.3° (c 5, water) (lit,[59] mp 194-196°, $[\alpha]_D^{27}$ -15.4° (c 1, water)).

I-2-2. (S)-β-Methyl-β-alanine: (S)-β-Me-β-Hala.

This ligand was derived from (S)-alanine by the method of Balenovic[60]; mp 211-213° (decomp); $[\alpha]_D^{15}$ +36.4° (c 2, water)(lit,[60] mp 212°; $[\alpha]_D^{19}$ +37.07° ± 1° (c 6, water)).

I-2-3. $(+)_D$-(1S,2S)-trans-2-aminocyclohexanecarboxylic acid: (S,S)-Hachc.

(1) (±)-N-Benzoyl-trans-2-aminocyclohexanecarboxylic acid.

(±)-Trans-2-aminocyclohexanecarboxylic acid was prepared from o-aminobenzoic acid by the action of metallic sodium in iso-amyl alcohol.[61,62] This was benzoylated by the reaction with benzoyl chloride in an usual method;[63] mp 226-227° (lit,[62] 226-227°).

(2) Optical resolution of (±)-N-benzoyl-trans-2-aminocyclohexanecarboxylic acid.

To a solution of 20.4 g (0.0826 mol) of (±)-N-benzoyl-trans-2-aminocyclohexanecarboxylic acid in 260 ml of boiling ethanol was added 10 g (0.0826 mol) of $(-)_D$-α-phenethylamine. After the solution resulted had been allowed to stand in a refrigerator, the crude less solubel diastereomer were collected by filtration; yield 13.6 g; $[\alpha]_{320}$ +59.7° (c 1, ethanol). Since it has been found by Nohira and co-workers[64] that the optical resolution of the benzoylate could be achieved by a preferential crystallization, the diastereomer obtained was used in the next step without further purification. The diastereomer was added in 4N sodium hydroxide in an ice-

bath and free α-phenethylamine separated out was removed by extraction with ether. The water layer was made acid to Congo red with 3N hydrochloric acid and the crude benzoylate deposited was collected by filtration; yield 9.0 g, $[\alpha]_{320}$ +128° (c 1, ethanol). This was recrystallized twice from boiling methanol to give pure $(+)_D$-N-benzoyl-trans-2-aminocyclohexanecarboxylic acid; yield 7.7 g; $[\alpha]_{315}$ +152° (c 1, ethanol), $[\alpha]_D^{19}$ +45.4° (c 1, ethanol); mp 250-251° (lit,[64] $[\alpha]_D^{20}$ +44.5° (c 0.67, ethanol); mp 257-258°).

The pure less soluble diastereomer was obtained by two recrystallization of the crude product obtained as described above from boiling ethanol; $[\alpha]_{320}$ +77.1° (c 1, ethanol), $[\alpha]_D^{18}$ +25.7° (c 2, ethanol); mp 199.5-200.5°. Anal. Calcd for $C_{22}H_{28}N_2O_3$: C, 71.70; H, 7.67; N, 7.60 %. Found: C, 71.52; H, 7.62; N, 7.66 %.

(3) (S,S)-Hachc.

A mixture of 6.6 g of the optically pure benzoylate obtained in (2) and 200 ml of concentrated hydrochloric acid was refluxed until the crystals of benzoylate had completely dissolved (about 60 hr). The solution obtained was cooled in a refrigerator for a few hours and the bezoic acid deposited was removed by filtration. The filtrate was concentrated to dryness on a vacuum evaporator and the residue was dissolved in L0 ml of water. After a small amount of insoluble materials had been removed by filtration, the filtrate was poured into a column (17 x 250 mm) containing

a cation-exchange resin (Dowex 50W-X8, 200-400 mesh, hydrogen form). The column was swepted with water and the eluates containing the desired aminocarboxylic acid were collected and concentrated to dryness. The white powder obtained was recrystallized from 70 % ethanol to give the dihydrate of the desired acid as transparent granular crystals; yield 3.6 g. Anal. Calcd for $C_7H_{13}NO_2 \cdot 2H_2O$: C, 46.90; H, 9.58; N, 7.87; H_2O, 20.10 %. Found: C, 46.99; H, 9.56; N, 7.69; H_2O, 20.10 %. This lost easily water of crystallization over anhydrous calcium chloride in a vacuum dessicator; Anal. Calcd for $C_7H_{13}NO_2$: C, 58.70; H, 9.17; N, 9.78 %. Found: C, 58.57; H, 9.31; N, 9.70 %, mp 250° (decomp); $[\alpha]_D^{16}$ +77.3° (c 2, water) (lit,[64] mp 264°; $[\alpha]_D^{17}$ +66.5° (c 2, water)).

I-2-4. $(+)_D$-(1S,2R)-cis-2-aminocyclohexanecarboxylic acid: (S,R)-Hachc.

The absolute configuration of this aminocarboxylic acid was confirmed in this work (see Section II-1-(2)).

(1) (±)-N-Bezyloxycarbonyl-cis-2-aminocyclohexanecarboxylic acid.

The (±)-cis-2-aminocyclohexanecarboxylic acid was prepared from cis-1,2-cyclohexanedicarboxylic acid according to the method of Armitage and co-workers;[65] 232-233° (lit,[65] mp 235°). Its benzyloxycarbonyl derivative was prepared by the reaction with benzyloxycarbonyl chloride in an usual method;[63] mp 129-130°. Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.95; H, 6.92; N, 5.05 %. Found: C, 64.86; H, 6.74; N, 5.08 %.

(2) Optical resolution of (±)-N-benzyloxycarbonyl-cis-2-aminocyclohexanecarboxylic acid.

To a solution of 27.7 g (0.1 mol) of (±)-N-benzyloxycarbonyl-cis-2-aminocyclohexanecarboxylic acid in 132 ml of hot ethyl acetate was added 12.1 g (0.1 mol) of $(-)_D$-α-phenethylamine. After the solution had been allowed to stand overnight at room temperature, the crude less soluble diastereomer deposited was collected by filtration; yield 17.7 g. This was recrystallized from boiling ethyl acetate. The optical purity of the diastereomer was checked by the optical rotation measurements of the benzyloxycarboxylate obtained by the method described below, because the diastereomer had very unstable water of crystallization and furthermore its optical rotation was very small in the range of 600-300 nm. Two recrystallization gave the pure less soluble diastereomer; yield 12.5 g; mp 135.5-137.5°; $[\alpha]_D^{22}$ +4.1° (c 5, ethanol). Anal. Calcd for $C_{23}H_{30}N_2O_4 \cdot 0.2H_2O$: C, 68.69; H, 7.63; N, 6.97 %. Found: C, 68.59; H, 7.71; N, 6.75 %. The crude benzyloxycarboxylate was obtained from 8.0 g of the diastereomer by the same procedure as that for the corresponding trans isomer described in I-2-3-(2). This was recrystallized twice from boiling 70 % methanol and further recrystallization did not give the change of its properties; yield 4.4 g, mp 125-126°; $[\alpha]_D^{22}$ +16.7° (c 5, ethanol), $[\alpha]_{295}$ +53.7° (c 5, ethanol). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.95; H, 6.92; N, 5.05 %. Found: C, 64.70; H, 6.86; N, 5.12 %.

(3) (S,R)-Hachc.

A solution of 2.8 g of the benzyloxycarboxylate obtained in (2) in 50 ml of methanol was subjected to catalytic reduction using a 10 % palladium on charcoal as catalyst in an usual method.[63] After completion of the reaction, the catalyst was removed by filtration and washed with a small amount of water. The combined filtrate and washings were concentrated to dryness on a vacuum evaporator. The desired acid of white crystals obtained was recrystallized once from 50% methanol; yield 1.2 g; mp 245° (decomp); $[\alpha]_D^{22.5}$ +19.2° (c 2.7, water). Anal. Calcd for $C_7H_{13}NO_2$: C, 58.70; H, 9.17; N, 9.78 %. Found: C, 58.44; H, 9.10; N, 9.75 %.

(4) $(+)_D$-(1S,2R)-N-Benzoyl-cis-2-aminocyclohexanecarboxylic acid.

This was prepared by the benzoylation of the $(+)_D$-(1S,2R)-cis-2-aminocyclohexanecarboxylic acid in an usual method;[63] mp 205.5-206.5°; $[\alpha]_D^{22}$ +38.0°, $[\alpha]_{346}$ +127.2° (c 2.95, 95 % ethanol)(lit,[66] mp 206.5-207°, $[\alpha]_{578}$ +41.9°, $[\alpha]_{346}$ +132° (0.31, 95 % ethanol).

I-3. Preparation of Complexes.

I-3-1. Nitlirotriacetato (nta) complexes; trans(N) and cis(N)-potassium (or sodium)(nitrilotriacetato)(aminocarboxylato)cobaltate(III): trans(N)- and cis(N)-K(or Na)-[Co(nta)(am)] (am = gly, (S)-ala, (S)-ser, (S)-val, sar, (S)-pro, β-ala, (R)-α-Me-β-ala, (S)-β-Me-β-ala, (S,S)-achc, (S,R)-achc, or γ-ambut).

The final products of all the desired complexes were air-dried at room temperature unless otherwise stated and the results of their chemical analyses were summarized in Table II (page 50).

(1) Preparation of reaction mixtures and separation of the trans(N) and cis(N) isomers.

To 3.92 g (0.02 mol) of H_3nta was added 2N potassium hydroxide (ca. 20 ml) until the pH reached 5.0-5.6 and to the resulted solution was added a solution of 5.0 g (0.02 mol) of cobalt(II) acetate tetrahydrate in 15 ml of water and then 3 g of lead dioxide. After the resulting mixture had been mechanically stirred at 50° for about 10 min (before sprlingly soluble blue substances begin to crystallize out), the desired aminocarboxylic acid (0.02 mol) and 3 g of lead dioxide were added to it and the mixture resulted was sterred at 50° during the following reaction time: 2 hr for α-aminocarboxylato complexes and 1 hr for the β- and γ-aminocarboxylato ones. After having been allowed to stand at room temperature, the reaction mixture was filtered and washed with a small amount of water. The combined

filtrate and washings were concentrated to about 20 ml on a vacuum evaporator. After removal of insoluble substances by filtration, the filtrate was poured dropwise with vigorous stirring in about 400 ml of ethanol (only in the (S)-pro complex, a small amount of ether was added additionally to it). it). Almost all fo the colored complexes were precipitated as a powder by this operation. The crude product precipitated was filtered ans washed ethanol and wther, and then dried over anhydrous calcium chloride in a vacuum desiccator. The yield was approximately 7 g.

About 7 g of each crude product obtained above was dissolved in a small amount of water and the insoluble substances were removed by filtration. The filtrate was adsorbed on a column (35 X 800 mm) containing an anion-exchange resin (Dowex 1-X8, 200-400 mesh, chloride form). After the column had been swepted with water, the adsorbed band was eluted with 0.07 M aqueous solution of potassium chloride at a rate of about 2.5 ml/min. After the elution for about 3 days, two colored bands, a reddish purple one and a violet one, were separately eluted in this order. The reddish purple band was confirmed to be trans(N) isomer and the violet one to be cis(N) isomer by the measurements of their absorption spectra (see Section II-3-1). In the sar, (S)-pro and γ-ambut complexes, the violet bands were not observed; only trans(N) isomer was obtained.

(2) Isolation of complexes.

(a) Each of the eluates in (1) was concentrated to several

milliliters on a vacuum evaporator below 40° and the potassium chloride deposited was removed by filtration. A small amount of methanol was added to the filtrate at about 40° and the potassium chloride deposited was removed again. After the concentration and the separation of potassium chloride were repeated a few times, the crystals of the desired complex began to crystallize out from the filtrate except for the five complexes described below. The complex deposited was collected by filtrationand recrystallized from warm water by adding methanol.

By the above treatment, the five complexes obtained as powders contaminated with a small amount of potassium chloride because of difficulty of their crystallization; therefore, they were treated as in (b) or (c).

(b) In the three complexes of them, the trans(N) isomers of (S)-val and (S)-pro complexes and the cis(N) one of (R)-α-Me-β-ala complex, each of the crude complexes was dissolved in a minimum amount of water and an appropriate amount of silver acetate was added to the solution in order to separate the contaminant potassium chloride. The resulting mixture was well stirred with a glass rod. The silver chloride precipitated was removed by filtration and to the filtrate a large amount of ethanol was added in order to precipitate almost all of the colored complexes. The powdery product was collected by filtration and washed well with ethanol, and then ether. It was recrystallized from a small amount of water by adding methanol, and then ethanol if necessary. The pure complex was obtained as a nonhygroscopic powder.

(c) In the other complexes, the trans(N) isomer of (R,S)-achc complex and the cis(N) one of β-ala complex, the counter ions were converted from potassium to sodium ones by the column chromatographic method. Each of the crude complexes (ca. 0.5 g) was dissolved in a small amount of water and the resulting solution was poured into a column (17 X 50 mm) containing a cation-exchange resin (Dowex 50W-X8, 200-400 mesh, sodium form). The colored eluate obtained by sweeping with water was concentrated to a few milliliters on a cacuum evaporator below 40°. To the concentrate was added a small amount of methanol and the crystalline complex deposited was filtered and recrystallized from warm water by adding methanol.

I-3-2. (R)- or (S)-Alaninate-N,N-diacetato ((R)- or (S)-alada) complexes; trans(N)- and cis(N)-potassium ((R)- or (S)-alaninate-N,N-diacetato)(aminocarboxylato)cobaltate(III); trans(N)- and cis(N)-K[Co((R)- or (S)-alada)(am)] (am = gly or β-ala for (S)-alada, and (S)-ala, (S)-pro, (R)-α-Me-β-ala, or (S)-β-Me-β-ala for both of (R)- and (S)-alada).

(1) Preparation of reaction mixtures and separation of trans(N) and cis(N) isomers.

The reaction mixture was prepared by a similar procedure to the used for the nta complexes described in I-3-1-(1), using (R)- or (S)-H_3alada (4.1 g, 0.02 mol) instead of H_3nta, after adding aminocarboxylic acid, two hour reaction was taken for α-aminocarboxylato complexes and one hour for β-aminocarboxylato ones. Each curde product obtained was chromatographed by the same procedure as that for nta

complexes. Two colored bands, a reddish purple one (trans(N) isomer) and a violet one (cis(N) isomer), were separately eluted in this order except for the γ-ambut or (S)-pro complex, in which only the reddish purple band was eluted.

(2) Separation of arrangement isomers.

(a) X-trans(N)- and X-cis(N)-[Co((S)-alada)(am)]$^-$ and Z-trans(N)- and Z-cis(N)-[Co((R)-alada)(am)]$^-$ complexes (isomer-i for each of the complexes).

From each of the eluates in (1), the pure crystalline complexes were obtained as a potassium salt by a similar procedure to that for the nta complexes described in I-3-1-(2-a). Only the trans(N) isomer of (R)-α-Me-β-ala complex was obtained as a nonhygroscopic powder by the same treatment as that for the complexes in I-3-1-(2-b). In all cases, the yield of the solid complex finally isolated was more than 80 % of the complex estimated on the basis of measurement of the absorption of the eluate separated by column chromatography.

(b) Purification of X-trans(N)-K[Co((S)-alada)(gly)] by diastereomer formation.

This experiment was carried out in order to examine whether the X-trans(N)-[Co((S)-alada)(gly)]$^-$ complex obtained in (a) is optically pure or not. A suspension of 1.0 g (0.0025 mol) of $(+)_D$-[Co(ox)(en)$_2$]I in 2.5 ml of water was stirred with 0.04 g of silver acetate until the brown crystals of the resolving agent went to sight. The silver iodide was filtered and washed with a small aount of water. The combined

filtrate and washings were warmed to 50°, and while 1.1 g (0.0025 mol) of the X-trans(N)-[Co((S)-alada)(gly)]·$3.5H_2O$ was dissoved in 1.5 ml of water at 50°. Both the solutions were mixed and the resulting solution was cooled in a refrigerator for a few four. The brownish-pink needle diastereomer deposited was collected by filtration and washed with water-methanol (1 : 1) and methanol and air-dried. The diastereomer was recrystallized from 15 ml of warm water (about 50°) by adding methanol; yield 1.1 g. The CD intensity of the potassium salt of the desired complex was unchanged by further recrystallization.* Anal. Calcd for $(+)_D$-[Co(ox)$(en)_2$]·X-trans(N)-[Co((S)-alada)-(gly)]·$5H_2O$: C, 26.02; H, 5.54; N, 12.14 %. Found: C, 25.95; H, 5.24; N, 12.21 %. The diastereomer (0.9 g) was dissolved in a minimum amount of water and the solution was poured into a column (10 x 50 mm) containing a cation-exchange resin (Dowex 50W-X8, 200-400 mesh, potassium form). By sweeping with water, the desired

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* The purity of the diastereomer was estimated as follows. An aqueous solution of the potassium salt was prepared from the diastereomer (about 0.03 g) by use of a column containing a cation-exchange resin (potassium form) as described in the next step to obtain the desired potassium salt from the pure diastereomer. The desired eluate was adjusted to a reasonable concentration by dilution with water and the CD intensity were determined from its absorption and CD spectra.

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complex, K[Co((S)-alada)(gly)], was eluted as a reddish purple solution, while the resolving agent, $(+)_{546}$-$[Co(ox)(en)_2]^+$, remained at top of the column. The reddish purple eluate was concentrated to a few milliliters below 40° on a vacuum evaporator. An appropriate amount of ethanol was gradually added to the solution. The plate crystals deposited were collected by filtration; yield 0.43 g. The CD spectrum of this complex completely conincided with that of the original complex used for the purification. This indicates that the original complex is optically pure.

(c) Y-trans(N)-K[Co((S)-alada)(gly)] (isomer-ii).

The X-trans(N)-K[Co((S)-alada)(gly)]·$3.5H_2O$ (isomer-i, 12.0 g) obtained in (a) was dissolved in 50 ml of water and 1.2 g of activated charcoal was added to the solution. After the resulting mixture had been kept with stirring at 70° for 1 hr, the charcoal was removed by filtration. To the filtrate was added 25 ml of ethanol and the prismatic crystals (isomer-i) deposited were removed by filtration. The filtrate was evaporated to a few milliliters on a vacuum evaporator below 30° and a small amount of methanol was added to the concentrated solution and the crystals deposited were removed by filtration. By this process, the crystalline complex of 9.9 g in total, which was the essentially pure X-trans(N) complex (isomer-i), was recovered from the original filtrate. To the final filtrate a large amount of ethanol was added in order to precipitate almost all of colored materials and the pinkish powder precipitated

was filtered and wahsed with ethanol and ether, and dried over anhydrous calcium chloride in a vacuum dessicator; yield 1.5 g of hygroscopic powder.

The crude product (0.6 g) dissolved in a minimun amount of water was chromatographed over an anion-exchange resin by a similar procedure as that described for the nta complexes (I-3-1-(1)). After about 15 days' elution, three colored bands, two partly overlapped reddish purple ones (trans(N) isomers) in dominant amount and a violet one (cis(N) isomer) in a trace amount, were eluted in this order. It was confirmed by the absorption and CD measurements of the fractionated eluates that the violet band consisted of the X-cis(N) complex isolated in (a) In the trans(N) isomers, the earlier eluted band consisted of isomer-i and the later eluted band another isomer, isomer-ii (Y-trans(N) isomer). The later eluted fractions, which showed a constant CD value, were collected and concentrated almost to dryness below 30° on a vacuum evaporator. To the residue a small amount of methanol was added and the potassium chloride deposited was removed by filtration. From the eluate, the isomer-ii was obtained as a hygroscopic powder contaminated with a small amount of potassium chloride because of difficulty of crystallization and it was dired over calcium chloride in a vacuum dessicator; yield 0.05 g. No elemental analysis was carried out.

The Y-trans(N) isomer (isomer-ii) isomerizes slowly to the X-trans(N) isomer (isomer-i) in water at room temperature. After

about 40 days, the absorption and CD spcetra of the solution become constant and their shapes are agree with those of the X-trans(N) isomer within experimintal error. The molar absorptivity (ε) and molar circular dichroism (Δε) of the Y-trans(N) isomer (isomer-ii) were determined from the result of the isomerization.

I-3-3. (R,S)-Alanine-N-iso-propionate-N-acetato ((R,S)-alaipa) complexes; trans(N)- and cis(N)-potassium ((R,S)-alaninate-N-iso-propionate-N-acetato)(glycinato)cobaltate(III): trans(N)- and cis(N)-K[Co((R,S)-alaipa)(gly)].

(1) Preparation of reaction mixture and separation of trans(N) and cis(N) isomers.

The reaction mixture was obtained by a similar procedure to that for the nta complexes descrubed in I-3-1-(1), using (R,S)-H_3alaipa (8.76 g, 0.04 mol) instead of H_3nta: after adding glycine, the mixture was allowed to react for 3 hr. The crude product obtained was chromatographed by the same procedure as that for the nta complexes. Two colored bands, a reddish purple one (trans(N) isomer) and a violet one (cis(N) isomer), were eluted separately in this order.

(2) Separation of arrangement isomers.

(a) X_SZ_R-trans(N)-K[Co((R,S)-alaipa)(gly)] (isomer-i).

The trans(N) eluate obtained above was treated in order to remove the contaminant potassium chloride as described for the nta complexes in I-3-1-(2-b). To the filtrate from the silver chloride a large amount of ethanol was gradually added and the plate crystals deposited were collected by

filtration. This was recrystallized from warm water (about 50°) by adding methanol; yield 1.8 g. This desired isomer was isolated almost quantitatively from the trans(N) eluate.

(b) $X_S Z_R$-cis(N)-K[Co((R,S)-alaipa)(gly)] (isomer-i).

From the cis(N) eluate the desired isomer was isolated almost quantitiatively as scaly crystals by a similar procedure to that for the corresponding trans(N) isomer in (a). The crystals were recrystallized from warm water (about 50°) by adding methanol; yield 1.1 g.

I-3-4. (S,S)-Alanine-N-iso-propionate-N-acetato ((S,S)-alaipa) complexes; trans(N)- and cis(N)-potassium- (or sodium)((S,S)-alaninate-N-iso-propionate-N-acetato)(glycinato)-cobaltate(III): trans(N)- and cis(N)-K (or Na) [Co((S,S)-alaipa)(gly)].

(1) Preparation of reaction mixture and separation of trans(N) and cis(N) isomers.

The reaction mixture was obtained by a similar procedure to that for the nta complexes described in I-3-1-(1), using (S,S)-H_3alaipa (8.8 g, 0.04 mol) instead of H_3nta: after adding glycine, the reaction time was taken for 2 hr. The crude product obtained was chromatographed by the same procedure as that for the nta complexes. Three colored bands, a reddish purple one (a mixture of trans(N) isomers) and two violet ones (cis(N) isomers), were eluted in this order.

(2) Separation of arrangement isomers.

(a) XY-trans(N)-Na[Co((S,S)-alaipa)(gly)] (isomer-i).

From the trans(N) eluate obtained in (1) the contaminant potassium chloride was removed by a similar procedure to that for the nta complexes in I-3-3-(2-b). From the filtrate from silver chloride, 3.5 g of the powdery product was obtained was obtained by addition of a large amount of ethanol. Take account of racemization of the (S,S)-H_3alaipa used as the starting material, the product was treated as follows. The product (2.70 g) in 7 ml of warm water (ca. 40°) was mixed with a warm solution (ca. 40°) containing the acetate of $(+)_{546}$-$[Co(ox)(en)_2]^+$ which was derived from $(+)_{546}$-$[Co(ox)(en)_2]I$ (2.76 g), silver acetate (1.23 g) and water (10 ml) as described for the (S)-alada complex (I-3-2-(2-b)). After cooling in a refrigerator overnight, the brownish-pink needle diasteromer deposited was collected by filtration and washed with water-methanol (1 : 1) and methanol and air dried; yield 3.3 g. The filtrate and washings contained another isomer (isomer-ii, XZ-trans(N) isomer) in a trace amount, but the isolation of this isomer was not attempted here and achieved by the method described in (b). The diastereomer was recrystallized from 30 ml of warm water by adding methanol; yield, 2.6 g. The optical purity of diastereomer was checked as for the (S)-alada complex (I-3-2-(2-b)).

Anal. Calcd for $(+)_{546}$-$[Co(ox)(en)_2]\cdot$XY-trans(N)-[Co-((S,S)-alaipa)(gly)]$\cdot 4.5H_2O$: C, 27.55; H, 5.65; N, 12.05 %. Found: C, 27.48; H, 5.50; N, 12.37 %.

The diastereomer (2.5 g) was converted to the sodium salt by using a cation-exchange resin of sodium form by the same procedure as that for the (S)-alada complex (I-3-2-(2-b)). The prismatic crystals (isomer-i) were obtained from the colored eluate, and recrystallized from water by adding methanol; yield 1.3 g. Attempts to crystallize the potassium salt of this complex were unsuccessful.

(b) XZ-trans(N)-K[Co((S,S)-alaipa)(gly)] (isomer-ii).

XY-trans(N)-Na[Co((S,S)-alaipa)(gly)]·H_2O (isomer-i, 5.2 g) obtained in (a) was treated with activated charcoal by the same procedure as that for the preparation of the Y-trans(N) (S)-alada complex (I-3-2-(2-c)). From the filtrate, the crystalline complex (isomer-i, 4.3 g in total) was recovered by a similar procedure to that for the (S)-alada complex. To the final filtrate was added a large amount of ehtanol and the powdery product precipitated was collected by filtration. The crude product obtained as sodium salt (0.5 g) was converted to the potassium salt by using a cation-exchange resin of potassium form (I-3-1-(2-c)). The plane crystals (isomer-ii) were obtained from the colored eluate and recrystallized from water by adding ethanol; yield, 0.2 g.

(c) XZ-cis(N)-K[Co((S,S)-alaipa)(gly)] (isomer-i).

From the cis(N) eluate early eluted in (1), the contaminant potassium chloride was removed by a similar procedure to that for the nta complex (I-3-1-(2-b)). The powdery product

obtained by addition of a large amount of ethanol was collected by filtration; yield 0.6 g. Attempts to obtain the crystalline complex from this product was unsuccessful. The diastereomer with $(+)_{546}$-$[Co(ox)(en)_2]^+$ using 0.5 g of the crude product was prepared by the same procedure as that for the (S)-alada complex (I-3-2-(2-c)). The diastereomer obtained was recrystallized from warm water by adding methanol; yield 0.6 g. The purity of the diastereomer was checked as for the (S)-alada complex. Anal. Calcd for $(+)_{546}$-$[Co(ox)(en)_2]\cdot$XY-cis(N)-[Co((S,S)-alaipa)(gly)]$\cdot 5H_2O$: C, 26.52; H, 5.86; N, 11.60 %. Found: C, 26.41; H, 5.59; N, 11.77 %.

An aqueous solution of the desired complex of potassium salt was obtained from the diastereomer (0.5 g) by use of a cation-exchange resin of potassium form (I-3-2-(2-b)). Attempts to obtain the crystalline complex from the solution was unsuccessful. To the concentrated aqueous solution of the complex was added a small amount of methanol and the powdery product precipitated was collected by filtration and washed with methanol and ether; yield 0.15 g of nonhygroscopic powder. Attempts of crystallization of the sodium salt or ammonium salt of this complex were also unsuccessful.

(d) XY-cis(N)-K[Co((S,S)-alaipa)(gly)] (isomer-ii).

The cis(N) eluate later eluted in (1) was concentrated to several milliliters and the potassium chloride deposited was removed by filtration. To the filtrate was added a

small amount of methanol and the potassiun chloride deposited was removed by filtration. When the contaminant potassium chloride was removed as much as possible by repeating this prcedure, the needle crystals (isomer-ii) crystallized out from the filtrate and were collected by filtration. The crystals contaminated with a small amount of potassium chloride were recrystallized from warm water by adding methanol; yield 4.7 g. Take account of racemization of the (S,S)-H_3alaipa ligand used, the diastereomer with $(+)_{546}$-[Co-(ox)(en)$_2$]$^+$, using 0.6 g of the product, was prepared by the same procedure as that for the (S)-alada complex (I-3-2-(2-b)). The pale-violet needle diastereomer obtained was recrystallized from warm water by adding methanol; yield 0.7 g. Anal. Calcd for $(+)_{546}$-[Co(ox)(en)$_2$]·XZ-cis(N)-[Co((S,S)-alaipa)(gly)]·2H_2O: C, 29.45; H, 5.26; N, 12.88 %. Found: C, 29.46; H, 5.28; N, 13.10 %. The desired complex of potassium salt was obtained from 1.0 g of diastereomer (I-3-2-(2-b)); yield 0.55 g. The CD spectrum of this complex completely coincided with that of the product obtained above.

<u>I-3-5. β-Alaninate-N,N-diacetato (β-alada) complexes; trans(N)- and cis(N)-potassium(β-alaninate-N,N-diacetato)-(aminocarboxylato)cobaltate(III): trans(N)- and cis(N)-K[Co-K[Co(β-alada)(am)]$^-$ (am = gly, (S)-ala or (S)-pro).</u>

(1) Preparation of reaction mixtures and separation of trans(N) and cis(N) siomers.

The reaction mixture were prepared by a similar

procedure to that for the nta complexes described in I-3-1-(1), using β-H_3alada (4.1 g, 0.02 mol) instead of the ntaH_3: before and after adding an aminocarboxylic acid, the reaction time was taken for 30 min and 1 hr respectively. Each of the crude products obtained was chromatographed by the same procedure as that for the nta complexes. Two colored bands a reddish purple one (a mixture of trans(N) isomers) and a violet one (a mixture of cis(N) isomers), were separately eluted in this order except for the (S)-pro complex, in which only the reddish purple band was eluted.

(2) Separation and optical resolution of arrangement isomers.

(a) Y-trans(N)-K[Co(β-alada)(gly)] (isomer-i).

The trans(N) eluate obtained in (1) was concentrated to several milliliters on a vacuum evaporator below 40° and the potassium chloride deposited was removed by filtration. To the filtrate a small amount of methanol was added and the potassium chloride deposited was removed again. After repeating this operation, the prismatic complex (isomer-i) began to crystallize out with a small amount of potassium chloride. The complex deposited was collected by filtration (the filtrate was reseved for the preparation of other isomers) and recrystallized from warm water by adding methanol; yield 0.1 g.

(b) Optical resolution of recemic modification, X- and Z-trans(N)-K[Co(β-alada)(gly)] (isomer-ii and -iii respectively).

The reserved filtrate from isomer-i was concentrated to

dryness below 40°. The resulting solid was contaminated with a small amount of potassium chloride; therefore it was treated with silver acetate as described for the nta complexes in I-3-1-(2-b). The powdery product obtained by addition of a large amount of ethanol was collected by filtration; yield 4.3 g. The PMR spectra showed that the product was a recemic complex (isomer-ii and -iii) and contaminated with about 3 % of isomer-i, but the product was used for next step without further purification.

The product (4.0 g) was dissolved in a warm solution (about 40°) containing the acetate of $(-)_{546}$-$[Co(ox)(en)_2]^+$ was obtained from $(-)_{546}$-$[Co(ox)(en)_2]I$ (3.9 g) and silver acetate (1.8 g) and water (12 ml). Repeating fractional crystallization by cooling in a refrigerator or by adding an appropriate amount of methanol, several diastereomers were obtained. The less soluble fractions with similar optical rotation values ($[\alpha]_{546}$ -270 to -350°) were combined and it was recrystallized several times from warm water by adding methanol; yield 0.8 g. $[\alpha]_{589}$ -532°, $[\alpha]_{546}$ -246°. Anal. Calcd for $(-)_{546}$-$[Co(ox)(en)_2]\cdot$X-trans(N)-$[Co(\beta\text{-alada})(gly)]\cdot 3H_2O$: C, 27.44; H, 5.23; N, 12.81 %. Found: C, 27.74; H, 5.37; N, 12.68 %. The diastereomer (0.6 g) was converted to the potassium salt by using a cation-exchange resin of potassium form (I-3-2-(2-b)). The reddish purple eluate was concentrated to a few milliliters below 40° on a vacuum evaporator. An appropriate amount of ethanol was gradually added to the solution. The needle crystals deposited were collected by filtration;

yield 0.2 g.

The more soluble diastereomers with similar rotations ($[\alpha]_{546}$ -500 to -620°) were treated likewise; yield 0.4 g, $[\alpha]_{589}$ -388°, $[\alpha]_{546}$ -690°. Anal. Calcd for $(-)_{546}$-$[Co(ox)(en)_2]\cdot$Z-trans(N)-$[Co(\beta\text{-alada})(gly)]\cdot 2H_2O$: C, 28.22; H, 5.06; N, 13.17 %. Found: C, 28.13; H, 5.29; N, 12.77 %. The optically active potassium salt (isomer-iii) was obtained from the diastereomer (0.3 g) as needle crystals by the same procedure to that for the enatiomer; yield 0.1 g.

After the completion of the preparation described above, it was found that the crystals of the racemic modification of β-alada complex (u-isomer) can be obtained as ammonium salt. Namely, the contaminant potassium chloride was removed from the trans(N) eluate obtained as described in (1) as much as possible as in (a) and to the final filtrate was added a large amount of ethanol. The powdery product obtained was passed through a cation-exchange resin (ammonium form) as described for the nta complexes (I-3-1-(2-c)). The colored eluates were collected and concentrated and a small amount of methanol was added to the concentrate. The crystalline complex deposited (u-isomer) was filtered and recrystallized from warm water by adding methanol. Anal. Calcd for u-trans(N)-$NH_4[Co(\beta\text{-alada})(gly)]\cdot H_2O$: C, 29.12; H, 4/89; N, 11.32 %. Found: C, 29.01; H, 4.89; N, 11.34 %.

(c) X- and Z-trans(N)-K[Co(β-alada)((S)-ala)] (isomer-i and -ii respectively).

The trans(N) eluate in (1) was concentrated almost to dryness below 40° on a vacuum evaporator. To the residue enough amount of methanol was added to dissolve the colored material at 50° and the potassium chloride deposited was removed by filtration. The filtrate was kept in a refrigerator overnight. The crude product deposited was collected by filtration (the filtrate was reserved for the preparation of another isomer, isomer-iii) and recrystallized from water by adding ethanol; yield 3.5 g. The PMR spectrum of this product indicated that it was a mixture of two isomers (isomer-i and -ii). A solution of 1.5 g of this product in 98 % methanol was poured into a column (35 x 800 mm) containing an anion-exchange resin (Dowex 1-X8, 200-400 mesh, chloride form), which was eluted with 0.05 % (W/V) solution of potassium chloride in 98 % methanol at a rate of about 1 ml/min. After about 33 days, two reddish bands, isomer-i and isomer-ii in this order, completely separated from each other. Each of the two eluted bands was collected in fractions, and their CD spectra showed that each band consisted of only one isomer. Each of the eluates was concentrated almost to dryness below 30° on a vacuum evaporator. To the residue a small amount of methanol was added and the potassium chloride deposited was removed by filtration. By repeating this process, potassium chloride was removed as mush as possible. An appropriate amount of ethanol was gradually added to the filtrate and the complex deposited as needle crystals was collected by filtration. Each of the complexes was recrystallized from methanol-water

(2 : 1) by adding ethanol; yield 0.4 g each for isomer-i and -ii.

(d) Y-trans(N)-K[Co(β-alada)((S)-ala)] (isomer-iii).

The reserved filtrate from the crude mixture of isomer-i and -ii was concentrated to dryness below 40°. In order to removed potassium chloride, it was treated with silver acetate as described for the nta complexes (I-3-1-(2-b)). The powdery product precipitated by addition of a large amount of ethanol was collected by filtration. The product was dissolved in a minimum amount of water. When an appropriate amount of ethanol was gradually added to the solution, a mixture of isomer-i and -ii crystallized out and was removed by filtration. By this process the crystalline complex (a mixture of isomer-i and -ii) was removed from the solution as much as possible. The final filtrate was concentrated to dryness on a vacuum evaporator; yield 0.5 g. The PMR spectrum of this product indicated that it was a mixture of three isomers, isomer-i and -i and -ii (about 40 % in total of the two isomers) and new isomer-iii (about 60 %). The separation of the new isomer from the mixture was carried out by the same chromatographic procedure as that for the separation of isomer-i and -ii. By the elution for about 25 days, two reddish purple bands which separated from each other were eluted. It was confirmed by CD measurements of the fractionized eluates that the earlier eluated band consists of isomer-iii and -i (eluted in this order, but partly overlapped) and later eluted band isomer-ii. The

earlier several fractions of the firstly eluted band, which showed a constant CD value, were collected, and the contaminants were removed as in the case of isomer-i or -ii. Finally, by the recrystallization from methanol-water (10 : 1) by adding ethanol, the pure isomer-iii complex was obtained as a nonhygroscopic powder; yield 0.05 g.

(e) X-, Y- and Z-trans(N)-K[Co(β-alada)((S)-pro)] (isomer-i, -ii and -iii respectively).

The trans(N) eluate in (1) was concentrated almost to dryness below 40° on a vacuum evaporator. To the residue at 50° just enough methanol to dissolve the colored material was added and the potassium chloride deposited was removed by filtration. To the filtrate was added a large amount of ethanol and ether to precipitate almost all of the colored complexes. The crude product was collected by filtration and dried under vacuum; yield 5.5 g. The separation of isomers was carried out using 1.5 g of the product by the same procedure as deiscribed for the (S)-ala complex in (c). After about 54 days' elutaion, three reddish purple bands, isomer-i, isomer-ii and isomer-iii, were eluted in this order and separated completely from one another. Each of the three eluates was concentrated to dryness below 30° on a vacuum evaporator. To the concentrate at 50° just enough methanol to dissolve the colored material was added and the potassium chloride deposited was removed by filtration. An appropriate amount of ethanol was gradually

added to the filtrate and the complex deposited was collected by filtration. Each of the complexes was recrystallized from methanol-water (20 : 1) by adding ethanol; yield 0.3 g of needle crystals for isomer-i; 0.03 g of powder for isomer-ii; 0.2 g of needle crystals for isomer-iii.

(f) Optical resolution of racemic modification, X- and Z-cis(N)-K[Co(β-alada)(gly)] (isomer-i and -ii respectively).

The cis(N) eluate in (1) was concentrated to several milliliters below 40° on a vacuum evaporator and the potassium chloride deposited was removed by filtration. By further addition of methanol to the filtrate, potasssium chloride was removed as much as possible. The final filtrate was evaporated to dryness below 40° and the resulting solid was treated as described for the nta complexes in I-3-1-(2-b), using silver acetate to remove contaminated potassium chloride. The powdery product precipitated by addition of a large amount of ethanol was collected and air-dried; yield 3.0 g. Although this product was a mixture of three isomers, isomer-i and isomer-ii (antipotal to each other and amounted about 94 % in total of the two isomers) and isomer-iii (about 6 %, the isolation of this isomer is described in (g)), it was used for next step without further purification.

The isomeric mixture (2.0 g) was dissolved in the solution containing the acetate of $(-)_{546}$-$[Co(ox)(en)_2]^+$ which was derived from $(-)_{546}$-[Co(ox)(en)]I (2.0 g) and silver acetate (0.9 g) and water (8 ml).

After cooling in a refrigerator overnight, the crude less soluble diastereomer deposited was filtered and washed with a small amount of cold water; yield 1.2 g. It was recrystallized a few times to constant rotation from warm water by adding methanol; yield 0.8 g of prismatic crystals; $[\alpha]_{589}$ -300, $[\alpha]_{546}$ +250°. Anal. Calcd for $(-)_{546}$-[Co(ox)-$(en)_2$]·Z-cis(N)-[Co(β-alada)(gly)]·$4H_2O$: C, 26.71; H, 5.39; N, 12.46 %. Found: C, 26.64; H, 5.48; N, 12.26 %.

To the filtrate from the less soluble diastereomer was added 5 ml of methanol and the solution was allowed to stand for 5 hr at room temperature. The crude more soluble diastereomer deposited was filtered and washed with a small amount of cold water; yield 0.6 g. Recrystallization was achieved as in the case of the less soluble diastereomer; yield 0.4 g of prismatic crystals; $[\alpha]_{589}$ -505°, $[\alpha]_{546}$ -1,130°. Anal. Calcd for $(-)_{546}$-[Co(ox)$(en)_2$]·X-cis(N)-[Co(β-alada)(gly)]·$6H_2O$: C, 25.36; H, 5.69; N, 11.83 %. Found: C, 25.42; H, 5.79; N, 11.62 %.

The desired potassium salts of these complexes, isomer-i and -ii, were obtained as crystalline powder from the less soluble diastereomer (0.6 g) and more soluble one (0.3 g), respectively, by the same procedure as that for the corresponding trans(N) isomer in (b); yield 0.2 g for isomer-i, 0.1 g for isomer-ii.

(g) Y-cis(N)-NH_4[Co(β-alada)(gly)] (isomer-iii).

The reaction mixture was prepared separately in three times scales of that described in (1) and the crude product obtained was chromatographed similarly. Several fractions

eluted first of the violet band (corresponding to approximately 15 % of the cis(N) isomer in total) were collected and the contaminant potassium chloride was removed by the same procedure as that for the nta complexes (I-3-1-(2-b)). The crude product obtained (0.4 g) was chromatographed again by a similar procedure (the elution rate was converted to 1.0 ml/min) as that described in (1). After the elution of 7 days, two violet bands, isomer-iii and the racemic modification (isomer-i and -ii), were eluted in this order and completely separated from each other. The eluates of the isomer-iii were collected and the contaminant potassium chloride was removed by the same procedure as that for the nta complexes (I-3-1-(2-b)). The crude product obtained as potassium salt was converted to ammonium salt using a cation-exchange resin of ammonium from by a similar procedure as that for the nta complexes (I-3-1-(2-c)). The complex obtained was recrystallized from warm water by adding methanol; yield 0.06 g of plate crystals. Attempts of crystallization of the potassium or sodium salt of this complex were unsuccessful.

(h) Z- and X-cis(N)-K[Co(β-alada)((S)-ala)] (isomer-i and -ii respectively).

The cis(N) eluate in (1) was concentrated to several milliliters below 40° on a vacuum evaporator and the potassium chloride precipitated was removed by filtration. When a small amount of methanol was added to the filtrate,

violet prismatic crystals (isomer-i) began to crystallize. After cooling in a refrigerator overnight, the complex was collected by filtration and recrystallized from warm water by adding methanol; yield 1.2 g. In order to remove potassium chloride in the filtrate from isomer-i, it was treated with silver acetate as desribed in I-3-1-(2-b)). The powdery product precipitated by adding a large amount of ethanol was collected by filtration and dissoved in a minimum amount of water. To the solution was gradually added a few milliliters of ethanol. The needle crystals (isomer-ii) depostied were collected by filtration and recrystallized from water by adding ethanol; yield 0.6 g.

(i) Y-cis(N)-K[Co(β-alada)((S)-ala)] (isomer-iii).

The filtrate from isomer-ii in (g) was concentrated to a few milliliters on a vacuum evaporator and to the concentrate a large amnount of ethanol was added to precipitate almost all of the colored complexes. The PMR spectrum of the product precipitated indicated that it was a mixture of three isomers, isomer-i and -ii (abouut 30 % in total of the two isomers) and new isomer-iii (about 70 %). The separation of new isomer from the mixture was carried out chromatographically as in I-3-1-(2). The column, the concentration of eluent and the elution rate were converted to 17 x 1,000 mm, 0.03 M and 1 ml/min, respectively. The attempt of elution for about 30 days indicated that no separation of the isomers was observed in appearance, but it was confirmed by CD measurements of the fractionized

eluates that the elution order was isomer-iii, isomer-ii, and isomer-i. Several fractions eluted first showed a constant CD; they were collected and the contaminant potassium chloride was removed as much as possible as in the isolation of the corresponding trans(N) isomers in (c). Because attempts to crystallize isomer-iii from the resulting filtrate were unsuccessful, the filtrate was evaporated to dryness on a vacuum evaporator below 30° and dried over calcium chloride in a vacuum dessicator. The final product contains a small amount of potassium chloride and was very hygroscopic; therefore no elemental analysis was carried out.

I-3-6. (S)-Alaninate-N-propionate-N-acetato ((S)-alapa) complexes; trans(N)-potassium- and cis(N)-ammonium((S)-alaninate-N-propionate-N-acetato)(glycinato)cobaltate(III): trans(N)-K- and cis(N)-NH_4[Co((S)-alapa)(gly)].

(1) Preparation of reaction mixture and separation of trans(N) and cis(N) isomers.

The reaction mixture was obtained by a similar procedure to that for the nta complexes described in I-3-1-(1), using (S)-H_3alapa (4.4 g, 0.02 mol) instead of ntaH_3: the reaction after the addition of glycine was for 1 hr. The crude product obtained was chromatographed by the same procedure as that for the nta complexes. Two colored bands, a reddish purple one (trans(N) isomer) and a violet one (cis(N) isomer), were eluted separately in this order.

(2) Separation of the arrangement isomers.

(a) $X_S Z_6$-trans(N)-K[Co((S)-alapa)(gly)] (isomer-i).

The trans(N) eluate obtained in (1) was concentrated to several milliliters below 40° on a vacuum evaporator and the potassium chloride deposited was removed by filtration. After repeating the concentration of the filtrate and removing potassium chloride resulted, the final filtrate was concentrated to dryness and the residue was treated with silver acetate in order to remove the contaminant potassium chloride as described for the nta complexes in I-3-1-(2-b). The prismatic crystals were obtained by dissolving the powdery product obtained in warm water and by adding methanol, and collected by filtraion; yield 2.8 g. Take account of racemization of the (S)-H_3alapa used as the starting material, the complex obained was purified by the formation of diastereomer with $(+)_{546}$-$[Co(ox)(en)_2]^+$ as follows. The complex (1.43 g, 0.003 mol as pentahydrate) was dissolved in a warm solution (about 50°) containing the acetate of $(+)_{546}$-$[Co(ox)(en)_2]^+$ which was derived from $(+)_{546}$-$[Co(ox)(en)_2]I$ (1.2 g, 0.003 mol) and silver acetate (0.53 g) and water (3 ml) as for the (S)-alada complex (I-3-2-(2-b)). After cooling in a refrigerator overnight, the brownish-pink needle diastereomer deposited was filtered and washed with water-methanol (1 : 1) and methanol and air-dried. The diastereomer was recrystallized once from 25 ml of water by adding methanol; yield 1.6 g. The purity of diastereomer was checked as described for the (S)-alada complex (I-3-2-(2-b)). Anal. Calcd for $(+)_{546}$-[Co(ox)-

$(en)_2]\cdot X_S Z_6$-trans(N)-[Co((S)-alapa)(gly)]$\cdot 1.5H_2O$: C, 29.87; H, 5.18; N, 13.06 %. Found: C, 29.74; H, 5.24; N, 13.10 %.

The desired complex of potassium salt was obtained from the diastereomer (1.2 g) by using a cation-exchange resin of potassium form as for the (S)-alada complex (I-3-2-(2-b)). The complex obtained was recrystallized from water by adding methanol; yield 0.6 g of plates.

(b) $X_S Z_6$-cis(N)-NH_4[Co((S)-alapa)(gly)] (isomer-i).

From the cis(N) eluate in (1) the contaminant potassium chloride was removed by the same procedure as that for the nta complexes using silver acetate (I-3-1-(2-b)); yield 3.6 g of a powder. The pale-violet diastereomer with $(+)_{546}$-$[Co(ox)(en)_2]^+$ was obtained as scales from the curde powdery product obtained (2.8 g) by a similar prodecure to that for the corresponding trans(N) isomer in (a), and the pure diastereomer was obtained by recrystallization from 20 ml of warm water (about 50°) by adding methanol; yield 3.0 g. Anal. Calcd for $(+)_{546}$-$[Co(ox)(en)_2]\cdot X_S Z_6$-cis(N)-[Co((S)-alapa)(gly)]$\cdot 2H_2O$: C, 29.45; H, 5.26; N, 12.88 %. Found: C, 29.68; H, 5.18; N, 13.05 %.

The desired complex of ammonium salt was obtained from the diastereomer (1.0 g) by using a cation-exchange resin of ammonium form as described for the (S)-alada complex (I-3-2-(2-b)). The scaly crystals obtained was recrystallized from water by adding methanol; yield 0.6 g. Attempts to crystallize the potassium or sodium salt of this complex were unsuccessful.

Table II. Chemical Analyses (%)

Label (isomer-)	Complex	C		H		N	
		Calcd	Found	Calcd	Found	Calcd	Found
	trans(N)-K[Co(nta)(gly)]·$2H_2O$	24.25	24.45	3.57	3.10	7.07	7.04
	trans(N)-K[Co(nta)((S)-ala)]·$2.5H_2O$	25.78	25.77	4.09	4.05	6.68	6.59
	trans(N)-K[Co(nta)((S)-val)]·$3H_2O$	28.95	28.80	4.87	4.70	6.14	6.08
	trans(N)-K[Co(nta)((S)-ser)]·H_2O	26.48	26.40	3.46	3.41	6.86	6.84
	trans(N)-K[Co(nta)((S)-pro)]·$3H_2O$	29.08	29.21	4.45	4.27	6.17	6.10
	trans(N)-K[Co(nta)(sar)]·H_2O	27.55	27.83	3.61	3.44	7.14	7.05
	trans(N)-K[Co(nta)(b-ala)]·$2H_2O$	26.34	26.01	3.94	3.98	6.83	6.79
	trans(N)-K[Co(nta)((R)-α-Me-β-ala)]	30.93	30.88	3.64	3.57	7.22	7.18
	trans(N)-K[Co(nta)((S)-β-Me-β-ala)]·$4.5H_2O$	27.33	27.44	5.22	4.97	5.80	5.85
	trans(N)-K[Co(nta)((S,S)-achc)]·$4.5H_2O$	30.65	30.45	5.35	5.45	5.50	5.43
	trans(N)-Na[Co(nta)((S,R)-achc)]·$4H_2O$	32.27	32.31	5.42	5.50	5.79	5.74
	trans(N)-K[Co(nta)(γ-ambut)]·$3H_2O$	27.15	27.22	4.57	4.31	6.33	6.22
	cis(N)-K[Co(nta)(gly)]·$2H_2O$	24.25	24.35	3.57	3.36	7.07	7.12
	cis(N)-K[Co(nta)((S)-ala)]·$2H_2O$	25.24	25.41	4.24	3.91	6.54	6.46

Table II. (continued)

Label (isomer-)	Complex	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
	cis(N)-K[Co(nta)((S)-val)]·$4H_2O$	27.85	28.02	5.11	4.63	5.91	5.91
	cis(N)-K[Co(nta)((S)-ser)]·$2H_2O$	25.36	25.09	3.79	3.81	6.57	6.54
	cis(N)-Na[Co(nta)(β-ala)]·$1.5H_2O$	28.06	27.77	3.93	3.14	7.27	7.27
	cis(N)-K[Co(nta)((R)-α-Me-β-ala)]·$3.5H_2O$	26.61	26.73	4.70	4.57	6.21	6.03
	cis(N)-K[Co(nta)((S)-β-Me-β-ala)]·$2.5H_2O$	27.71	27.72	4.43	4.36	6.47	6.38
	cis(N)-K[Co(nta)((S,S)-achc)]·$3.5H_2O$	31.77	31.60	5.14	4.93	5.70	5.53
	cis(N)-K[Co(nta)((S,R)-achc)]·$3.5H_2O$	31.77	32.00	5.14	5.19	5.70	5.67
i	X-trans(N)-K[Co((S)-alada)(gly)]·$3.5H_2O$	24.72	24.63	4.39	4.41	6.41	6.49
ii	Y-trans(N)-K[Co((S)-alada)(gly)][a]		—		—		—
i	X-trans(N)-K[Co((S)-alada)((S)-ala)]·$2H_2O$	28.30	28.52	4.28	4.24	6.60	6.91
i	Z-trans(N)-K[Co((R)-alada)((S)-ala)]·$2H_2O$	28.30	28.00	4.28	4.50	6.60	6.84
i	X-trans(N)-K[Co((S)-alada)((S)-pro)]·H_2O	33.33	33.30	4.20	4.37	6.48	6.29
i	Z-trans(N)-K[Co((R)-alada)((S)-pro)]·$2H_2O$	32.00	31.89	4.49	4.63	6.22	6.08
i	X-trans(N)-K[Co((S)-alada)(β-ala)]·$3H_2O$	27.15	27.17	4.57	4.69	6.33	6.26

Table II. (continued)

Label (isomer-)	Complex	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
i	X-trans(N)-K[Co((S)-alada)((R)-α-Me-β-ala)]·$3H_2O$	28.95	28.81	4.87	4.87	6.14	6.07
i	Z-trans(N)-K[Co((S)-alada)((R)-α-Me-β-ala)]·$4.5H_2O$	27.33	27.52	5.22	5.26	5.80	5.84
i	X-trans(N)-K[Co((S)-alada)((S)-β-Me-β-ala)]·$3H_2O$	28.95	29.09	4.87	4.78	6.25	6.14
i	Z-trans(N)-K[Co((R)-alada)((S)-β-Me-β-ala)]·$2H_2O$	30.14	29.93	4.61	4.70	6.39	6.32
i	X-cis(N)-K[Co((S)-alada)(gly)]·$3H_2O$	25.24	25.12	4.24	4.23	6.54	6.48
i	X-cis(N)-K[Co((S)-alada)((S)-ala)]·$3H_2O$	27.15	27.34	4.57	4.55	6.33	6.37
i	Z-cis(N)-K[Co((R)-alada)((S)-ala)]·$3H_2O$	27.15	27.60	4.57	4.48	6.33	6.34
i	X-cis(N)-K[Co((S)-alada)(β-ala)]·H_2O	29.56	29.27	3.98	4.02	6.90	6.79
i	X-cis(N)-K[Co((S)-alada)((R)-α-Me-β-ala)]·$3.5H_2O$	28.39	28.42	4.99	5.05	6.02	6.03
i	Z-cis(N)-K[Co((R)-alada)((R)-α-Me-β-ala)]·$3H_2O$	28.95	29.05	4.87	5.03	6.14	6.27
i	X-cis(N)-K[Co((S)-alada)((S)-β-Me-β-ala)]·$4.5H_2O$	27.33	27.44	5.22	4.97	5.80	5.85
i	Z-cis(N)-K[Co((R)-alada)((S)-β-Me-β-ala)]·$3H_2O$	28.95	28.90	4.87	4.83	6.14	6.06
i	X_SZ_R-trans(N)-[Co((R,S)-alaipa)(gly)]·H_2O	29.56	29.30	4.00	4.10	6.90	7.17
i	X_SZ_R-cis(N)-[Co((R,S)-alaipa)(gly)]·$4.5H_2O$	25.56	25.32	4.95	4.84	5.97	6.05

Table II. (continued)

Label (isomer-)	Complex	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
i	XY-trans(N)-Na[Co((S,S)-alaipa)(gly)]·H_2O	30.78	30.55	4.14	4.09	7.18	7.19
ii	XZ-trans(N)-K[Co((S,S)-alaipa)(gly)]·$4H_2O$	26.09	26.10	4.83	4.85	6.09	6.32
i	XZ-cis(N)-K[Co((S,S)-alaipa)(gly)]·$3H_2O$	27.15	27.35	4.57	4.33	6.33	6.58
ii	XY-cis(N)-K[Co((S,S)-alaipa)(gly)]·$3H_2O$	27.15	27.03	4.57	4.53	6.33	6.40
i	Y-trans(N)-K[Co(β-alada)(gly)]·$2H_2O$	26.34	26.59	3.94	3.96	6.82	6.76
ii	X-trans(N)-K[Co(β-alada)(gly)]·$3H_2O$	25.24	25.17	4.24	4.18	6.54	6.44
iii	Z-trans(N)-K[Co(β-alada)(gly)]·$3H_2O$	25.24	24.80	4.24	4.10	6.54	6.53
i	X-trans(N)-K[Co(β-alada)((S)-ala)]·$5H_2O$	25.11	25.43	5.07	5.18	5.86	5.81
ii	Z-trans(N)-K[Co(β-alada)((S)-ala)]·$4H_2O$	26.09	26.01	4.81	4.81	6.08	5.98
iii	Y-trans(N)-K[Co(β-alada)((S)-ala)]·$3H_2O$	27.15	27.28	4.57	4.36	6.33	6.33
i	X-trans(N)-K[Co(β-alada)((S)-pro)]·$3H_2O$	30.77	30.80	4.74	4.68	5.98	5.58
ii	Y-trans(N)-K[Co(β-alada)((S)-pro)]·$2.5H_2O$	31.37	31.44	4.62	4.64	6.10	5.78
iii	Z-trans(N)-K[Co(β-alada)((S)-pro)]·$3H_2O$	30.77	30.73	4.74	4.91	5.98	5.76

Table II. (continued)

Label (isomer-)	Complex	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
i	Z-cis(N)-K[Co(β-alada)(gly)]·2.5H_2O	25.78	26.16	4.09	4.35	6.68	6.69
ii	X-cis(N)-K[Co(β-alada)(gly)]·2.5H_2O	25.78	25.63	4.09	4.36	6.68	6.44
iii	Y-cis(N)-NH_4[Co(β-alada)(gly)]·H_2O	29.12	29.11	4.89	4.89	11.32	11.40
i	Z-cis(N)-K[Co(β-alada)((S)-ala)]·2.5H_2O·0.5KCl	25.52	25.43	4.08	4.04	5.95	5.94
ii	X-cis(N)-K[Co(β-alada)((S)-ala)]·4H_2O	26.09	26.09	4.81	4.84	6.08	6.03
iii	Y-cis(N)-K[Co(β-alada)((S)-ala)][a]		—		—		—
i	X_SZ_6-trans(N)-K[Co((S)-alapa)(gly)]·5H_2O	25.11	25.10	5.07	4.93	5.86	5.85
ii	X_SZ_6-cis(N)-NH_4[Co((S)-alapa)(gly)]·4H_2O	27.33	27.36	5.98	5.80	9.57	9.78

a) Not isolated; see Experimental Section.

I-4. Isomer equilibrium experiments.

(1) $[Co((S)\text{-alada})(gly)]^-$ complex.

The equilibrium experiments were carried out by using the three isomers of this complex, X-trans(N), Y-trans(N), and X-cis(N), as starting materials. For each of the X-trans(N) and X-cis(N) isomers, the complex (1.00 g for the X-trans(N) isomer and 1.02 g for the X-cis(N) one) was dissolved in 4 ml of water and to the solution 0.1 g of activated charcoal was added. After the resulting mixture was stirred at 70° for 1 hr, the activated charcoal was removed by filtration, and washed with a small amount of warm water. A small amount of the equlibrium mixture obtained was separated and after an appropriate dilution with water its absorption and CD spectra were measured in order to compare with those of the equilibrium mixture from the Y-trans(N) isomer described below. The remaining equilibrium mixture was chromatographed by the procedure similar to that for the nta complexes (I-3-1-(1)). The eluates of the trans(N) and cis(N) isomers were collected separately. After an appropriate dilution, the absorption and CD spectra of the eluates were measured and the contents of the trans(N) and cis(N) isomers were estimated by comparing the absorbance of the first absorption maxima (assuming that each of the trans(N) and cis(N) eluates consists of only one arrangement isomer, i.e., X-trans(N) and X-cis(N) isomers respectively). The equilibrium mixture from the Y-trans(N) isomer was obtained by use of the isomer (0.1 g) containing

a small amount potassium chloride by the same procedure as above and its absorption and CD spectra were measured after an appropriate dilution.

(2) $[Co(N\text{-}O_3)(gly)]^-$ ($N\text{-}O_3$ = nta, (S)-alada, (R,S)- and (S,S)-alaipa, β-alada, or (S)-alapa) complex.

The following isomers of the gly complexes were used as the starting materials of equilibration: trans(N) nta, X-trans(N) (S)-alada, X_SZ_R-trans(N) (R,S)-alaipa, XY-trans(N) (S,S)-alaipa, u-trans(N) β-alada (ammonium salt, see Section I-3-5-(2-b)), and X_SZ_6-trans(N) (S)-alapa. The equilibriun mixtures were obtained by using 5-15 g of the gly complexes by the same procedure as that described in (1). For example, the isomer distribution of the (S)-alada complex was estimated qualitatively from the experiments described in I-3-2-(2-c). Namely, the essentially pure X-trans(N) isomer was obtained by the fractional crystallization from the equilibrium mixture in an 82,5 % yield. From the results of the column chromatographic separation of the remainder from the X-trans(N) isomer, it was found that the cis(N) eluate consist mostly of the X-cis(N) isomer and it was contianed in a 0.8 % yield, and that the Y-trans(N) isomer was contained in a very small amount. Similar experiments were also performed for the other complexes except for the nta complex. In the case of nta complex for which the arrangement isomer is impossible, the equilibrium mixture obtained was chromatographed as it is and the extents of the trans(N) and

cis(N) isomers in the mixture were determined as for the (S)-alada complex in (1).

I-5. Deuterium exchange experiments.

The partial deuteration of the trans(N)-[Co(nta)-(β-ala)]·$2H_2O$ was carried out as follows. The nta complex (1.0 g) was dissolved in 4 ml of deuterium oxide and the pD of the solution was adjusted to 10.0 by addition of a small amount of potassium carbonate. The empirical formula pD = "pH" + 0.4[67] was employed to correct the values measured with a Hitachi-Horiba M-5 pH meter. The solution was allowed to stand at room temperature (~ 25°) for 9 hr. During the reaction the pD of the solution dropped slowly, and the pD was maintained in the range of 9.6-10.0 by addition of potassium carbonate. When to the reaction mixture ethanol was added dropwise with stirring until a slight cloudiness persisted, immediately the partially deuterated complex crystallized out. The complex was collected by filtration in a 92 % yield and provided to the PMR measurement. The trans(N)-[Co((S)-alada)(β-ala)]·H_2O was deuterated for 22 hr under the same condition as above and the deuterated complex was obtained in an 88 % yield.

I-6. Estimation of the formation of trans(N) and cis(N) isomers.

The % formation of the trans(N) and cis(N) isomers versus reaction time for the $[Co(nta)(gly)]^-$ complex was

estimated as follows. The preparation reaction was carried out under the same condition as that for the preparation of this complex (I-3-1-(1)). The reaction vessel, however, was converted to a 100 ml Erlenmeyer flask with a stopper from a beaker to prevent the weight loss upon concentration. A weighted amount (about 1.0 g) of the reaction mixture was picked up with vigorous stirring at the desired times and insoluble materials were removed by filtration, and washed with a small amount of hot water. The combined filtrate and washings were chromatographed by a similar procedure to that described for the nta complexes (I-3-1-(1)), and the eluates of the trans(N) and cis(N) isomers were collected separately. The yields of the isomers were determined from the absorption measurements of the eluates.

I-7. Measurements.

The electronic absorption spectra were measured with a Beckman DU spectrophotometer and Shimadzu QV-50 or UV-200 spectrophotometer. The CD spectra were recorded with a Jasco Model ORD/UV-5 spectropolarimeter fitted with a CD attachment or Rousel-Jouan dichrographe. All the measurements were made for aqueous solutions in the range of 1.7-4.8 x 10^{-3} M concentration in an 1 cm quartz cell for the absorption spectra and an 1 or 2 cm quartz cell for the CD spectra at room temperature.

The specific rotations were measured in a 10 cm cell with a Hitachi PO-B polarimeter using a sodium D line light source or Jasco Model ORD/UV-5 spectropolarimeter. The data

obtained from the former apparatus were given with the symbol $[\alpha]_D$ and those from the latter one were estimated from the optical rotatory dispersion curves and given with the symbol, for example, $[\alpha]_{589}$.

The PMR spectra of the complexes were measured with a Japan Electon Optics JNM-4H-100 spectrometer operating at 100 MHz, in deuterium oxide solutions at 23-30° unless otherwise stated, the internal temperature of probe. When the overlapping with HOD signal was present, the overlapped signal was explored by the measurements in an acidic deuterium oxide solution (the addition of a few drops of 20 % deuterium hydrochloric acid in the deuterium oxide solution) or at an elevated temperature (below 50°). As an internal standard, tert-butyl alcohol or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) were used. Chemical shifts, when tert-bytyl alcohol was used, are referred to DSS as zero; tert-butyl alcohol is shifted 1.234 ppm down field from DSS. All of the PMR spectra were taken under conditions where the nitrogen protons of aminocarboxylate exchange with solvent.

Chapter II. Results and Discussion

II-1. Stereochemistry of ligands.

(1) Nitrilotricarboxylic acid.

The ligand (R)-H_3alada was derived from (R)-alanine and the other optically acitve nitrilotricarboxylic acid, (S)-H_3alada, (S,S)-H_3alaipa and (S)-H_3alapa, were derived from (S)-alanine as described in Experimental Section. Since the reaction does not involve the cleavage of the bonds to the asymmetric center, the absolute configurations of asymmetric center in these ligands are known. However, it is anticipated that the partial racemization takes place under the conditions employed in the preparation. As described in Experimental Section (I-1-1-(2-b)), optically pure (S)-H_3alada was recovered from the X-trans(N)-[Co-((S)-alada)(gly)]$\cdot 3.5H_2O$ and its specific rotation is slightly large compared with that of (S)-H_3alada used for the preparation of complexes. Taking into account the fact that the (S)-H_3alada recovered from the complex was purified by ion-exchange chromatography, the (R)- and (S)-H_3alada used for the preparation of complexes are essentially optically pure. In the cases of the (S,S)-H_3alaipa and (S)-H_3alapa ligands, the possibility of the partially racemized ligand was removed by the purification of the complex as described in Experimental Section.

(2) Aminocarboxylato ligands.

The absolute configurations of all the optically active α-aminocarboxylates are known and those of the β-amino-

carboxylates, (R)-α-Me-β-ala,[68] (S)-β-Me-β-ala[59] and (S,S)-achc,[69] have been determined by means of the chemical interconversion to the compounds of which the absolute configurations are known. Cis-2-aminocyclohexanecarboxylic acid was first resolved into the optical antipodes in this work and its absolute configuration was determined as follows. The benzoylation of $(+)_D$-cis-2-aminocyclohexanecarboxylic acid gave (1S,2R)-$(+)_D$-cis-2-benzoylaminocyclohexane-carboxylic acid of which the absolute configuration has been determined.[70] Accordingly, the absolute configuration of $(+)_D$-cis-2-aminocyclohexanecarboxylic acid is concluded to be (1S,2R).

II-2. Purity of arrangement isomers.

Several arrangement isomers are possible for the complexes with the nitrilotricarboxylato ligands except nta. The arrangement isomers were separated by ion-excahnge chromatography, fractional crystallization, or optical resolution. Each of the complexes isolated is not a mixture of the arrangement isomers but just one isomer. This fact was confirmed on the basis of the separation behaviors by ion-exchange column chromatography and CD and/or PMR behaviors of the fractions. In particular, the PMR spectra are useful for this purpose. In the trans(N)-$[Co((S,S)-alaipa)(gly)]^-$ complex, for example, it can be expected that the PMR spectra of the three possible isomers consist of the identical PMR pattern (one AB and two AX_3 patterns for (S,S)-alaipa protons and one AB pattern for gly protons, see

Section II-5), but that their spectra have differences in the chemical shift and the coupling constants. Two of the three possible isomers were obtained in this work and their PMR spectra are shown in Fig. 3. All the signals observed for each of the isomers can be assigned without considering the existence of more than one isomer as indicated above the spectra. From this observation, it can be concluded that each of the complexes obtained is only one species of the possible isomers.

II-3. Structural assignment of complexes.

II-3-1. Geometrical isomers, trans(N) and cis(N).

It has been well established that trans(N) and cis(N) isomers of a $[Co^{III}(N)_2(O)_4]$ type complex can be identified from the splitting patterns of their first spin-allowed d-d absorption bands as will be described in Section II-4. On this basis, it is concluded that the complexes obtained from the reddish-purple band in the ion-exchange chromatographic separation are trans(N) isomers and those from the violet ones cis(N) isomers.

II-3-2. Arrangement isomers.

(1) (R)- and (S)-alada, and (R,S)- and (S,S)-alaipa complexes.

Figure 4 shows the structure of nta moiety in a nta complex which is a parent complex. In the alada and alaipa complexes, one or two of the six hydrogen atoms of nta are substituted with methyl groups. A molecular model examination shows that the two in-plane five-membered chelate rings of

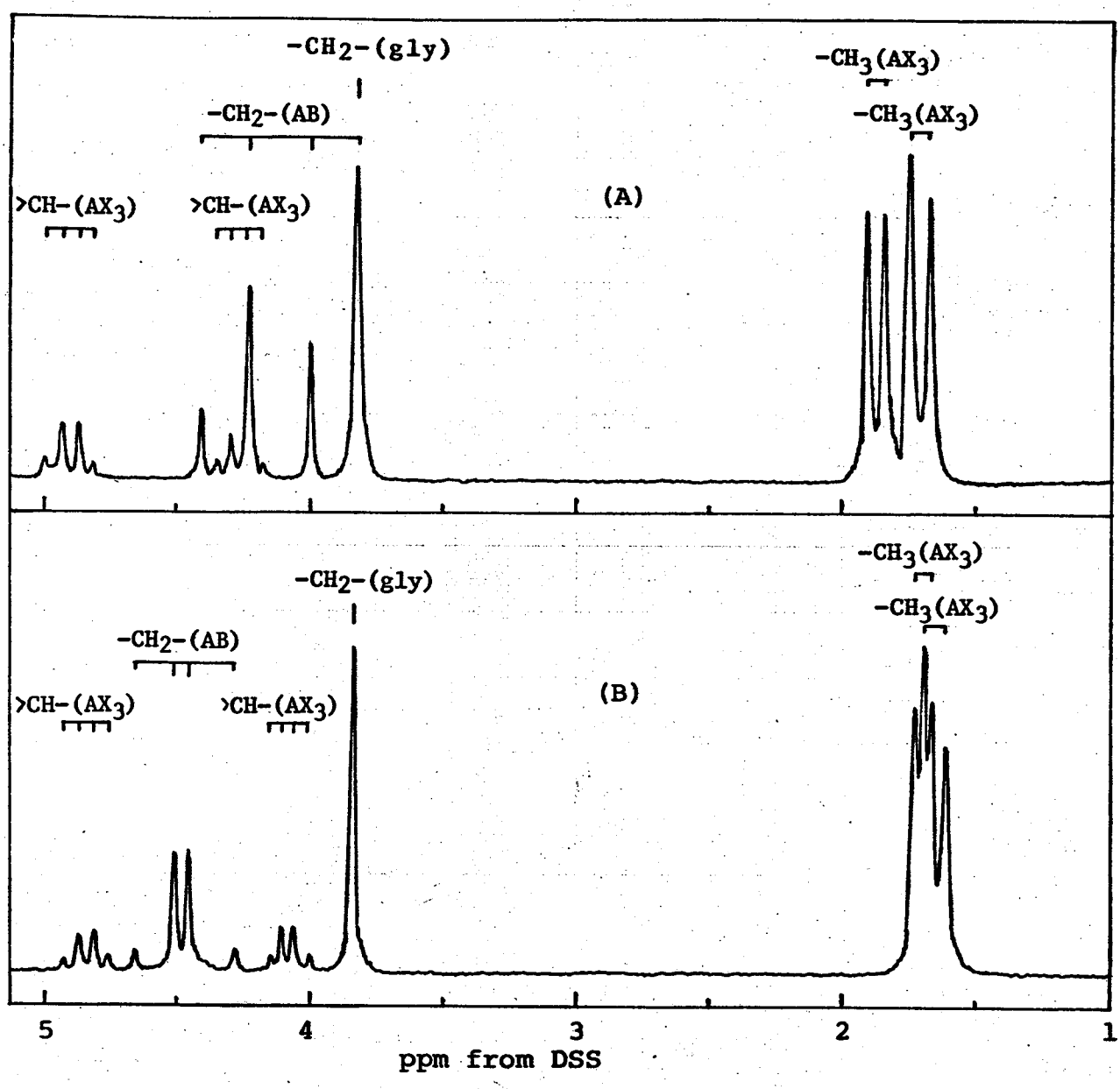


Fig. 3. PMR spectra of trans(N)-[Co((S,S)-alaipa)(gly)]$^-$: (A) XY- (isomer-i), and (B) XZ- (isomer-ii).

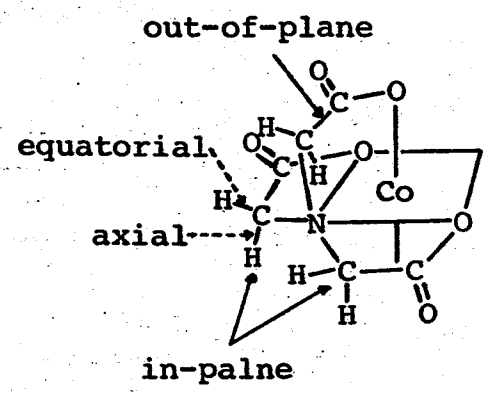


Fig. 4. Structure of coordinated nta.

the nta are forced to take a non-planar conformation, and substituents on chelate rings is in the equatorial or axial disposition (Fig. 4).

In the preparation of $[Co((R,S)\text{-alaipa})(gly)]^-$ complex (Section I-3-3), only one isomer (isomer-i) of the possible arrangement isomers was obtained stereoselectively for each of the trans(N) and cis(N) complexes. Figure 5 shows the PMR spectra of the (R,S)-alaipa complexes obtained and it is apparent that each of the spectra consists of one AX_3 and one A_2 patterns due to the (R,S)-alaipa protons and one A_2 pattern due to the gly protons. Such spectrum is expected for the X_SZ_R- and X_RZ_S-isomers which have a plane of symmetry, while the more complicated spectrum (two AX_3 and one AB patterns due to (R,S)-alaipa protons and one AB patterns for gly protons) is expected for the other isomers. Judging from the PMR behavior for the related complexes in this work, it is unlikely that the simplification of spectra due to the accidental overlapping of signals take place for the signals due to the (R,S)-alaipa protons. From this

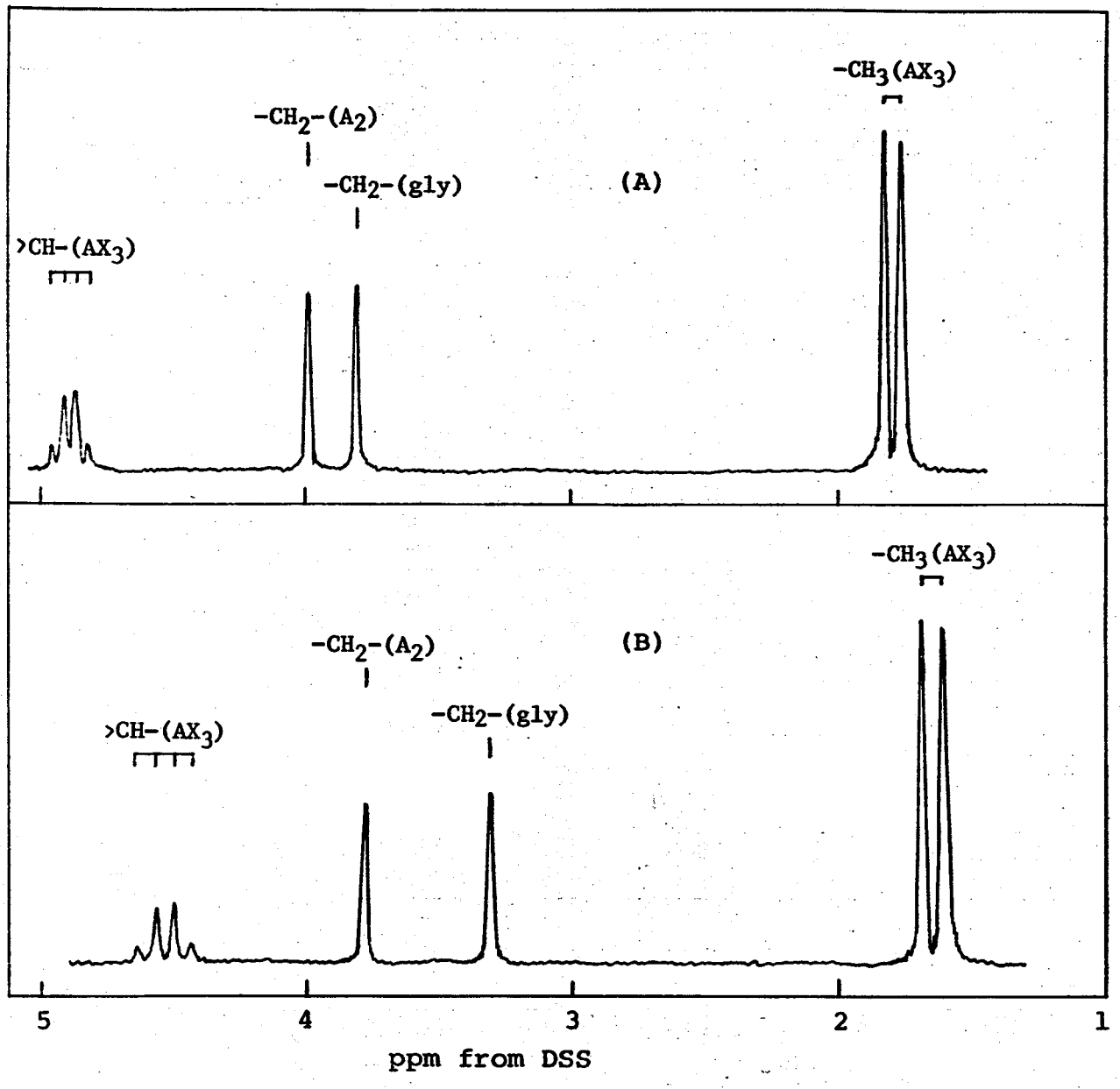


Fig. 5. PMR spectra of $[Co((R,S)\text{-alaipa})(gly)]^-$:

(A) X_SZ_R-trans(N)- (isomer-i), (B) X_SZ_R-cis(N)- (isomer-i).

consideration, it is concluded that each of the (R,S)-alaipa complexes obtained is either X_SZ_R- or X_RZ_S-isomer.

The equilibrium experiment of the (R,S)-alaipa complexes on activated charcoal indicates that the isomer-i of trans(N) is much more stable than the other possible isomers (Section II-7). The structure of coordinated (R,S)-alaipa in the X_SZ_R- and X_RZ_S-isomers are shown in Fig. 6. A molecular

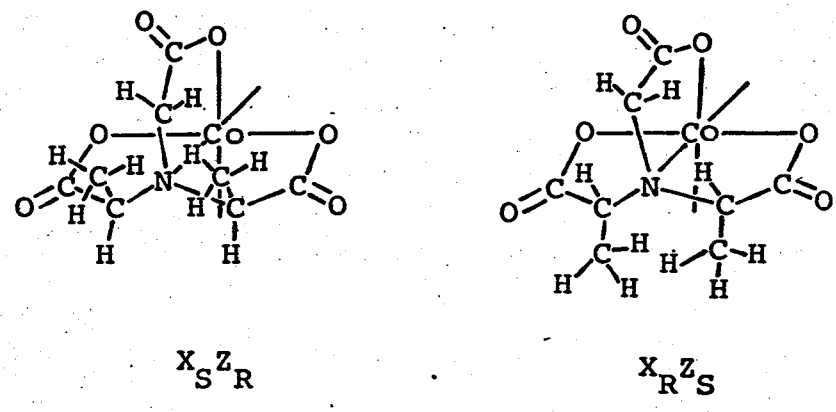


Fig. 6. Two structures of coordinated (R,S)-alaipa.

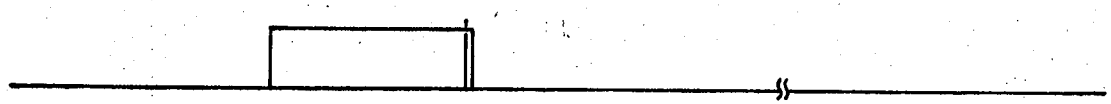
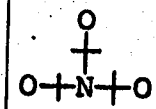
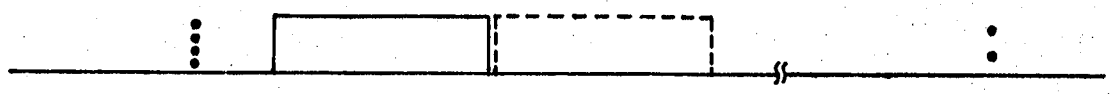
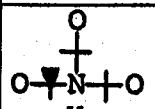
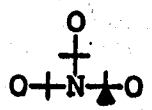
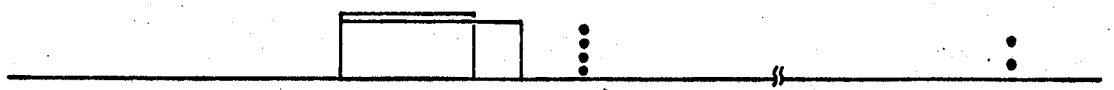
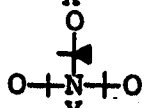
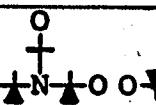
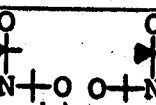
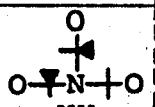
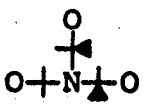
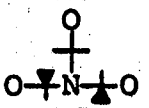
model examination indicates that in the X_RZ_S-isomer severe steric hindrance exists between the two axial methyl groups regardless of the variation of conformation of the coordinated (R,S)-alaipa ligand. In contrast to this, there is no such a hindrance in the X_SZ_R-isomer. Thus, the trans(N) (R,S)-alaipa complex (isomer-i) obtained is confidently assigned to the X_SZ_R-isomer (see Section II-7). In the cis(N) (R,S)-alaipa complex, it is impossible to evaluate the relative stabilities between the possible arrangement isomers, because no cis(N) isomer was recognized in the equilibrium

mixture of the (R,S)-alaipa complex. As described above, however, only one arrangement isomer of the cis(N) isomer was obtained stereoselectively as for the corresponding trans(N) isomer. A molecular model examination indicates that in the X_RZ_S-isomer of cis(N), the axial methyl groups interact strongly with the amino protons of the bidentate ligand gly, in addition to severe steric hindrance between the two methyl groups. From these situations, the cis(N) (R,S)-alaipa complex (isomer-i) obtained is assigned also to the X_SZ_R-isomer.

For the trans(N)-$[Co(N\text{-}O_3)(gly)]^-$ ($N\text{-}O_3$ = (S)-alada and (R,S)- or (S,S)-alaipa) type complexes, the possible isomers and isolated ones are shown in Table III. The PMR spectra of the isomer-i and -ii of the (S)-alada complex are shown in Fig. 7(A and B), the spectra of the other complexes are shown in Figs. 3 and 5, and then that of the corresponding nta complex in Fig. 15. The assignment of these spectra are easily made as indicated above the spectra (Section II-5), and the spectral data for the nitrilotricarboxylato ligand protons are shown schematically in Table III.

As will be described in Section II-5-(2), it was confirmed that whether an AB pattern due to the N-acetate methylene protons of nitrilotricarboxylato ligands is due to the out-of-plane ring or in-plane one can be determined on the basis of the magnitude of the geminal coupling constant (J_{AB}) of the AB pattern. The distinction of the AB patterns is indicated in Table III and provides the following

Table III. PMR Spectra (100 MHz) in D_2O and Structural Assignments of trans(N)-$[Co(N\text{-}O_3)(gly)]^-$ Complexes.

Complex isolated	Schematic PMR spectra[a)]	Assignment	Possible isomers
nta			
(S)-alada isomer-i		 X	 Z
isomer-ii		 Y	
(R,S)-alaipa isomer-i		 X_SZ_R	 X_RZ_S  X_SY_R b)  Y_RZ_S b)
(S,S)-alaipa isomer-i		 XY	 YZ
isomer-ii		 XZ	

5.0 4.5 4.0 2.0 1.5

ppm from DSS

a) The following symbols are used (the position of vertical line shows the chemical shift): ⌐¬, AB quartet (in-plane), ⌐¬, AB quartet (out-of-plane); |, singlet; ⋮, AX_3 quartet; ⋮, AX_3 doublet. b) The antipode is also possible.

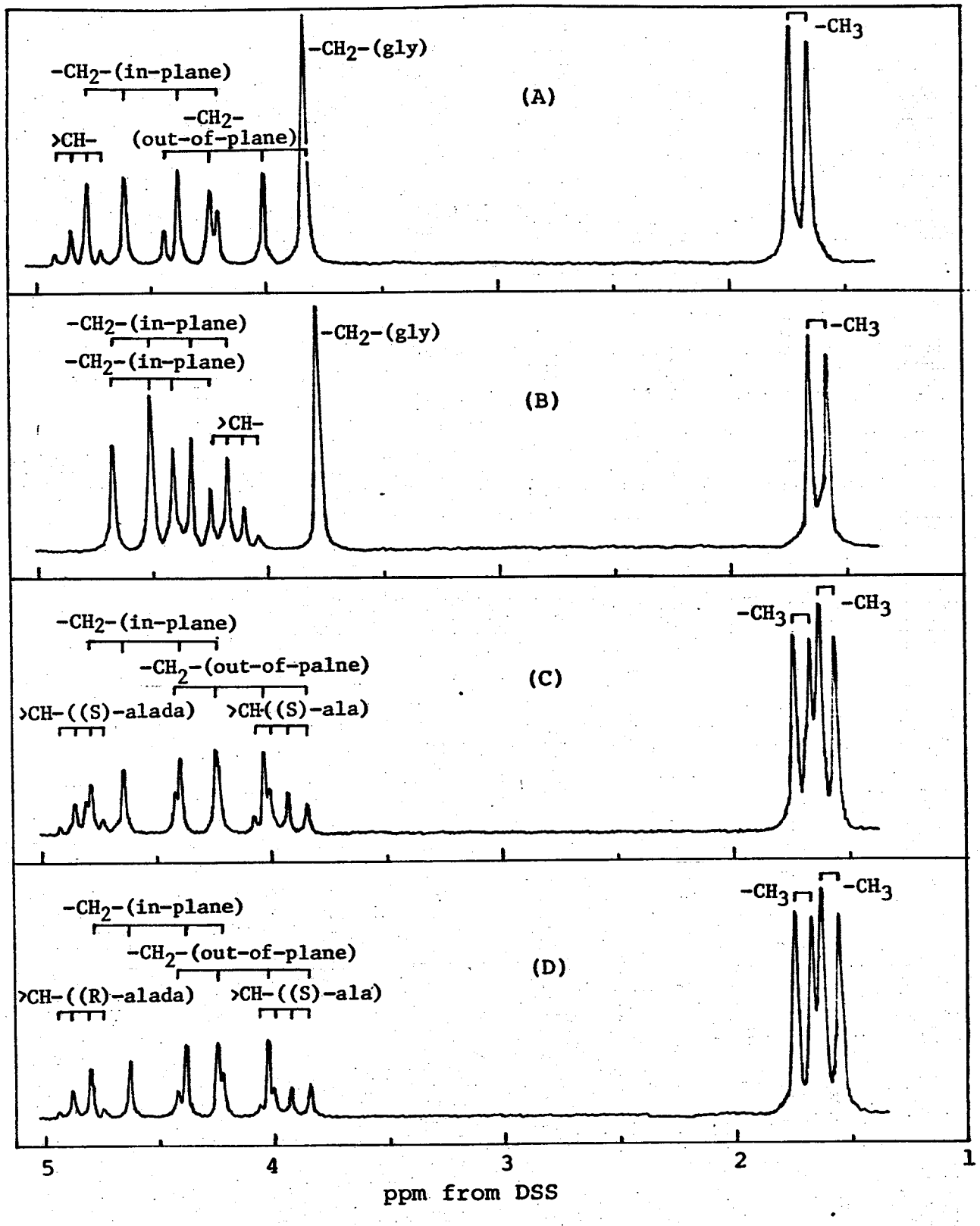


Fig. 7. PMR spectra of (A) X-trans(N)-[Co((S)-alada)(gly)]$^-$ (isomer-i), (B) Y-trans(N)-[Co((S)-alada)(gly)]$^-$ (isomer-ii), (C) Z-trans(N)-[Co((R)-alada)((S)-ala)]$^-$ (isomer-i), (D) X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$ (isomer-i).

information. The isomer-ii of (S)-alada complex exhibits two in-plane N-acetate rings and the isomer-ii of (S,S)-alaipa complex exhibits one out-of-plane N-acetate ring. Accordingly, the former complex is assigned unequivocally to Y-isomer and the latter to XZ-isomer. From the similar consideration, the isomer-i of the (S)-alada complex is assigned to either X- or Z-isomer and the isomer-i of the (S,S)-alaipa complex to either XY- or YZ-isomer.

In the PMR studies of a series of cobalt(III) complexes containing ethylenediamine-N,N'-(S)-iso-propionate or -(R)-iso-propionate ligand, Schoenberg and co-workers pointed out that replacing a proton by a methyl group on N-acetate methylene protons has little effect for the chemical shift of the signal due to the remaining methine protons.[71] The methine quartet of the isomer-i of (S)-alada and those of the isomer-i and -ii of the (S,S)-alaipa complex at the lower field are quite similar in their chemical shifts to that of the X_SZ_R-trans(N) (R,S)-alaipa complex where two methine protons are present only in the axial positions, while those of the isomer-ii of the (S)-alada complex, and of isomer-i and -ii of the (S,S)-alaipa complex at the higher field are different remarkably from that of the X_SZ_R-trans(N) (R,S)-alaipa complex, as seen in Table III. From this observation, it is considered that the former quartets near at 4.85 ppm due to the axial methine protons and the latter ones (near at 4.2 ppm) due to the other methine protons. Namely, the isomer-i of the (S)-alada complex, the isomer-i and -ii of the (S,S)-alaipa complex have an axial methine

proton in analogy with the (R,S)-alaipa complex. These assignments are consistent with the information based on the J_{AB} values for the isomer-i of the (S)-alada complex and the isomer-i of the (S,S)-alaipa complex. On these bases, the isomer-i of the (S)-alada complex and the isomer-i of the (S,S)-alaipa complex may be assigned to X-isomer and XY-isomer respectively. The results of the structural assignments are summarized in Table III.

For all the complexes in Table III, the following observation provides further support for the structural assignment of the complexes. The chemical shift values are closely related to "position" where the individual protons are situated. Namely, the signals of the methine or methylene protons on the in-plane N-acetate rings appear at 4.3 - 4.9 ppm and those on the out-of-plane appear at 3.9 - 4.4 ppm. Furthermore, the chemical shift correlations of the signals due to the methyl protons between these complexes also support the above assignment. It was confirmed by the spin-decoupling technique that in the isomer-ii of the (S,S)-alaipa complex the methyl doublet at 1.88 ppm constitute an AX_3 pattern with the methine quartet at 4.22 ppm which was assigned to the equatorial methine proton, and hence the doublet is assigned to the axial methyl protons. The doublet of the isomer-ii of (S,S)-alaipa complex at 1.88 ppm differs obviously in the chemical shift from those of the other complexes and then the axial methyl group is present only in the isomer-ii of the (S,S)-alaipa complex.

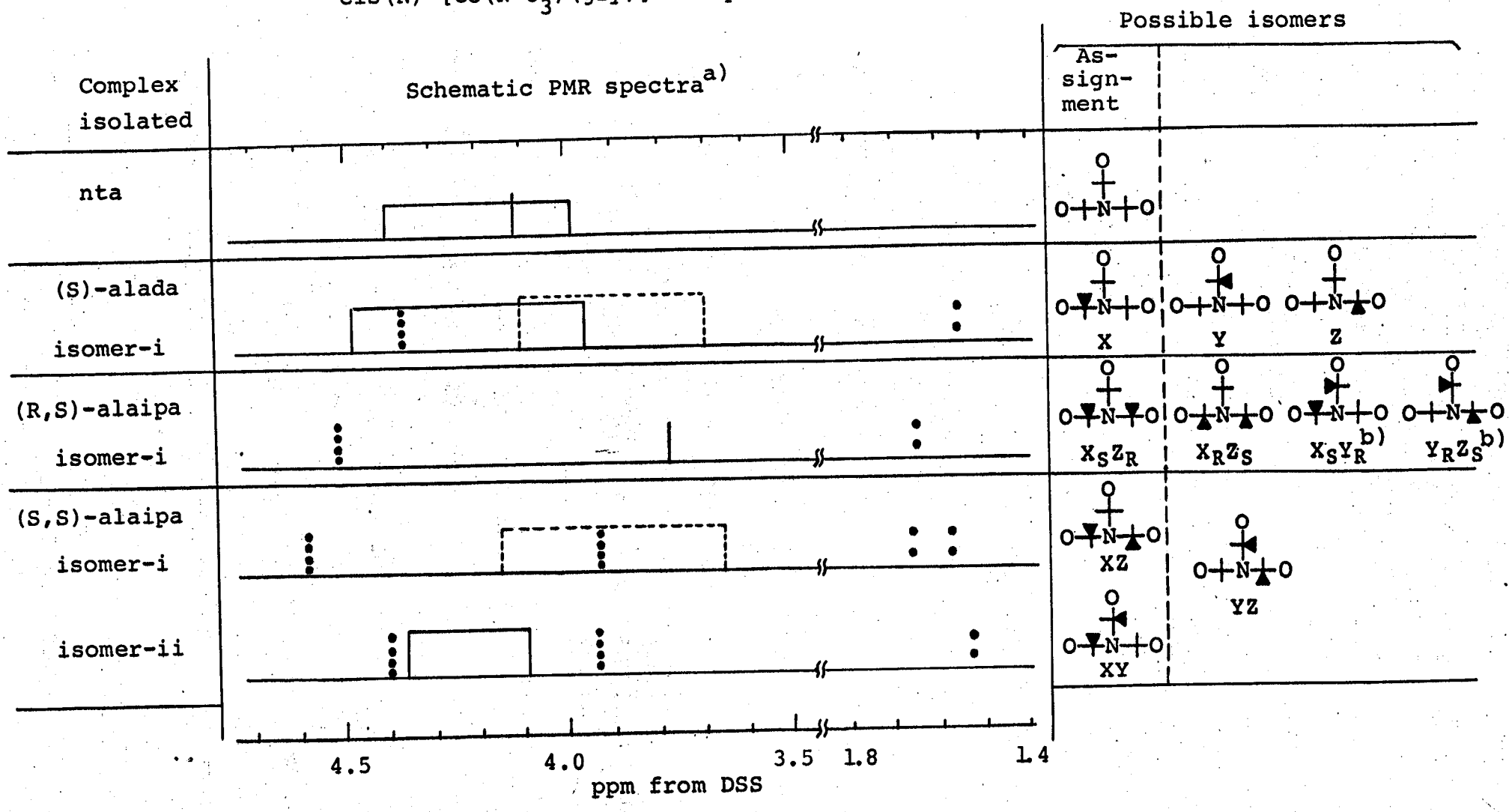
Similar examination for the structural assignment was

also undertaken for the analogous complexes of the following types; cis(N)-[Co(N-O_3)(gly)]$^-$ and trans(N)-[Co(N-O_3)(β-ala)]$^-$. The result for the former complexes is summarized in Table IV and that of the latter ones are reproduced from the related work[72] in Table V. The structural assignments of the complexes obtained for these type complexes can be performed by the same arguments as for the trans(N)-[Co(N-O_3)(gly)]$^-$ type complex and their results are shown in Table IV and V.

As seen in Table III - V, the arrangement isomers obtained are common in the three type complexes, except for the fact that the Y-cis(N)-[Co((S)-alada)(gly)]$^-$ complex was not obtained. In the preparation of these complexes, the stereoselective formation was observed and the predominance for formation is very similar for the same arrangement isomers in the three type complexes (see Experimental Section and Reference 72). Furthermore, the relationships between the PMR behaviors of the arrangement isomers obtained in a certain type complex are very similar between the three type complexes (Table III - V). These similarities support the above structural assignments for the three type complexes, because it is reasonable to consider that the difference in the bidentate ligand moiety has little effect for the stereoselective formation and PMR behaviors of the present complexes.

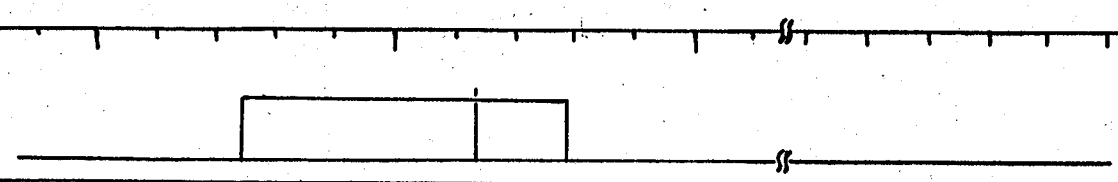
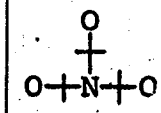
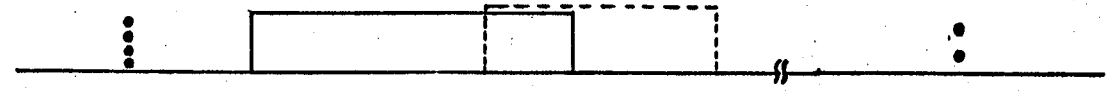
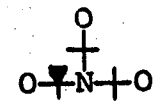
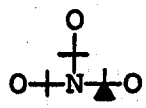
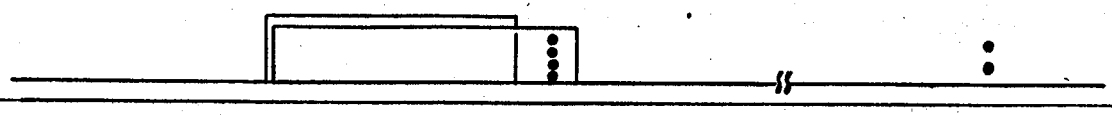
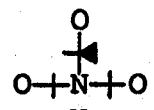
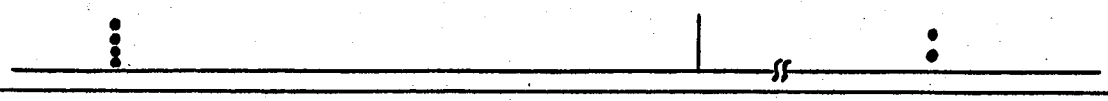
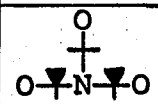
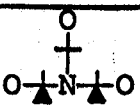
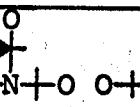
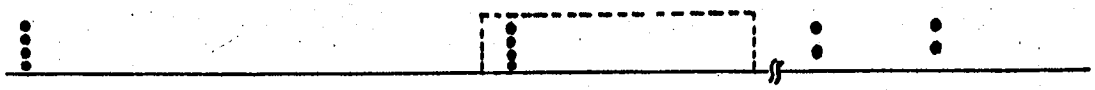
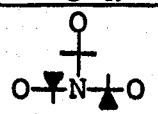
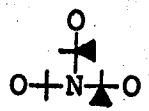
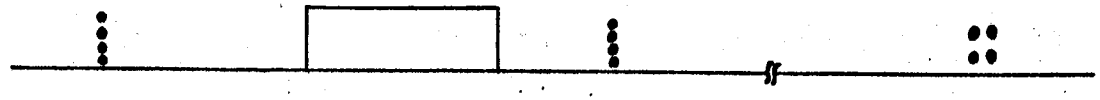
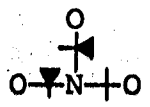
For the cis(N)-[Co(N-O_3)(β-ala)]$^-$ type complex, only the nta and (S)-alada complexes were prepared and other complexes were not attempted to obtain. The PMR data are similarly shown in Table VI. For the cis(N) (S)-alada complex, only one isomer (isomer-i) was obtained in

Table IV. PMR Spectra (100 MHz) in D_2O and Structural Assignments of cis(N)-$[Co(N\text{-}O_3)(gly)]^-$ Complexes.



a) and b) the same as the footnote in Table III.

Table V. PMR Spectra (100 MHz) in D_2O and Structural Assignments of trans(N)-$[Co(N\text{-}O_3)(\beta\text{-ala})]^-$ Complexes.

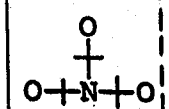
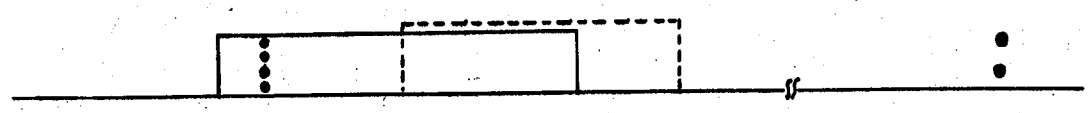
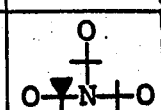
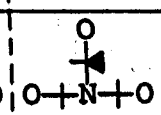
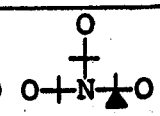
Complex isolated	Schematic PMR spectra[a)]	As-sign-ment	Possible isomers
nta			
(S)-alada isomer-i		 X	 Z
isomer-ii		 Y	
(R,S)-alaipa isomer-i		 X_SZ_R	 X_RZ_S  X_SY_R[b)] Y_RZ_S[b)]
(S,S)-alaipa isomer-i		 XZ	 YZ
isomer-ii		 XY	

5.0 4.5 4.0 2.0 1.5

ppm from DSS

a) and b) the same as the footnote in Table III.

Table VI. PMR Spectra (100 MHz) in D_2O and Structural Assignments of cis(N)-$[Co(N\text{-}O_3)(\beta\text{-ala})]^-$ Complexes.

Complex isolated	Schematic PMR spectra[a)]	Possible isomers: Assignment		
nta				
(S)-alada isomer-i		 X	 Y	 Z

4.5 4.0 3.5 1.8 1.4

ppm from DSS

a) the same as the footnote in Table III.

predominant yield as for the (S)-alada complexes of the above three type. The J_{AB} value indicates that the (S)-alada complex obtained is either X- or Z-isomer. Furthermore, the signals for the nitrilotricarboxylato ligand protons of the nta and (S)-alada complexes are very similar in the chemical shift values to those of the corresponding cis(N)-$[Co(N\text{-}O_3)(gly)]^-$ complexes respectively (Tables IV and VI). From these facts, it is concluded that the cis(N)-[Co((S)-alada)(β-ala)]$^-$ complex (isomer-i) obtained is X-isomer.

A number of trans(N)- and cis(N)-[Co((R)- or (S)-alada)-(am)]$^-$ type complexes containing various optically active α- or β-aminocarboxylate as am were prepared. For all the complexes, only one arrangement isomer (isomer-i for each of the complexes) was obtained stereoselectively as for the corresponding complexes with optically inactive amino-carboxylates of which the structures were assigned above. The PMR spectra and their assignments of the trans(N)-[Co-((S)-alada)((S)-ala)]$^-$ and trans(N)-[Co((R)-alada)((S)-ala)]$^-$ complexes are shown in Fig. 7(C and D). Each of the (S)-ala complexes is indicated to be either X- or Z-isomer on the basis of the J_{AB} values of the AB patterns. The PMR spectra of the (S)-ala complexes are indistinguishably similar over whole range of magnetic fields to each other, and then the two AB patterns and one AX_3 pattern due to the (R)- or (S)-alada protons of these complexes are quite similar in their chemical shift values to those due to the (S)-alada protons of the X-trans(N)-[Co((S)-alada)(gly)]$^-$ complex. From these facts, it is reasonable to conclude that the

trans(N)-[Co((S)-alada)((S)-ala)]$^-$ complex obtained (isomer-i) is X-isomer, while the trans(N)-[Co((R)-alada)-((S)-ala)]$^-$(isomer-i) is Z-isomer, because with respect to the coordinated alada the Z-isomer of the (R)-alada complex is antipodal to the X-isomer of the (S)-alada complex. The quite similar behaviors are observed for the (R)-alada and (S)-alada complexes with the other optically active aminocarboxylates. Thus, all the (S)-alada complexes can be assigned to the X-isomer and all the (R)-alada complexes to the Z-isomer as shown in Table II.

(2) β-alada and (S)-alapa complexes.

As shown in Table I, the three arrangement isomers are possible for each of the trans(N)- and cis(N)-[Co(β-alada)-(gly)]$^-$ complexes. Two (X- and Z-isomers: u-isomers) of the three isomers are unsymmetrical and antipodal to each other and another one (Y-isomer: s-isomer) is symmetrical and optically inactive. The two isomers of the trans(N) gly complex, isomer-ii and -iii, were optically active and their CD spectra indicated that the isomers were antipodal to each other(Section II-6). Accordingly it is obvious that the isomer-ii and -iii of the trans(N) gly complex are u-isomers, and hence the remaining unresolving complex, isomer-i, is s-isomer. From the same consideration, the isomer-i and -ii of the cis(N) gly complex are u-isomers and the isomer-iii is s-isomer. The absolute configuration of the u-isomers (the distinction between the X- and Z-isomers) in the trans(N) gly and cis(N) gly complexes

will be determined on the basis of their CD behaviors (Section II-6).

From the construction of molecular model of the trans(N)- and cis(N)-[Co(β-alada)(gly)]$^-$ complexes, it is expected for the s-isomers that the PMR signals due to β-alada protons consist of one AB pattern due the four methylene protons on the two in-plane N-acetate rings, which are in the same environment, and one AA'BB' pattern due to the four ethylene protons of the out-of-plane N-propionate ring. In the u-isomers, one AB pattern is expected for each of the in-plane and out-of-plane N-acetate protons and one ABCD pattern is expected for four in-plane N-propionate protons. The expectation is realized in Figs. 8 and 9: the signals for the N-propionate protons of the s-trans(N)- and s-cis(N)-[Co(β-alada)(gly)]$^-$ constitute typical AA'BB' patterns which have the midpoint at 2.19 and 2.75 ppm respectively, and the u-trans(N) and u-cis(N) complexes show complicated spectra as expected for the ABCD pattern. Judging from intensity integrations, the signals near 2.8, 3.3-3.6, and 3.8-4.1 ppm for the u-trans(N) gly complexes correspond to two, one and one protons, respectively, and signals resemble to these are also observed for u-cis(N) gly complex near 2.8, 3.0-3.3, and 3.5-3.65 ppm, although the signals in the last named region are most likely hidden by other intense signals.

In the trans(N)- and cis(N)-[Co(β-alada)(am)]$^-$ type complexes with optically active aminocarboxylates, three arrangement isomers were obtained for each of the trans(N)

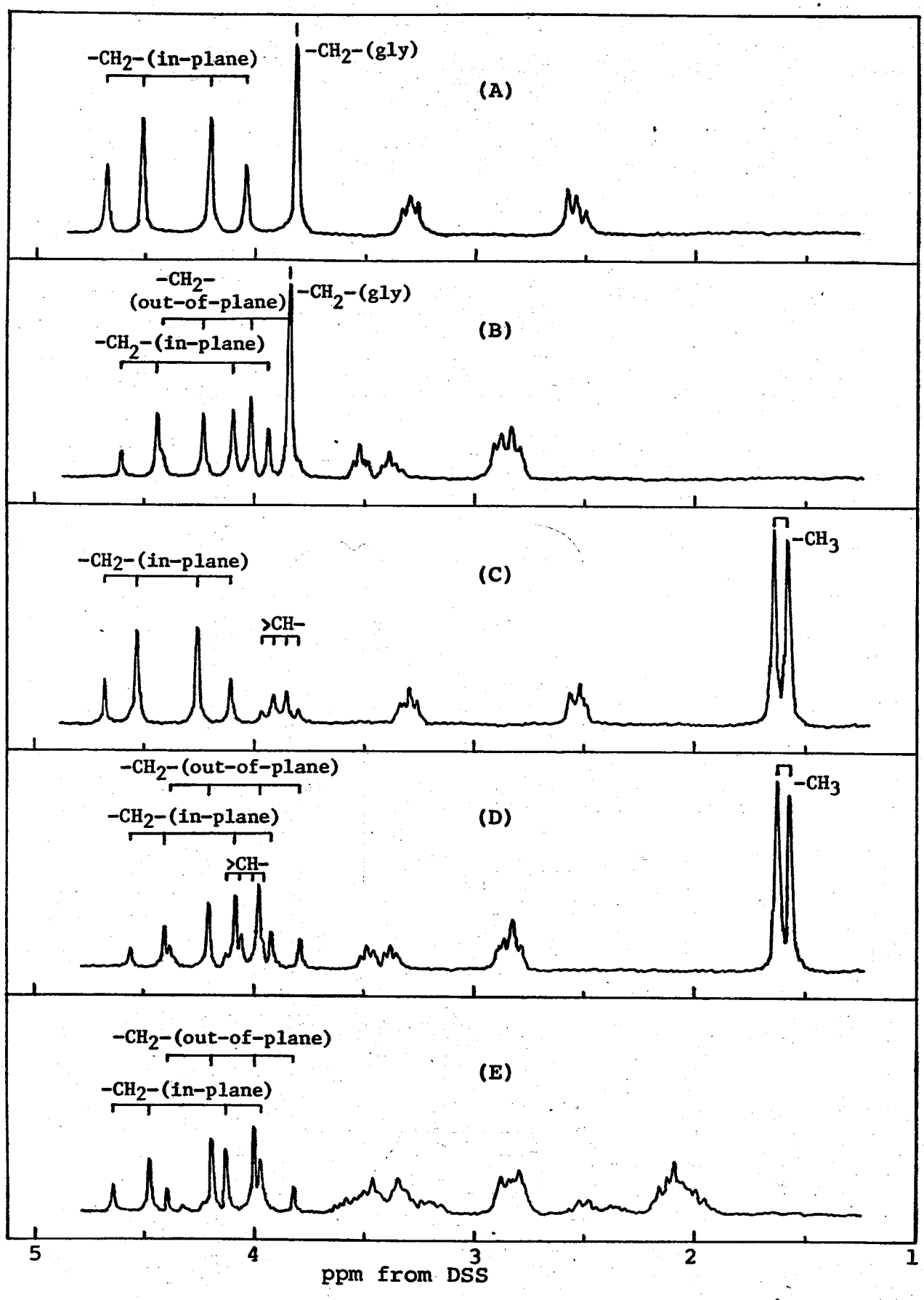


Fig. 8. PMR spectra of (A) Y(s)-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-i), (B) X(u)-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-ii), (C) Y(s)-trans(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-iii), (D) X(u)-trans(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-i), and (E) X(u)-trans(N)-[Co(β-alada)((S)-pro)]$^-$ (isomer-i).

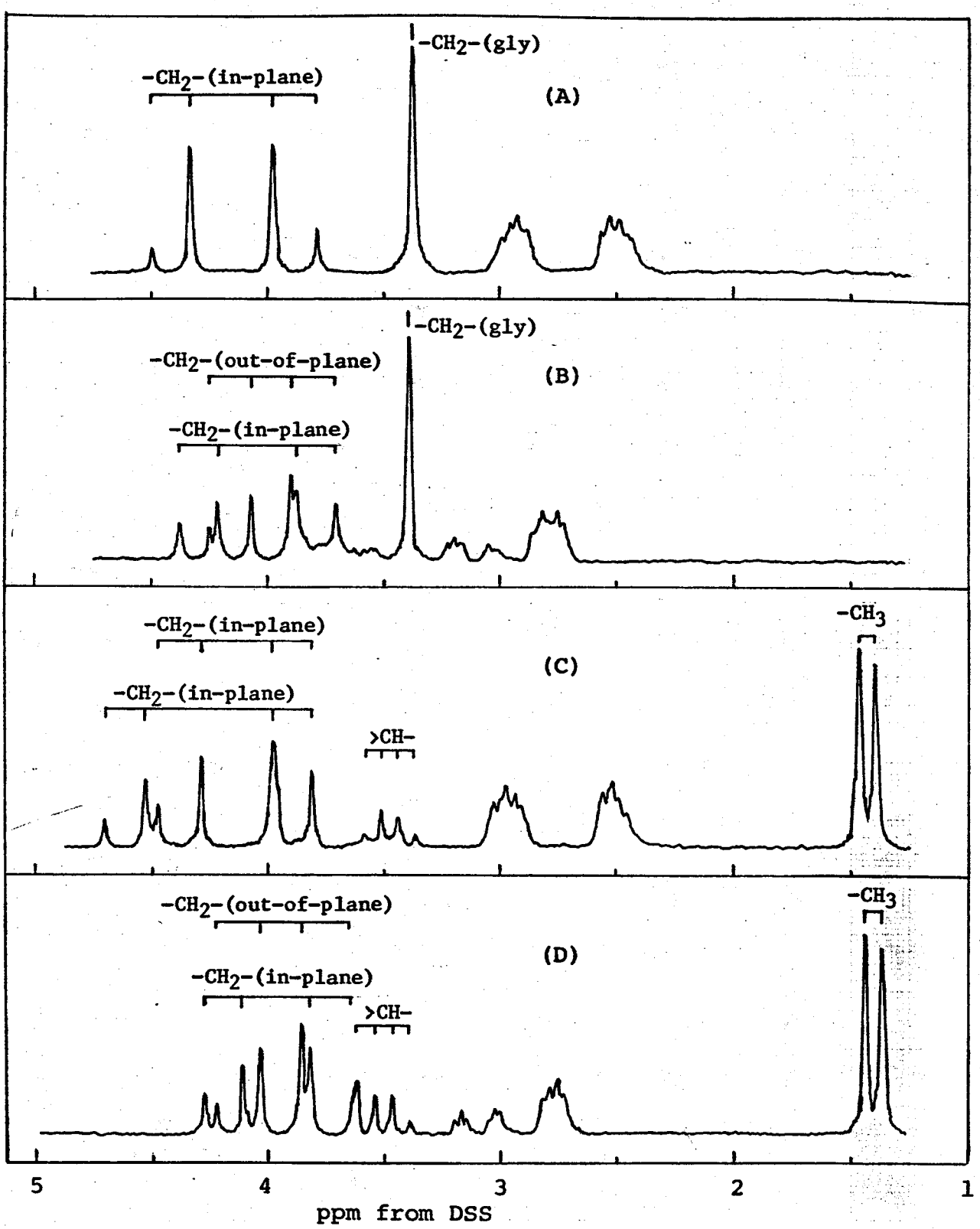


Fig. 9. PMR spectra of (A) Y(s)-cis(N)-[Co(β-alada)(gly)]$^-$ (isomer-i), (B) Z(u)-cis(N)-[Co(β-alada)(gly)]$^-$ (isomer-ii), (C) Y(s)-cis(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-iii), and (D) X(u)-cis(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-ii).

(S)-ala, cis(N) (S)-ala and trans(N) (S)-pro complexes. The representative PMR spectra of the complexes are shown in Figs. 8 and 9. In the trans(N)-[Co(β-alada)((S)-ala)]$^-$ complex, it is indicated on the basis of the J_{AB} values of the AB pattern that the isomer-iii has the two in-plane N-acetate rings and each of the isomer-i and -ii has the one in-plane and one out-of-plane N-acetate rings (Section II-5-(2)). Furthermore, the signals of β-alada protons of the trans(N) (S)-ala complexes are quite similar in the chemical shift values and splitting patterns to those of the corresponding isomers of the trans(N)-[Co(β-alada)(gly)]$^-$ complex (Fig. 8); namely, the isomer-iii resembles the s-isomer of the trans(N) gly complex and the isomer-i and -ii resemble the u-isomer of the trans(N) gly complex. From these observations, it is concluded that the isomer-iii of the trans(N) (S)-ala complex is s-isomer and the isomer-i and -ii are u-isomers. From the same consideration, the arrangement isomers of the cis(N) (S)-ala and trans(N) (S)-pro complexes can be assigned as shown in Table II (Figs. 8 and 9). The absolute configuration of the u-isomers of these complexes will be assigned in Section II-5.

The representative absorption sepctra of trans(N)- and cis(N)-[Co(β-alada)(am)]$^-$ type complexes are shown in Figs. 10 and 11. The similarlity of spectra of the present β-alada complexes lead to the same conclusion as the above assignment based on the PMR spectra. In each of the trans(N) gly and cis(N) gly complexes, the absorption curves of the s- and u-isomers are clearly differ in the first and second

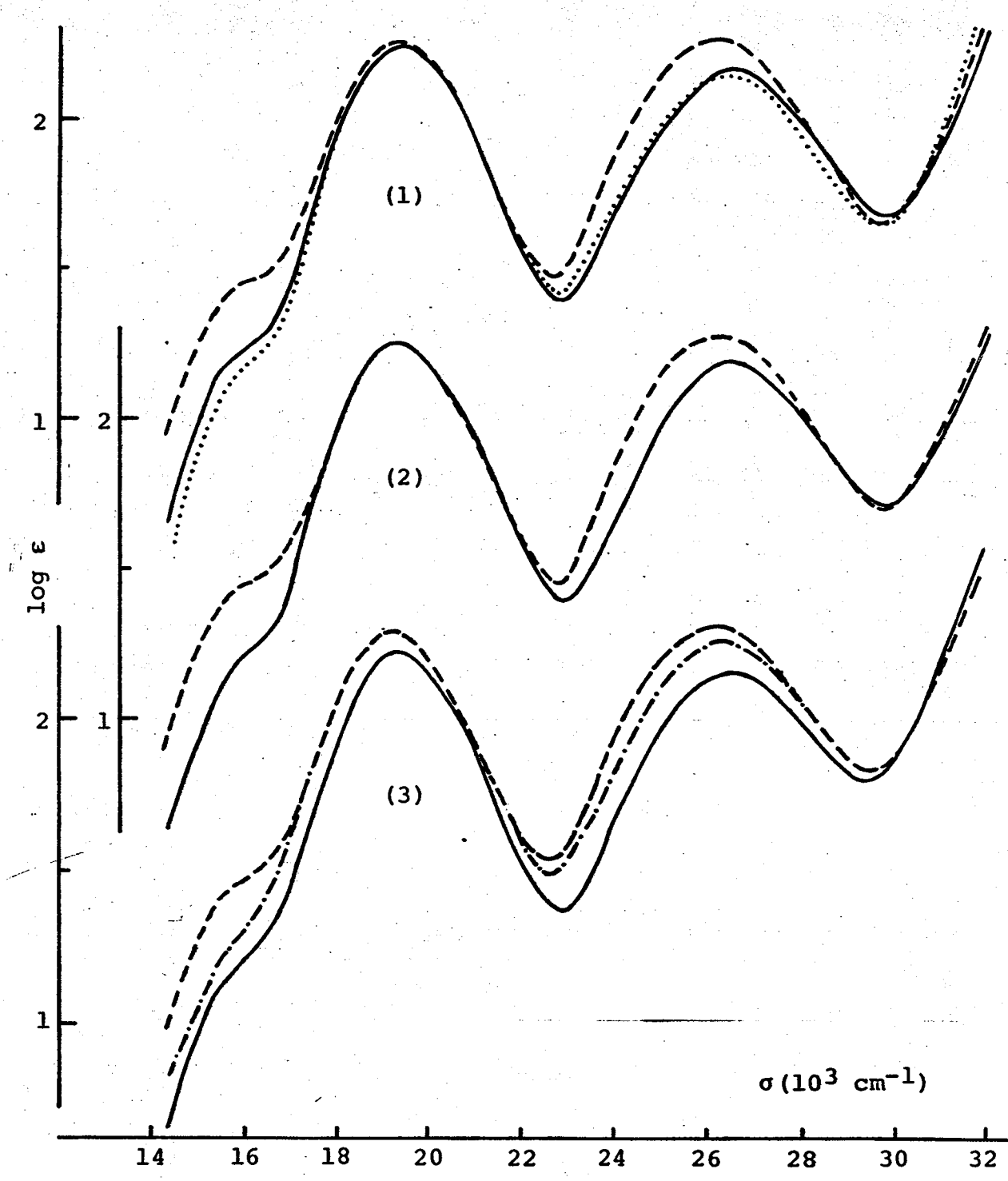


Fig. 10. Absorption spectra of trans(N)-[Co(β-alada)(am)]$^-$ type and trans(N)-[Co((S)-alapa)(gly)]$^-$ complexes.

(1) -----, Y(s)-gly (isomer-i); ———, X(u)-gly (isomer-ii); ·····, X_SZ_6-trans(N)-[Co((S)-alapa)(gly)]$^-$ (isomer-i)

(2) -----, Y(s)-(S)-ala (isomer-iii); ———, Z(u)-(S)-ala (isomer-ii)

(3) -----, Y(s)-(S)-pro (isomer-ii); ———, X(u)-(S)-pro (isomer-i); -·-·-, Z(u)-(S)-pro (isomer-iii)

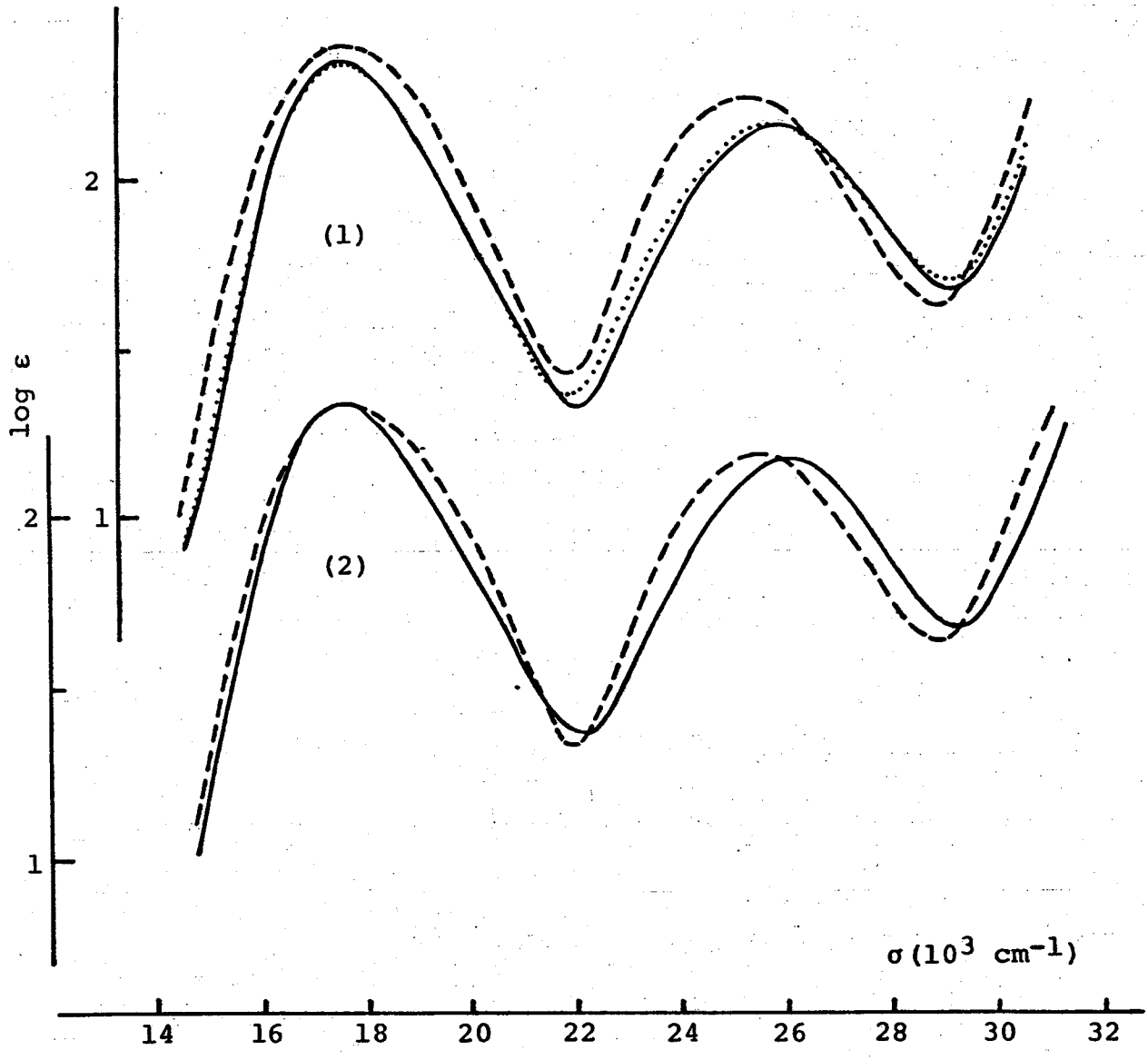


Fig. 11. Absorption spectra of cis(N)-[Co(β-alada)(am)]$^-$ type and cis(N)-[Co((S)-alapa)(gly)]$^-$ complexes.

(1) -----, Y(s)-gly (isomer-i); ———, Z(u)-gly (isomer-ii); ·····, X_SZ_6-cis(N)-[Co((S)-alapa)(gly)]$^-$ (isomer-i)

(2) -----, Y(s)-(S)-ala (isomer-iii); ———, X(u)-(S)-ala (isomer-ii)

absorption bands from each other as can be seen in Figs. 10 and 11 (see Section II-4). The s- and u-isomers of the trans(N) (S)-ala and trans(N) (S)-pro complexes are very similar to the s- and u-isomers of the trans(N) gly complexes respectively (Fig. 10). A similar relationship is observed between the cis(N) gly and cis(N) (S)-ala complexes (Fig. 11).

In the preparation of $[Co((S)\text{-alapa})(gly)]^-$ complex, only one arrangement isomer (isomer-i) was obtained for each of the trans(N) and cis(N) isomers of the complex. From the isomer equilibrium experiment of the $[Co(N\text{-}O_3)\text{-}(gly)]^-$ type complexes, it was found that there was the following correlations for each of the trans(N) and cis(N) isomers (Section II-7). In the (S)-alada, (R,S)- and (S,S)-alaipa complexes, the methyl group of the N-isopropionate ring prefer to take the equatorial position on the in-plane ring to the other positions. On the other hand, in the β-alada complex the β-alada ligand prefer to take the u-structure than the s-structure. Applying these ocrrelations for the present (S)-alapa complexes, it is expected that the X_SZ_6-isomer is most stable of the six isomers possible for each of the complexes, because it can be considered that the structure of the X_SZ_6-isomer of (S)-alapa complex consist of a combination of the X-isomer of (S)-alapa complex and the Z(u)-isomer of β-alada complex. This expectation seems to be reasonable from the stereochemical consideration of the coordinated (S)-alapa ligand (Section II-7). The equilibrium experiment of the $[Co((S)\text{-alapa})(gly)]^-$ complex indicates that the isomer

(isomer-i) obtained in the preparation is much more stable than the other arrangement isomers for each of the trans(N) and cis(N) isomers. Thus, it may be reasonable to assign both of the trans(N) and cis(N) (S)-alapa complexes obtained to X_SZ_6-isomer. These assignments are strongly supported from the relationships between the CD spectra of the (S)-alapa complexes and those of the related complexes.

The PMR and absorption spectra of the (S)-alapa complexes provide some informations for the structural assignment. The informations support the result of the above assignment, although do not provide a conclusive evidence. The absorption are shown in Figs. 10 and 11 along with those of trans(N)- and cis(N)-$[Co(\beta\text{-alada})(gly)]^-$ complexes. The absorption spectra of the trans(N) and cis(N) (S)-alapa complexes are quite similar to those of the u-trans(N) and u-cis(N) β-alada complexes respectively. Figure 12 shows that the PMR spectra of the (S)-alapa complexes and the simple and sharp signals can be assigned as indicated above the spectra (Section II-5-(1)). The broad and complicated signals near 2.85, 3.4-3.6 and 3.8-4.1 ppm for the trans(N) (S)-alapa complex are assigned to the ethylene protons of (S)-alapa and quite similar in the splitting patterns and chemical shift values to the signals of the ethylene protons for the u-trans(N)-$[Co(\beta\text{-alada})(gly)]^-$ complex (Fig. 8). Similarly, the signals near 2.75, 3.0-3.3 and 3.5 ppm due to the ethylene protons of the cis(N) (S)-alapa complex are similar to

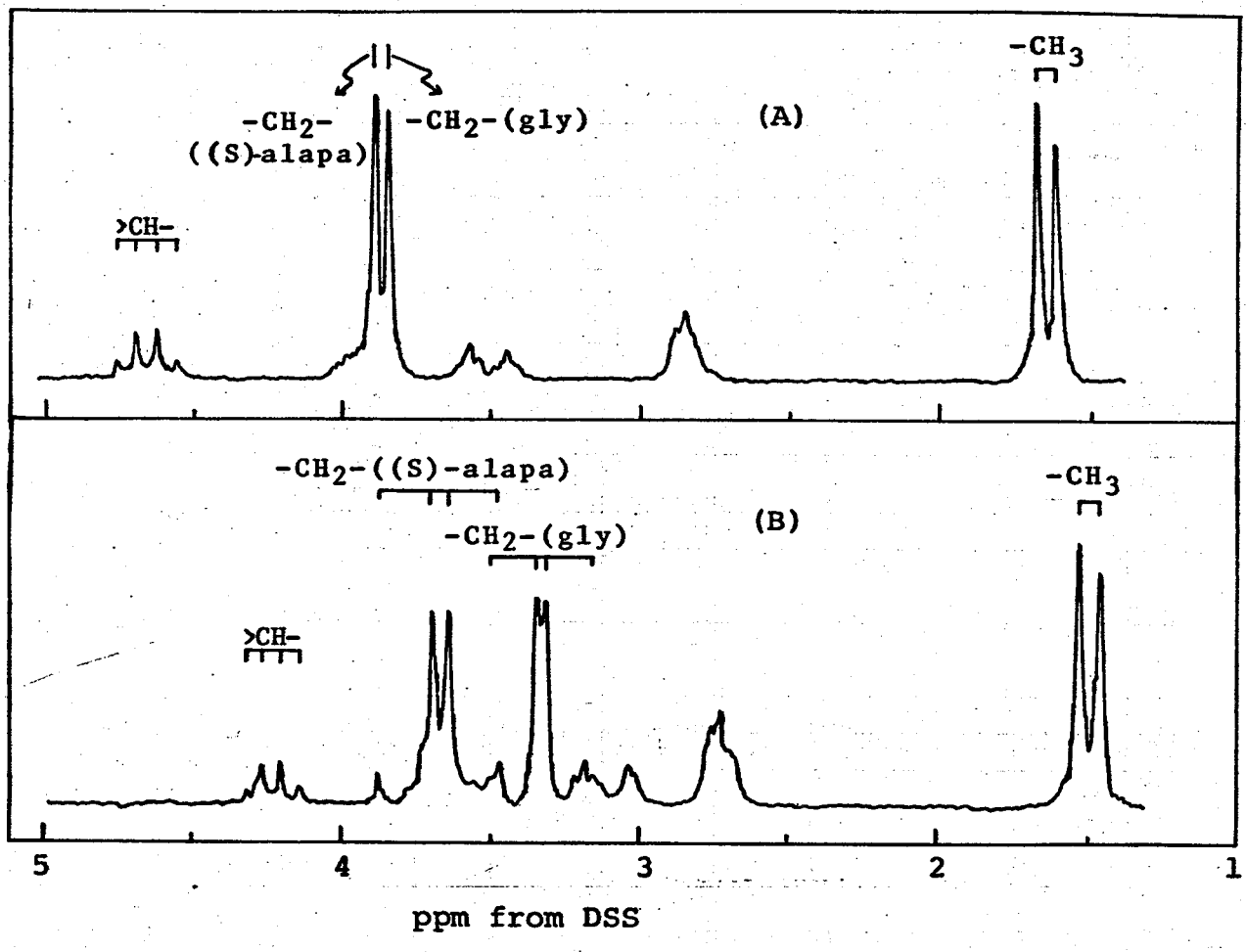


Fig. 12. PMR spectra of $[Co((S)\text{-alapa})(gly)]^-$:

(A) X_SZ_6-trans(N) (isomer-i), and (B) X_SZ_6-cis(N) (isomer-i).

those for the u-cis(N)-[Co(β-alada)(gly)]$^-$ complex (Fig. 9). These observations indicate that each of the trans(N) and cis(N) (S)-alapa complexes is u-type isomer (one of X_SZ_6-, Y_SZ_6-, Y_SX_6- and Z_SX_6-isomers). In the cis(N) (S)-alapa complex, the AB pattern due to the N-acetate methylene protons of (S)-alapa appears and its J_{AB} value indicates that the cis(N) (S)-alapa complex has the out-of-plane N-acetate ring, that is, it is either X_SZ_6- or Z_SX_6-isomer (Section II-5-(2)). Unfortunately, the signal for the N-acetate methylene protons of (S)-alapa collapses into a singlet in the trans(N) (S)-alapa complex (Fig. 12). Accordingly, the suggestion for the structural assignment can not be obtained from the J_{AB} value.

II-4. Electronic absorption spectra.

The spin allowed d-d transition bands of trans(N)- and cis(N)-$[Co(N)_2(O)_4]$ type complexes have been widely investigated with those of many other type complexes.[17,20,73-79] When only coordinated atoms around the central ion is taken into consideration, these complexes have holohedlized tetragonal symmetry. Under the tetragonal (D_{4h}) symmetry, the T_{1g} (O_h) level which is the first excited state for a low-spin cobalt(III) complex is split into A_2 and E levels.[75-79] In the trans(N)-$[Co(N)_2(O)_4]$ type complexes, there is a stronger field strength along the unique axis (N-N) than in the plane perpendicular to it, while in the cis(N) complexes there is a weaker one along unique axis (O-O) than the plane of perpendicular to it. Thus, it is expected that the A_2 level lies lower in energy than the E level in the trans(N) complexes and the relationship in the levels are reversed for the cis(N) complexes. Furthermore, it is expected that the tetragonal splitting in a trans(N) complex amounts to twice that in a cis(N) complex.

The d-d absorption data of the complexes obtained in this work are summarized in Table VII and the representative curves are shown in Figs. 8, 9, 13, and 14. These complexes are divided into two groups on the basis of the splitting pattern of their first d-d absorption bands. The first group has a shoulder at the lower energy side of the major peak (506 - 526 nm), and the second group has a vague

Table VII. Electronic Absorption Spectral Data of $[Co(N\text{-}O_3)(am)]^-$ Complexes.[a)]

Complex ion	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
trans(N)-[Co(nta)(gly)]$^-$	ca. 16.0sh[b)]	1.2_5	26.70	2.22
	19.57	2.20		
trans(N)-[Co(nta)((S)-ala)]$^-$	ca. 16.0sh	1.2_5	26.85	2.24
	19.57	2.21		
trans(N)-[Co(nta)((S)-val)]$^-$	ca. 16.0sh	1.3_0	26.88	2.24
	19.53	2.21		
trans(N)-[Co(nta)((S)-ser)]$^-$	ca. 16.0sh	1.2_5	26.81	2.24
	19.53	2.23		
trans(N)-[Co(nta)((S)-pro)]$^-$	ca. 16.0sh	1.3_0	26.67	2.28
	19.49	2.23	26.67	2.28
trans(N)-[Co(nta)(sar)]$^-$	ca. 16.0sh	1.2_5	26.74	2.27
	19.49	2.23		
trans(N)-[Co(nta)(β-ala)]$^-$	ca. 15.9sh	1.3_5	26.35	2.26
	19.42	2.33		
trans(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$	ca. 15.9sh	1.3_5	26.46	2.27
	19.46	2.36		

Table VII. (continued)

Complex ion	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
trans(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$	ca. 15.9sh	1.3_0	26.46	2.26
	19.42	2.32		
trans(N)-[Co(nta)((S,S)-achc)]$^-$	ca. 15.9sh	1.3_5	26.53	2.29
	19.49	2.38		
trans(N)-[Co(nta)((S,R)-achc)]$^-$	ca. 15.9sh	1.3_5	26.46	2.28
	19.42	2.36		
trans(N)-[Co(nta)(γ-ambut)]$^-$	ca. 15.7sh	1.4_0	25.91	2.26
	19.01	2.31		
cis(N)-[Co(nta)(gly)]$^-$	17.61	2.34	26.01	2.23
cis(N)-[Co(nta)((S)-ala)]$^-$	17.48	2.33	26.04	2.23
cis(N)-[Co(nta)((S)-val)]$^-$	17.48	2.32	25.97	2.22
cis(N)-[Co(nta)((S)-ser)]$^-$	17.51	2.32	25.97	2.22
cis(N)-[Co(nta)(β-ala)]$^-$	17.18	2.34	26.81	2.27
cis(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$	17.18	2.31	25.77	2.25
cis(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$	17.18	2.34	25.71	2.28
cis(N)-[Co(nta)((S,S)-achc)]$^-$	17.18	2.34	25.74	2.28
cis(N)-[Co(nta)((S,R)-achc)]$^-$	17.17	2.34	25.74	2.28

Table VII. (continued)

	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
X-trans(N)-[Co((S)-alada)(gly)]$^-$	ca. 16.0sh	1.2_5	26.74	2.23
	19.65	2.26		
Y-trans(N)-[Co((S)-alada)(gly)]$^-$ c)	ca. 16.0sh	1.2_5	26.88	2.22
	19.57	2.20		
X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$	ca. 16.0sh	1.3_0	26.74	2.23
	19.65	2.27		
Z-trans(N)-[Co((R)-alada)((S)-ala)]$^-$	ca. 16.0sh	1.3_0	26.74	2.23
	19.65	2.27		
X-trans(N)-[Co((S)-alada)((S)-pro)]$^-$	ca. 16.0sh	1.2_0	26.67	2.26
	19.51	2.26		
Z-trans(N)-[Co((R)-alada)((S)-pro)]$^-$	ca. 16.0sh	1.2_5	26.67	2.25
	19.53	2.25		
X-trans(N)-[Co((S)-alada)(β-ala)]$^-$	ca. 15.9sh	1.3_0	26.25	2.28
	19.46	2.40		
X-trans(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$	ca. 15.9sh	1.3_0	26.39	2.26
	19.46	2.40		

Table VII. (continued)

	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
Z-trans(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$ ca.	15.9sh	1.4_0	26.39	2.30
	19.49	2.44		
X-trans(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$ ca.	15.9sh	1.3_5	26.32	2.28
	19.46	2.41		
Z-trans(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$ ca.	15.9sh	1.3_0	26.32	2.27
	19.46	2.39		
X-cis(N)-[Co((S)-alada)(gly)]$^-$	17.61	2.37	25.91	2.24
X-cis(N)-[Co((S)-alada)((S)-ala)]$^-$	17.61	2.37	25.97	2.22
Z-cis(N)-[Co((R)-alada)((S)-ala)]$^-$	17.61	2.36	25.94	2.23
X-cis(N)-[Co((S)-alada)(β-ala)]$^-$	17.21	2.36	25.77	2.26
X-cis(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$	17.18	2.37	25.71	2.27
Z-cis(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$	17.18	2.38	25.77	2.27
X-cis(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$	17.18	2.28	25.58	2.29
Z-cis(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$	17.18	2.39	25.58	2.29

Table VII. (continued)

Complex ion	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
$X_S Z_R$-trans(N)-[Co((R,S)-alaipa)(gly)]$^-$	ca. 16.0sh	1.2_5	26.60	2.23
	19.76	2.27		
$X_S Z_R$-cis(N)-[Co((R,S)-alaipa)(gly)]$^-$	17.79	2.34	25.84	2.16
XY-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$	ca. 16.0sh	1.2_0	26.85	2.23
	19.67	2.25		
XZ-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$	ca. 16.0sh	1.2_0	26.85	2.25
	19.69	2.29		
XZ-cis(N)-[Co((S,S)-alaipa)(gly)]$^-$	17.61	2.32	25.81	2.21
XY-cis(N)-[Co((S,S)-alaipa)(gly)]$^-$	17.62	2.34	26.04	2.22
Y-trans(N)-[Co(β-alada)(gly)]$^-$	ca. 16.0sh	1.45	26.04	2.28
	19.34	2.25		
X-trans(N)-[Co(β-alada)(gly)]$^-$	ca. 16.0sh	1.2_0	26.53	2.17
		(1.2_0) d)		(2.17) d)
	19.34	2.24		
		(2.23) d)		

Table VII. (continued)

Complex ion	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
X-trans(N)-[Co(β-alada)((S)-ala)]$^-$	ca. 16.0sh	1.2_0	26.53	2.19
	19.31	2.26		
Z-trans(N)-[Co(β-alada)((S)-ala)]$^-$	ca. 16.0sh	1.2_0	26.60	2.20
	19.31	2.25		
Y-trans(N)-[Co(β-alada)((S)-ala)]$^-$	ca. 16.0sh	1.44	26.11	2.27
	19.31	2.24		
X-trans(N)-[Co(β-alada)((S)-pro)]$^-$	ca. 16.0sh	1.2_0	26.46	2.17
	19.19	2.23		
Y-trans(N)-[Co(β-alada)((S)-pro)]$^-$	ca. 16.0sh	1.48	25.97	2.32
	19.12	2.28		
Z-trans(N)-[Co(β-alada)((S)-pro)]$^-$	ca. 16.0sh	1.3_0	26.25	2.26
	19.05	2.29		
Z-cis(N)-[Co(β-alada)(gly)]$^-$	17.61	2.35	26.11	2.16
		(2.34)[d]		(2.15)[d]
Y-cis(N)-[Co(β-alada)(gly)]$^-$	17.78	2.38	25.41	2.24
Z-cis(N)-[Co(β-alada)((S)-ala)]$^-$	17.61	2.36	26.11	2.15

Table VII. (continued)

Complex ion	Band I		Band II	
	σ_{max}	$\log\varepsilon_{max}$	σ_{max}	$\log\varepsilon_{max}$
X-cis(N)-[Co(β-alada)((S)-ala)]$^-$	17.61	2.34	26.11	2.18
Y-cis(N)-[Co(β-alada)((S)-ala)]$^-$ e)	17.73	—	25.58	—
X_SZ_6-trans(N)-[Co((S)-alapa)(gly)]$^-$	ca. 16.0sh 19.38	1.1_5 2.24	26.46	2.16
X_SZ_6-cis(N)-[Co((S)-alapa)(gly)]$^-$	17.62	2.34	25.84	2.16

a) The wave numbers are given in 10^3 cm^{-1}.

b) "sh" means a shoulder band.

c) No elemental analysis carried out, but the ε_{max} value was estimated on the sasis of the isomerization experiment (Experimental Section I-3-2-(c)).

d) The values in parentheses are for the antipode.

e) The ε_{max} value has not been obtained because of the lack of elemental analysis. Electronic absorption curve in Fig. 11 was drawn by assuming the ε_{max} value of the first absorption band to be the same as the mean value (ε_{max} = 225) for those of the corresponding Z- and X-isomers.

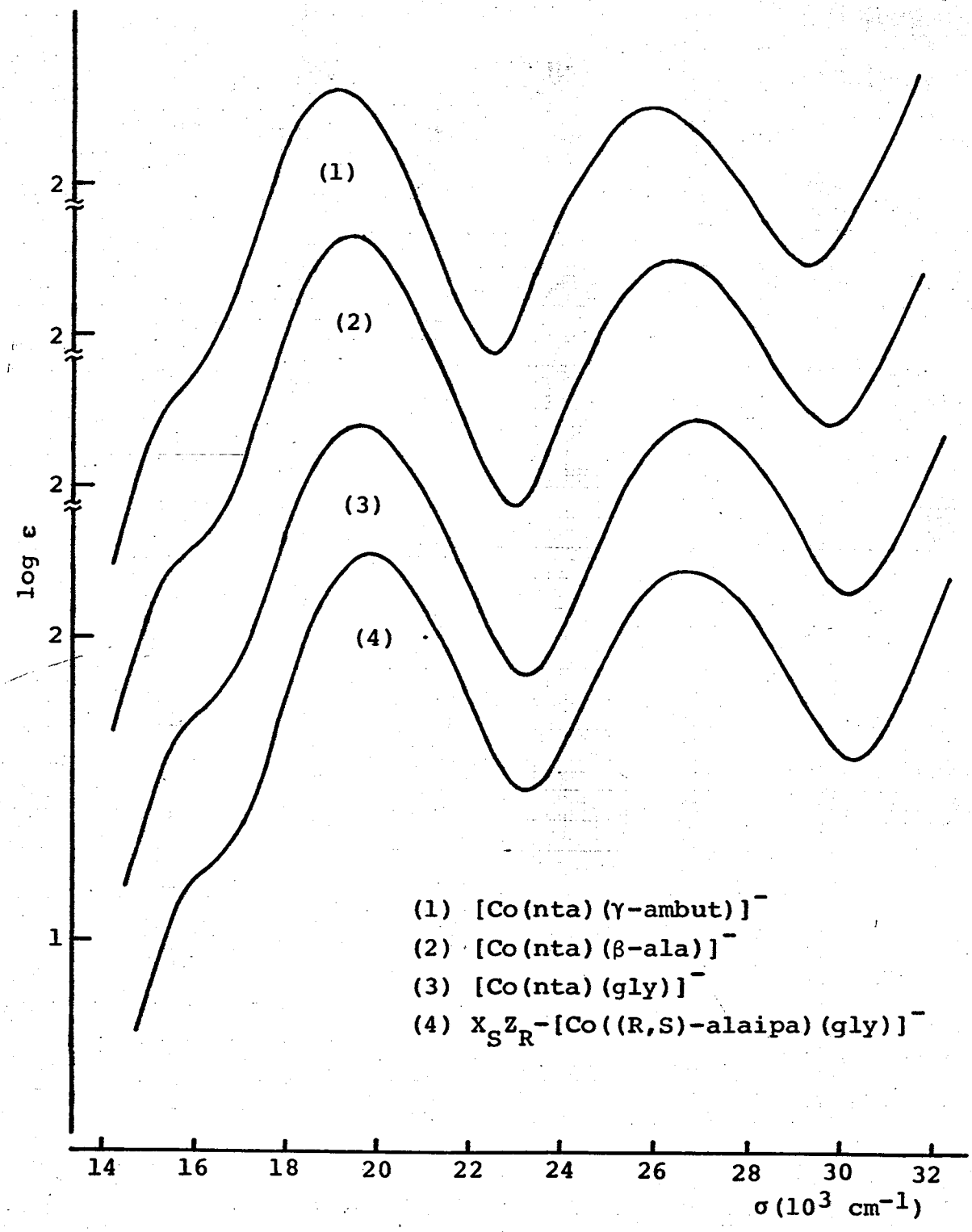


Fig. 13. Absorption spectra of trans(N)-$[Co(N\text{-}O_3)(am)]^-$ complexes.

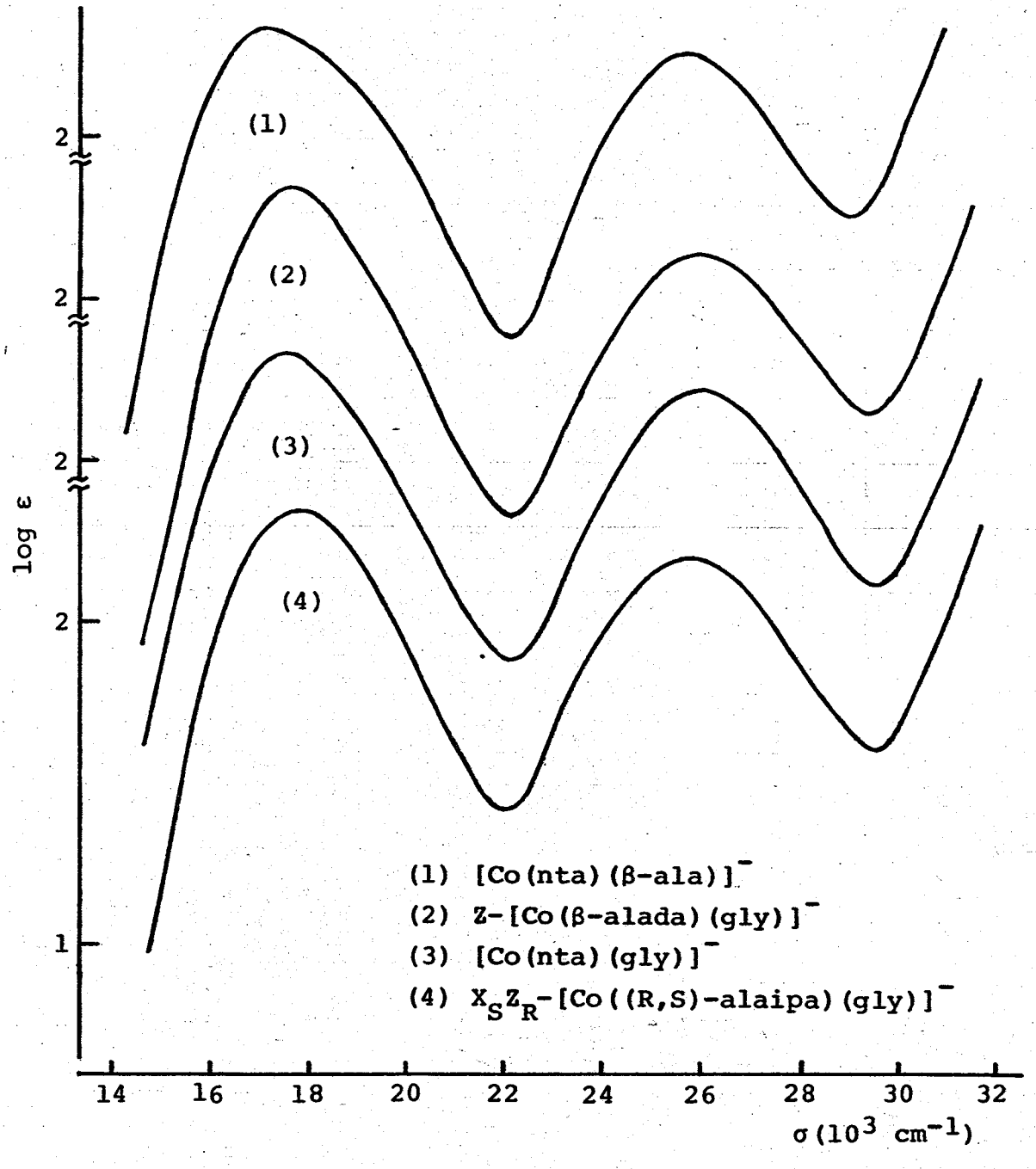


Fig. 14. Absorption spectra of cis(N)-$[Co(N\text{-}O_3)(am)]^-$ complexes.

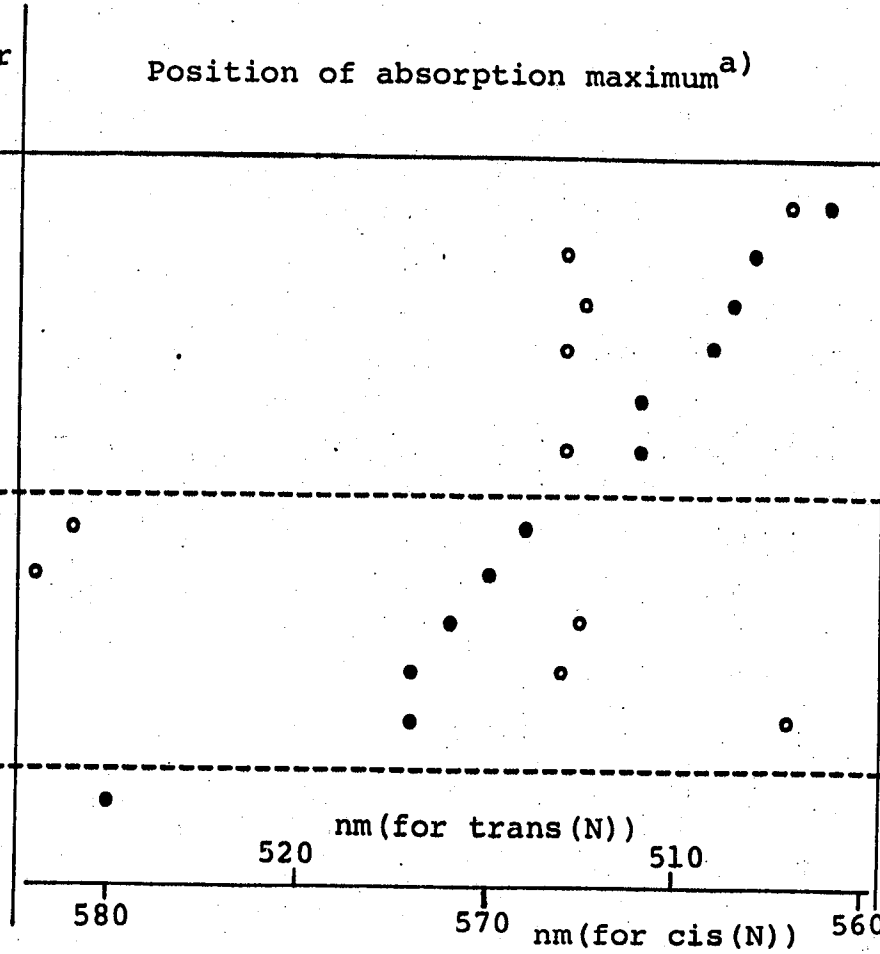
shoulder at the higher energy side of the major peak (562 - 582.5 nm). The complexes which belong to the first group exhibits greater splittings than those of the second group. By referring to the general consideration mentioned above, it is concluded that the first group has trans(N) structure and the second cis(N) one.

A series of trans(N)- and cis(N)-$[Co(N\text{-}O_3)(am)]^-$ type complexes were prepared in this work, and so it is worthwhile to examine the correlation between the structure of complexes and their absorption behaviors. For the complexes with the optically inactive aminocarboxylato ligand, gly, β-ala or γ-ambut, the maximum position of major peak in the first absorption band are presented schematically to facilitate a comparison in Table VIII. The trans(N) complexes are arranged from the top of the column in the order of the decreasing wave number of their absorption maxima. All the complexes consist of four chelate rings and they are classified into three types, 5-5-5-5, 5-5-5-6 and 5-5-5-7, on the basis of the chelate ring size as shown in Table VIII.

All the trans(N) complexes in Table VIII show the reasonable correlation among their first absorption bands. The absorption maxima are closely related to the three types classified above. That is, they shift to lower energy with the increase of the size of the fourth ring. The same relationship is also substantiated for the second absorption maxima of these complexes (Table VII). The following behavior of the absorption maxima by the substitution of methyl group for a hydrogen atom on a

Table VIII. Maximum positions and half-value widths of the first absoption band for trans(N)- and cis(N)-$[Co(N\text{-}O_3)(am)]^-$ complexes

trans(N)- and cis(N)-$[Co(N\text{-}O_3)(am)]^-$	Size of the four chelate rings	Position of absorption maximum[a)]	Half-value width (cm^{-1}) trans(N)	Half-value width (cm^{-1}) cis(N)
X_SZ_R-[Co((R,S)-alaipa)(gly)]$^-$	5-5-5-5		3230	3360
XZ-[Co((S,S)-alaipa)(gly)]$^-$			3280	3530
XY-[Co((S,S)-alaipa)(gly)]$^-$			3270	3470
X-[Co((S)-alada)(gly)]$^-$			3170	3420
Y-[Co((S)-alada)(gly)]$^-$			3250	—
[Co(nta)(gly)]$^-$			3290	3240
X-[Co((S)-alada)(β-ala)]$^-$	5-5-5-6		3030	3770
[Co(nta)(β-ala)]$^-$			3090	4040
X_SZ_6-[Co((S)-alapa)(gly)]$^-$			3010	3200
u-[Co(β-alada)(gly)]$^-$			3100	3070
s-[Co(β-alada)(gly)]$^-$			3100	3600
[Co(nta)(γ-ambut)]$^-$	5-5-5-7		3030	—



a) ●, for trans(N); ○, for cis(N)

nitrilotricarboxylato ligand is interesting, though the difference of the maximum position is very subtle. The absorption maxima shift to higher energy with the increase of the number of methyl groups substituted on the nta or β-alada moiety of the parent gly or β-ala complex. From the maximum data of the trans(N) gly and β-ala complexes, the present nitrilotricarboxylato ligands can be arranged in a series according to decreasing D_q values (decreasing ligand field strength): (R,S)-alaipa > (S,S)-alaipa > (S)-alada > nta > (S)-alapa > β-alada.

The cis(N) complexes corresponding to these trans(N) ones were obtained except two complexes, Y-cis(N)-[Co-((S)-alada)(gly)]$^-$ and cis(N)-[Co(nta)(γ-ambut)]$^-$. Between the chelate ring size and the first absorption maxima of the cis(N) complexes, there is not clear correlation as observed in the trans(N) complexes, as can be seen in Table VIII. This difference of the absorption behaviors between the trans(N) and cis(N) complexes may be ascribed to the fact that the splitting of the A_2 and E components is larger in the trans(N) complexes than in the cis(N) ones, and hence in the latter complexes the maximum position is easy to be affected by the relative intensity of the two components or splitting width. This situation is suggested by the fact that the half-value widths of the first absorption band vary more widely in the cis(N) complexes than in the trans(N) ones, as shown in Table VIII.

The absorption spectra of the nta, (R)- and (S)-alada and β-alada complexes with various optically active α- or

β-aminocarboxylates were also measured. Their absorption curves are very similar in the maximum position and the shape of the first and second absorption bands to the absorption curve of the corresponding gly or β-ala complex listed in Table VIII (Table VII). It is noted here that in the complexes with (S)-pro, especially in the β-alada complexes, the first absorption maxima shift appreciably to lower energy than that in the corresponding gly complex. Such a shift of the complex with (S)-pro has been also observed for cobalt(III) complexes of some other types,[14,21,37,80-82] such as $[Co((S)\text{-pro})_3]$.[83]

In the first absorption band of trans(N)-$[Co(N)_2(O)_4]$ type complexes, it may be of interest that the intensity ratio of a sub- and major-band, $\{\varepsilon_{max}(sub)/\varepsilon_{max}(major)\}$, is smaller in the complexes with tridentate or quadridentate ligand (0.03 - 0.28[74,84-89]) than in the complexes with bidentate one (0.45 - 0.48).[17,18,90] This situation also stands for the present trans(N) complexes (0.08 - 0.16).

In each of the trans(N)- and cis(N)-$[Co(\beta\text{-alada})(gly)]^-$ type complexes, it was pointed out in Section II-3-2-(2) that the absorption behaviors in the first and second absorption band regions clearly differ between the s- and u-isomers. In the case of the trans(N) complexes, the ratio mentioned above is about 0.16 and 0.10 for the s- and u-isomers, respectively. Furthermore, the second absorption band of the s-isomer is higher in intensity than its first absorption band unlike the u-isomer, and then the second absorption maximum of the s-isomer shifts to lower energy

than that of the u-isomer. The difference between the s- and u-isomers in the cis(N) complexes is observed in the shape of the first absorption band and maximum position of the second one. As described in Section II-3-2-(2), these absorption behaviors can be utilized as a means of structural assignment of the trans(N) or cis(N) (S)-alapa complex, which has the chelate skelton same as the β-alada complex.

II-5. Proton magnetic resonance spectra of complexes.

Proton magnetic resonance (PMR) spectra has been widely used to study the structures of cobalt(III) complexes containing aminocarboxylate ligands.[13,53,71,91-105] In particular, simple and sharp signals due to a simple spin-system, as for the methylene protons of N-acetate chelate ring, provide a powerful information for the structural assignment of complexes. Such patterns were observed for most signals due to the nitrilotricarboxylato ligand protons of the present complexes. As described in Section II-3, the characteristics of PMR spectra, PMR pattern, geminal coupling constant and chemical shift correlation, were used in order to assign the arrangement isomers.

(1) Proton magnetic resonance pattern.

The three feet of nitrilotricarboxylato ligand in the present complexes consist of an appropriate combination of the three kinds of chelate rings, N-acetate, N-propionate and N-iso-propionate. As well known, either A_2 or AB splitting pattern is expected for the N-acetate protons ($-CH_2-$), either AA'BB' or ABCD pattern for the N-propionate protons ($-CH_2CH_2-$), and AX_3 pattern for N-iso-propionate protons ($-CH(CH_3)-$). From the PMR studies of the complexes similar to the present ones, it has been found that the distinction of the two possible splitting patterns for the former two chelate rings are consistent with the speculation based on a consideration of a simple molecular model,

although a simplification of spectrum takes place occationally owing to an accidental overlapping of signals. In the present type complexes, the PMR pattern become simple when the complex has a plane of symmetry through coordinated oxygen and nitrogen atoms of the out-of-plane ring and central cobalt atom. Namely, the splitting patterns for the N-acetate and N-propionate protons of out-of-plane rings are A_2 and AA'BB', respectively. Furthermore, the signals due to two chelate ring protons of in-plane are completely overlapped, because the two rings are in the same environment. In fact, the signals due to the nta protons of the trans(N)- and cis(N)-$[Co(nta)(am)]^-$ type complex with optically inactive aminocarboxylates consist of one singlet and one AB quartet (see Section II-5-(2)). In the trans(N)- and cis(N)-$[Co((R,S)\text{-alaipa})(gly)]^-$ complexes, two types of the arrangement isomers are possible: one has a symmetry of plane and the other does not. Accordingly, these two type complexes should give different PMR patterns from each other. This situation was used for the assignment of arrangement isomers of the (R,S)-alaipa complexes (Section II-3-2-(1)). Similar situation is also applicable for the arrangement isomers of trans(N)- and cis(N)-$[Co(\beta\text{-alada})(gly)]^-$ complexes (Section II-3-2-(2)).

On the other hand, the PMR pattern is helpless for the structural assignment of the arrangement isomer of the complexes with (R)- and (S)-alada , (S,S)-alaipa and (S)-alapa, because the same pattern is expected for the

arrangement isomers possible for each of these complexes. For all complexes with these ligands in this work, the PMR patterns just as expected are observed for the signals due to the N-acetate and N-iso-propionate protons of the aminocarboxylato ligands, except the fact that in the trans(N)-[Co((S)-alapa)(gly)]$^-$ complexes the signal due to the N-acetate protons of (S)-alapa appears as singlet, but not AB pattern. These observations make sure that a simple pattern observed for the (R,S)-alaipa protons of the (R,S)-alaipa complexes is not due to an accidental overlapping of signals.

(2) Geminal coupling constant of N-acetate protons.

Sudmeier and co-workers pointed out that the magnitude of N-acetate geminal coupling constant (J_{AB}) for multidentate aminocarboxylato cobalt(III) complexes fall into two categories, the one 16.0 ± 0.5 Hz for in-plane N-acetate ring and the other of 18.0 ± 0.5 Hz for out-of-plane N-acetate ring.[106] More recently, the validity of this rule is confirmed for many similar aminocarboxylato cobalt(III) complexes .[54,97,107,108] Accordingly, this provides a powerful information for the assignment of the possible isomers for multidentate aminocarboxylato cobalt(III) complex with N-acetate chelate ring. However, the PMR spectrum of the complex related directly to the present type complexes is reported only for the two complexes, [Co(nta)(OH)(OH_2)]$^-$ and [Co(nta)(OH_2)$_2$].[109] The above rule is applicable for these comlexes, but it is adopted only for the in-plane

N-acetate rings because the signal of the ouf-of-plane ring is a singlet.

The PMR spectra of the trans(N)- and cis(N)-[Co(nta)-(am)]$^-$ type complexes with optically inactive aminocarboxylates are shown in Fig. 15. The signlet and AB quartet are assigned undoubtly to the signals due to the out-of-plane and in-plane N-acetate protons respectively as described in (1). In the gly complexes, the singlet of the methylene protons of gly is distinguishable from that of the out-of-plane methylene protons of nta, because the gly protons couple with the neighboring amino protons in acidic D_2O solution. The AB quartets of these nta complexes, which assigned to the signals of in-plane N-acetate protons, have the J_{AB} values in the range of 16.2 - 17.1 Hz.

In the trans(N) and cis(N)-[Co(β-alada)(gly)]$^-$ complexes, the assignment to the s- and u-isomers could be undoubtedly accomplished on the basis of the criteria other than the J_{AB} value (Section II-3). The representative PMR spectra of these complexes are shown in Figs. 8 and 9 (Section II-3). The s-isomers of the β-alada complexes exhibit one AB pattern due to the two in-plane N-acetate protons and the J_{AB} values are 16.8 and 17.0 Hz respectively. On the other hand, the u-isomers show the two AB patterns due to the in-plane and out-of-plane N-acetate rings and the J_{AB} values differ clearly in the magnitude from each other. The smaller and larger J_{AB} are in the range of 15.9 - 16.8 Hz and 18.1 - 18.7 Hz, respectively.

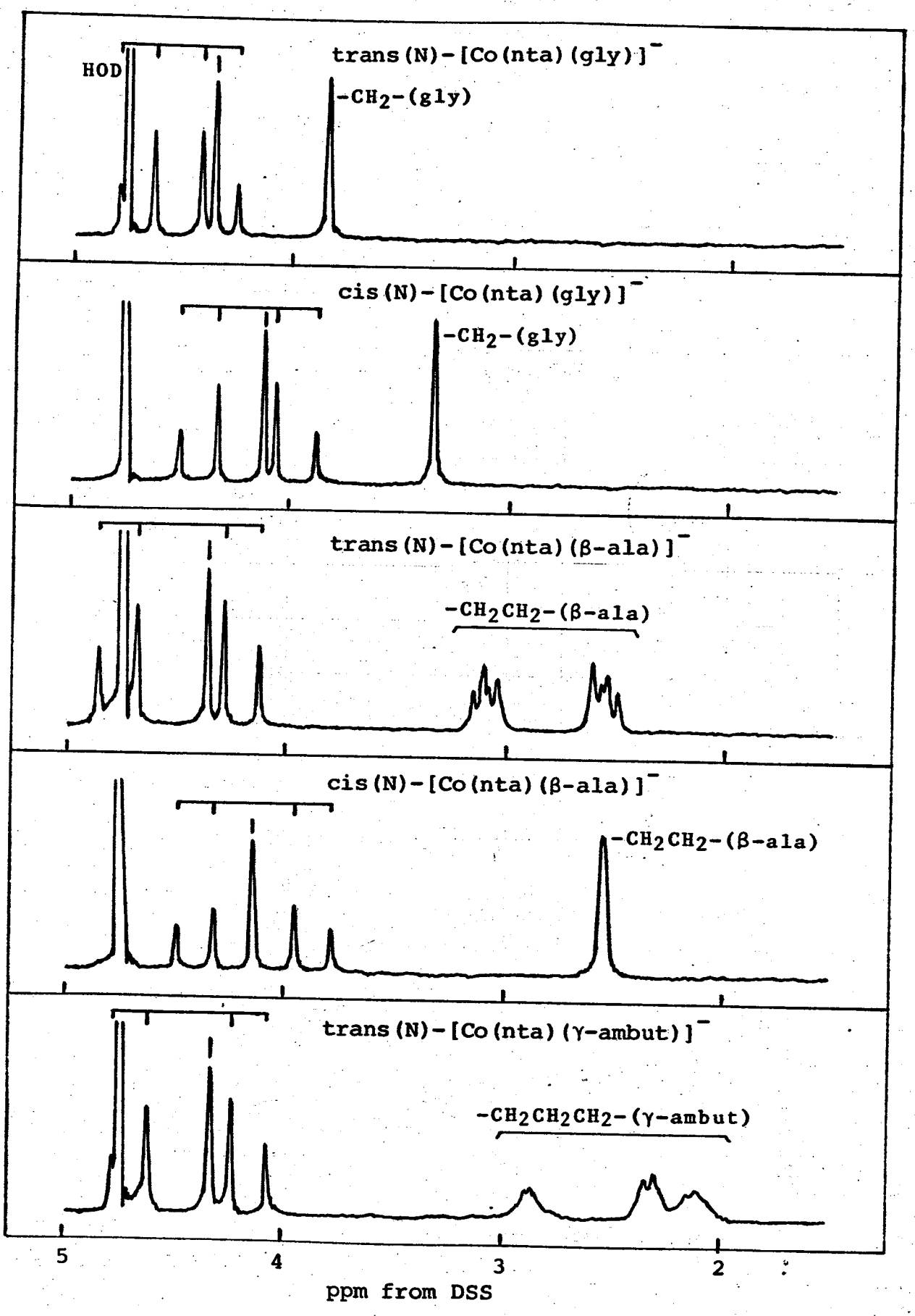


Fig. 15. PMR spectra of trans(N)- and cis(N)-$[Co(nta)(am)]^-$ complexes.

It has been known that in the cobalt(III) complexes with the aminocarboxylato ligands having N-acetate ring, such as ethylenediamine-N,N,N',N'-tetraacetate (edta), certain N-acetate methylene protons undergo deuterium exchange in basis or acidic D_2O solution.[93,96,103,106,107,110-114] In these studies, it have been established that the out-of-plane N-acetate protons rapidly undergo deuterium excahnge, while the in-plane ones do so only with difficulty or not at all.[96,103,106,107,110-114] Terril and Reilley proposed on the basis of the kinetic study and stereochemical consideration that the differnce in ability of the nonequivalent N-acetate rings to undergo deuterium exchange is a function of ring strain.[112] Very recently, this proposal was supported from the deuterium exchange experiment for the cobalt(III) complexes with (S)-asparate as a tridentate.[105] A molecular model examination shows that the N-acetate chelate rings of the present type complexes are very similar in the stereochemistry (bending and strain) to the corresponding ring of the $[Co(edta)]^-$ type complexes. Accordingly, it is expected that the preferential deuteration of the out-of-plane ring take place for the present complexes. In fact, this expectation realized for the trans(N)-$[Co(nta)(\beta\text{-ala})]^-$ complex. The deuteration of the nta complex was carried out in basic D_2O solution (pD 9.5 - 9.9) at room temperature. After deuteration for 9 hr, partially deuterated complexes were isolated from the solution (Experimemntal Section I-5). The PMR spectrum of the complex obtained was measured in D_2O solution at an elevated temperature (40°) in order to avoid

the overlapping with HOD signal. The PMR spectrum and spectral assignment of the nondeuterated complex are shown in Fig. 15. After deuteration (Fig. 16), the singlet become very small in intensity, while the AB quartet remains unchanged (the intensity of signal can be estimated by comparison with that of the ethylene protons of β-ala which do not undergo deuterium exchange (vide infra)). This observation proves that the out-of-plane protons more rapidly undergo deuterium exchange than the in-plane ones.

The deuteration of X-trans(N)-[Co((S)-alada)(β-ala)]$^-$ complex was carried out for 22 hr under the same condition as for the nta complex. The PMR spectrum of the deuterated complex is shown with that of the nondeuterated complex in Fig. 17. The spectral assignment of the nondeuterated complex can be easily made as indicated in Fig. 17(A). After the deuteration (Fig.17(B)), the quartet (labeled as AB-1, J_{AB} = 18.1 Hz) at the higher field become very small in intensity, while the AB quartet (labeled as AB-2, J_{AB} = 16.3 Hz) at the lower field remains essentially unchanged. The change of signal intensity due to deuterium exchange can be estimated on the basis of the intensity of the doublet of β-alada methyl protons which ought not to undergo deutrium exchange (through this deuteration, the ethylene protons of β-ala do not undergo deuterium exchange). Two new signals (indicated by the vertical arrow) appear almost near at calculated chemical shift of the individual protons for the AB-1. These signals are assigned to the remaining methylene protons which are, in effect, decoupled by deuteration of

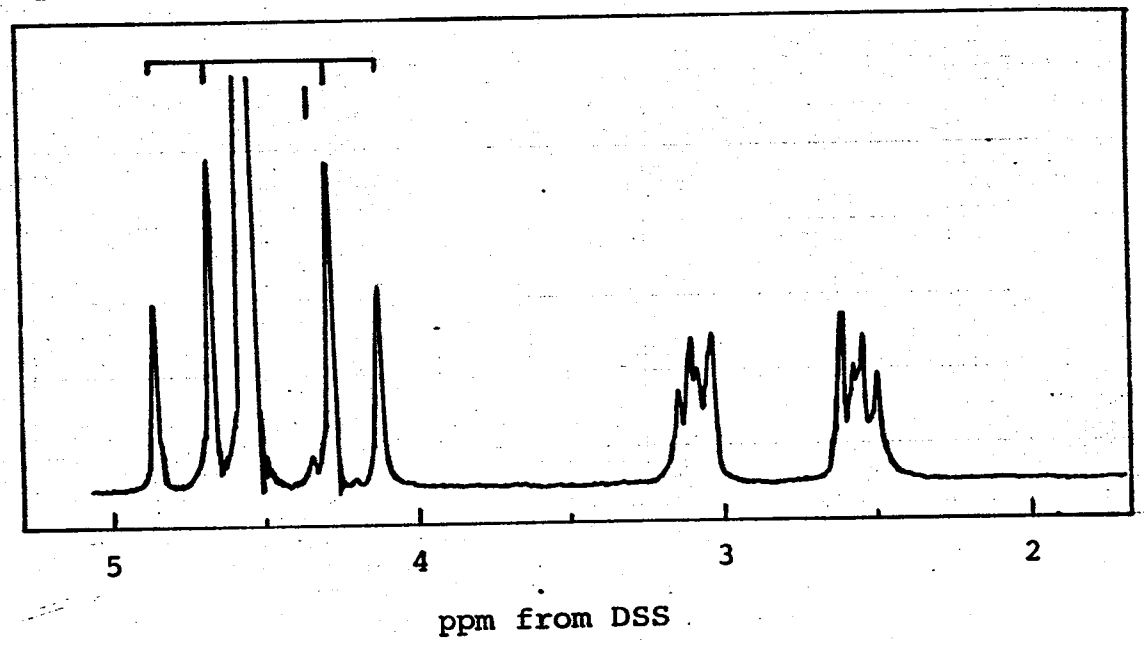


Fig. 16. PMR spectra at 40° of trans(N)-$[Co(nta)(\beta\text{-ala})]^-$ complex in D_2O solution after deuteration in basic D_2O solution for 9 hr.

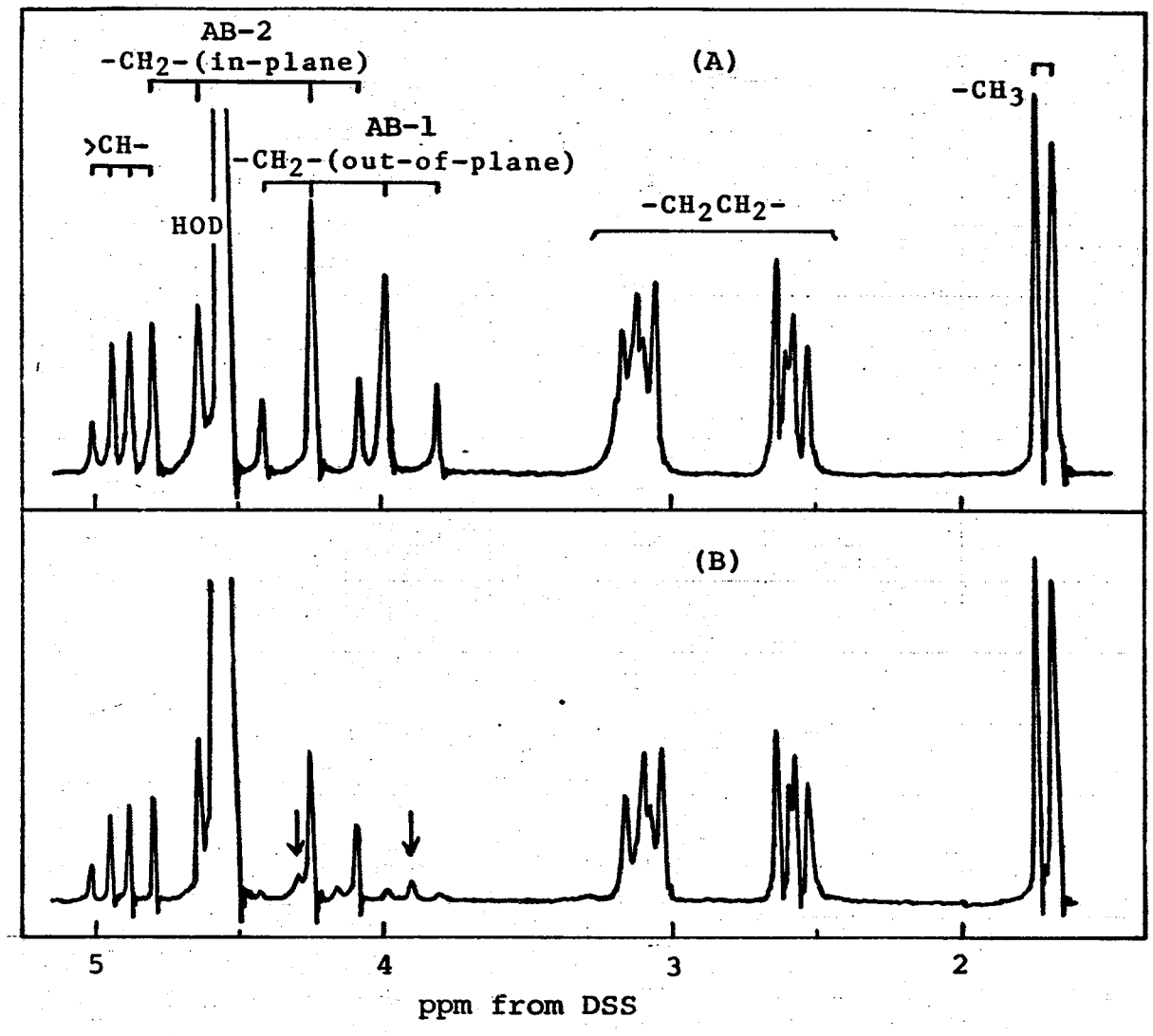


Fig. 17. PMR spectra at 40° of trans(N)-[Co((S)-alada)-(β-ala)]$^-$ complexes in D_2O solution: (A) before deuteration, and (B) after deuteration in basic D_2O solution for 22 hr.

their geminal protons. This result shows that the methylene protons corresponding to the AB-1 are deuterated more rapidly than those corresponding to the AB-2. On this basis, the AB pattern (AB-1) which has J_{AB} = 18.1 Hz is the signal of the out-of-plane ring and the AB pattern (AB-2) which has J_{AB} = 16.3 Hz is that of the in-plane ring.

From these observations, Sudmeier's rule appears to apply also for the complexes containing the present nitrilotricarboxylato ligands, although in some cases the J_{AB} values deviate somewhat from the range of J_{AB} value reported by Sudmeier and co-workers (vide infra).

The AB patterns observed for the present complexes can be classified into two categories according to the magnitude of the J_{AB} values. On this basis, each of the AB patterns was assigned to either the in-plane or out-of-plane N-acetate ring. The J_{AB} values are summarized as follows; 15.5 - 16.8 Hz for the in-plane N-acetate rings of trans(N) complexes and 16.5 -17.3 for those of cis(N) complexes, and 18.1 - 18.8 Hz for the out-of-plane N-acetate rings of both the trans(N) and cis(N) complexes. The many J_{AB} values for the in-plane rings, particularly for those of the cis(N) complexes, are considerably larger than the value (16.5 ± 0.5 Hz) estimated by Sudmeier and co-workers, but such large values (16.8 - 17.1 Hz) were observed for the cis(N)-$[Co(nta)(gly)]^-$, cis(N)-$[Co(nta)(\beta\text{-ala})]^-$, and s-trans(N)- and s-cis(N)-$[Co(\beta\text{-alada})(gly)]^-$ complexes for which the assignment of signals is quite certain.

II-6. Circular dichroism spectra of complexes.

II-6-1. General consideration.

There have been many studies concerning the circular dichroism (CD) spectra of the complexes with the ligands containing the asymmetric carbon atom such as optically active α-aminocarboxylates.[1-3,10-22,25-30,39-43] The optical activity of these complexes is contributed from the configurational effect due to the chiral distribution of chelate rings or the vicinal effect due to the optically active ligand or from both of them. So far, some interesting informations have been obtained experimentally. For example, the absolute configuration of complexes with respect to the distribution of chelate rings can be determined using empirical relationships.[5] It has been found for several cobalt(III) complexes that the configurational and vicinal contributions to CD are almost separable and additve.[10-23] Furthermore, a plausible explanation have been offered for the CD contributions of the complexes which have only the vicinal effect.[2] At the present time, however, there is no unifying theoretical model in accounting for the experimental data. In these circumstances, it is thought to be desirable to study more in detail the CD behaviors of various kinds of optically active complexes.

The CD contributions of the complexes which have only the vicinal effect have been studied for the complexes of limit types, such as the square planar,[38-43] or praseo-like complexes,[32-37] and hence it is of interest

to study the CD contribution of the complexes of another type which have the vicinal effect. Recently, optically active cobalt(III) complexes which have a new source of chirality have been reported,[44-47] and such studies may be important in elucidation of the origin of optical activity. From these viewpoints, the CD contributions of the complexes with general formula (nitrilotricarboxylato)(aminocarboxylato)-cobaltate(III) will be examined in this Section. The optical activity of these complexes is contributed from the vicinal effect due to the optically active nitrilotricarboxylates or aminocarboxylates, or from "arrangement" chirality effect due to the optically inactive nitrilotricarboxylate, and furthermore from a combination of these effects.

II-6-2. $[Co(nta)(am)]^-$ complexes.

The CD spectra of the nta complexes containing optically active α- or β-aminocarboxylato ligands are shown with the representative absorption (AB) spectra in Figs. 18-23, and the CD data are summarized in Table IX. The CD curves of the nta complexes are contributed only by the vicinal effect of the optically active α- or β-aminocarboxylato ligand.

The CD curves of the trans(N) nta complexes with (S)-α-aminocarboxylato ligands are very similar to each other, though the (S)-pro complex is rather differs in the whole shape from the other complexes (Fig 18), and the same relationship is also true for the cis(N) complexes with (S)-α-aminocarboxylates (Fig. 19). The difference of the trans(N) (S)-pro complex from the other trans(N) complexes

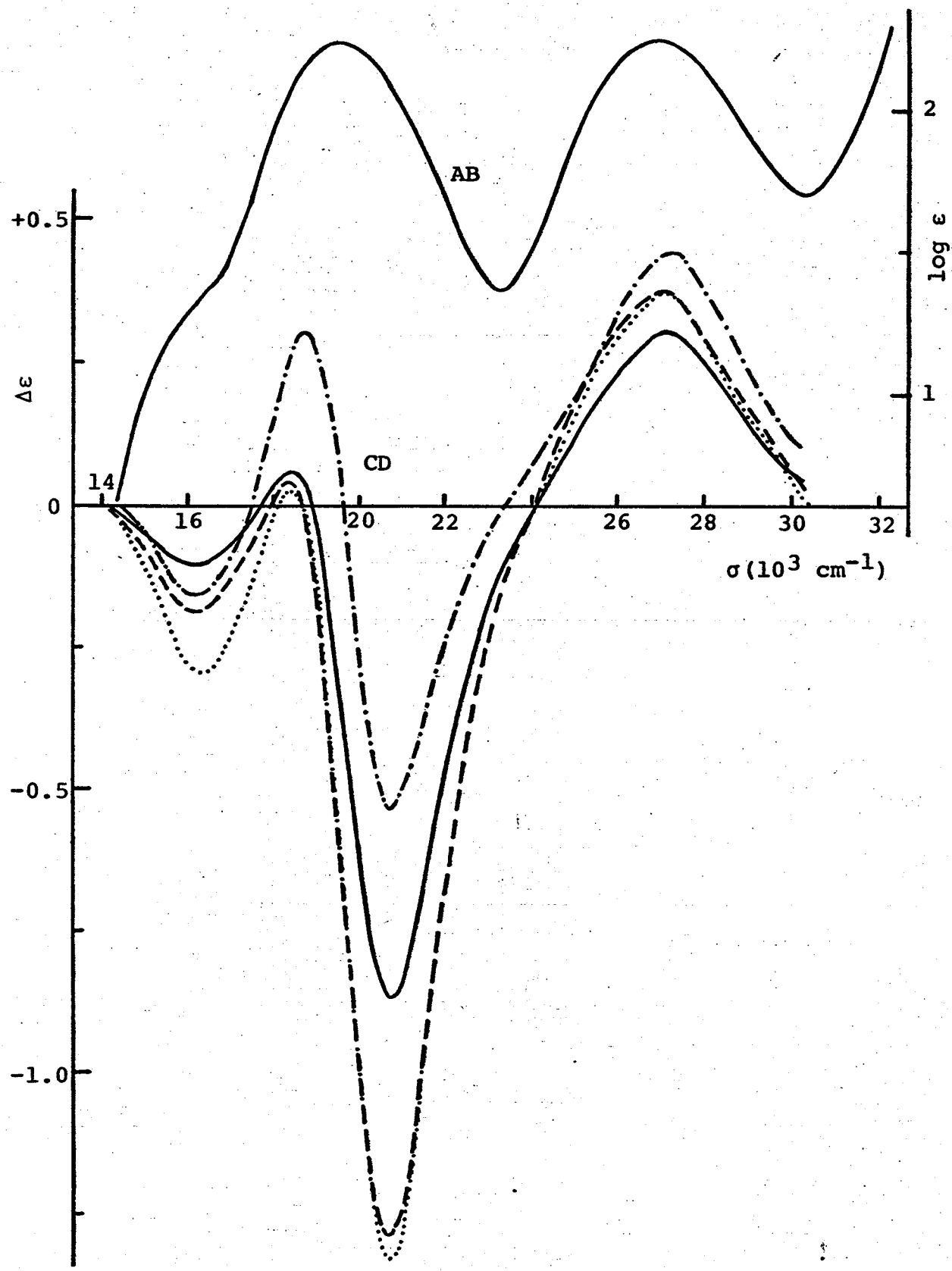


Fig. 18. CD curves of trans(N)-[Co(nta)(α-am)]⁻: ———, (S)-ala; -----, (S)-ser; ·····, (S)-val; -·-·-, (S)-pro, and AB curve of trans(N)-[Co(nta)((S)-ala)]⁻.

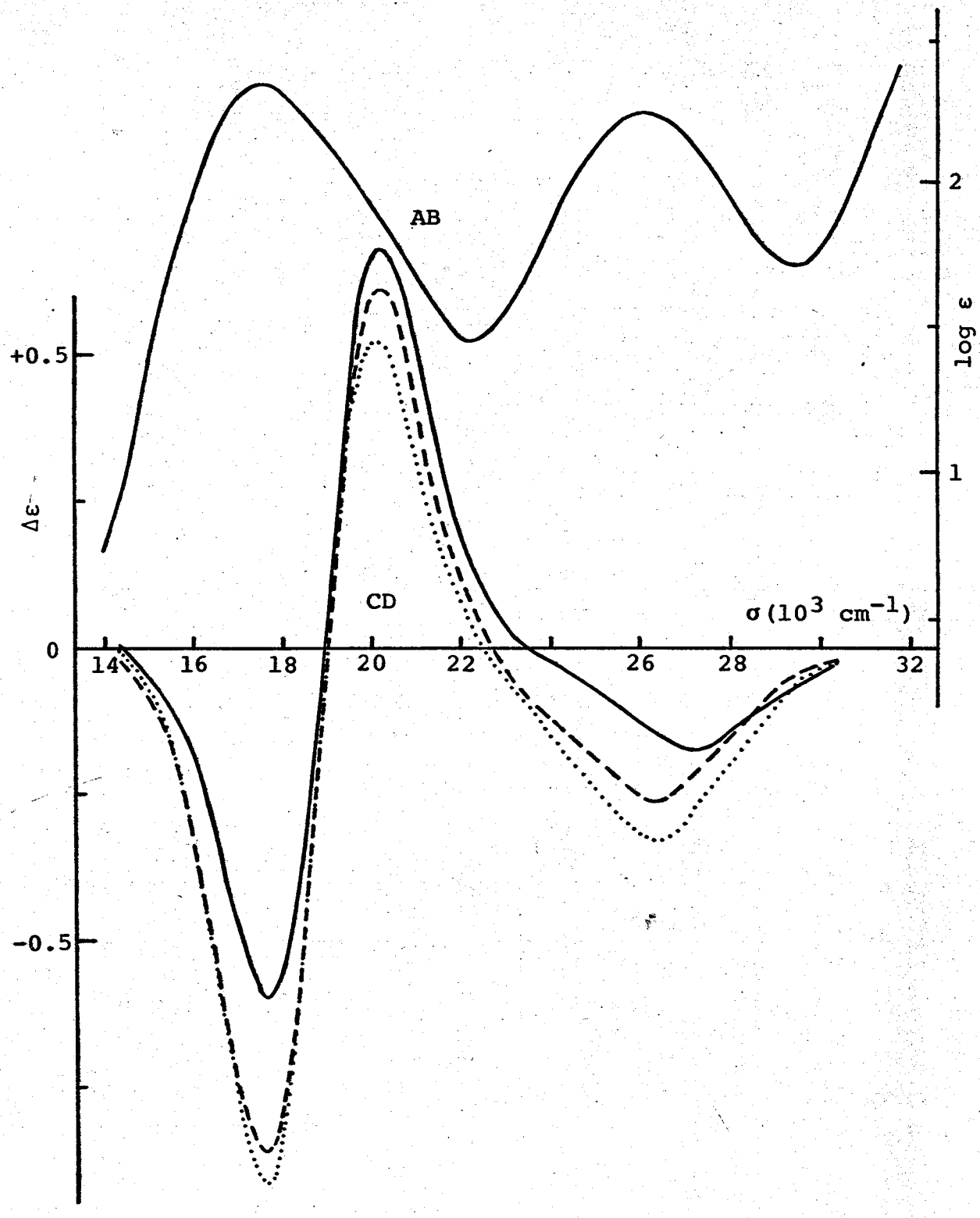


Fig. 19. CD curves of cis(N)-[Co(nta)(α-am)]$^-$: ———, (S)-ala; -----, (S)-ser; ·····, (S)-val, and AB curve of cis(N)-[Co(nta)((S)-ala)]$^-$.

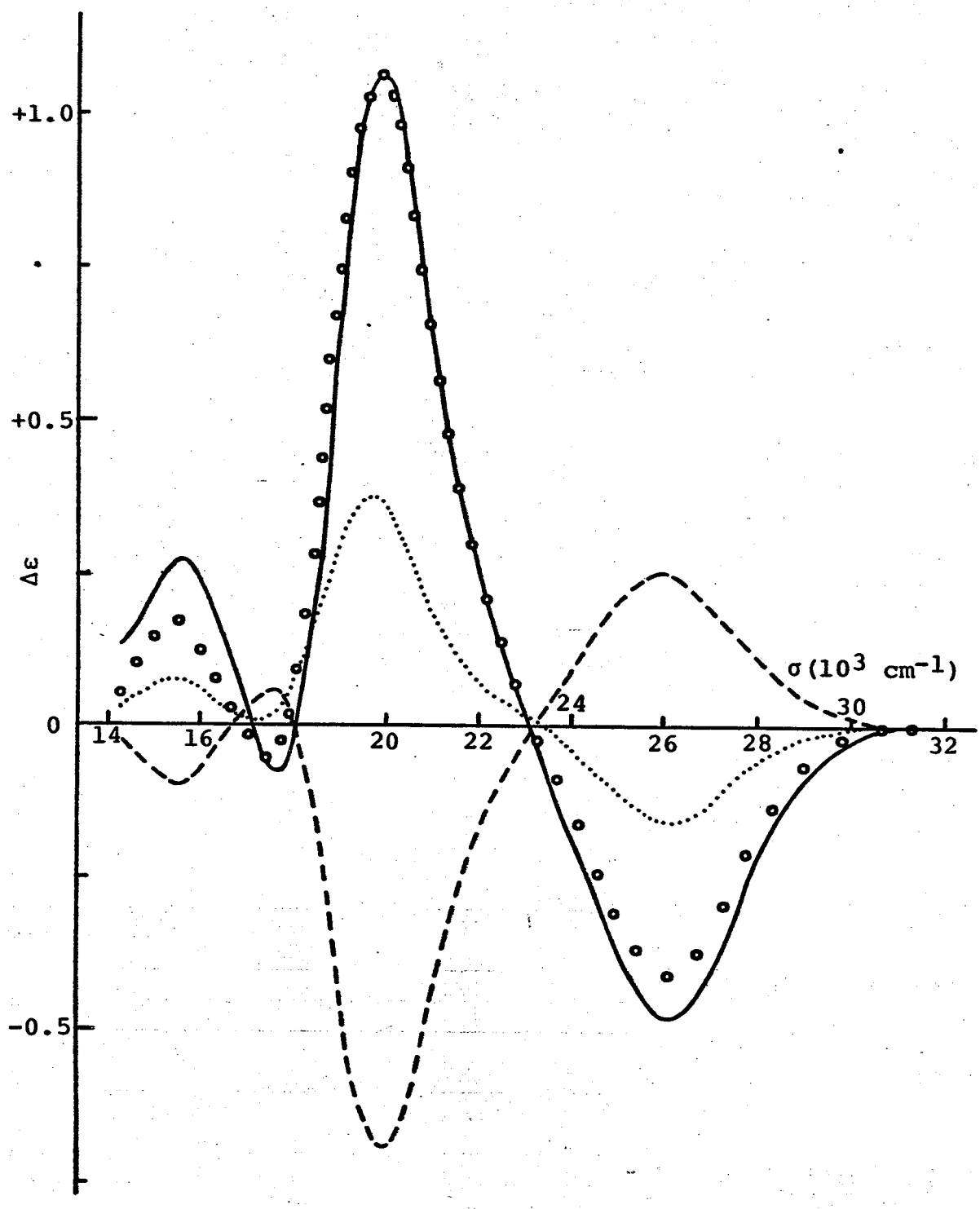


Fig. 20. CD curves and curve analysis of trans(N)-$[Co(nta)(\beta\text{-am})]^-$.

(1) -----, $[Co(nta)((R)\text{-}\alpha\text{-Me-}\beta\text{-ala})]^-$

(2) ·····, $[Co(nta)((S)\text{-}\beta\text{-Me-}\beta\text{-ala})]^-$

(3) ———, $[Co(nta)((S,S)\text{-achc})]^-$

(4) ∘∘∘∘∘, calculated curve, (2) - (1)

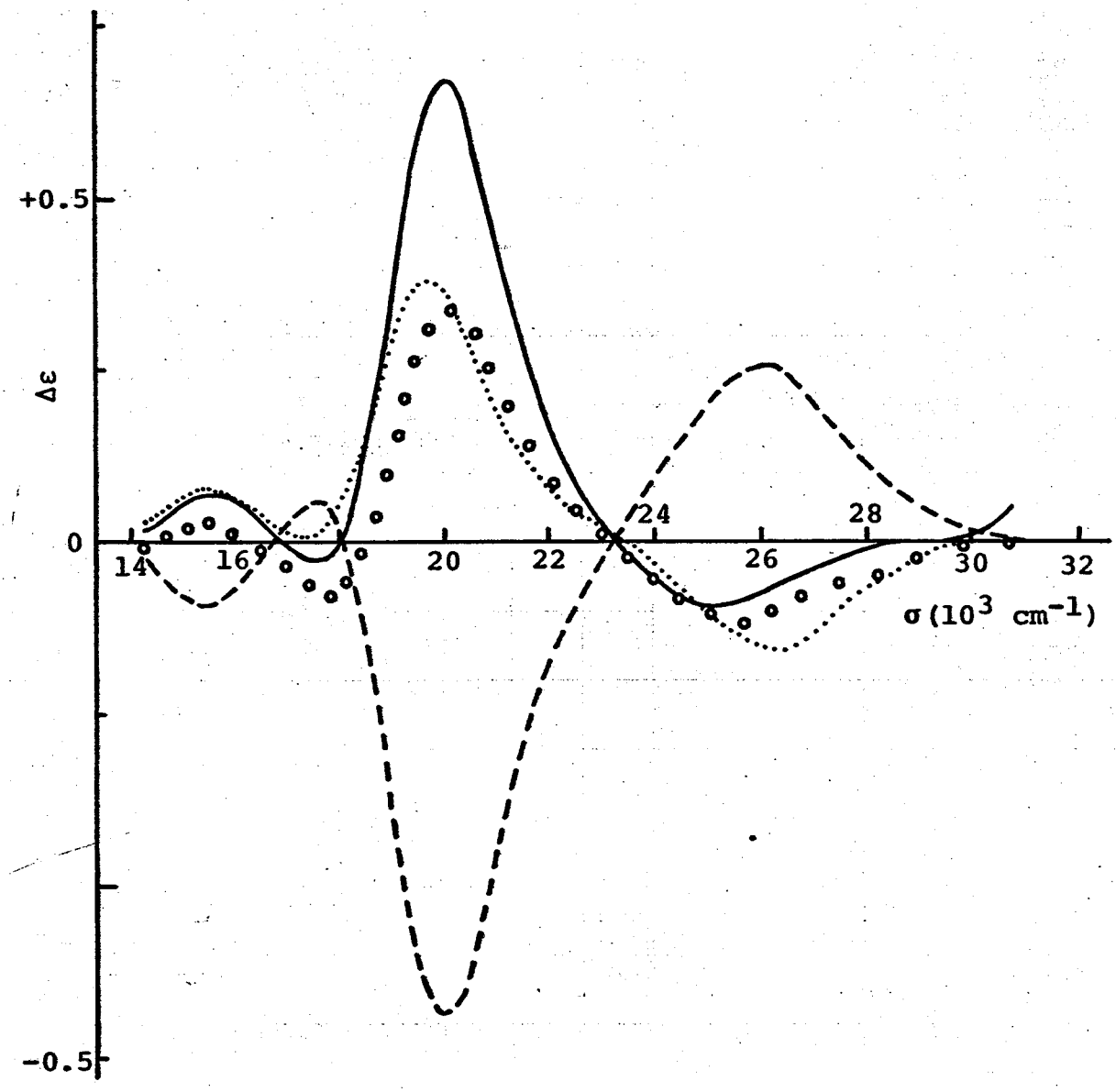


Fig. 21. CD curves and curve analysis of trans(N)-$[Co(nta)(\beta\text{-am})]^-$.

(1) -----, $[Co(nta)((R)\text{-}\alpha\text{-Me-}\beta\text{-ala})]^-$

(2) •••••, $[Co(nta)((S)\text{-}\beta\text{-Me-}\beta\text{-ala})]^-$

(3) ———, $[Co(nta)((S,R)\text{-achc})]^-$

(4) ooooo, calculated curve, -(1) - (2)

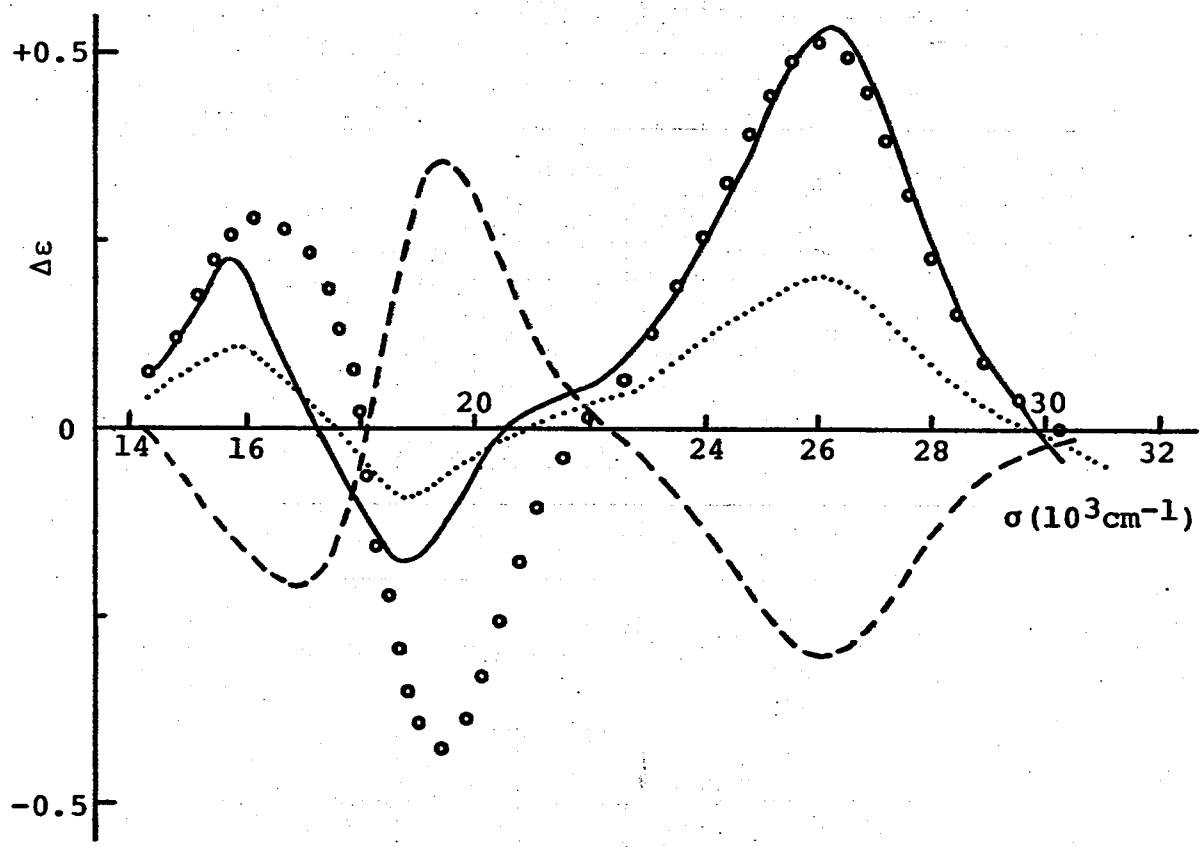


Fig. 22. CD curves and curve analysis of cis(N)-$[Co(nta)(\beta\text{-am})]^-$.

(1) -----, $[Co(nta)((R)\text{-}\alpha\text{-Me-}\beta\text{-ala})]^-$

(2) ·····, $[Co(nta)((S)\text{-}\beta\text{-Me-}\beta\text{-ala})]^-$

(3) ———, $[Co(nta)((S,S)\text{-achc})]^-$

(4) ∘∘∘∘∘, calculated curve, (2) - (1)

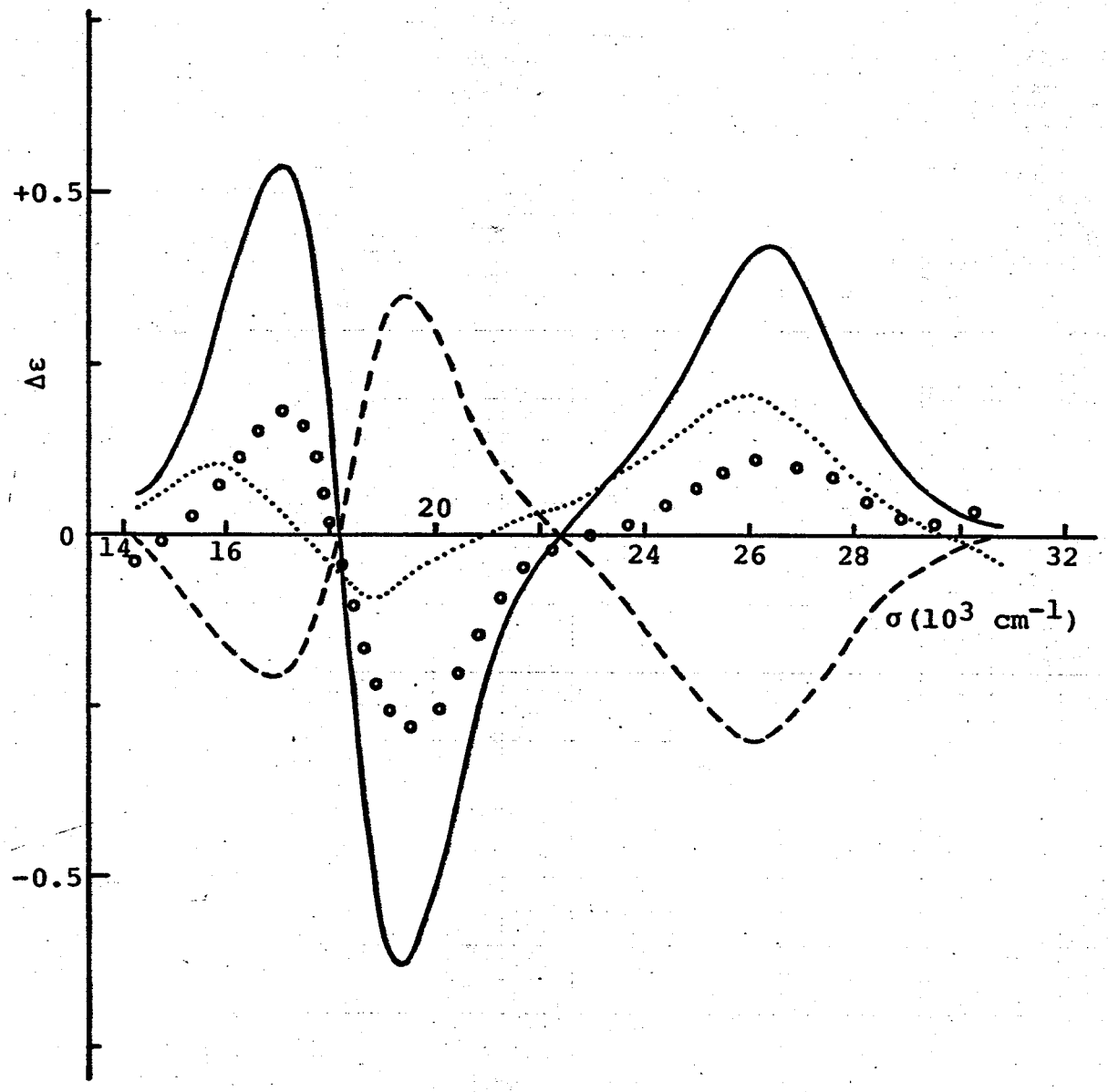


Fig. 23. CD curves and curve analysis of cis(N)-$[Co(nta)(\beta\text{-am})]^-$.

(1) -----, $[Co(nta)((R)\text{-}\alpha\text{-Me-}\beta\text{-ala})]^-$

(2) ·····, $[Co(nta)((S)\text{-}\beta\text{-Me-}\beta\text{-ala})]^-$

(3) ———, $[Co(nta)((S,R)\text{-achc})]^-$

(4) ∘∘∘∘∘, calculated curve, -(1) - (2)

Table IX. CD Spectral Data of $[Co(nta)(am)]^-$ Complexes[a)]

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
trans(N)-[Co(nta)((S)-ala)]$^-$	16.1	-0.10	27.2	+0.30
	18.4	+0.06		
	20.8	-0.87		
trans(N)-[Co(nta)((S)-val)]$^-$	16.3	-0.29	27.1	+0.37
	18.5	+0.02		
	20.7	-1.32		
trans(N)-[Co(nta)((S)-ser)]$^-$	16.2	-0.19	27.0	+0.38
	18.4	+0.04		
	20.7	-1.29		
trans(N)-[Co(nta)((S)-pro)]$^-$	16.2	-0.16	27.2	+0.45
	18.8	+0.31		
	20.7	-0.54		
trans(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$	15.5	-0.10	26.0	+0.26
	17.7	+0.06		
	20.0	-0.70		
trans(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$	15.5	+0.08	26.2	-0.16
	19.7	+0.38		

Table IX. (continued)

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
trans(N)-[Co(nta)((S,S)-achc)]$^-$	15.6	+0.28	26.2	-0.48
	17.7	-0.08		
	19.9	+1.07		
trans(N)-[Co(nta)((S,R)-achc)]$^-$	15.6	+0.07	25.3	-0.10
	17.6	-0.03		
	20.0	+0.67		
cis(N)-[Co(nta)((S)-ala)]$^-$	17.7	-0.60	27.2	-0.17
	20.2	+0.68		
cis(N)-[Co(nta)((S)-val)]$^-$	17.7	-0.91	26.3	-0.33
	20.1	+0.53		
cis(N)-[Co(nta)((S)-ser)]$^-$	17.6	-0.87	26.6	-0.26
	20.1	+0.61		
cis(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$	16.8	-0.21	26.0	-0.31
	19.4	+0.36		
cis(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$	15.9	+0.11	26.0	+0.20
	18.8	-0.09		

Table IX. (continued)

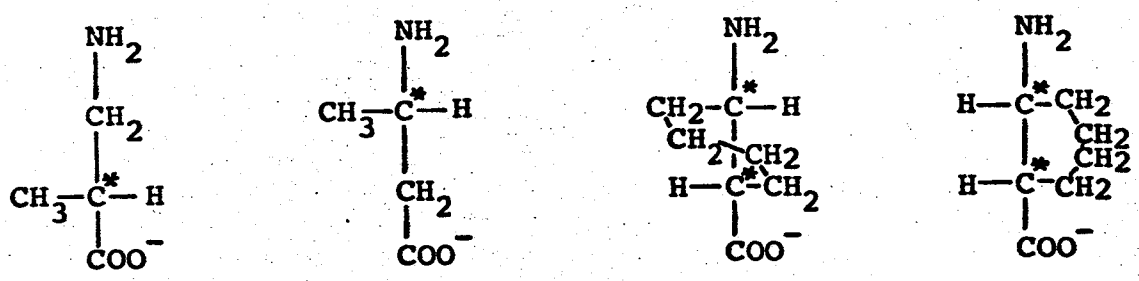
Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
cis(N)-[Co(nta)((S,S)-achc)]$^-$	15.7	+0.22	26.2	+0.54
	18.8	-0.18		
cis(N)-[Co(nta)((S,R)-achc)]$^-$	17.0	+0.54	26.4	+0.43
	19.4	-0.63		

a) The wave numbers are given in 10^3 cm^{-1}.

may be related to the CD contribution due to the asymmetric nitrogen donor atom of (S)-pro, which is known to take only (S) configuration by coordination.[39,40,48,49] Such an anomalous CD behavior has been observed for the metal complexes with usual α-aminocarboxylates of some other types.[26,39,40,43]

In the first and second absorption band region, the CD curves of the cis(N) nta complexes with the β-aminocarboxylato ligands are quite similar in the splittings and general shapes to each other, and also to those of the cis(N) nta complexes with (S)-aminocarboxylates (Figs. 19 and 22). The similar relationships are observed for the corresponding trans(N) complexes, though it seems that the trans(N) (S)-β-Me-β-ala complex lacks a negative CD component near at 17,500 cm^{-1} (Figs. 18 and 20). In the α-Me-β-ala and β-Me-β-ala complexes, the signs of CD components of the complexes with these ligands of (S) configuration are (+), (-), (+) and (-) for the trans(N) complexes and (-), (+) and (-) for the cis(N) complexes listing from lower energy side. It is noteworthy that the inverse sequence of signs, (-), (+), (-) and (+) for the trans(N) complexes and (+), (-) and (+) for the cis(N) complexes, are found for the (S)-α-aminocarboxylato complexes.

The (R)-α-Me-β-ala and (S)-β-Me-β-ala ligands have one asymmetric carbon atom, while the (S,S)-achc and (S,R)-achc ligands have two such atoms. The Fisher projection formulas of these ligands are shown in Fig. 24. In order



(R)-α-Me-β-ala (S)-β-Me-β-ala (S,S)-achc (S,R)-achc

Fig. 24. Fisher projection formulas of the optically active β-aminocarboxylates.

to examine details of the vicinal CD contribution due to the β-aminocarboxylato ligand in the nta complexes with these β-aminocarboxylates, the calculated CD curves for each of the trans(N) achc and cis(N) achc complexes were derived from the observed CD curves of the (R)-α-Me-β-ala and (S)-β-Me-β-ala complexes by the following formulas.

$$\Delta\varepsilon\{(S,S)\text{-achc}\}_{calcd} = -\Delta\varepsilon\{(R)\text{-}\alpha\text{-Me-}\beta\text{-ala}\}_{obs} + \Delta\varepsilon\{(S)\text{-}\beta\text{-Me-}\beta\text{-ala}\}_{obs}$$

$$\Delta\varepsilon\{(S,R)\text{-achc}\}_{calcd} = -\Delta\varepsilon\{(R)\text{-}\alpha\text{-Me-}\beta\text{-ala}\}_{obs} - \Delta\varepsilon\{(S)\text{-}\beta\text{-Me-}\beta\text{-ala}\}_{obs}$$

where Δε{β-am} is the calculated (subscript calcd) or observed (subscript obs) CD curve of the nta complexes with the β-am in the brace. The calculated curves for the four achc complexes are shown in Figs. 20-23. As can be seen in Fig. 20, it is noted that the observed CD curve of the trans(N) (S,S)-achc complex is fairly perfectly reproduced from those of the trans(N) (R)-α-Me-

β-ala and (S)-β-Me-β-ala complexes by the upper formula. This means a simple additivity between the CD contribution of two adjacent asymmetric carbon atoms in the six-membered chelate ring. In each of the other achc complexes, the splitting pattern well corresponds between the observed and calculated curves (Figs. 21-24). However, there is considerable deviation in the intensity for a part of or all of the CD components.

Similar examinations have been made for the complexes with (R,R)-trans-1,2-diaminocyclohexane[24,32,33,38] or (R,S)-2,3-diaminobutane[34] complexes. In several square planar complexes of these diamine ligands, the CD intensity is approximately proportional to the number of asymmetric carbon atom.[38] On the contrary, in several praseo type octahedral complexes, the CD intensity is approximately proportional to the number of chelate rings having chiral conformation.[24,32,33] The additivity observed for the trans(N) (S,S)-achc complex resembles to the behavior of square planar diamine complexes. On the other hand, the observed curve of the cis(N) (S,R)-achc complex is of two- or threefold intensity as compared with the corresponding calculated curve. Such a relationship do not belong to both of the relationships observed for the diamine complexes.

In these circumstances, it is difficult to offer a consistent explanation through the results observed for the four achc complexes. The following situations should be considered in explanation of the CD behaviors

of the complexes with β-aminocarboxylates. The six-membered chelate ring of chelated b-aminocarboxylate must be deviate considerably from flatness as found from X-ray diffraction studies.[5] Accordingly, it may be reasonable to assume that the CD curve of the complex with optically active β-aminocarboxylate is contributed from the chiral conformation of β-aminocarboxylato chelate as well as from the asymmetric carbon atom. Furthermore, the (S,S)-achc and (S,R)-achc ligands have structures such as two methyl groups attached to the α- and β-carbon atoms on β-ala (correspond to α-Me-β-ala and β-Me-β-ala respectively) are jointed by an ethylene bridge. This situation will provide an additional contribution to the optical activity of the achc complexes.

II-6-3. $[Co((R)-\text{ or }(S)-alada)(am)]^-$ and $[Co((S,S)-alaipa)-(gly)]^-$ complexes.

The CD spectra of $[Co((R)-\text{ or }(S)-alada)(am)]^-$ complexes are shown in Figs. 25-31 and Table X. The CD curves of the Z-trans(N)-$[Co((R)-alada)((S)-ala)]^-$ and X-trans(N)-$[Co((S)-alada)((S)-ala)]^-$ complexes are composed of two different vicinal CD contributions, one due to the quadridentate ligand, (R)- or (S)-alada, and the other due to the bidentate ligand (S)-ala, while the CD curve of the X-trans(N)-$[Co((S)-alada)(gly)]^-$ complex is composed only of the vicinal contribution due to the (S)-alada. In these complexes, the structures of the (S)-alada and (R)-alada moieties coordinated are antipodal to each other (Table I),

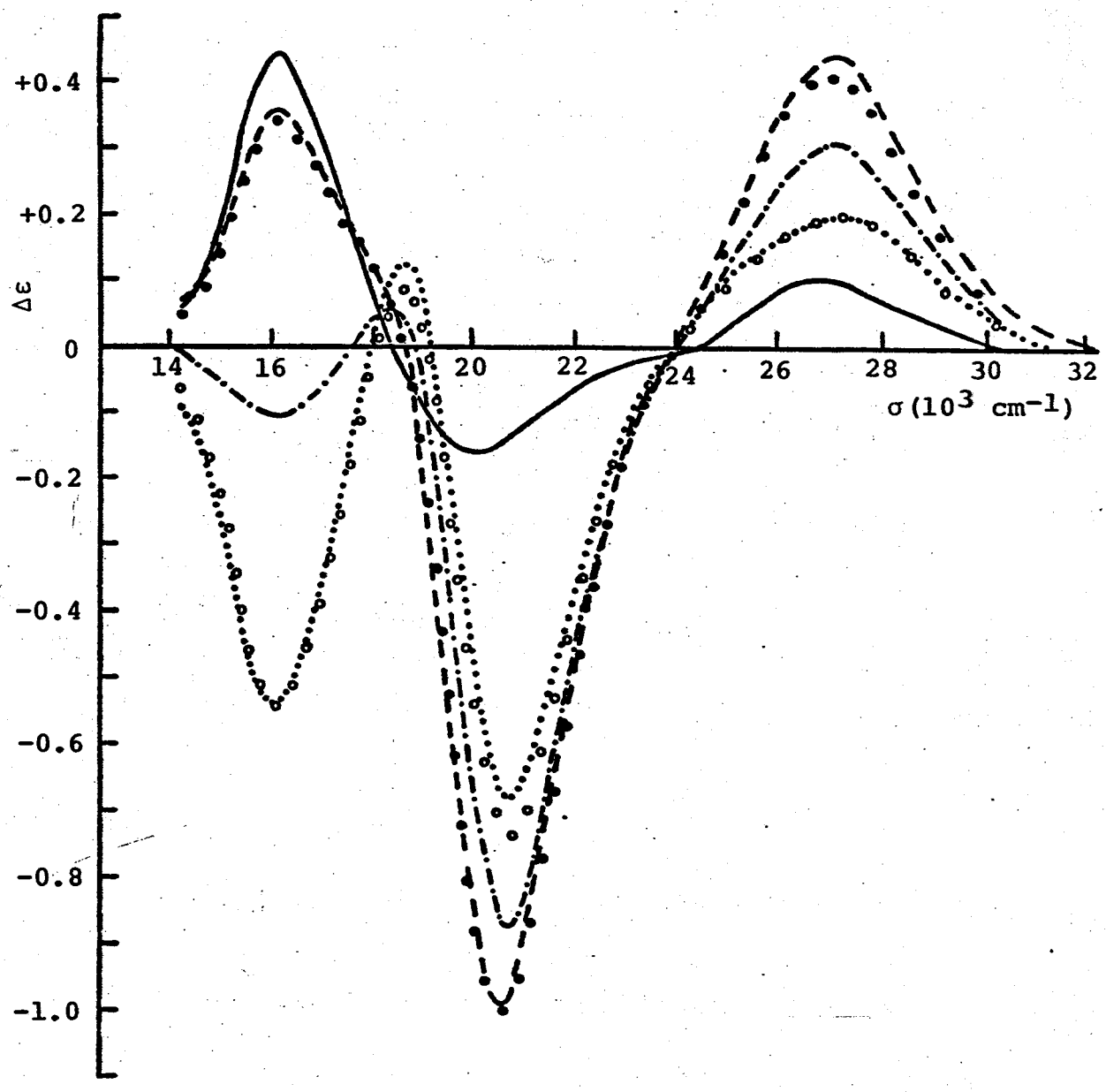


Fig. 25. CD curves of trans(N)-[Co((R)- or (S)-alada)(α-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, trans(N)-[Co(nta)((S)-ala)]$^-$
(2) ———, X-trans(N)-[Co((S)-alada)(gly)]$^-$
(3) -----, X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$
(4) ·····, Z-trans(N)-[Co((R)-alada)((S)-ala)]$^-$
(5) •••••, calculated curve, (1) + (2)
(6) ○○○○○, calculated curve, (1) - (2)

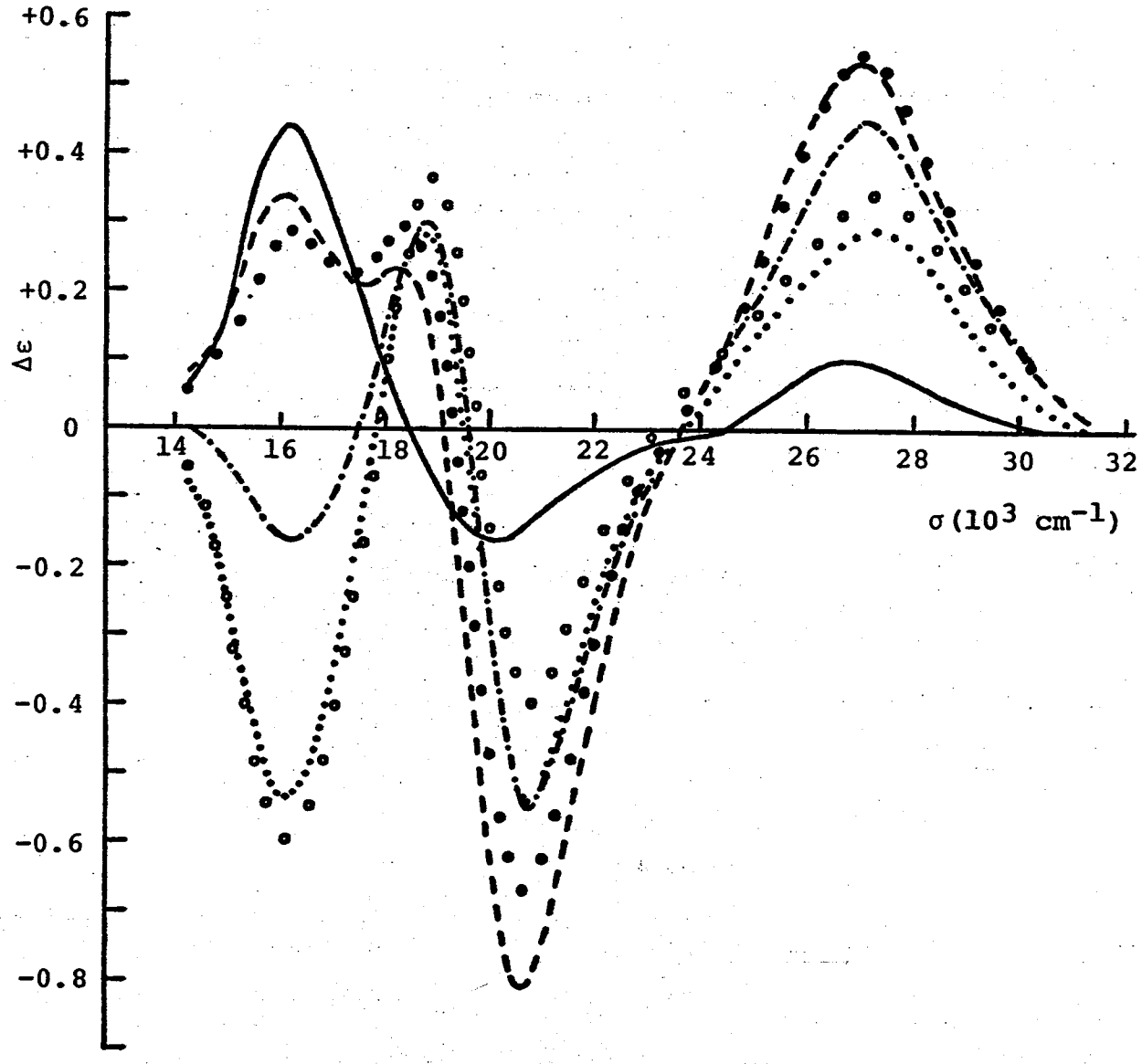


Fig. 26. CD curves of trans(N)-[Co((R)- or (S)-alada)(α-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, trans(N)-[Co(nta)((S)-pro)]$^-$

(2) ———, X-trans(N)-[Co((S)-alada)(gly)]$^-$

(3) -----, X-trans(N)-[Co((S)-alada)((S)-pro)]$^-$

(4) ·····, Z-trans(N)-[Co((R)-alada)((S)-pro)]$^-$

(5) •••••, calculated curve, (1) + (2)

(6) ∘∘∘∘∘, calculated curve, (1) - (2)

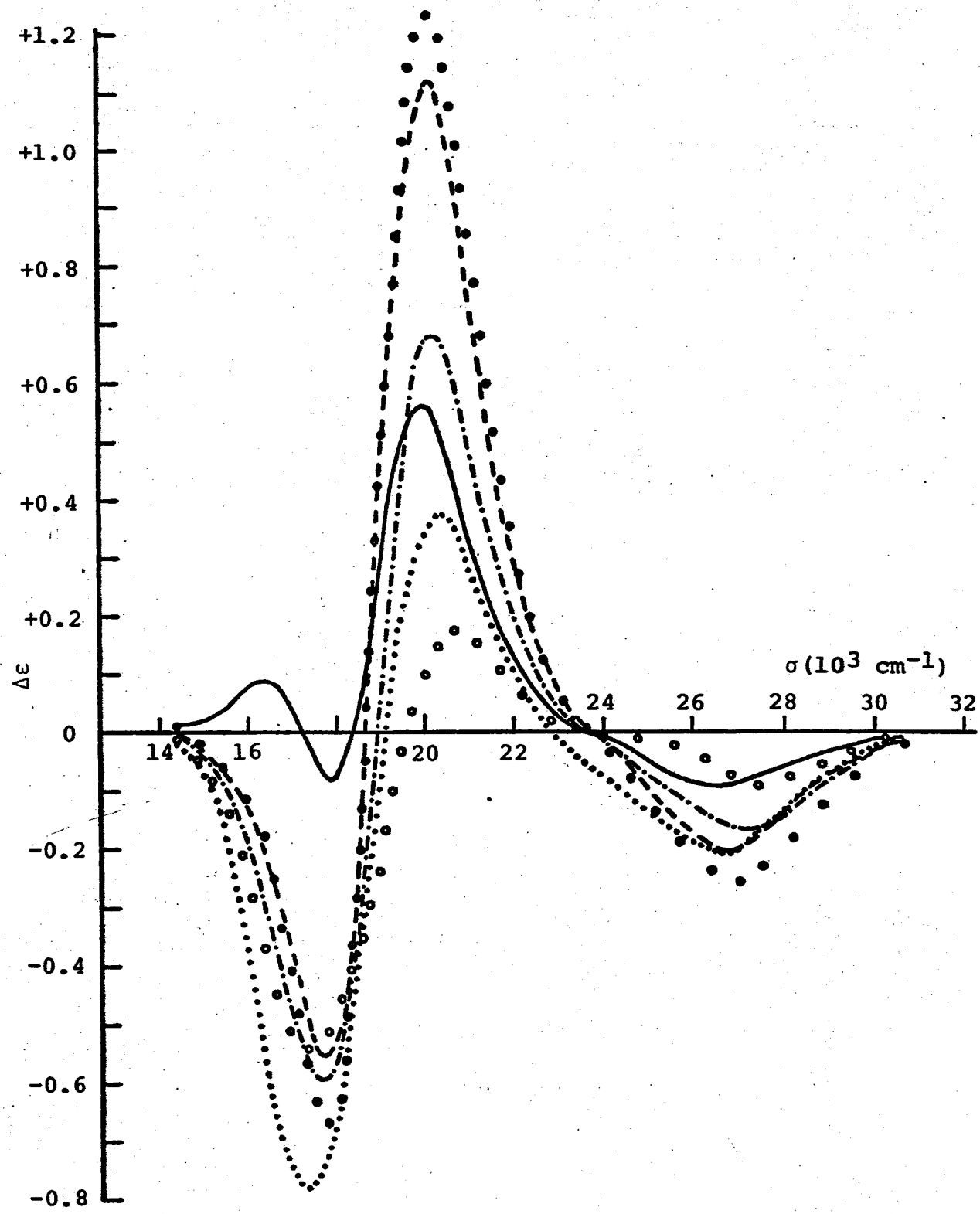


Fig. 27. CD curves of cis(N)-[Co((R)- or (S)-alada)(α-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, cis(N)-[Co(nta)((S)-ala)]$^-$

(2) ———, X-cis(N)-[Co((S)-alada)(gly)]$^-$

(3) -----, X-cis(N)-[Co((S)-alada)((S)-ala)]$^-$

(4) ·····, Z-cis(N)-[Co((R)-alada)((S)-ala)]$^-$

(5) •••••, calculated curve, (1) + (2)

(6) ∘∘∘∘∘, calculated curve, (1) - (2)

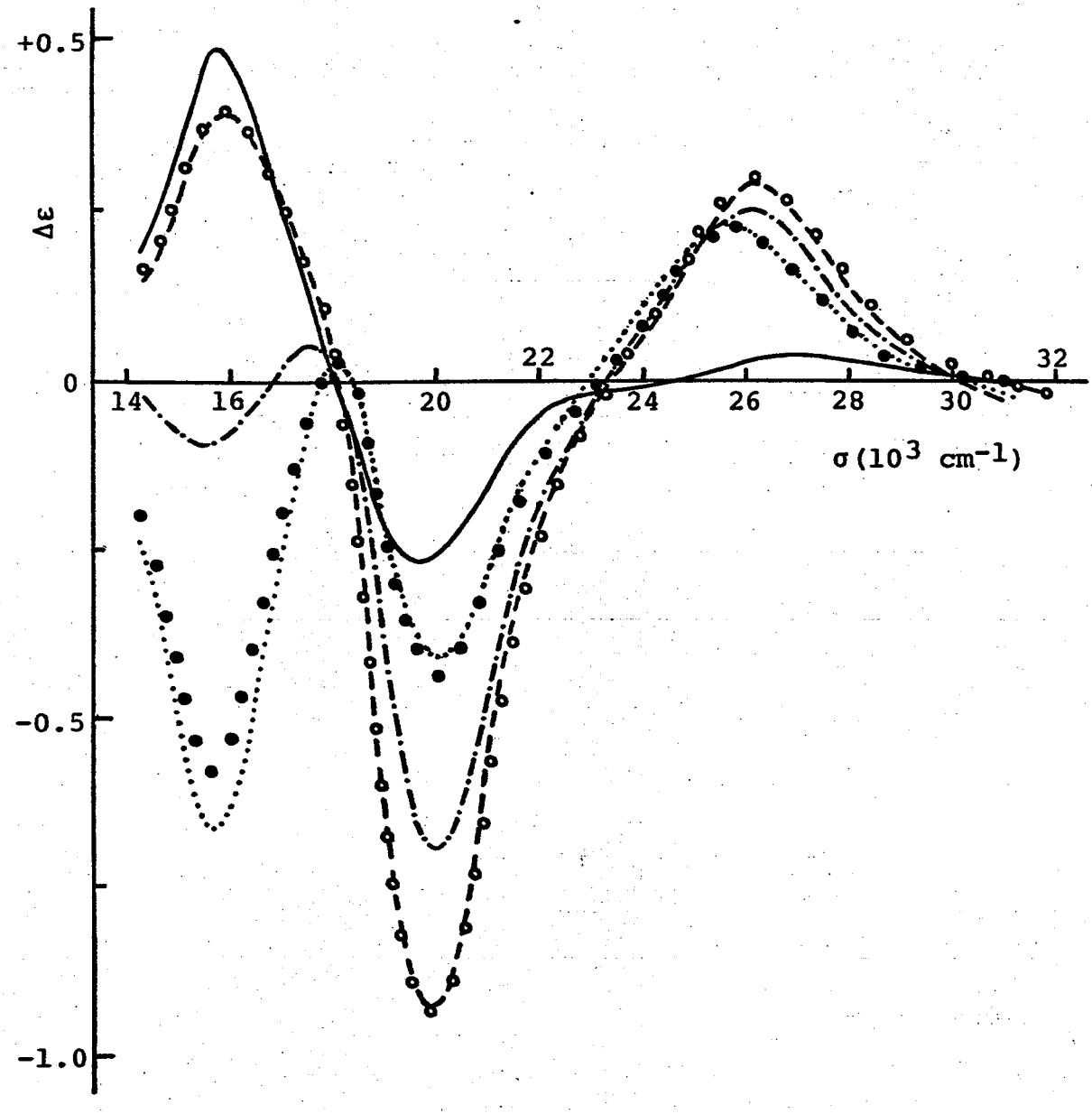


Fig. 28. CD curves of trans(N)-[Co((R)- or (S)-alada)(β-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, trans(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$

(2) ———, X-trans(N)-[Co((S)-alada)(β-ala)]$^-$

(3) -----, X-trans(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$

(4) ·····, Z-trans(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$

(5) ∘∘∘∘∘, calculated curve, (1) + (2)

(6) •••••, calculated curve, (1) - (2)

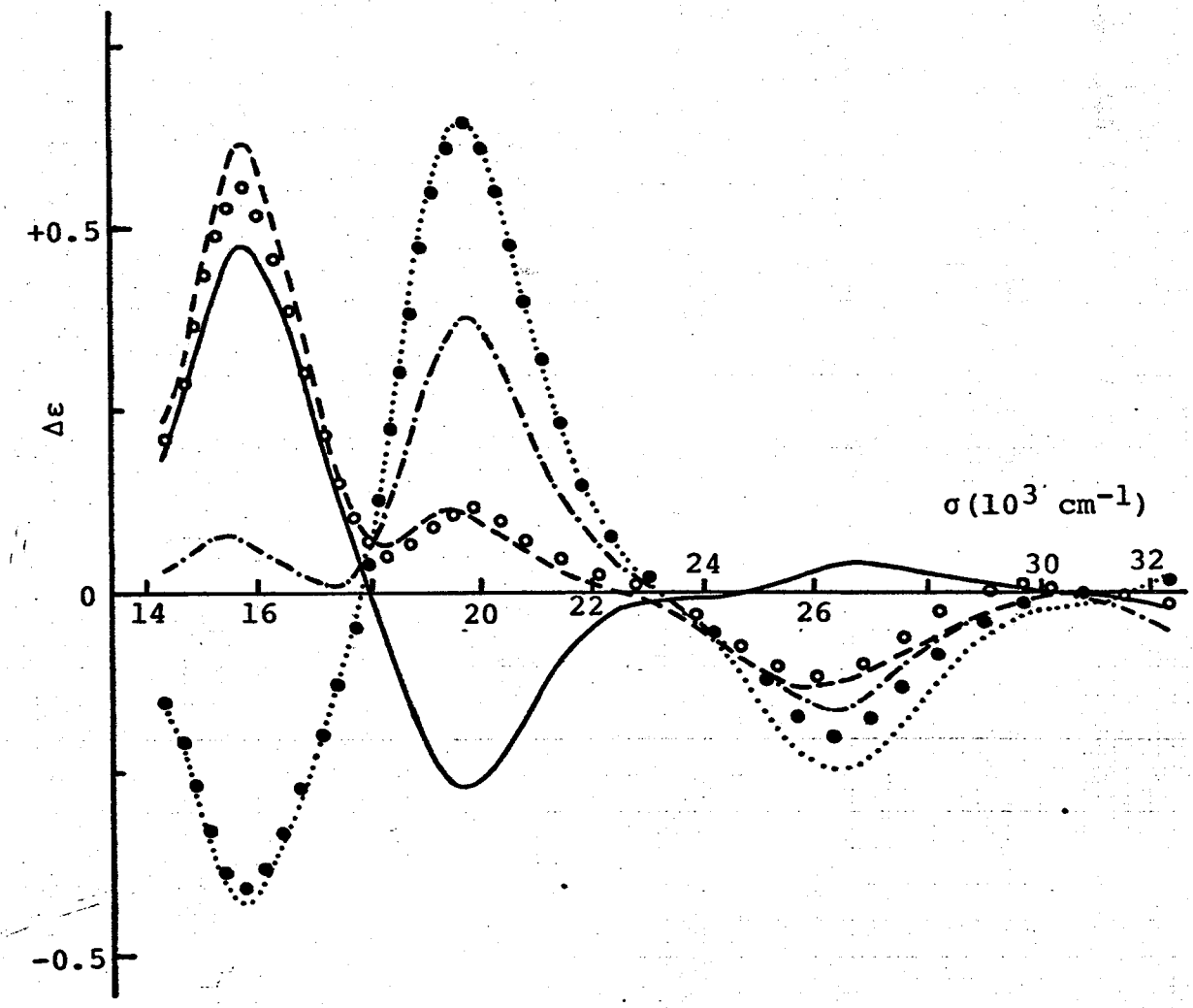


Fig. 29. CD curves of trans(N)-[Co((R)- or (S)-alada)(β-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, trans(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$
(2) ———, X-trans(N)-[Co((S)-alada)(β-ala)]$^-$
(3) -----, X-trans(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$
(4) ·····, Z-trans(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$
(5) ○○○○○, calculated curve, (1) + (2)
(6) ●●●●●, calculated curve, (1) - (2)

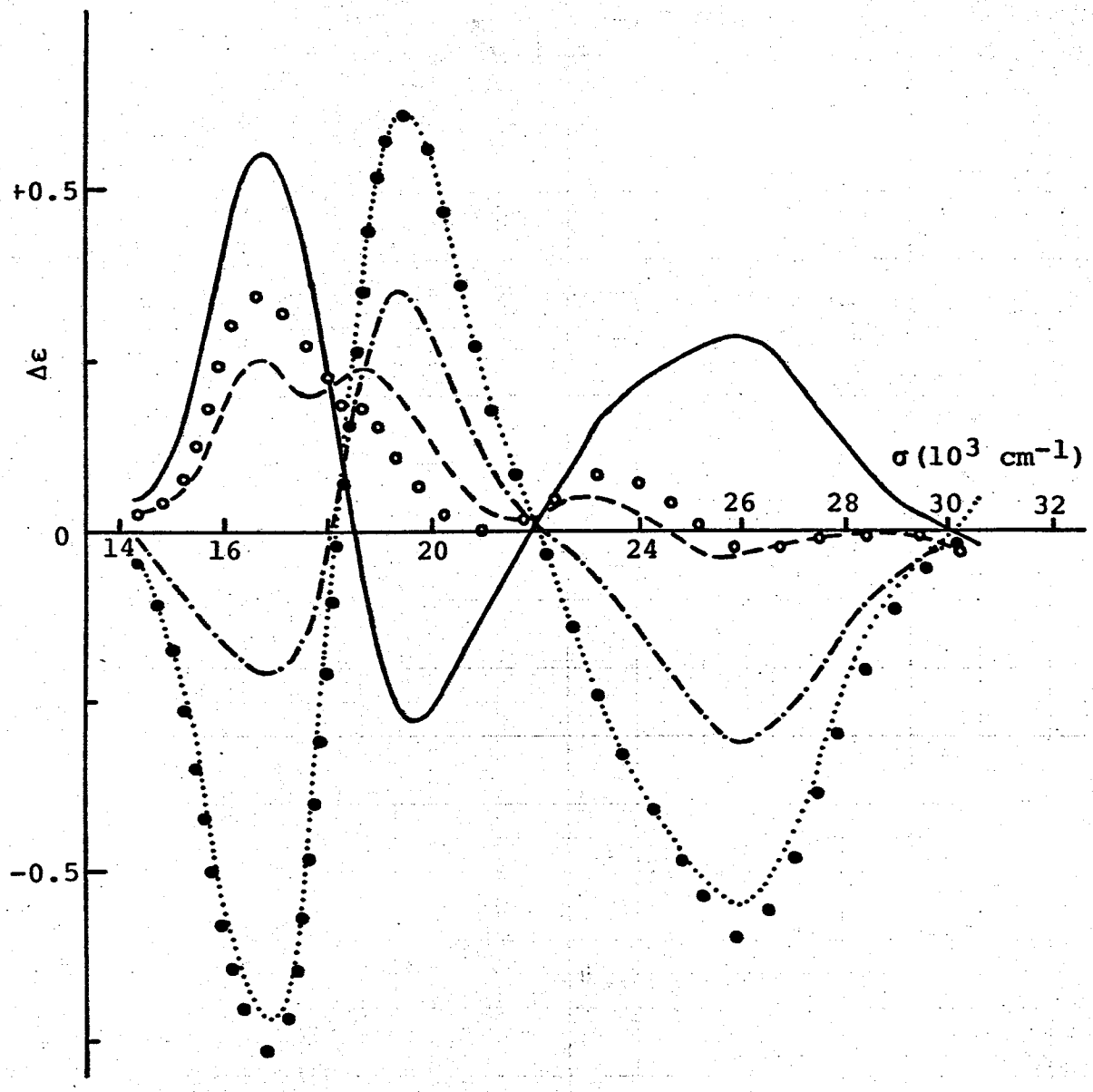


Fig. 30. CD curves of cis(N)-[Co((R)- or (S)-alada)(β-ala)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, cis(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$

(2) ———, X-cis(N)-[Co((S)-alada)(β-ala)]$^-$

(3) -----, X-cis(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$

(4) ·····, Z-cis(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$

(5) ∘∘∘∘∘, calculated curve, (1) + (2)

(6) •••••, calculated curve, (1) - (2)

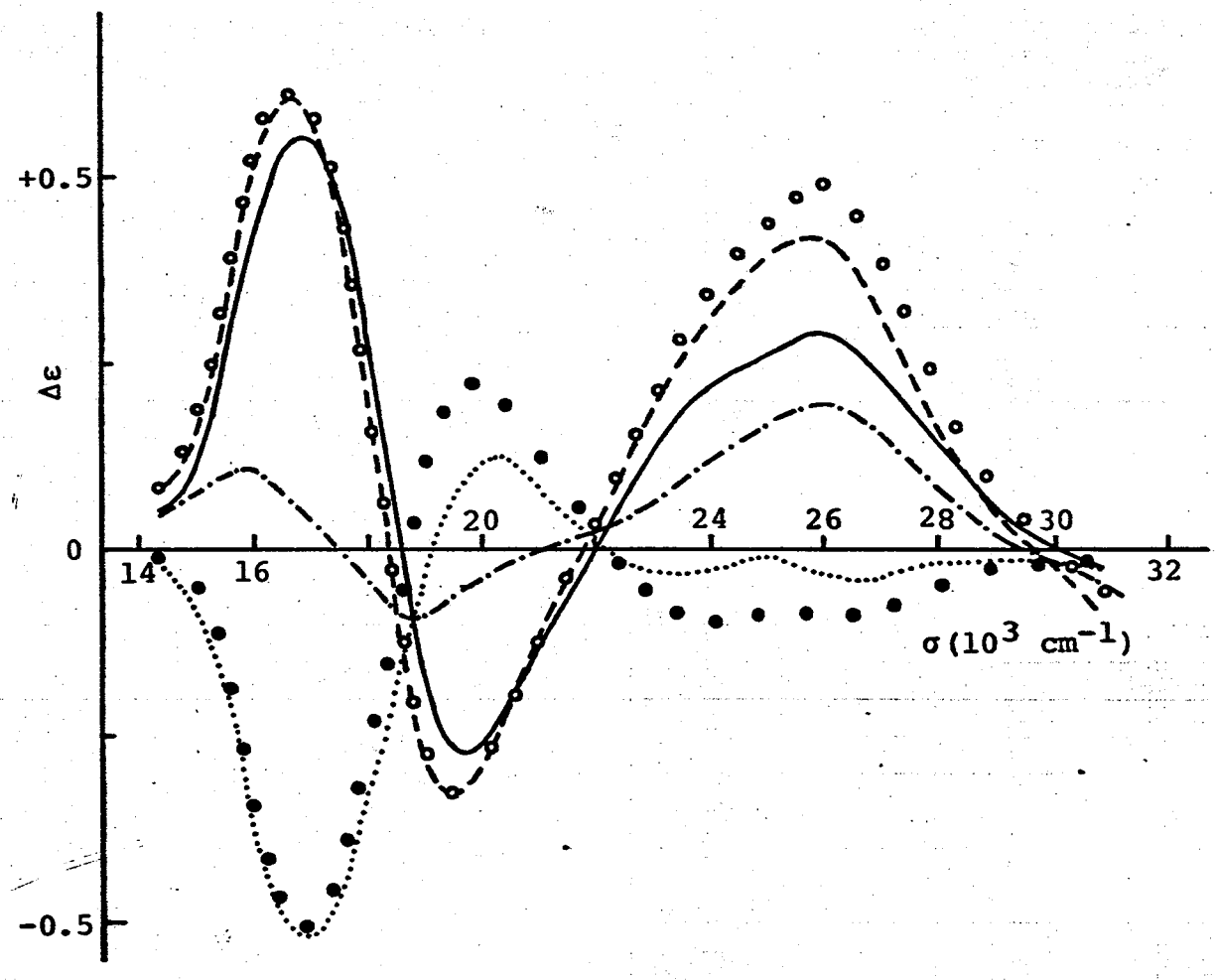


Fig. 31. CD curves of cis(N)-[Co((R)- or (S)-alada)(β-am)]$^-$ and the related complex, and curve analyses.

(1) -·-·-, cis(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$
(2) ———, X-cis(N)-[Co((S)-alada)(β-ala)]$^-$
(3) -----, X-cis(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$
(4) ·····, Z-cis(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$
(5) ∘∘∘∘∘, calculated curve, (1) + (2)
(6) •••••, calculated curve, (1) - (2)

Table X. CD Spectral Data of $[Co(N\text{-}O_3)(am)]^-$ ($N\text{-}O_3$ = (R)- or (S)-alada, (S,S)-alaipa) Complexes[a)]

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
X-trans(N)-[Co((S)-alada)(gly)]$^-$	16.1	+0.50	27.0	+0.12
	19.8	-0.19		
Y-trans(N)-[Co((S)-alada)(gly)]$^-$[b)]	15.9	+0.33	25.8	+0.06
	20.5	-0.11		
X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$	16.2	+0.35	27.1	+0.44
	20.6	-0.10		
Z-trans(N)-[Co((R)-alada)((S)-ala)]$^-$	16.1	-0.54	27.2	+0.20
	18.8	+0.12		
	20.8	-0.68		
X-trans(N)-[Co((S)-alada)((S)-pro)]$^-$	16.1	+0.34	27.1	+0.53
	18.4	+0.23		
	20.7	-0.81		
Z-trans(N)-[Co((R)-alada)((S)-pro)]$^-$	16.2	-0.54	27.4	+0.29
	18.8	+0.28		
	20.8	-0.55		

Table X. (continued)

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
X-trans(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$	15.9	+0.40	26.2	+0.30
	19.9	-0.94		
Z-trans(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$	15.7	-0.67	25.5	+0.23
	18.1	+0.03		
	20.1	-0.41		
X-trans(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$	15.7	+0.62	26.0	-0.13
	19.5	+0.11		
Z-trans(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$	15.7	-0.42	26.4	-0.24
	19.6	+0.65		
X-cis(N)-[Co((S)-alada)(gly)]$^-$	16.4	+0.09	26.2	+0.09
	17.9	-0.09		
	20.0	+0.57		
X-cis(N)-[Co((S)-alada)((S)-ala)]$^-$	17.7	-0.56	26.0	-0.20
	20.2	+1.12		
Z-cis(N)-[Co((R)-alada)((S)-ala)]$^-$	17.3	-0.79	26.5	-0.20
	20.3	+0.37		
X-cis(N)-[Co((S)-alada)(β-ala)]$^-$	16.8	+0.56	26.0	+0.29
	19.8	-0.27		

Table X. (continued)

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
X-cis(N)-[Co((S)-alada)((R)-α-Me-β-ala)]$^-$	16.8	+0.26	23.0	+0.05
	18.8	+0.25	25.6	-0.03
Z-cis(N)-[Co((R)-alada)((R)-α-Me-β-ala)]$^-$	16.9	-0.72	25.9	-0.55
	19.5	+0.63		
X-cis(N)-[Co((S)-alada)((S)-β-Me-β-ala)]$^-$	16.7	+0.61	25.8	+0.42
	19.6	-0.33		
Z-cis(N)-[Co((R)-alada)((S)-β-Me-β-ala)]$^-$	16.9	-0.53	23.4	-0.03
	20.3	+0.12	26.6	-0.03
XY-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$	16.1	+0.75	26.6	+0.08
	20.0	-0.30		
XZ-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$	16.3	+0.20	26.2	+0.23
	20.0	-0.44		
XZ-cis(N)-[Co((S,S)-alaipa)(gly)]$^-$	17.2	+0.85	25.6	+0.85
	19.7	-0.17		
XY-cis(N)-[Co((S,S)-alaipa)(gly)]$^-$	16.6	+0.34	25.8	-0.06
	19.8	+0.34		

a) The wave numbers are given in 10^3 cm^{-1}.

b) No elemental analysis was carried out, and the $\Delta\varepsilon_{ext}$ value was estimated from the isomerization experiment (Experimental Section I-3-2-(c)) and CD curve in Fig. 32 was drawn on the basis of the same estimation.

and hence the former two complexes are diastereomeric to each other. The trans(N)-[Co(nta)((S)-ala)]$^-$ complex has the vicinal contribution due to the (S)-ala ligand. If the vicinal contributions due to the two kinds of optically active ligand in a complex are separable and additive, the following relationships will hold between these four complexes.

$$\Delta\varepsilon\{X\text{-}((S)\text{-alada}, (S)\text{-ala})\} = \Delta\varepsilon\{X\text{-}((S)\text{-alada}, gly)\} + \Delta\varepsilon\{nta, (S)\text{-ala}\}$$

$$\Delta\varepsilon\{Z\text{-}((R)\text{-alada}, (S)\text{-ala})\} = -\Delta\varepsilon\{X\text{-}((S)\text{-alada}, gly)\} \Delta\varepsilon\{nta, (S)\text{-ala}\}$$

where $\Delta\varepsilon\{X\text{-}((S)\text{-alada}, (S)\text{-ala})\}$, for example, is the observed CD curve of the X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$ complex and $\Delta\varepsilon\{nta, (S)\text{-ala}\}$ is that of the trans(N)-[Co-(nta)((S)-ala)]$^-$ complex. The calculated CD curve for the X-trans(N)-[Co((S)-alada)((S)-ala)]$^-$ or Z-trans(N)-[Co-((R)-alada)((S)-ala)]$^-$ complex was derived by applying the above relationships to the observed CD curves of the X-trans(N)-[Co((S)-alada)(gly)]$^-$ and trans(N)-[Co(nta)-((S)-ala)]$^-$ complexes, and the resulted CD curves agree quite well with the corresponding observed CD curves as can be seen in Fig. 25. Similar good agreement of the observed CD curves with the calculated ones is also realized for the trans(N) (S)-pro and cis(N) (S)-ala complexes, though there are some differences in the intensities only for the Z-cis(N)-[Co((R)-alada)((S)-ala)]$^-$ complex (Figs. 26 and 27). The same examination was conducted for the (R)- or (S)-alada

complexes with the β-aminocarboxylates (R)-α-Me-β-ala and (S)-β-Me-β-ala, using Δε{X-((S)-alada, β-ala) instead of Δε{X-((S)-alada, gly)} in the above relationships. For all of the β-aminocarboxylato complexes, the calculated CD curve is also quite agree with the observed one (Figs. 28-31). These facts indicate that the additivity of the two kinds of vicinal contribution is almost perfect and each of the vicinal effects due to the two optically active ligands in a complex contribute independently to the optical activity of the complex.

The CD spectra of each two arrangement isomers of the trans(N)- and cis(N)-[Co((S,S)-alaipa)(gly)]$^-$ complexes are shown in Figs. 32 and 33 and Table X. These complexes have a vicinal contribution due to the (S,S)-alaipa ligand, which has two asymmetric carbon atoms. In the (S,S)-alaipa complexes, a molecular model examination shows that there is a considerable crowding between the methyl group of the ligand and some nonbonded atoms in the complex. Such crowding may be relieved by distortion of the conformation of the three chelate rings around the nitrogen atom. The distorted conformation of the (S,S)-alaipa ligand must be chiral because the (S,S)-alaipa ligand itself is chiral. This chiral conformation is expected to contribute to the optical activity of the complex. Accordingly it may be reasonable to assume that in the (S,S)-alaipa complexes the vicinal effect due to the (S,S)-alaipa ligand consists of two kinds of CD contribution, one due to the asymmetric carbon atoms and the other due to the chiral conformation.

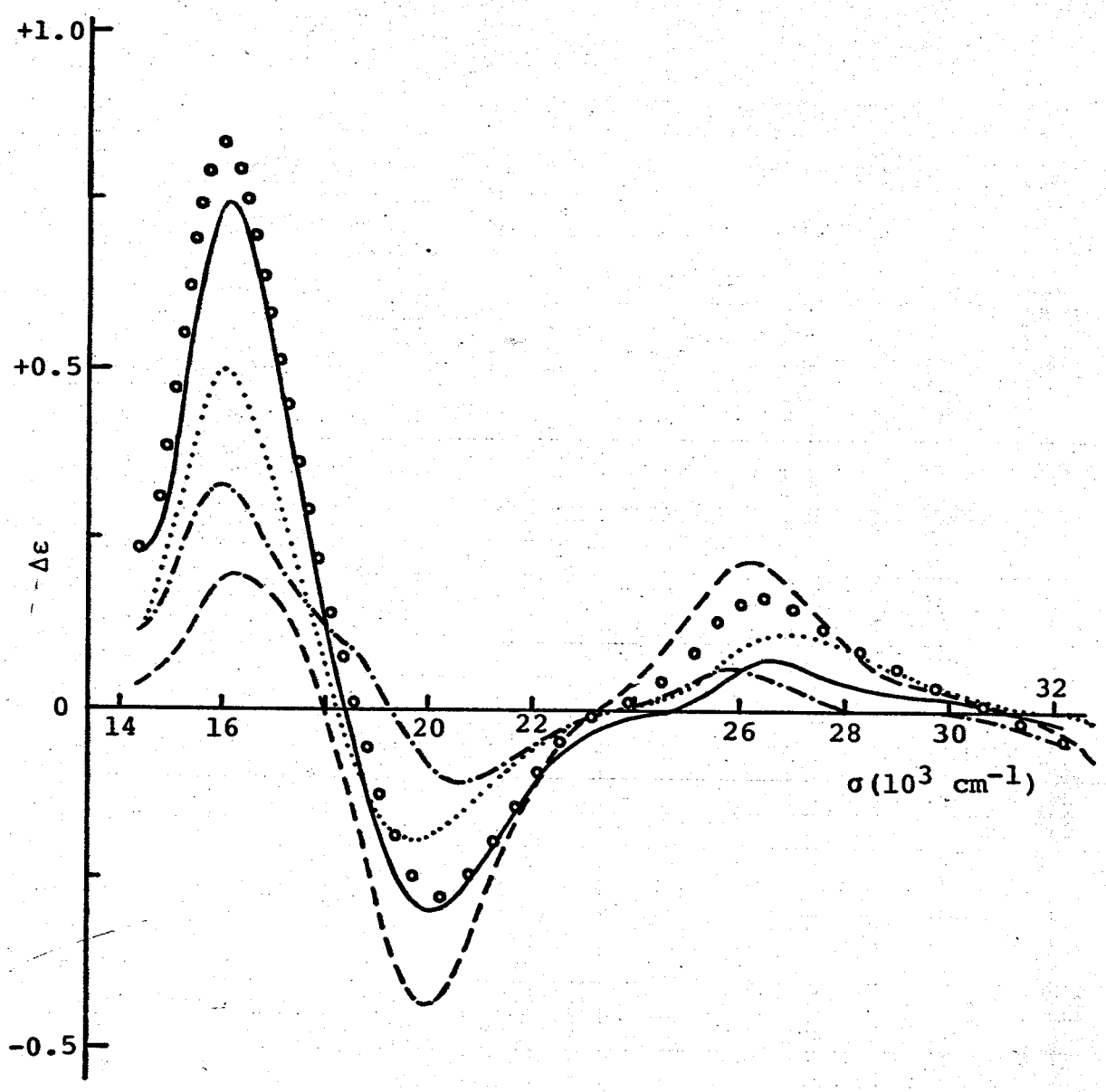


Fig. 32. CD curves of trans(N)-[Co((S,S)-alaipa)(gly)]$^-$ and the related complexes, and curve anasysis.

(1) •••••, X-trans(N)-[Co((S)-alada)(gly)]$^-$
(2) -•-•-, Y-trans(N)-[Co((S)-alada)(gly)]$^-$
(3) ———, XY-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$
(4) -----, XZ-trans(N)-[Co((S,S)-alaipa)(gly)]$^-$
(5) ∘∘∘∘∘, calculated curve, (1) + (2)

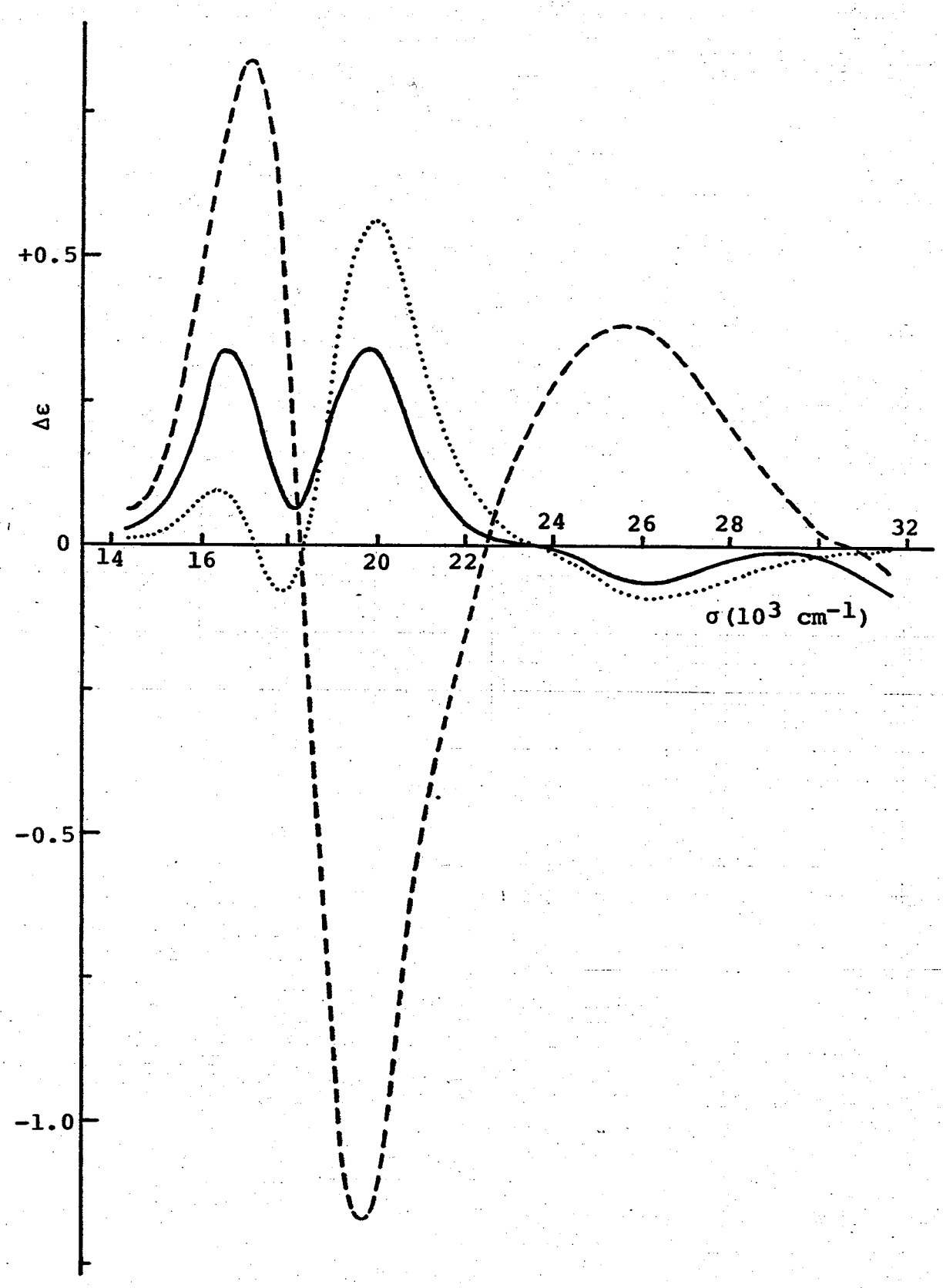


Fig. 33. CD curves of cis(N)-[Co((S,S)-alaipa)(gly)]$^-$: ———, XY-; -----, XZ-, and of X-cis(N)-[Co((S)-alada)-(gly)]$^-$ (·····).

Similar situation is considered for the vicinal contribution due to the complexes with (S)-alada. At the present time, it is difficult to evaluate separately the two kinds of CD contributions in the (S)-alada and (S,S)-alaipa complexes. However, the following CD behaviors are noted in the CD curves of these complexes.

The XY-trans(N) (S,S)-alaipa complex has one asymmetric carbon atom on each of the X- and Y-chelate rings of the coordinated (S,S)-alaipa. On the other hand, the two arrangement isomers, X- and Y-, of the trans(N)-[Co((S)-alada)(gly)]$^-$ complex have one asymmetric carbon atom on X- and Y-chelate rings respectively. It is noteworthy that the CD curve of the (S,S)-alaipa complex is very well reproduced by summing up the CD curves of the two isomers of the (S)-alada complex as can be seen in Fig. 32. This is well explained by assuming that the CD curve in these complexes are contributed mostly from the asymmetric carbon atoms and the contributions are almost additive. Furthermore, it is noted that these three complexes are quite similar in their splitting patterns to one another. The same examination of the CD curves can not be made for the corresponding cis(N) complexes because the Y-isomer of the (S)-alada complex was not obtained. However, the general CD pattern of the X-cis(N) (S)-alada and XY-cis(N) (S,S)-alaipa complexes are similar to each other as in the case of the trans(N) complex (Fig. 32). Next, it seems that the CD curve of the XZ-cis(N) (S,S)-alaipa complex take an anomalous behavior. Namely, the CD curve of this complex is clearly different

in the general pattern and intensity from those of the related complexes, X-cis(N) (S)-alada and XY-cis(N) (S,S)-alaipa, while the CD curve of the XZ-trans(N) (S,S)-alaipa are similar in the splitting pattern to the other complexes in Fig. 32. A molecular model consideration indicated that there is remarkable steric hindrance in the XZ-cis(N) (S,S)-alaipa complex of these complexes; the methyl group on Z-chelate ring interacts strongly with the amino protons of gly in the apical postions (Section II-7). From this fact, it is considered that the anomalous CD behavior observed for the XZ-cis(N) (S,S)-alaipa complex arises from the conformational contribution due to the (S,S)-alaipa ligand which is distorted by the remarkable interaction.

II-6-4. $[Co(\beta\text{-alada})(am)]^-$ and $[Co((S)\text{-alapa})(gly)]^-$ complexes.

Although both β-alada and gly ligands in the trans(N)- and cis(N)-$[Co(\beta\text{-alada})(gly)]^-$ complexes are optically inactive, the two isomer, X- and Z-, which were obtained by the optical resolution of the u-isomer of the complexes, are optically active and antipodal to each other. This is proved by the fact that the CD curves of the isomers are of mirror image as can be seen in Figs. 37-39 and Table XI. The CD curves of these complexes are contributed from the chiral arrangement of the three feet of the tripod-like ligand β-alada. Cobalt(III) complexes with similar tripod-like ligands such as 4-diethylenetriaminemonoacetate[51,52] and β-aminoethyliminodiacetate[53] have been prepared, but no

attempt was made to obtain the optically active complexes. The contribution to CD due to the chiral coordination of β-alada is named "arrangement" contribution in this report, since the chirality results from the difference of arrangement of the β-alada chelate rings. On the other hand, the s(Y)-isomer of the trans(N)- or cis(N)-[Co(β-alada)-(gly)]$^-$ complex has not the arrangemnt chirality, and so it is optically inactive.

The s-trans(N)- and s-cis(N)-[Co(β-alada)((S)-am)]$^-$ complexes with an optically active (S)-α-aminocarboxylato ligand ((S)-am) have only the vicinal contribution due to the (S)-am. As expected, the CD curve of the s-trans(N)-[Co(β-alada)((S)-ala)]$^-$ complex is very similar to that of the trans(N)-[Co(nta)((S)-ala)]$^-$ complex; the optical activity of the latter complex is contributed only by the optically active (S)-α-aminocarboxylato ligand as described in Section II-6-2 (Fig. 34). Similar CD relationships are also recognized for the s-cis(N) (S)-ala and s-trans(N) (S)-pro complexes (Figs. 35 and 36).

The u-trans(N)- and u-cis(N)-[Co(β-alada)((S)-am)]$^-$ complexes have both of the arrangement and vicinal contributions, and the two u(X and Z)-isomers of the complex are diastereomeric to each other. For the trans(N)- and cis(N)-[Co((R)- or (S)-alada)((S)-am)]$^-$ complexes, it was confirmed that the two kinds of vicinal contributions in a complex are separable and almost additive on the CD curve in the preceding Section. If the additivity rule between the arrangement and vicinal contributions is correct here,

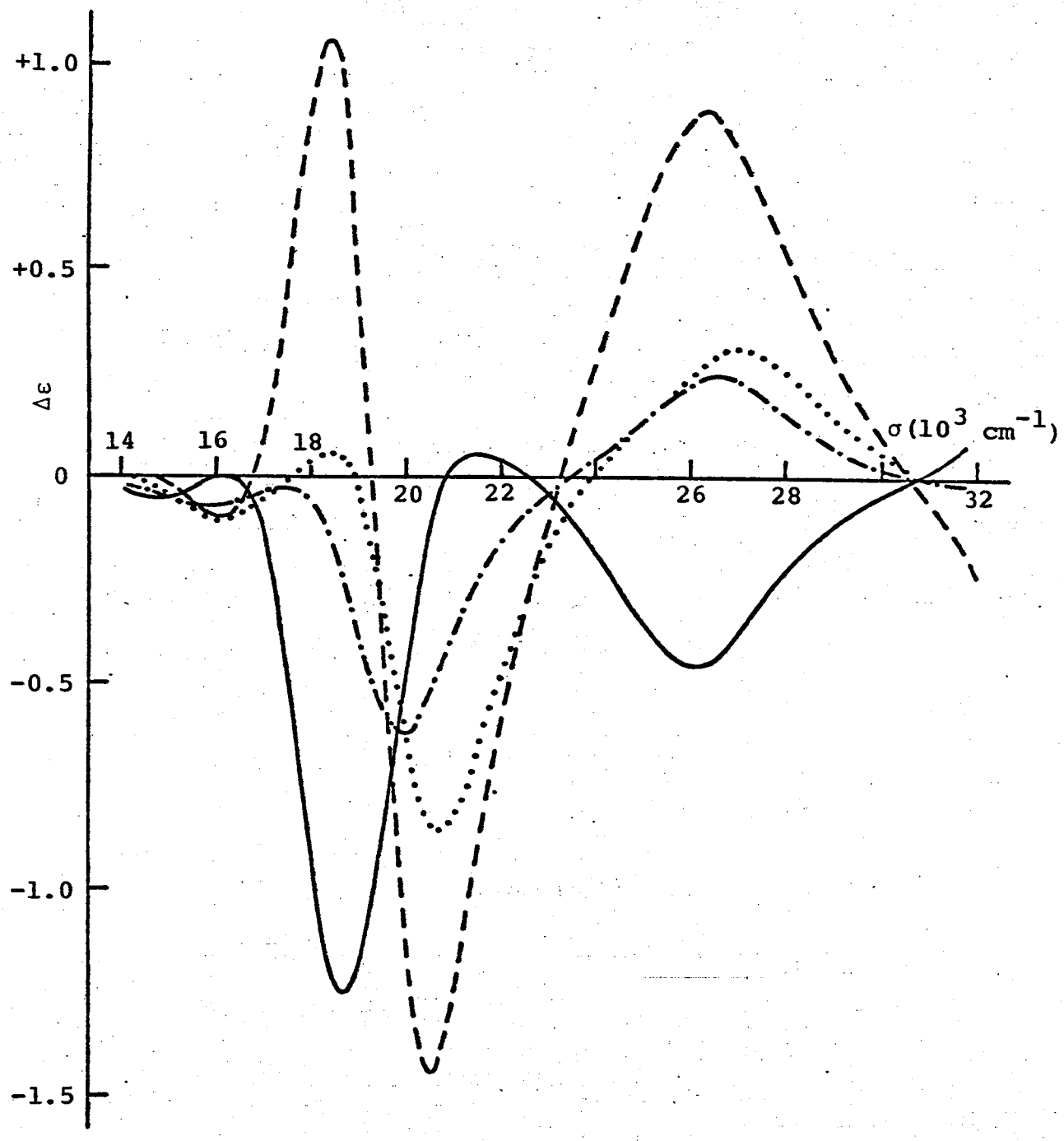


Fig. 34. CD curves of trans(N)-[Co(β-alada)((S)-ala)]$^-$: ———, X- (isomer-i); -----, Z- (isomer-ii); -·-·-, Y- (isomer-iii), and of trans(N)-[Co(nta)((S)-ala)]$^-$ (·····).

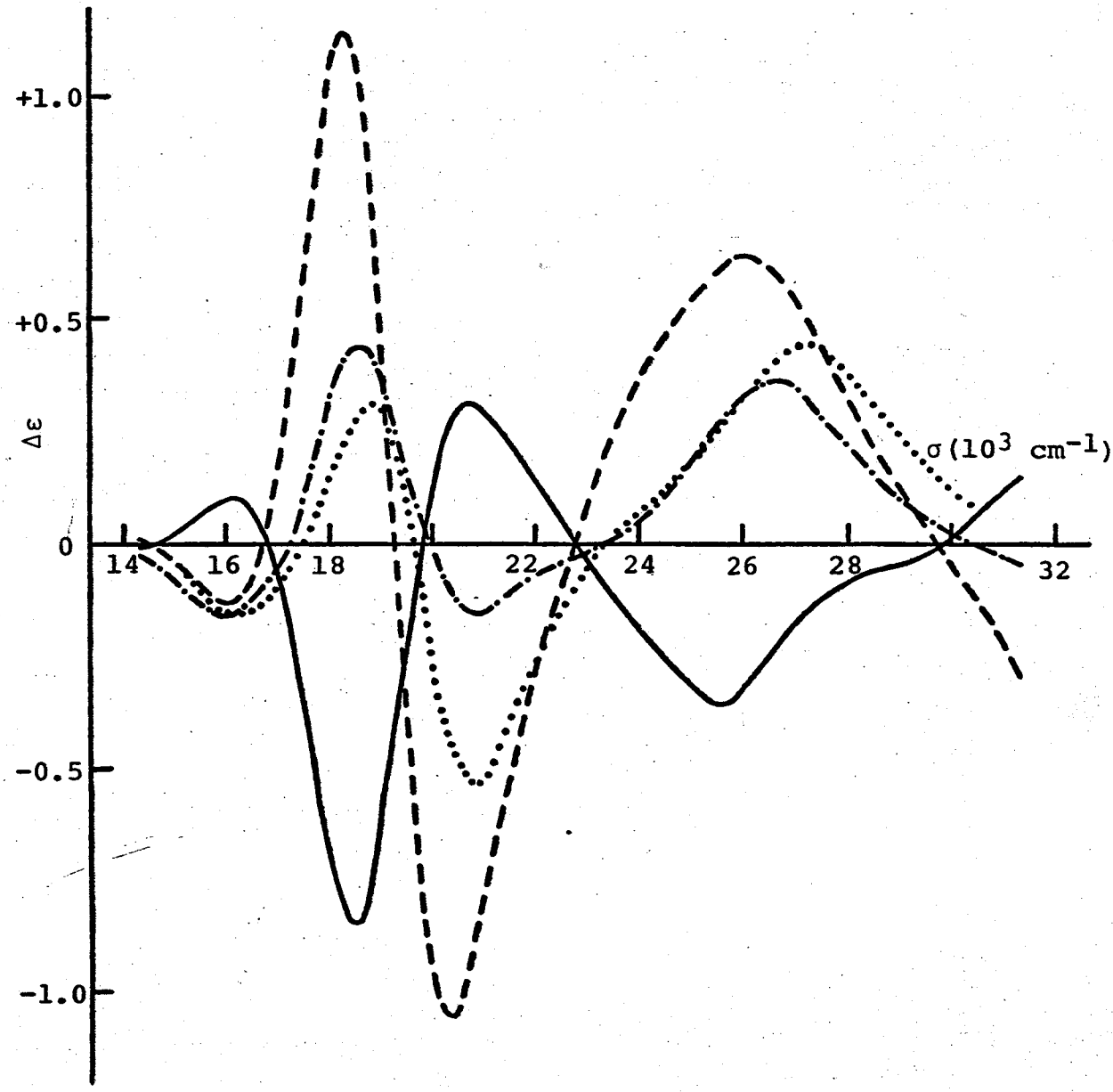


Fig. 35. CD curves of trans(N)-[Co(β-alada)((S)-pro)]$^-$: ———, X- (isomer-i); -----, Z- (isomer-iii); -·-·-, Y- (isomer-ii), and of trans(N)-[Co(nta)((S)-pro)]$^-$ (·····).

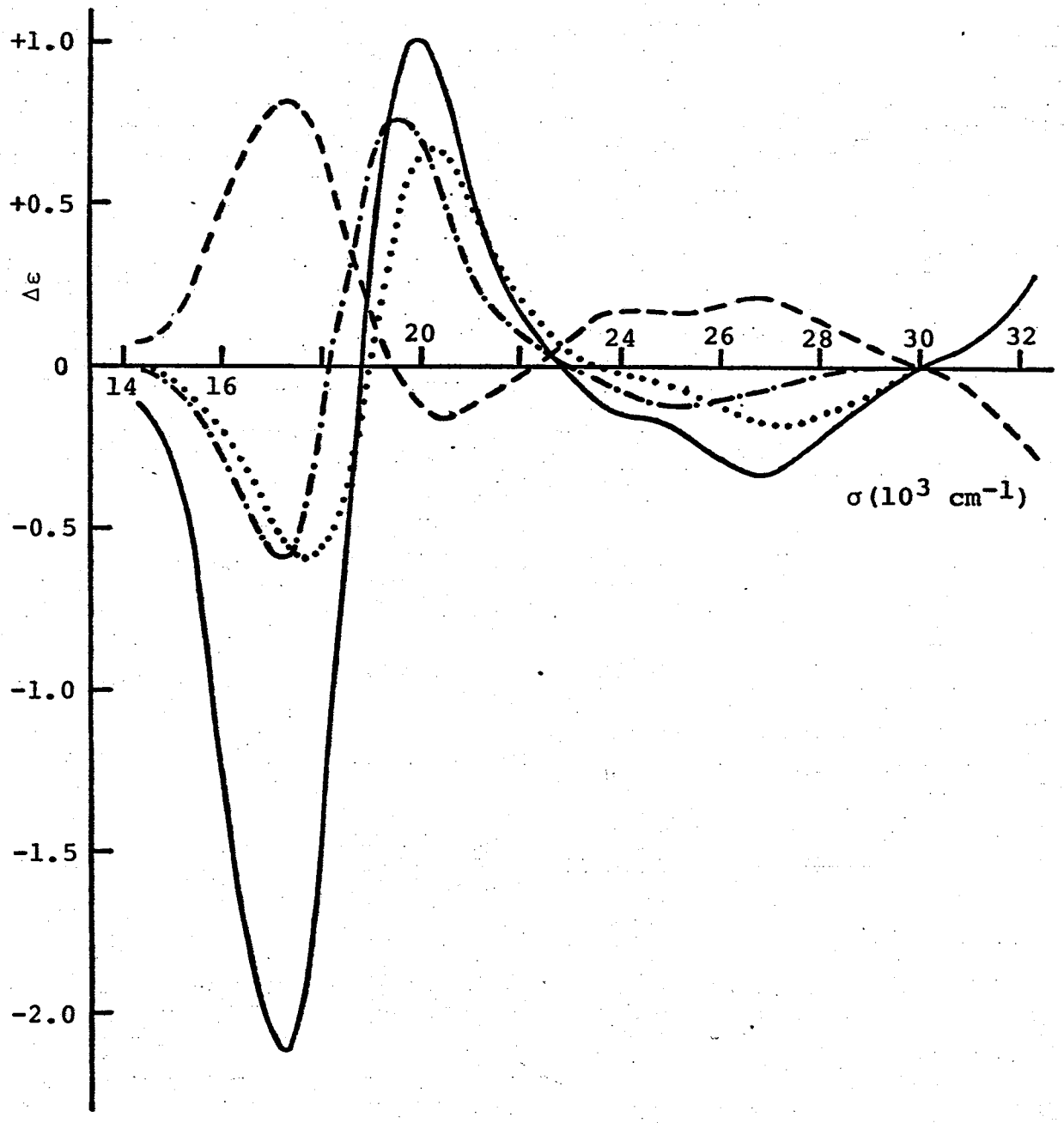


Fig. 36. CD curves of cis(N)-[Co(β-alada)((S)-ala)]$^-$: ———, X- (isomer-ii); -----, Z- (isomer-i); -·-·-, Y- (isomer-iii), and of cis(N)-[Co(nta)((S)-ala)]$^-$ (·····).

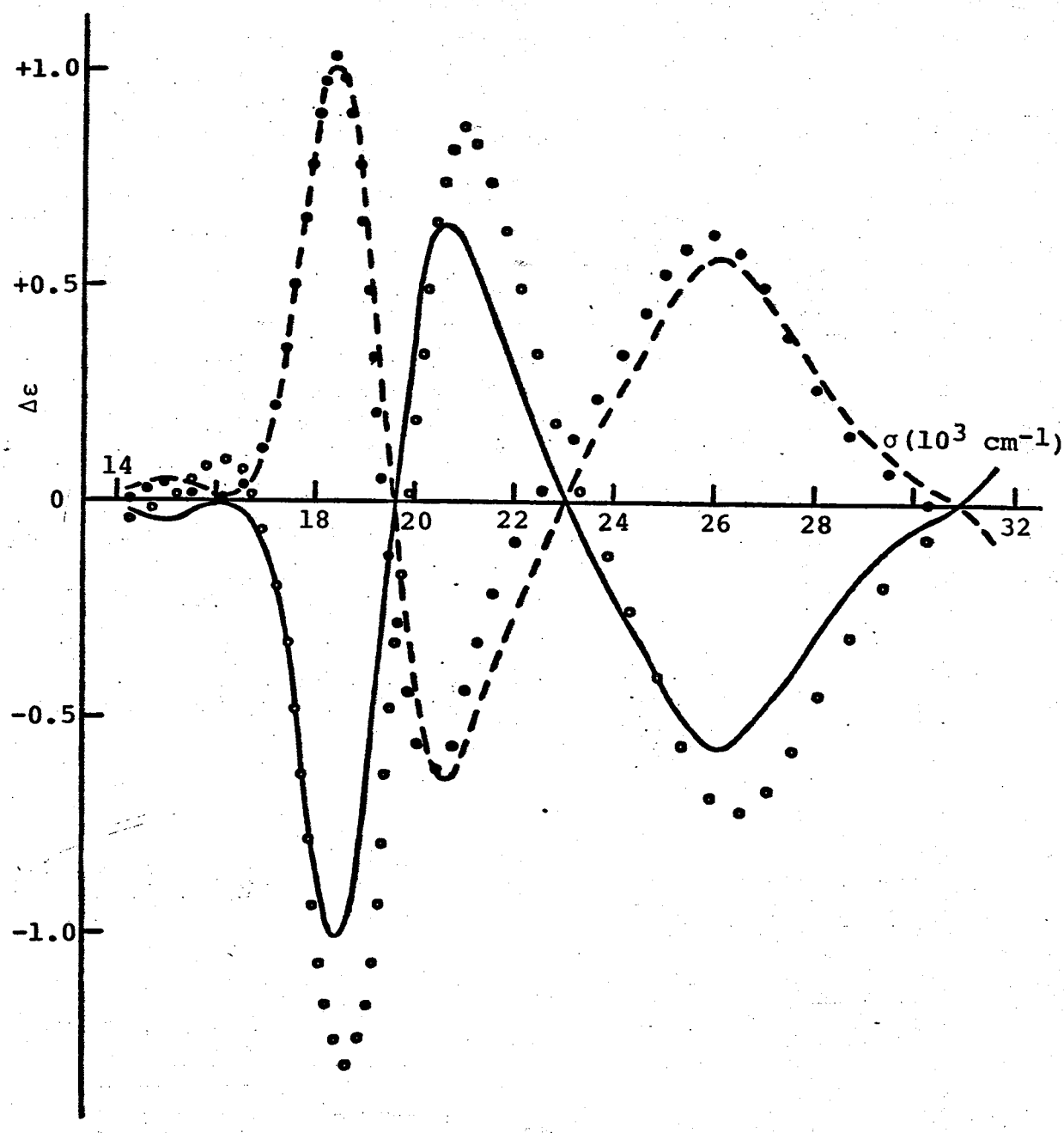


Fig. 37. CD curves of trans(N)-[Co(β-alada)(gly)]$^-$, and curve analyses of trans(N)-[Co(β-alada)((S)-ala)]$^-$.

———, X-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-ii)

-----, Z-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-iii)

ooooo, calculated curve, X-trans(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-i) minus trans(N)-[Co(nta)((S)-ala)]$^-$

•••••, calculated curve, Z-trans(N)-[Co(β-alada)((S)-ala)]$^-$ (isomer-ii) minus trans(N)-[Co(nta)((S)-ala)]$^-$

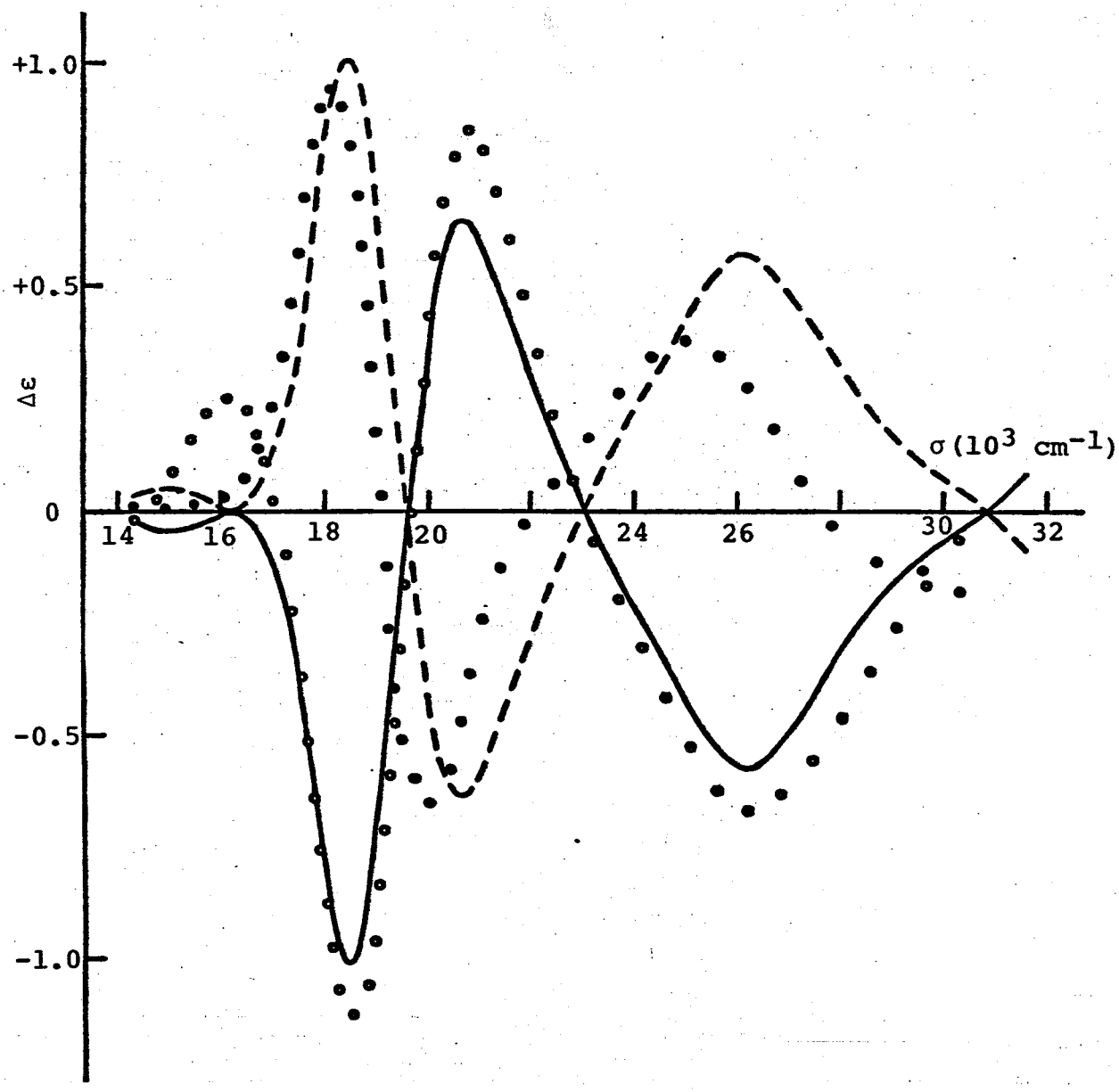


Fig. 38. CD curves of trans(N)-[Co(β-alada)(gly)]$^-$, and curve analyses of trans(N)-[Co(β-alada)((S)-pro)]$^-$.

———, X-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-ii)

-----, Z-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-iii)

∘∘∘∘∘, calculated curve, X-trans(N)-[Co(β-alada)((S)-pro)]$^-$ (isomer-i) minus trans(N)-[Co(nta)((S)-pro)]$^-$

•••••, calculated curve, Z-trans(N)-[Co(β-alada)((S)-pro)]$^-$ (isomer-iii) minus trans(N)-[Co(nta)((S)-pro)]$^-$

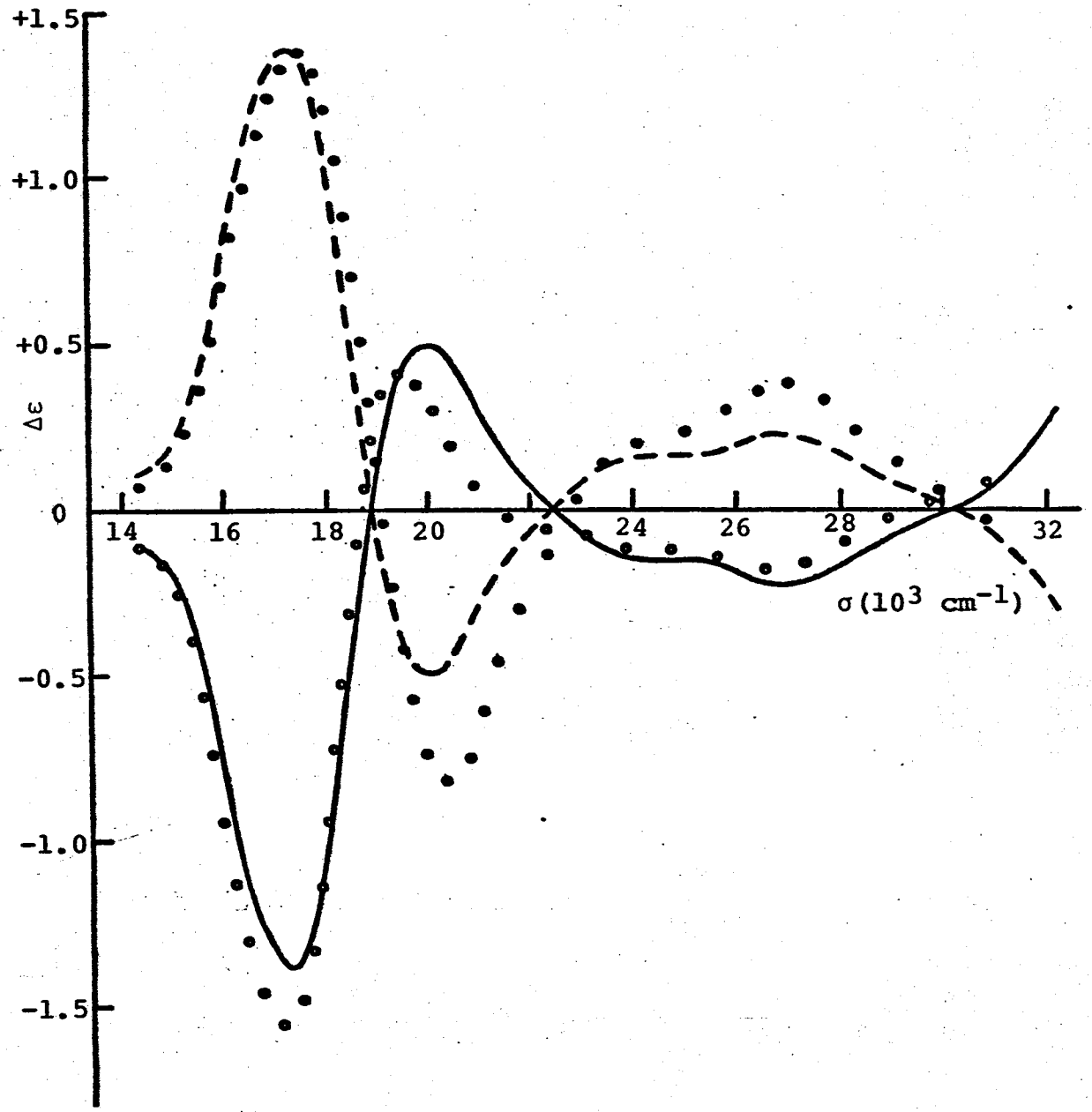


Fig. 39. CD curves of cis(N)-[Co(β-alada)(gly)]⁻, and curve analyses of cis(N)-[Co(β-alada)((S)-ala)]⁻.

———, X-cis(N)-[Co(β-alada)(gly)]⁻ (isomer-iii)

-----, Z-cis(N)-[Co(β-alada)(gly)]⁻ (isomer-ii)

∘∘∘∘∘, calculated curve, X-cis(N)-[Co(β-alada)((S)-ala)]⁻ (isomer-ii) minus cis(N)-[Co(nta)((S)-ala)]⁻

•••••, calculated curve, Z-cis(N)-[Co(β-alada)((S)-ala)]⁻ (isomer-i) minus cis(N)-[Co(nta)((S)-ala)]⁻

Table XI. CD Spectral Data of $[Co(N\text{-}O_3)(am)]^-$ ($N\text{-}O_3$ = β-alada and (S)-alapa) Complexes[a)]

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
X-trans(N)-[Co(β-alada)(gly)]$^-$	15.0	-0.05 (+0.05)[b)]	26.1	-0.58 (+0.57)[b)]
	18.4	-1.02 (+1.00)[b)]		
	20.6	+0.56 (-0.66)[b)]		
X-trans(N)-[Co(β-alada)((S)-ala)]$^-$	15.0	-0.05	26.1	-0.45
	18.8	-1.26		
	21.5	+0.05		
Z-trans(N)-[Co(β-alada)((S)-ala)]$^-$	16.1	-0.10	26.3	-0.88
	18.4	+1.05		
	20.5	-1.46		
Y-trans(N)-[Co(β-alada)((S)-ala)]$^-$	16.6	-0.08	26.5	+0.25
	20.0	-0.62		

Table XI. (continued)

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
X-trans(N)-[Co(β-alada)((S)-pro)]$^-$	16.1	+0.10	25.6	-0.35
	18.5	-0.85		
	20.7	+0.31		
Y-trans(N)-[Co(β-alada)((S)-pro)]$^-$	15.9	-0.16	26.5	+0.36
	18.6	+0.44		
	20.7	-0.15		
Z-trans(N)-[Co(β-alada)((S)-pro)]$^-$	16.1	-0.14	26.0	-0.65
	18.2	+1.16		
	20.3	-1.06		
Z-cis(N)-[Co(β-alada)(gly)]$^-$	17.2	-1.41	ca. 24.5sh	-0.15
		(+1.38)[b]		(+0.16)[b]
	20.0	+0.50	26.8	-0.21
		(-0.50)[b]		(+0.22)[b]
Z-cis(N)-[Co(β-alada)((S)-ala)]$^-$	17.3	-2.08	ca. 24.2sh	-0.11
	19.9	+1.00	26.9	-0.34
X-cis(N)-[Co(β-alada)((S)-ala)]$^-$	17.2	+0.81	ca. 24.4sh	+0.16
	20.4	-0.15	26.7	+0.21

Table XI. (continued)

Complex ion	Band I		Band II	
	σ_{ext}	$\Delta\varepsilon_{ext}$	σ_{ext}	$\Delta\varepsilon_{ext}$
Y-cis(N)-[Co(β-alada)((S)-ala)]$^{-}$ c)	17.1	-	25.1	-
	19.5	+		
X_SZ_6-trans(N)-[Co((S)-alapa)(gly)]$^{-}$	15.7	+0.41	26.0	+0.75
	18.2	+1.05		
	20.4	-1.00		
X_SZ_6-cis(N)-[Co((S)-alapa)(gly)]$^{-}$	17.1	+1.78	23.9	+0.25
	20.0	-0.51	26.5	+0.23

a) The wave numbers are given in 10^3 cm^{-1}.

b) The values in parentheses are for the antipode.

c) The $\Delta\varepsilon_{ext}$ value has not obtained because of the lack of elemental analysis. CD curve in Fig. 36 was drawn by assuming the e value of the first absorption band to be the same as the mean value (ε_{max} = 225) for those of the corresponding Z- and X-isomers.

the following relationships will hold for each diastereomeric pair of u-trans(N) (S)-ala, u-trans(N) (S)-pro and u-cis(N) (S)-ala complexes.

$$\Delta\varepsilon\{X\text{-}(\beta\text{-alada, gly})\} = \Delta\varepsilon\{X\text{-}(\beta\text{-alada, (S)-am})\} - \Delta\varepsilon\{\text{nta, (S)-ala}\}$$

$$\Delta\varepsilon\{Z\text{-}(\beta\text{-alada, gly})\} = \Delta\varepsilon\{Z\text{-}(\beta\text{-alada, (S)-am})\} - \Delta\varepsilon\{\text{nta, (S)-ala}\}$$

where $\Delta\varepsilon\{X\text{-}(\beta\text{-alada, gly})\}$, for example, is the observed CD curve of the X-trans(N)- or X-cis(N)-[Co(β-alada)(gly)]$^-$ complex, and $\Delta\varepsilon\{\text{nta, (S)-ala}\}$ is the observed CD curve of the trans(N)- or cis(N)-[Co(nta)((S)-am)]$^-$ complex. The calculated CD curve obtained by subtracting the CD curve of the trans(N)-[Co(nta)((S)-ala)]$^-$ complex from that of the isomer-i of trans(N)-[Co(β-alada)((S)-ala)]$^-$ complex agrees well with the observed CD curve of the isomer-ii of trans(N)-[Co(β-alada)(gly)]$^-$ complex, while the calculated CD curve from the isomer-ii of the trans(N)-[Co(β-alada)((S)-ala)]$^-$ complex agrees with the observed curve of the isomer-iii of trans(N)-[Co(β-alada)(gly)]$^-$ complex (Fig. 37). Similar agreement is also substantiated for the u-trans(N) (S)-pro and u-cis(N) (S)-ala complexes as seen in Figures 21 and 22. These facts indicate that the additivity rule is maintained also between the vicinal and arrangement contributions.
In consequence, it is possible to point out, based on the above relationships, that the each isomer-i of the trans(N) (S)-ala and trans(N) (S)-pro complexes has the absolute configuration of chelate ring arrangement of β-alada same

as the isomer-ii of trans(N)-[Co(β-alada)(gly)]$^-$ complex, and that the isomer-i of cis(N)-[Co(β-alada)((S)-ala)]$^-$ complex and the isomer-ii of cis(N)-[Co(β-alada)(gly)]$^-$ complex have the same configuration.

The optical activity of the X_SZ_6-trans(N)- and X_SZ_6-cis(N)-[Co((S)-alapa)(gly)]$^-$ complexes is contributed from the chirality of the coordinated (S)-alapa ligand. This chirality can be considered to consist of a combination of the chirality of (S)-alada coordinated with the X-arrangement and the chirality of β-alada coordinated with the Z-arrangement The CD spectra of the (S)-alapa complexes are shown in Figs. 40 and 41 and Table XI. The CD curve of the X_SZ_6-trans(N)-[Co((S)-alapa)(gly)]$^-$ complex agrees well with the calculated CD curve obtained by summing up the observed curves of the X-trans(N)-[Co((S)-alada)(gly)]$^-$ complex and of the isomer-iii of trans(N)-[Co(β-alada)(gly)]$^-$ complex, as can be seen in Fig. 41. This good agreement indicates the validity of the structural assignment of the trans(N) (S)-alapa complex described in Section II-3-2-(2). As described in the preceding Section, it was suggested that the CD curve of the X-trans(N)-[Co((S)-alada)(gly)]$^-$ complex is contributed mostly from the asymmetric carbon atom of the (S)-alada ligand. From this agreement of the CD curves, therefore, it may be reasonable to assume that the CD curve of the trans(N) (S)-alapa complex consists of two contributions, one from the asymmetric carbon atom and the other from the chiral chelate ring arrangement of (S)-alapa, and that the two contributions are separable

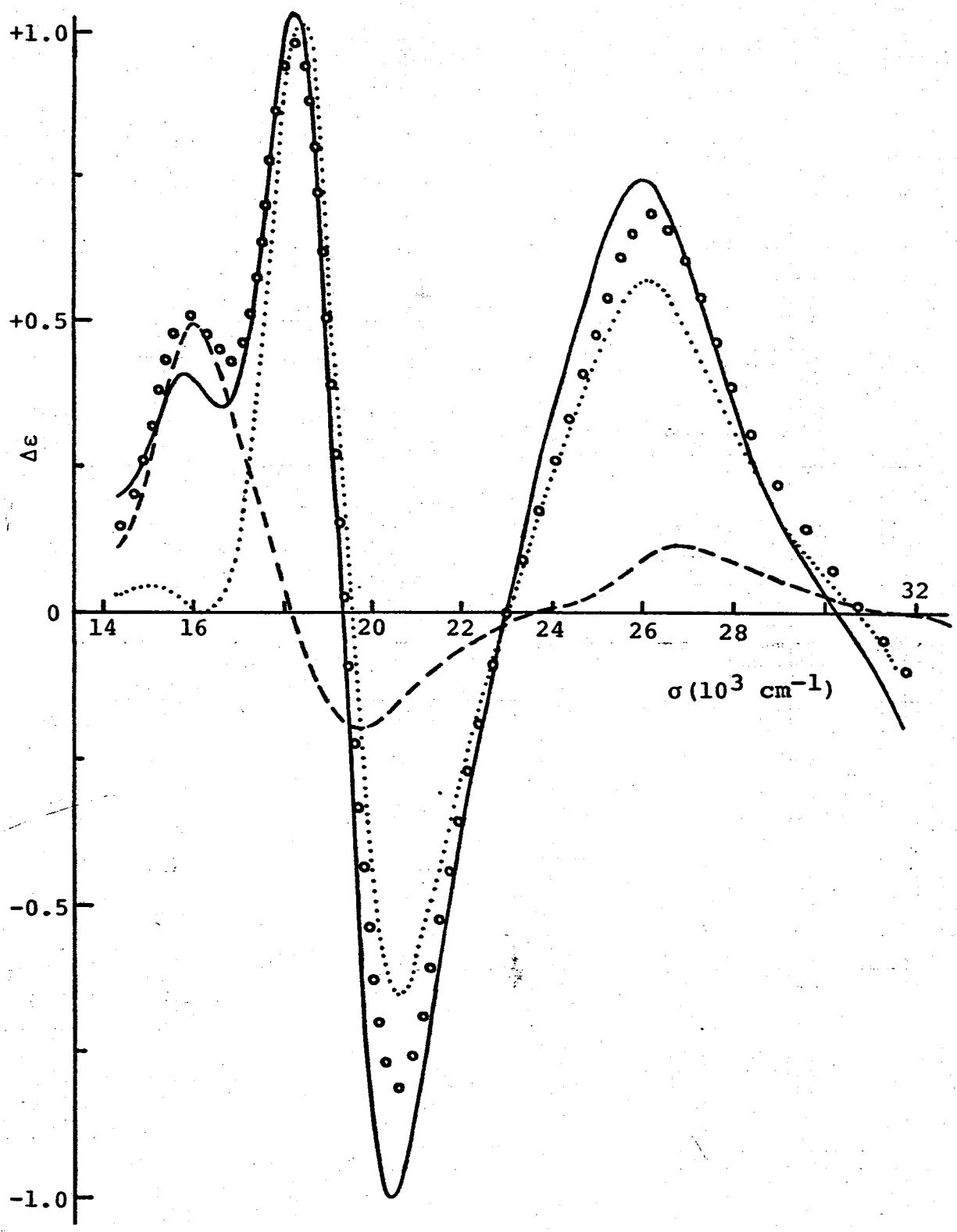


Fig. 40. CD curves of trans(N)-[Co((S)-alapa)(gly)]$^-$ and the related complexes, and curve analysis.

(1) -----, X-trans(N)-[Co((S)-alada)(gly)]$^-$

(2) ·····, Z-trans(N)-[Co(β-alada)(gly)]$^-$ (isomer-iii)

(3) ———, X_SZ_6-trans(N)-[Co((S)-alapa)(gly)]$^-$

(4) ∘∘∘∘∘, calculated curve, (1) + (2)

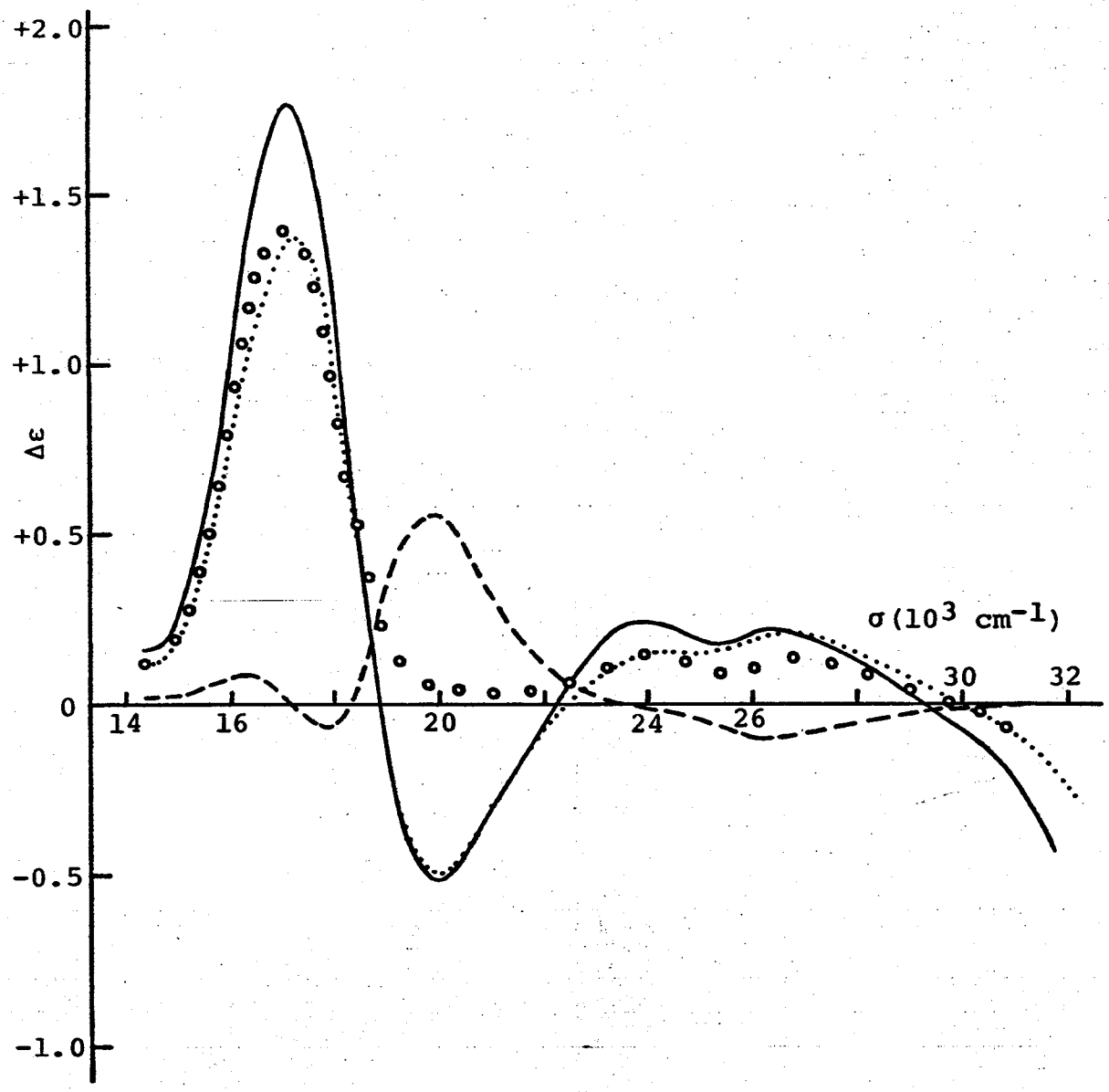


Fig. 41. CD curves of cis(N)-[Co((S)-alapa)(gly)]$^-$ and the related complexes, and curve analysis.

(1) -----, X-cis(N)-[Co((S)-alada)(gly)]$^-$

(2) ·····, Z-cis(N)-[Co(β-alada)(gly)]$^-$ (isomer-ii)

(3) ———, X_SZ_6-cis(N)-[Co((S)-alapa)(gly)]$^-$

(4) ∘∘∘∘∘, calculated curve, (1) + (2)

and almost additive. Now, the nitrogen atom of (S)-alapa ligand becomes asymmetric by coordination to cobalt(III) ion, having the (S) configuration in the X_SZ_6-isomer, because all of the three feet of the ligand differ to each other. The above agreement of the CD curve, however, indicates that the contribution due to the asymmetric nitrogen atom is very small for the trans(N) (S)-alapa complex, Douglas and co-workers[54] have prepared the $[Co(eddda)]^-$ ($eddda^{4-}$ = ethylenediamine-N,N'-diacetate-N,N'-dipropionate) complex, which has a very similar asymmetric nitrogen atom to the (S)-alapa complex. On the basis of analysis of the CD curves of the eddda complex and its analogous complexes, they have proposed that an asymmetric nitrogen atom make only a minor contribution to the optical activity when the three groups about the nitrogen atom are similar. It seems likely that the same situation is also the case for the present trans(N) (S)-alapa complex, because the (S)-alapa ligand has quite similar three groups about the nitrogen atom, namely acetate, propionate and iso-propionate. From these considerations, it is concluded that the absolute configuration of the isomer-iii of trans(N)-$[Co(\beta\text{-alada})(gly)]^-$ complex is Z, in which the Z-chelate ring is six-membered in the same manner as the X_SZ_6-trans(N)-$[Co((S)\text{-alapa})(gly)]^-$ complex, and accordingly that of the isomer-ii of the β-alada complex is X.

Figure 41 shows the CD curve of the X_SZ_6-cis(N)-$[Co((S)\text{-alapa})(gly)]^-$ complex and the same examination on the CD

curves as in the corresponding trans(N) complex. The observed and calculated CD curves agree in their general shapes to each other, though the latter curve lacks the component near at 20,000 cm^{-1} and there are some differences in the intensities. From this fact, the absolute configuration of the isomer-ii of cis(N)-[Co(β-alada)(gly)]$^-$ complex can be assigned to Z, and the isomer-iii to X.

The relative configuration with respect to the chelate ring arrangement of β-alada between the u-trans(N)- and u-cis(N)-[Co(β-alada)(gly)]$^-$ complexes and the corresponding complexes with (S)-ala or (S)-pro ligands has been confirmed as described above. On this basis, the absolute configurations of the β-alada complexes with (S)-ala and (S)-pro can be determined as shown in Table II.

III-7. Relative stability of complexes.

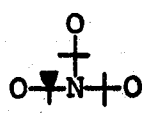
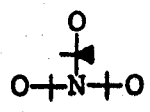
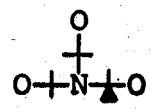
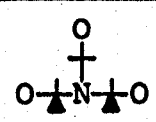
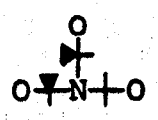
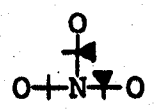
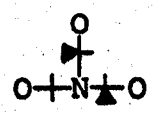
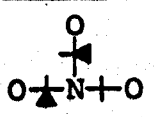
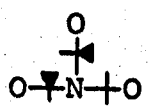
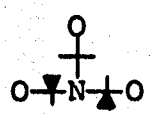
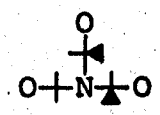
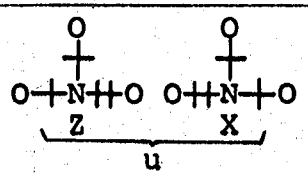
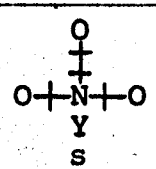
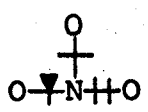
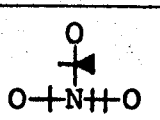
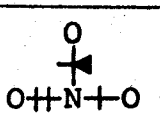
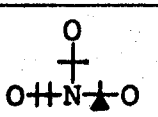
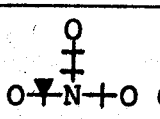
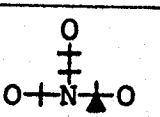
The stereoselectivity between the stereoisomers possible for a complex has been observed for a large number of cobalt(III) complexes and the relationships between stereoselectivities and the molecular structures of the isomers have been widely investigated.[54,108,115-128] In general, the relative stabilities of the isomers are experimentally evaluated from the isomer distribution at equilibrium and the equilibration is established by a treatment in the presence of activated charcoal in a solution.[122-128]

In the preparation of present complexes, which is the direct method from cobalt(II) salt, the stereoselective formations were observed between the possible isomers, trans(N) and cis(N) isomers and arrangement isomers. However, this preparation method is not at an equilibrium condition because of the absence of activated charcoal. The X-trans(N)- and cis(N)-$[Co((S)\text{-alada})(gly)]^-$ complexes were separately treated with activated charcoal in water at 70° for 1 hr (Experimental Section I-4). The column chromatographic separation and subsequent electronic absorption and CD measurements indicated that the products from both complexes consisted of essentially the same composition. Namely, the contents of the trans(N) and cis(N) isomers were quite similar, that is, about 92 and 1 % respectively based on the complex used for the equilibrium experiment. Furthermore, the CD spectra of the trans(N) eluates from both of the separations were identical to each

other and the same relationship was observed for the cis(N) eluates. On the other hand, when the Y-trans(N)-[Co((S)-alada)(gly)]$^-$ complex was treated under the same condition, the absorption and CD spectra of the reaction mixture were almost identical with those from the corresponding X-trans(N) or cis(N) isomer. These observations indicate that the equilibration between the isomers possible for the (S)-alada complex is established with the present treatment with activated charcoal.

The equilibration of the [Co(N-O_3)(gly)]$^-$ type complexes, where N-O_3 = (S)-alada, (R,S)-alaipa, (S,S)-alaipa, β-alada, or (S)-alapa, was carried out by use of the trans(N) complexes which were obtained predominantly in this work (Section I-4). In each of these gly complexes, the contents of the isomers in equilibrium mixtures were examined qualitatively and from the results for the trans(N) isomers the relative stabilities of the arrangement isomers are estimated as summarized in Table XII. In all cases, the equilibration lay to one isomer, which is trans(N) isomer and corresponds to "most stable" isomer in Table XII. The most stable isomers were obtained as pure crystals in the range of 58 - 91 % yields (based on the complex used to the equilibrium experiment) from the equilibrium mixtures. The desired complexes in the remainder were mostly trans(N) isomer, and the cis(N) isomer was contained in very samll amount or not contained as described below. Thus, the presence of one more arrangement isomer of trans(N) for each of the (S)-alada and (S,S)-alaipa and β-alada complexes

Table XII. Relative Stability of the Arrangement Isomers of trans(N)-$[Co(N\text{-}O_3)(gly)]^-$ Complexes

N-O_3	Most stable	Less stable	Unstable[a)]
(S)-alada	 X	 Y	 Z
(R,S)-alaipa	 X_SZ_R		 X_RZ_S  X_SY_R  Y_SZ_R  Y_RZ_S  X_RY_S
(S,S)-alaipa	 XY	 XZ	 YZ
β-alada	 u	 s	
(S)-alapa	 X_SZ_6		 Y_SZ_6  Y_SX_6  Z_SX_6  X_SY_6  Z_SY_6

a) Existence of these isomers was not recognized.

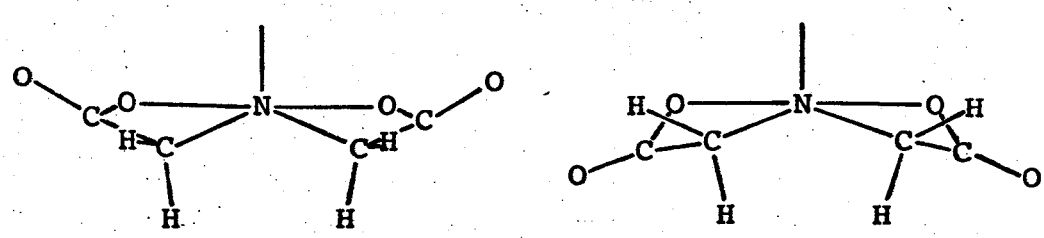
was recognized. In this work, the less stable isomers of the former two complexes were obtained from the equilibrium mixture (see Experimental Section). For the trans(N) isomers of the present gly complexes, the existence of any arrangement isomer other than the isomers mentioned here could not be recognized.

The cis(N) isomers were separated from the remainder by ion-exchange chromatography. In all the gly complexes, the contents of the cis(N) isomers in the equilibrium mixture were estimated to be less than 2 % (based on the complex), and each of the cis(N) eluates consists mostly of the arrangement isomer obtained predominantly in the preparation in this work, except for the (R,S)-alaipa complex in which case no existence of the cis(N) isomer was recognized. This observation indicates that the most stable arrangement isomer is common in the trans(N) and cis(N) isomers for each of the gly complexes, except for the (R,S)-alaipa complex for which such an estimation is impossible.

The trans(N)-$[Co(N\text{-}O_3)(gly)]^-$ type complexes with (S)-alada, (R,S)- and (S,S)-alaipa as a $N\text{-}O_3$ are C-methyl substituted derivatives of the trans(N)-$[Co(nta)(gly)]^-$ complex. In the nta of the nta complex, there are three different protons, i.e., axial and equatorial protons (on the in-plane rings) and out-of-plane protons (Fig. 4). The three arrangement isomers possible for the (S)-alada complex correspond to the derivatives in which each one of the three different nta protons are substituted by one methyl group. The stereoselectivity observed for the

(S)-alada complex shows that the relative stabilities of the arrangement isomers increases in the following order of the positions of methyl substituents, axial < out-of-plane < equatorial. This correlation also explains the results of stereoselectivities for the (R,S)- and (S,S)-alaipa complexes with two methyl groups as can be seen in Table XII, although is not applicable for the X_RY_S-, X_SY_R- and X_RZ_S-isomers of the (R,S)-alaipa complex because of a severe steric hindrance between the two methyl groups in the complex (vide infra). Thus, it is found that there is a reasonable correlation as above between the stabilities of isomers and the positions of methyl groups in these complexes.

Furthermore, the extent of isomer distribution observed for these complexes showed that the methyl group in the equatorial position remarkably increase the relative stability of the isomers compared with those in the other positions. Similar relationship was observed for the corresponding cis(N) complexes. From a molecular model examination, an explanation for these observations can be offered for the simplest (S)-alada complex as follows. When the nta moiety in the parent nta complex is considered, the conformation of the two in-plane rings is considerably flexible and two forms as shown in Fig. 42 can be considered as extreme conformations. In the (S)-alada complex, steric interaction should be considered mainly between the substituted methyl group and one proton of the methylene group on the neighbouring ring. Such an interaction is



I II

Fig. 42. Two extreme conformational forms of the in-plane chelate rings of coordinated nta (pictured looking along the N-Co bond).

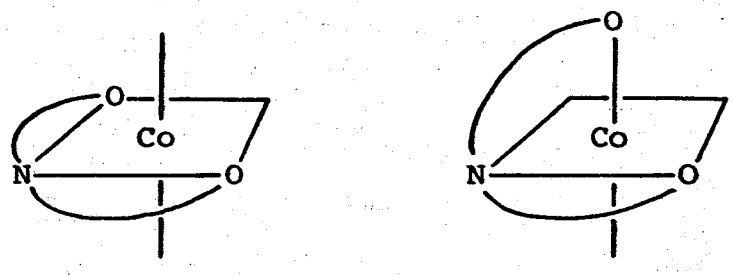
significantly affected by whether form I or II was taken for the complex. The interaction is very similar between the three arrangement isomers in form II, while it is more relieved in the X-isomer than the other isomers in form I. Furthermore, the interaction between the methyl group and other atoms in the complex is also very similar between the three isomers in form II, while in form I the interaction is probable only for the Y- and Z-isomers; in the Y-isomer the methyl group interacts with the carbonyl group of one in-plane ring and in the Z-isomer with the atoms in the apical position of the gly ligand (oxygen atom and amino hydrogen atoms for the trans(N) and cis(N) isomers respectively). Thus, it may be reasonable to consider that the X-isomer of the (S)-alada complex takes the conformation near to form I and is more stabilized than the other isomers.

The preference of form I may be supported from the following consideration with respect to the conformation of the nta complex. The X-ray diffraction studies of a number of metal complexes with chelated α-aminocarboxylate have been reported and their results showed that the conformation of the five-membered chelate ring of the α-aminocarboxylate vary in large extent between various complexes.[50] Such a large variation has been pointed out to be due to the low tortional barrier to rotation about the C-C bond in the chelate ring.[2] Form I and II of the coordinated nta differ mainly in the tortional angle about the C-C bond in the in-plane rings. Accordingly, it is expected that there is no significant difference in the conformational energy between the two forms. However, it is noted in the in-plane rings that the tortional rotation about C-N bond is strongly restricted because of the rigid span of the quadridentate nta lignd, differing from the cases of simple α-aminocarboxylato chelates. For this reason, form II is forced nearly to the eclipsed conformation with respect to the C-N bond, while form I is nearly in the staggered conformation. From these situations, it is considered that the nta coordinates preferably in the conformation near to form I.

As mentioned above, severe steric hindrance exist between the two methyl groups in the X_RZ_S-, X_SY_R- and Y_SZ_R-isomers of the (R,S)-alaipa complex. From this reason, the isomer obtained for each of the trans(N) and cis(N) (R,S)-alaipa complexes was confirmed to be X_SZ_R-isomer,

not but X_RZ_S-isomer (Section II-3-2-(2)). In the X_RZ_S-isomer, the two methyl groups are in the most remote position when the isomer takes form I (Fig. 42). Even in this conformation the distance between the two carbon atoms of methyl groups is estimated to be approximately 2.1 Å. This situation indicates that steric hindrance enough to deny the possibility of the X_RZ_S-isomer exists between the two methyl groups regardless of the variation of conformation. On the other hand, the two methyl groups of the X_SZ_R-isomer have no noticeable steric interaction with other atoms in the complex, particularly when the isomer take form I.

The equilibrium experiment of the $[Co(\beta\text{-alada})(gly)]^-$ complex showed in both of the trans(N) and cis(N) isomers that the u-isomer is more stable than the s-isomer. The β-alada ligand forms two five-membered rings and one six-membered one by coordination to the cobalt ion. Many cotahedral metal complexes containing O,N,O-tridentate ligands, such as iminodiacetate(ida)[56,74,82,84,87,88,101,109,129-131] and sarcocinate-N-monoacetate (sarmp),[56,74,87,88] have been reported. In these tridentate ligands, two coordination forms, meridional and facial, are possible as shown in Figs. 43. The ida-like ligands form two five-membered chelate rings, while the sarmp-like ligands form each one of five- and six-membered rings. From the studies of stereoselectivity for these complexes, it has been found that the ida-like ligands strongly prefer the facial coordination to the meridional one and that the sarmp-like



meridional facial

Fig. 43. Two possible coordination forms of O,N,O-tridentate ligand.

ligands are possible to take both the meridional and facial coordinations.[56,74,84,87,88,101,109,129,131] As indicated by the workers, these situations may be expected by the facts that in the ida-like ligands the meridional coordination is very strained in the C-N-C angle,[109] while the facial one is relatively strain free, and that the meridional coordination in the sarmp-like ligands is in less strained circumstances than that in the ida-like ligands.[74,87] When these stereochemical relationships are applied for the present β-alada complex, it is indicated that the s-isomer is less stable than the u-isomer because the less prefered meridional coordination of the two five-membered rings exists in the former isomers. Furtheremore, it is noted from a molecular model examination that the out-of-plane six-membered ring in the s-isomer differs in the steric circumstances from the six-membered ring in the facial coordination of the complexes with the sarmp-like ligands.

Namely, the six-membered ring of the sarmp-like ligands can take relatively freely a prefered conformation, probably, chair or twisted-boat one. On the other hand, it seems difficult in the case of the s-isomer to take such a conformation because the coplanarity of the O-Co-N-C atoms of the six-membered ring is strongly required owing to the existence of the two in-plane rings. This also indicates that the s-isomer is less stable. These considerations well explain the difference of stability between the u- and s-isomers observed for the β-alada complex.

For all of the $[Co(N\text{-}O_3)(gly)]^-$ type complexes mentioned above, the equilibrium experiments indicate that the trans(N) isomer is extremely stable than the cis(N) one. The same was observed for the corresponding nta complex; the extents of the trans(N) and cis(N) isomers in the equilibrium mixture were of about 93 and 1 % respectively (based on the complex used for the equilibrium experiment). From a molecular model examination, it seems that these observations are related to the interligand steric interaction between the nitrilo-tricarboxylato and aminocarboxylato ligands in a complex. The apical site with respect to the in-plane rings of nitrilotricarboxylato ligands is clearly in sterically more crowded circumstances than the other coordination site, and of two coordination groups of gly ligand the amino group is bulkier than the carboxyl donor oxygen atom. Thus, it is expected that the steric interaction is stronger in the cis(N) isomer than in the trans(N) one.

In the cis(N) nta complex, for example, the considerable interaction is probable regardless of the variation of the chelate ring conformation in the complex; the amino protons of gly interact with the axial protons of the in-plane rings of nta in form I and with the carbonyl carbon atoms of the in-plane rings in form II (Fig. 42). In the XZ-cis(N) (S,S)-alaipa complex, which has a methyl group in the axial position, there is severe steric interaction between the methyl group and the amino protons of gly ligand. In Section II-3-4, it was suggested that the anomalous CD behavior of this complex is caused by this steric interaction.

It is of interest to compare the stereochemistry of the $[Co(nta)(gly)]^-$ complex with that of the $[Co(taa)(gly)]^-$ (taa = tris(2-aminoethyl)amine) complex,[82,132] because their chelate skeltons are very similar to each other. The structure of the coordinated taa is shown in Fig. 44. The

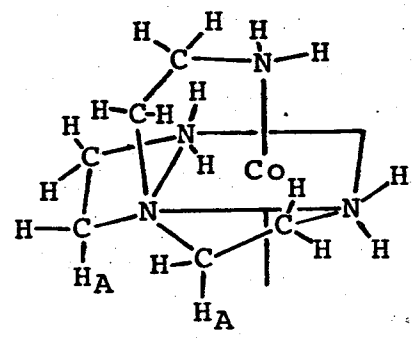


Fig. 44. Structure of the coordinated taa.

two isomers are possible for the taa complex depending on the coordination mode of the gly ligand in analogy with the nta complex. It has been found that one isomer of the taa complex, which coordinates the carboxyl oxygen atom of gly in the apical position, yielded stereoselectively in a peptide cleavage reaction.[82] From the X-ray diffraction and energy minimization analyses, it has been pointed out that the low stability of another isomer, which coordinate the amino group in the apical position, was caused mainly by the steric interaction between the amino protons of gly and the H_A protons of taa (Fig. 44).[132] Such an interation is very similar to the interaction pointed out for the cis(N) isomer of nta complex which take the conformation of form I.

In spite of the low stability, the cis(N) isomers were obtained in relatively good yields in the present preparation. This situation is explained by considering that the cis(N) isomer is more rapidly formed than the trans(N) isomer in the preparation. In fact, when the reaction time was prolonged than that adopted in the present procedure the yield of the cis(N) isomer decreased with the increase in reaction time. As a typical example, the % yield of the trans(N) and cis(N) isomers versus reaction time for the $[Co(nta)(gly)]^-$ complex in the present preparation procedure is shown in Fig. 45. Similar behaviors were observed in process of the preparation of all the complexes in this work except for the complexes with sar and (S)-pro. A molecular model examination shows that the steric interaction between the in-plane rings of the nitrilotricarboxylate and

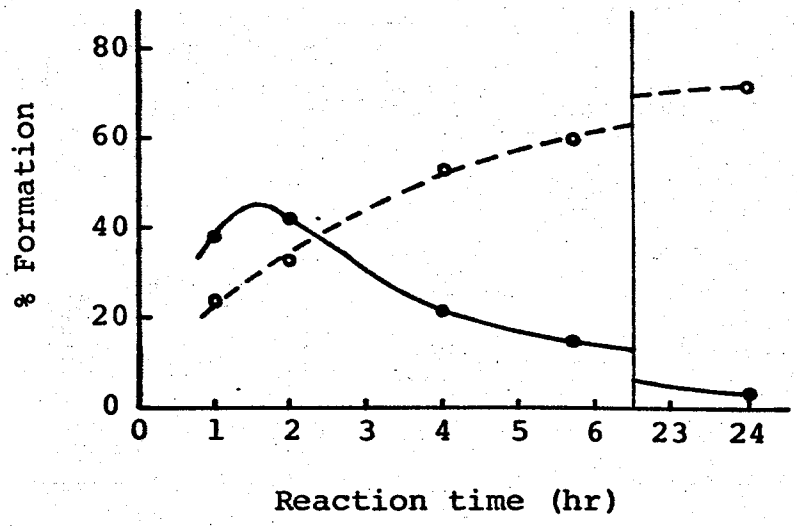


Fig. 45. Plots of % formation versus reaction time in the preparation of $[Co(nta)(gly)]^-$ complex: trans(N) isomer (--∘--), cis(N) isomer (—•—).

the aminocarboxylate is remarkable in the complexes with sar or (S)-pro, which has the substituent on the nitrogen atom. For the nta complex of sar, and the nta, (S)-alada and β-alada complexes of (S)-pro, as expected, the formation of the cis(N) isomer was not recognized regardless of the reaction time.

Concluding Remarks

1) About 60 new complexes of trans(N)- and cis(N)-(nitrilotricarboxylato)(aminocarboxylato)cobalt(III) type have been prepared. Except for nta, the nitrilotricarboxylato ligands, (R)- and (S)-alada, (R,S)- and (S,S)-alaipa, β-alada, and (S)-alapa, have nonidentical feet and in the complexes with these ligands several stereoisomers are possible with respect to the arrangement of the three feet. The stereoisomers have been separated by optical resolution, fractional crystallization, or ion-exchange column chromatography. The structures of isomers have been assigned on the basis of electronic absorption and PMR spectra, and from the stereochemical consideration.

2) From the electronic absorption behavior, the nitrilotricarboxylato ligands in this work can be arranged in a series according to decreasing D_q values: (R,S)-alaipa > (S,S)-alaipa > (S)-alada > nta > (S)-alapa > β-alada.

3) The CD curves of the optically acitve complexes in this work are contributed from the vicinal effect or the arrangement effect or a combination of them. In the complexes having two different optically active ligands, such as X-[Co((S)-alada)((S)-ala)]$^-$ and Z-[Co((R)-alada)-((S)-ala)]$^-$ complexes, it has been found that the CD contributions from the two kinds of vicinal effects are separable and almost additive. Furthermore, such a

additivity rule holds also between the vicinal and arrangement contributions, for example, as observed for the X- and Z-[Co(β-alada)((S)-ala)]$^-$ complexes. The arrangement effect is a novel source for the optical activity and its contribution to the CD is intermediate in the intensity between those for the configurational and vicinal effects. The CD curve of the $X_S Z_6$-[Co((S)-alapa)(gly)]$^-$ complex can be reproduced by summing up those of the X-[Co((S)-alada)(gly)]$^-$ and Z-[Co(β-alada)(gly)]$^-$ complexes. The CD curve of the trans(N)-[Co(nta)((S,S)-achc)]$^-$ complex is reproduced well by subtracting that of the trans(N)-[Co(nta)((R)-α-Me-β-ala)]$^-$ complex from that of the trans(N)-[Co(nta)((S)-β-Me-β-ala)]$^-$ complex. Such a relationship holds also at least for the splitting pattern for some other complexes with the ligands having two asymmetric carbon atoms in a ligand, though there is considerable deviation in the intensity.

4) The X- and Z-isomers of each of the trans(N)- and cis(N)-[Co(β-alada)(gly)]$^-$ complexes are antipodal to each other. The absolute configurations of these complexes have been determined on the basis of the CD spectra by connecting those with the corresponding (S)-alada and (S)-alapa complexes. Furthermore, the absolute configurations of the β-alada complexes with optically active aminocarboxylate, (S)-ala or (S)-pro, instead of gly, were determined by applying the additivity of the vicinal and arrangement CD contributions mentioned in 3).

5) For the $[Co(N\text{-}O_3)(gly)]^-$ type complexes with the nitrilotricarboxylato $(N\text{-}O_3)$ ligands, the relative stability of the isomers has been examined by the equilibrium experiment on activated charcoal. The relative stability of the arrangement isomers in the (S)-alada, (R,S)- and (S,S)-alaipa complexes can be related to the "position" where the methyl substituent is situated and the stability of the isomers increases in the following order: axial (in-plane) < out-of-plane < equatorial (in-plane). In the β-alada and (S)-alapa complexes, the u-isomer is more stable than the s-isomer, and then in all complexes the trans(N) isomer are much more stable than the cis(N) isomers. These observations can be explained from a molecular model examination by considering the intraligand or interligand steric interaction in a complex.

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