Metal Complexes of Peptides. II.[1] Circular Dichroism Spectra and Absolute Configuration of Bis(dipeptidato)cobalt(III) Complexes

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Type $[Co(dipeptidato)_2]^-$ complexes (dipeptidato denotes dianions of glycylglycine, -β-alanine, -L-alanine, and -L-leucine, β-alanylglycine and -L-alanine, L-alanylglycine and -β-alanine, L-leucylglycine, and L-prolylglycine) and the complex $[Co(gly\text{-}gly)(L\text{-}pro\text{-}gly)]^-$ were prepared by a method using lead dioxide as an oxidizing agent, and these complexes were separated into two diastereomers or enantiomers by column chromatography. The absolute configurations of the optical isomers were determined on the basis of their circular dichroism patterns in the ligand transition region.

A great number of metal complexes with various peptides have been studied as enzymatic metal complexes.[2-14] However, coordination behaviors of peptides to metal ions are delicately different among metals and peptides. It is very interesting to characterize systematically metal complexes with various peptides. It is well-known that cobalt(III) ion produces stable peptide complexes.[1,3,13-20]

According to X-ray crystallographic studies of bis(glycylglycinato)cobalt(III) complex,[21,22] two glycylglycinates are coordinated to cobalt(III) in the meridional (mer) configuration as terdentate ligand. In our previous studies concerning mixed-ligand complexes containing both dipeptidate and iminodiacetate or *N*-methyliminodiacetate,[1,23] it was demonstrated by ^1H and ^{13}C NMR data that the dipeptidate coordinates to cobalt(III) in mer disposition.

Recently, Boas *et al.*[20] studied several preparative methods for type $[Co(\alpha_1\text{-}\alpha_2)_2]^-$ complexes ($\alpha_1\text{-}\alpha_2$ denotes dianion of dipeptide) and their configurations by ^1H NMR, circular dichroism (CD) spectroscopy in the d-d transition region, and column chromatography.

In the present paper, we will describe the preparation of new type bis(dipeptidato)cobalt(III) complexes containing L-proline or β-alanine residue and discuss their absolute configurations on the basis of absorption and CD spectral data.

Experimental

Ligands. Glycyl-β-alanine (H_2gly-β-ala), β-alanylglycine (H_2β-ala-gly), L-alanyl-β-alanine (H_2L-ala-β-ala), and β-alanyl-L-alanine (H_2β-ala-L-ala) were prepared by the method described in our previous paper.[1] Glycylglycine (H_2gly-gly), glycyl-L-leucine (H_2gly-L-leu), L-leucylglycine (H_2L-leu-gly) were obtained commercially from Protein Research Foundation, glycyl-L-alanine (H_2gly-L-ala) and L-alanylglycine (H_2L-ala-gly) from Fluka Chemical Company, and L-prolylglycine (H_2L-pro-gly) from Sigma Chemical Company. These purchased dipeptides were used without further purification.

Preparation of Complexes. Two Diastereomers of Potassium Bis(L-prolylglycinato)cobaltate(III), K[Co(L-pro-gly)$_2$]: L-Prolylglycine (3.44 g, 0.02 mol) was dissolved in 20 cm^3 of water, and the solution was adjusted to pH 9—9.5 with a 1 M† NaOH solution. An aqueous solution containing cobalt(II) chloride hexahydrate (2.37 g, 0.01 mol) in 10 cm^3 of water was added drop by drop to the above peptide solution, keeping the pH of the solution at *ca.* 9 with a NaOH solution. The mixed solution was oxidized with lead dioxide (5 g) at 40 °C for 1 h with stirring. The resulting solution was filtered to remove insoluble materials, and the purple filtrate was chromatographed on a QAE-Sephadex A-25 column (4.7 cm × 90 cm, Cl^- form). The positively charged and neutral complexes were removed by flushing the column with water. The adsorbed band was separated into violet and purple bands by elution with an 0.05 M KCl solution. Each eluted solution was concentrated to a small volume by a rotary evaporator at 35—40 °C. A large amount of methanol was added to the concentrated solution, and then potassium chloride which deposited was removed by filtration. The filtrate was concentrated again to a few milliliters, and the residual KCl in the solution was removed completely by using a Sephadex G-10 column. The early eluted isomer ($R(C_2)$-K[Co(L-pro-gly)$_2$]·3H_2O) was crystallized by addition of ethanol to the concentrated aqueous solution and by keeping the solution in a refrigerator for a few days. The crystals were filtered and washed with 90% ethanol, 99.5% ethanol, and then acetone. The late eluted isomer ($S(C_2)$-K[Co(L-pro-gly)$_2$]·3.5H_2O) was isolated as needle crystals by addition of acetone to the methanolic solution and by keeping the solution in a refrigerator for a few days. The crystals were filtered and washed with acetone. Both complexes were dried over calcium chloride in a desiccator under reduced pressure.

The diastereomers of other bis(dipeptidato)cobalt(III) complexes with L-alanyl-β-alaninate, β-alanyl-L-alaninate, glycyl-L-leucinate, L-leucylglycinate, glycyl-L-alaninate, or L-alanylglycinate were prepared and separated by the same procedure as that used for the complex K[Co(L-pro-gly)$_2$] described above, except that the pH of the reaction solutions containing the dipeptide ligands with β-alanyl or β-alanine residue was adjusted to 8—8.5. Crystallization of these complexes was carried out from the concentrated aqueous solutions by addition of methanol or acetone.

Two Diastereomers of Potassium(glycylglycinato)(L-prolylglycinato)cobaltate(III), K[Co(gly-gly)(L-pro-gly)]: The preparation and chromatographic separation for the diastereomers of this mixed ligand complex were carried out by the method similar to that used for the complex K[Co(L-pro-gly)$_2$], except that a mixture of glycylglycine (1.32 g, 0.01 mol) and L-prolylglycine (1.72 g, 0.01 mol) was used instead of L-prolylglycine. However, in this case an adsorbed band was separated into five ([Co(L-pro-gly)$_2$]$^-$ ($R(C_2)$-isomer), [Co(gly-gly)(L-pro-gly)]$^-$ ($R(C_2)$-isomer), [Co(gly-gly)$_2$]$^-$, [Co(gly-gly)(L-pro-gly)]$^-$ ($S(C_2)$-isomer), and [Co(L-pro-gly)$_2$]$^-$ ($S(C_2)$-isomer)) by continuous development using six QAE-Sephadex columns (4.7 cm × 90 cm, Cl^- form). Two diastereomers (second and forth eluates) of the mixed ligand complex were

† 1 M = 1 mol dm^{-3}.

Table 1. Analytical data of the bis(dipeptidato)cobalt(III) complexes

Complex	Elution order	C(%)		H(%)		N(%)	
		Found	(Calcd)	Found	(Calcd)	Found	(Calcd)
$Ba[Co(gly\text{-}\beta\text{-}ala)_2]_2\cdot 4H_2O$		26.50	(26.58)	4.44	(4.46)	12.22	(12.40)
$K[Co(\beta\text{-}ala\text{-}L\text{-}ala)_2]\cdot 2H_2O$	1	32.23	(32.00)	5.58	(5.37)	12.59	(12.44)
$K[Co(\beta\text{-}ala\text{-}L\text{-}ala)_2]\cdot 4H_2O$	2	29.97	(29.63)	5.61	(5.81)	11.16	(11.52)
$K[Co(L\text{-}ala\text{-}\beta\text{-}ala)_2]\cdot 3H_2O$	1	30.67	(30.77)	5.61	(5.60)	12.07	(11.96)
$K[Co(L\text{-}ala\text{-}\beta\text{-}ala)_2]\cdot 1.5H_2O$	2	32.65	(32.67)	5.22	(5.25)	12.46	(12.69)
$K[Co(L\text{-}pro\text{-}gly)_2]\cdot 3H_2O$	1	33.86	(34.15)	4.92	(5.32)	11.49	(11.38)
$K[Co(L\text{-}pro\text{-}gly)_2]\cdot 3.5H_2O$	2	33.69	(33.54)	5.40	(5.43)	10.76	(11.17)
$K[Co(gly\text{-}gly)(L\text{-}pro\text{-}gly)]\cdot 2.5H_2O$	1	30.02	(29.80)	4.97	(4.77)	12.67	(12.63)
$K[Co(gly\text{-}gly)(L\text{-}pro\text{-}gly)]\cdot 4H_2O$	2	28.14	(28.09)	4.91	(5.14)	12.04	(11.91)

isolated as needle crystals of reddish-purple color.

Barium Bis(glycyl-β-alaninato)cobaltate(III) Tetrahydrate and Potassium Bis(β-alanylglycinato)cobaltate(III) Monohydrate, $Ba[Co(gly\text{-}\beta\text{-}ala)_2)]_2\cdot 4H_2O$ and $K[Co(\beta\text{-}ala\text{-}gly)_2]\cdot H_2O$:[1] These complexes were obtained by the method similar to that used for $K[Co(L\text{-}pro\text{-}gly)_2]$. However, since the potassium salt of bis(glycyl-β-alaninato)cobaltate(III) complex was hygroscopic, it was converted to the barium salt using a small SP-Sephadex C-25 column (Ba^{2+} form).

The analytical data of the newly prepared complexes are listed in Table 1.

Partial Resolution of $[Co(gly\text{-}\beta\text{-}ala)_2]^-$. Racemic $Ba[Co(gly\text{-}\beta\text{-}ala)_2]_2\cdot 4H_2O$ (*ca.* 0.2 g) was dissolved in a small amount of water and loaded on a QAE-Sephadex column (4.7 cm × 90 cm, Cl^- form). An adsorbed band was developed with an 0.1 M L-histidinium chloride solution. After the development had been repeated about twenty-five times using a circulating micropump, the broadened band was eluted fractionally. The first and last fractions exhibited optical rotations of (−) and (+) signs at 589 nm, respectively. Each fraction was concentrated by a rotary evaporator until crystals of L-histidinium chloride appeared. The L-histidinium chloride was removed by filtration, and methanol was added to the filtrate to deposit out the residual L-histidinium chloride. After the removal of L-histidinium chloride, the methanolic solution was evaporated again almost to dryness. The resulting residue was dissolved in a small amount of water and chromatographed to remove completely the L-histidinium chloride and to convert the complex to the potassium salt using a small SP-Sephadex column (K^+ form). The crude complex was purified using a Sephadex G-10 column. The CD spectra of the optically active complexes were measured without isolating them as crystals, and the $\Delta\varepsilon$ values of the complexes were calculated from the absorption spectral data of the racemic complexes. The main CD band in the first absorption region showed negative and positive signs for the two isomers from the first and last fractions, respectively.

Partial resolution of racemic $[Co(\beta\text{-}ala\text{-}gly)_2]^-$ and $[Co(gly\text{-}gly)_2]^-$ was also carried out by the method similar to that used for the complex $[Co(gly\text{-}\beta\text{-}ala)_2]^-$. However, in the case of the complex $[Co(\beta\text{-}ala\text{-}gly)_2]^-$ the $(+)_{589}$- and $(-)_{589}$-isomers were obtained from the first and last fractions, respectively, and the elution order of the enantiomers was opposite to the cases of the complexes $[Co(gly\text{-}\beta\text{-}ala)_2]^-$ and $[Co(gly\text{-}gly)_2]^-$.

Measurements. The absorption and CD spectra were measured by a Hitachi 557-type spectrophotometer and a JASCO J-22 spectropolarimeter, respectively.

Results and Discussion

Boas *et al.*,[20] trying seven preparative methods for type $[Co(dipeptidato)_2]^-$ complexes, adopted the method starting from cobalt(III) hydroxide oxide. In the present study, however, we used the preparative method based on oxidizing cobalt(II) by lead dioxide, which is not included in the above seven methods. The present method is featured by rapid reaction, minor by-products, comparable yields of two diastereomeric complexes, and prevention of the hydrolysis of dipeptide.

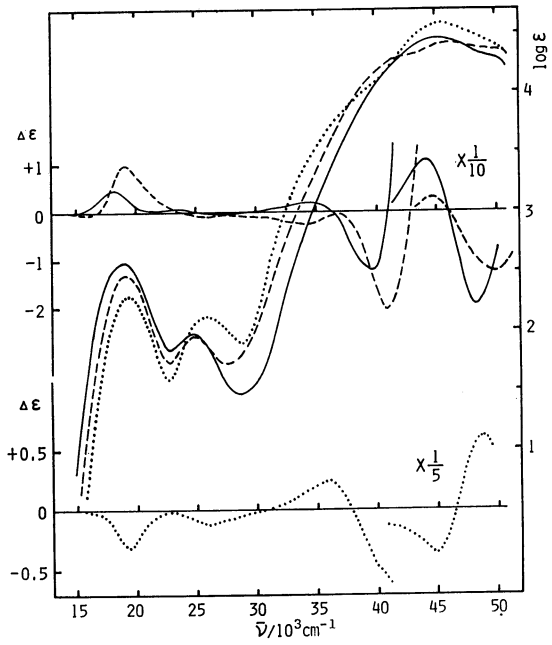

Fig. 1. Absorption (racemate) and CD (last fraction resolved by column chromatography) spectra: $[Co(gly\text{-}gly)_2]^-$ (——), $[Co(gly\text{-}\beta\text{-}ala)_2]^-$ (------), and $[Co(\beta\text{-}ala\text{-}gly)_2]^-$ (····).

Absorption Spectra. Absorption spectral data of the complexes bis(dipeptidato)cobalt(III) examined are summarized in Table 2. These complexes show a slight difference in their spectral behaviors. Figure 1 shows a comparison of absorption curves among the complexes $[Co(gly\text{-}gly)_2]^-$, $[Co(gly\text{-}\beta\text{-}ala)_2]^-$, and $[Co(\beta\text{-}ala\text{-}gly)_2]^-$. The first and second absorption maxima shift to the higher energy side in the order of gly-gly, gly-β-ala,

TABLE 2. ABSORPTION DATA OF M[Co(dipeptidato)$_2$] COMPLEXES

	Complex	Elution order	$\bar{\nu}_{max}$[a] (log ε) d-d Transition 1st band	d-d Transition 2nd band	Ligand transition band	$\varepsilon_I/\varepsilon_{II}$[b]
1	K[Co(gly-gly)$_2$]·1.5H$_2$O		18.94(2.57)	24.69(1.97)	45 25(4 45)	1.30
2	Ba$_{0.5}$[Co(gly-β-ala)$_2$]·2H$_2$O		19.16(2.48)	24.88(1.96)	46.30(4.41)	1.27
3	K[Co(β-ala-gly)$_2$]·H$_2$O		19.38(2.30)	25.84(2.13)	45 46(4 57)	1 08
4	S(C$_2$)-K[Co(gly-L-ala)$_2$]·H$_2$O	1	18.98(2 60)	24.75(1.94)	44 84(4 44)	1 34
5	R(C$_2$)-K[Co(gly-L-ala)$_2$]·2.5H$_2$O	2	18.90(2.59)	24.75(2 07)	45 25(4 48)	1 25
6	S(C$_2$)-K[Co(L-ala-gly)$_2$]·1.5H$_2$O	1	18.98(2.63)	24 88(2 01)	45 45(4 51)	1 31
7	R(C$_2$)-K[Co(L-ala-gly)$_2$]·2.5H$_2$O	2	18.90(2.59)	24.69(2 07)	45 25(4 49)	1 25
8	S(C$_2$)-K[Co(gly-L-leu)$_2$]·3H$_2$O	1	19.23(2.51)	25.51(2 03)	46.51(4.31)	1 24
9	R(C$_2$)-K[Co(gly-L-leu)$_2$]·3.5H$_2$O	2	19.16(2.58)	25.00(2.14)	46 30(4.43)	1 21
10	S(C$_2$)-K[Co(L-leu-gly)$_2$]·5.5H$_2$O	1	19.16(2.63)	25.25(2 02)	46 84(4 50)	1.30
11	R(C$_2$)-K[Co(L-leu-gly)$_2$]·4H$_2$O	2	19.05(2 62)	25 00(2 10)	46 51(4 50)	1 25
12	S(C$_2$)-K[Co(β-ala-L-ala)$_2$]·2H$_2$O	1	19.38(2 27)	26 32(1 99)	45 05(4 50)	1 14
13	R(C$_2$)-K[Co(β-ala-L-ala)$_2$]·4H$_2$O	2	19.31(2 28)	25 97(2 30)	45 05(4 55)	0 99
14	S(C$_2$)-K[Co(L-ala-β-ala)$_2$]·3H$_2$O	1	19 23(2 57)	25 00(2 06)	46 08(4 47)	1 25
15	R(C$_2$)-K[Co(L-ala-β-ala)$_2$]·1.5H$_2$O	2	19.16(2.39)	25 00(1 90)	46 51(4 36)	1 24
16	R(C$_2$)-K[Co(L-pro-gly)$_2$]·3H$_2$O	1	18.25(2 64)	24.10(2 00)	44 25(4 47)	1 32
17	S(C$_2$)-K[Co(L-pro-gly)$_2$]·3.5H$_2$O	2	18.55(2 66)	24 39(2 07)	44 84(4 53)	1.29
18	R(C$_2$)-K[Co(gly-gly)(L-pro-gly)]·2.5H$_2$O	1	18.80(2.56)	24 63(2 04)	44 64(4 47)	1 25
19	S(C$_2$)-K[Co(gly-gly)(L-pro-gly)]·4H$_2$O	2	18.73(2 62)	24 57(2 02)	44 84(4 46)	1.30

a) In the unit of 10^3 cm^{-1}. b) Molar extinction coefficient ratio of the first and second absorption maxima.

and β-ala-gly complexes. Such a shift of the maximum positions may be attributed to a delicate difference in the ligand field strength of coordinated dipeptidates or in the stability of dipeptidato complexes; it follows that the six-membered chelate ring (β-alanyl ring) in the N-terminal side is less strained than the five-membered chelate ring (glycyl ring). The order of the stability of these dipeptidato complexes quite agrees with that established by Nakahara *et al.* for copper(II) complexes of dipeptides[24] and tripeptides[25] containing glycine and/or β-alanine residues.

Difference between the type [Co(β-ala-α_2)$_2$]$^-$ and [Co(α_1-β-ala)$_2$]$^-$ or [Co(α_1-α_2)$_2$]$^-$ (α denotes α-amino acid residue) complexes is also observed in the intensity ratio of the first to second absorption maximum ($\varepsilon_I/\varepsilon_{II}$) (Table 2). It is interesting that the $\varepsilon_I/\varepsilon_{II}$ ratios of the diastereomeric complexes indicate higher values for the early eluted isomers (S(C$_2$)-isomers) than for the late eluted ones (R(C$_2$)-isomers), except for the [Co(L-pro-gly)$_2$]$^-$ complexes.

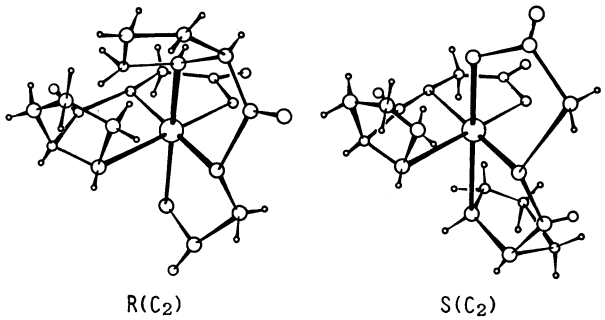

Fig. 2. Possible structures of two diastereomers in [Co(L-pro-gly)$_2$]$^-$ complex.

Figure 2 shows the two diastereomeric structures of the complex [Co(L-pro-gly)$_2$]$^-$. With the notation, proposed by Boas *et al.*[20] for the bis(dipeptidato)cobalt(III) type complexes, applied to the case of complex [Co(L-pro-gly)$_2$]$^-$, a diastereomer assuming the R(C$_2$) configuration has a larger steric compression between the two pyrrolidine rings in the complex molecule than the other assuming the S(C$_2$) configuration. As shown in Table 2, the first and second absorption maxima of the early eluted isomer (violet isomer) locate toward the longer wavelength side by as much as 300 and 290 cm^{-1}, respectively, than those of the late eluted isomer (purple isomer). Consequently, it is expected from these spectral behaviors that the former isomer assumes a structure of larger steric compression than the latter isomer, hence the configurations of the early and late eluted isomers can be assigned to R(C$_2$) and S(C$_2$), respectively.

Circular Dichroism Spectra and Absolute Configurations. The CD spectral data of all the complexes are listed in Table 3, and their absolute configurations and the elution order of the diastereomers are shown in Table 2. The CD spectra of the complexes examined may be divided into three band regions in the d-d transition range 15000—30000 cm^{-1}, the charge transfer range 30000—40000 cm^{-1}, and the ligand transition range 40000—50000 cm^{-1}. Figure 3 shows the CD curves of the two pairs of diastereomers in the complexes [Co(L-pro-gly)$_2$]$^-$ and [Co(gly-gly)(L-pro-gly)]$^-$. These diastereomers exhibit quite similar CD patterns in the first and second absorption regions. Therefore, in these cases it is difficult to assign their absolute configurations from their CD patterns only for the d-d transition region. On the other hand, the CD curves of the pair of diastereomers in the range of

TABLE 3. CD DATA OF M[Co(dipeptidato)$_2$] COMPLEXES

Complex	$\bar{\nu}_{ext}$[a] (log ε)				
	1st band region	2nd band region	Charge transfer band region		Ligand transition band region
1[b]	18.18(+0.41)	23.53(+0.04)	34.25(+0.18)	39.53(−1.25)	44.05(+11.00)
		27.32(−0.02)			48.08(−19.70)
2[b]	16.26(−0.012)	25.97(−0.07)	34.25(−0.27)	40.82(−2.07)	44.84(+2.94)
	19.17(+1.00)				50.00(−12.42)
3[b]	19.31(−0.31)	25.97(−0.12)	35.97(+0.23)	*ca.*40.0(−0.45)	44.84(−1.78)
					48.78(+3.00)
4	19.76(−4.127)	24.69(+0.618)	34.48(+0.426)	38.00(−0.350)	43.29(−16.59)
					49.50(+18.32)
5	17.39(+0.299)	25.64(−0.641)	35.34(+0.706)	38.76(+0.965)	47.17(−16.17)
	20.00(−1.911)				
6	19.72(−2.243)	25.84(+0.518)	31.25(+0.050)		43.86(−9.171)
					48.54(+18.66)
7	17.61(+1.857)	24.94(+1.795)	34.97(+2.082)	39.53(−2.588)	43.86(+12.88)
	20.08(−4.260)				48.08(−29.25)
8	19.27(−3.424)	26.32(−0.234)	33.56(+0.501)		42.74(−10.03)
					49.02(+15.81)
9	19.57(−3.035)	25.19(−0.900)	33.11(+0.307)	40.65(−2.479)	43.48(+1.024)
					46.73(−10.24)
10	19.76(−3.047)	25.45(+0.807)	34.22(+0.331)		43.10(−7.921)
					48.31(+13.50)
11	17.39(+1.598)	24.69(+1.612)	34.60(+2.310)	39.37(−2.700)	43.48(+10.67)
	19.80(−5.221)				47.62(−29.65)
12	19.05(−3.847)	25.97(−1.642)	32.47(+0.823)		44.05(−13.02)
	21.37(+0.905)				48.78(+5.923)
13	19.19(−2.273)	25.97(−0.839)	33.67(−0.574)	37.19(+1.146)	44.64(+4.788)
	21.28(+0.441)			40.82(−1.699)	48.31(−8.428)
14	16.53(+0.076)	25.71(+0.827)	33.67(+1.573)	37.59(−1.114)	44.25(−3.714)
	19.69(−5.419)			40.65(+0.801)	49.75(+33.87)
15	18.32(+1.480)	25.13(+0.638)	29.94(−0.120)	41.15(−7.727)	44.84(+13.97)
	20.37(−0.542)				49.75(−35.58)
16	17.27(+3.720)	24.15(+2.811)	29.59(−0.551)	38.46(−1.361)	42.19(+7.061)
	19.49(−3.589)		33.90(+2.015)		46.51(−28.24)
17	17.24(+1.933)	24.69(+1.481)	32.79(+0.174)	38.17(−2.730)	42.92(−16.41)
	19.72(−3.048)				47.17(+25.97)
18	17.67(+1.716)	24.51(+0.825)	29.85(−0.100)	39.06(−2.090)	43.10(+6.844)
	20.00(−1.298)		33.90(+0.721)		47.17(−19.72)
19	17.24(+0.348)	25.00(+0.719)		37.74(−0.777)	43.10(−10.30)
	19.88(−1.610)				47.39(+20.60)

a) In the unit of 10^{-3} cm^{-1}. b) The isomer was obtained from the last fraction when the complex was chromatographed on a QAE-Sephadex C-25 column with an 0.1 M L-histidinium chloride solution.

40000—50000 cm^{-1} show antipodal CD patterns with opposite signs, which may be related to the absolute configurations of the diastereomeric complexes. Namely, in the complex [Co(L-pro-gly)$_2$]$^-$ the CD curve of the early eluted isomer assigned to the R(C_2) shows plus and minus peaks at 42190 and 46510 cm^{-1}, respectively, and that of the late eluted isomer assigned to the S(C_2) shows minus and plus peaks at 42920 and 47170 cm^{-1}, respectively. Quite similar CD patterns are observed also for the pair of the diastereomers of the complex [Co(gly-gly)(L-pro-gly)]$^-$ (Fig. 3). Therefore, we can assign the early and late eluted isomers the configurations R(C_2) and S(C_2), respectively.

However, the observed CD spectra of the present diastereomers are produced as a sum of the configurational and vicinal contributions. Figure 4 shows only the configurational CD curves (obtained through subtraction of values for the early eluted diastereomer from those for the late eluted) for the diastereomeric complexes. The configurational CD curves in the d-d transition region exhibit quite similar patterns to each other for the L-ala-gly and L-leu-gly complexes of the gly-L-ala and gly-L-leu complexes, but those of the L-pro-gly, L-ala-β-ala, and β-ala-L-ala complexes do not indicate such a similarity among them. On the other hand, the configurational CD curves in the region of 40000—50000 cm^{-1} show the same patterns (plus and minus signs from the longer wavelength side) for

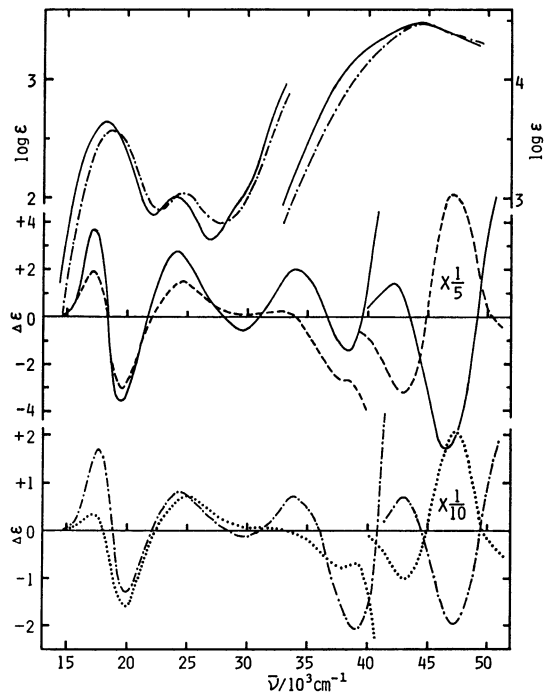

Fig. 3. Absorption and CD spectra of the dipeptidato complexes: early (——) and late (------) eluted diastereomers of [Co(L-pro-gly)$_2$]$^-$; early (-·-·-·) and late (·····) eluted diastereomers of [Co(gly-gly)(L-progly)]$^{-1}$.

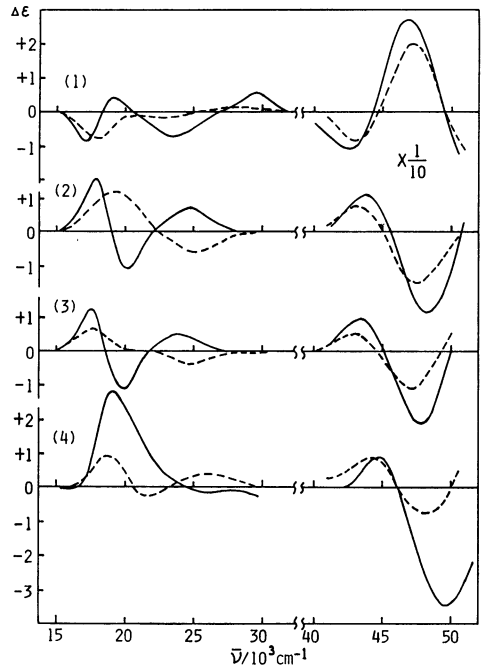

Fig. 4. Configurational CD curves calculated for the dipeptidato complexes: [(late eluted diastereomer)—(early eluted diastereomer)]/2. (1) [Co(L-pro-gly)$_2$]$^-$ (——) and [Co(gly-gly)(L-pro-gly)]$^-$ (------), (2) [Co(L-ala-gly)$_2$]$^-$ (——) and [Co(gly-L-ala)$_2$]$^-$ (------), (3) [Co(L-leu-gly)$_2$]$^-$ (——) and [Co(gly-L-leu)$_2$]$^-$ (------), (4) [Co(L-ala-β-ala)$_2$]$^-$ (——) and [Co(β-ala-L-ala)$_2$]$^-$ (------).

complexes (2)—(4) in Fig. 4. From a comparison of these CD patterns with those of the L-pro-gly and (gly-gly)(L-pro-gly) complexes one can assign the absolute configurations to the paired diastereomers in complexes (2)—(4). Namely, the R(C_2) and S(C_2) configurations can be assigned to the late and early eluted diastereomers of complexes (2)—(4), respectively, as shown in Table 2. These configurational assignments for the gly-L-ala, L-ala-gly, gly-L-leu, and L-leu-gly complexes are quite in agreement with those by Boas *et al.*[20]

An analogous discussion can be made for the complexes [Co(gly-gly)$_2$]$^-$, [Co(gly-β-ala)$_2$]$^-$, and [Co(β-ala-gly)$_2$]$^-$ which were partially resolved by column chromatography[26] using an 0.1 M L-histidinium chloride solution. Figure 1 shows the CD spectra of their first fractions ((+)$_{589}$-[Co(gly-gly)$_2$]$^-$, (+)$_{589}$-[Co(gly-β-ala)$_2$]$^-$, and (−)$_{589}$-[Co(β-ala-gly)$_2$]$^-$). The CD patterns in the ligand transition region exhibit plus and minus signs in the range 40000—50000 cm^{-1} for the gly-gly and gly-β-ala complexes. Therefore, the R(C_2) configuration can be assigned to the first fractions ((+)$_{589}$-isomer) of these complexes. The elution order of the two enantiomers in the complex [Co(gly-gly)$_2$]$^-$ was the same as that Gillard *et al.*[15,20] obtained with a starch column. On the other hand, the first fraction ((−)$_{589}$-isomer) of the complex [Co(β-ala-gly)$_2$]$^-$ shows the CD pattern with opposite (minus and plus) signs which can be assigned to the S(C_2) configuration.

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