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Studies of Amino Acid Complexes of the Type $[Co(aa)_2dipy]X$ and $[Co(aa)_2phen]X$[1]

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Complexes of the types $[Co(aa)_2dipy]X$ and $[Co(aa)_2phen]X$ (where aa is the anion of glycine, (*S*)-alanine, (*S*)-hydroxyproline, or allohydroxy-(*R*)-proline, and dipy and phen are dipyridyl and 1,10-phenanthroline, respectively) were prepared. Only one geometrical isomer was isolated for each complex and two isomers, (+)D and (−)D, were separated for the complexes containing optically active amino acids. These complexes were characterized by pmr, absorption, and circular dichroism spectra, and their absolute configurations were assigned as Λ-trans(N) for the (+)D isomer.

Recently it has been shown that metal complexes with optically active amino acids are diastereomeric with significantly different physical and spectral properties. This has been observed not only for tris(amino acidato) complexes[3−8] but also for bis-[9−10] and mono(amino acidato)[9,11−13] complexes. Thus, it is possible, in some cases, to separate the dissymmetrical isomers without the usual resolution process. Matsuoka and coworkers[10] succeeded in separating all six of the possible isomers of the $Co(ox)((S)\text{-ser})_2^-$ complex ion.

In the present paper the structures and absolute configurations of the new complexes $[Co(aa)_2dipy]X$ and $[Co(aa)_2phen]X$ will be discussed on the basis of their pmr, absorption, and circular dichroism (CD) spectra.

Experimental Section

Source of Materials.—Amino acids were obtained from Nutritional Biochemical Corp., Cleveland, Ohio, except for (−)D-allohydroxy-(*R*)-proline which came from Sigma Chemical Co., St. Louis, Mo. Dipyridyl and 1,10-phenanthroline were obtained from Aldrich Chemical Co. Other chemicals were reagent grade.

Preparations. **(±)-[Co(gly)$_2$dipy]Br.**—To a stirred solution of dipyridyl (13.2 g, 0.02 mol) and glycine (3.0 g, 0.04 mol) in methanol (10 ml) was added $Co(NO_3)_2\cdot 6H_2O$ (5.8 g, 0.02 mol) in 40 ml of H_2O. Lead dioxide (8 g, excess) was added gradually to the dark orange solution with vigorous stirring. The color of the solution turned dark red. The solution was heated at 65° for 5–6 min and air was blown over the surface of the solution for 30 min to complete oxidation. The insoluble residue was removed by filtration and washed with a small amount of water. The filtrate and washings were combined and poured into a cation-exchange resin column (Dowex 50W-X8, 200–400 mesh, K form, 26 mm × 500 mm). Elution was carried out at a rate of about 1 ml/min. The purple and pink solutions (neutral complexes) were swept out with water and then the purple solution of bis(glycinato)diaquo complex ion was eluted with 0.1 *M* KBr solution. The orange solution of $[Co(gly)_2dipy]Br$, obtained by elution using 0.2 *M* KBr solution, was evaporated to dryness below 35° using a vacuum evaporator. The residue was dissolved in methanol and the solution was filtered. The crude complex was obtained by adding a large amount of acetone to the filtrate. It was recrystallized by dissolving in the minimum amount of water to which methanol–acetone (1:1) mixture and a few drops of concentrated HBr were added. This solution was allowed to stand in a refrigerator overnight. The orange crystals deposited were filtered and washed with methanol–acetone (1:2) mixture and then acetone and air dried. The yield was 2.2 g.

(+)D-[Co(gly)$_2$dipy]Br.—The freshly precipitated silver antimonyl tartrate, from silver nitrate (0.8 g, 4.7 mmol) and potassium antimonyl tartrate (2 g, 6 mmol), was added to the solution of the racemate (4 g, 9 mmol) in water (20 ml) and stirred well. The AgBr precipitated was removed by filtration and washed with 5 ml of water. To the combined solution of filtrate and washings was added methanol (70 ml), and this solution was cooled in an ice bath for about 2 hr. The diastereomer which deposited was filtered and washed with methanol–acetone (1:1) mixture and then acetone and air dried. The diastereomer was recrystallized by dissolving in the minimum quantity of water, followed by the gradual addition of just enough methanol to produce turbidity. The solution was filtered and then cooled in an ice bath for 3 hr. The crystals were separated, washed, and dried as before. The diastereomer was easily soluble in water but insoluble in methanol and in acetone. The optical rotation was constant after two recrystallizations; $[\alpha]_D$ +138°.

A solution of the diastereomer (2.5 g) in a small amount of water was mixed with $BaBr_2\cdot 2H_2O$ (0.8 g) with vigorous stirring and filtered. The orange crystals of the bromide salt, deposited by adding methanol–acetone (1:2) mixture to the filtrate, followed by cooling, were collected by filtration and washed with methanol–acetone (1:1) mixture and then acetone. Recrystallization was carried out as for the racemate; $[M]_D$ +919°. *Anal.* Calcd for $CoC_{14}H_{16}N_4O_4Br$: C, 37.94; H, 3.65; N, 12.64. Found for the racemic complex: C, 37.81; H, 3.85; N, 12.79. Found for the (+)D isomer: C, 37.98; H, 3.80; N, 12.74.

(−)D-[Co((*S*)-ala)$_2$dipy]NO$_3\cdot$NH$_4$NO$_3\cdot$H$_2$O and (+)D-[Co((*S*)-ala)$_2$dipy]I.—The crude (*S*)-alanine complex was obtained by a procedure similar to that of the glycine complex except for elution with NH_4NO_3 instead of KBr. It was also easily isolated as the bromide salt by elution with KBr; the (±)D complex (an active racemate) was obtained as a KBr double salt in this way. The presence of K^+ in the double salt was confirmed by the formation of a precipitate with $Na_3[Co(NO_2)_6]$ solution. The (−)D isomer (nitrate salt, $[M]_D$ −2050°) was separated as needle-shaped crystals by dissolving the crude complex in warm methanol which was then cooled in an ice bath. The crude (+)D isomer was obtained from the filtrate by addition of an acetone–ether (1:1) mixture. Since the nitrate salt was difficult to purify, the (+)D isomer was changed into the iodide salt by adding NaI to a concentrated aqueous solution to isolate the complex as needle-shaped crystals. The iodide salt was recrystallized

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from methanol by adding an acetone–ether (1:1) mixture; $[M]_D$ +1250°. *Anal.* Calcd for (+)D-[Co((*S*)-ala)$_2$dipy]I, $CoC_{16}H_{20}N_4O_4I$: C, 37.08; H, 3.90; N, 10.80. Found: C, 36.80; H, 4.10; N, 10.92. Calcd for (−)D-[Co((*S*)-ala)$_2$dipy]NO_3·NH_4NO_3·H_2O, $CoC_{16}H_{26}N_7O_{11}$: C, 34.85; H, 4.76; N, 17.9. Found: C, 34.90; H, 4.98; N, 17.40. Calcd for (±)-[Co((*S*)-ala)$_2$dipy]Br·KBr·H_2O, $KCoC_{16}H_{22}N_4O_5Br_2$: C, 31.58; H, 3.62; N, 9.21; Br, 26.32. Found: C, 31.40, 31.23; H, 4.02, 3.98; N, 8.39; Br, 26.97.

(−)D-[Co((*S*)-hpro)$_2$dipy]NO_3 and (+)D-[Co((*S*)-hpro)$_2$-dipy]NO_3.—The (*S*)-hydroxyproline complex was prepared by the method used for the glycine complex. The orange eluate obtained using 0.25 *M* NH_4NO_3 solution was condensed to 100 ml in a vacuum evaporator at 35°, and about twice that volume of acetone was added. The pinkish orange crystals separated on standing in a refrigerator overnight. Recrystallization was carried out from warm water (60°) containing NH_4NO_3; $[M]_D$ −1100°.

The filtrate from the (−)D isomer was condensed to about 30 ml, a large amount of methanol–acetone (1:5) mixture was added, and the solution was kept in a refrigerator for several hours. The (+)D isomer separated as orange, needle-shaped crystals which were recrystallized from water–methanol (1:1) mixture to which was added a few drops of a saturated solution of NH_4NO_3 and then acetone; $[M]_D$ +1540°. *Anal.* Calcd for $CoC_{20}H_{24}N_5O_9$: C, 44.69; H, 4.51; N, 13.06. Found for the (+) and (−) isomers, respectively: C, 44.58, 44.76; H, 4.65, 4.51; N, 12.91, 12.93.

(+)D-[Co(al-(*R*)-hpro)$_2$dipy]NO_3 and (−)D-[Co(al-(*R*)-hpro)$_2$dipy]NO_3·NH_4NO_3.—The allohydroxy-(*R*)-proline complexes were separated by the same procedure used for the (*S*)-hydroxyproline complex. The stereochemistry of the ligand is described near the end of the Results and Discussion. The solubilities of the (+)D and (−)D isomers correspond to those of the (−)D and (+)D isomers of the (*S*)-hydroxyproline complex, respectively; $[M]_D$ +1500°, $[M]_D$ −2300°. *Anal.* Calcd for (+)-[Co(al-(*R*)-hpro)$_2$dipy]NO_3, $CoC_{20}H_{24}N_5O_9$: C, 44.69; H, 4.51; N, 13.06. Found: C, 44.59; H, 4.66; N, 13.26. Calcd for (−)D-[Co(al-(*R*)-hpro)$_2$dipy]NO_3·NH_4NO_3, $CoC_{20}H_{28}N_7O_{12}$: C, 38.90; H, 4.58; N, 15.88. Found: C, 38.68; H, 4.57; N, 15.77.

(±)-[Co(gly)$_2$phen]Br·3H_2O.—To a suspension of 1,10-phenanthroline (4.4 g, 0.02 mol) and glycine (3.0 g, 0.04 mol) in water (50 ml) was added $Co(NO_3)_2$·$6H_2O$ (5.8 g, 0.02 mol) with stirring. Lead dioxide (8.0 g) was added gradually to the dark orange solution with vigorous stirring, and the suspension was heated for 10 min at 65°. Air was blown over the surface of the solution for 30 min, and the solution was filtered. The dark red solution was poured into the cation-exchange column. The elution was carried out as for (±)-[Co(gly)$_2$dipy]Br. The orange eluate was evaporated to dryness, and (±)-[Co(gly)$_2$phen]Br was extracted with methanol and filtered. A large amount of acetone was added to the filtrate and the solution was allowed to stand in a refrigerator for several hours. The orange crystals which deposited as needles were filtered and washed with 80% acetone and then 100% acetone. Recrystallization was carried out from a small amount of water by adding a methanol–acetone (1:2) mixture until slight turbidity appeared. The resulting solution was kept in a refrigerator overnight to yield crystals (2.0 g).

(+)D-[Co(gly)$_2$phen]Br·3H_2O.—The freshly prepared silver antimonyl tartrate, from potassium antimonyl tartrate (1.3 g, 3.9 mmol) and silver nitrate (0.6 g, 3.5 mmol), was added to the solution of the racemate (3.0 g, 7 mmol) in water (30 ml) and stirred well. The precipitated AgBr was removed by filtration and washed with water (5 ml). Methanol (100 ml) was added to the combined filtrate and washings, and the solution was cooled in an ice bath for 2 hr. The diastereomer (needle crystals) was filtered and washed with methanol and then acetone. It was recrystallized from water to which methanol was added, as before. The observed optical rotation was constant after two recrystallizations; yield 1.7 g; $[\alpha]_D$ +249°.

The diastereomer (1.7 g) was suspended in a solution of $BaBr_2$·$2H_2O$ (0.4 g) in 8 ml of water, with stirring. The solution was filtered to remove the barium antimony tartrate precipitate, which was washed with 2 ml of water. To the combined filtrate and washings was added 50 ml of acetone. This solution was kept in an ice bath for several hours. The orange crystals which deposited as needles were filtered and washed with acetone. Recrystallization was carried out from the minimum amount of water by adding acetone, followed by cooling in a refrigerator; yield *ca.* 0.5 g; $[M]_D$ +1675°. *Anal.* Calcd for $CoC_{18}H_{22}N_4O_7Br$ (trihydrate): C, 36.87; H, 4.26; N, 10.75. Found for racemate and (+) isomer, respectively: C, 36.84, 36.52; H, 4.14, 4.11; N, 10.90, 10.64.

(±)-[Co((*S*)-ala)$_2$phen]Br·3H_2O and (+)D-[Co((*S*)-ala)$_2$-phen]Br·3H_2O.—The orange eluate, obtained by the same procedure as that used for (±)-[Co(gly)$_2$phen]Br·$3H_2O$, was evaporated to 20–30 ml below 35° in a vacuum evaporator. The (±) isomer was separated by adding a large amount (*ca.* 300 ml) of methanol–acetone (1:1) mixture to the combined solution, followed by cooling in an ice bath. The orange crystals were filtered and washed with methanol–acetone (1:2) and then with acetone. The crude (+)D isomer was obtained by adding ether to the filtrate.

The (±) complex was recrystallized from the minimum amount of water by adding a methanol–acetone (1:2) mixture containing a few drops of concentrated HBr, followed by cooling in a refrigerator overnight.

The (+)D isomer was recrystallized from methanol by adding acetone containing HBr; $[M]_D$ +1440°. *Anal.* Calcd for $CoC_{18}H_{20}N_4O_4Br$ (trihydrate): C, 39.35; H, 4.85; N, 10.21. Found for racemate and (+) isomer, respectively: C, 39.46, 39.71; H, 4.72, 5.10; N, 10.49, 10.16.

Attempts to isolate the (−)D isomer as the bromide or nitrate salt were unsuccessful because the (±) complex has lower solubility.

(+)D-Co((*S*)-hpro)$_2$phen]NO_3·0.5NH_4NO_3·2H_2O and (−)D-[Co((*S*)-hpro)$_2$phen]NO_3·2H_2O.—The crude complex was obtained by the same procedure as that used for the corresponding glycine complex except that NH_4NO_3 solution was used for elution. The pinkish orange eluate was evaporated to 20 ml, methanol (50 ml) and a large amount of an acetone–ether (1:1) mixture were added, and the mixture was allowed to stand for several hours. The crude complex which deposited was filtered and washed with acetone. The (−)D isomer did not dissolve when the crude complex was suspended in methanol (50 ml). The (+)D isomer was separated from the methanolic solution by adding acetone–ether (1:1). As the (+)D isomer was still contaminated with the (−)D isomer, extraction with methanol was repeated. The total yield of the (−)D isomer was 0.5 g and that of the (+)D isomer was *ca.* 4.5 g.

The (−)D isomer was recrystallized from the minimum amount of water containing a few drops of HNO_3 by adding methanol–acetone (1:1). The molar rotation of the orange complex deposited as needle-shaped crystals was $[M]_D$ −1490°.

Recrystallization of the (+)D isomer was carried out from water containing a few drops of saturated NH_4NO_3 solution by addition of methanol–acetone (1:2). The molar rotation of the pinkish orange complex which deposited as needle crystals was $[M]_D$ +2040°. *Anal.* Calcd for (+)-[Co((*S*)-hpro)$_2$phen]NO_3·0.5NH_4NO_3·$2H_2O$, $Co_2H_{44}H_{60}N_{12}O_{25}$: C, 41.4; H, 4.75; N, 13.19. Found: C, 41.11; H, 4.88; N, 13.39. Calcd for (−)-[Co((*S*)-hpro)$_2$phen]NO_3·2H_2O, $CoC_{22}H_{28}N_5O_{11}$: C, 44.22; H, 4.73; N, 11.72. Found: C, 44.44; H, 5.13; N, 11.99.

[Co(NH_3)$_4$((*S*)-hpro)]SO_4·1.5H_2O.—(*S*)-Hydroxyproline (2.7 g) was dissolved in 18 ml of 1 *M* NaOH solution and 10 ml of water was added. The solution was warmed to 60° and [Co(NH_3)$_4$(H_2O)Cl]SO_4 (5.6 g) was added gradually. To the violet solution was added 1.5 ml of 2 *M* aqueous ammonia followed by heating at 70–75° for 2 hr. After cooling to room temperature, the resulting solution was poured into a cation-exchange column (Dowex 50W-X8, 200–400 mesh, H form, 21 mm × 100 mm). The neutral and univalent complexes were eluted, respectively,

with water and 0.25 *M* $(NH_4)_2SO_4$ solution. The $Co(NH_3)_4((S)\text{-hpro})^{2+}$ ion was eluted with 1 *M* $(NH_4)_2SO_4$ solution and the orange eluate was evaporated to dryness in a vacuum evaporator below 35°. A large amount of $(NH_4)_2SO_4$ was removed by dissolving the residue in a small quantity of water followed by the addition of methanol. The crude complex, obtained by evaporating to dryness the methanolic solution, was recrystallized from water by adding methanol. The orange crystals which deposited were filtered and washed with a water–methanol (1:1) mixture, methanol, and then acetone; yield 1.0 g. *Anal.* Calcd for $Co_2C_{10}H_{46}N_{10}O_{17}S_2$ (sesquihydrate): C, 15.79; H, 6.18; N, 18.42. Found: C, 15.70; H, 6.13; N, 18.30.

Measurements.—The CD spectra were obtained in aqueous solution using a Roussel-Jouan Dichrograph. The optical rotations were measured in aqueous solution in a 1- or 4-dm tube at room temperature. Optical isomers are characterized here by the sign of rotation at the sodium D line. The absorption spectra were recorded on a Cary Model 14 spectrophotometer, and the nmr spectra were recorded on a Varian A-60 analytical spectrometer, using DSS (2,2-dimethyl-2-silapentane-5-sulfonate) as an internal standard.

Results and Discussion

These complexes are easily soluble in water except for (−)D-$[Co((S)\text{-hpro})_2dipy]NO_3$. All of the phenanthroline complexes contain water of crystallization and they are more soluble than the corresponding dipyridyl complexes. For the (*S*)-alanine and (*S*)-hydroxyproline complexes, the (+)D isomers are more soluble in water and in methanol than are the (−)D isomers. The ratio of the isomers isolated, (+)D:(−)D, was about 7:10. Four of the complexes were isolated as double salts from solutions containing large amounts of KBr or NH_4NO_3. For each of these complexes one isomer could be isolated without the inert salt. The presence of K^+ was confirmed by qualitative tests, but such tests for NH_4^+ were inconclusive because of interference caused by the complex cation.

For either $[Co(aa)_2dipy]X$ or $[Co(aa)_2phen]X$, six isomers are possible, Δ- and Λ-trans(O) (C_2 symmetry), Δ- and Λ-trans(N) (C_2 symmetry), and Δ- and Λ-cis(O)cis(N) (C_1 symmetry), as shown in Figure 1. The

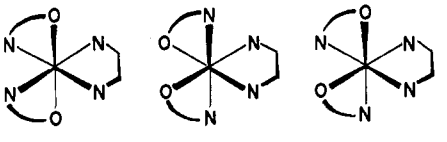

Figure 1.—One set of optical isomers (all Λ) for complex ions of the type $Co(aa)_2(diamine)^+$.

absolute configurations are designated according to the IUPAC tentative rules.[14] In this case the convention is equivalent to using a pseudo-C_3 axis (defined by the three chelate rings).

It is well known that the first absorption band of a trans$(O)_2(N)_4$ type of complex shows much larger splitting than for the corresponding cis$(O)_2(N)_4$ type of complex.[15–18] As seen in Figures 2–6, the present complexes do not show any splitting in the first band, suggesting that they are cis(O) rather than trans(O) isomers. One does not expect sufficient differences in the absorption spectra to allow one to distinguish between trans(N) and cis(O)cis(N) isomers.

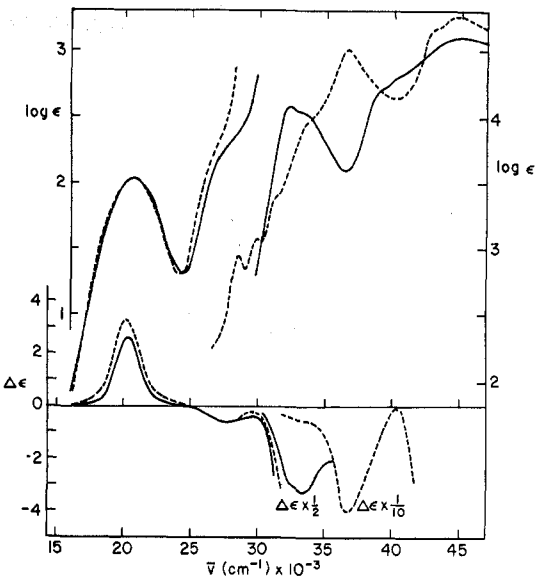

Figure 2.—Absorption and CD curves of (+)D-$[Co(gly)_2dipy]Br$ (——) and of (+)D-$[Co(gly)_2phen]Br\cdot 3H_2O$ (– – –).

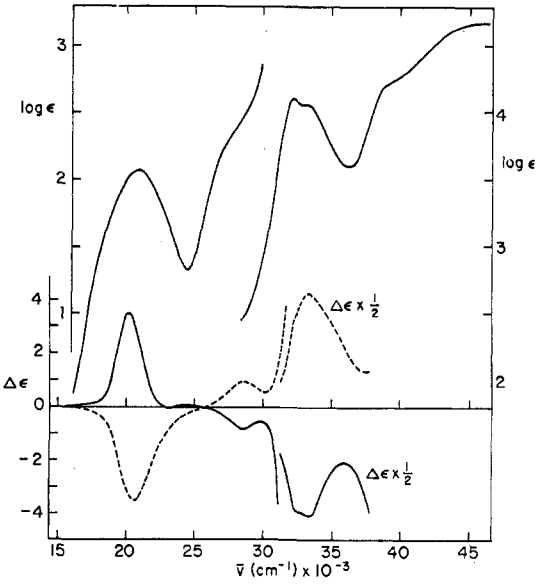

Figure 3.—Absorption and CD curves of (+)D-$[Co((S)\text{-ala})_2dipy]I$ (——) and the CD curve of (−)D-$[Co((S)\text{-ala})_2dipy]NO_3\cdot NH_4NO_3\cdot H_2O$ (– – –).

Circular Dichroism.—The CD spectra (Figures 2–6) show one dominant peak in the first band region, supporting the conclusion from absorption spectra that the compounds reported are not trans(O) isomers. More pronounced splitting in the absorption and CD spectra is apparent for complexes with a tetragonal field as observed for *trans*(N)-$Co(aa)_2C_2O_4^-$ [10] and *trans*(O)-$Co(en)(gly)_2^+$.[19]

Assignment of the absolute configurations of the

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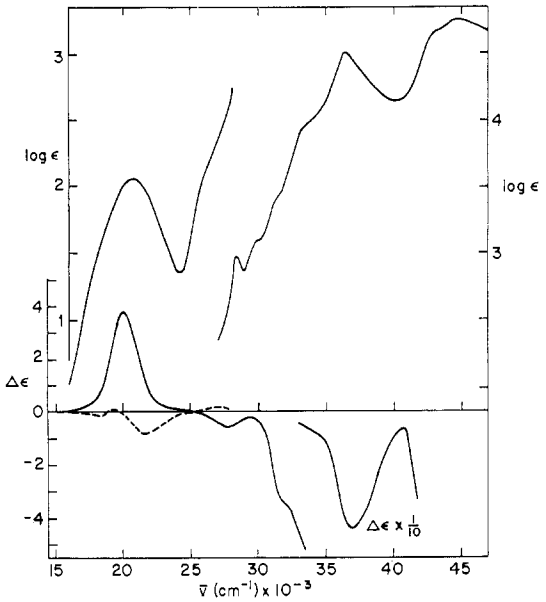

Figure 4.—Absorption and CD curves of the (+)D isomer (——) and the CD curve of the (±) isomer (---) of [Co((*S*)-ala)$_2$phen]-Br·3H$_2$O.

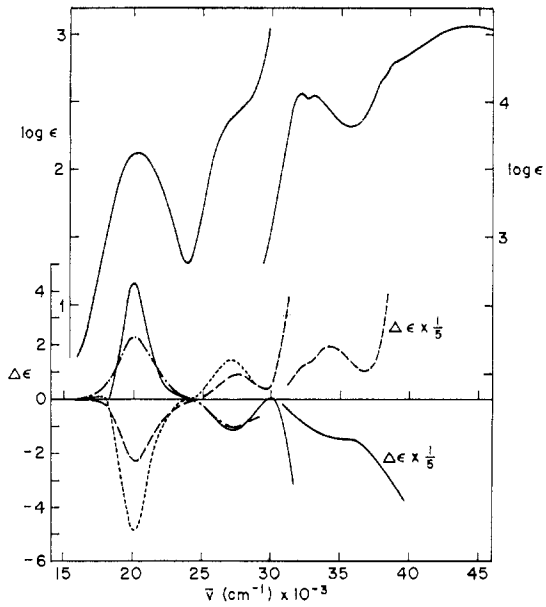

Figure 5.—Absorption and CD curves of the (+)D isomer (—) and the CD curve of the (−)D isomer (– – – –) of [Co((*S*)-hpro)$_2$-dipy]NO$_3$ and the CD curves of the (+)D isomer (·–·–·) and (−)D isomer (· · · ·) of [Co(al-(*R*)-hpro)$_2$dipy]NO$_3$.

complexes reported here can be made by comparison of the CD spectra in the first absorption band region with that of Λ-(+)D-[Co(en)$_3$]Cl$_3$.[20] The major CD peak in the visible region (Figures 2–6 and Table I) is positive for each (+)D isomer and negative for each (−)D isomer. On this basis, the assignments are Λ-(+)D and Δ-(−)D, consistent with the pmr results (*vide infra*).

Assignments of absolute configurations of dipy and phen complexes have been made from CD spectra[21-31] in the region of the ligand $\pi-\pi^*$ transitions (ultraviolet). Two intense CD peaks of opposite sign are observed for (phen)$_3$ or (dipy)$_3$ complexes in this region. Only one dominant CD peak is observed here for the phen complexes (*ca.* 37,000 cm^{-1}, Figures 2 and 4) and one peak with a shoulder is observed for the dipy complexes (*ca.* 34,000 cm^{-1}, Figures 2 and 3). Hidaka and Douglas[23] reported a CD spectrum for (−)$_{589}$-[Co(en)$_2$-phen]I$_3$ which is strikingly similar to those of Figures 4 and 6. From the dominant CD peak in the visible region, as related to that of Δ-[Co(en)$_3$]Cl$_3$, one can assign the Δ configuration to (−)$_{589}$-[Co(en)$_2$phen]I$_3$. Here, as for Co(gly)$_2$phen$^+$ and Co((*S*)-ala)$_2$phen$^+$, the CD peak at 35,000–37,000 cm^{-1} is opposite in sign to the prominent peak in the visible region. Thus the sign of this peak for a phen transition also indicates

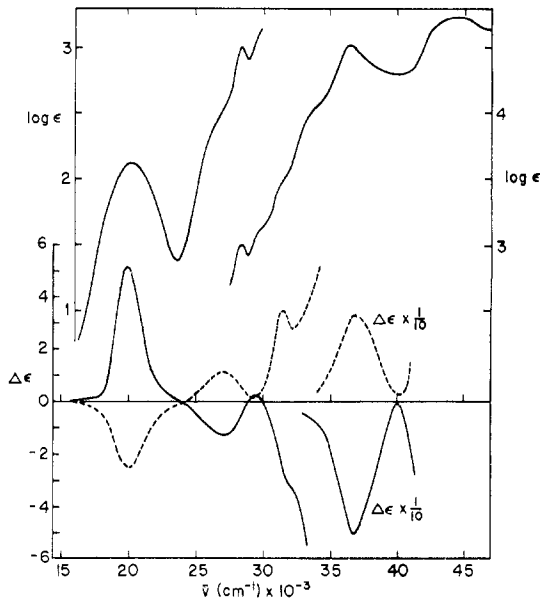

Figure 6.—Absorption and CD curves of the (+)D isomer (—) and the CD curve of the (−)D isomer (---) of [Co((*S*)-hpro)$_2$phen]-NO$_3$.

that (+)D-((*S*)-ala)$_2$phen$^+$ (Figure 4) has the Λ configuration, as assigned above.

Vicinal Contributions.—Douglas and coworkers[4,11,12,32] have shown that the contributions to the optical activity from the chirality of chelate rings and the presence of an optically active ligand are separable and additive. It is of interest to examine the vicinal contribution of more than one optically active center in a ligand. The isomers of the (*S*)-hydroxyproline complex are similar to those of the alanine complexes in solubilities and absorption spectra. An additional negative low-

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TABLE I

ABSORPTION AND CD SPECTRAL DATA

Complex ions	ν_{max}, cm^{-1}	Log ϵ	ν, cm^{-1}	$\epsilon_l - \epsilon_r$
(+)D-[Co(gly)$_2$dipy]Br	20,750	2.03_5	20,200	+2.635
	(28,000)[a]		27,780	−0.587
	32,250	4.08_4	(32,300)	(−5.6)
	(33,200)	(4.02)	33,330	−6.57
	(39,100)	(4.2)		
	(40,300)	(4.3)		
	45,100	4.59_3		
(+)D-[Co((*S*)-ala)$_2$dipy]I[b]	20,830	2.06_5	20,240	+3.50
	(28,000)		28,500	-0.83_6
	32,250	4.10	(32,400)	−7.60
	33,300	4.05_3	33,330	−8.21
	(39,000)	(4.2)		
	45,900	(4.66)		
(+)D-[Co((*S*)-hpro)$_2$dipy]-NO_3[b]	20,370	2.12_7	17,830	−0.116
			20,080	+4.35
	(27,600)		27,400	−1.09
			29,850	$+0.09_4$
	32,050	4.06_6	(32,300)	(−4.0)
	33,100	4.04_5	(34,000)	(−6.5)
	(37,800)	(4.14)		
	(38,800)	(4.28)		
	44,200	4.55_6		
(+)D-[Co(gly)$_2$phen]Br·$3H_2O$	20,660	2.025	20,120	+3.32
	(28,000)		27,000	-0.63_3
	28,500	2.94		
	30,030	3.07		
	(31,300)	(3.40)		
	(33,700)	(3.95)	(33,400)	(−5.6)
	36,640	4.51	36,640	−39.8
	(43,200)	(4.65)		
	44,750	4.75_1		
(+)D-[Co((*S*)-ala)$_2$phen]Br·$3H_2O$	20,740	2.05_2	20,080	+3.82
	(27,500)		27,780	-0.62_2
	28,420	2.96_1		
	30,030	3.086		
	(31,400)	(3.38)	(31,800)	(−3.3)
	(33,500)	(3.92)		
	36,500	4.50_2	36,780	−44.2
	(43,000)	(4.65)		
	44,650	4.47_9		
(+)D-[Co((*S*)-hpro)$_2$phen]-$NO_3 \cdot 0.5NH_4NO_3 \cdot 2H_2O$[b]	20,280	2.121	19,960	+5.15
	(27,200)		27,360	-1.24_3
	28,420	3.005		
	(29,900)	(3.12)	29,400	-0.27_9
	(31,400)	(3.45)	(31,800)	(−3.0)
	(33,600)	(3.97)		
	36,500	4.519	36,780	−49.8
	(43,000)	(4.66)		
	44,430	4.72_5		
$[Co(NH_3)_4((S)\text{-hpro})]SO_4 \cdot 1.5H_2O$	20,120	1.90_3	17,860	−0.065
			19,760	+0.594
			22,020	−0.262
	28,500	1.99	28,720	−0.105

[a] Parentheses indicate approximate value. [b] Only one of two isomers is listed.

energy peak appears in the CD spectrum for the (+)D-Co((*S*)-hpro)$_2$dipy$^+$ complex ion (Figure 5). This is absent for the corresponding (−)D isomer and for both isomers of the alanine complex. Three CD peaks in the first band region are observed[11,17] for complex ions of the type $Co(NH_3)_4((S)\text{-aa})^{2+}$, including $Co(NH_3)_4((S)\text{-hpro})^{2+}$. The CD curve for $Co(NH_3)_4((S)\text{-hpro})^{2+}$ is very similar to that for $Co(NH_3)_4((S)\text{-pro})^{2+}$,[17] so that the second asymmetric center (at the 4 carbon) makes little vicinal contribution. In Figure 7, one-fourth of the sum of the CD curves for (+)D- and (−)D-Co((*S*)-hpro)$_2$phen$^+$ (and for the corresponding dipy complex) is plotted to represent the contribution of one coordinated (*S*)-hpro, since the Δ and Λ spiral contributions cancel. The resulting curves are of similar form and intensity to that for $Co(NH_3)_4((S)\text{-hpro})^{2+}$, indicating the similarity of and essentially additivity

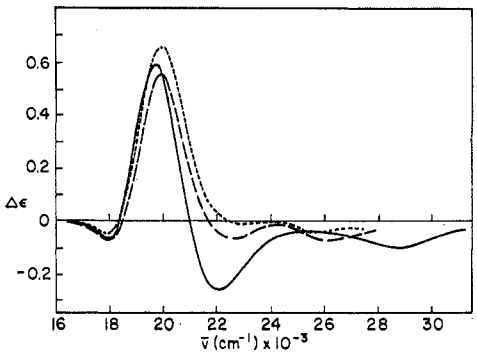

Figure 7.—CD curves of $[Co(NH_3)_4((S)\text{-hpro})]SO_4 \cdot 1.5H_2O$ (—), and one-fourth of the sum of the CD curves for (+)D- and (−)D-[Co((*S*)-hpro)$_2$dipy]NO_3 (---), and one-fourth of the sum of the CD curves for (+)D- and (−)D-[Co((S)-hpro)$_2$phen]NO_3 (· · · ·).

of the vicinal and any conformational effect of (*S*)-hpro in these three cases.

The variation in the CD curve shapes for the optical isomers and the curve for the unresolved (±)-Co((*S*)-ala)$_2$phen$^+$ ion (Figure 4) indicate the presence of three components in the first band region for this case also. In all cases except for (+)D-Co((*S*)-hpro)$_2$dipy$^+$ and the (−)D-allohydroxy-(*R*)-proline complex, the lowest energy CD peak is swamped out by the dominant neighboring peak. This dominant CD peak in comparison to the (*S*)-alanine complexes is the basis for assigning the isomers of the Co((*S*)-hpro)$_2$dipy$^+$ ion as (+)D-Λ-trans(N) and (−)D-Δ-trans(N).

Allohydroxy-(*R*)-proline has the opposite configuration of (*S*)-proline, but the configuration at the 4 carbon is the same as for (*S*)-hydroxyproline. Salts of (+)D-Co((*S*)-hpro)$_2$dipy$^+$ and (−)D-Co(al-(*R*)-hpro)$_2$dipy$^+$ correspond in solubilities and their CD curves are nearly mirror images (Figure 5). The same is true for the opposite pair of isomers. Thus the change in configuration of the 4 carbon makes little contribution to the CD spectra and hence its vicinal contribution is small.

Nuclear Magnetic Resonance.—The proton resonance of the CH_2 group of chelated glycinate ion shows a typical single AB pattern in the 196–243-Hz region for each of the ions (±)-Co(gly)$_2$dipy$^+$ (δ 3.64 and 3.42 ppm, J = 17.4 Hz) and (±)-Co(gly)$_2$phen$^+$ (δ 3.82 and 3.52 ppm, J = 17.2 Hz). This is the result expected for a trans(N) isomer since the CH_2 groups are equivalent. In the structure with C_1 symmetry (Figure 1) the CH_2 groups are not equivalent and two AB patterns would be expected. The pmr data (Figure 8) are in agreement with the trans(N) structure for the corresponding (*S*)-alanine complexes also. Since significant pmr shifts are observed for diastereomers, one can be confident that the symmetry is not C_1 with the expected splitting unresolved by the A-60.

For the (+)D and (−)D isomers of the (*S*)-alanine complexes, only two resonances, derived from coupling of a $-CH_3$ group with a single α proton, are observed in the 76–95-Hz region. Such resonances of the methyl group have been observed for $Co((S)\text{-ala})_2(NO_2)_2^-$

(C_2 symmetry)[33] and Co((*S*)-ala)$_3$ (C_3 symmetry).[7] The methyl group of the (+)D isomer resonates at higher field than in the case of the (−)D isomer (Figure 8). This shift to higher field[34] strongly suggests that

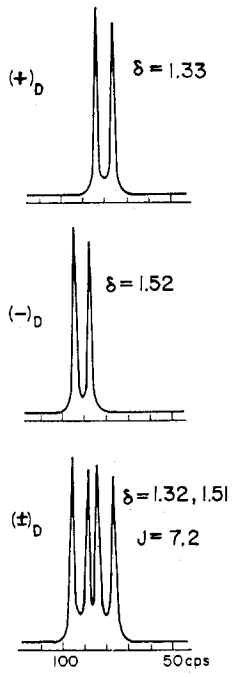

Figure 8.—Pmr spectra of (+)D-, (−)D-, and (±)-Co((*S*)-ala)$_2$-dipy$^+$ in D_2O with DSS as the internal standard.

shielding of the methyl protons by the π-electron cloud of the dipy or phen ligand is greater for the (+)D isomer than for the (−)D isomer. The methyl group is in the π-electron cloud region (over the aromatic ring) for the Λ-trans(N) configuration, so this should be the (+)D isomer. The methyl group is far removed from this region for the Δ-trans(N) configuration which is assigned to the (−)D isomer. The use of pmr spectra for assigning absolute configurations has been well established.[35-38] The pmr pattern for the methyl protons in the unresolved (±) complex with (*S*)-alanine appears as a superposition of the spectra for the (+)D and (−)D isomers (Figure 8). The chemical shifts were 1.32 ppm for (+)D-[Co((*S*)-ala)$_2$phen]Br·3H_2O and 1.33 and 1.54 ppm for the corresponding (±) complex. Data were not obtained for the (−) isomer.

The α protons of (*S*)-alanine in the complexes in the trans(N) structure are not subject to the compression noted[39] for *trans*(O)-Co(en)((*S*)-ala)$_2^+$. The present results in comparison to theirs confirm the elimination of the trans(O) structure. Instead of compression one finds that the –CH resonance occurs at higher field for (−)D-[Co((*S*)-ala)$_2$dipy]NO_3·NH_4NO_3·H_2O (δ 3.64 ppm) than for the (+)D isomer (δ 3.91 ppm). The shift is even greater than for the methyl protons. The shift of the –CH resonance to higher field for the (+)D isomer is consistent with the assignment of this to the Λ configuration. In the Λ configuration the α proton is above the π-electron cloud of dipy, but it is far removed from this region in the Δ configuration. Unfortunately good data could not be obtained in this region for the corresponding phen complexes. For the trans(O) structure the Δ configuration would cause some steric compression of the methyl protons, while the Λ configuration would cause compression of the α protons. In each case the proton is in a deshielding region. Shifts in the opposite direction to that observed would be expected for either effect.

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