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Optical Activity, Absolute Configuration, and Rearrangement Reactions of Tris Amino Acid Complexes of Cobalt(III) with L-Alanine, L-Leucine, and L-Proline[1a]

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Eleven of the twelve possible isomers of Co(III) with L-alanine, L-leucine, and L-proline have been prepared and separated. Their electronic absorption spectra and circular dichroism spectra are reported. In some cases proton magnetic resonance spectra are reported. The nmr spectra of the L-alanine complexes show the red isomers to be *cis* and the violet isomers to be *trans*. The absence of one L-proline isomer is predictable on steric grounds and allows an assignment of absolute configuration. The same steric interaction is manifest in the nmr spectra of the L-leucine complexes and confirms the assignment. The circular dichroism spectra of the *cis* complexes show apparent splitting of the higher energy absorption band into three electronic components. This is inconsistent with the molecular symmetry, and a possible explanation for the artifact is proposed. The net rotational strength of the first absorption band of a Δ molecule is negative, a result that is consistent with the $Co(en)_3^{3+}$ ion. The *cis*-Δ-tris(L-prolinato)cobalt(III) complex rearranges in aqueous solution to the corresponding *trans*-Δ complex. This rules out internal twist mechanisms and is explained by a bond rupture mechanism. A similar rearrangement of an L-leucine complex suggests the same mechanism.

Introduction

Recently renewed interest has been shown in the earlier[2,3] preparative work on the isomerism of cobalt(III) amino acid complexes. Dunlop and Gillard[4] have separated the four isomers of tris(L-alaninato)cobalt(III) and tentatively assigned their absolute configuration on the basis of the relative stabilities of the isomers. Douglas and Yamada[5] have isolated the same four isomers, namely two *cis*, facial (β and β') isomers and two *trans*, peripheral (α and α') isomers. The latter workers deduced absolute configurations from the circular dichroism (CD) spectra as follows: $\beta = \Lambda$, $\beta' = \Delta$, $\alpha = \Delta$, $\alpha' = \Lambda$. The validity of the technique used for the α and α' isomers is open to question and will be discussed herein. Since the ligand is optically active, spatial and chemical differences will arise between the Δ and Λ[6] absolute configurations within each geometrical form. Such effects have been referred to as stereospecificity[7] and some implications in the case of chelating diamines have been reviewed by Corey and Bailar.[8] Only a very small specificity is detectable in the relative stabilities of bis(L-alaninato)copper(II) and *dl*-alaninatocopper(II).[9] Previous workers had failed to observe this.[10] The small magnitude of the effect in these square-planar complexes as compared to the six-coordinate tris complexes suggests that its principal origin is the direct interaction of neighboring chelate rings. This work describes the use of amino acids that deliberately accentuate the stereospecific effects in such a way that an assignment of absolute configuration can be made. We have incidentally proven the earlier assignment of *cis* and *trans* isomers correct and have studied some interconversion reactions.

Experimental Section

Materials.—L-Leucine, L-alanine, and L-proline were obtained from the Aldrich Chemical Co., Inc. Reagent grade cobalt salts were used. Hexaamminecobalt(III) trichloride was prepared in the normal way.[11] Alumina used in the chromatography was the Merck acid-washed variety.

Preparation and Separation of *trans*-Tris(L-leucinato)cobalt(III) Isomers.—Both (+) and (−) isomers were obtained by the carbonate method of Mori, *et al.*[3] $Co(NO_3)_2 \cdot 6H_2O$, 17.4 g (0.06 mole), in 30 ml of water and 6 ml of 30% H_2O_2 (excess) were mixed in a dropping funnel and added dropwise to a slurry of 30.3 g of $KHCO_3$ (0.3 mole) in 30 ml of H_2O at 0°. After the addition, the mixture was stirred at 0° for 1 hr, 23.7 g of L-leucine (0.18 mole) dissolved in 180 ml of 1 *N* HCl (0.18 mole) was added slowly with stirring and the mixture heated cautiously to boiling in a large flask. It was boiled under reflux for 2 hr. After cooling the crude product was filtered and dried in air at 100°; yield (crude) 24.2 g (89.5%). The crude material was extracted three times with boiling ethanol and the filtrate evaporated to dryness. The product was dissolved in the minimum volume of 85% ethanol–water and chromatographed on an alumina column, 140 cm high and 4 cm in diameter. The eluant was 85% ethanol–water. The separation of the (+) and (−) isomers was not complete. One hundred 5-ml fractions were collected, and the distribution of the isomers was determined by circular dichroism and optical absorption of the fractions. The (+) isomer appeared first. The first 15 fractions, mostly (+) isomer, were removed and the remainder evaporated and rechromatographed. The first and second halves of the eluted material were then rechromatographed separately and by a suitable division of the collected fractions almost pure samples of

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(2) J. Lifschitz, *Z. Physik. Chem.*, **114**, 493 (1925).

(3) M. Mori, M. Shibata, E. Kyono, and M. Kanaya, *Bull. Chem. Soc. Japan*, **34**, 1837 (1961).

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(5) B. E. Douglas and S. Yamada, *Inorg. Chem.*, **4**, 1561 (1965).

(6) T. S. Piper, *J. Am. Chem. Soc.*, **83**, 3908 (1961).

(7) A. M. Sargeson, "Chelating Agents and Metal Chelates," F. P. Dwyer and D. P. Mellor, Ed., Academic Press Inc., New York, N. Y., 1964.

(8) E. J. Corey and J. C. Bailar, *J. Am. Chem. Soc.*, **81**, 2620 (1959).

(9) C. R. Hare, Paper 99, Division of Inorganic Chemistry, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965.

(10) R. D. Gillard, H. M. Irving, R. Parkins, N. C. Payne, and L. D. Pettit, *Chem. Commun.*, 81 (1965).

(11) J. Bjerrum and J. P. Reynolds, *Inorg. Syn.*, **2**, 217 (1946).

(+) and (−) isomers were obtained. The (+) isomer was purified by slow crystallization from evaporating ethanol, giving dark violet needles. The (−) isomer was purified by the slow addition of water to a methanol solution. The first crop was a mixture and was rejected but subsequent crops were pure. The purity of the isomers was checked by rechromatographing them separately and recording the ratio of the circular dichroism maximum to the absorption coefficient maximum as a function of fraction number. In 35 fractions of the (+) isomer collected this factor was a constant for the first 30 but decreased rapidly in the last five fractions showing contamination by the (−) isomer. The (−) isomer showed no contamination when the same technique was applied. Yields of pure material: (+) isomer, 1.45 g; (−) isomer, 1.03 g.

trans-(+)-[Co(L-leu)$_3$]·2H$_2$O.—The dihydrate was dried under vacuum at room temperature. Dark violet prismatic crystals resulted.

Anal. Calcd for $CoN_3C_{18}H_{40}O_8$: C, 44.53; N, 8.65; H, 8.32. Found: C, 44.46; N, 8.39; H, 8.39.

trans-(−)-[Co(L-leu)$_3$]·3H$_2$O.—The light violet needles were dried overnight *in vacuo* at room temperature.

Anal. Calcd for $CoN_3C_{18}H_{42}O_9$: C, 43.00; N, 8.39; H, 8.42. Found: C, 43.15; N, 8.52; H, 8.55.

trans-(−)-[Co(L-leu)$_3$]·H$_2$O.—When the trihydrate was pumped at 0.005 mm pressure overnight at 56°, the monohydrate was obtained.

Anal. Calcd for $CoN_3C_{18}H_{36}O_7$: C, 46.29; N, 8.99; H, 8.21. Found: C, 46.91; N, 9.05; H, 8.29.

Preparation and Separation of *cis*-Tris(L-leucinato)cobalt(III) Isomers.—Both (+) and (−) isomers were obtained from the preparation of Mori, *et al.*[3] Hexaamminecobalt(III) chloride (5.43 g, 0.02 mole) was boiled with 8.0 g of L-leucine (0.06 mole) and 2.45 g of NaOH (0.06 mole) in 50 ml of water until no more ammonia was evolved—about 2 hr. On cooling, the violet-red solid was separated by filtration and washed with hot ethanol to remove the *trans* isomers. The red residue was repeatedly extracted with small portions of concentrated HCl, until the extracts became colorless—150 ml in all. The concentrated HCl solution was poured into an equal volume of water and allowed to cool when red needlelike crystals formed. A second crop was obtained by evaporation of half-volume on a steam bath and pouring again into an equal volume of water. On standing overnight, a crop of good purity crystals of the (−) isomer separated. The (+) isomer was obtained from the residue of the HCl extraction by dissolution in 50% H_2SO_4 and careful dilution of this solution with water.

cis-(+)-[Co(L-leu)$_3$]·3H$_2$O.—This complex is hygroscopic after drying *in vacuo* and the equilibrium composition appears to be the trihydrate.

Anal. Calcd for $CoN_3C_{18}H_{42}O_9$: C, 43.00; N, 8.39; H, 8.42. Found: C, 43.52; N, 8.21; H, 8.30.

cis-(−)-[Co(L-leu)$_3$·2H$_2$O.—This complex forms red needles of the dihydrate. *Anal.* Calcd for $CoN_3C_{18}H_{40}O_8$: C, 44.53; N, 8.65; H, 8.32. Found: C, 44.45; N, 8.54; H, 8.01.

Preparation and Separation of Tris(L-prolinato)cobalt(III) Complexes.—In this case the method using hexaaminecobalt(III) as a precursor failed to give any product after 24-hr boiling under reflux. The carbonate method described above however gave reasonable yields. The procedure was the same. After boiling under reflux for 1.5 hr, a reddish purple solid was removed by filtration. It was washed with alcohol and water and was soluble only in 50% H_2SO_4 from which it was recrystallized unchanged. The circular dichroism (CD) and absorption spectrum shows it to be the *cis*-(+) isomer. The filtrate from the reaction mixture was passed through a cation-exchange resin in the hydrogen ion form and evaporated to dryness. The solid was extracted with ethanol, leaving a red residue. This was thoroughly washed with ethanol and dissolved in warm water to give, on evaporation, small red prisms of the *cis*-(−) isomer. The purple mother liquor was chromatographed on the same alumina column as described above. Two small unidentified violet bands appeared from the column first, followed by the *trans*-(−) isomer. Careful observation of the CD of fractions from the column showed no contamination with the *trans*-(+) isomer. The *trans*-(−) isomer was purified by the addition of acetone to an aqueous solution until cloudiness just appeared. It was allowed to stand at 0° when dark lustrous prisms separated. On exposure to air these broke up giving finely divided semicrystalline material. Further crops were obtained by the addition of more acetone and recooling. The final crops gave platelike crystals which were stable in air. After drying *in vacuo* at room temperature the first crop is anhydrous and the last crops are in the monohydrate form. No material identifiable as the *trans*-(+) isomer was obtained.

cis-(+)-[Co(L-pro)$_3$].—This compound was dried under vacuum at room temperature.

Anal. Calcd for $CoN_3C_{15}H_{24}O_6$: C, 44.88; N, 10.47; H, 5.98. Found: C, 44.57; H, 10.44; H, 5.99.

cis-(−)-[Co(L-pro)$_3$]·$^1/_2$H$_2$O.—This compound was dried under vacuum at room temperature.

Anal. Calcd for $CoN_3C_{15}H_{25}O_{6.5}$: C, 43.85; N, 10.23; H, 6.09. Found: C, 43.72; N, 9.72; H, 6.13.

trans-(−)-[Co(L-pro)$_3$].—This compound was dried under vacuum at room temperature.

Anal. Calcd for $CoN_3C_{15}H_{24}O_6$: C, 44.88; N, 10.47; H, 5.98. Found: C, 44.71; N, 10.03; H, 6.09.

trans-(−)-[Co(L-pro)$_3$]·H$_2$O.—This compound was dried under vacuum at room temperature. Fine purple plates formed.

Anal. Calcd for $CoN_3C_{15}H_{26}O_7$: C, 42.93; N, 10.02; H, 6.20. Found: C, 43.16; N, 9.44; H, 6.40.

Preparation and Separation of Tris(L-alaninato)cobalt(III) Complexes.—We have prepared three of these complexes from cobalt(III) hydroxide by the method first described by Ley and Winkler.[12] Cobalt(III) hydroxide was prepared by treating 5.1 g of $Co(NO_3)_2 \cdot 6H_2O$ (0.02 mole) with excess alkaline sodium perborate, $NaBO_3 \cdot 4H_2O$, followed by repeated washing in a centrifuge. The hydroxide was boiled for 8 hr with 5.0 g of L-alanine (0.06 mole) in 100 ml of water in a covered beaker, the volume being kept constant. The hot solution was filtered, concentrated to 30 ml, and allowed to cool. Violet needles of the *trans*-(+) isomer separated and were removed by filtration; 100 ml of ethanol was added to the filtrate and a red-violet solid slowly separated. This was extracted with a small volume of water to give a red solution and a violet residue. After a second precipitation with ethanol and extraction with water, the red solution was allowed to evaporate, giving a small yield of red needles of the *cis*-(−) isomer. The remaining ethanolic solution was evaporated to dryness and dissolved in the minimum volume of 50% ethanol–water and chromatographed on alumina. One small unidentified violet band separates first, followed by a band containing the *trans*-(−) isomer. A small reddish band which travels much more slowly is probably more of the *cis*-(−) isomer. The alcohol solution of the *trans*-(−) isomer was evaporated to dryness, dissolved in water, and allowed to crystallize slowly.

The *cis*-(+) isomer was obtained from the hexaaminecobalt(III) reaction as a red product insoluble in every solvent except 50% sulfuric acid.

cis-(+)-[Co(L-ala)$_3$].—This compound is a red, insoluble powder.

Anal. Calcd for $CoN_3C_9H_{18}C_6$: C, 33.45; N, 13.00; H, 5.57. Found: C, 34.18; N, 12.92; H, 5.62.

cis-(−)-[Co(L-ala)$_3$].—This compound exists as red needles.

Anal. Calcd for $CoN_3C_9H_{18}O_6$: C, 33.45; H, 5.57. Found: C, 33.57; H, 6.33.

trans-(+)-[Co(L-ala)$_3$]·$^1/_2$H$_2$O.—This complex is the hemihydrate after drying under vacuum at room temperature.

Anal. Calcd for $CoN_3C_9H_{19}O_{6.5}$: C, 32.51; N, 12.64; H, 5.72. Found: C, 32.56; N, 12.30; H, 5.71.

trans-(−)-[Co(L-ala)$_3$].—This compound was dried under vacuum at 60°. A violet powder formed.

Anal. Calcd for $CoN_3C_9H_{18}O_6$: C, 33.45; N, 13.00; H, 5.57. Found: C, 33.17; N, 12.68; H, 5.86.

(12) H. Ley and H. Winkler, *Ber.*, **42**, 3894 (1909).

Equilibrium Measurements.—In the equilibration of the *trans*-L-leucine complexes the 1-butanol solutions were boiled under reflux until no further change in the CD spectrum was observed, roughly 3 hr. A very small amount of red insoluble *cis* isomer was removed by filtration, the solution was evaporated, and the residue was chromatographed in 85% ethanol–water on an alumina column. The total violet effluent from the column was collected, evaporated, redissolved in ethanol, and analyzed by CD and absorption measurements. In a second experiment the equilibrated 1-butanol solution was analyzed using CD and absorption measurements directly, by comparison with the spectra of the components in the same solvent.

The equilibration of the *cis*-(−)-L-proline complex was carried out in a thermostated cell housing at 80° in neutral aqueous solution. Equilibration was complete after about 6 hr and was followed by very slow decomposition. The solution was analyzed by CD measurements.

Instrumental Measurements.—The nmr spectra were recorded on a Varian A-60 analytical spectrometer, using TMS as an internal standard. The absorption spectra were taken on a Cary Model 14 RI recording spectrophotometer, and the CD measurements were made on a Roussel–Jouan Dichrographe.

Results and Discussion

(A) Characterization of Isomers.—The four possible isomers of [Co(L-ala)$_3$] and [Co(L-leu)$_3$] and three isomers of [Co(L-pro)$_3$] were prepared by existing methods[3,12] and separated by column chromatography and solubility differences. In general the *cis* isomers are red and the *trans* isomers violet. The characterization of the configurational isomers relies on their circular dichroism (CD) spectra and in what follows the (+) and (−) signs refer to the sign of the net rotational strength of the low-energy absorption band. In the work of Douglas[5] α and β are (+) isomers and α' and β' are (−) isomers. The CD and absorption spectra are shown in Figures 1–8.

Note the similarity of the spectra of any one isomer irrespective of the amino acid. The absorption spectra are similar to those previously reported,[3] similar band shapes and intensities being observed. The exceptions are the *cis*-L-proline isomers, where intensity relationships are somewhat different and where the bands occur at lower energy (Figures 1 and 2). However, comparison with the spectrum of *trans*-(−)-[Co(L-pro)$_3$] (Figure 4) shows that the lower energy band occurs at higher energy in the *cis* complexes and is more symmetrical. The characterization of the *cis*-L-proline complexes is confirmed by the similarity of their CD spectra to those of the other *cis* complexes (Figures 5 and 6).

The solubilities of the isomers differ markedly. In general *cis* isomers are much less soluble than *trans* isomers and (+) isomers are much less soluble than (−) isomers. The *cis*-(+) isomers only dissolve in 50% H_2SO_4 or stronger acid. The remaining alanine complexes are soluble in water but only the *trans*-(−) isomer has any ethanol solubility. The *trans* isomers of leucine are soluble in alcohols, but not in water. The *cis*-leucine isomers dissolve in strong acids. The *trans*-(−)-L-proline complex is very water soluble. The *cis*-(−)-L-proline isomer is moderately water soluble but the *cis*-(+) isomer is very insoluble.

(B) Geometrical Isomerism.—Figure 9 and Table I show the proton nmr resonances and relative band areas of *cis*-(−)-[Co(L-ala)$_3$] and *trans*-(−)-[Co(L-ala)$_3$] in D_2O solution. The methyl resonance at ~110 cps from TMS is a simple doublet for the *cis* isomer.

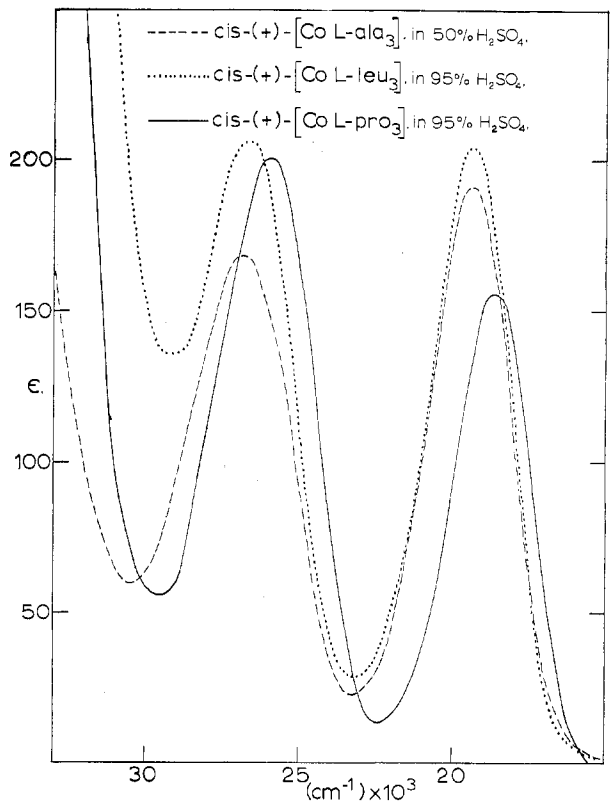

Figure 1.—Absorption spectra of *cis*-(+)-[Co(L-amino acid)$_3$] complexes.

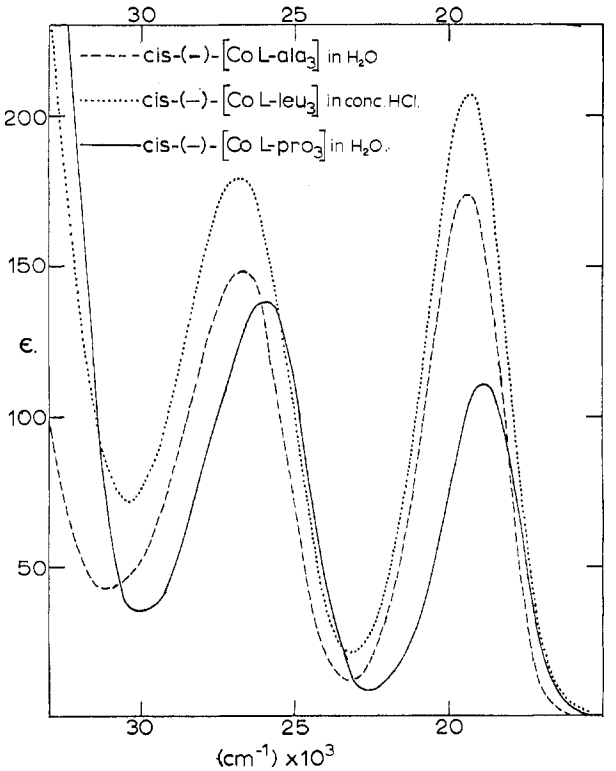

Figure 2.—Absorption spectra of *cis*-(−)-[Co(L-amino acid)$_3$] complexes.

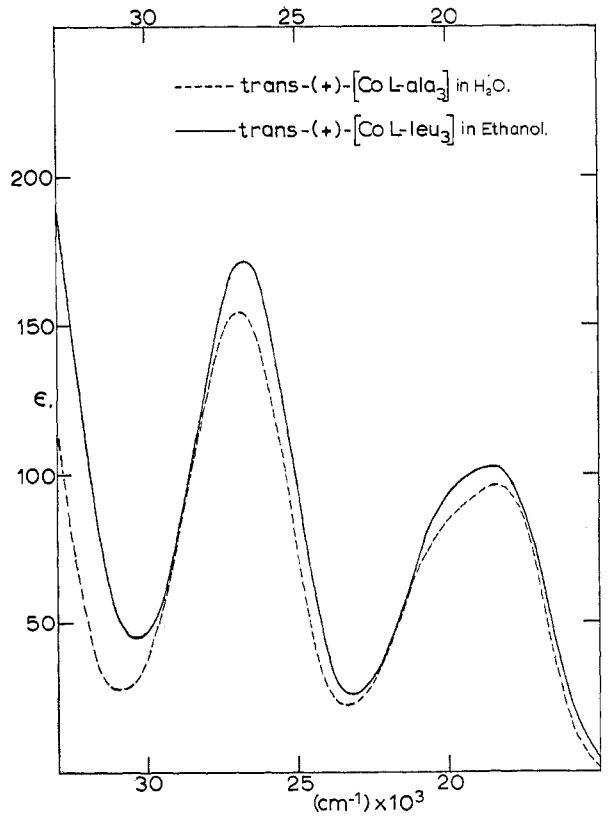

Figure 3.—Absorption spectra of *trans*-(+)-[Co(L-amino acid)$_3$] complexes.

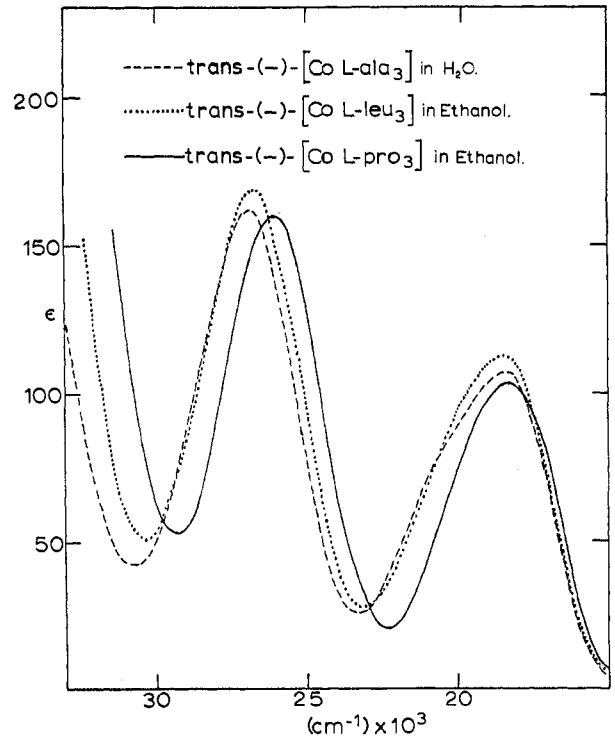

Figure 4.—Absorption spectra of *trans*-(−)-[Co(L-amino acid)$_3$] complexes.

By contrast the *trans* isomer shows five lines in the ratio 1:2:1:1:1, corresponding to three doublets. The spectrum of the *cis* isomer is clearly consistent with its threefold symmetry, all methyl groups being

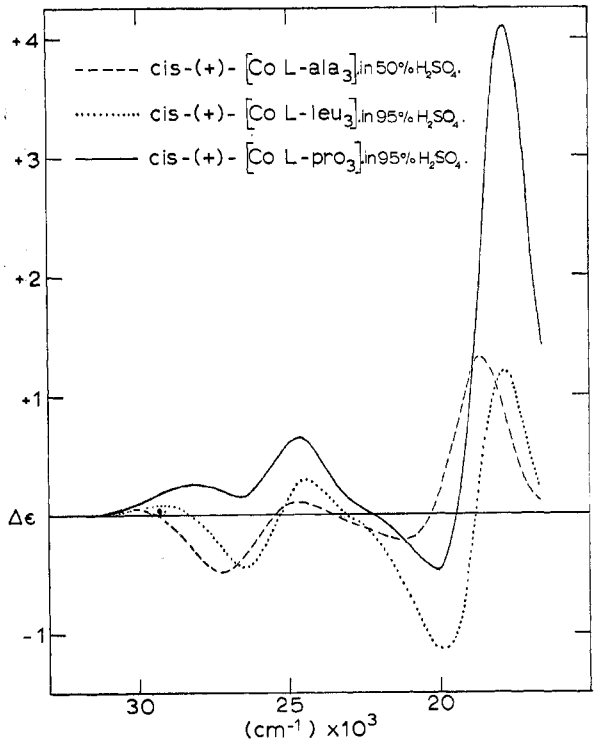

Figure 5.—CD spectra of *cis*-(+)-[Co(L-amino acid)$_3$] complexes.

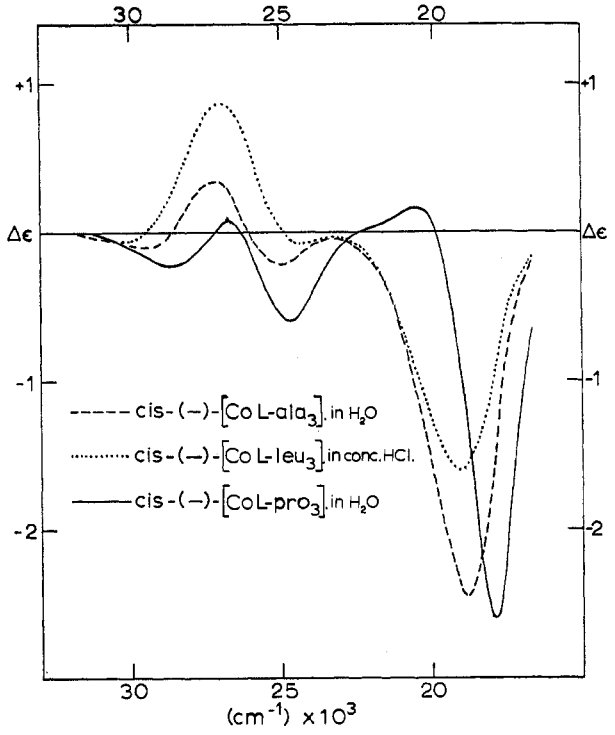

Figure 6.—CD spectra of *cis*-(−)-[Co(L-amino acid)$_3$] complexes.

equivalent. The *trans* isomer with no symmetry elements shows the expected splitting. The large difference in chemical shift of one doublet from the other two can be related to the near equivalence of two chelate rings with respect to the pseudo-threefold axis of the molecule compared to the third ring (see Figure 10).

The resonances of the α carbon atom protons are

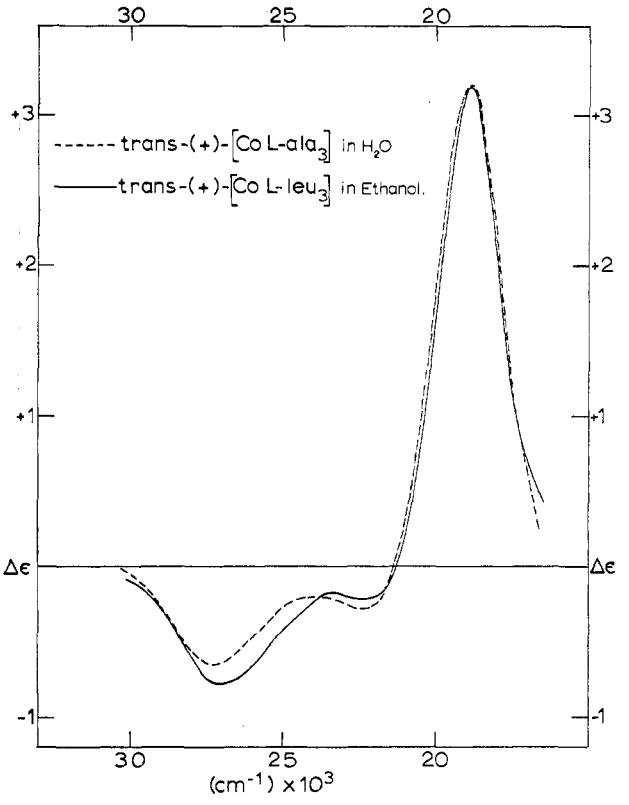

Figure 7.—CD spectra of *trans*-(+)-[Co(L-amino acid)$_3$] complexes.

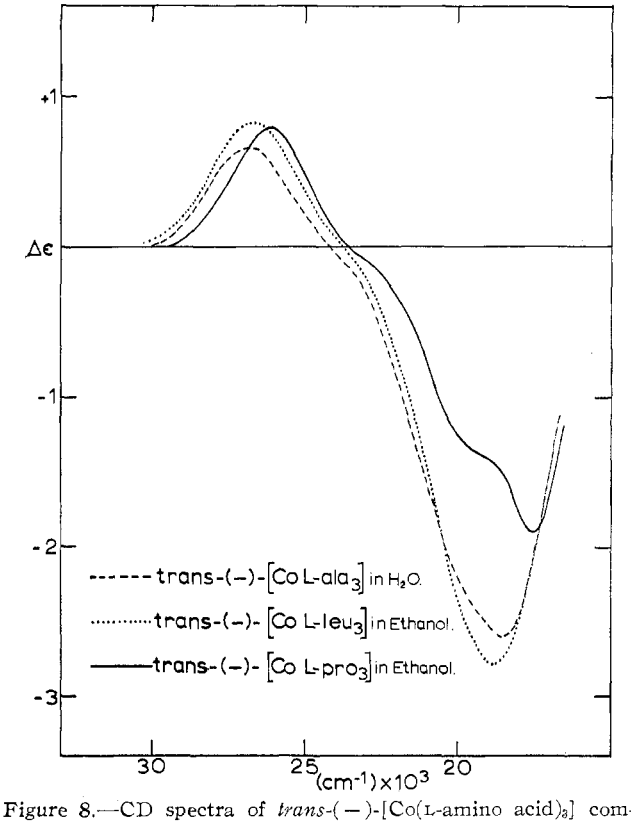

Figure 8.—CD spectra of *trans*-(−)-[Co(L-amino acid)$_3$] complexes.

consistent with the methyl resonances. The *cis* compound shows a simple quartet in the ratio 1:3:3:1 due to coupling with the methyl protons and having J = 7.0 cps. The *trans* compound has a more complex spectrum in this region, in which three sets of quartets with J = 7.0 cps can be traced.

TABLE I

METHYL PROTON CHEMICAL SHIFTS

Compound	Solvent	Chemical shift[a,b]
cis-(−)-[Co(L-ala)$_3$]	D_2O	107.5 (1), 114.5 (1)
trans-(−)-[Co(L-ala)$_3$]	D_2O	105.0 (1), 112.2 (2), 113.7 (1), 119.3 (1), 120.7 (1)
trans-(+)-[Co(L-ala)$_3$][c]	D_2O	106.0 (1), 112.5 (3), 119.5 (2)
trans-(+)-[Co(L-leu)$_3$]	CD_3OD	55.4 (1), 57.3 (2), 60.7 (2), 63.0 (3), 66.0 (1), 69.9 (2), 76.8 (1)
trans-(−)-[Co(L-leu)$_3$]	CD_3OD	60.6 (1), 64.1 (2), 65.6 (1), 69.4 (2)

[a] In cps at 60 Mc downfield from TMS. [b] Relative peak areas in parentheses. [c] Saturated solution in D_2O, 0.08%, signal averaging employed.

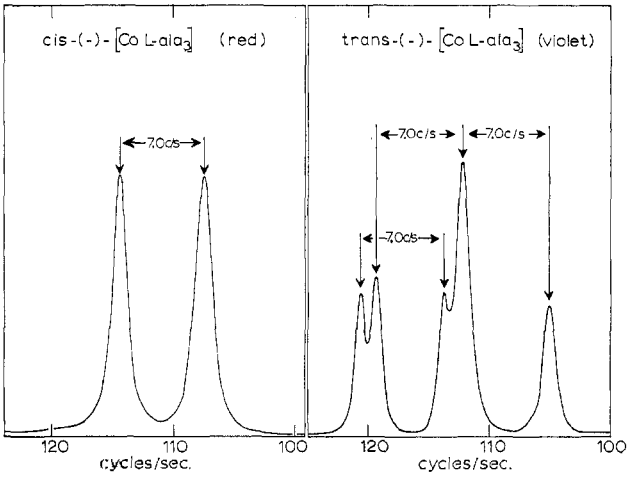

Figure 9.—Methyl proton resonances.

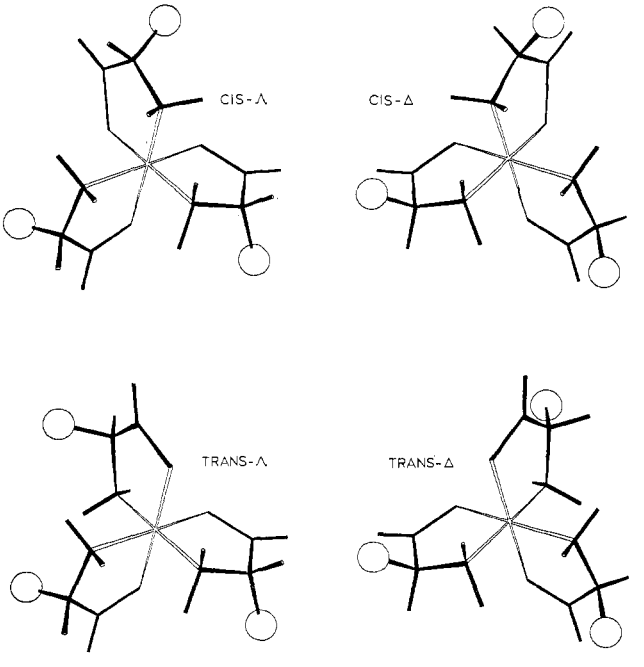

Figure 10.—Steric distribution of alkyl groups in the isomers of [Co(L-amino acid)$_3$] complexes.

(C) **Configurational Isomerism.**—Figure 10 shows the spatial distribution of the alkyl substituents in the four isomers arising with any one L-amino acid. In the

alanine and leucine complexes these are the methyl and *sec*-butyl groups, respectively. In the L-proline complexes a three-membered aliphatic chain links the α carbon atom to the nitrogen atom. The figures indicate either a pseudo-axial or pseudo-equatorial arrangement of these groups with respect to the threefold or (in the case of *trans* isomers) pseudo-threefold axis of the molecules. The Λ molecules, both *cis* and *trans*, have pseudo-equatorial substituents while the Δ molecules have pseudo-axial components. In the case of the Δ-*trans* molecule two substituents are axially disposed at one end of the pseudo-threefold axis and the third at the opposite end. Furthermore, there is one isomer, Λ-*trans*, which has an exceptionally small distance between two of its alkyl groups. In no other isomer is such a close distance of approach realized. When the alkyl group is *sec*-butyl an appreciable "clash" is possible in certain rotational conformations. When the amino acid is L-proline the conformation of the alkyl ring is practically rigid and the steric interaction implied in the Λ-*trans* configuration appears prohibitively large. This interaction is illustrated in Figure 11. With this amino acid only the Λ-*cis* molecule shows no steric interaction. The Δ molecules show an interaction between the axial groups which is greater in the *cis* isomer, in which three groups are involved, than in the *trans* isomer, where only two groups interact.

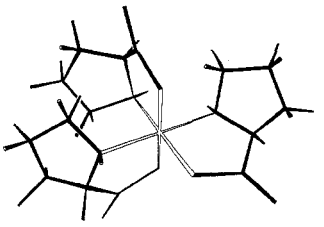

Figure 11.—Steric interaction of two L-proline residues in *trans*-Λ-[Co(L-pro)$_3$].

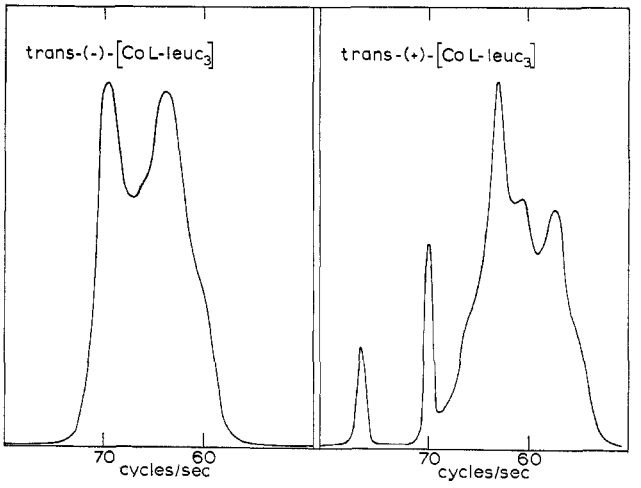

Figure 12.—Methyl proton resonances.

Our assignment of absolute configuration is based primarily on the yields of the various isomers of the L-proline complexes, where the steric factors are most accentuated. The preparation, from tris(carbonato)-cobalt(III), generally favors the formation of *trans* isomers. When the ligands are L-leucine and L-alanine, almost equal yields of (+)- and (−)-*trans* isomers are obtained. In a typical preparation of the L-proline complexes the yields were *cis*-(+) = 0.76 g, *cis*-(−) = 0.11 g, *trans*-(−) = 1.48 g. No *trans*-(+) isomer could be recovered from the preparation (see Experimental Section). The *trans*-(−) isomer, however, crystallized in two forms; both gave identical CD and absorption spectra.

The yields given above are undoubtedly governed by mechanistic and kinetic factors; however, if it is assumed that the activation energy of the transition state in the formation reaction is related to the free energy of the final product, then the relative yields of the isomers may be related to their stabilities. On this basis the missing *trans*-(+) isomer is identified as *trans*-Λ because of the prohibitive steric hindrance in this case. From the sign of the circular dichroism it follows that the *cis*-(+) isomer is also Λ and the *cis*-(−) isomer is Δ. The yields of these isomers support this assignment. The high yield of the *cis*-(+)-Λ molecule is related to the absence of the axial steric interactions in this case.

The importance of the axial and equatorial disposition of the alkyl groups is indicated by the solubility differences of the various isomers. Douglas, *et al.*,[5] point out this effect but their discussion of the solubilities of the L-alanine complexes is incorrect. They indicate that the *trans*-(+) or α isomer is more soluble than the *trans*-(−) or α' isomer. Contrary to this and in agreement with the authors experimental details, we find the water solubility of the *trans*-(+) isomer to be 0.1% by weight, whereas the *trans*-(−) isomer is extremely soluble. The difficulty arises from the configurations of the *trans* isomers proposed by Douglas, *et al.*,[5] which we now suggest to be incorrect. From our assignment of configuration, it is the *trans*-(+) or α isomer which has the Λ absolute configuration and therefore equatorial alkyl groups. The experimental solubilities then follow the same pattern as the *cis* isomers, Δ molecules with axial groups being more soluble than Λ molecules with equatorial groups. Steric interference with lattice forces has been proposed to explain this.[5]

The nmr spectra of the L-leucine complexes support the present assignment of absolute configuration. We have examined the proton resonances of both *trans* isomers in perdeuteriomethanol solution. The results are shown in Table I. The methyl resonances, which are more clearly defined than the remainder, occur at about 60 cps downfield from TMS. The spectra are shown in Figure 12. The *trans*-(−) isomer has a relatively simple spectrum whose peak areas suggest two doublets centered at 67 cps with almost identical chemical shifts and one doublet centered at 63 cps. This pattern is almost identical with that observed in the corresponding L-alanine isomer (see Figure 9) except that the resonances of the leucine isomer occur at higher fields and the coupling constants are smaller.

This is due to the greater distance of the leucine methyl groups from the electrophilic metal ion.

The breadth of the leucine resonances deserves comment. Each *sec*-butyl group has two methyl groups which, when the total molecule is considered, are not related by a C_2 axis. However, if the *sec*-butyl group is freely rotating, they will experience virtually the same average environment. It is this nonequivalence which accounts for the line width. The lines were not appreciably narrowed by raising the sample temperature to 65°.

The analysis of the spectrum of the *trans*-(+)-leucine isomer is illustrated in Figure 13. The numbers at the base of the peaks indicate their relative areas. The sum of these numbers is twelve. The total number of methyl groups in the molecule is six, each of which should provide a doublet resonance by coupling with its single α proton. This implies that the peaks with unit area represent one resonance of a single methyl group. If it is assumed that the coupling constants are of the order of 5.0 to 7.0 cps and that the coupling constants of the two methyl groups on a single alkyl chain are very similar, then the analysis of the spectrum is straightforward. The peak of intensity 2 at 69.9 cps, 6.9 cps from that at 76.8 cps, implies a second doublet having one resonance at 69.9 cps and the other at 63.0 cps. Similarly the unit intensity peaks at 66.0 and 55.4 cps imply that the other resonances of their doublets are common at 60.7 giving J = 5.3 cps. This leaves two resonances, each with intensity 2, at 63.0 and 57.3 cps, which correspond to two virtually degenerate doublets with J = 5.7 cps. By a comparison of the circular dichroism spectra the absolute configuration of this isomer can be correlated with that assigned to the L-proline isomers. It is found that it is just this *trans*-(+) molecule in which the steric "clash" of alkyl groups is expected. This correlation procedure should be reliable because the same ring sizes and coordinating atoms are involved in all these complexes. The features of the nmr spectrum are then easily explained if the two alkyl groups involved in the "clash" no longer have free rotation. For one alkyl chain we observe two high-field doublets with J = 6.9 cps and for the other, two lower field doublets with J = 5.3 cps. The third alkyl group which is not involved in the clash is free to rotate and preserves the essential degeneracy of its methyl resonances exactly as in the other isomer. There are other possible assignments of the spectrum but the essential point is that the two methyl groups on any one alkyl chain must have appreciably different chemical shifts. This is good evidence for the steric "clash" and therefore for the correctness of the assignment of absolute configuration.

In support of this, the *trans*-(+)-L-alanine isomer, having the same absolute configuration, has a methyl resonance spectrum almost identical (although not so well resolved) with that of the *trans*-(−)-isomer (see Table I). In this case the alkyl groups are too small to interact and no anomalies are observed.

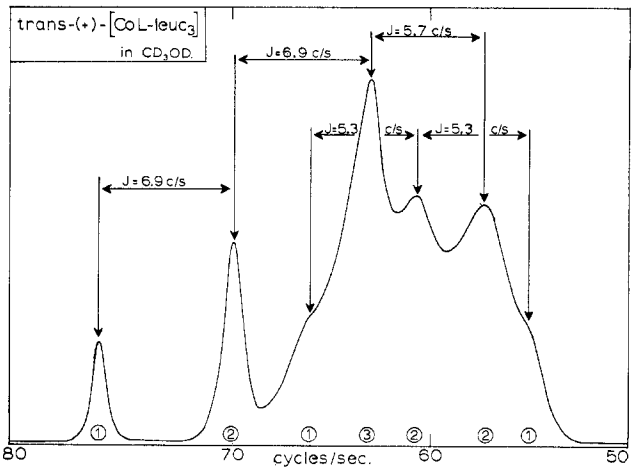

Figure 13.—Analysis of the methyl proton resonance spectrum of *trans*-(+)-[Co(L-leu)$_3$].

(D) Electronic Spectra.—The electronic absorption spectra of all the complexes are given in Figures 1–4, and the corresponding CD spectra in Figures 5–8. The following points arise from these spectra.

(1) The absorption spectra are alike regardless of the ligand and mostly[13] agree with previous work.[3,5] There are small differences in absorption intensity and band shape between (+) and (−) isomers. The absorption of the L-proline isomers occurs at lower energies, as expected from the smaller ligand field of the secondary amine group. By contrast there are major differences between isomers in the circular dichroism spectra. While the general characteristics of any one isomer are preserved when the ligand is changed (and serve to identify it), all four isomers have distinct CD spectra. For the L-alanine complexes these generally[13] agree with previous work.[5]

The spectra of the (+) isomers are not mirror images of those of the corresponding (−) isomers. This is due to the influence of the additional asymmetry of the amino acid carbon atom and has been referred to as "the vicinal effect."[14] The separable spectroscopic "vicinal effect" has been used[5] to assign the positions of the component electronic transitions of the *trans* complexes. The central A_2 peak (D_3 parentage) is of opposite sign to its neighbors and is correlated by its wavelength with the CD maximum of the "configurational effect"; hence the absolute configuration is obtained by analogy with $Co(en)_3^{3-}$ ion. However, Mason[15] has shown that the two components of the CD spectrum of $Co(en)_3^{3+}$ whose maxima are separated by ~3000 cm^{-1} in solution are due to the cancellation of two very intense CD components of opposite sign which, from the polarized crystal spectrum, have

(13) The absorption and CD spectra of the *trans*-(−) isomer in ref 4 show the compound to be clearly impure. ϵ_{max} for the first absorption band is given as 60 and the CD in this region as two negative peaks both with $\Delta\epsilon_{max} = -0.8$. Both the present work and ref 5 indicate ϵ_{max} for the first band as 100, and a CD with a single negative peak having $\Delta\epsilon_{max} = -2.4$. A doubling of this CD peak is always observed when the complex is contaminated with *trans*-(+) isomer, and the abundance of impurity in this case is 30%. This invalidates the authors discussion of the relative abundance of *trans*-(+) and -(−) isomers.

(14) C. T. Liu and B. E. Douglas, *Inorg. Chem.*, **3**, 1356 (1964).

(15) A. J. McCaffery and S. F. Mason, *Mol. Phys.*, **6**, 359 (1963).

maxima separated by ~30 cm^{-1}. It is therefore inappropriate to correlate the CD maxima of the "configurational effect" with any of the components of the "vicinal effect" on the basis of wavelength unless it can be shown that similar cancellation is not occurring in either or both of these effects.

It is not clear how the ligand asymmetry is communicated to the metal chromophoric electrons. It may be due to direct mixing of the asymmetric carbon and metal orbitals (although this seems unlikely from energy considerations), or to specific distortions of the individual chelate rings, or to distortions of the molecule as a whole. The latter can arise either from steric interactions between chelate rings or solvation differences between the isomers. Some evidence for this last mechanism is provided by strong solvent effects on the circular dichroism. This is illustrated for the *cis*-(−)-L-leucine isomer in Figure 14. The sign of the net rotational strength of the higher energy absorption band changes completely as the solvent is changed from hydrochloric acid to dimethylformamide. The latter solvent also causes a drastic increase in absorption intensity in both absorption bands and shifts them to lower energy (Figure 14). This reduction in Dq is consistent with some coordination of dimethylformamide on the C_3 axis, which is the most accessible direction of approach. The *cis*-(+) isomer shows similar effects, but the absorption spectra of the *trans* complexes are relatively insensitive to the same solvent changes. The CD spectra of the *trans* complexes are, however, affected in a regular way by changing the solvent from sulfuric acid to dimethylformamide, as shown for the *trans*-(+)-L-leucine isomer in Figure 15. While a weak positive component in the higher energy band disappears, a weak negative component appears in the lower energy band. External solvent effects are then profoundly affecting the metal chromophores, just as ion-pairing effects have been shown to influence the metal chromophores of optically active complex ions.[16]

(2) The CD spectra of the *cis* complexes show apparently three components in the higher energy absorption band. In the rigorous C_3 symmetry of these complexes the T_2 level can only be resolved into A and E components by the ligand field. Further splitting by a spin–orbital coupling mechanism may be ruled out because of the absence of first-order spin–orbital coupling of the singlet states. On the other hand, if the A and E components have rotational strength of opposing signs and also have different band widths, then the sum of the two components could give the observed CD spectrum with no additional postulates. If the amplitude of both components is large, only small differences in band width can provide this effect. This kind of superimposition is supported by the behavior of the curves in different solvents (Figure 14).

The theory for the optical activity of tris-chelate complexes of Co(III) with D_3 symmetry,[17,18] which is based on the static trigonal field distortion of the ions, predicts only strong rotational strengths in the A_2 and E_a components of the magnetically allowed lower

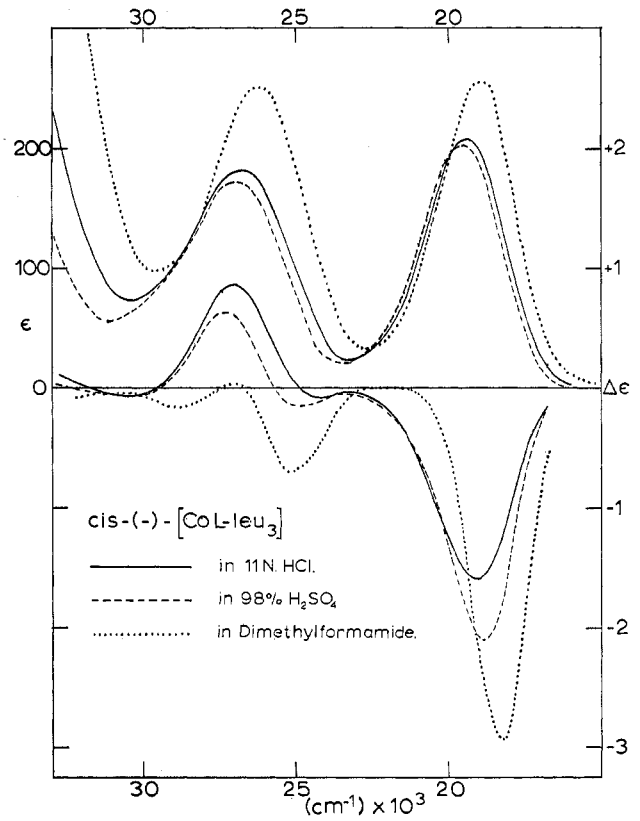

Figure 14.—Effect of solvent on absorption and CD spectra of a *cis* complex.

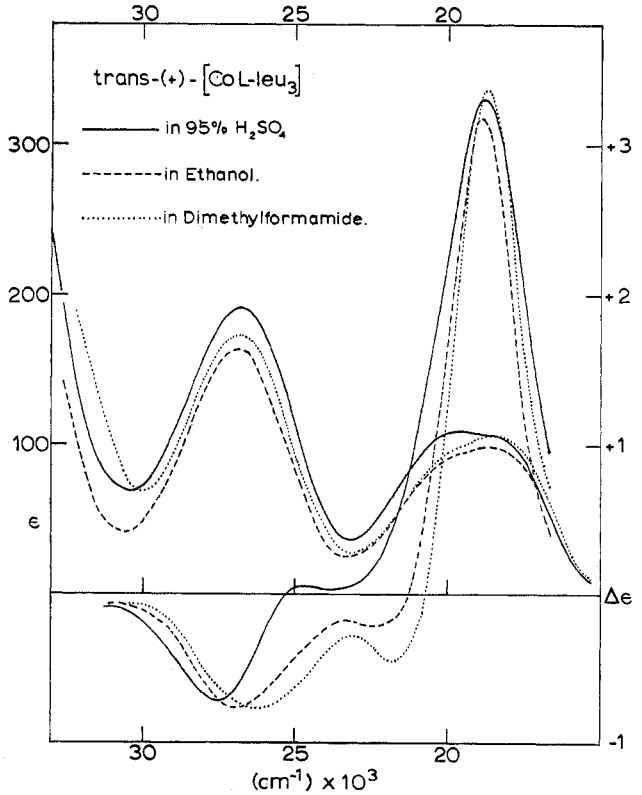

Figure 15.—Effect of solvent on absorption and CD spectra of a *trans* complex.

(16) S. F. Mason and B. J. Norman, *Chem. Commun.*, 73 (1965).
(17) T. S. Piper and A. G. Karipides, *Mol. Phys.*, **5**, 475 (1962).
(18) T. S. Piper and A. G. Karipides, *J. Chem. Phys.*, **40**, 674 (1964).

energy absorption band. Weak activity arising from configuration interaction appears in the E_b component of the upper band. In D_3 symmetry activity in the A_1 component is strictly forbidden. The observed activity in this component in the *cis*-amino acid complexes can arise from two causes. First, in the strict C_3 symmetry of the molecule both the T_1 and T_2 octahedral states are resolved into A and E components, and the higher energy A state can now also gain activity by configuration interaction. Second, Weigang[19] has recently shown that weak circular dichroism ($\Delta\epsilon \sim 1.0$ l. mole^{-1} cm^{-1}) in a magnetically "forbidden" absorption band may arise from a vibronic mechanism, whereby a vibration of the correct symmetry may mix the "forbidden" state with one that is magnetically "allowed." The similarity of the circular dichroism curve in the low-energy absorption region to that of $Co(en)_3^{3+}$ suggests that the sign of the trigonal field parameter in the present complex is negative, consequently the two E components should have rotational strengths of the same sign.[18] Therefore the two A components also must have identical signs. This discussion suggests that the apparent number and sign of CD components may be confused by differences in the band width of the components. For example, the CD spectrum of the *trans*-(−)-L-proline complex (Figure 8) apparently shows two negative components in the low-energy region, one appearing as a pronounced shoulder. It seems much more likely this is due to the weak A component of positive sign and narrower band width superimposed on the strong E component.[20]

(3) From the present assignment of absolute configuration the net rotational strength of a Δ molecule is negative in the low-energy absorption band. This is the same sign as found in Δ-$Co(en)_3^{3+}$ and Δ-$Co(L\text{-}pn)_3^{3+}$ (where L-pn = L-propylenediamine), for which the absolute configurations have been determined by X-ray methods.[21] Both ionic and molecular orbital models[17,18] for the activity predict that the sign of the rotational strength inverts if the chelate angle changes from azimuthal contraction to azimuthal expansion. Saito[22] has recently shown that the $Co(L\text{-}pn)_3^{3+}$ ion exhibits contraction of the chelate ring. No crystal structure of a Co(III) amino acid complex is available. However, structures for Cu(II) amino acid complexes[23] show the O–Cu–N angle to be about 85°. The metal–nitrogen distances in the bis-diamine complexes of Cu(II) and the tris-diamine complexes of Co(III) are 2.00 A in both cases.[21,24] It may be concluded that the two ions are of similar size and that the O–Co–N angle in the Co(III) amino acid complexes will also be less than 90° and show azimuthal contraction. In other words, the sign of the circular dichroism for a known absolute configuration observed in the present work is consistent, in terms of the existing theoretical models, with the sign of the dichroism in the other cases in which the absolute configuration is known.

(E) **Rearrangement Reactions.**—Most of the isomers described above are only soluble in strongly polar or reactive solvents and few underwent isomerization without solvation and decomposition preceding rearrangement. Two systems were found to rearrange without undue decomposition. The *trans*-(−)-tris(L-leucinato)cobalt(III) complex, when boiled in 1-butanol for 4 hr at 117°, gave an equilibrium mixture with the *trans*-(+)-tris(L-leucinato)cobalt(III) complex. During this time a very small quantity of insoluble red *cis* isomer was precipitated. Two separate determinations of the equilibrium constant were made by CD measurements and the following results were obtained: λ (in mμ), % (−) isomer for two runs: 600, 42.9, 43.3; 590, 42.1, 45.4; 580, 41.0, 43.5; 570, 41.7, 42.8; 560, 43.1, 42.5; 550, 43.9, 41.9; 540, 43.5, 42.7; 530, 43.5, 41.3; 520, 44.2, 41.3; 510, 43.0, 41.2; 500, 48.5, 40.8; 410, 45, 40; 400, 48, 34; 390, 50, 38.5; 380, 46, 41.5; 370, 45, 41.2; 360, 43.5, 43.5; 350, 41.3, 49.0. The weighed mean is 42.6%, the standard derivation 1.45. These figures give an equilibrium constant

$$K_1 = \frac{[(-)\text{ isomer}]}{[(+)\text{ isomer}]} = 0.742 \pm 0.05 \text{ at } 117°$$

An approximate first-order rate constant for the reaction in which the (−) isomer goes to the (+) isomer was obtained by quenching the boiling reaction mixture in cold water at regular intervals and observing the CD. The following data were obtained: t (in min), % (−) isomer at three wavelengths: 5, 88.0, 87.3, 88.2; 15, 65.5, 63.7, 66.0; 30, 49.0, 47.6, 50.3; 45, 45.4, 44.5, 46.4. This gave $k_{(-)\rightarrow(+)} = 6.4 \times 10^{-4}$ sec^{-1}.

Second, the *cis*-(−)-tris(L-prolinato)cobalt(III) complex isomerized in neutral aqueous solution at 80° to an equilibrium mixture with the corresponding *trans*-(−) isomer. The reaction was followed by the change in the CD spectrum. After equilibrium had been reached the absorption spectrum showed that 20.1% of the optically active complexes had decomposed. The CD curve was analyzed by comparing the circular dichroism at two wavelengths at a number of points in the spectrum. The results are given in Table II from which the equilibrium constant is

$$K_2 = \frac{[trans\text{-}(-)]}{[cis\text{-}(-)]} = 3.9 \pm 0.6 \text{ at } 80°$$

When the same reaction was attempted in 0.1 N perchloric acid solution at 80°, no reaction was observed after 20 hr.

Three mechanisms have been considered for the rearrangement of unsymmetrical acetylacetone complexes and the implications of each mechanism in

(19) O. E. Weigang, *J. Chem. Phys.*, **42**, 2244 (1965).

(20) These components are defined in the C_3 *cis* complexes but for simplicity the same nomenclature is used in the *trans* complexes. We assume here that the activity arises primarily from the trigonal component of the ligand field and that the lower symmetry of the *trans* complexes is a second-order effect. This assumption is supported by the absence of any splitting in the absorption spectrum.

(21) Y. Nakatsu, M. Shiro, Y. Saito, and H. Kuroya, *Bull. Chem. Soc. Japan*, **30**, 158 (1957); Y. Saito, H. Iwasaki and H. Ota, *ibid.*, **36**, 1543 (1963).

(22) Y. Saito, private communication.

(23) G. A. Barclay and F. S. Stephens, *J. Chem. Soc.*, 2027 (1963); A. M. Mathieson and H. K. Welsh, *Acta Cryst.*, **5**, 599 (1953).

(24) B. W. Brown and E. C. Lingafelter, *ibid.*, **17**, 254 (1964).

TABLE II

EQUILIBRATION OF L-PROLINE ISOMERS

Wavelength, A	(ΔOD) × 10³ [a]	K [b]
5100	−4.80	4.21
4100	+0.45	
4200	−0.22	3.49
3800	+3.00	
5700	−9.37	4.02
5000	−4.28	
5800	−8.77	4.43
4800	−3.00	
5500	−8.25	4.47
3800	+3.00	
5000	−4.27	3.17
4000	+2.85	
5600	−9.15	3.63
4000	+1.50	
5080	−4.72	4.00
4250	−1.87	
	Mean = 3.9 ± 0.6	

[a] Concentration = 8.24×10^{-4} M, 5-cm cell. [b] In H_2O at 80°.

terms of reaction products given.[25] The trigonal twist mechanism involves a trigonal prismatic transition state and provides for inversion of the molecule without *cis–trans* isomerization. In the rhombic twist mechanism, inversion of a *cis* isomer is always accompanied by isomerization so that a *cis*-Λ molecule yields a *trans*-Δ molecule. The bond rupture or dissociative mechanism provides a path for any one isomer to be converted to any of the others, although not necessarily with equal activation energies.

The *cis*-(−)-tris(L-prolinato)cobalt(III) complex undergoes *cis–trans* isomerization without inversion, so that only the bond-rupture mechanism is possible in this case. However, since this reaction is totally inhibited in 0.1 N perchloric acid, the bond rupture must be base catalyzed. An SN1CB mechanism seems reasonable.

The *trans*-(−)-tris(L-leucinato)cobalt(III) complex undergoes inversion without isomerization, so that any of the mechanisms could apply. However, the formation of a small quantity of *cis* isomer during the reaction suggests that a bond rupture or rhombic twist mechanism is operating. The yield of *cis* isomers in such rearrangements will be low as any *cis–trans* equilibrium will favor the *trans* isomer on statistical grounds.

The equilibrium constants raise two points. First, the *cis–trans* equilibrium constant (K_2) for the L-proline complexes shows that the *trans* isomer is slightly more stable than expected from statistical arguments. The molecular diagrams (Figure 10) show that axial steric interactions are more pronounced in the *cis* isomer. Furthermore, the *cis* isomers have a higher dipole moment and are therefore inherently less stable.

Second, the *trans*-(+)-tris(L-leucinato)cobalt(III) complex is slightly more stable in 1-butanol solution than the *trans*-(−) isomer. It is this *trans*-(+) isomer which exhibits the steric "clash." The stability conferred by the pseudo-equatorial nature of the alkyl groups is then sufficient to outweigh this interaction. It is probably because of this equatorial stability that Lifschitz[2] failed to isolate the *cis*-(−)-tris(L-alaninato)-cobalt(III) complex which has axial alkyl groups and is always obtained in smaller yields than the *cis*-(+) isomer with equatorial groups.

Summary

The important conclusions of this work are now summarized.[26]

(1) The red compounds of tris(amino acid)cobalt(III) complexes have been shown to belong to the *cis* or "facial" series, while the violet compounds belong to the *trans* or "peripheral" series.

(2) The complexes which have net negative rotational strength in the low-energy absorption band have been shown to have the Δ absolute configuration. The argument, which is a steric one, allows the assignment in uncharged complexes. It is applied in two independent cases and is based only on the absolute configuration of the amino acid.

(3) The circular dichroism spectra provide a case where the number of apparent circular dichroism components exceeds the number of electronic components of the absorption band. This should be considered when assignments of molecular symmetry are based on the number of circular dichroism components in an absorption band.

(4) Some rearrangement reactions of these complexes are shown to support a bond rupture mechanism rather than internal twisting mechanisms. One of the rearrangements is base catalyzed.

Acknowledgments.—We gratefully acknowledge support from the National Science Foundation. We thank Mr. J. A. Stanko for useful discussions and Mr. J. Nemeth and his staff for the microanalytical work.

(25) R. C. Fay and T. S. Piper, *Inorg. Chem.*, **3**, 348 (1964).

(26) A preliminary, two-dimensional X-ray structure of *trans*-(+)-tris(L-alaninato)cobalt(III) [M. G. B. Drew, J. H. Dunlop, R. D. Gillard, and D. Rogers, *Chem. Commun.*, 42 (1966)] confirms the absolute configurations found in this work.