with respect to tris(cysteinato)cobalt(III). The red complex is S,O coordinated, and the green one is S,N coordinated. The isomerization between these two complexes is irreversible: treatment of the red isomer with hot sodium cysteinate at pH 11–12 results in rapid formation of the green isomer.

Oxidation Mechanism.—There is an equilibrium between the 1:1 and 1:2 complexes, and the latter complex is a main species in the presence of excess cysteine. This violet tris complex decomposes into the red complex rapidly at room temperature. In view of these facts, the catalytic oxidation of cysteine may be explained reasonably in the following manner. The red-violet color observed in the presence of excess cysteine is not due to a 1:2 complex as postulated by Martell and Calvin[13] but to a 1:3 complex. This tris complex decomposes into a bis complex and then into ferrous ion and cystine as suggested by many workers. This scheme is outlined in Chart I.

Acknowledgment.—The authors are indebted to Dr. S. Okuzawa for many helpful discussions.

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[13] A. E. Martell and M. Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., New York, N. Y., 1952, p 384.

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Stereochemistry of Complexes of Multidentate Ligands. II. Geometrical and Optical Isomers of Bis(2,3-diaminopropionato)cobalt(III) Ion

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Reaction of DL-2,3-diaminopropionic acid with tris(carbonato)cobaltate(III) ion gives the expected five geometrical isomers of bis(2,3-diaminopropionato)cobalt(III) ion. The five are separated by ion-exchange chromatography. Formation of the complex with either enantiomeric 2,3-diaminopropionic acid gives three optically active geometrical isomers of specific absolute configuration. Uv, ORD, and CD data for these isomers are used in determining the geometry of the several complex ions.

Introduction

Only a few complexes of cobalt(III) and tridentate ligands have been prepared and studied. The bis-cobalt(III) complex of 1,2,3-triaminopropane has been prepared.[1] Also, the 2:1 diethylenetriamine:cobalt(III) and the 2:1 imidodiacetate:cobalt(III) complexes are known.[2,3] Recently, Legg and Cooke[4] prepared the first cobalt(III) complexes containing two different tridentate ligands and investigated the stereochemistry of the complex ions.

In this paper we report the preparation and separation of all of the possible geometrical and optical isomers of the bis-cobalt(III) complex of L-2,3-diaminopropionic acid, of D-2,3-diaminopropionic acid, and of racemic 2,3-diaminopropionic acid. In both of the first two cases, formation of three optically active geometrical isomers is expected. In the third case, five geometrical isomers are expected to form because of the possibility of having the two ligands in the complex possess opposite absolute configurations. In all cases separation of the geometrical isomers was effected by ion-exchange chromatography.

2,3-Diaminopropionic acid, like 1,2,3-triaminopropane, is constrained to occupy an octahedral face about the cobalt atom when coordinated. Unlike 1,2,3-triaminopropane, 2,3-diaminopropionic acid contains an asymmetric carbon atom. For octahedral complexes of this ligand, in a given geometrical isomer, the absolute configuration of the ligands (if both ligands have the same absolute configuration) specifies the absolute configuration of the complex ion. The geometries and configurations of the complexes are assigned on the basis of visible–uv, ORD, and CD spectra and less soluble diastereomers data.

Experimental Section

Reagents.—Commercial reagent grade chemicals were used throughout, except where otherwise indicated.

Ligands.—L-2,3-Diaminopropionic acid hydrochloride was purchased from the California Corp. for Biochemical Research, Los Angeles, Calif. *Anal.* Calcd for $C_3H_9N_2O_2Cl$: C, 25.63; H, 6.45; N, 19.92. Found: C, 25.82; H, 6.5; N, 19.9; $[\alpha]_D$ +25.6°.

D-2,3-Diaminopropionic acid hydrochloride was prepared from D-asparagine (Nutritional Biochemicals Corp.) by means of a Hoffmann degradation of N-acetyl-D-asparagine followed by acid hydrolysis of the glyoxalidonecarboxylic acid, according to the method of Karrer and Schlosser.[5] *Anal.* Found: C, 25.32; H, 6.37; N, 20.02; $[\alpha]_D$ −24.0°.

DL-2,3-Diaminopropionic acid hydrobromide was prepared by the amination under pressure of 2,3-dibromopropionic acid, according to the literature method.[6] *Anal.* Calcd for C_3H_9-

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[1] F. G. Mann and W. J. Pope, *Proc. Roy. Soc.* (London), **A107**, 80 (1925).

[2] F. G. Mann, *J. Chem. Soc.*, 461 (1934).

[3] M. Mori, M. Shibata, E. Kyuno, and F. Maryama, *Bull. Chem. Soc. Japan*, **35**, 75 (1962).

[4] J. I. Legg and D. W. Cooke, *Inorg. Chem.*, **5**, 594 (1966).

[5] P. Karrer and A. Schlosser, *Helv. Chim. Acta*, **6**, 411 (1923).

[6] K. Poduska, J. Rudinger, and F. Sorm, *Collection Czech. Chem. Commun.*, **20**, 1174 (1955).

N_2O_2Br: C, 19.47; H, 4.90; N, 15.14. Found: C, 19.51; H, 4.88; N, 15.11.

Preparation of Complexes.—The complexes of the D and the L ligands were prepared identically. A 3.44-g sample of the 2,3-diaminopropionic acid hydrochloride was dissolved in 49.1 ml of 0.50 M HCl. The solution was warmed slightly on the steam bath, and the equivalent amount of freshly prepared sodium tris(carbonato)cobaltate(III) trihydrate was added in portions. A 0.2-g sample of activated charcoal was added then to the solution. The solution was heated for 4 hr on the steam bath. The resulting red reaction mixture was filtered and the charcoal was carefully extracted with hot water to recover any traces of the least soluble isomer which crystallized on it. This solution was used directly on the ion-exchange column for isomer separation. The complexes with DL ligand were also prepared in this way except that an equivalent amount of the 2,3-diaminopropionic acid hydrobromide was used.

Separation of Isomers.—The red solutions from preparations described above were each deposited on ion-exchange columns and eluted slowly (1 drop every 12 sec). The separations generally took 4–5 weeks. The columns were 5.0 × 60 cm and were packed with 50–100 mesh Dowex 50W-X8 cation-exchange resin in the ammonium form. The eluent was 0.25 M ammonium bromide. Three distinctly colored bands developed and were collected from the column which contained the complexes of the L ligand and also from the column which contained the complexes of the D ligand. Five separate bands developed and were collected from the DL column. The solutions containing these bands were evaporated to small volume in a rotary evaporator. In cases of the less soluble isomers, a red product precipitated immediately and was recrystallized from water. The solutions of the more soluble isomers were evaporated to dryness and the ammonium bromide was removed by extraction with absolute alcohol in a Soxhlet extractor. Analyses of the bromides are given in Table I except for the fifth isomer off the DL column which was isolated and analyzed as the chloride. *Anal.* Calcd for $CoC_6H_{14}O_4N_4Cl$: C, 23.99; H, 4.70; N, 18.65. Found: C, 23.68; H, 4.92; N, 18.02.

Table I
Analyses of Isomers of
Bis(2,3-diaminopropionato)cobalt(III) Bromide

Isomer	% C	% H	% N
	Calcd for $CoC_6H_{14}O_4N_4Br$		
	20.85	4.05	16.20
	Found		
L-1	20.80	4.11	16.54
L-2	20.93	4.08	16.30
L-3	21.16	4.07	15.37
D-1	21.41	4.07	15.95
D-2	21.42	4.10	16.32
D-3	21.12	4.15	16.36
DL-1	21.00	4.12	16.16
DL-2	20.82	4.19	16.22
DL-3	20.80	3.93	16.13
DL-4	21.03	4.24	16.11

Resolutions.—Isomer DL-3 was resolved in the following way. A 0.0584-g sample (0.1693 × 10^{-3} mole) of the analytically pure isomer was dissolved in 25 ml of water. To the solution was added 0.0738 g (0.1693 × 10^{-3} mole) of silver *d*-α-bromocamphor-π-sulfonate. The solution was digested on the steam bath for 1 hr, and the silver bromide was removed by filtration. Slow evaporation gave a crop of purple-red crystals. These were removed by filtration and washed with cold water and cold ethanol. A solution of this product in water gave a CD spectrum that did not change during subsequent recrystallization. Therefore the *d*-α-bromocamphor-π-sulfonate salt was converted to the bromide by addition of ammonium bromide and recrystallization. The CD curve of this bromide salt is the same as the CD curve of the *d*-α-bromocamphor-π-sulfonate salt except for the absence of the *d*-α-bromocamphor-π-sulfonate peak in the ultraviolet region. Isomers DL-1, DL-2, and DL-4 were resolved in the same way.

Electronic Absorption Spectra.—Spectra were recorded at room temperature using a Jasco ORD/UV/CD-5 spectrophotometer.

Optical Rotatory Dispersion and Circular Dichroism.—These curves were recorded at room temperature using the same instrument.

Analyses.—Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich., and Micro-Tech. Laboratories Inc., Skokie, Ill.

Discussion

2,3-Diaminopropionic acid contains an asymmetric carbon atom and exists therefore in the enantiomeric forms shown in Figure 1. The absolute configurations of the enantiomers of this ligand are known from chemical correlations with asparagine and serine.[5]

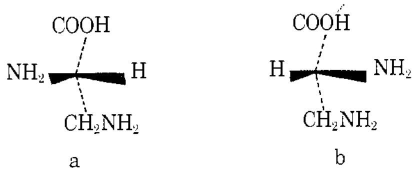

Figure 1.—(a) L-2,3-Diaminopropionic acid and (b) D-2,3-diaminopropionic acid.

The bis(2,3-diaminopropionato)cobalt(III) ion has five possible geometrical isomers (Figure 2). The isomers are named by considering first the spatial relationship of the two oxygen atoms, then of the two α-nitrogen atoms, and finally of the two β-nitrogen atoms. Three of these geometries require the two ligand molecules in the complex to have the same absolute configuration. The other two geometries require ligand molecules of opposite absolute configurations. If pure D-2,3-diaminopropionic acid is coordinated to cobalt(III), formation of only the *trans,cis,cis*, *cis,cis,trans*, and *cis,trans,cis* isomers is possible; in the other geometries at least one of the ligand donor groups always points out in the wrong direction. If pure L ligand is coordinated to cobalt(III), the enantiomers of the same three geometrical isomers result. Only with DL-2,3-diaminopropionic acid can all five possible geometrical isomers form.

It proves possible to separate and isolate the various sets of geometrical isomers by using cation-exchange column chromatography. With D-2,3-diaminopropionic acid or with L-2,3-diaminopropionic acid as the ligand, three colored bands develop when the complexation reaction mixture is eluted on the column. With DL ligand, five bands develop. Thus 11 bands are isolated. This is in accord with the theoretical expectation. The bands are designated here as D-1, D-2, D-3, L-1, L-2, L-3, DL-1, DL-2, DL-3, DL-4, and DL-5. The ORD measurements show that the compounds of the three D bands are severally the mirror images of the compounds of the three L bands. The ORD and CD spectra for the three isomers from the reaction with L ligand are given in Figures 3 and 4.

Since the complexes exhibit uv–visible spectra (Fig-

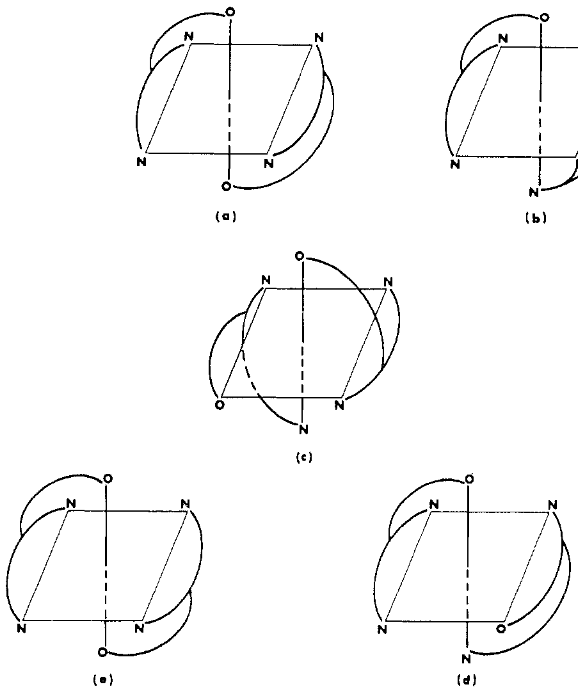

Figure 2.—Geometrical isomers of bis(2,3-diaminopropionato)-cobalt(III) ion: (a) *trans,cis,cis*, (b) *cis,cis,trans*, (c) *cis,trans,cis*, (d) *cis,cis,cis*, (e) *trans,trans,trans*. (a), (b), and (c) require two ligands of the same absolute configuration—L in the above representations; (d) and (e) require that the two ligands have opposite absolute configurations.

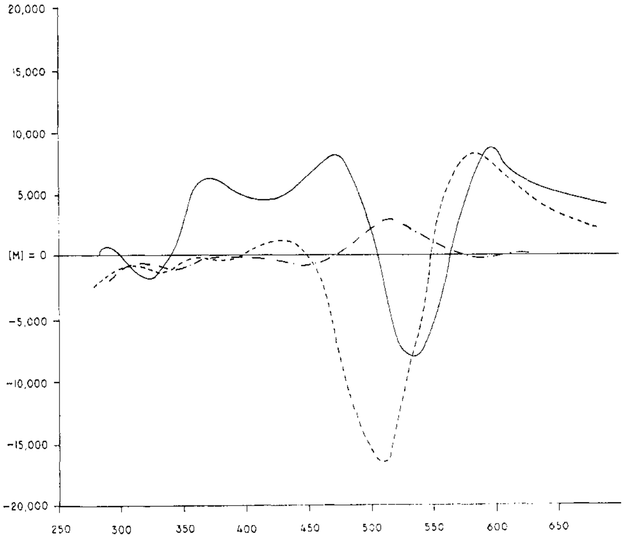

Figure 3.—Molar rotation of: (———) *trans,cis,cis*-bis(L-2,3-diaminopropionato)cobalt(III) ion (L-1); (– – – –) isomer L-2; (– · – ·) isomer L-3. Wavelength in millimicrons.

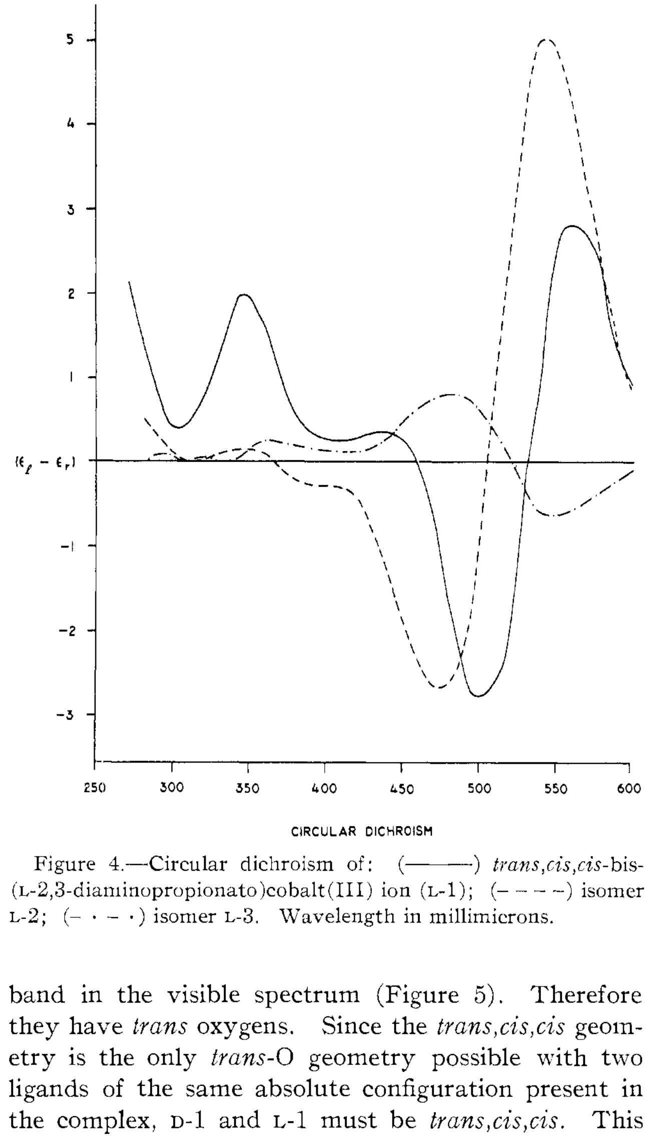

Figure 4.—Circular dichroism of: (———) *trans,cis,cis*-bis-(L-2,3-diaminopropionato)cobalt(III) ion (L-1); (– – – –) isomer L-2; (– · – ·) isomer L-3. Wavelength in millimicrons.

ure 5) which agree with the crystal field considerations for *cis* and *trans* isomers as established by Ballhausen and Jørgensen,[7] Moffitt and Ballhausen,[8] and Yamatera,[9] it is possible immediately to assign geometries to isomers D-1 and L-1. These two isomers are of the type bis(carboxylic acid)tetraamminecobalt(III) and show a shoulder on the high-energy side of the long-wavelength band in the visible spectrum (Figure 5). Therefore they have *trans* oxygens. Since the *trans,cis,cis* geometry is the only *trans*-O geometry possible with two ligands of the same absolute configuration present in the complex, D-1 and L-1 must be *trans,cis,cis*. This means that L-1 is of the geometry and configuration represented in Figure 2a and that D-1 is the mirror image of the representation in Figure 2a.

DL-1 and DL-5 also show shoulders on the high-energy sides of their long-wavelength bands in the visible spectrum. They both therefore must also be considered *trans*-O isomers. Since DL-1 is followed from the column by two *cis*-O isomers (as are both L-1 and D-1), it must also have the *trans,cis,cis* geometry and consist of a racemic mixture of D-1 and L-1. DL-5 then has the *trans,trans,trans* geometry as this is the only other *trans*-O geometry.

D-2, D-3, L-2, L-3, DL-2, DL-3, and DL-4 are all *cis*-O isomers according to their visible spectra. DL-2 and DL-4 were resolved with the *d*-α-bromocamphor-π-sulfonate ion. The resolution of DL-2 gave in the first crop an optically active ion whose CD curve in the visible region was identifiable with the CD curve of D-2. In a like way, the resolution of DL-4 gave in the first crop with *d*-α-bromocamphor-π-sulfonate an ion identifiable by comparison of CD curves with L-3. Also resolved with the same resolving agent was DL-1. This resolution, by giving in the first crop an ion identifiable with D-1 by comparison of CD curves,

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[7] C. J. Ballhausen and C. K. Jørgensen, *Kgl. Danske Videnskab. Selskab, Mat. Fys. Medd.*, **29**, 14 (1955).

[8] W. J. Moffitt and C. J. Ballhausen, *J. Inorg. Nucl. Chem.*, **2**, 178 (1956).

[9] H. Yamatera, *Bull. Chem. Soc. Japan*, **31**, 95 (1958).

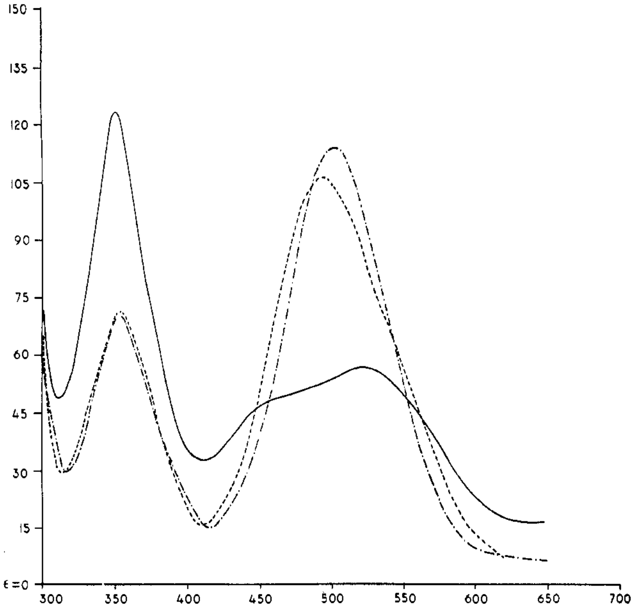

Figure 5.—Absorption spectra of (———) *trans,cis,cis*-bis-(L-2,3-diaminopropionato)cobalt(III), (– – – –) isomer L-2, and (– · – ·) isomer L-3 *vs.* wavelength in millimicrons.

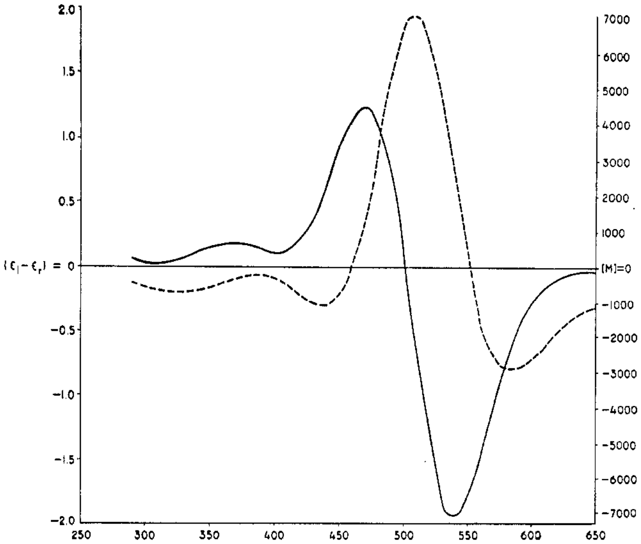

Figure 6.—Molar rotation (– – – –) and circular dichroism (———) of $(+)_{546}$-*cis,cis,cis*-L-2,3-diaminopropionato-D-2,3-diaminopropionatocobalt(III) ($(+)_{546}$-DL-3) *vs.* wavelength in millimicrons.

TABLE II

C_2-AXIS RING CHIRALITIES

Compound	Ring chiralities ONα–ONα	NαNβ–NαNβ	ONα–NαNβ	NαNβ–ONα	Abs config
trans,cis,cis-Bis(L-2,3-diaminopropionato)-cobalt(III) bromide[a]	Λ	Δ	Δ	Δ	Δ_{C_2}
cis,cis,trans-Bis(L-2,3-diaminopropionato)-cobalt(II) bromide[a]	Λ	Δ	Λ	Λ	Λ_{C_2}
cis,trans,cis-Bis(L-2,3-diaminopropionato)-cobalt(III) bromide[a]	Δ	Λ	. . .	. . .	. . .
cis,cis,cis-L-2,3-Diaminopropionato-D-2,3-diaminopropionatocobalt-(III) bromide[a,b]	Δ	Δ	Δ	Λ	Δ_{C_2}

[a] The enantiomer represented in Figure 2. [b] Chiralities along pseudo-C_2 axis.

verified the visible spectrum identification of DL-1 as a racemic mixture of D-1 and L-1. Since D-1, DL-2, and DL-4 are thus identified as racemic mixtures of the three geometrical isomers that require the two coordinated ligands to have the same absolute configurations, DL-3 and DL-5 must be the two geometrical isomers that require the two coordinated ligands to have opposite absolute configurations. Since DL-5, as deduced above from the visible spectra, is the *trans,trans,trans* geometrical isomer, DL-3 is the *cis,cis,cis* geometrical isomer. This conclusion was made certain by the resolution of DL-3 into optical isomers having CD and ORD curves different from the CD and ORD curves of any of the other optical isomers (Figure 6). Finally, the fact that DL-1, DL-2, DL-3, and DL-4 are resolvable verifies the assignment of DL-5 to the *trans,trans,trans* geometry—the only centrosymmetric geometry.

It now remains to determine whether L-2 (and thus D-2 and DL-2) has the *cis,trans,cis* geometry and L-3 (and thus D-3 and DL-4) the *cis,cis,trans* geometry, or *vice versa.* In Table II is given a summary of the C_2-axis ring chiralities for all of the possible pairs of rings in the four optically active geometrical isomers. Also given is the label for the absolute configuration as determined by the ring-pairing method of Legg and Douglas.[10]

From Table II it can be seen that the *trans,cis,cis* and *cis,cis,trans* geometrical isomers should have opposite absolute configurations when both are prepared with ligands of the same absolute configuration. This difference in absolute configuration provides a potential means of identification of L-2 and L-3. Resolution of DL-1, DL-2, and DL-4 gave, respectively, D-1, D-2, and L-3 in the less soluble *d*-α-bromocamphor-π-sulfonate salts. By the method of less soluble diastereomers then, it can be concluded that L-1 and L-2 have like absolute configurations and L-3 has the opposite absolute configuration. If L-3 and L-1 have opposite absolute configurations, L-3 is the *cis,cis,trans*-bis(L-2,3-diaminopropionato)cobalt(III) ion because L-1 is known to be the *trans,cis,cis*-bis(L-2,3-diaminopropionato)cobalt(III) ion and the *trans,cis,cis* and *cis,cis,trans* isomers have, by the ring-pairing method, opposite absolute configurations. L-2 cannot be the *cis,cis,trans* isomer by this method because it and L-1 have the same absolute configuration.

By this assignment, L-2 has the geometry and configuration represented in Figure 2c, and L-3, the geometry and configuration represented in Figure 2b; D-2 and D-3 are represented by the mirror images of Figure 2c and b, respectively.

Although the method of less soluble diastereomers has been shown to be unreliable at times,[11] it has been pointed out that in the applications where the method

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(10) J. I. Legg and B. E. Douglas, *J. Am. Chem. Soc.*, **88**, 2697 (1966).

(11) K. Garbett and R. D. Gillard, *J. Chem. Soc.*, 6084 (1965).

gave incorrect results, the diastereomers under comparison did not have the same crystalline morphology.[12] The above identification thus rests on the assumption that the crystals of the less soluble DL-1, DL-2, and DL-4 diastereomers with *d*-α-bromocamphor-π-sulfonate ion are isomorphous. This seems likely enough since the diastereomers under comparison are formed from geometrical isomers. Still, it cannot be considered unequivocal.

Also, this assignment can be correct only insofar as the conclusion that the chelate ring arrangement in the *trans,cis,cis* isomer is opposite in absolute configuration to the ring arrangement in the *cis,cis,trans* isomer. It should be brought out that the conclusion is not dependent upon the actual labels assigned the ring arrangements by the ring-pairing method, but only upon the assumption that the two labels are different.

Further, it is possible to make the reverse assignment of geometry to isomers L-2 and L-3 using the CD curves.

It is known that either L-2 or L-3 is the *cis,trans,cis* isomer. If it is assumed that the CD curve of the *cis,trans,cis* isomer is due mostly to the vicinal effect caused by the two L ligands (see Table II), then the subtraction of the CD curve of the *cis,trans,cis* isomer from the CD curve of the *cis,cis,trans* isomer would be expected to give approximately the pure configurational CD curve of the *cis,cis,trans* isomer. Furthermore, subtraction of the CD of *cis,trans,cis* from that of *trans,cis,cis* (L-1) gives approximately the pure configurational CD of the *trans,cis,cis* isomer if it is assumed that the vicinal effect of two L ligands with oxygens *cis* is about equal to the vicinal effect of two L ligands with oxygens *trans*. In Figure 7 are shown the results of (L-1) − (L-2) and (L-1) − (L-3) (because either L-2 or L-3 could be *cis,trans,cis* and so represent the vicinal effect CD) and (L-3) − (L-2). The mirror image of this third curve of course represents (L-2) − (L-3). If the absolute configuration of *trans,cis,cis* isomer (L-1) is indeed Δ_{C_2}, then, according to the reasoning used by Legg, Cooke, and Douglas,[13] this *trans*-bis(carboxylic acid)tetraamminecobalt(III) complex should have a positive longest wavelength CD extremum. Only (L-1) − (L-3) gives this. In a similar way, a Λ_{C_2} *cis*-bis(carboxylic acid)tetraamminecobalt complex should also have a positive longest wavelength CD extremum. Only (L-2) − (L-3) gives this. Thus it can be concluded that the CD curve of L-3 represents the vicinal effect and therefore L-3 is the *cis,trans,cis* isomer, which means of course that L-2 is the *cis,cis,trans* isomer.

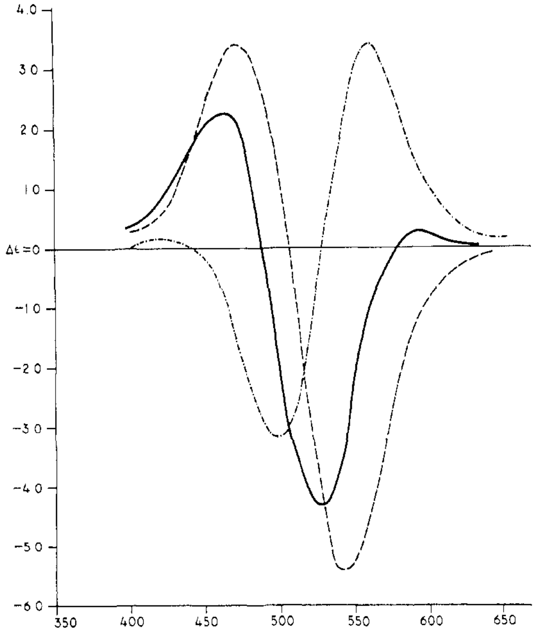

Figure 7.—Subtraction of CD of L-2 from that of L-1 (———), subtraction of CD of L-2 from that of L-3 (– – – –), and subtraction of CD of L-3 from that of L-1 (– · – ·) plotted *vs.* wavelength in millimicrons.

This assignment depends not only on the fact that the absolute configurations of the *trans,cis,cis* and *cis,cis,trans* isomers formed with two L ligands are opposite, but also on the fact that the labels, Δ_{C_2} and Λ_{C_2}, respectively, given the two by the ring-pairing methods are correct.

Considering the assumptions involving the vicinal effect that are made in the above line of reasoning and the dependence of the assignment on the ring-pairing method to give the correct label for the absolute configuration, this second method cannot be considered any more nearly definitive than the method involving the less soluble diastereomers.

Definitive assignment of the geometries awaits X-ray single-crystal methods. Once the geometries of L-2 and L-3 are definitely known, it will be possible to consider the CD curves on a basis of certainty.

Acknowledgment.—Financial assistance furnished by the National Institutes of Health through Grant GM-14254-02 is gratefully acknowledged.

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[12] K. Garbett and R. D. Gillard, *J. Chem. Soc., Sect. A*, 802 (1966).

[13] J. I. Legg, D. W. Cooke, and B. E. Douglas, *Inorg. Chem.*, **6**, 700 (1967).