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Circular Dichroism of a Cobalt(III) Complex of Ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionic Acid[1]

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One geometrical isomer of the cobalt(III) complex of ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionic acid has been prepared and resolved into optical isomers. Absorption, infrared, circular dichroism, and pmr spectra were used to characterize the species as a hexadentate complex with the two glycinate rings in trans positions.

Introduction

Although there are now general methods for relating the absolute configurations of optically active metal chelates,[3,4] the effects of chelate ring size and arrangement around the central metal ion on the circular dichroism spectra are still little understood.

The ethylenediaminetetraacetatocobaltate(III) ion ($Co(EDTA)^-$, see Figure 1) has three chelate rings which form a girdle around the cobalt ion, the ethylenediamine ring, and two of the glycinate rings (G rings). The other two glycinate rings (R rings) lie in planes approximately perpendicular to each other and to the plane of this girdle. Bond length and bond angle data[5] indicate that the G glycinate rings are considerably more strained than the R rings.

Compounds with the microsymmetry *cis*-$[CoN_2O_4]$ and related to the $Co(EDTA)^-$ structure are of interest for the study of factors contributing to the optical activity and stereospecificity in these systems. As part of this general study, we report here the preparation, characterization, and optical activity of the cobalt(III) complex of ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionic acid (H_4EDDDA). Studies of complexes of ethylenediaminediacetic-*N*,*N*′-di-2-propionic acid (H_4EDPA)[6] and ethylenediamine-*N*,*N*′-disuccinic acid (H_4EDDS)[7] have recently been published. The reactions of both of these ligands with trivalent cobalt were reported to be stereospecific. Three isomers of $Co(\text{L-asp})_2^-$ ion (L-asp = L-aspartate ion) have been separated and characterized by absorption, circular dichroism,[8] and proton magnetic resonance[9] spectra. One of these isomers corresponds to the $Co(EDDS)^-$ complex ion which was reported[7] (H_4EDDS was prepared by joining two L-H_2asp molecules by an ethylene linkage).

H_4EDDDA is closely related to H_4EDTA, but on hexadentate coordination it forms three five- and two six-membered chelate rings. Three geometric isomers which differ in the number (0, 1, or 2) of six-membered rings lying in the girdle plane are possible (Figure 2). The effect of position of the six-membered rings on the optical activity should be clarified if the circular dichroism (CD) of resolved species of these three isomers could be measured. However, as the G rings are strained in $Co(EDTA)^-$, one might expect the more flexible β-alaninate rings to coordinate preferentially in these positions and it may not be possible to obtain all isomers.

Experimental Section

Reagents.—All reagents and solvents were obtained commercially and used without further purification.

Physical Measurements.—Electronic spectra were recorded at room temperature on a Cary Model 14 recording spectrophotometer using a tungsten lamp and a hydrogen lamp (<350 nm).

Proton magnetic resonance spectra were obtained on a Varian A-60 spectrometer (60 MHz). The solvent was D_2O and sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was added to serve as internal standard. The circular dichroism curves were recorded at room temperature with a Roussel-Jouan Dichrograph using a Sylvania Sun Gun light source. Infrared spectra were recorded on a Beckman IR4 or a Beckman IR8 infrared spectrometer. Cellex AE anion-exchange cellulose obtained from Bio-Rad Laboratories was used for ion-exchange studies. Chemical analyses were done by Alfred Bernhardt, Elbach, West Germany.

Ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionic Acid.—3-Chloropropionic acid (54 g, 0.5 mol) was dissolved in 40 ml of water and cooled in an ice bath. A cooled solution of KOH (28 g, 0.5 mol) in 40 ml of water was added dropwise, the rate of addition being adjusted so that the temperature remained below 20°. Ethylenediamine-*N*,*N*′-diacetic acid (42 g, 0.25 mol) dissolved in 40 ml of water containing KOH (28 g, 0.5 mol) was added to the above solution. The solution was heated on a steam bath to 80° and an additional 28 g of KOH in 50 ml of water was added to keep the pH near 8. The solution was evaporated to 100 ml and cooled to 0°. The KCl which deposited was separated by filtration. The filtrate was diluted to 150 ml and the pH was reduced to 3–4 by adding concentrated hydrochloric acid. A white precipitate formed when this solution was cooled. The precipitate was recrystallized from boiling water, washed with ethanol and then acetone, and dried at 80°; yield 25–30%; mp 190 ± 5°. *Anal.* Calcd for $C_{12}H_{20}N_2O_8$: C, 45.0; H, 6.3; N, 8.74. Found: C, 44.9; H, 6.2; N, 8.65.

Preparation of Potassium Ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionatocobaltate(III) Dihydrate, $K[Co(EDDDA)]\cdot 2H_2O$.—Ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-di-3-propionic acid (6.4 g, 0.02 mol) was dissolved in 20 ml of hot water containing potassium acetate (8 g, 0.08 mol). Cobalt(II) chloride hexahydrate (4.8 g, 0.02 mol) was added to this solution which was then heated quickly to 90°. Eight milliliters of 3% H_2O_2 was added gradually, causing the solution to turn deep purple. The purple solution was evaporated to 20 ml and allowed to stand at 0° for 12 hr. At the end of this time the purple crystals which had formed were collected by filtration and further solid was obtained by adding a small amount of ethanol to the cooled filtrate. The purple solid was recrystallized from (1:1) ethanol–water solution, filtered, washed with acetone, and air-dried at room temperature. *Anal.* Calcd for $KCoC_{12}N_2O_8H_{16}\cdot 2H_2O$: C, 32.0; H, 4.4; N, 6.24. Found: C, 31.2; H, 4.2; N, 6.30.

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[2] Research Associate, 1969–1970.

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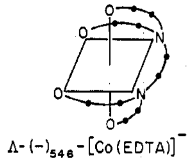

Figure 1.—Absolute configuration of Λ-(−)$_{546}$-[Co(EDTA)]$^-$.

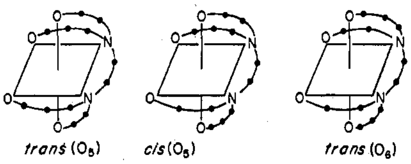

Figure 2.—Three possible isomers of Λ-[Co(EDDDA)]$^-$.

The complex was converted to its silver salt by mixing warm solutions of the complex and silver nitrate. The silver salt (1.1 g) and (−)$_{546}$-[Co(en)$_2$ox]Br (0.9 g) were stirred together in 10 ml of water at 60° for 5 min. The AgBr was filtered and washed with 5 ml of warm water. The combined filtrate and washing were cooled and, as the solid formed, it was filtered and the solution was cooled further to yield more solid. Circular dichroism spectra of solutions of each portion of solid were obtained and portions giving similar spectra were combined. Two major fractions were collected, corresponding to the expected diastereoisomers, and these were recrystallized from water; only one recrystallization was required to achieve constant spectral characteristics. The enantiomers were obtained by precipitating the resolving cation as the iodide, filtering, and inducing crystallization of the filtrate by the addition of a small amount of ethanol. Recrystallization did not change the $\Delta\epsilon$ values and mirror image CD curves were obtained for the enantiomers.

Results and Discussion

Characterization of the Acid. Infrared Spectrum.—The most interesting region of the infrared spectrum for complexes of carboxylates is that of the asymmetric carbonyl stretching frequency, 1750–1550 cm^{-1}. It has been shown[10] that the frequency of this absorption can be used to gain insight into the bonding situation of the carboxylate group. The Nujol mull spectrum of the ligand, H_4EDDDA, showed two strong bands in this region at 1700 and 1580 cm^{-1}. These bands correspond to the asymmetric carbonyl stretch of protonated and free carboxylate groups, respectively. This does not parallel the case for H_4EDTA where a single strong band at 1698 cm^{-1} was interpreted[11] to mean that this polyacid existed completely in the protonated form. The data from the present study suggest that H_4EDDDA, unlike H_4EDTA, might exist as a zwitterion. This would leave two carboxylate groups protonated and a possibility of four isomers. Two carboxylate bands were recently observed in the 1700–1550-cm^{-1} range for H_4EDDS[7] but the existence of zwitterions was not discussed.

The basicity difference between the carboxylate groups of the glycinate and β-alaninate arms seems likely to determine the most stable isomer. The isomer formed might be expected to have either both glycinate arms protonated or both glycinate arms unprotonated. It must be remembered, however, that the spectra were measured in the solid state and intermolecular H bonding may play an important role in determining the most stable structure.

Nmr Spectrum.—The 60-MHz proton magnetic resonance spectrum of the ligand in D_2O–NaOD solution (pH or pD ~10) is entirely consistent with the expected structure. Under the conditions used, all of the carboxylate groups would be unprotonated. The spectrum consists of two singlets at 3.85 and 3.71 ppm and what initially appeared to be two triplets at lower field. On closer examination this is found to be an A_2B_2 pattern centered at 3.10 ppm. The two major peaks in the pattern occur at 3.50 and 2.70 ppm and each has smaller peaks toward the center of the pattern separated by 14 and 13 Hz. The A_2B_2 pattern is expected from β-alaninate arms and the singlets are from glycinate arms and the diamine bridge. The presence of an A_2B_2 pattern instead of two triplets suggests the influence of rotamers.

Cobalt(III) Complex.—Diastereoisomers could not be formed using resolved [Co(en)$_2$ox]Br and K[Co(EDDDA)]. Resolution was obtained using Ag[Co(EDDDA)] and [Co(en)$_2$ox]Br though both diastereoisomers have very high solubilities. A small amount of the purple diastereoisomer was dissolved in water and added to an anion-exchange column packed with Cellex AE cellulose. The column was eluted with water, resulting in the formation of a purple band at the top of the column. The column was then eluted with 0.01 *N* KCl with a drop rate of about 4 min^{-1}. The band descended the column slowly, showing no evidence for more than a single band. The visible electronic absorption spectra of five fractions from the column were identical in peak positions and shape, suggesting the presence of only one isomer in significant quantity.

Infrared Spectrum of the Complex.—Strong bands at 1620 and 1570 cm^{-1} were observed in the Nujol mull infrared spectrum of the complex. The former band occurs in the region assignable to the asymmetric carbonyl stretching frequency of a coordinated glycinate group. The 1570-cm^{-1} band, however, occurs in the region usually associated with free carboxylate groups.[10] The presence of uncomplexed carboxylate groups is inconsistent with the nmr data reported below and with the problems encountered in trying to prepare pentadentate derivatives containing a coordinated halide ion. The infrared spectrum of Co(EDDS)$^-$ also showed two bands but Rose and Neal were able to show that the lower energy peak lies in the region associated with the asymmetric carbonyl stretch of a β-alaninate ring.[7] Similar results were found[8] for Co(asp)$_2^-$. Further support for this assignment was obtained from the infrared spectrum of the ethylenediaminetetrapropionatocobaltate(III) ion[12] where a single strong band was observed at 1575 cm^{-1}.

Nmr Spectrum of the Complex.—The 60-MHz nmr spectrum of the complex in D_2O showed a single, well-resolved AB pattern at low field, running into a very complex group of bands at higher field (Figure 3). The AB pattern is centered at 3.88 ppm with δ_A 4.25 ppm, δ_B 3.52 ppm, $\delta_A - \delta_B = 0.73$ ppm, and $J_{AB} = -18.4$ Hz (the negative sign of J_{AB} is assumed[13]). The complex pattern upfield is presumed to result from overlapping AA′BB′ patterns of the ethylenediamine and propionate rings. The AB patterns of glycinate rings

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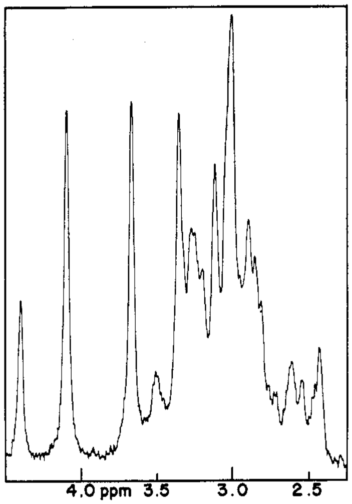

Figure 3.—Pmr spectrum of K[Co(EDDDA)] in D_2O at 60 MHz *vs.* DSS as internal standard.

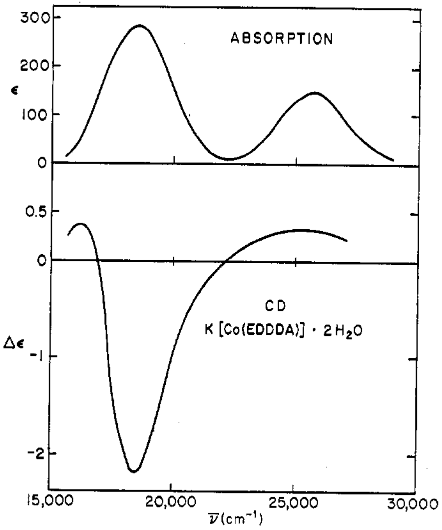

Figure 4.—Absorption and circular dichroism curves for K[Co-(EDDDA)]·$2H_2O$.

coordinated to cobalt(III) are not encountered so far upfield. The occurrence of only one AB pattern strongly suggests that both glycinate rings in the complex are equivalent. This is expected for the two isomers in which the glycinate rings are related by a twofold symmetry axis. The cis(O_5)cis(O_6) isomer (Figure 2) should give two AB patterns.

A recent publication[13] has pointed out that proton geminal coupling constants (J) for cobalt(III)–aminocarboxylate compounds fall into two categories, those in the range -16 ± 0.5 Hz for in-plane (G) glycinate rings and those in the range -18 ± 0.5 Hz for out-of-plane (R) glycinate rings. The J value (-18.4 Hz) for the Co(EDDDA)$^-$ AB pattern is typical for out-of-plane glycinate rings. This supports the assignment of the species present to the trans(O_5) structure (Figure 2).

Legg and coworkers[14] have indicated a relationship between the chemical shift difference for A and B protons and the orientation of coordinated glycinate groups for cobalt(III)–aminocarboxylate complexes. The $\delta_A - \delta_B$ values for R rings are 0 for Co(EDTA)$^-$ and 0.529 ppm[15] for Co(1,3-PDTA)$^-$, with smaller changes for G rings. The $\delta_A - \delta_B$ value of 0.73 ppm for Co-(EDDDA)$^-$ is resonable for an R ring in a complex with even more relief of strain in the girdle plane than for Co(1,3-PDTA)$^-$.

Electronic Absorption and Circular Dichroism.—The electronic absorption spectrum of Co(EDDDA)$^-$ in aqueous solution (Figure 4) shows two visible region absorption bands (18,500 cm^{-1}, $\epsilon = 290$; 25,700 cm^{-1}, ϵ 150) which are similar in position and shape, but lower in intensity, compared to those[7,16,17] of Co-(EDTA)$^-$. This decrease in intensity would be predicted for a vibronic mechanism when flexibility is introduced into the ligand ring system. It is also likely that the more strained Co(EDTA)$^-$ will have the larger asymmetric perturbation to the cubic field, giving the greater static contribution to the intensity.

The maximum symmetry of these complexes of hexadentate ligands is C_2, but the absence of splitting of the two bands suggests pseudooctahedral symmetry. The lower energy bands for Co(EDTA)$^-$ and Co-(EDDDA)$^-$ are so similar that Dq must be almost identical for the two complexes. The greater asymmetry observed[7] in this band for the Co(EDDS)$^-$ species suggests an increase in the in-plane field strength with respect to the out-of-plane field strength, supporting the use of the D_{4h} model in that case. The Dq value for EDDS was found to be about the same as that of EDTA, or even slightly greater. Thus the presence of six-membered amino acid chelate rings formed by the hexadentate ligand did not weaken the field strength, as noted[8] also for *cis-N*-[Co(L-asp)$_2$]$^-$.

The more intense band system in the ultraviolet region [42,000 cm^{-1}, ϵ 11,600; 38,300 cm^{-1} (sh), ϵ 9900] is almost certainly a ligand to metal charge-transfer transition of an effectively nonbonding carboxylate electron. No intense absorption is observed below 43,000 cm^{-1} for the parent acid, so it seems unlikely that this region is dominated by intraligand transitions.

The CD spectrum shows peaks of opposite sign at 16,200 cm^{-1} ($\Delta\epsilon \pm 0.4$) and 18,400 cm^{-1} ($\Delta\epsilon \pm 2.2$) under the first absorption band. The isomer with a positive CD peak at 16,200 cm^{-1} (Figure 4) was obtained from the less soluble diastereomer. Three peaks would be expected under this envelope if the effective symmetry were C_2. Three CD peaks are observed in the first band region for Co(EDDS)$^{-}$ [7] and [Co(en)(mal)$_2$]$^-$ (mal = malonate),[16] both *cis*-[Co-N_2O_4] complexes. The CD spectral results of the isomers of [Co(L-asp)(ida)]$^-$ (ida = iminodiacetate ion)[18] in comparison to others suggest that three transitions under the first band are rather general, although one of them is often masked.[17] The absolute configurations are known to be Λ[19] for $(-)_{546}$-Co(EDTA)$^-$,[20] $(-)_{546}$-Co(en)(mal)$_2$$^-$,[21] and Co(EDDS)$^-$ (EDDS prepared

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from L-aspartic acid).[7] All three of these complexes with the Λ configuration have positive lowest energy CD peaks, as observed also for a series of complexes[17] related to Co(EDTA)$^-$.

Where two transitions are apparent for complexes of the type considered here under the first ($^1T_{1g}$) absorption band, a tetragonal field approximation has been used.[4,7] If the in-plane crystal field strength is greater than the out-of-plane field strength, as for *cis*-[Co-N_2O_4] complexes, then the transition to the ^1E level will be at lower energy. The lowest energy CD peak of both Co(EDTA)$^-$ and Co(EDDDA)$^-$ would be assigned to the $^1A_1 \rightarrow {}^1E(D_{4h})$ transition. On this basis the isomer of Co(EDDDA)$^-$ for which the CD curve is shown in Figure 4 would be assigned the Λ configuration, corresponding to that of $(-)_{546}$-[Co(EDTA)]$^-$. In cases where three CD peaks under the first absorption band [Co(EDDS)$^-$ and Co(en)(mal)$_2{}^-$] indicate the complete removal of degeneracy, it might be better to use the actual C_2 symmetry as applied in several complexes[4,17,22] related to Co(EDTA)$^-$. These complexes are related to Co(en)(mal)$_2{}^-$ (of known absolute configuration), which, in turn, can be related to *cis*-$[Co(en)_2X_2]^{n+}$ complexes, which were correlated[23] with $Co(en)_3{}^{3+}$. Here the A(C_2) component, of lowest energy, has been regarded as retaining the CD sign[4,23] of the parent $E_a(D_3)$ transition. The positive lowest energy CD peak (Figure 4), if treated as the A(C_2) component, indicates a Λ configuration for the isomer represented by the CD curve. The intensity criterion[23] which identifies the transition related to $E_a(D_3)$ as the dominant CD peak under the first absorption band fails in the present case.

The Co(EDDS)$^-$ complex has been shown to form stereospecifically,[7] giving the Λ configuration (EDDS from L-asp) with the six-membered rings in plane.[24] It is also considered most likely that the six-membered rings of Co(EDDDA)$^-$ would prefer the in-plane position in order to relieve the strain of the G rings. Thus Co(EDDDA)$^-$ should be even more closely related to Co(EDDS)$^-$ than to Co(EDTA)$^-$. The relative heights of the two visible region absorption bands for Co(EDDDA)$^-$ are more similar to those of Co(EDDS)$^-$ than those of Co(EDTA)$^-$. The CD spectra are also very similar except that the highest energy CD peak of the three in the first-band region appears to be masked in the case of Co(EDDDA)$^-$. The signs and relative intensities of the two low-energy CD peaks (see Figure 4 and ref 7) are similar, favoring the same configuration (Λ) for both complexes. The CD spectra of the isomers[8] of Co(L-asp)$_2{}^-$ are not as similar to that of Co(EDDDA)$^-$ as is that of Co(EDDS)$^-$. The latter two complexes contain coordinated asymmetric nitrogen atoms; Co(L-asp)$_2{}^-$ does not. Of a series of model complexes[17] related to Co(EDTA)$^-$, the one for which the CD spectrum is most similar to that of Co(EDDDA)$^-$ is Co(EDTP)$^-$ (EDTP = the anion of ethylenediaminetetrapropionic acid). An important structural feature which these two complexes would have in common is the relief of strain of the G rings if the six-membered rings are in plane for Co(EDDDA)$^-$, as seems most likely.

Considerable effort has been made to prepare and resolve chloro, bromo, and nitro complexes containing pentadentate EDDDA. These efforts have been largely unsuccessful. A blue tar was obtained from a concentrated hydrochloric acid solution of K[Co(EDDDA)]. When the tar was dissolved in water, a purple solution with the same absorption spectrum as Co(EDDDA)$^-$ was obtained.

The reluctance of the ligand to function as a pentadentate donor to cobalt(III) suggested that it might function as a hexadentate donor to larger metal ions. It was hoped that a hexadentate complex with chromium(III) could be prepared and resolved. It appears that such a complex has been obtained, but the solid has not yet been isolated in any quantity owing to its exceptionally high solubility in water and a tendency to form tars in the atmosphere. However, a successful resolution of the 1,3-PDTA complex of chromium(III), previously shown to be hexadentate,[25] has been obtained.[12]

In conclusion, we find that a single geometrical isomer of Co(EDDDA)$^-$ is obtained from the reaction of EDDDA^{4-} with $CoCl_2$ in the presence of H_2O_2. The isomer is deduced to be the trans(O_5) isomer (glycinate rings trans, Figure 2) from the nmr evidence and by analogy with Co(EDDS)$^-$. Difficulties in preparing complexes of the pentadentate ligand can be attributed to the easing of ring strain as compared with Co(EDTA)$^-$.

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