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Some Amino Acid Cobalt(III) Complexes Containing Tetradentate Macrocyclic Amine Ligands[1]

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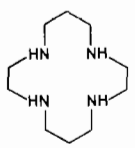
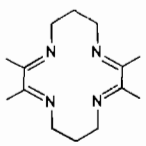
The preparation and circular dichroism (CD) spectra of a series of complexes of the type trans-[Co([14]aneN$_4$)(amH)$_2$]$^{3+}$ and trans-[Co(Me$_4$[14]teteneN$_4$)(amH)$_2$]$^{3+}$ (amH = glycine, S-alanine, S-phenylalanine and S-leucine) are reported. Cis-[Co([14]aneN$_4$)ox]ClO$_4$ has been prepared and resolved. The optically active complexes trans-[Co([14]aneN$_4$)X$_2$]$^{n+}$ (X = Cl, glycine and S-alanine) were prepared via the oxalato complex. Comparison of CD spectra indicates that the transitions arising from the $^1A_1 \rightarrow {}^1E_g(D_{4h})$ state in particular are influenced by the axial ligand.

Introduction

Complexes such as $[Co(NH_3)_5L]^{n+}$ containing optically active ligands (L) have been studied here[2] and elsewhere[3,4,5] in order to evaluate vicinal effects. We were interested in extending the study to *trans*-[N$_4$ macrocycle L$_2$]$^{n+}$ complexes where the macrocycle might be expected to impart stability and permit the study of a variety of ligands in the axial positions. A concurrent study of similar complexes of linear tetraamine ligands has been reported.[6] Cobalt(III) diacidotetraamine complexes of the 14-membered macrocyclic amines 1,4,8,11-tetraazacyclo-tetradecane ([14]aneN$_4$)[7] and 2,3,9,10-tetramethyl-1,4,8,11-tetraazacyclo-tetradeca-1,3,8,10-tetraene (Me$_4$[14]teteneN$_4$)[8] have been prepared and characterized previously.[9] The macrocycle ([14]aneN$_4$) appears to favor the *trans* geometry[10] with monodentate extracyclic ligands but by stereoretentive substitution the corresponding *cis* complexes have also been reported.[11,12] Me$_4$[14]teteneN$_4$ is a ligand containing two α-diimine groupings and retaining strictly the *trans* configuration due to the inflexibility of the structure.



[14]aneN$_4$



Me$_4$[14]teteneN$_4$

In order to understand better the various stereochemical and electronic relationships that accompany the formation of macrocyclic complexes, a series of *trans*-bis(amino acid)tetraaminecobalt(III) complexes containing oxygen-coordinated glycine, S-alanine, S-phenylalanine and S-leucine[13] were prepared using both macrocyclic tetraamines. In the present study the preparation, electronic and circular dichroism (CD) spectra are reported. For comparison, *cis*-[Co([14]aneN$_4$)ox]ClO$_4$ was newly prepared and resolved. Optically active *trans*-[Co([14]aneN$_4$)Cl$_2$]ClO$_4$, *trans*-[Co([14]aneN$_4$)(glyH)$_2$]$^{3+}$ and *trans*-[Co([14]aneN$_4$)(S-alaH)$_2$]$^{3+}$ were prepared from the resolved oxalato complex.

Experimental

The amino acids used were purchased from Nutritional Biochemicals Corporation, Cleveland, Ohio. [14]aneN$_4$ was prepared by the method of Barefield and Wagner[14] and *trans*-[Co([14]aneN$_4$)Cl$_2$]Cl was obtained using the procedure by Bosnich, *et al.*[7] The methods of Busch and co-workers[8] were used to prepare *trans*-[Co(Me$_4$[14]teteneN$_4$)Br$_2$]Br. All other reagents were obtained commercially and used without further purification.

Preparation of trans-Diaquo-2,3,9,10-tetramethyl-1,4,8,11-tetraazocyclotetradeca-1,3,8,10-tetraene-cobalt(III) Perchlorate Monohydrate, trans-[Co(Me$_4$[14]teteneN$_4$)(H$_2$O)$_2$]ClO$_4$·H$_2$O

A 2.07 g sample (3.8 mmol) of *trans*-[Co(Me$_4$[14]teteneN$_4$)Br$_2$]Br was ground for 75 min in a mortar with AgClO$_4$ (2.48 g, 12 mmol) which had been dissolved in 5 ml of water containing 2 drops of concentrated HClO$_4$ (60–62%). During the grinding, the color changed from green to red–violet. The mixture was then washed into a beaker using 100 ml of water which had been acidified to a pH of 2 with HClO$_4$. This mixture was covered and stirred for 30 min. After filtration of AgBr, the red–violet solution was rotary

evaporated to dryness. The resulting violet material was recrystallized from a minimum of hot acidified absolute methanol. Light violet crystals were obtained on cooling; these were filtered, washed with ether and vacuum dried over anhydrous calcium chloride. Yield: 86.6%. *Anal.* Calcd. for $CoC_{14}H_{30}N_4O_{15}Cl_3$: C, 25.48; H, 4.58; N, 8.49. Found: C, 25.46; H, 4.63; N, 8.19.

Preparation of trans-Bis(amino acid)-2,3,9,10-tetramethyl-1,4,8,11-tetraazacyclotetradeca-1,3,8,10-tetraenecobalt(III) Perchlorate Monohydrate Complexes, trans-[Co(Me$_4$[14]teteneN$_4$)(amH)$_2$](ClO$_4$)$_3$·H$_2$O. Trans-[Co(Me$_4$[14]teteneN$_4$)(glyH)$_2$]ClO$_4$)$_3$·H$_2$O

Trans-[Co(Me$_4$[14]teteneN$_4$)(H$_2$O)$_2$](ClO$_4$)$_3$·H$_2$O (0.65 g, 1 mmol) and glycine (0.19 g, 2.5 mmol) were added to 5 ml of water and the mixture was heated several hr on a steam bath. With cooling and slow evaporation under an air jet the product crystallized. The red–violet crystals were recrystallized from a minimum of warm water. *Anal.* Calcd. for $CoC_{18}H_{36}N_6O_{17}Cl_3$: C, 27.93; H, 4.68; N, 10.86. Found: C, 27.91; H, 4.72; N, 10.85.

Corresponding complexes of optically active amino acids were prepared as described for the glycine complex, substituting S-alanine, S-phenylalanine, or S-leucine for the glycine.

Anal. Calcd. for the S-alanine complex *trans*-[Co(Me$_4$[14]teteneN$_4$)(S-alaH)$_2$](ClO$_4$)$_3$·H$_2$O, $CoC_{20}H_{40}N_6O_{17}Cl_3$: C, 29.95; H, 5.02; N, 10.48. Found: C, 29.88; H, 5.09; N, 10.51.

Anal. Calcd. for the S-phenylalanine complex *trans*-[Co(Me$_4$[14]teteneN$_4$)(S-phalaH)$_2$](ClO$_4$)$_3$·H$_2$O, $CoC_{32}H_{48}N_6O_{17}Cl_3$: C, 40.28; H, 5.07; N, 8.80. Found: C, 40.27; H, 5.31; N, 9.06.

Anal. Calcd. for the S-leucine complex *trans*-[Co(Mc$_4$[14]teteneN$_4$)(S-leuH)$_2$](ClO$_4$)$_3$·H$_2$O, $CoC_{26}H_{52}N_6O_{17}Cl_3$: C, 35.24; H, 5.91; N, 9.48. Found: C, 35.12; H, 6.12; N, 9.63.

Preparation of the trans-Bis(amino acid)-1,4,8,11-tetraazacyclotetradecanecobalt(III) Perchlorate Complexes, Trans-[Co([14]aneN$_4$)(amH)$_2$](ClO$_4$)$_3$. Trans-[Co([14]aneN$_4$)(glyH)$_2$](ClO$_4$)$_3$

Equimolar amounts of *trans*-[Co([14]aneN$_4$)Cl$_2$]Cl and glycine were dissolved in water (80 ml/mmol of complex) and the solution adjusted to pH 5.5 using 5*M* NaOH. The solution was then heated on a steam bath for 1 hr with checks to make sure the pH remained about 5.5. The pH was then adjusted to 8.5 and heating was continued for an additional 3 hr. After the addition of a stoichiometric amount of $LiClO_4$ and evaporating, violet *trans*-[Co([14]aneN$_4$)(glyH)$_2$](ClO$_4$)$_3$ crystallized. After cooling, the violet product was filtered, washed with absolute methanol and recrystallized from a minimum of hot water. Yield: 34%. *Anal.* Calcd. for $CoC_{14}H_{34}N_6Cl_3O_{16}$: C, 23.75; H, 4.84; N, 11.87. Found: C, 23.96; H, 5.28; N, 12.01.

Trans-[Co([14]aneN$_4$)(S-alaH)$_2$](ClO$_4$)$_3$

This preparation was identical to that of *trans*-[Co([14]aneN$_4$)(glyH)$_2$](ClO$_4$)$_3$ using S-alanine in place of glycine. Yield: 49%. *Anal.* Calcd. for $CoC_{16}H_{38}N_6Cl_3O_{16}$: C, 26.11; H, 5.20; N, 11.42. Found: C, 26.68; H, 5.85; N, 11.81.

Trans-[Co([14]aneN$_4$)(S-phalaH)$_2$](ClO$_4$)$_3$

A mixture of freshly prepared Ag_2O (4.5 mmol) and *trans*-[Co([14]aneN$_4$)Cl$_2$]Cl (1.09 g, 3 mmol) was shielded from the light and stirred for 30 min in 40 ml of water. The resulting precipitate was filtered and the filtrate adjusted to pH of 5.5 using aqueous $HClO_4$. S-phenylalanine (0.99 g, 6 mmol) was added and the resulting red solution was heated at 50° C for 20 hr. After cooling to room temperature the solution was filtered, $LiClO_4 \cdot 3H_2O$ (1.44 g, 9 mmol) was added to the filtrate and, with slow evaporation under an air jet at room temperature, the violet product crystallized. After cooling, the crystals were filtered, air dried and recrystallized from a minimum of hot water. *Anal.* Calcd. for $CoC_{28}H_{46}N_6Cl_3O_{16}$: C, 37.87; H, 5.22; N, 9.46. Found: C, 38.41; H, 5.43; N, 9.48.

Trans-[Co([14]aneN$_4$)(S-leuH)$_2$](ClO$_4$)$_3$

This procedure was similar to that of the S-phenylalanine complex using S-leucine in place of the S-phenylalanine. *Anal.* Calcd. for $CoC_{22}H_{50}N_6Cl_3O_{16}$: C, 35.15; H, 6.14; N, 10.24. Found: C, 35.65; H, 6.28; N, 10.41.

Preparation and Resolution of cis-Oxalato-1,4,8,11-tetraazacyclotetradecanecobalt(III) Perchlorate, cis-[Co([14]aneN$_4$)ox]ClO$_4$

A solution containing *trans*-[Co([14]aneN$_4$)Cl$_2$]Cl (5.5 g, 15 mmol) and potassium oxalate hydrate (2.7 g, 15 mmol) in 60 ml of water was adjusted to pH 8.5 and heated on a steam bath for 6 hr. The deep-pink solution was then filtered, $LiClO_4 \cdot 3H_2O$ (2.4 g, 15 mmol) was added and with stirring the product precipitated. After cooling the light-pink solid was filtered and recrystallized from a minimum of hot water. Yield: 1.8 g (26%).

Resolution

A suspension of *cis*-[Co([14]aneN$_4$)ox]ClO$_4$ (1.78 g, 4 mmol) in 30 ml of water was stirred with an excess of Dowex 1–8X anion-exchange resin in the Cl^- form. The deep-pink solution was then filtered and the resin was washed with small volumes of water until the washings were colorless. The filtrate and washings were combined with Ag(–)$_{546}$-[Co(EDTA)][15] (1.82 g, 4 mmol) and the resulting slurry was stirred for several min at 50° C. The AgCl was removed and the filtrate was evaporated to 20 ml. An equal volume of 95% EtOH was added and the solution was left at room temperature overnight. About 0.8 g of solid was re-

moved and recrystallized twice to constant rotation by dissolving in a minimum of water and adding 95% EtOH, $\Delta\varepsilon_{496} = -2.91$ (assuming a 1:1 diastereoisomer, M.W. 695). The filtrate was saved for recovery of the other isomer. This solid was redissolved and the $(-)_{546}$-[Co(EDTA)]$^-$ was removed by treatment of the solution with Dowex I–8X anion-exchange resin in the Cl^- form. The resin was removed and, after the addition of excess $LiClO_4$, the product crystallized. It was filtered and recrystallized from warm water by cooling in ice, $\Delta\varepsilon_{444} = -2.35$. The other isomer was obtained in a similar fashion from the filtrate which had been saved after removal of the less soluble diastereoisomer. About 0.3–0.5 g of each isomer was obtained. The less soluble diastereoisomer with $(-)_{546}$-[Co(EDTA)]$^-$ gave (–)-*cis*-[Co([14]aneN$_4$)ox]ClO_4 with $\Delta\varepsilon_{555} + 1.89$, $\Delta\varepsilon_{494} = -2.31$. *Anal.* Calcd. for $CoC_{12}H_{24}N_4O_8Cl$: C, 32.26; H, 5.41; N, 12.54. Found: C, 32.46; H, 5.45; N, 12.50.

Preparation of Optically Active trans-Dichloro(1,4,8,11-tetraazacyclotetradecane)cobalt(III) Perchlorate, trans-[Co([14]aneN$_4$)Cl$_2$]ClO$_4$

$(+)_{546}$-*cis*-[Co([14]aneN$_4$)ox]ClO_4 (0.1 g) was dissolved in 30 ml of methanol saturated with dry HCl gas. After heating the solution at 50° C for 6 hr a few drops of concentrated $HClO_4$ were added. Evaporation under a jet of air at room temperature gave green crystals of *trans*-[Co([14]aneN$_4$)Cl$_2$]ClO_4. These were filtered, washed with ether and air dried. *Anal.* Calcd. for $CoC_{10}H_{24}N_4Cl_3O_4$: C, 27.95; H, 5.63; N, 13.04. Found: C, 28.13; H, 5.86; N, 12.75. $\Delta\varepsilon_{602} = 1.43$. The absorption and CD spectra were measured in acetonitrile solution because of rapid aquation in aqueous solution.

Active trans-[Co([14]aneN$_4$)Cl$_2$]$^+$→Active trans-[Co([14]aneN$_4$)(glyH)$_2$]$^{3+}$

Trans-[Co([14]aneN$_4$)Cl$_2$]ClO_4 (0.0100 g) and 0.4 g of glycine were suspended in 5 ml of water and the mixture was warmed at 50° C for 1.5 hr. At this time the solution was spectrophotometrically identical to a solution containing *trans*-[Co([14]aneN$_4$)(glyH)$_2$]$^{3+}$ (isolated above) and excess glycine. $\Delta\varepsilon_{504} = -0.33$.

Active trans-[Co([14]aneN$_4$)Cl$_2$]$^+$→Active trans-[Co([14]aneN$_4$)(S-alaH)$_2$]$^{3+}$

This procedure was identical to that for glycine, substituting the same weight of S-alanine for the glycine. $\Delta\varepsilon_{514} = -0.57$.

Spectra

The absorption spectra were recorded on a Cary 14 spectrophotometer at room temperature using a tungsten source. The CD spectra were recorded on a Roussel–Jouan Dichrograph using a tungsten source. Optical isomers are denoted by (+) or (–), the sign of the dominant CD band.

Analysis

Elemental analyses were performed by Chemalytics, Inc., Tempe, Arizona.

Results and Discussion

The [14]aneN$_4$–amino acid Co(III) complexes were prepared starting with *trans*-[Co([14]aneN$_4$)Cl$_2$]Cl. In earlier studies[7] it was found that replacement of the Cl^- by other unidentate ligands produces *trans* products. The replacement of Cl^- by the amino acids glycine or S-alanine under slightly basic conditions gave *trans*-bis(amino acid) complexes, as verified from their absorption spectra (see below). Amino acids with larger substituents (*e.g.*, S-phenylalanine and S-leucine) gave lower yields of the *trans* product using the same procedure. There was some indication that the yield was lower because of formation of some chelated *cis* product. Better yields of *trans* product were obtained by first removing Cl^- using a stoichiometric amount of Ag_2O, followed by addition of acid to form the diaquo complex, and finally by addition of the amino acid. This procedure using Ag_2O may be used for all of the amino acids considered. The *trans*-[Co(Me$_4$[14]teteneN$_4$)(S-amino acid)$_2$](ClO$_4$)$_3$ complexes were obtained in good yields from the reaction of excess amino acid with *trans*-[Co(Me$_4$[14]teteneN$_4$)(H$_2$O)$_2$](ClO$_4$)$_3$ above 70° C.

The electronic absorption spectra for the [Co([14]aneN$_4$)(amino acid)$_2$]$^{3+}$ complexes (Figure 1) are in accord with theoretical expectations[16] for complexes of the type *trans*-[CoA$_4$B$_2$]. They agree well with those reported[17] for *trans*-[Co(en)$_2$(OCOR)$_2$]$^+$, *trans*-[Co(NH$_3$)$_4$(OCOR)$_2$]$^+$ and for the closely related linear tetraamine complex ions[18] *trans*-[Co(2,3,2-tet)(glyH)$_2$]$^{3+}$ and *trans*-[Co(3,2,3-tet)(glyH)$_2$]$^{3+}$. These results, with the large splitting within the lower energy $T_{1g}(O_h)$ band, confirm the characterization of the complexes reported here as *trans* isomers containing oxygen bonded amino acids. For the [Co(Me$_4$[14]teteneN$_4$)(amino acid)]$^{3+}$ complex ions only the *trans* configuration is possible because of the rigidity of the Me$_4$[14]teteneN$_4$ macrocycle. The absorption bands (Figure 2) are shifted to higher energy for the Me$_4$[14]teteneN$_4$ complexes because of the greater field strength of the Me$_4$[14]teteneN$_4$ ligand[8] compared to [14]aneN$_4$. Only two *d–d* absorption bands appear. The second band (*ca.* 22.5 *k*K) appears as a shoulder on the intense ultraviolet charge transfer or ligand absorption band which is characteristic of complexes of ligands of this type containing diimine groupings. The third band (*ca.* 27 *k*K) observed for the [14]aneN$_4$ complexes is completely obscured.

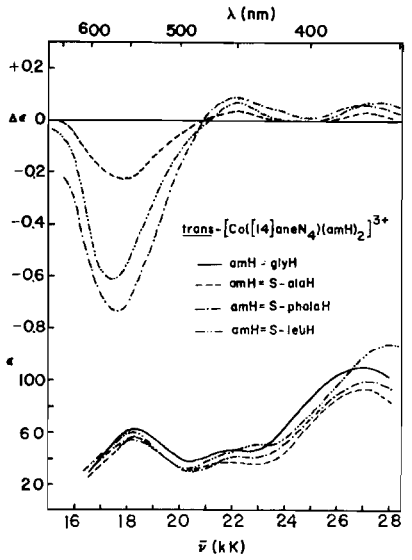


Figure 1. Circular dichroism and absorption spectra of *trans*-$[Co([14]aneN_4)(S\text{-}alaH)_2]^{3+}$ (---), *trans*-$[Co([14]aneN_4)(S\text{-}phalaH)_2]^{3+}$ (- · - ·), *trans*-$[Co([14]aneN_4)(S\text{-}leuH)_2]^{3+}$ (- · · - · · -), and the absorption spectra for *trans*-$[Co([14]aneN_4)(glyH)_3]^{3+}$ (——).

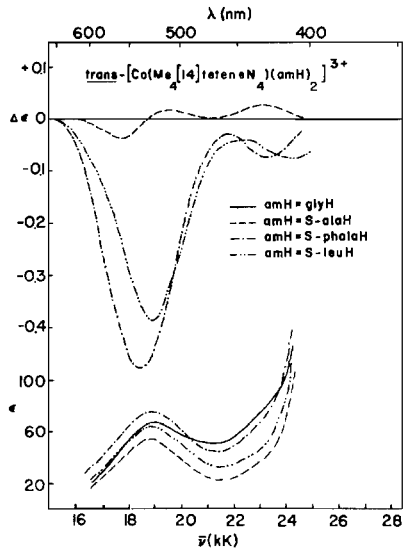


Figure 2. Circular dichroism and absorption spectra of *trans*-$[Co(Me_4[14]teteneN_4)(S\text{-}alaH)_2]^{3+}$ (---), *trans*-$[Co(Me_4[14]teteneN_4)(S\text{-}phalaH)_2]^{3+}$ (- · - ·), *trans*-$[Co(Me_4[14]teteneN_4)(S\text{-}leuH)_2]^{3+}$ (- · · - · · -), and the absorption spectra for *trans*-$[Co(Me_4[14]teteneN_4)(glyH)_2]^{3+}$ (——).

The absorption spectra for both series of complexes (Figures 1 and 2) are consistent with D_{4h} symmetry. The $^1T_{1g}(O_h)$ band is split into ^1E_g and $^1A_{2g}$ components. Since the weaker field ligand atoms (O) are along the unique axis, the lower energy band corresponds to the transition $^1A_{1g} \rightarrow {}^1E_g$ and the next to $^1A_{1g} \rightarrow {}^1A_{2g}$.

In the CD spectra (Figures 1 and 2) for complexes of both series, except for $[Co(Me_4[14]teteneN_4)(S\text{-}alaH)_2](ClO_4)_3$, there is a single negative CD peak of significant intensity in this region of the ^1E_g absorption band. Two CD peaks of low intensities appear in the region for $[Co(Me_4[14]teteneN_4)(S\text{-}alaH)_2]^{3+}$. This case is unusual because of the very low CD peak intensities and the removal of the degeneracy of the ^1E_g band to give two components. The lower energy CD peaks for each of the other $Me_4[14]teteneN_4$ complexes (Figure 2) are somewhat steeper on the higher energy side, even though the next peak has the same sign. This suggests that there is a positive component which is completely cancelled. The net rotational strength remains negative. The CD peaks in the region of the A_{2g} absorption band are positive for the [14]$aneN_4$ complexes and *trans*-$[Co(Me_4[14]teteneN_4)(S\text{-}alaH)_2]^{3+}$, but negative for the other $Me_4[14]teteneN_4$ complexes.

Optical Activity and the Topology of [14]aneN$_4$

It has been observed[7] that substitution reactions can occur in [14]$eneN_4$ complexes with complete retention of configuration of the ligand. Interconversion of *trans* to *cis* topology is possible by a simple displacement of a nitrogen along an edge of the octahedron. *Cis-trans* interconversion can occur with or without inversion of configuration for one or more nitrogen atoms. Such inversion can be achieved *via* proton exchange, which is favored at high pH. The most favorable folded arrangements of [14]$aneN_4$ in *cis*-$[Co([14]aneN_4)C_2O_4]ClO_4$ are shown in Figure 3. The four asymmetric nitrogens in structures I and II have the absolute configurations RRRR and RRRS,[19] respectively. Struc-

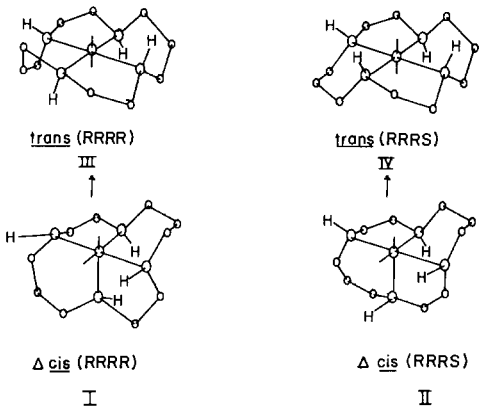


Figure 3. The interrelation of absolute configurations of the secondary nitrogen atoms for *Δ cis* and *trans*-[14]$aneN_4$ complexes.

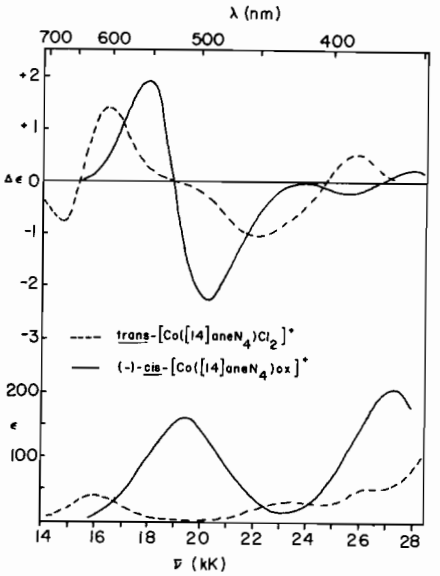


Figure 4. Circular dichroism and absorption spectra of *cis*-$[Co([14]aneN_4)ox]^+$ (——) in aqueous solution and active *trans*-$[Co([14]aneN_4)Cl_2]^+$ (---) in acetonitrile.

ture I has C_2 symmetry, but there is no C_2 symmetry axis for II because of inversion of one nitrogen. Structure III has D_2 symmetry. This is a strain-free structure which was not considered in earlier work.[7]

The CD and electronic spectra for the newly resolved (–)-*cis*-$[Co([14]aneN_4)ox]ClO_4$ are shown in Figure 4. The two broad, symmetrical absorption bands at 19.4 and 27.3 *k*K may be assigned, respectively, to the $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ electronic transitions of Co(III) assuming O_h symmetry. In the CD spectrum there are positive (lower energy) and negative peaks within the $^1T_{1g}$ absorption band. These transitions have been used previously for the assignment of absolute configurations for oxalato complexes with C_2 symmetry. As described by Mason[20,21] and Brubaker[22], the dominant band in this region may be related to the $^1A_1 \rightarrow {}^1A_2$ (E_a parentage) transition, which if negative corresponds to a Δ absolute configuration. Accordingly, (–)-*cis*-$[Co([14]aneN_4)ox]ClO_4$ shows a more intense negative band and might be assigned the Δ configuration. This is a tentative assignment since, on the basis of the ring-pairing approach,[23] there is no net chirality if one considers the 5-membered and 6-membered chelate rings as equivalent. The Δ chirality shown for structure I or II (Figure 3) is that defined by the 5-membered chelate rings.

Upon conversion of (–)-*cis*-$[Co([14]aneN_4)ox]^+$ to *trans*-$[Co([14]aneN_4)Cl_2]^+$, optical activity is retained. Under the acidic conditions used, I and II are expected to produce III and IV, respectively. The high CD intensities (Figure 4) are indicative of high stereoselectivity in the conversion, and of large contributions to the rotational strength from the asymmetric nitrogen atoms and fixed chelate ring conformations. Such high CD intensities might argue in favor of structure III where all secondary nitrogens have the R configuration and all chelate rings are chiral. The sign pattern for the CD curve of active *trans*-$[Co([14]aneN_4)Cl_2]^+$ is the same as that observed for *trans*-(RR)-$[Co(2,3,2\text{-tet})Cl_2]^+$ [24] and *trans*-(R_NR_N)-$[Co(SS)\text{-dime-}2,3,2\text{-tet}(Cl)_2]^+$.[25] In the case of these two complexes of linear tetraamines and for structure III the 5-membered chelate rings have the δ conformation. In structure IV one nitrogen has the S configuration and the 6-membered ring between the R and S nitrogen is folded and achiral. The $\Delta\varepsilon$ values are of comparable magnitude for the *cis* and *trans* complex ions, even though the ε values are much lower for the *trans* complex. The lowest energy $^1E_a(D_{4h})$ absorption band for *trans*-$[Co([14]aneN_4)Cl_2]^+$ is seen to give two components of opposite signs in the CD spectrum, verifying the identification of this absorption band as ^1E_a, using D_{4h} symmetry, but revealing the lower true symmetry of the complex. Correspondingly, the second absorption band and the negative CD peak at *ca.* 22.1 *k*K can be assigned to the $^1A_1 \rightarrow {}^1A_2$ (D_{4h}) transition.

Replacement of the chloride ions by amino acids in the optically active *trans*-dichloro complex produces an optically active *trans*-$[Co([14]aneN_4)(glyH)_2]^{3+}$ complex ion with lower CD peak intensities (Figure 5), comparable to those observed (Figure 1) for corresponding complexes which derive their activity solely from the presence of optically active amino acids. The marked decrease in CD intensities suggests some racemization of the nitrogens of the macrocycle, accompanied by inversion of the chelate rings. This is likely to occur in the presence of the large excess of amino acid during the 1.5 hour heating (50° C) period. The

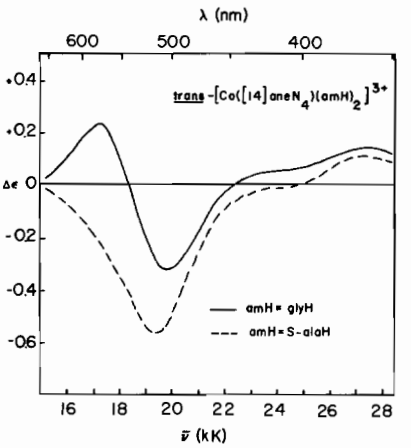


Figure 5. Circular dichroism spectra of active *trans*-$[Co([14]aneN_4)(glyH)_2]^{3+}$ (——), and active *trans*-$[Co([14]aneN_4)(S\text{-alaH})_2]^{3+}$ (---).

reaction was allowed to proceed until the absorption spectrum agreed with that of the *trans*-[Co([14]aneN$_4$)(amino acid)$_2$]$^{3+}$ prepared from the inactive dichloro complex. Prolonged heating gave lower activity, but also poorer conversion to the bis(amino acid) complex. The active *trans*-[Co([14]aneN$_4$)Cl$_2$]$^+$ loses activity quickly in aqueous solution. On standing the color changes from green to violet. This is most likely aquation followed by or concurrent with racemization. In 10% aqueous HCl the color changes are much slower. The green to violet color change is observed but activity is lost only slowly. In basic solution (pH ~ 8) the color changes in the time of mixing and racemization is complete in a matter of minutes.

The *trans*-[Co([14]aneN$_4$)(S-alaH)$_2$]$^{3+}$ complex ion obtained from the optically active *trans*-dichloro complex gives a single negative CD peak (Figure 5) in the $E_g(D_{4h})$ absorption band region. This peak is more than twice as intense as for the corresponding complex in Figure 1 and the peak for the complex prepared from the optically active macrocycle is at higher energy, so some activity of the macrocyclic ring is retained. If one subtracts the CD curve in the 15–22 *k*K region for the active *trans*-[Co([14]aneN$_4$)(glyH)$_2$]$^{3+}$ complex ion from that for the corresponding S-alanine complex (both in Figure 5), there is one negative peak similar in shape and position of the maximum to that of Figure 1, corresponding to the "vicinal" contribution of two alanine ligands coordinated along the z axis. It appears that the optically active macrocycle contributes significantly to the intensities of both peaks in the $E_g(D_{4h})$ region, but the axially coordinated S-amino acid ligands contribute more to the higher energy (negative) peak, cancelling the positive peak. Brubaker and Fitzgerald[6] noted that axially coordinated, optically active amino acids contributed significantly to the rotatory strength of the $^1E_g(D_{4h})$ transition for Co(III) complexes of linear tetraamines, but that their contribution to the rotatory strength of the $^1A_{2g}(D_{4h})$ is negligible. These authors attributed the rotatory strength of the $^1A_{2g}(D_{4h})$ transition in *trans*-[Co(–)-5-me-3,2,3-tet)(amino acid)$_2$]$^{3+}$ complex ions to the in-plane contribution from the optically active tetraamine. The CD curves for the complexes containing the optically active macrocycle (Figure 5) show opposite signs in the region of the $^1A_{2g}(D_{4h})$ transition (*ca.* 22 *k*K), while there is a positive CD peak in this region for the corresponding complex ions of the inactive macrocycle (Figure 1). However, no distinct peaks corresponding to the $^1A_{2g}(D_{4h})$ transition appears in the former case (Figure 5). One cannot say whether the sign of the $^1A_{2g}(D_{4h})$ peak is reversed when the macrocycle becomes optically active, or whether it is masked by overlap with one of the components of the $E_g(D_{4h})$ transition.

The contributions to the rotatory strength for the amino acids reported here are in the order phenylalanine > leucine ≫ alanine for the complexes of both macrocyclic ligands (Figures 1 and 2).

The CD curve for active *trans*-[Co([14]aneN$_4$)(glycine)$_2$]$^{3+}$ (Figure 5) shows two peaks of opposite sign in the region of the lowest energy absorption band. The complexes containing optically active amino acids all gave a single CD peak in this region (Figures 1 and 5). Similar results were observed for corresponding complexes of an optically active linear tetraamine,[6] *trans*-[Co(–)-5-me-3,2,3-tet(Cl$_2$)]$^+$.

The reversal of signs for the CD peaks in going from the active dichloro complex (–, +, –, starting from low energy) to the active diglycinato complex (+, –, +) is unexpected. The axial substitution is expected to occur with retention of configuration of the nitrogens of the macrocycle, or with some racemization, but not with inversion. However, the CD spectra for these complexes were obtained in acetonitrile and water, respectively. The dichloro complex aquates rapidly in water and the substitution reaction was carried out in water only because the amino acids are not sufficiently soluble in acetonitrile. Essentially enantiometric CD curves have been obtained for *trans*-(R,R)-[Co($NH_2C_3H_6NHC_2H_4NHC_3H_6NH_2$)Cl$_2$]$^+$ in water and dimethylsulfoxide,[26] so that the reversal in signs does not necessarily mean inversion of configuration of the macrocycle. Yet conversion of the optically active *trans*-[Co(–)-5-me-3,2,3-tet(Cl)$_2$]$^+$ gives the same sign pattern of CD peaks in water as observed for the corresponding *trans*-bis(amino acid) complex in acetonitrile.[6] These linear tetraamine complexes are similar to those reported here except for the presence of a methyl substituent and the closing of the macrocyclic ring. One would not expect solvent reversal of signs in one of these cases only, or reversal of the order (in energies) of the two rhombic components in one case only. Since we cannot be certain of the configuration and conformation of the macrocyclic ring, it would be purely speculative to try to rationalize the change in CD sign patterns in terms of regional rules.

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