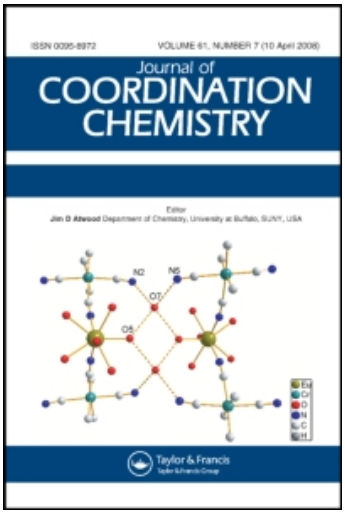

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OPTICALLY ACTIVE BIS(BIQUANIDE)COBALT(III) COMPLEXES CONTAINING AMINO ACIDS

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OPTICALLY ACTIVE BIS(BIQUANIDE)COBALT(III) COMPLEXES CONTAINING AMINO ACIDS

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Biguanide-amino acid complexes of the type $Co(am)(Hbg)_2^{3+}$, where am is the anion of glycine, sarcosine, L-alanine, L-valine, L-isoleucine, or L-proline, have been prepared and resolved. The absorption, circular dichroism (CD) and proton magnetic resonance spectra (for the alanine and valine complexes) are reported. For some salts of some of the complexes of optically active amino acids, one pure optical isomer could be obtained by slow crystallization from from the reaction solution. One optical isomer of the complexes containing optically active amino acids is present in the reaction mixture to a slightly greater extent than the other. The effects of hydroxide ion and heating on equilibration was studied. Assignments of absolute configurations were made from the CD spectra.

INTRODUCTION

The complexes of biguanide, $Hbg = NH\{C(NH_2)NH\}_2$, have caused disagreement concerning the interpretation of circular dichroism (CD) spectra and assignments of absolute configurations. The $(-)_{589}$-$[M(Hbg)_3]^{3+}$ complexes of Co(III) and Cr(III) have been assigned the same[1] and opposite[2] absolute configurations. The absolute configurations of these isomers of both complexes are now known to be the same from X-ray crystallographic studies.[2,3] The assignment for the Co(III) complex based on the CD of the region of the *d-d* transitions was interpreted as contradicting that based on the ligand transitions in the ultraviolet region.[2,4] This case is one of those involving uncertainties regarding the possible reversals of signs and ordering of the trigonal components of the first absorption band, $T_{1g}(O_h)$, as well as ambiguities in the ligand absorption region.

Effort has been made to relate the CD data for $Co(Hbg)_3^{3+}$ to those for $Co(en)_3^{3+}$ by studying the mixed complexes[4] $Co(en)(Hbg)_2^{3+}$ and $Co(en)_2(Hbg)^{3+}$ The present work reports studies of the amino acid complexes $Co(am)(Hbg)_2^{3+}$ to be related to the thoroughly studied $Co(am)(en)_2^{2+}$ complexes.

EXPERIMENTAL

Preparation and Optical Resolution

A series of bis(biguanide)-amino acid complexes was prepared employing glycine (glyH), L-alanine(L-alaH), sarcosine(sarH), L-valine(L-valH), L-isoleucine(L-isoleuH) and L- proline (L-proH). The general procedure is illustrated by the preparation of the glycinato complex.

$[Co(gly)(Hbg)_2]I_2$ Eight grams of $[Co(Hbg)_2(NH_3)_2](OH)_3 \cdot H_2O$ (prepared by the method of Dutta and Sarkar[5]) and 1.64 g of glycine were dissolved in 100 ml of water and the solution was heated in a water-bath (60°) until the evolution of NH_3 ceased (about 3 hr). The solution was neutralized with HCl and allowed to stand overnight at room temperature. A small amount of orange material [tris(biguanide)complex] deposited. After filtration of this product, 10 g of NaI was added to the filtrate and then the solution was allowed to stand at room temperature for 2 or 3 hr. The dark-red crystals of $[Co(gly)(Hbg)_2]I_2$ were filtered and washed with methanol-water (2:1) mixture. This product, which was contaminated with the tris(biguanide) complex, was recrystallized from 90 ml of hot water (yield: 8.05 g).

Resolution

Four grams of $[Co(gly)(Hbg)_2]I_2$ was dissolved in 130 ml of water, and 2.2 g of $K[SbOtart] \cdot 0.5H_2O$ was dissolved in 35 ml of water. The latter solution was added dropwise to the former, with stirring, and then the resulting suspension was allowed to stir for 2 hr. The pink precipitate was filtered and washed with cold water and methanol, and then air dried. The yield of the diastereoisomer was 3.20 g. The diastereoisomer, which is slightly soluble in water, was

suspended in 20 ml of water. After 20 g of KI was added, the suspension was stirred vigorously for 15 min. The dark-red crystalline precipitate, which formed immediately, was filtered and washed with methanol-water (1:1) and then with methanol-acetone (1:1) (yield: 1.84 g). The crude $(-)$-$[Co(gly)(Hbg)_2]I_2$, which contained a trace of diastereoisomer, was dissolved in a minimum amount of water and the diastereoisomer was removed by filtration. The filtrate was concentrated with an air stream and the dark-red crystals of $(-)_{589}$-$[Co(gly)(Hbg)_2]I_2$ were filtered. The recrystallization was repeated to the attainment of constant $\Delta\epsilon$.

$(-)_{589}$-[Co(L-ala)(Hbg)$_2$]I$_2$ The $[Co(L\text{-}ala)(Hbg)_2]I_2$ complex was obtained (yield 7.36 g) from 7.2 g of $[Co(Hbg)_2(NH_3)_2](OH)_3 \cdot H_2O$ and 1.8 g of L-alanine. The resolution of the L-alaninato complex is similar to that of the glycinato complex.

$(+)_{589}$-[Co(sar)(Hbg)$_2$]I$_2$ The racemate $[Co(sar)(Hbg)_2]I_2$, was obtained (yield: 8.4 g) from 7.2 g of $[Co(Hbg)_2(NH_3)_2](OH)_3 \cdot H_2O$ and 1.8 g of sarcosine. The less soluble diastereoisomer was obtained by a method similar to that of the glycinato complex. The diastereoisomer was suspended in a small amount of water and excess KI was added. The resulting solution was evaporated with an air stream. White material, which precipitated at first, was removed by filtration and then the filtrate was evaporated to dryness. The resulting solid was suspended in a large amount of acetone (*ca.* 200 ml) and stirred. The white material dissolved and the complex was recovered by filtration. The crude $(+)_{589}$-sarcosinato complex was recrystallized from methanol to constant $\Delta\epsilon$.

$(-)_{589}$-[Co(sar)(Hbg)$_2$](ClO$_4$)$_2$ When the original solution containing the less soluble diastereoisomer was evaporated rapidly to dryness, the $(-)_{589}$ isomer was obtained. The crude $(-)_{589}$ isomer was recrystallized from methanol by addition of $NaClO_4$.

$(-)_{589}$-[Co(L-val)(Hbg)$_2$](Cl$_4$)$_2$ · 1.5H$_2$O The preparation was the same as that in glycinato complex except for using L-valine instead of glycine and $NaClO_4$ instead of KI. The yield was 6.0 g from 5.0 g of $[Co(Hbg)_2(NH_3)_2](OH)_3 \cdot H_2O$ and 1.7 g of L-valine. Optically pure $(-)_{589}$-$[Co(L\text{-}val)(Hbg)_2](ClO_4)_2 \cdot 1.5H_2O$ was obtained from the reaction solution by slow crystallization.

$(+)_{589}$-[Co(L-val)(Hbg)$_2$]Cl$_2$ · 1.5H$_2$O The preparation of the $(+)_{589}$ isomer was similar to that of the $(-)_{589}$ isomer except for the use of LiCl instead of $NaClO_4$.

$(+)_{589}$-[Co(L-isoleu)(Hbg)$_2$]I$_2$ This complex precipitated as an oily product on addition of KI to the reaction solution. The product was separated from the solution by decantation and leached with acetone until it solidified. The crude complex was dissolved in water and crystallized slowly as the $(+)_{589}$ isomer.

$(-)_{589}$-[Co(L-pro)(Hbg)$_2$](ClO$_4$)$_2$ The pure $(-)_{589}$ isomer was prepared by a method similar to that of the $(-)_{589}$ valinato complex.

Analytical data for all compounds are given in Table I.

Measurements

The electronic absorption spectra were measured using a Hitachi Spectrophotometer EPS-3T. The CD spectra were recorded on Varian–Cary 61. The pmr spectra were recorded on Varian A-60 using sodium trimethylsilylpropane sulfonate as an internal standard.

TABLE I
Elemental analyses with calculated percentages in parentheses

Compound C	C (%)	H (%)	N (%)
$(-)_{589}$-$[Co(gly)(Hbg)_2]I_2$	12.49 (12.24)	2.95 (3.08)	25.99 (26.16)
$(-)_{589}$-$[Co(L\text{-}ala)(Hbg)_2]I_2$	14.29 (13.94)	3.25 (3.34)	25.90 (25.55)
$(-)_{589}$-$[Co(L\text{-}val)(Hbg)_2](ClO_4)_2 \cdot 1.5\,H_2O$	17.99 (17.92)	4.60 (4.51)	25.63 (25.54)
$(+)_{589}$-$[Co(L\text{-}val)(Hbg)_2]Cl_2 \cdot 1.5\,H_2O$	22.55 (22.75)	5.80 (5.73)	32.35 (32.42)
$(+)_{589}$-$[Co(L\text{-}isoleu)(Hbg)_2]I_2$	19.11 (18.62)	4.45 (4.06)	24.28 (23.88)
$(-)_{589}$-$[Co(L\text{-}pro)(Hbg)_2](ClO_4)_2$	18.42 (18.83)	3.88 (3.86)	26.49 (26.83)
$(+)_{589}$-$[Co(sar)(Hbg)_2]I_2$	14.14 (13.94)	3.46 (3.34)	25.61 (25.55)
$(-)_{589}$ $[Co(sar)(Hbg)_2](ClO_4)_2$	15.77 (15.34)	3.70 (3.68)	27.65 (28.11)

RESULTS AND DISCUSSION

Beautiful crystalline products, expected to contain $(+)_{589}$-$[Co(L\text{-}ala)(Hbg)_2]^{2+}$, $(-)_{589}$-$[Co(L\text{-}isoleuc)(Hbg)_2]^{2+}$ and the $(+)_{589}$ and $(-)_{589}$ isomers of $Co(L\text{-}leuc)(Hbg)_2^{2+}$, were obtained, but the samples gave unsatisfactory elemental analyses. The spectra checked with expectation and several anions were tried for isolation of the complexes. The analytical results did not agree with the formulation as guanylurea complexes, as encountered in earlier work on biguanide complexes.[4]

For most of the other complexes containing the optically active amino acids, only one of the two diastereomers (Λ or Δ containing the L-amino acid) was obtained directly from the aqueous reaction solution. The complex of L-alanine was isolated as the $(-)_{589}$ isomer when it was crystallized as the perchlorate salt. However, for other salts, i.e., iodide, bromide, or chloride, a diastereomeric racemate separated. The complex of L-valine was obtained as the $(-)_{589}$ isomer when it was crystallized as the perchlorate, iodide, or bromide, but the chloride salt separated directly from the reaction solution as the $(+)_{589}$ isomer. Both isomers were obtained optically pure on slow crystallization, suggesting a second order asymmetric resolution. Only the $(-)_{589}$ isomer crystallized for the complex of L-proline for any of these salts (ClO_4^-, I^-, Br^-, or Cl^-). In the cases where the optically pure diastereoisomers were obtained upon slow crystallization, the reaction solution from which they were obtained showed only weak configurational activity (Table II). The diastereomeric mixtures obtained from the reaction solutions were resolved, following the procedure used for the glycinato complex, as a check on the optical purity of the diastereomeric salts obtained directly.

TABLE II
CD spectra of the reaction solutions in the first band region

	before neutrallization		after neutrallization	
	ν(kK)	$\Delta\epsilon_{max}$	ν(kK)	$\Delta\epsilon_{max}$
$[Co(L\text{-}ala)(Hbg)_2]^{2+}$	17.30	−0.44	17.83	−0.28
	20.12	+1.02	20.62	+0.55
$[Co(L\text{-}val)(Hbg)_2]^{2+}$	17.36	−1.20	17.92	−0.86
	20.62	+2.79	20.88	+1.86

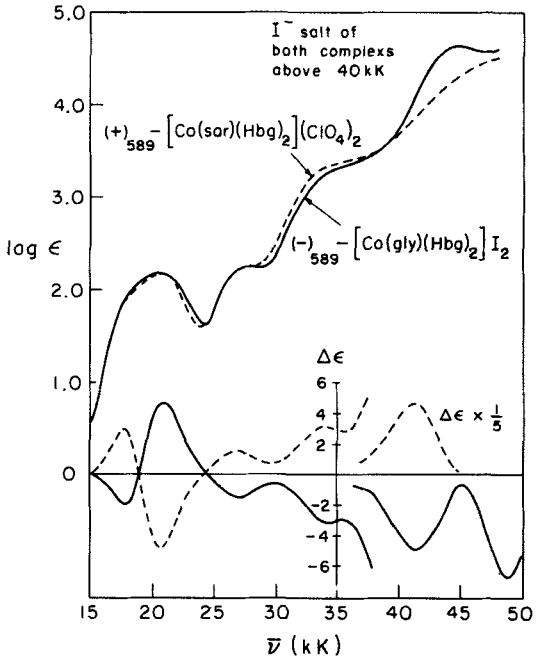

FIGURE 1 Absorption and circular dichroism $(-)_{589}$-$[Co(gly)(Hbg)_2]I_2$ (——) and $(+)_{589}$-$[Co(sar)(Hbg)_2](ClO_4)_2$ (– – –).

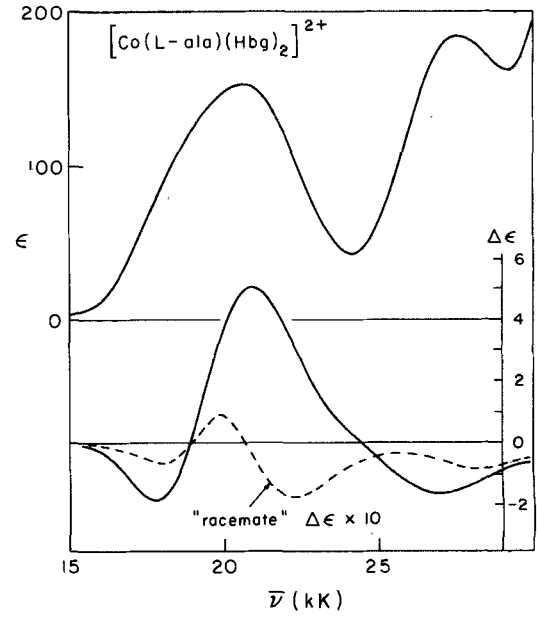

FIGURE 2 Absorption and circular dichroism curves for $(-)_{589}$-$[Co(L\text{-}ala)(Hbg)_2]I_2$. The CD curve for the active racemate obtained from the reaction solution is shown (– – –).

TABLE III
Absorption and CD data of the complexes in aqueous solutions[a]

	Absorption		CD	
	ν(kK)	log ϵ_{max}	ν(kK)	$\Delta\epsilon_{max}$
$(-)_{589}$-[Co(gly)(Hbg)$_2$]$^{2+}$	20.53	2.17	17.70	−1.95
			20.92	+4.73
	27.62	2.25	26.95	−1.52
	(34.5)sh	3.30	34.25	−3.21
			41.49	−25.1
			49.02	−34.1
$(-)_{589}$ [Co(L-ala)(Hbg)$_2$]$^{2+}$	20.58	2.19	17.83	−1.88
			20.96	+5.04
	27.47	2.27	27.03	−1.64
	(34.5)sh	3.30	(34.5)sh	−3.80
			41.15	−27.8
			49.02	−31.9
$(-)_{589}$-[Co(L-val)(Hbg)$_2$]$^{2+}$	20.66	2.19	17.83	−1.93
			20.96	+5.26
	27.47	2.27	26.95	−1.67
	(34.5)sh	3.33	(34.5)sh	−4.38
			41.32	−29.9
			48.78	−33.3
$(+)_{589}$-[Co(L-val)(Hbg)$_2$]$^{2+}$			17.76	+1.47
			21.14	−5.47
			26.74	+1.51
			(34.5)sh	+3.33
			41.32	+23.8
			48.78	+31.1
$(+)_{589}$-[Co(L-isoleu)(Hbg)$_2$]$^{2+}$	20.45	2.23	17.76	+1.40
			21.10	−5.62
	27.40	2.31	26.74	+1.52
	(34.5)sh	3.34	(35.1)sh	+3.58
			41.15	+22.9
			48.78	+32.0
$(-)_{589}$-[Co(L-pro)(Hbg)$_2$]$^{2+}$	20.62	2.24	17.64	−2.13
			20.58	+6.36
	27.25	2.27	26.67	−1.57
	(33.9)sh	3.34	(33.9)sh	−3.12
			41.15	−29.5
			48.31	−28.2
$(+)_{589}$-[Co(sar)(Hbg)$_2$]$^{2+}$	20.49	2.18	17.57	+2.99
			20.70	−4.91
	27.55	2.26	26.81	+1.52
	(34.5)sh	3.34	33.67	+3.09
			41.15	+22.9
			48.31	+29.9

[a]approximate position of shoulders are given in parentheses

Effects of Heating and Base

The neutralized reaction solutions gave CD spectra similar to those of the $(-)_{589}$ isomers (Table II and III). The intensities of the CD peaks (using absorption peak intensities to determine concentrations) were nearly the same as those observed after heating aqueous solutions of the $(-)_{589}$ isomers for one hour at *ca.* 80° (Table IV). The CD intensities showed no

TABLE IV
CD data of the complexes[a] (A) in 0.1 M NaOH aqueous solutions and (B) after heating in water (diastereoisomeric equilibrium mixture)

	(A)		(B)[b]	
	ν(kK)	$\Delta\epsilon_{max}$	ν(kK)	$\Delta\epsilon_{max}$
$(-)_{589}$-[Co(L-ala)(Hbg)$_2$]I_2	17.24	−0.52	17.79	−0.30
	20.41	+1.10	20.58	+0.65
	(28.3)sh	−0.65	27.25	−0.27
	31.25	−0.73		
	39.37	−2.88		
$(-)_{589}$-[Co(L-val)(Hbg)$_2$]$(ClO_4)_2 \cdot 1.5\ H_2O$	17.21	−1.37	17.89	−0.83
	20.53	+3.07	20.83	+1.75
	(28.1)sh	−1.49	27.10	−0.63
	31.25	−2.07		
	3.37	−8.76		
$(+)_{589}$-[Co(L-isoleu)(Hbg)$_2$]I_2	17.18	−1.23	17.92	−0.72
	20.53	+2.84	20.88	+1.55
	(28.2)sh	−1.43	27.25	−0.59
	31.15	−1.93		
	39.37	−8.30		
$(-)_{589}$-[Co(L-pro)(Hbg)$_2$]$(ClO_4)_2$	17.04	−2.32	17.54	−0.64
	20.24	+6.19	20.53	+2.79
	(28.2)sh	−2.14	26.67	−0.63
	30.58	−2.76		
	39.06	−15.4		

[a]Approximate positions of shoulders are given in parentheses.
[b]Data for the visible region only.

further change after heating for one hour and standing at room temperature for six days. The same CD curve was obtained by heating either the $(+)_{589}$ or $(-)_{589}$ isomer of Co(L-val)(Hbg)$_2^{2+}$. The same results were obtained for the two isomers of Co(L-ala)(Hbg)$_2^{2+}$ even though good analytical data could not be obtained for the $(+)_{589}$ isomer. These facts suggest that the CD spectra after heating are those of the diastereoisomeric equilibrium mixtures and that the $(-)_{589}$ isomer is favored in each case.

The equilibrium constants were calculated from the CD data in the *d-d* band region. The values for the ratio [$(-)_{589}$ isomer] / [$(+)_{589}$ isomer] were estimated to be 1.3 for the L-alaninato, 2.0 for the L-valinato, 1.7 for the L-isoleucinato, and 2.5 for the L-prolinato complexes. Buckingham *et al.*[6] found the equilibrium constant (Λ/Δ at 34.3°) to be 1.0 for Co(L-ala)(en)$_2^{2+}$ and 1.7 for Co(L-val)(en)$_2^{2+}$. It seems that the stereoselectivity is somewhat greater for the bis(biguanide) complexes, even though a smaller steric interaction might have been expected because of the nearly planar biguanide chelate rings.[2,3]

The absorption and CD spectra of the reaction solution before neutralization are very similar to those of resolved complexes in alkaline solution (Tables II and IV). The effect of base on the absorption spectra for other complexes was similar to that shown (Figure 3) for Co(L-pro)(Hbg)$_2^{2+}$, but the CD spectra for other complexes were altered to a much greater extent (Table IV). In 0.1 M NaOH solution, the diastereoisomeric equilibrium was established very rapidly. The glycinato complex lost all activity within *ca.* 5 minutes. Little optical activity remained for the sarcosinato complex after two minutes is alkaline solution and there was no detectable activity after six minutes. The CD intensities for the complexes of optically active amino acids changed rapidly with the addition of base, but remained unchanged after *ca.* five minutes. The same CD curves were obtained in 0.1 M NaOH for both (+) and (−) isomers of Co(L-val)(Hbg)$_2^{2+}$ and also for the two isomers of the L-alaninato complex.

There are two effects to be considered in basic solution in addition to establishing diastereomeric

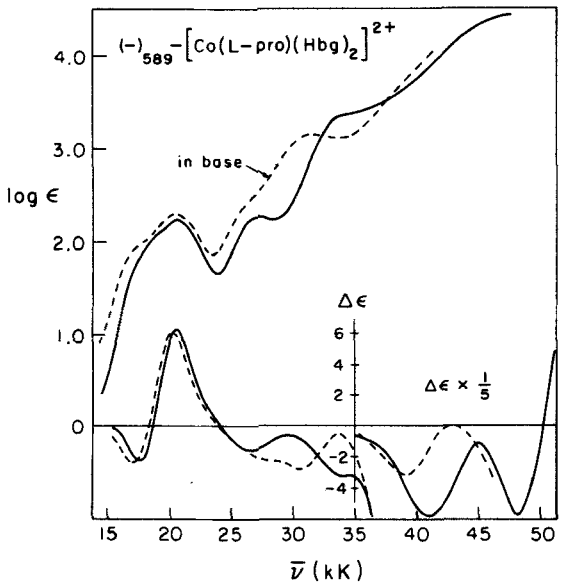

FIGURE 3 Absorption and circular dichroism curves for $(-)_{589}$-[Co(L-pro)(Hbg)$_2$](ClO$_4$)$_2$ in water (——) and 0.1 M NaOH (– – –).

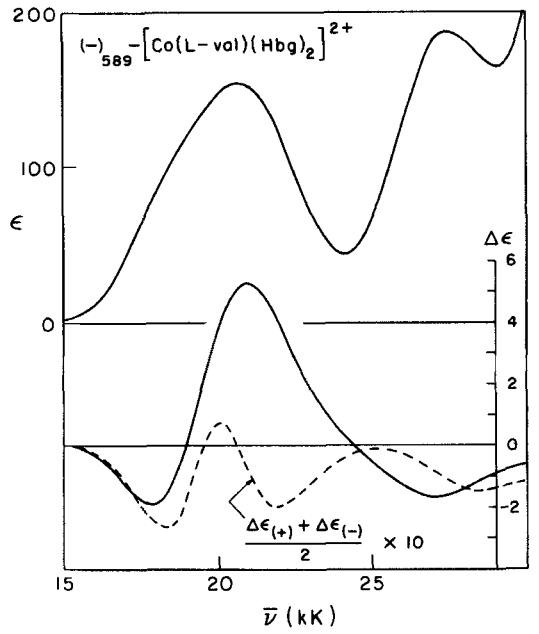

FIGURE 4 Absorption and circular dichroism curves for $(-)_{589}$-[Co(L-val)(Hbg)$_2$](ClO$_4$)$_2$ · 1.5H$_2$O and the average of the CD curves for the two optical isomers (– – –).

equilibrium. One is deprotonation of the biguanide ligand, Hbg, to form the anion bg$^-$, changing the charge on the complex ion. The other effect is that of electrolytes in altering CD spectra. The CD intensities were increased[4] in basic solution for Co(Hbg)$_3^{3+}$ and Co(en)(Hbg)$_2^{3+}$.

It is believed that essentially the same diastereomeric equilibrium mixture is obtained in basic solution or by heating. Heating in the absence of base weakened the CD intensities for Co(L-val)(Hbg)$_2^{2+}$ without altering the curve shapes greatly. The peak positions were altered significantly in basic solution for the reasons noted above. When the basic solution was neutralized the optical activity was essentially the same as that of the complex heated in neutral solution. The same result was achieved by treating the complex with activated charcoal for six hours at room temperature. Only the L-prolinato complex showed little change in the CD spectrum in the visible region in basic solution, although the CD intensities were decreased by about 5% after one hour. Perhaps the diastereomeric equilibrium is established more slowly at room temperature in this case.

Absorption and Circular Dichroism Spectra

The absorption and CD data for the complexes studied are presented in Table III. All of the complexes show similar absorption and CD spectra (Figures 1, 2, 3, and 4). The absorption spectra all show shoulders on the lower energy side of the first bands. Most complexes of the CoN_5O type containing amine ligands show shoulders on the higher energy side of the first band. In such cases the unique tetragonal axis, using effective D_{4h} symmetry, is the O–N axis, corresponding to the weaker field. If the ligand field of the biguanide is sufficiently weaker[4] to reverse the direction of the tetragonal splitting, the strongest field ligand would be the amine of the amino acid. The strongest field would be along an axis defined by the amine ligand trans to one end of a biguanide ligand. The two weaker field axes would have biguanide groups trans to one another and a biguanide group trans to the carboxylate of the amino acid anion. Presumably the field strengths along these axes would not be so different as to lower the effective symmetry from tetragonal to rhombic, at least with regard to the absorption spectra.

In alkaline solution, the shoulder on the lower energy side of the first band becomes more pronounced, but the position of the main band is not altered (Table IV, Figure 3). Since the anionic bg^- ligand is lower in the spectrochemical series[4] than Hbg, one would expect the tetragonal splitting to be enhanced on the basis just presented.

In the first absorption band region, all of these complexes show two CD bands of opposite signs, with the one at higher energy much more intense (Table III, Figures 1–4). The positions of these CD bands nearly coincide with the peak and shoulder of the first absorption band. The CD spectra of $(-)_{589}$-$[Co(Hbg)_3]^{3+}$ and $(+)_{589}$-$[Co(en)(Hbg)_2]^{3+}$ are similar[4] and the CD spectrum of $Co(en)(Hbg)_2^{3+}$ in the visible region is very similar to the spectra reported here (Figure 1–4). Igi and coworkers[4] assigned the Λ configuration to these complexes, which have the same CD sign patterns as shown for $(-)_{589}$-$[Co(gly)(Hbg)_2]^{2+}$ (Figure 1). The corresponding isomers, all $(+)_{589}$, of the other amino acids with the same CD sign pattern should also have the Λ configuration. From the equilibrium studies of the complexes containing L-amino acids, this is the more stable isomer, although Δ-$(-)_{589}$-$[Co(L\text{-}val)(en)_2]^{2+}$ is the more stable isomer.[6]

The $Co(L\text{-}ala)(NH_3)_4^{2+}$ ion shows three CD peaks of alternating sign (−, +, −) in the first absorption band region.[7] This seems to be the general pattern, although the weak center peak can be completely cancelled by the neighboring peaks, as for $Co(L\text{-}val)(NH_3)_4^{2+}$, giving two negative CD peaks.[6] These two peaks correspond to the two negative peaks of the L-ala complex. The active racemate of $Co(L\text{-}ala)(Hbg)_2^{2+}$ shows a CD curve (Figure 2) similar to that of $Co(L\text{-}ala)(NH_3)_4^{2+}$ except for relative peak intensities. The sum of the CD intensities of the (+) and (−) isomers of $Co(L\text{-}val)(Hbg)_2^{2+}$ (Figure 4) is even more similar in relative peak intensities to the CD curves of typical $Co(L\text{-}am)(NH_3)_4^{2+}$ complex ions and the "vicinal effect" curves of $Co(L\text{-}am)(en)_2^{2+}$ complex ions.[8]

The CD curve of the two isomers of $Co(sar)(Hbg)_2^{2+}$ (one given in Table III and Figure 1) are mirror images of one another, indicating that the optical isomers are also exact mirror images. The CD curve differs significantly from that of the corresponding L-ala complex only in that the intensity of the lowest energy peak is greater for the sarcosine complex. This can be attributed to the contribution of the asymmetric coordinated nitrogen atom. Sarcosine has been found to coordinate stereospecifically[9] in $Co(en)_2(sar)^{2+}$. The $Co(NH_3)_4(sar)^{2+}$ ion can be resolved[9] and its CD curve is quite different from those of other amino acids which contain only asymmetric carbon atoms.[7]

Only one isomer was isolated for $Co(L\text{-}pro)(Hbg)_2^{2+}$. This is to be expected because of the second order asymmetric synthesis observed for some of the other optically active amines, resulting in one pure optical isomer crystallizing slowly in high yield from the reaction solution. Only one isomer was isolated for $Co(en)_2(L\text{-}pro)^{2+}$ also.[10] Proline is more rigid than the other amino acids and it contains both asymmetric nitrogen and carbon. The contribution from this source accounts for the unusual CD intensities in the first band region (Figure 3 and Table III).

The absorption spectra of all of the complexes reported are similar in the region of the second *d-d* absorption band (27.5 kK) and the ligand absorption. Complexes as iodide salts showed an additional absorption band at 44.5 kK. The presence of I^- did not affect the CD spectra. The band at about 34.5 kK corresponds to the charge-transfer band reported for other biguanide complexes.[4] This band is shifted to lower energy (*ca.* 32 kK) in alkaline solution (Figure 3). There is one CD peak near the energy of this absorption band that shifts in the same direction in alkaline solution. In the studies of $Co(Hbg)_3^{3+}$ and $Co(en)(Hbg)_2^{3+}$ the CD peaks in the 41-46 kK region were assigned to the intra-ligand π-π^* transition,[2,4] but this assignment has been questioned.[3] The interpretation of the CD spectrum in the ligand absorption region for biguanide complexes is questionable and cannot serve as a basis for assigning absolute configurations.

The proton magnetic resonance spectra were measured in D_2O solutions. For $(-)_{589}$-$[Co(L\text{-}ala)(Hbg)_2]^{2+}$ the methyl doublet occurs at 1.39 ppm with a coupling constant of 7.2 cps. After heating on a steam bath for 15 minutes, the resulting diastereomeric equilibrium mixture showed two doublets with the same coupling constant (7.2 cps) centred at 1.39 and 1.43 ppm. The latter doublet can be attributed to the $(+)_{589}$ isomer. The doublet at 1.39 ppm is more intense, in accordance with the indications from CD data that the $(-)_{589}$ isomer is favored at equilibrium.

Valine has two methyl groups and $(-)_{589}$-$[Co(L\text{-}val)(Hbg)_2]^{2+}$ shows two doublets at 1.04 and 0.81 ppm, both with a coupling constant of 6.8 cps. For the $(+)_{589}$ isomer the doublets occur (same J) at 1.05 and 0.89 ppm. The equilibrium mixture exhibits three clear methyl doublets with the one at 1.04 ppm of greatest intensity because it occurs for each isomer. The intensity of the doublet at 0.82 ppm is higher than that at 0.88 ppm because of the greater amount of the $(-)_{589}$ isomer. Similar pmr results[11] were obtained for the enantiomers of $Co(L\text{-}val)(en)_2^{2+}$.

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