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Synthesis and Spectral Characterization of the Mixed-Ligand Complexes [*N*-(Carboxymethyl)-L-histidinato][amino acidato]cobalt(III), Co(*N*-Cm-L-Hist)(AA)

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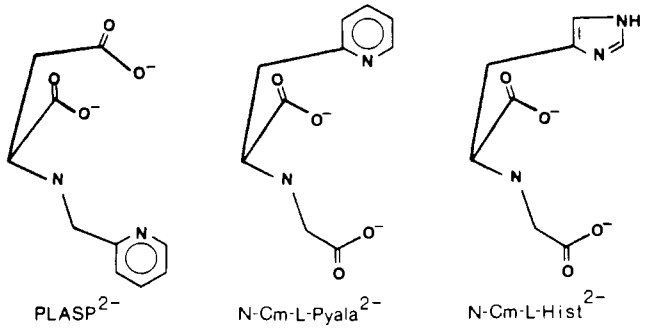
The ligand *N*-(carboxymethyl)-L-histidinate, *N*-Cm-L-Hist^{2-}, was prepared by $NaBH_4$ reduction of the Schiff base formed from L-histidinate and glyoxylate. Several Co(III) mixed-ligand complexes of the form Co(*N*-Cm-L-Hist)(AA) (where AA^- is one of the following: D- or L-valinate (Val^-), α-aminoisobutyrate (α-$AIBA^-$), D-threoninate (Thr^-), D-asparaginate (D-AsN^-)) were prepared by $K_2S_2O_8$ oxidation of Co(II) to Co(III) in the presence of *N*-Cm-L-Hist^{2-} and AA^-. Although there are four possible geometrical isomers, the only one isolated was the facial isomer. In this isomer the carboxylate group of the *N*-carboxymethyl moiety is coordinated trans to the imidazole group of *N*-Cm-L-Hist^{2-}. This structural assignment was based on visible spectra of the Co(*N*-Cm-L-hist)(AA) complexes. The use of D,L-Val^-, D,L-Thr^-, or D,L-AsN^- in the synthesis produced only the *fac*-Co(*N*-Cm-L-Hist)(D-AA) complexes. The CD spectra of the Co(*N*-Cm-L-Hist)(AA) complexes were resolved into two contributions, one from the optically active portion of the amino acidate ring (*Y*) and the other from the rest of the molecule (*X*). Features of the CD spectra are compared with those of spectra of related complexes in the literature. The ^{13}C and ^1H NMR spectra of the complexes are also reported.

Introduction

Previous work in our laboratory has shown that the overall structures of Co^{III}[Y][AA] complexes, where Y is either *N*-(carboxymethyl)-L-β-(2-pyridyl)-α-alaninate, *N*-Cm-L-Pyala^{2-}, or *N*-(2-pyridylmethyl)-L-aspartate, PLASP^{2-}, and



AA^- is a bidentate amino acidate, are determined by a combination of electronic, structural, and steric factors.[1-3] For the Co(*N*-Cm-L-Pyala)(AA) and the Co(PLASP)(AA) complexes in which no steric interaction between the amino acidate chelate ring and the pyridyl ring is evident, the facial isomers having nitrogen coordinated trans to oxygen (Figure 1a,b) appear to be favored.[1-3] Coordination of PLASP^{2-}, as shown in Figure 1a, gives the least strained bond angle around the secondary amino nitrogen and is presumably favored structurally over the more strained structure in which the pyridyl group is trans to the α-CO_2^- of PLASP^{2-}.[1,2] On the other hand, the meridional isomer of Co(*N*-Cm-L-Pyala)(AA) in which the pyridyl group is coordinated trans to the amino nitrogen of the amino acidate (Figure 1c) appears to be the favored isomer when steric interaction between the amino acidate chelate ring and the pyridyl ring is present in the facial isomer as in the Co(*N*-Cm-L-Pyala)(L-Val) complex.[3] In order to compare the effects of substituting an imidazole group for a pyridyl group in the above complexes, we prepared the structurally similar ligand *N*-(carboxymethyl)-L-histidinate, *N*-Cm-L-Hist^{2-}, and its Co(III) mixed amino acidate, Co(*N*-Cm-L-Hist)(AA), complexes where the amino acidate is either α-aminoisobutyrate (α-$AIBA^-$), D-threoninate (D-Thr^-), D-asparaginate (D-AsN^-), or D- or L-valinate (Val^-). It is also of interest to compare the spectra of the Co(*N*-Cm-L-Hist)(AA) complexes to those of the corresponding Co(*N*-Cm-L-Pyala)(AA) and Co(PLASP)(AA) complexes.

Experimental Section

Preparation of *N*-(Carboxymethyl)-L-histidine, *N*-Cm-L-HistH_2. To a solution of L-histidine (12.0 g, 77 mmol) in 50 mL of water was added enough base (~6 N NaOH) to bring the histidine solution to pH 9.8-10.0. The solution was then placed in an ice bath. Next a solution of glyoxylic acid hydrate (13.0 g, 170 mmol) in 35 mL of water was added dropwise to the histidine solution over a period of 45 min. So that pH 9.8-10.0 might be maintained, 6 N NaOH was added simultaneously with the glyoxylic acid solution. Upon addition of the glyoxylic acid solution, the reaction solution acquired a light yellow color. The solution was stirred for 1 h, and a solution of $NaBH_4$ (1.50 g, 40 mmol) in 20 mL water was added dropwise. The addition of the $NaBH_4$ resulted in the partial disappearance of the yellow color. To maintain pH 9.8-10.0, we added ~2 N HCl periodically during the borohydride addition. The solution was stirred for 30 min, and $NaBH_4$ (1.50 g, 40 mmol) in 20 mL of water was again added; the solution was stirred for an additional 3 h. Next, the solution was brought to pH 3.5 with 6 N HCl and removed from the ice bath. The acidified solution was reduced to half its volume in a rotary evaporator and placed on a Dowex 50W-X8 ion-exchange column (2.6 × 85 cm, 400 mL of resin, 100-200 mesh) in the H^+ form. After it was washed with 1 L of water (eluant pH 5-6), the product was eluted off with 0.25 N aqueous NH_3. Fractions (25 mL) were collected, and those of pH 3.5 were combined and reduced to near dryness. The resulting slurry was treated with 250 mL of absolute ethanol, chilled to -10 °C in a freezer, and then filtered. Additional fractions of product were obtained by reducing the ethanol solution to near dryness and adding more absolute ethanol. The total yield was 14.2 g (86%). Anal. Calcd for *N*-Cm-L-HistH_2, $C_8H_{11}N_3O_4$: C, 45.07; H, 5.16; N, 19.72. Found: C, 45.11; H, 5.27; N, 19.64.

Preparation of [*N*-(Carboxymethyl)-L-histidinato][amino acidato]cobalt(III) Complexes, Co(*N*-Cm-L-Hist)(AA). To a solution containing *N*-Cm-L-HistH_2 (0.54 g, 2.5 mmol), amino acid (AAH) (2.5 mmol), and $CoSO_4 \cdot 7H_2O$ (0.70 g, 2.5 mmol) in 15 mL of water was added 7.5 mL of 1 N NaOH. The initial pH was between 9 and 10. Next 0.1 g of activated charcoal was added to the reaction mixture. This was followed by the addition over a 30-min period of a solution containing $K_2S_2O_8$ (0.40 g, 1.5 mmol) in 15 mL of water. The solution began to turn reddish purple, and the pH began dropping. The solution was heated at 50-60 °C for 1 h to give a final pH 5.0-6.0 and a deep reddish purple solution. The individual complexes were isolated and purified as described below.

Isolation of [Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$ Using D-Val^-. The complex [Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$ precipitated out of the reaction mixture and was filtered off with the activated carbon. The

(1) Meiske, L. A.; Angelici, R. J. *Inorg. Chem.* **1980**, *19*, 3783.
(2) Meiske, L. A.; Jacobson, R. A.; Angelici, R. J. *Inorg. Chem.* **1980**, *19*, 2028.
(3) Meiske, L. A.; Angelici, R. J., *Inorg. Chem.*, companion paper in this issue.

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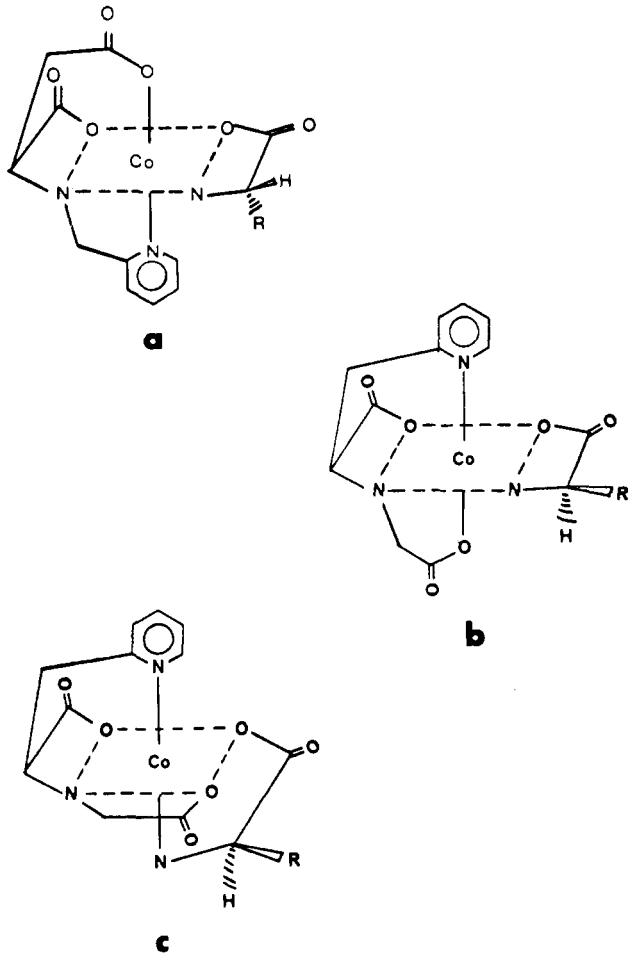

Figure 1. Structures of (a) *fac*-Co(PLASP)(AA), (b) *fac*-Co(*N*-Cm-L-Pyala)(AA), and (c) *mer*-Co(*N*-Cm-L-Pyala)(AA) complexes.

product was isolated by extraction with hot water and filtering off the carbon. The extraction was repeated with hot water until the filtrate was colorless. The filtrates were combined and reduced to dryness. Reduction and filtration of the reaction mixture yielded additional fractions of product. The yield of [Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$ was 293 mg (30%). Anal. Calcd for [Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$, $C_{13}H_{19}N_4O_6Co\cdot{}^1/_2H_2O$: C, 39.50; H, 5.06; N, 14.18. Found: C, 39.60; H, 5.00; N, 14.26.

Isolation of [Co(*N*-Cm-L-Hist)(L-Val)]·4H$_2$O Using L-Val$^-$. The activated carbon was filtered off, and the reaction mixture was reduced to 5–10 mL under vacuum. The reduced solution was placed on a Dowex 50W-X8 ion-exchange column (2.4 × 60 cm, 200–400 mesh) in the Na^+ form and eluted with water to give an initial band containing various anionic and decomposition products. The second and major band, containing the product, was collected and reduced to a few milliliters under vacuum. To force precipitation, we added a large volume (100–150 mL) of absolute ethanol. The resulting slurry was chilled at −10 °C overnight and filtered. The yield of [Co(*N*-Cm-L-Hist)(L-Val)]·4H_2O was 470 mg (41%). Anal. Calcd for [Co(*N*-Cm-L-Hist)(L-Val)]·4H_2O, $C_{13}H_{19}N_4O_6Co\cdot 4H_2O$: C, 34.07; H, 5.90; N, 12.23. Found: C, 34.37; H, 6.03; N, 12.37.

Isolation of [Co(*N*-Cm-L-Hist)(D-Val)]·H$_2$O Using D,L-Val$^-$. The Co(*N*-Cm-L-Hist)(D-Val) that precipitated out of the reaction mixture was filtered off with the activated carbon and extracted as described above in the isolation of the D-Val$^-$ complex. The filtered reaction solution was reduced in volume to give additional fractions of the D-Val$^-$ complex. Chromatography of the remaining reaction solution as described in the section on the isolation of Co(*N*-Cm-L-Hist)(L-Val) (see above) yielded a red band containing only the D-Val$^-$ complex. The yield of [Co(*N*-Cm-L-Hist)(D-Val)]·H_2O was 362 mg (36% based on total D- and L-Val$^-$). Anal. Calcd for [Co(*N*-Cm-L-Hist)(D-Val)]·H_2O, $C_{13}H_{19}N_4O_6Co$: C, 38.62; H, 5.20; N, 13.86. Found: C, 38.21; H, 5.19; N, 13.89.

Isolation of Co(*N*-Cm-L-Hist)(α-AIBA). The complex Co(*N*-Cm-L-Hist)(α-AIBA) was isolated and chromatographed in a manner

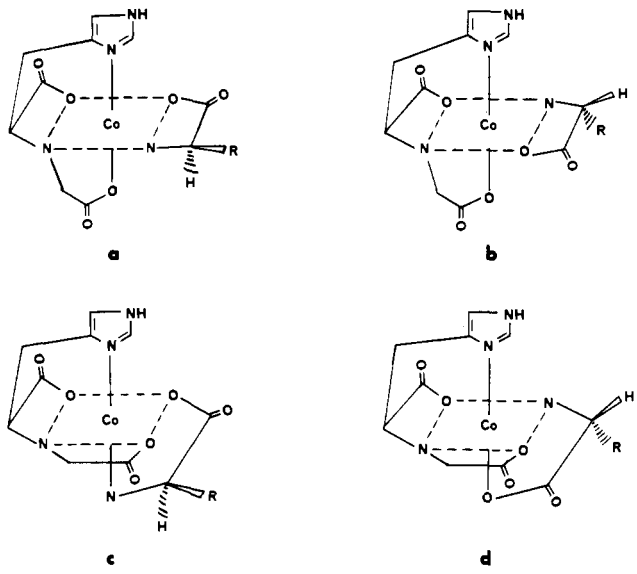

Figure 2. The four possible geometrical isomers of [Co(*N*-Cm-L-Hist)(D-AA)]: (a) *fac*; (b) *mer*-*N*-Cm-CO_2^-; (c) *mer*-AA$^-$ amino; (d) *mer*-AA$^-$$CO_2^-$.

identical with that described for the [Co(*N*-Cm-L-Hist)(L-Val)]·4H_2O complex above. The yield was 247 mg (27%). Anal. Calcd for Co(*N*-Cm-L-Hist)(α-AIBA), $C_{12}H_{18}N_4O_6Co$: C, 38.72; H, 4.84; N, 15.06. Found: C, 38.29; H, 4.70; N, 15.10.

Isolation of [Co(*N*-Cm-L-Hist)(D-Thr)]·H$_2$O Using D,L-Thr$^-$ and of [Co(*N*-Cm-L-Hist)(D-AsN)]·2H$_2$O Using D,L-AsN$^-$. These two complexes were isolated and purified in the same manner as that described for the isolation of [Co(*N*-Cm-L-Hist)(D-Val)]·H_2O using D,L-Val$^-$. The yields of [Co(*N*-Cm-L-Hist)(D-Thr)]·H_2O and [Co(*N*-Cm-L-Hist)(D-AsN$^-$)]·2H_2O were 332 mg (34% based on total D- and L-Thr$^-$) and 410 mg (45% based on total D- and L-AsN$^-$), respectively. Anal. Calcd for [Co(*N*-Cm-L-Hist)(D-Thr)]·H_2O, $C_{12}H_{17}N_4O_7Co\cdot H_2O$: C, 35.48; H, 4.68; N, 13.80. Found: C, 35.52; H, 4.79; N, 13.83. Calcd for [Co(*N*-Cm-L-Hist)(D-AsN)]·2H_2O $C_{12}H_{16}N_5O_7Co\cdot 2H_2O$: C, 32.96; H, 4.58; N, 16.02. Found: C, 33.03; H, 4.51; N, 16.31.

Spectra. Visible spectra were measured in water at room temperature with a Cary Model 14 spectrophotometer. Circular dichroism spectra were measured in water at room temperature with a Jasco ORD/UV/CD-5 spectrophotometer. The ^{13}C and ^1H NMR spectra were recorded on a Jeol FX90Q Fourier transform NMR spectrometer at room temperature. The ^{13}C NMR spectra of the more soluble complexes and all the ^1H NMR spectra were recorded in 99.7% D_2O, while the ^{13}C NMR spectra of the less soluble complexes were recorded in 70% H_3PO_4(aq). The proton chemical shifts are reported in ppm downfield from Me_4Si with *tert*-butyl alcohol (δ 1.23) as an internal standard. The ^{13}C chemical shifts are also given in ppm downfield from Me_4Si with 1,4-dioxane (δ 67.0) as the internal standard.

Results and Discussion

Figure 2 shows the four possible geometric isomers of the Co(*N*-Cm-L-Hist)(D-AA) complexes. The structure in Figure 2a has a facial arrangement of oxygen atoms. The three meridional isomers in Figure 2b–d are denoted *mer*-*N*-Cm-CO_2^-, *mer*-AA$^-$ amino, and *mer*-AA$^-$$CO_2^-$, with the terms *N*-Cm-$CO_2^-$, AA$^-$ amino, and AA$^-$$CO_2^-$ being used to denote which group is coordinated trans to the imidazole group.

Visible Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes. The visible spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) in water is shown in Figure 3 and is typical of the other Co(*N*-Cm-L-Hist)(AA) visible spectra, whose maxima are presented in Table I. The visible spectra of these Co(*N*-Cm-L-Hist)(AA) complexes, which have a symmetrical peak at 511 ± 1 nm and a somewhat lower intensity peak at 353 ± 3 nm, are comparable to those reported for the facial isomers of the Co(*N*-Cm-L-Pyala)(AA) and Co(PLASP)(AA) mixed-ligand complexes.[1,3] The major differences in the visible spectra of the facial Co(*N*-Cm-L-Pyala)(AA) (with symmetrical peaks at

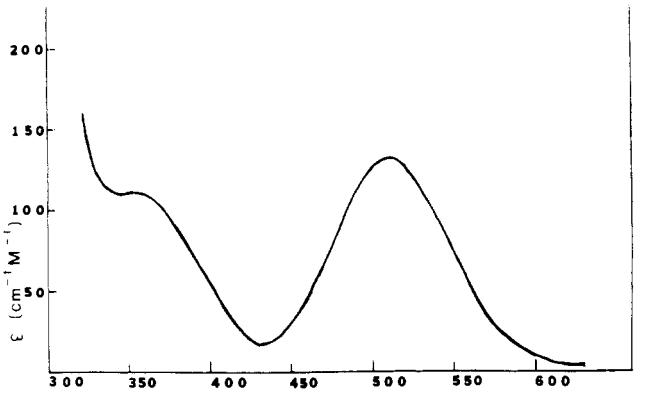

Figure 3. Visible spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) in water.

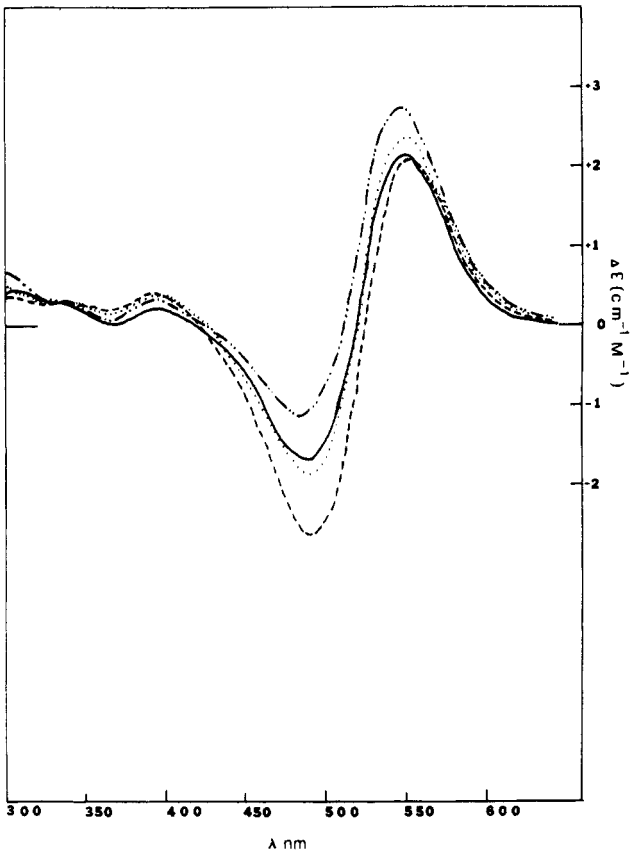

Figure 4. CD spectra of Co(*N*-Cm-L-Hist)(AA) complexes: α-AIBA⁻ (—); L-Val⁻ (- - -); D-Val⁻ (-·-·-); [(D + L)/2]-Val⁻ (···).

Table I. Visible Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes in H_2O

complex	λ, nm	ϵ^a	λ, nm	ε
[Co(*N*-Cm-L-Hist)(α-AIBA)]	510	138	355	121
[Co(*N*-Cm-L-Hist)(L-Val)]·$4H_2O$	512	139	353	130
[Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$	511	138	353	117
[Co(*N*-Cm-L-Hist)(D-Val)]·$^1/_2H_2O$[b]	510	142	353	115
[Co(*N*-Cm-L-Hist)(D-Thr)]·H_2O[b]	511	138	352	121
[Co(*N*-Cm-L-Hist)(D-AsN)]·$2H_2O$[b]	510	136	350	114

[a] Units for ε are cm^{-1} M^{-1}. [b] Obtained from preparations using D,L-AA⁻.

522 nm, ε = 165, and 370 nm, ε = 132) and the facial Co(*N*-Cm-L-Hist)(AA) complexes are a decrease in ε and a shift to higher energy (a 10-nm shift for the lower energy band and a 20-nm shift for the higher energy band) when imidazole is substituted for pyridine in the coordination sphere. A similar decrease in extinction coefficients but smaller shifts (10 nm) in the higher energy band have been noted before for some

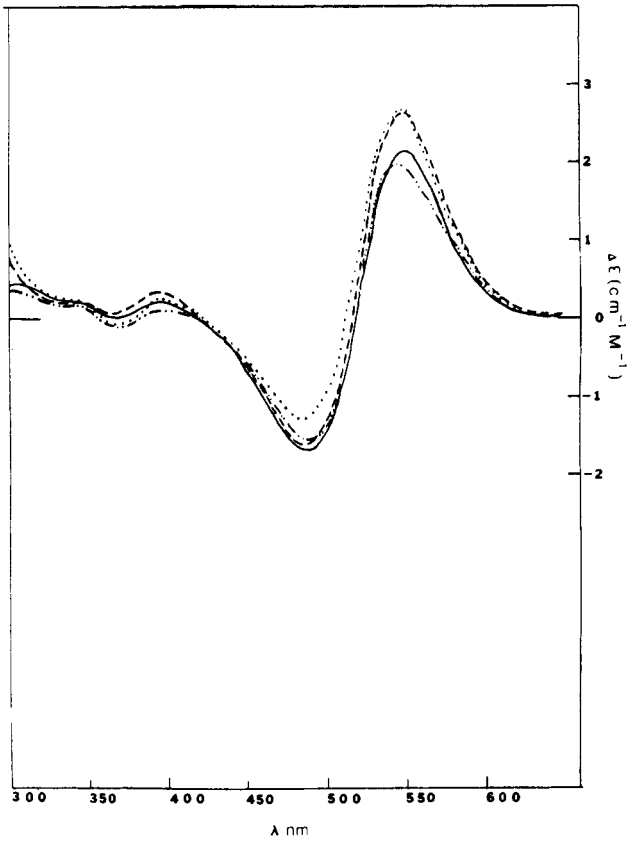

Figure 5. CD spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) (—) and CD spectra of Co(*N*-Cm-L-Hist)(AA) complexes isolated from reactions using D,L-AA⁻ as starting material, D-Val⁻ (···), D-Thr⁻, (- - -), and D-AsN⁻ (-·-·-).

Table II. CD Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes in H_2O

	band I				band II			
AA⁻	λ, nm	$\Delta\epsilon^a$	λ, nm	Δε	λ, nm	Δε	λ, nm	Δε
α-AIBA⁻	545	+2.14	484	−1.68	394	+0.23	340	+0.29
L-Val⁻	553	+2.38	490	−2.66	393	+0.41	340	+0.31
D-Val⁻	546	+2.73	485	−1.13	395	+0.32	340	+0.33
D-Val⁻[b]	547	+2.68	485	−1.25	396	+0.29	340	+0.25
D-Thr⁻[b]	547	+2.64	485	−1.60	393	+0.37	340	+0.25
D-AsN⁻[b]	547	+1.94	485	−1.54	396	+0.12	340	+0.25

[a] Units for Δε are cm^{-1} M^{-1}. [b] Obtained from preparations using D,L-AA⁻.

$Co^{III}N_4O_2$ complexes containing imidazole and pyridine.[4] The similarity of the absorption maxima and extinction coefficients for the complexes listed in Table I suggests that the coordination sphere around the Co(III) is identical for all of the complexes. Since there is only one facial isomer (Figure 2a) possible for the Co(*N*-Cm-L-Hist)(AA) complex, the complexes listed in Table I are assigned that structure. Further evidence for this assignment may be obtained from their CD, ^1H NMR, and ^{13}C NMR spectra, which are discussed below.

Circular Dichroism Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes. The circular dichroism spectra (visible region only) of the Co(*N*-Cm-L-Hist)(AA) complexes in water are shown in Figures 4 and 5, and numerical values for their minima and maxima are listed in Table II. These spectra are all similar in shape, varying only in intensity. They can be divided into two major bands (Table II), with band I in the region from 480 to 555 nm and band II in the region from 340 to 400 nm.

(4) Ebner, S. R.; Angelici, R. J. *Inorg. Chem.* **1980**, *19*, 1031.

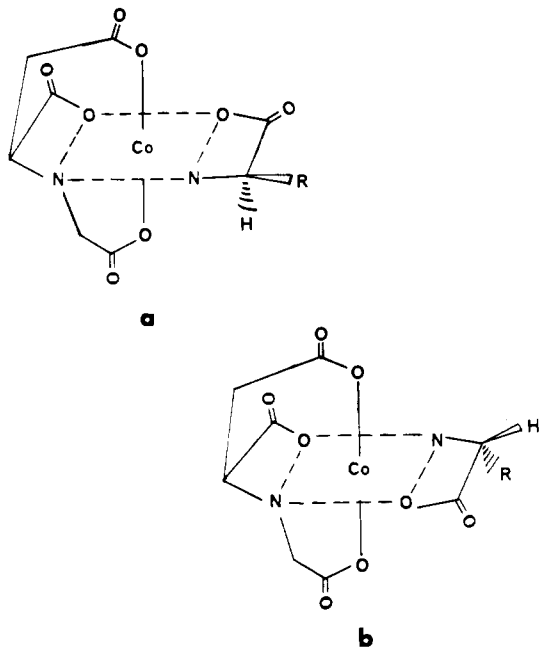

Figure 6. (a) cis-N,cis-O_5 and (b) trans-N,cis-O_5 Co(*N*-Cm-L-Asp)(D-AA).

Band I of *fac*-Co(*N*-Cm-L-Hist)(α-AIBA) with a positive peak at 545 nm and a negative peak at 468 nm is very similar in its overall shape to band I of *fac*-Co(*N*-Cm-L-Pyala)(α-AIBA) with a positive peak at 557 nm and a negative peak at 488 nm. Band I of the other *fac*-Co(*N*-Cm-L-Hist)(AA) complexes in Table II is also similar in shape to band I of the *fac*-Co(*N*-Cm-L-Pyala)(AA)[3] and cis-N, cis-O_5 Co(*N*-Cm-L-Asp)(AA) complexes (Figure 6a) where *N*-Cm-L-Asp^{3-} is the tetradentate *N*-(carboxymethyl)-L-aspartate ligand.[5] This similarity seems reasonable since these three complexes, *fac*-Co(*N*-Cm-L-Hist)(AA), *fac*-Co(*N*-Cm-L-Pyala)(AA), and Co(*N*-Cm-L-Asp)(AA), are structurally identical in terms of the size and position of their chelate rings, each containing one six-membered ring and three five-membered rings. They differ only in the type of donor group (either imidazole, pyridyl, or carboxylate, respectively) coordinated trans to the *N*-carboxymethyl carboxylate group. As noted above for their visible spectra, the circular dichroism spectral intensities ($\Delta\epsilon$) of the Co(*N*-Cm-L-Hist)(AA) complexes are lower than the $\Delta\epsilon$ values for the corresponding facial Co(*N*-Cm-L-Pyala)(AA) complexes. Thus substitution of imidazole for pyridine also causes a decrease in $\Delta\epsilon$ values. This trend has also been reported for the $Co(Pyala)_2^+$, Co(Pyala)$(Hist)^+$, and $Co(Hist)_2^+$ complexes, where $Pyala^-$ is β-(2-pyridyl)-α-alaninate and $Hist^-$ is histidinate.[4]

Band II consists of two low-intensity positive peaks. The position and intensity of these higher energy peaks do not vary significantly from one amino acidate to another.

A comparison of the CD curves in Figures 4 and 5 reveals that the CD curve of the L-Val^- complex lies lower than that of the α-$AIBA^-$ complex and that the D-amino acidate complex curves are higher than that of the α-$AIBA^-$ complex. Since the Co(*N*-Cm-L-Hist)(AA) complexes all have the same basic structure, the differences in their CD spectra must be related to the differences at the α-carbon of their amino acidates. This has been noted in the CD spectra of the facial Co(PLASP)(AA) and meridional Co(*N*-Cm-L-Pyala)(AA) complexes. In those cases, their CD spectra were resolved into a *Y* term representing the contribution of amino acidate chelate ring bending and an *X* term representing the contribution of the rest of the complex. With use of a similar approach, the value of $\Delta\epsilon$ at a given wavelength in the CD spectrum of a Co(*N*-Cm-L-Hist)(AA) complex can be expressed as

$$X + Y_{\text{D or L}} = \text{CD[Co(}N\text{-Cm-L-Hist)(D- or L-AA)]} \quad (1)$$

if it is assumed that $Y_D = -Y_{L'}$ then

$$X = \{\text{CD[Co(}N\text{-Cm-L-Hist)(L-AA)] + CD[Co(}N\text{-Cm-L-Hist)(D-AA)]}\}/2 \quad (2)$$

The *X* value has been calculated with use of the CD spectra of the Co(*N*-Cm-L-Hist)(D-Val) and Co(*N*-Cm-L-Hist)(L-Val) complexes and is given in Figure 4. It should be noted that the CD spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) is essentially the same as that of the calculated *X* term (Figure 4). Thus, as in the case of facial Co(PLASP)(α-AIBA) and *mer*-Co(*N*-Cm-L-Pyala)(α-AIBA), the assumption that *X* is essentially equal to the observed spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) can be made. The *X* term for the *N*-Cm-L-$Hist^{2-}$ complexes consists of a positive peak at ~550 nm and a negative peak at 470 nm. This is different than the two positive peaks at 545 nm and 495 nm for the Co(PLASP)(AA) *X* term and the single negative peak at 488 nm for the *mer*-Co(*N*-Cm-L-Pyala)(AA) *X* term.

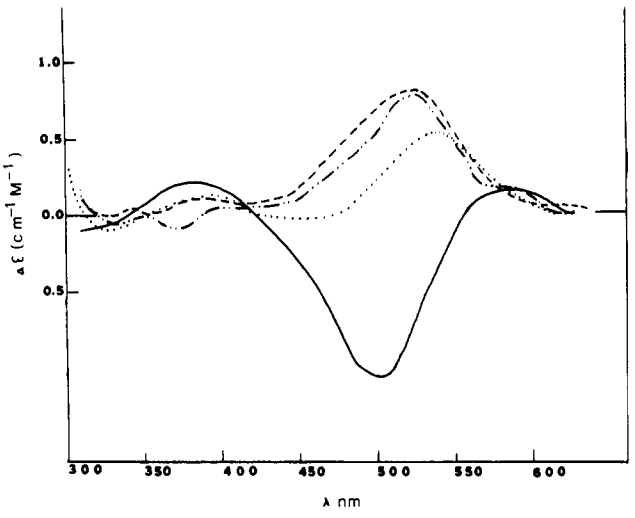

Figure 7. *Y* contribution to the Co(*N*-Cm-L-Hist)(AA) CD spectra of D-Val^- (---), L-Val^- (—), D-Val^- (-··-) isolated from the reaction using D,L-Val^- in the synthesis, and D-Thr^- (···) isolated from the reaction using D,L-Thr^- in the synthesis.

Calculations of the various *Y* terms, assuming that *X* is equal to the CD spectrum of Co(*N*-Cm-L-Hist)(α-AIBA) were made with use of eq 1; these values are given in Figure 7 for D-Val^-, L-Val^-, and D-Thr^-. A comparison of the *Y* terms for L-Val^- and D-Val^- shows that to a first approximation the assumption of $Y_D = -Y_L$ in formulating eq 2 for the present system is valid. Since the CD spectrum of Co(*N*-Cm-L-Hist)(D-AsN) is very similar to that of the α-AIBA complex, no attempt was made to calculate a *Y* term for D-AsN^-. The assignment of this complex as the D-AsN^- isomer is discussed in the ^1H NMR section below.

The *Y* term for D-Val^- in Co(*N*-Cm-L-Hist)(D-Val) with its positive peak at ~510 nm is comparable to the positive low-energy peak of the *Y* terms calculated for other D-amino acidates in the Co(PLASP)(D-AA) and Co(*N*-Cm-L-Pyala)(D-AA) complexes. Similarly the negative peak at ~510 in the *Y* term of L-Val^- in *fac*-Co(*N*-Cm-L-Hist)(L-Val) is comparable to the negative low-energy peak in the *Y* terms of the *fac*-Co(PLASP)(L-AA) and *mer*-Co(*N*-Cm-L-Pyala)(L-AA) complexes. Since the general shapes and intensities of the *Y* terms in the various complexes listed above vary considerably, only the signs of the low-energy peaks are compared. It should be noted that the Val^- complex prepared with

(5) Colomb, G.; Bernauer, K. *Helv. Chim. Acta* **1977**, *60*, 459.

Table III. Proton NMR Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes in D_2O[a]

	N-Cm-L-Hist^{2-}				AA$^-$		
compd	α-H	β-H	*N*-Cm-H	imidazole	α-H	β-H	γ-H
N-Cm-L-HistH_2	3.99 t	3.38 d	3.65 m	7.38 s[b]			
				8.61 s[c]			
Co(*N*-Cm-L-Hist)(α-AIBA)	3.92 t	3.42 d	3.51 d	7.18 s		1.43 s	
			4.31 d	7.50 s[c]		1.46 s	
Co(*N*-Cm-L-Hist)(L-Val)	3.89 t	3.34 d	3.44 d	7.14 s	3.69 d	2.27 m	0.86 d[d]
			4.35 d	7.43 s[c]			0.96 d
Co(*N*-Cm-L-Hist)(D-Val)	3.93 t	3.45 d	3.50 d	7.19 s	3.54 d	2.2 m	0.89 d[d]
			4.34 d	7.46 s[c]			1.03 d
Co(*N*-Cm-L-Hist)(D-Val)[e]	3.93 t	3.44 d	3.51 d	7.19 s	3.55 d	2.26 m	0.89 d[d]
			4.34 d	7.47 s[c]			1.04 d
Co(*N*-Cm-L-Hist)(D-Thr)[e]	3.92 t	3.45 d	3.54 d	7.17 s	3.50 d	4.4 m	1.26 d
			4.35 d	7.54 s[c]			
Co(*N*-Cm-L-Hist)(D-AsN)[e]	3.91 t	3.42 d	3.54 d	7.16 s	3.74 t	2.87 m	
			4.32 d	7.80 s[c]			

[a] The chemical shifts (δ) are referenced to *t*-BuOH (δ 1.23); t = triplet, d = doublet, s = singlet, and m = multiplet. [b] The imidazole protons are given as singlets although they are doublets with a coupling constant of ~1 Hz. [c] This chemical shift is assigned to the proton on the 2-carbon of the imidazole. [d] J = 7 Hz. [e] Complex prepared with D,L-AA$^-$.

use of D,L-Val$^-$ has a *Y* term that is essentially the same as that for the Co(*N*-Cm-L-Hist)(D-Val) complex; similarly the *Y* term for the Thr$^-$ complex prepared with use of D,L-Thr$^-$ is characteristic of a D-AA$^-$. Thus, the only complexes isolated with use of D,L-AA$^-$ in their syntheses are the Co(*N*-Cm-L-Hist)(D-AA) complexes. Further evidence for this assignment may be seen in their ^1H and ^{13}C NMR spectra to be discussed below.

A comparison of the CD curves and minimum and maximum values reported previously for the cis-N, cis-O_5 and trans-N, cis-O_5 Co(*N*-Cm-L-Asp)(D- and L-AA) complexes (Figure 6) shows that their overall shapes and intensities are also related to changes at the α-carbon of the amino acidates.[5] (The amino acidate of the trans-N, cis-O_5 isomer (Figure 6b) has its α-CO_2^- coordinated trans to the α-CO_2^- of *N*-Cm-L-Asp^{3-} and its amino group trans to the *N*-Cm-L-Asp^{3-} amino group.) Thus, their CD spectra can also be divided into *X* and *Y* terms. From an examination of the CD curves and values of their minima and maxima, the sign of the low-energy peak of the *Y* term for both cis-N, cis-O_5 and trans-N, cis-O_5 is found to be positive for D-amino acidates and negative for L-amino acidates.

Thus, there appears to be a general trend in the sign of the low-energy peak of the *Y* terms for the *fac*-Co(PLASP)(AA), *fac*- and *mer*-Co(*N*-Cm-L-Pyala)(AA), *fac*-Co(*N*-Cm-L-Hist)(AA), and Co(*N*-Cm-L-Asp)(AA) complexes. For D-amino acidates the sign of the low-energy peak of the *Y* term is positive, and for L-amino acidates it is negative. As discussed for the Co(PLASP)(AA) complexes, *Y* may represent the contribution of amino acidate chelate ring bending to the overall CD spectrum.[1]

^1H NMR Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes. The ^1H NMR spectra of the Co(*N*-Cm-L-Hist)(AA) complexes and the free ligand *N*-Cm-L-HistH_2 in 99.7% deuterium oxide are given in Table III. Chemical shifts of protons in the coordinated *N*-Cm-L-Hist^{2-} ligand are assigned as follows: a triplet centered at δ ~3.92 for the α-proton, a doublet centered at δ 3.45 for the β-protons, two doublets (J = 18 Hz) centered at δ ~3.50 and 4.35 for the *N*-carboxymethyl protons, a singlet at δ ~7.17 for the proton on the imidazole 4-carbon, and a singlet varying from δ 7.43 to 7.80 for the proton on the imidazole 2-carbon. The α-proton and *N*-carboxymethyl protons of the *N*-Cm-L-Hist^{2-} ligand are comparable to those of the *N*-Cm-L-Pyala^{2-} cobalt analogues, where the α-proton occurs at δ 3.9 and the *N*-carboxymethyl protons occur as two doublets at δ 3.56 and 4.37 with J = 18 Hz.[3]

The spectrum of the complex isolated from the preparation using D,L-AsN$^-$ indicates that only one diastereomer is present. The downfield shift of the proton on the imidazole 2-carbon of this complex as compared to those of the other complexes in Table III suggests that the AsN$^-$ complex is *fac*-Co(*N*-Cm-L-Hist)(D-AsN). A similar deshielding of the 2-pyridyl proton in *fac*-Co(PLASP)(L-AsN)[1] and especially in *fac*-Co(*N*-Cm-L-Pyala)(D-AsN)[3] was attributed to the polar amide group of AsN$^-$, which is on the same side of the complex as the imidazole ring.

The assignments of the various protons in the coordinated amino acidates are also given in Table III. A comparison of the α-protons for the L-Val$^-$ and D-Val$^-$ complexes reveals that the α-proton of L-Val$^-$ is deshielded relative to the α-proton of D-Val$^-$. Since the α-proton of L-Val$^-$ is positioned nearly in the plane of the imidazole ring, which is pointing between the α-carbon and the α-carboxylate (this has been found for the pyridine ring of Co(*N*-Cm-L-Pyala)(D-Thr)[6]), it is deshielded relative to the α-proton of D-Val$^-$, which is on the opposite side of the chelate ring.

A similar argument can be used to explain why the γ-methyl groups of D-Val$^-$ are deshielded relative to those of the L-Val$^-$ complex. In the D-Val$^-$ complex, the γ-methyls are positioned in the plane of the imidazole ring (as is the α-H of the L-Val$^-$ analogues) and are deshielded relative to the γ-methyls of the L-Val$^-$ complex, which are on the opposite side of the chelate ring. It should be noted that the assignment of the Val$^-$ complex prepared with use of D,L-Val$^-$ as the Co(*N*-Cm-L-Hist)(D-Val) diastereomer is based upon the fact that its proton NMR is identical with that of the complex obtained from D-Val$^-$ (Table III). This conclusion is consistent with that noted in the CD discussion.

The proton NMR spectrum of the complex isolated with use of D,L-Thr$^-$ in the synthesis gives a doublet at δ 1.26 for the γ-methyl protons and a doublet at δ 3.50 for the α-proton. Since no other doublets were observed, the complex prepared with use of D,L-Thr$^-$ is either Co(*N*-Cm-L-Hist)(D-Thr) or Co(*N*-Cm-L-Hist)(L-Thr) instead of the D,L-Thr complex. Since the calculated *Y* contribution to the CD spectrum of the complex is characteristic of D-amino acidates, the complex is formulated as Co(*N*-Cm-L-Hist)(D-Thr).

^{13}C NMR Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes. The ^{13}C NMR spectra of the free ligand *N*-Cm-L-HistH_2 and the Co(*N*-Cm-L-Hist)(AA) complexes in D_2O and 70% H_3PO_4 are given in Table IV. The assignment of the resonances for the histidinate portion of the free ligand is consistent with that reported for histidine.[7] The chemical shifts of the *N*-Cm-L-

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Table IV. ^{13}C NMR Spectra of the Co(*N*-Cm-L-Hist)(AA) Complexes in D_2O[a]

	N-Cm-L-Hist^{2-}					*N*-Cm-L-Hist^{2-}			AA$^-$			
	α-CO_2^-	*N*-Cm-CO_2^-	α-C	β-C	*N*-Cm-C	5-C	4-C	2-C	α-CO_2^-	α-C	β-C	γ-C
Co(*N*-Cm-L-Hist)(α-AIBA)	184.1	183.5	67.7	26.9	57.3	132.3	117.8	136.7	189.8	61.5	28.3 26.8	
Co(*N*-Cm-L-Hist)(D-Val)[b]	185.5	184.2	67.9	27.0	57.7	132.0	118.7	136.4	186.7	64.3	30.1	16.1 18.3
Co(*N*-Cm-L-Hist)(D-Val)[b,c]	185.5	184.2	68.0	26.9	57.7	131.8	118.8	136.3	186.6	64.5	30.3	16.1 18.2
Co(*N*-Cm-L-Hist)(L-Val)	184.0	183.4	67.6	26.6	57.6	132.2	117.6	136.7	186.7	63.4	30.2	16.0 18.1
Co(*N*-Cm-L-Hist)(D-Thr)[b,c]	185.4	184.4	67.9	26.9	58.1	131.6	118.4	137.2	185.4	67.7	64.3	18.6
Co(*N*-Cm-L-Hist)(D-AsN)[c]	184.0	183.6	67.8	26.8	57.0	132.0	117.3	138.3	184.4	55.0	35.4	175.2
Co(*N*-Cm-L-Hist)(D-AsN)[b,c]	185.4	184.4	68.1	27.0	57.7	131.5	118.2	138.0	185.1	55.7	35.2	175.9
N-Cm-L-HistH_2	171.9	171.3	61.3	25.4	48.8	127.8	118.1	134.4				

[a] Chemical shifts are given relative to 1,4-dioxane (δ 67.0 downfield from Me_4Si) as an internal reference. [b] Solvent is 70% H_3PO_4 (aq). [c] Complex prepared with D,L-AA$^-$ in the synthesis.

Hist^{2-} ligand in the complexes remain constant and do not seem to be affected by the amino acidate. This is consistent with assigning the same structure (Figure 2a) to all the Co(*N*-Cm-L-Pyala)(AA) complexes listed in Table IV. The spectra obtained in 70% H_3PO_4 are nearly identical with those obtained in D_2O, with only the carboxylate carbons being shifted up to 1.5 ppm downfield. This could be due to some protonation of these carboxylates by the H_3PO_4 solvent. The chemical shifts of the amino acidates correspond well with those reported for the various *fac*-Co(PLASP)(AA) and *fac*-Co(*N*-Cm-L-Pyala)(AA) complexes.[1,3]

It may be noted that all the carbon resonances occur as distinct singlets (protons were broad-band decoupled), and no evidence for the presence of other isomers was found. This is consistent with the CD and proton NMR spectra, which indicated that only the Co(*N*-Cm-L-Hist)(D-AA) complexes were isolated from reactions using D,L-AA$^-$.

Conclusion

Previously we concluded that for several $Co^{III}N_3O_3$ complexes, the stability of the isomer isolated may be attributed to a combination of electronic, structural, and steric factors. The facial isomer of the Co(PLASP)(AA) complexes (Figure 1a) was favored by having the tetradentate ligand in the least strained configuration and by not having trans-amino groups, which are observed in related systems to avoid coordinating trans to each other.[1,2] This preferred facial mode of coordination is consistent with an earlier theoretical account of bonding in transition-metal complexes, which stated that the most stable isomer for low-spin d^6 $ML_3L'_3$ complexes should be facial if there is no steric interaction present.[8] Also, as noted for the $Co^{III}N_4O_2$, Co(Pyala)$_2^+$, and $Co^{III}N_3O_3$, *fac*- and *mer*-Co(L-Pyala)(X), complexes where X is either aspartate or iminodiacetate, amino groups avoid coordinating trans to each other.[4,9] Similar coordination trends have been reported for other Co(III) mixed-ligand complexes.[10]

Both the *fac* and *mer* isomers (Figure 1b,c) of Co(*N*-Cm-L-Pyala)(AA) were isolated. The stability of the *fac* isomer was expected on the basis of the least strained tetradentate ligand geometry[11-14] and the absence of trans amino groups. The *mer* isomer, however, involved the strained configuration of the ligand; its stability was attributed to the presence of the favorable coordination of an amino group trans to pyridine.[3] Moreover, bending of the chelate ring for the L-AA$^-$ complexes was proposed to favor the *mer* isomer.

Replacement of the pyridine group in Co(*N*-Cm-L-Pyala)(AA) by imidazole gives the Co(*N*-Cm-L-Hist)(AA) complexes, which have been isolated as the *fac* isomer only. This isomer appears to be favored by its least strained geometry for the tetradentate ligand[11-14] and the lack of trans-amino groups. The absence of the *mer*-Co(*N*-Cm-L-Hist)(AA) isomer (Figure 2c) is presumably due to the strained geometry of the tetradentate ligand. Unlike the *mer*-Co(*N*-Cm-L-Pyala)(AA), which contains a stabilizing *trans*-amino–pyridine structure,[4,9] *mer*-Co(*N*-Cm-L-Hist)(AA) contains a *trans*-amino–imidazole unit, which is presumably less favorable. Because of the smaller size of the imidazole ring, there is probably also less steric repulsion between this ring and L-amino acidates, which would favor the *mer* isomer. Repulsion between the larger pyridine ring and the L-AA$^-$ chelate ring in the *fac* structure was proposed to account for the formation of the *mer* isomer in the Co(*N*-Cm-L-Pyala)(L-AA) system.[3]

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Registry No. Co(*N*-Cm-L-Hist)(α-AIBA), 79872-89-2; Co(*N*-Cm-L-Hist)(L-Val), 79872-90-5; Co(*N*-Cm-L-Hist)(D-Val), 79951-63-6; Co(*N*-Cm-L-Hist)(D-Thr), 79872-91-6; Co(*N*-Cm-L-Hist)(D-AsN), 79872-92-7; *N*-Cm-L-HistH_2, 79872-85-8; L-histidine, 71-00-1; glyoxalic acid, 298-12-4.

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