Chromium(III) Complexes with Amino Acids. III. Chromium(III) Complexes with Acidic, Basic and Carbamoyl Amino Acids

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Syntheses by both the isothermal matrix in a solid state and by the usual solution method have been tried for chromium(III) complexes with L- and DL-asparagine, L- and DL-aspartic acid, L- and DL-glutamine, L- and DL-glutamic acid, L- and DL-lysine, and L-ornithine. $[Cr(L\text{-}aspNH_2)_3]\cdot 2H_2O$, $[Cr(DL\text{-}aspNH_2)_3]\cdot 3H_2O$, $(NH_4)_2[Cr(L\text{-}asp)_2][Cr(D\text{-}asp)_2]\cdot 4H_2O$, and $(+)[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl\cdot 4H_2O$ were obtained by the matrix method in the solid state, while $[Cr(L\text{-}aspNH_2)_3]\cdot 2H_2O$, $[Cr(DL\text{-}aspNH_2)_3]\cdot 2H_2O$, and $(+)[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl\cdot 4H_2O$ were prepared by the usual solution method. The preparation of chromium(III) complexes with other amino acids was not successful. A new type of complex of chromium(III) containing terdentate DL-aspartic acid and a new mixed chromium(III) complex containing three different ligands (L-lysine, ammine, and aqua) were prepared.

Chromium(III) complexes containing terdentate amino acids have not yet been isolated. Amino acids which act as terdentate ligands are classified into amino dicarboxylic (acidic), diamino carboxylic (basic), and carbamoyl amino carboxylic acids (carbamoyl amino acid). In the chromium(III) complexes with L-asparagine,[1] L-aspartic acid,[2] L-glutamine, or L-lysine,[3] all the amino acids work as bidentate ligands. In the present work, attempts were made to prepare chromium(III) complexes with α-amino acids (L- and DL-aspartic acid, L- and DL-glutamic acid, L-ornithine, L- and DL-lysine, L- and DL-asparagine, and L- and DL-glutamine) by applying the methods described in Ref. 4, and to study the difference in complexation among neutral amino acids,[4,5] acidic, basic, and carbamoyl amino acids.

Experimental

Preparation of Chromium(III) Complexes. The methods of preparation are essentisally the same as those reported in our previous papers.[4,5]

a) Preparation by Means of Solid State Reaction: The reaction temperature, the mole ratios of amino acids to the starting complex, $[Cr(NH_3)_6](NO_3)_3$, and the reaction time are listed in Table 1.

The reaction products with L- and DL-asparagine were dissolved in water, after which the solutions were kept standing at room temperature for one or two days. Tris(L-asparaginato) and tris(DL-asparaginato)chromium(III) were obtained as pink powder. By the same method, a complex with DL-aspartic acid was obtained as ammonium bis(DL-aspartato)chromate(III) after the solution had stood for two weeks. When the reaction product with L-lysine monohydrochloride was kept standing at room temperature for one or two days, bis(L-lysinato)ammineaquachromium(III) chloride was obtained as pink crystals. In the case of DL-lysine, a mixture of pink powder and free amino acid was obtained. However, the desired complexes could not be separated from the mixture. From the reaction products with L-aspartic acid, L- and DL-glutamine, and L-ornithine, oily substances were obtained, and crystallizations were not successful. In the case of the L- and DL-glutamic acid, the reaction products dissolved in water were kept standing at room temperature for four or five days to give purple crystals. However, the results of the elementary analysis of these crystals were coincident with the composition of neither a tris-type nor a dihydro-bridged dimer complex.

Table 1. Mole ratios of amino acids to the starting complex, the reaction temperature, and the reaction time

Amino acid	Mole ratio	Reaction temperature (°C)	Reaction time (min)
L-Asparagine	2.5	135	60
DL-Asparagine	2.5	135	60
DL-Aspartic acid	2.5	125	120
L-Lysine	5	135	35

b) Preparation by the Reaction in Solution: Hexaamminechromium(III) nitrate (3.4 g), and L-asparagine (4.0 g) were dissolved in water (50 ml), and the mixture was heated on a water-bath until pink crystals began to appear. The pink crystals were tris(L-asparaginato)chromium(III). By the same method, a complex with DL-asparagine was precipitated as a tris-type one. Hexaamminechromium(III) nitrate (3.4 g) and L-lysine monohydrochloride (5.4 g) were dissolved in water (50 ml), and the mixture was concentrated on a water-bath to one-fifth of its orginal volume. When the resulting solution was kept standing at room temperature for one or two weeks, bis(L-lysinato)ammineaquachromium(III) chloride were gradually deposited as pink crystals. In the case of DL-lysine or L-ornithine, a mixture of pink crystals and amino acid was obtained but the pink crystals could not be separated from the mixture.

Attempts to prepare of chromium(III) complexes with other amino acids were not successful, only oily substances were obtained in those cases.

The analytical data of these complexes are given in Table 2.

Apparatus. The absorption spectra were measured with a Hitachi 139 spectrophotometer. The IR spectra were measured with a Hitachi EPI-G3 infrared spectrophotometer in Nujol mull. The CD spectra were recorded on a JASCO Model ORD/UV-5 spectrophotometer with a CD attachment.

Results and Discussion

The absorption spectra of $[Cr(L\text{-}aspNH_2)_3]$ were measured in the solid state and in a perchloric acid solution. The spectrum of $[Cr(DL\text{-}aspNH_2)_3]$ was measured in the solid state, while those of $NH_4[Cr(DL\text{-}asp)_2]$ and $[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl$ were measured in aqueous solutions. The numerical data of their maxima are summarized in Table 3. The values of the absorption maxima of $[Cr(L\text{-}aspNH_2)_3]$ in 20%$HClO_4$ and in

Table 2. Analytical data

	C (%)		H (%)		N (%)	
	Calcd	Found	Calcd	Found	Calcd	Found
$[Cr(L\text{-}aspNH_2)_3]\cdot 2H_2O$[a]	29.94	29.97	5.25	4.93	17.46	17.69
$[Cr(DL\text{-}aspNH_2)_3\cdot 3H_2O$[a]	28.86	28.74	5.46	4.88	16.83	16.72
$NH_4[Cr(DL\text{-}asp)_2]\cdot 2H_2O$[a]	25.17	25.09	4.94	4.89	11.44	11.41
$[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl\cdot 4H_2O$[a]	29.70	29.26	8.12	7.56	14.44	14.22
$[Cr(L\text{-}aspNH_2)_3]\cdot 2H_2O$[b]	29.94	30.60	5.25	4.85	17.46	17.83
$[Cr(DL\text{-}aspNH_2)_3]\cdot 2H_2O$[b]	29.94	29.69	5.25	4.86	17.46	17.93
$[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl\cdot 4H_2O$[b]	29.70	29.47	8.12	7.28	14.44	14.78

a) By the solid state reaction. b) By the reaction in solution.

Table 3. Absorption maxima of chromium(III) complexes

	$\nu_1/10^3$ cm^{-1}	(log ε)	$\nu_2/10^3$ cm^{-1}	(log ε)	
$[Cr(L\text{-}aspNH_2)_3]$[a]	19.3		26.1		Reflactance
$[Cr(L\text{-}aspNH_2)_3]$[a]	18.7	(1.82)	25.1	(1.64)	20%$HClO_4$
$[Cr(DL\text{-}aspNH_2)_3]$[a]	19.8		26.2		Reflactance
$NH_4[Cr(DL\text{-}asp)_2]$[a]	19.5	(1.98)	26.0	(1.56)	H_2O
$[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl$[a]	19.5	(1.66)	26.5	(1.68)	H_2O
$[Cr(L\text{-}aspNH_2)_3]$[b]	19.3		26.2		Reflactance
$[Cr(DL\text{-}aspNH_2)_3]$[b]	19.9		26.2		Reflactance
$[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl$[b]	19.5	(1.68)	26.5	(1.69)	H_2O

a) By the solid state reaction. b) By the reaction in solution.

the solid state differ from each other. The data suggest that this complex undergoes acid hydrolysis or some other chemical reaction in perchloric acid and that the behavior is similar to that of complexes with L- and DL-alanine.[4,5] The absorption maxima of $[Cr(L\text{-}aspNH_2)_3]$ and $[Cr(DL\text{-}aspNH_2)_3]$ in the solid state are nearly the same as those for chromium(III) complexes with neutral amino acids with the *fac*-structure. Thus, the present complexes of the tris-type have the *fac*-structure.

The spectrum of $NH_4[Cr(DL\text{-}asp)_2]$ is shown in Fig. 1. It may be seen that the second absorption band gives a lower molar extinction coefficient than does the first band and that the absorption curve of this complex is nearly the same as that of the corresponding *cis*(N)-*trans*(O_5) cobalt(III) complex.[6] The complex was adsorbed on an anion exchanger (Dowex 1X8, Cl-form). When a 0.01M NaCl solution was passed through a column of the exchanger, a pink solution was eluted. The spectrum of the eluted solution agreed with that of the original complex. Further, Nessler's reaction for this complex was positive. These results indicate that an ammonia molecule was not coordinated in this complex. In the complex of DL-aspartic acid, there are two possibilities whether both L- and D-aspartic acid are contained, or either. Concerning the geometrical isomers, the former type has one *trans*- and two *cis*-forms, while the latter has one *trans*- and one *cis*-form. The possible geometrical isomers are all shown in Fig. 2.

The reaction product in the solid state with L-aspartic acid was dissolved in water, and the solution was adsorbed on an anion exchanger (Dowex 1 X8, Cl-form). Upon elution with water, one violet band was seen. By eluting with 0.01M NaCl, two pink bands were completely separated. However, the isolation of compounds from these fractions was not carried out. The violet band described above was not adsorbed on a cation exchanger (Dowex 50W X2, H-form). Therefore, this

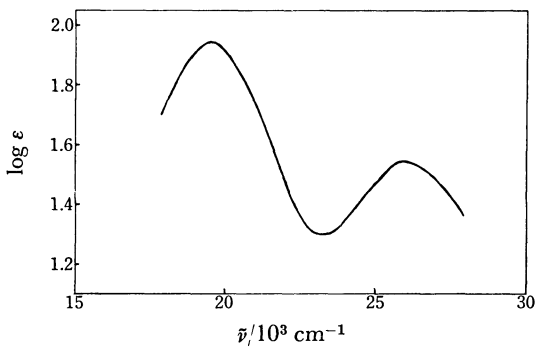

Fig. 1. The absorption spectrum of $(NH_4)_2[Cr(L\text{-}asp)_2]$-$[Cr(D\text{-}asp)_2]$.

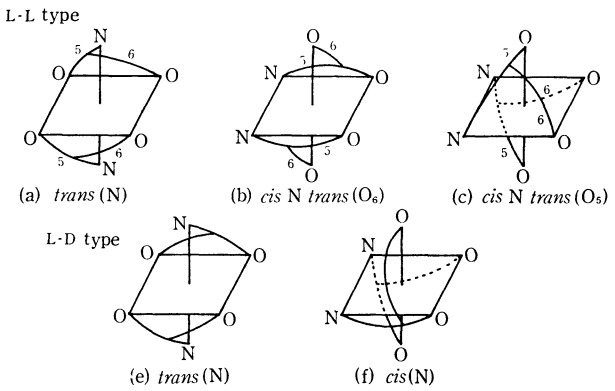

Fig. 2. The possible structures of bis(aspartato)chromate(III) ion.

band is considered to contain a noncharge species. The isolation of the compound from this fraction was also not carried out. By applying the method described above, the reaction product with DL-aspartic acid in the solid state was separated by chromatography. The results were similar to those for the complex with L-aspartic acid. Therefore, the chromium(III) ion was coordinated with two ions of either L- or D-aspartic acid in the bis(DL-aspartato)chromate(III) complex. The spectrum for the ammonium bis(DL-aspartato)-chromate(III) which had been eluted from the ion exchanger agreed with that of the first eluted band of the complex with L-aspartic acid. This complex shows no CD. Therefore, the bis(DL-aspartato)chromate(III) complex was concluded to consist of a racemic structure of $NH_4[Cr(L\text{-}asp)_2]$ and $NH_4[Cr(D\text{-}asp)_2]$. The geometrical structure of the first eluted band of the *cis*-type in the bis(L-aspartato)cobaltate(III) ion has been assigned to *cis*(N)-*trans*(O_5) [Fig. 2 (c)];[6] therefore, the structure of the bis(L-aspartato)chromate(III) ion is assigned to (c) in Fig. 2.

The absorption and CD spectra of $[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl$ are shown in Fig. 3. In this complex, six geometrical isomers are possible; they are given in Fig. 4. It is obvious from Fig. 3 that the molar extinction coefficent of the first absorption band is nearly equal to that of the second absorption band, both showing no splitting. The maximum of the first absorption band of this complex is at a frequency nearly equal to those of *fac*-(amino acidato)chromium(III) complexes. The CD spectrum of this complex is shown in Fig. 3. Mizuochi *et al.*[3] reported that the bis(L-lysinato)diaquachromium(III) complex has a *cis* structure with respect to the nitrogen or the oxygen atoms of lysine. These facts lead to presume that the structure of $[Cr(L\text{-}lys)_2(NH_3)(H_2O)]^+$ has a *cis-cis* structure with respect to the nitrogen or the oxygen atoms, (f) in Fig. 4.

The CD spectra for $[Cr(L\text{-}aspNH_2)_3]$ and $[Cr(DL\text{-}aspNH_2)_3]$ were not measured, because these substances were not soluble in common solvents (H_2O, MeOH, EtOH, DMF and DMSO).

The chromium(III) complexes with acidic, basic, or

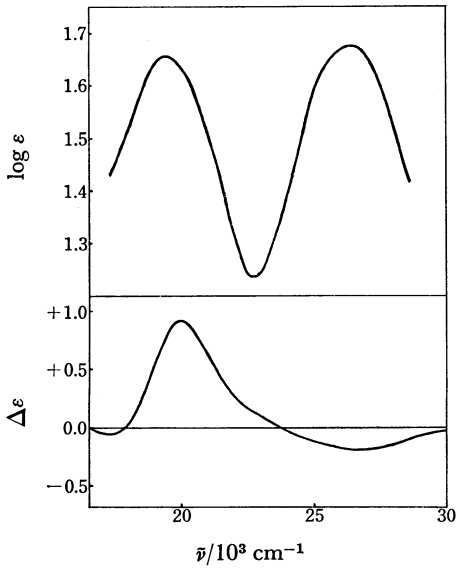

Fig. 3. The absorption and CD spectra of $[Cr(L\text{-}lys)_2(NH_3)(H_2O)]Cl$.

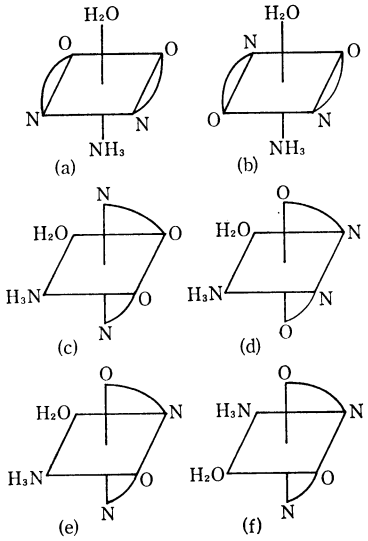

Fig. 4. The possible structures of $[Cr(L\text{-}lys)_2(NH_3)(H_2O)]^+$ ion.

Table 4. Chromium(III) complexes with acidic, basic, and carbamoyl amino acids

Starting material	$[Cr(NH_3)_6](NO_3)_3$		$Cr(OH)_3$	$CrCl_3$
Amino acid	Solid	Solution		
L-Asp	—	—		$[Cr(L)_3]$[2]
DL-Asp	$[Cr(L)_2]$	—		
L-Glu	—	—		
DL-Glu	—	—		
L-Lys	$[Cr(L)_2AB]$	$[Cr(L)_2AB]$		$[Cr(L)_2B_2]$[3]
DL-Lys	mixture	mixture		
L-Orn	—	mixture		
$L\text{-}AspNH_2$	$[Cr(L)_3]$	$[Cr(L)_3]$	$[Cr(L)_3]$[1]	$[Cr(L)_3]$[3]
$DL\text{-}AspNH_2$	$[Cr(L)_3]$	$[Cr(L)_3]$		
$L\text{-}GluNH_2$	purple	—	$[Cr(L)_3]$[3]	$[Cr(OH)(L)_2B]$[3]
$DL\text{-}GluNH_2$	purple	—		

L: amino acid, A: NH_3, B, H_2O, —: not crystallized.
Mixture: pink crystal and amino acid. Purple: no pure purple compound.

carbamoyl amino acids were synthesized both in the solid state and in solution. These synthesized complexes are given in Table 4, together with a description of the preparation by the solution method when chromium(III) hydroxide and chromium(III) chloride are used as the starting materials as reported by Volshtein[1,2] and Mizuochi.[3] Only $(NH_4)_2[Cr(L\text{-asp})_2][Cr(D\text{-asp})_2]$ contained terdentate amino acids. Bis(L-aspartato)chromate(III) was not crystallized. Volshtein obtained $Ag_3[Cr(L\text{-asp})_3]$,[2] but the tris-asp complex was not isolated in the present work. When silver nitrate was added to solution eluted by chromatography, the tris-asp complex was not precipitated. The reason for this is not clear.

When a mixture of bis(L-lysinato)ammineaquachromium(III) chloride and L-lysine·HCl in water was heated on a water-bath, a tris-type complex was not prepared and only the starting substances were recovered. Mizuochi *et al.*[3] reported the method of preparing $[Cr(L\text{-lys})_2(H_2O)]Cl$, but not for $[Cr(L\text{-lys})_3]$. The absorption curves of crude pink complexes with DL-lysine and L-ornithine were similar to that of $[Cr(L\text{-lys})_2(NH_3)(H_2O)]Cl$; and therefore, those complexes may be bis-type complexes. Thus, the synthesis of a tris-type complex of basic amino acid seems to be difficult.

In the present work, tris(L- or DL-asparaginato)chromium(III) complexes were prepared by both methods, solid state and solution. These carbamoyl amino acids are regarded as neutral amino acids. In a previous paper, we reported that the solution containing hexaamminechromium(III) nitrate and neutral amino acid naturally neutralized during the course of reaction.[4] In the case of asparagine, the reacting solution is also expected to be naturally neutralized to yield a tris-type complex. However, tris-type complexes with L- and DL-glutamine, as well as asparagine, were not obtained. The reason for this is not clear.

No terdentate bis-type chromium(III) complex could be obtained, except for those with DL-aspartic acid. This might be due to the instability of seven- or eight-membered ring in a bis-type complex, except for the complexes of aspartic acid and asparagine.

In a previous paper,[5] we reported that the preponderance of the formation of one optical isomer is changed depending upon the kind of solvent dissolving the product of the solid state reaction; when reaction products were dissolved in methanol (+) isomers were obtained, while (−) isomers were obtained in ethanol. However, in the present work, the reaction products with amino acids used in the solid state reaction were all insoluble in ethanol. L- and DL-aspartic acid, L- and DL-lysine, L-ornithine and L-glutamine are soluble, but the other amino acids are insoluble in methanol. The complexes with L- and DL-aspartic acid, L-ornithine, and L-glutamine were prepared as oily substances. The complexes with L- and DL-lysine were obtained as pink crystals. However, the results of the elemental analysis of these complexes show a mixture of $[Cr(lys)_2(NH_3)(H_2O)]Cl$ and $[Cr(lys)_2(NH_3)_2]Cl$. These complexes could not be separated, and the relation between the formation of optical isomers and the solvent was not investigated.

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