Chromium(III) Complexes with Amino Acids. I. Chromium(III) Complexes with Glycine and *dl*-α-Amino Acids

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(Received September 10, 1975)

A comparison has been made between the synthesis carried out by the isothermal matrix method in solid state and that by the usual method in solution for chromium(III) complexes with glycine and *dl*-α-amino acids (alanine, aminobutyric acid, norvaline, norleucine, valine, isoleucine and leucine). The effect of the length of the skeletal carbon chain or the presence of the side chain in α-amino acids on the formation of complexes was investigated. The complexes with α-amino acids which have a normal chain were obtained in *fac*-structure except for norleucine complexes, whereas the complexes with α-amino acids which have a side chain were obtained only in dimer-type by the matrix method in solid state. The chromium(III) complexes with *dl*-α-amino acids were all prepared as tris-type structure, except for α-aminobutyric acid and valine, whereas all the complexes of dimer-type structure were prepared in solution, except for alanine and norleucine.

A number of chromium(III) complexes with natural amino acids are known.[1-10] However, no systematic studies have been carried out on the effect of the length of the skeletal carbon chain or the presence of a side chain in α-amino acids upon the formation of complexes. No studies have been reported on the difference between racemic- and L-amino acids in the complexation. All the tris-type chromium(III) complexes with the natural α-amino acids are of *fac*-structure, no *mer*-form being obtained as crystals. The preparation of purple *mer*-$[Cr(gly)_3]$ has been claimed by Israily.[11] However, Gillard *et al.* reported that this purple fraction is a hydrated dihydroxobridged dimer, $[Cr_2(gly)_4(OH)_2]\cdot 6H_2O$.[12] In the present work, attempts were made to prepare chromium(III) complexes with glycine and racemic amino acids (where racemic amino acids= alanine, aminobutyric acids, norvaline, norleucine, valine, isoleucine and leucine) by the isothermal matrix method in solid state and by the method in solution where hexaamminechromium(III) nitrate was used as the starting material.

Experimental

Preparation of Chromium(III) Complexes. There are two methods for the preparation of chromium(III) complexes with natural α-amino acids according to the mode of starting.

a) Preparation by Solid State Reaction: Hexaamminechromium(III) nitrate was mixed with α-amino acids in a mortar. The mixture was heated at 135±1 °C in a Toyoroshi electronic drying oven. The mole ratios of the amino acids to the starting complex and the heating time applied are given in Table 1.

Table 1. Mole ratios of amino acids to the starting complex and the reaction times at 135±1 °C

α-Amino acid	Mole ratio	Reaction time (min)
Glycine	3	45
α-Alanine	2.5	60
α-Aminobutyric acid	3	60
Norvaline	4	60
Valine	3	60
Isoleucine	2	50
Leucine	3	40

The reaction products containing glycine and *dl*-α-alanine were dissolved in water and kept standing at room temperature overnight. $[Cr(gly)_3]\cdot H_2O$ and $[Cr(\alpha\text{-ala})_3]$ were obtained as red or pink crystals. The reaction products containing *dl*-α-alanine, *dl*-α-aminobutyric acid and *dl*-norvaline were dissolved in methanol. After removal of residues by filtration, the filtrates were kept standing at room temperature for one or two days. $[Cr(\alpha\text{-ala})_3]$, $[Cr(\alpha\text{-ambut})_3]\cdot H_2O$ and $[Cr(norval)_3]\cdot H_2O$ were gradually deposited as pink crystals. When the reaction products containing *dl*-valine, *dl*-isoleucine and *dl*-leucine were dissolved in methanol, the complexes could not be crystallized. However, when water was used as a solvent, *dl*-μ-hydroxo-tetrakis(amino acidato)dichromium(III) complexes were obtained as light purple crystals, where amino acids are *dl*-α-aminobutyric

Table 2. Analytical data (by the solid state reaction)

Complexes	C (%)		H (%)		N (%)	
	Calcd	Found	Calcd	Found	Calcd	Found
$[Cr(gly)_3]\cdot H_2O$	24.66	24.39	4.83	5.00	14.38	14.04
$[Cr(\alpha\text{-ala})_3]$	34.18	33.64	5.74	5.85	13.29	13.20
$[Cr(\alpha\text{-ambut})_3]\cdot H_2O$	38.18	37.40	6.96	7.03	11.17	11.07
$[Cr(norval)_3]\cdot H_2O$	43.06	42.20	7.71	7.79	10.04	10.48
$[Cr(norval)_3]\cdot 2H_2O$	41.28	41.11	7.39	7.81	9.63	9.61
$[Cr(OH)(\alpha\text{-ambut})_2]_2\cdot 3H_2O$	31.07	31.07	6.84	6.45	9.06	9.92
$[Cr(OH)(norval)_2]_2\cdot 2H_2O$	37.62	38.36	7.26	6.94	8.77	9.12
$[Cr(OH)(val)_2]_2\cdot 2H_2O$	37.62	38.57	7.26	7.18	8.77	8.74
$[Cr(OH)(leu)_2]_2\cdot 4H_2O$	39.45	40.73	8.00	7.82	7.67	8.12
$[Cr(OH)(isoleu)_2]_2\cdot 4H_2O$	39.45	38.58	8.00	7.54	7.67	7.70

Table 3. Analytical data (by the solution state reaction)

Complexes	C (%)		H (%)		N (%)	
	Calcd	Found	Calcd	Found	Calcd	Found
$[Cr(\alpha\text{-ala})_3]$	34.18	33.30	5.74	5.64	13.29	13.18
$[Cr(norval)_3]\cdot 3H_2O$	39.61	39.93	7.92	7.06	9.24	9.30
$[Cr(norleu)_3]\cdot 2H_2O$	45.18	44.19	8.43	7.98	8.78	8.74
$[Cr(leu)_3]\cdot 2H_2O$	45.18	44.99	8.43	7.99	8.78	8.46
$[Cr(OH)(gly)_2]_2$	22.13	21.70	5.83	5.82	10.81	10.23
$[Cr(OH)(\alpha\text{-ambut})_2]_2\cdot 2H_2O$	32.99	33.74	6.53	5.98	9.62	9.85
$[Cr(OH)(norval)_2]_2\cdot 2H_2O$	37.62	37.05	7.26	6.70	8.77	8.52
$[Cr(OH)(val)_2]_2\cdot 2H_2O$	37.62	38.10	7.26	6.90	8.77	9.10
$[Cr(OH)(isoleu)_2]_2\cdot 4H_2O$	39.45	39.02	8.00	7.72	7.67	7.80

acid, *dl*-norvaline, *dl*-valine, *dl*-isoleucine and *dl*-leucine. The reaction product containing *dl*-norvaline was washed with water and the residue was dissolved in DMF. After filtration, the filtrate was evaporated until its volume was reduced to one-third. To this was added water until pink crystals began to appear. The crystals have the same composition as that of the product deposited from the methanolic solution, but the amount of the water of crystallization contained is two, instead of one mole. The analytical data are given in Table 2.

b) *Preparation by the Reaction in Solution*: Hexaamminechromium(III) nitrate (345 mg) and glycine (225 mg) were dissolved in water (10 ml) and the mixture was heated on a waterbath until a small quantity of purple crystals began to appear. The purple crystals formed were removed by filtration while hot. When the filtrate was cooled to room temperature, red crystals were precipitated, which were contaminated by some amount of purple crystals. The red compound was separated by decantation in ethanol. The red and the purple crystals are considered to be tris- and binuclear-type chromium(III) complexes, respectively.

By the same method as described above, the complex with *dl*-alanine was precipitated only as of tris-type. The complexes with *dl*-aminobutyric acids, valine and isoleucine were precipitated as hydroxo bridging dimer complexes. The complexes with *dl*-norvaline was first precipitated as pink crystals. After they had been removed by filtration, water was added to the filtrate until the volume became equal to the original one. By heating the resulting solution on a waterbath, pink and purple crystals were precipitated. Pure $[Cr(OH)(dl\text{-norval})_2]_2\cdot 2H_2O$ was precipitated by repeating the same procedure. Pink crystals were dissolved in DMSO because of contamination by a small quantity of the purple crystals. After filtration, the filtrate was added dropwise to water, causing instant precipitation of $[Cr(dl\text{-norval})_3]\cdot 3H_2O$ as pink crystals. The complexes with norleucine and leucine were precipitated as red-purple crystals. The crystals were dissolved in DMF and after removal of residues by filtration, the filtrate was added dropwise into water. $[Cr(dl\text{-norleu})_3]\cdot 2H_2O$ and $[Cr(dl\text{-leu})_3]\cdot 2H_2O$ were precipitated almost instantly. The analytical data of these complexes are given in Table 3.

Apparatus. The UV spectra were measured with a Hitachi 139 spectrophotometer. The IR spectra were measured with a Hitachi EPI-G3 infrared spectrophotometer in Nujol mull.

Results and Discussion

UV Absorption Spectra. Mizuochi *et al.*[10] measured all the UV absorption spectra of the chromium(III) complexes of tris-type with amino acids in a 20% perchloric acid solution except the spectrum of tris(L-leucinato)chromium(III) complex which was measured in methanol and DMF. Gillard *et al.*[12] reported that the values found for the absorption maxima of *fac*-tris(glycinato)chromium(III) complex in solid state (530 nm) and in 70% $HClO_4$ solution (539 nm) differ from each other, suggesting the occurrence of some chemical reactions during the course of dissolution.

Table 4. Absorption maxima of tris-type chromium(III) complexes

	$\bar{\nu}_1$(log ε)	$\bar{\nu}_2$(log ε)	Solvent	Reflectance method	
				$\bar{\nu}_1$	$\bar{\nu}_2$
Solid state reaction					
Gly	18.6(1.63)	25.0(1.56)	60%$HClO_4$	19.8	26.0
Ala	18.7(1.76)	25.1(1.67)	20%$HClO_4$	19.4	25.7
Ambut	18.6(1.75)	25.0(1.64)	20%$HClO_4$	19.4	25.6
Norval	19.3(2.13)	25.4(2.06)	DMF	19.4	25.9
Solution state reaction					
Ala				19.4	25.7
Norval	19.3(2.11)	25.4(2.01)	DMSO	19.4	25.9
Norleu	19.3(2.39)	25.5(2.23)	DMSO		
Isoleu	19.1(2.26)	25.4(2.14)	DMSO		
Leu	19.3(2.19)	25.6(2.13)	DMSO		
				($\bar{\nu} \times 10^3$ cm^{-1})	

The UV absorption spectra of chromium(III) complexes of tris-type with glycine, alanine and aminobutyric acid were measured in both solid state and in perchloric solution. The absorption spectra of chromium(III) complexes with other amino acids of tris-type were measured in DMF or DMSO. Their maxima are summarized in Table 4. The spectra of tris(glycinato)chromium(III) complex in 60% perchloric acid and in solid state are shown in Fig. 1. These data suggest that this complex undergoes acid hydrolysis or chemical reaction on dissolution in perchloric acid. The spectra of tris(norvalinato)-chromium(III) complex in DMSO and in solid state are shown in Fig. 2. It can be seen that the absorption curve in DMSO is similar to that in solid state except for slight shifts of the peak to longer wave number region in solid state. This indicates that the latter complex is significantly stable even in DMSO solution.

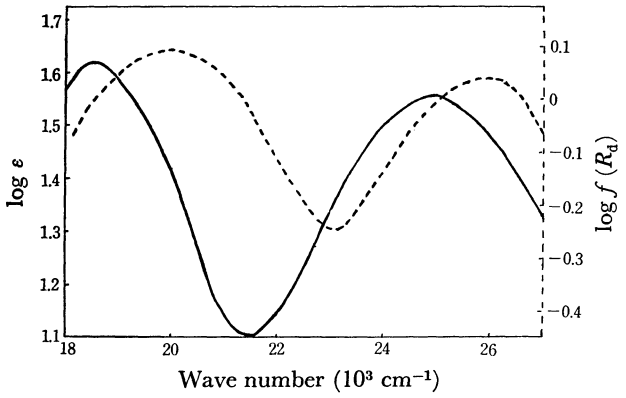

Fig. 1. The absorption spectra of tris-glycinatochromium(III) complex in 60% $HClO_4$ solution (—) and in solid state (---).

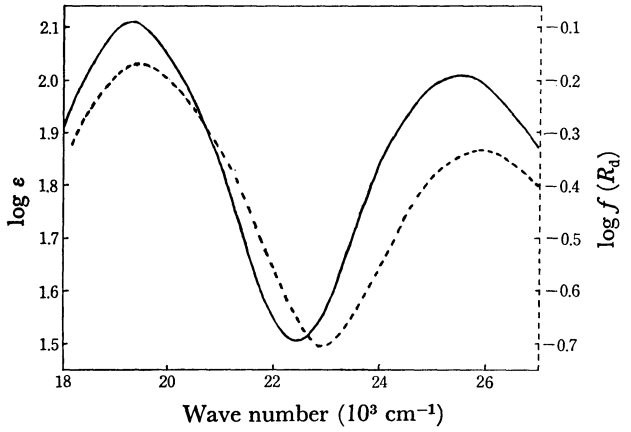

Fig. 2. The absorption spectra of tris-norvalinatochromium(III) complex in DMSO solution (—) and in solid state (---).

For all the $[Co(O)_n(N)_{6-n}]$ series, the predicted shift of the first and second absorption bands has been discussed by Matsuoka *et al.*[13] In the present paper, their calculations were applied to these chromium(III) complexes. The value 21.9×10^3 cm^{-1} and 28.3×10^3 cm^{-1} were obtained for the maxima of the first and the second bands, respectively, in the $[Cr(en)_3]^{3+}$ complex, and 17.5×10^3 cm^{-1} and 23.8×10^3 cm^{-1} for those in the $[Cr(ox)_3]^{3-}$ complex. The maxima of the first and the second absorption bands in *fac*-$[Cr(O)_3(N)_3]$ were calculated to be 19.7×10^3 cm^{-1} and 26.1×10^3 cm^{-1}, respectively. The absorption maxima of these chromium(III) complexes in solid state and in DMF or DMSO solution (Table 4) coincide with the wave numbers obtained by the above calculation. This suggests that the tris-type chromium(III) complexes we prepared have the *fac*-form. Although the absorption maxima of tris-glycinato, alaninato and aminobutyrato complexes in perchloric acid differ from those predicted, the values obtained by Gillard *et al.*,[12] Nakahara[14] (glycine) and Mizuochi *et al.*[10] (alanine and aminobutyric acid) agreed with those obtained in perchloric acid solution (Table 4).

The results indicate that *fac*-tris(amino acidato)-chromium(III) complexes are unstable in acid solution, the stability differing substantially from that of the corresponding cobalt(III) complexes in acid. Tris-(amino acidato)chromium(III) complexes become easily soluble in organic solvent, with increase in the length of the skeletal carbon chain of α-amino acid.

IR Spectra. Infrared absorption spectra were measured in the range 4000—400 cm^{-1}. The spectra of tris-type chromium(III) complexes with glycine, α-alanine and α-aminobutyric acid agree with those of the corresponding chromium(III) complexes of *fac*-form as reported by Mizuochi *et al.*[10] No *fac*-form of chromium(III) complexes with norvaline and norleucine could be found. The preparation of purple chromium-(III) complex with α-aminobutyric acids was reported but no spectrum. The spectrum of purple chromium(III) complex with aminobutyric acid agrees with that for the corresponding chromium(III) complex, *cis*-$[Cr(OH)(ambut)_2H_2O]$, which they prepared. However, it is doubtful whether the assignment of this structure is correct, since, the di-μ-hydroxotetrakis(glycinato)-dichromium(III) shown by X-ray diffraction analysis and magnetic measurement,[15] was assigned to hydroxo-aquo complex. The purple crystals with glycine and L-phenylalanine were confirmed to have the dimer structure by magnetic measurement.[16]

Table 5. Chromium(III) complexes with *dl*-α-amino acids

Amino acid	$[Cr(L)_3]$	$[Cr(OH)(L)_2]_2$
Glycine	◑	○
α-Alanine	◑	
α-Aminobutyric acid	●	◑
Norvaline	◑	◑
Norleucine	○	
Valine		◑
Isoleucine	○	◑
Leucine	○	◑

L=amino acid.
● Complexes prepared by the solid method.
◑ Complexes prepared by both methods.
○ Complexes prepared by the solution method.

The chromium(III) complexes with various *dl*-amino acids of the type $[CrL_3]$ and $[Cr(OH)L_2]_2$, where L denotes amino acid, were synthesized in the solid state and in solution (Table 5). Preparation of chromium(III) complexes with natural *dl*-α-amino acids carried out by the two methods may be charactrized as follows: i) Solid State Reaction. The complexes with *dl*-α-amino acids which have no side chain were prepared as tris-type structure, except for *dl*-norleucine. The complexes of dimer-structures were prepared with α-aminobutyric acid and norvaline. Taking account of the carbon skeleton in *dl*-amino acids, when the reaction product is dissolved in water, complexes with glycine and α-alanine are obtained as tris-type, but those with α-aminobutyric acid and norvaline in which the length of carbon chain is longer than that of alanine are obtained as the dimer type. When the reaction product is dissolved in methanol, the complex with glycine can not be crystallized, but the complexes with other amino acid are obtained as tris-type. The preparation of tris-type chromium(III) complex with norleucine

was not successful. However, the solid state reaction of norleucine was similar to that of other amino aicds. Thus, the complexes of *fac*-structure can be easily separated from the dimer type, when the solvent is changed. This is advantageous for the preparation of tris-type complexes in a solid method than in the solution method. The complexes with valine, isoleucine and leucine which have a side chain were obtained only as the dimer-type. ii) Solution State Reaction. The chromium(III) complexes with racemic α-amino acids have all been prepared with tris-type structure, except for α-aminobutyric acid and valine. All the complexes with dimer-structure have been prepared, except for alanine and norlecine. Preparation in solution method seems more convenient than that in solid state. A mixture of tris- and dimer-complexes is prepared by the solution method. It should be separated into components by another method.

Taking account of the carbon skeleton in racemic amino acids, we obtained dimer-type complexes containing glycine and α-aminobutyric acid and tris-type complexes containing α-alanine and norvaline. Complexes with racemic α-amino acids appear predominantly with dimer- and tris-structures, alternatively, depending on the length of the carbon skeleton. However, this can not always be applied to complexes with norleucine, since it gave only a tris-type structure.

Complexes with isoleucine and leucine which have a side chain were obtained with tris- and dimer-type structures. However, the complex with valine which has a methyl group in the β-position, as well as isoleucine, was obtained with only a dimer-type structure.

The present method in solution state using hexaamminechromium(III) nitrate is very simple as compared with the usual method in the same state, using chromium(III) hydroxide and chromium(III) chloride as a starting material. It is necessary to remove unreacted hydroxide using chromium(III) hydroxide and to neutralize the reactant solution in the method using chromium(III) chloride, but it is not necessary to separate unreacted substance in the dissolved state and the reactant solution naturally neutralized in the method using hexaamminechromium(III) nitrate.

No circular dichroism was observed for tris-type. All tris-type chromium(III) complexes were in *fac*-structure, no *mer*-form being obtained.

The authors wish to thank Professor R. Tsuchiya, Kanazawa University, for valuable discussions and suggestions.

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