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The Chromium(III) Complexes with Natural α-Amino Acids[1]

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The following chromium(III) complexes with natural α-amino acids were prepared: $[Cr(\alpha\text{-ambut})_3]\cdot 2H_2O$ (red) (I), $(-)_{546}$-$[Cr(l\text{-leu})_3]\cdot 2H_2O$ (red) (II), $(+)_{546}$-$[Cr(l\text{-leu})_3]\cdot 2H_2O$ (red) (III), $[Cr(l\text{-glu})_3]\cdot 2H_2O$ (red) (IV), $(+)_{546}$-$[Cr(l\text{-lys})_2(H_2O)_2]Cl\cdot 3H_2O$ (red) (V), $[Cr(OH)(\alpha\text{-ambut})_2(H_2O)]\cdot H_2O$ (light purple) (VI), $[Cr(OH)(l\text{-val})_2(H_2O)]\cdot H_2O$ (light purple) (VII), $[Cr(OH)(l\text{-leu})_2(H_2O)]\cdot H_2O$ (light purple) (VIII) and $[Cr(OH)(l\text{-glu})_2(H_2O)]\cdot H_2O$ (light purple) (IX), where α-ambut, *l*-leu, *l*-glu, *l*-lys, and *l*-val are the basic forms of α-amino-n-butyric acid, *l*-leucine, *l*-glutamine, *l*-lysine and *l*-valine, respectively. From the results of electronic and infrared absorption spectra, molar conductivities and behaviors toward ion exchangers, the composition and structures of the complexes were determined. The striking information obtained is that the complexes (I)—(IV) are considered to have all the β-form unlike the corresponding cobalt(III) complexes having both α- and β-forms. On the basis of ORD and CD measurements, the complexes (II), (III), and (V) were found to be optically active.

A number of transition metal complexes with various amino acids are already known. Within the limits of chromium(III) as a central metal ion, the complexes with synthetic amino acids such as NTA (nitrilotriacetic acid)[3] and IDA (iminodiacetic acid)[4] and their derivatives[5–8] have been prepared, their chemical properties and structures being investigated.

Of the natural amino acids, however, studies on the complexes are rare except for the tris-type complexes containing glycine[9,10] α-alanine,[11–15] asparagine[16], or *l*-aspartic acid.[17] In the present work, attempts were made to prepare chromium(III) complexes with various natural α-amino acids in tris- or bis-type and to investigate which type of complex can be successfully synthesized in each natural α-amino acid and which form of complex can be obtainable in two geometrically possible isomers.

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Experimental

Preparation of Chromium(III) Complexes. Preparation of the chromium(III) complexes with natural α-amino acids carried out in the present work was classified into the following three methods depending upon the kinds of chromium(III) salts used as the starting material.

1. *Method using Chromium(III) Hydroxide*: This is essentially the same as the method by Ley and Winkler.[9] To a solution of *l*-glutamine (45 g, 0.3 mol) was added a slight excess of freshly prepared chromium(III) hydroxide (12 g, 0.12 mol), and the mixture was heated on a water bath until a reddish violet solution was obtained. This was filtered at once to remove unreacted hydroxide. The filtrate was evaporated to a half volume and cooled to room temperature. After adding a small amount of ethanol, the mixture was kept in a refrigerator overnight in order to precipitate the unreacted amino acid. After being filtered, the filtrate was kept to stand at room temperature for two or three days. Pink crystals were gradually precipitated.

The yield was about 10%. Found: C, 34.33; H, 6.03; N, 15.92%. Calcd for $[Cr(l\text{-glu})_3]\cdot 2H_2O$ (*l*-glu=*l*-glutamine): C, 34.38; H, 5.92; N, 16.05%.

By applying the same method as described above, the corresponding complexes with glycine, *d,l*,α-alanine and *l*-asparagine were prepared in better yields (about 30%) than in *l*-glutamine.

2. *Method using Chromium(III) Chloride*: This is similar to the method reported by Green and Ang,[15] and by Volshtein and Molosnova.[16] To a solution of α-amino-*n*-butyric acid (30 g, 0.3 mol), for example, was added an aqueous solution of chromium(III) chloride hexahydrate (27 g, 0.1 mol), and the mixture was heated on a water bath until it turned to violet. The color changed again to reddish violet by the dropwise addition of potassium hydrogen carbonate (30 g, 0.3 mol). On heating the solution, pink crystals began to appear on the wall of the evaporating dish. The filtrate was cooled to room temperature and kept standing overnight. Fine pink crystals were obtained.

The yield was about 10%. Found: C, 36.51; H, 7.10; N, 10.65%. Calcd for $[Cr(\alpha\text{-ambut})_3]\cdot 2H_2O$ (α-ambut=α-amino-*n*-butyric acid): C, 37.02; H, 6.90; N, 10.71%.

The yields for the complexes with glycine, *d,l*-α-alanine, and *l*-asparagine prepared by applying this method were all 30%.

The complex with *l*-lysine obtained by the same method was bis-type. Found: C, 30.79; H, 7.67; N, 12.52%. Calcd for $[Cr(l\text{-lys})_2(H_2O)_2]Cl\cdot 2H_2O$ *l*-lys=*l*-lysine: C, 30.80; H, 7.77; N, 11.98%.

By using a similar method except that 0.2 moles of the desired amino acid, instead of 0.3 moles, were employed as a starting material and the mixed solution was kept standing at room temperature for about one week instead of overnight after the addition of potassium hydrogen carbonate, the bis-type complexes with *l*-glutamine, α-amino-n-butyric acid, *l*-leucine, and *l*-valine were obtained as light purple crystals. For *l*-glutamine complex, Found: C, 31.21; H, 6.11; N; 13.49%. Calcd for $[Cr(OH)(l\text{-glu})_2(H_2O)]\cdot H_2O$: C, 30.36; H, 5.82; N, 14.17%. For α-amino-n-butyric acid complex, Found: C, 32.38; H, 6.63; N, 9.34%. Calcd for $[Cr(OH)(\alpha\text{-ambut})_2(H_2O)]\cdot H_2O$: C, 31.05; H, 6.79; N, 9.06%. For *l*-leucine complex, found: C, 41.39; H, 7.94; N, 7.91%. Calcd for $[Cr(OH)(l\text{-leu})_2(H_2O)]\cdot H_2O$ (*l*-leu=*l*-leucine): C, 40.75; H, 7.69; N, 7.92%. For *l*-valine complex, Found: C, 35.75; H, 6.81; N, 8.34%. Calcd for $[Cr(OH)(l\text{-val})_2(H_2O)]\cdot H_2O$ (*l*-val=*l*-valine): C, 35.60; H, 6.89; N, 8.31%.

The chromium(III) complex with leucine in tris-type was prepared by a different method from that mentioned above, though chromium(III) chloride was used as starting material in the same manner. 26.6 g (0.1 mol) of chromium(III) chloride hexahydrate in 200 m*l* of 80% methanol and 39.3 g (0.3 mol) of *l*-leucine were mixed and the mixture was heated in a round flask equipped with a reflux condenser. As the reaction proceeded, the color of the solution turned from green to violet. After the reaction was completed, a mixture of methanol and aqueous ammonia (0.3 mol) was gradually added dropwise to the solution, whereby its color became reddish. The solution was filtered and cooled to room temperature. A small amount of methanol having been added, the mixture was kept in a refrigerator for two days to let ammonium chloride precipitate. The filtrate was evaporated to half its volume under reduced pressure and was kept standing at room temperature after repeated filtration. Pink crystals were obtained, soluble in methanol. After removal of the crystals, the filtrate was kept at room temperature for a long time. Another crop of crystals was obtained, insoluble in methanol but soluble in *N,N*-dimethylformamide (DMF). In spite of this difference in solubility, the chemical composition of the two complexes obtained above is expressed by $[Cr(l\text{-leu})_3]\cdot 2H_2O$.

Soluble in methanol: Found: C, 44.09; H, 7.57; N, 8.45%.

Soluble in DMF: Found: C, 45.39; H, 8.73; N, 8.52%.

Calcd for $[Cr(l\text{-leu})_3]\cdot 2H_2O$: C, 45.17; H, 8.42; N, 8.78%.

Preparation of Cobalt(III) Complexes. In order to compare the UV and IR spectra of the chromium(III) complexes with those of the corresponding cobalt(III) ones, the latter were also prepared by known methods.[18,19]

Apparatus. The molar conductivities and UV spectra were measured with a Yokogawa Universal Bridge BV-Z-12A and with a Hitachi EPS Spectrophotometer, respectively. The IR spectra were measured with a JASCO DS-301 and a JASCO Model IR-E Infrared Spectrophotometers both in KBr disk and in nujol mull. The optical rotatory dispersion (ORD) and circular dichroism (CD) curves were recorded with a JASCO Optical Rotatory Dispersion Recorder, Model UV-S attached with a CD recorder. The quantity of crystalline water contained in these compounds was estimated from the TG curve measured with a Shimadzu TM-1A Thermanobalance and a MOM Derivatograph Typ-OD-102.

Results and Discussion

UV Absorption Spectra. The UV absorption spectra of the chromium(III) complexes with amino acids in tris-type, together with those in bis-type with glycine or *l*-lysine, were measured in 20% perchloric acid solution except for that of tris-*l*-leucinatochromium(III) complexes measured in methanol and DMF and that of the corresponding cobalt(III) complexes measured in 60% perchloric acid solution. The numerical data of their maxima are summarized in Table 1. The spectra of tris(*l*-leucinato)chromium(III) and tris(*l*-glutaminato)chromium(III) are shown in Figs. 1 and 2, respectively, together with

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Table 1. Absorption maxima of the chromium(III) and cobalt(III) complexes

	Cr(III)		Co(III)	
	ν_1(log ε)	ν_2(log ε)	ν_1(log ε)	ν_2(log ε)
gly[11]			57.7(2.16)	79.6(2.06)
α-ala[16]	56.0(1.85)	75.4(1.75)	58.0(2.22)	80.4(2.21)
l-glu	56.1(1.95)	76.0(1.84)	57.0(2.32)	79.2(2.30)
α-ambut	55.8(1.87)	75.0(1.79)	57.3(2.35)	79.8(2.30)
l-leu	57.8(1.67)	76.9(1.79)	58.0(2.27)	80.4(2.26)
gly[a]	57.3(1.64)	76.7(1.57)		
l-lys[a]	57.5(1.56)	78.7(1.58)		

a) Bis-type complexes. Others: tris-typecomplexes.

those of the corresponding cobalt(III) complexes of β-form.

It is known that there are two geometrical isomers in tris-type amino acid complexes, *i.e.*, *mer* (*cis*, *trans*) and *fac* (*cis*, *cis*) type with respect to the nitrogen or oxygen atoms coordinating to central metal, the former called α-form (violet) and the latter β-form (red).

It was pointed out[20] that the main difference between the absorption curves in these two isomers appears predominantly in the first band; *viz.*, the first band of the α-form isomer shows some splitting, while that of the β-form isomer does not. Although the positions giving the maximum absorbancies for these chromium(III) complexes are shifted to a somewhat lower frequency region compared with those for the corresponding cobalt(III) complexes, the shapes of the bands for the chromium(III) complexes prepared in the present work are nearly the same as those for the corresponding cobalt(III) ones assigned to β-form. This suggests that the chromium(III) complexes in tris-type have also the β-form.

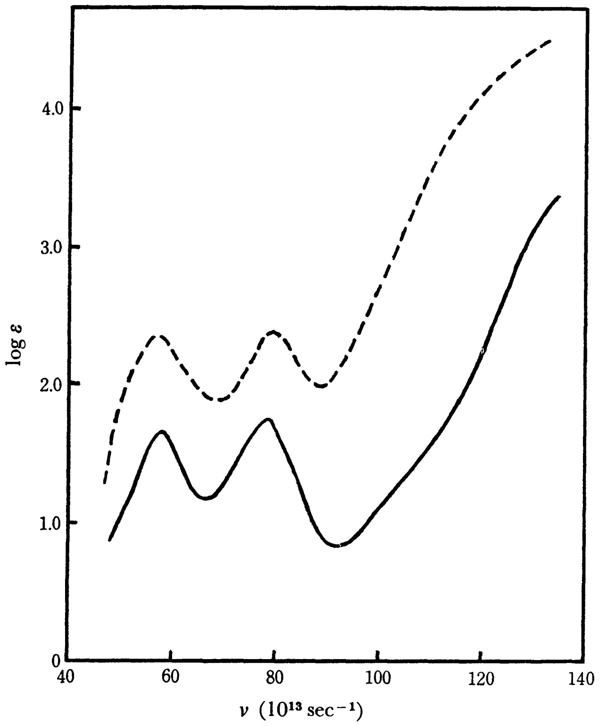

Fig. 1. Electronic absorption spectra of [Cr(*l*-leu)$_3$] in methanol (——) and of β-[Co(*l*-leu)$_3$] in 60% perchloric acid solution (----).

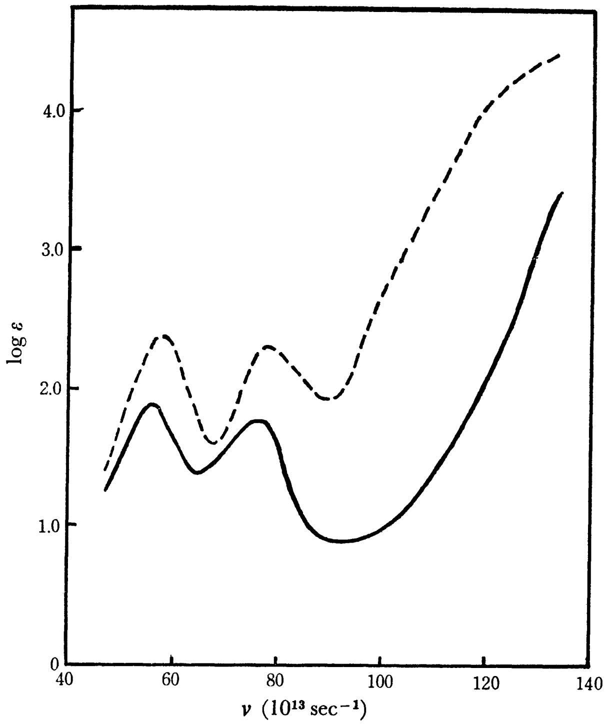

Fig. 2. Electronic absorption spectra of [Cr(*l*-glu)$_3$] in 20% perchloric acid (——) and of β-[Co(*l*-glu)$_3$] in 60% perchloric acid solutions (----).

The spectra of bis(*l*-lysinato)- and bisglycinatodiaquochromium(III) complexes are shown in Fig. 3. In bis(*l*-aminato)diaquochromium(III) complexes, five geometrically possible isomers are considered, which are given in Fig. 4. It is obvious from Fig. 3 that the first absorption band not only gives a higher molar absorption coefficient than the second band but also shows no splitting. This leads us to presume the coordinating structure of these bisaminatodiaquo complexes to be (e) in Fig. 4, which is not trans structure with respect to nitrogen or oxygen atoms.

Since the absorption spectra could not be measured in aqueous solution owing to much smaller solubility in water, those for hydroxobisaminatoaquo complexes, $[Cr(OH)Am_2(H_2O)]\cdot H_2O$, where Am=*l*-

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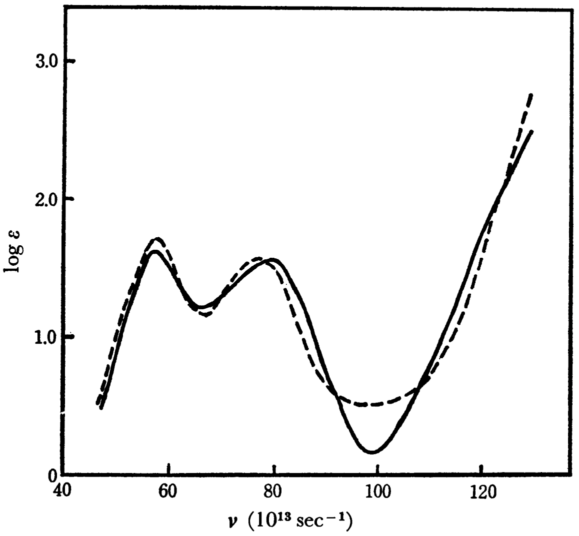

Fig. 3. Electronic absorption spectra of $[Cr(l\text{-lys})_2(H_2O)_2]Cl$ (——) and of $[Cr(gly)_2(H_2O)_2]NO_3$ (----) in aqueous solutions.

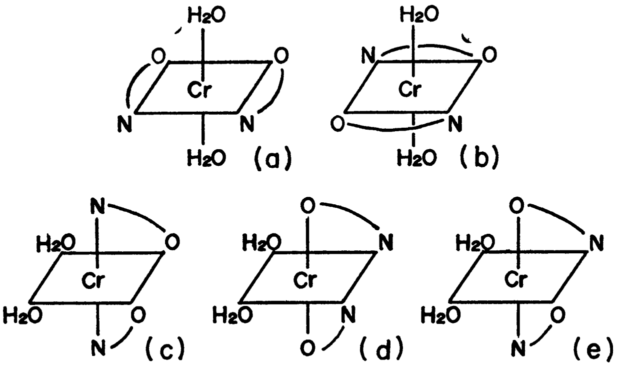

Fig. 4. Five geometrically possible isomers for $[CrL_2(H_2O)_2]^+$, where L denotes bidentate amino acid.

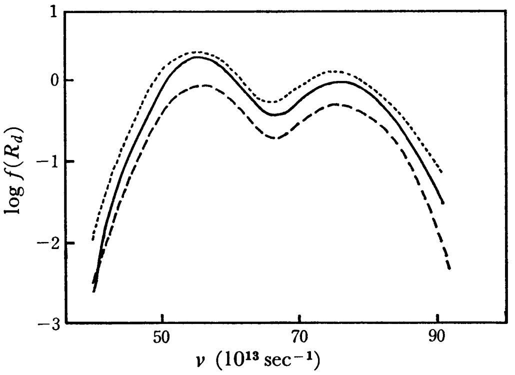

Fig. 5. Absorption spectra of $[Cr(OH)(\alpha\text{-ambut})_2(H_2O)]$ (——), $[Cr(OH)(l\text{-leu})_2(H_2O)]$ (— —) and $[Cr(OH)(l\text{-val})_2(H_2O)]$ (----) by the diffuse reflectance method.

glutamine, α-amino-*n*-butyric acid, *l*-leucine, or *l*-valine, were obtained by the diffuse reflectance method. The representative spectra for the chromium(III) complexes with α-amino-*n*-butyric acid, *l*-leucine and *l*-valine are shown in Fig. 5.

The first absorption peaks appear at 55, 56, and 55 × 10^{13} sec^{-1} and the second peaks appear at 76, 75.5, and 75.5 × 10^{13} sec^{-1} for α-amino-*n*-butyric acid, *l*-leucine and *l*-valine, respectively, as seen in Fig. 5. From the features of the absorption curves in this figure, where the first absorption bands do not show appreciable splitting, having higher absorption coefficients than the second bands, the hydroxobisaminatoaquochromium(III) complexes seem to have (e) structure in Fig. 4, containing OH and H_2O ligands in *cis* sites.

IR spectra. Infrared absorption spectra were measured over the range of 4000—700 cm^{-1}. The spectra of the chromium(III) complexes with glycine,

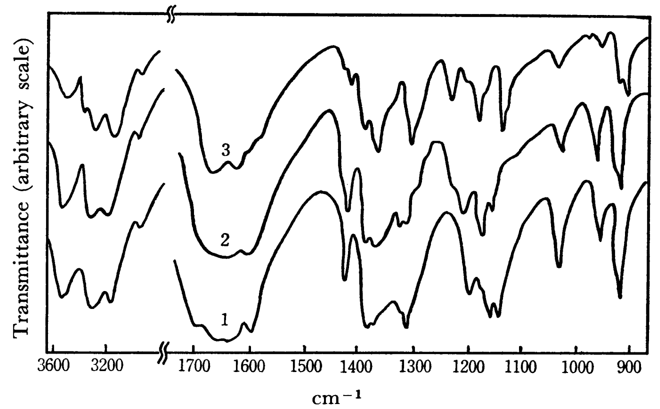

Fig. 6. IR spectra of $[Cr(gly)_3]$ (1), β-$[Co(gly)_3]$ (2), and α-$[Co(gly)_3]$ (3).

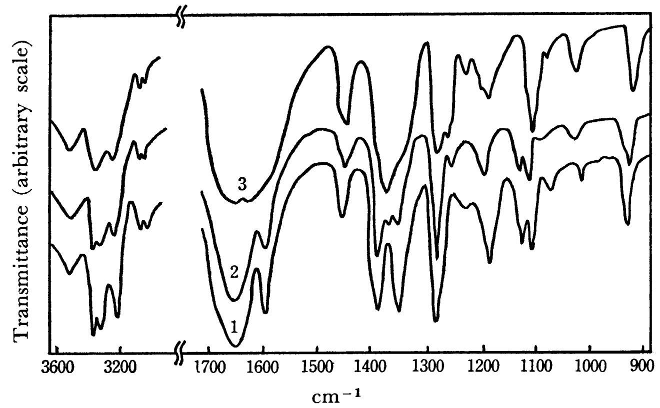

Fig. 7. IR spectra of $[Cr(\alpha\text{-ala})_3]$ (1), β-$[Co(\alpha\text{-ala})_3]$ (2), and α-$[Co(\alpha\text{-ala})_3]$ (3).

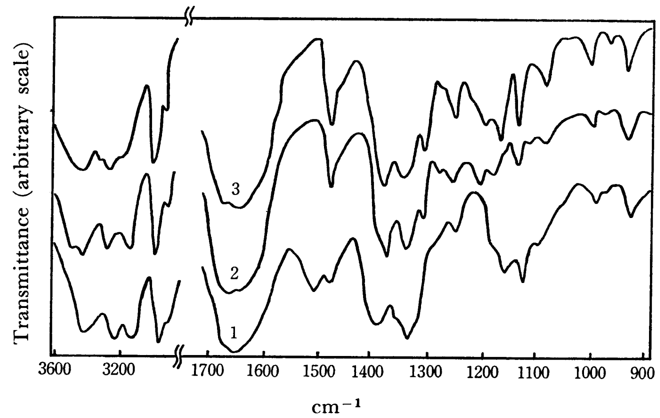

Fig. 8. IR spectra of $[Cr(l\text{-leu})_3]$ (1), β-$[Co(l\text{-leu})_3]$ (2), and α-$[Co(l\text{-leu})_3]$ (3).

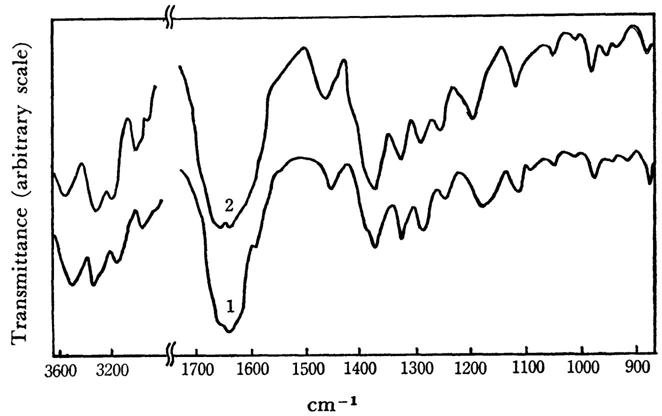

Fig. 9. IR spectra of $[Cr(\alpha\text{-ambut})_3]$ (1) and β-$[Co(\alpha\text{-ambut})_3]$ (2).

d,l-α-alanine, *l*-leucine, α-amino-*n*-butyric acid, and *l*-glutamine in tris-type are shown in Figs. 6—10, together with those of the corresponding cobalt(III) complexes in both α- and β-forms, though the α-forms of cobalt(III) complexes with α-amino-*n*-butyric acid and with *l*-glutamine could not be found.

The spectral curves for the chromium(III) complexes are extremely analogous to those for the corresponding cobalt(III) complexes in β-form rather than those in α-form, especially in several wave number regions, 3180—3400 cm^{-1} (NH_2 stretching), 1600—1650 cm^{-1} (NH_2 bending), 1350—1420 cm^{-1} (COO^- stretching) and 1100—1200 cm^{-1} (CH_2 deformation). It can be assumed from IR spectra that the tris-type of chromium(III) complexes have the same β-structure as the corresponding cobalt(III) complexes.

Behaviors toward Ion Exchangers and Molar Conductivity. Bisglycinatodiaquochromium(III) nitrate and bis(*l*-lysinato)diaquochromium(III) chloride were adsorbed by Cl^--form exchanger and their molar conductivity data measured in 1×10^{-3} mol/*l* were 69.5 and 202.4 mho cm^{-1}, respectively. This suggests that the above two complexes are 1 : 1 valency type, the complex cation being univalent as expected.

On the other hand, hydroxoaminatoaquochromium(III) complexes were adsorbed by neither cation nor anion exchangers and their conductivities could not be measured owing to insolubility in water. This is in line with the behavior of their non-electrolytes.

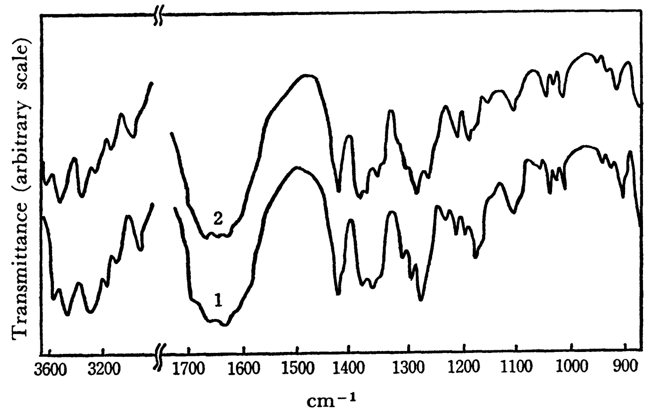

Fig. 10. IR spectra of $[Cr(gly)_3]$ (1) and β-$[Co(gly)_3]$ (2).

ORD and CD Spectra. The optical rotatory dispersion, circular dichroism, and absorption curves for tris(*l*-leucinato)chromium(III) soluble in methanol and in DMF and those for bis(*l*-lysinato)diaquochromium(III) chloride measured in water are given in Figs. 11 and 12, respectively. The molar rotations for two tris(*l*-leucinato)chromium(III) complexes were $[M]_{546}=-3496$ and $+5932$ respectively, and

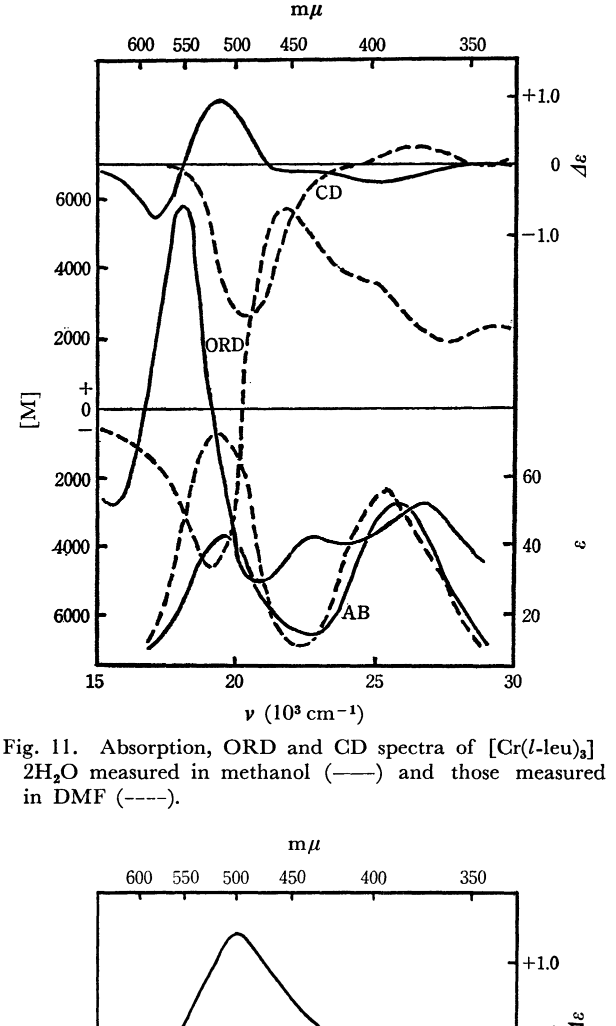

Fig. 11. Absorption, ORD and CD spectra of $[Cr(l\text{-leu})_3]$ $2H_2O$ measured in methanol (——) and those measured in DMF (----).

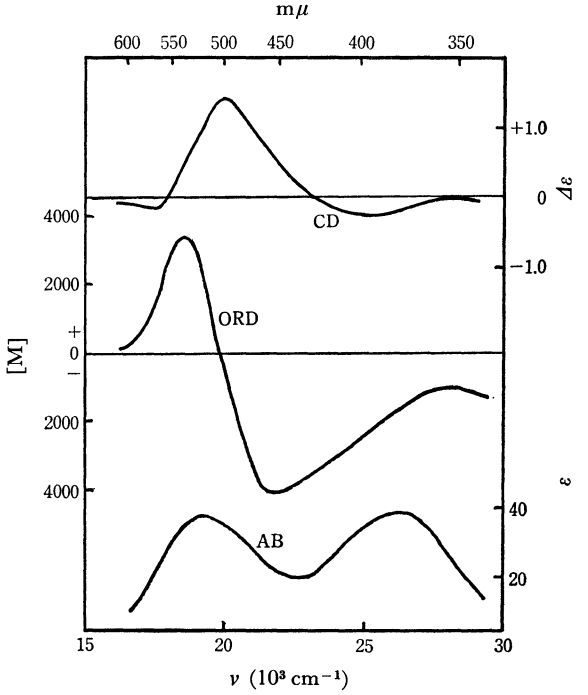

Fig. 12. Absorption, ORD and CD spectra of $[Cr(l\text{-lys})_2(H_2O)_2]Cl\cdot3H_2O$.

Table 2. Chromium(III) complexes with α-amino acids prepared

Amino acid	$[CrL_3]$	$[CrL_2(H_2O)_2]X$	$[Cr(OH)L_2(H_2O)]$
Glycine	○	○	○
α-Alanine	○		○
l-Aspartic acid	○		
l-Asparagine	○		
α-Aminobutyric acid	◑		◑
l-Leucine	◑		◑
l-Glutamine	◑		◑
l-Lysine		◑	
l-Valine			◑

○: Complexes already prepared
◑: Complexes prepared in this work

that for bis(*l*-lysinato)diaquochromium(III) chloride was $[M]_{546}=+2867$.

The chromium(III) complexes with various amino acids in the types, $[CrL_3]$, $[CrL_2(H_2O)_2]X$ and $[Cr(OH)L_2(H_2O)]$, where L denotes amino acid and X denotes Cl^- or NO_3^-, were synthesized, and they are summarized in Table 2 together with those reported.

The tris-type chromium(III) complexes were all of *β*(*fac*)-structure, though in the corresponding cobalt(III) complexes both α- and β-forms have been found. The reason why α-form can not be obtained as crystals in the preparative conditions of the chromium(III) complexes with natural amino acids is not clear as yet.

An attempt to prepare the α-form of the chromium(III) complexes may be examined with the following ideals. Since the isomers (a) and (b), two of the bis-aminatodiaquochromium(III) complexes depicted in Fig. 4, have *trans*-structure, the introduction of the third chelation of amino acid into them is impossible without the movement of chelating ligands already coordinated. On the contrary, in the *cis*-isomers (c), (d), and (e), the probability of the formation of the α-form complexes will amount to 5/6 by introducing the third chelation.

As an example, the preparation of a α-form chromium(III) complex in crystalline state was attempted by using *d*,*l*-α-alanine as the third bidentate ligand to be introduced into bisglycinatodiaquochromium(III) nitrate, and violet crystals were obtained. Taking account of the color of the crystals, the complexes are considered to have α-form structure and the starting bisglycinato complex to have cis-structure of either (c), (d), or (e).