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The Preparation and Stereoselectivity of $[Cr(L\text{- or }D\text{-}ala)_x(L\text{-}leu)_{3-x}]$ and the Possibility of the Optical Resolution of DL-Alanine

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Synopsis. *fac*-(+)$_{546}$-$[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ and *fac*-(−)$_{546}$-$[Cr(D\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ were prepared by the method using an ethanol solution, with $[Cr(L\text{-}leu)_2(NCS)(OH_2)]$(leu=leucinato) with L- or D-alanine used as the starting material respectively. Also, *fac*-$[Cr(L\text{- or }D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ was obtained from the filtrate, the standing temperatures were 5, 25, 40, and 55 °C. The optical purity of *fac*-(Λ)-$[Cr(L\text{- or }D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ increases with the rise in the standing temperature. In the case of DL-alanine, $[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ and $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ were obtained during heating and from the filtrate respectively. By using this procedure, the possibility of the optical resolution of DL-alanine was shown.

We reported previously that tris(amino acidato)chromium(III) complexes which exhibit very high stereoselectivities were obtained by a solid state reaction[2,3] or by use of an ethanol solution.[3] However, no study has been reported concerning the preparation of chromium(III) mixed amino acidato complexes except for that of Watabe et al.[4] It is interesting to study the stereoselectivity in the case of the chromium(III) complexes involving different kinds of amino acid ligands.

We will report here the preparation of some new (mixed amino acidato) chromium(III) complexes containing L-leucine and L- or D-alanine, using $[Cr(L\text{-}leu)_2(NCS)(OH_2)]$ as the starting material. A very high stereoselectivity was also remarked in the cases of the (mixed amino acidato) chromium(III) complexes.

An optical resolution of DL-alanine based on the different reactivities of $[Cr(L\text{-}leu)_2(NCS)(OH_2)]$ to L- and D-alanine is suggested.

Experimental

a) Preparation of the Starting Material, $[Cr(L\text{-}leu)_2(NCS)(OH_2)]\cdot H_2O$. A solution of Reinecke's salt, $NH_4[Cr(NH_3)_2(NCS)_4]\cdot H_2O$ (2×10^{-2} mol),[5] and L-leucine (6×10^{-2} mol) in 200 cm^3 of H_2O was evaporated to dryness in an evaporating dish on a water bath. The residue was washed with 80 cm^3 of H_2O. After air-drying, the solid was dissolved in 200 cm^3 of ethanol. After filtration, the filtrate was added to 400 cm^3 of H_2O, causing an immediate precipitation of the purple crystals. These crystals were subsequently dried overnight at 55 °C; yield, 21%. Found: C, 37.91; H, 6.72; N, 10.93%. Calcd for $CrC_{13}H_{26}O_5N_3S$: C, 38.39; H, 6.89; N, 10.34%.

b) Preparation of (Mixed Amino Acidato)Chromium(III) Complexes, $[Cr(L\text{- or }D\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ and $[Cr(L\text{- or }D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$. A solution of $[Cr(L\text{-}leu)_2(NCS)(OH_2)]\cdot H_2O$ (406 mg: 1×10^{-3} mol) in 50 cm^{-3} of ethanol was added to L-alanine (89 mg: 1×10^{-3} mol). After the addition of 0.5 cm^3 of butylamine, the mixed solution was refluxed for 5 hours at 75 °C. Pink crystals were deposited during the heating. After immediate filtration and washing with ethanol and methanol, $[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ was obtained.

The filtrate was separated into four portions, which were then placed in sealed flasks. They were kept at 5, 25, 40, and 55 °C respectively. The crystals grown in the flasks were filtered after 10 days. In spite of the difference in the standing temperature, only pink crystals of $[Cr(L\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ were obtained.

By the same method, in the case of D-alanine $[Cr(D\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ was obtained as a purplish pink powder during the heating. From the filtrate, $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ was obtained. With the use of DL-alanine $[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$ was obtained during the heating and $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$ was obtained from the filtrate. The yields and elementary analyses are summarized in Table 1.

Measurements. The VIS-UV spectra were measured with a Hitachi 124 spectrophotometer in DMSO. The CD measurements were made with a JASCO-J-500A spectropolarimeter in DMSO.

Table 1. Analytical Data and Yields of $[Cr(ala)_x(L\text{-}leu)_{3-x}]$(10 Days Standing)

Complex		C	H	N	Yield%
$CrC_{12}H_{27}O_{7.5}N_3$	Calcd.	37.37	7.00	10.90	
(1) $[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$[a]	Obsd.	37.42	6.80	10.55	16—22
(2) $[Cr(D\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$[a]	Obsd.	37.85	6.93	10.56	10—15
(3) $[Cr(L\text{-}ala)_2(L\text{-}leu)]\cdot 1.5H_2O$[a]	Obsd.	37.74	6.79	10.75	16—22
$CrC_{15}H_{32}O_8N_3$	Calcd.	41.28	7.85	9.63	
(4) $[Cr(L\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[b]	Obsd.	41.38	7.87	9.43	8— 9
(5) $[Cr(L\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[c]	Obsd.	41.76	7.78	9.60	38—45
(6) $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[b]	Obsd.	41.59	7.83	9.52	8— 9
(7) $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[c]	Obsd.	41.48	7.92	9.33	38—43
(8) $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[b]	Obsd.	41.80	7.67	9.42	7— 9
(9) $[Cr(D\text{-}ala)(L\text{-}leu)_2]\cdot 2H_2O$[c]	Obsd.	41.20	7.72	9.88	39—45

x=1 or 2. (1)(4)(5) obtained using L-alanine. (2)(6)(7) obtained using D-alanine. (3)(8)(9) obtained using DL-alanine. a) The reaction product during heating. b) Standing temperature: 5 °C. c) Standing temperature: 55°C.

Table 2. Absorption Maxima and CD Maxima of Mixed Chromium(III) Complexes with L-Leucine and L-, D-, or DL-Alanine (10 Days Standing)

Complex	AB		CD	
	nm (log ε)	nm (log ε)	nm (Δε)	nm (Δε)
(1) [Cr(L-ala)$_2$(L-leu)]$^{a)}$	520 (2.15)	393 (2.04)	505 (2.38)	389 (−0.32)
(2) [Cr(L-ala)(L-leu)$_2$]$^{b)}$	515 (2.11)	393 (1.98)	495 (−1.25)	385 (0.06)
(3) [Cr(L-ala)(L-leu)$_2$]$^{c)}$	515 (2.17)	392 (2.03)	490 (−0.72)	383 (0.06)
(4) [Cr(L-ala)(L-leu)$_2$]$^{d)}$	520 (2.16)	390 (2.04)	518 (0.95)	395 (−0.14)
(5) [Cr(L-ala)(L-leu)$_2$]$^{e)}$	520 (2.18)	393 (2.05)	505 (1.76)	390 (−0.25)
(6) [Cr(D-ala)$_2$(L-leu)]$^{a)}$	517 (2.18)	391 (2.08)	496 (−1.81)	385 (0.43)
(7) [Cr(D-ala)(L-leu)$_2$]$^{b)}$	515 (2.10)	394 (1.99)	495 (−1.05)	384 (0.13)
(8) [Cr(D-ala)(L-leu)$_2$]$^{c)}$	515 (2.11)	393 (2.02)	493 (−0.65)	383 (0.17)
(9) [Cr(D-ala)(L-leu)$_2$]$^{d)}$	519 (2.10)	394 (2.01)	516 (1.05)	394 (−0.28)
(10) [Cr(D-ala)(L-leu)$_2$]$^{e)}$	520 (2.15)	394 (2.04)	506 (2.03)	392 (−0.53)
(11) [Cr(L-ala)$_2$(L-leu)]$^{a)}$	520 (2.16)	393 (2.03)	505 (2.32)	389 (−0.32)
(12) [Cr(D-ala)(L-leu)$_2$]$^{b)}$	515 (2.11)	390 (2.00)	495 (−1.05)	385 (0.13)
(13) [Cr(D-ala)(L-leu)$_2$]$^{c)}$	516 (2.12)	391 (1.98)	492 (−0.66)	383 (0.08)
(14) [Cr(D-ala)(L-leu)$_2$]$^{d)}$	517 (2.13)	392 (1.99)	515 (1.02)	393 (−0.26)
(15) [Cr(D-ala)(L-leu)$_2$]$^{e)}$	520 (2.15)	393 (1.98)	505 (1.95)	390 (−0.42)

(1)—(5) obtained using L-alanine. (6)—(10) obtained using D-alanine. (11)—(15) obtained using DL-alanine. a) The reaction product during heating. b) Standing temperature: 5 °C. c) Standing temperature : 25 °C. d) Standing temperature: 40 °C. e) Standing temperature: 55 °C.

Results and Discussion

The absorption spectral data of the mixed-tris type complexes are listed in Table 2. No splitting of the first band was observed, and the absorption coefficient of the first band is larger than that of the second band. These finding agree well with those of the reported *fac*-tris(amino acidato)chromium(III) complexes,$^{3)}$ suggesting a *fac*-structure of the present tris type mixed amino acidato complexes.

The CD spectra of (+)$_{546}$-[Cr(L-ala)$_2$(L-leu)] and (−)$_{546}$-[Cr(D-ala)(L-leu)$_2$] in DMSO are shown in Fig. 1, while the numerical data are summarized in Table 2. They are very similar in shape and peak position to those of (+)$_{546}$-and (−)$_{546}$-[Cr(AA)$_3$](AA=amino acidato).$^{3)}$ Comparing the CD curves of the present complexes with those reported for Λ- and Δ-[Cr(AA)$_3$], the configuration of the present complexes can be identified as Λ for the (+)$_{546}$- and Δ for the (−)$_{546}$-isomers.

As is shown in Fig. 1, the Δε values of the major components of the first absorption band of [Cr(L-ala)$_2$(L-leu)] and [Cr(D-ala)(L-leu)$_2$] were +2.38 (505 nm) and −1.81 (495 nm) respectively. We have previously reported that the absolute configuration of [Cr(L-ala)$_3$] was the Λ(+) form.$^{3)}$ On the other hand, the tris complex containing D-alanine, which was prepared according to the literature,$^{3)}$ is Δ form (Δε=−2.41 (495 nm)). Thus, L- and D-alanine favor the Λ(+) and the Δ(−)-product respectively. From these results, it may be seen that the absolute configuration of the mixed tris-type complexes obtained is dependent on the that of the two alanine molecules coordinated. The reason for this may be the difference in the solubilities of the diastereoisomers, although this is still not clear.

The CD spectra of [Cr(L-ala)(L-leu)$_2$], which was obtained at 5, 25, 40, and 55 °C, are shown in Fig. 2, while the numerical data are summarized in Table 2,

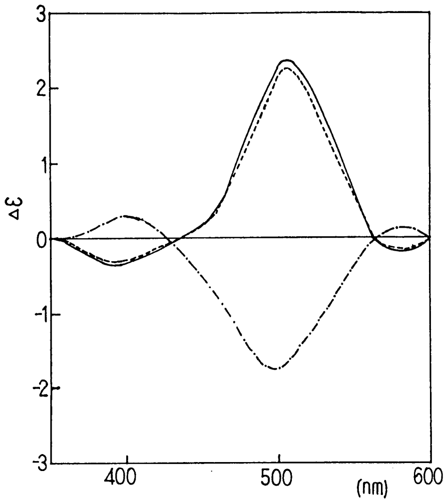

Fig. 1. The CD spectra of *fac*(+)$_{546}$-[Cr(L-ala)$_2$(L-leu)] (——), *fac*(−)$_{546}$-[Cr(D-ala)$_2$(L-leu)] (— • —), and *fac*(+)$_{546}$-[Cr(L-ala)$_2$(L-leu)](Used DL-alanine) (----).

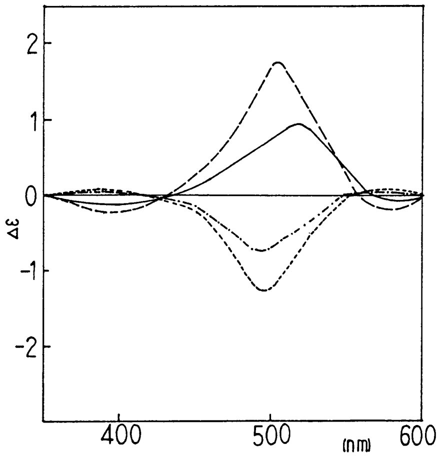

Fig. 2. The CD spectra of [Cr(L-ala)(L-leu)$_2$] obtained at each standing temperature. 55 °C (— —), 40 °C (——), 25 °C (— • —), 5 °C (----).

together with those of [Cr(D-ala)(L-leu)$_2$]. The peak positions and the signs of $\Delta\varepsilon$ of $(-)_{546}$-[Cr(L- or D-ala)(L-leu)$_2$] obtained at 5 °C and of $(+)_{546}$-[Cr(L- or D-ala)(L-leu)$_2$] obtained at 55 °C appear to be similar to those of $(+)_{546}$- and $(-)_{546}$-[Cr(AA)$_3$] respectively. Thus, the configurations of the present complexes can be identified as Λ for $(+)_{546}$- and Δ for $(-)_{546}$-isomers. On the other hand, the CD data of [Cr(L- or D-ala)(L-leu)$_2$] obtained at 25 °C or 40 °C suggest that the products are mixtures of Λ- and Δ-isomers. It was found that the ratio of the Λ-isomer to the Δ-isomer increases with a rise in the standing temperature, irrespective with the difference in the optical isomer of alanine involved.

The preparation of [Cr(L-leu)$_3$] was undertaken according to the present method. The $\Delta\varepsilon$ values of the tris complex obtained at 55 °C and at 5 °C are −0.316 and −0.583 respectively. It may be suggested that the ratio of the Λ-isomer to the Δ-isomer increases with a rise in the standing temperature. However, the ratio of the increase of the Λ-isomer of [Cr(L-leu)$_3$] is smaller than that of [Cr(L-ala)(L-leu)$_2$)]. The solubilities of [Cr(L-leu)$_3$] and [Cr(L-ala)(L-leu)$_2$] obtained at 5 °C and at 55 °C were investigated in an ethanol solution, which was added to KNCS at 5 °C and 55 °C. Nor was [Cr(L-leu)$_3$] dissolved in the solution at each temperature. On the other hand, the $(-)_{546}$-[Cr(L-ala)(L-leu)$_2$] obtained at 5 °C was dissolved at 55 °C, but was not dissolved at 5 °C. The $(+)_{546}$-[Cr(L-ala)(L-leu)$_2$] obtained at 55 °C was slightly dissolved at 55 °C, but was not dissolved at 5 °C. From these results, the stereoselectivity of [Cr(L-ala)(L-leu)$_2$] obtained after standing seems to be brought about by the difference in the solubility of the $(-)_{546}$-isomer, which arises from the difference in the standing temperature.

The characteristic feature of the present method of preparation is that it gives two different types of products.

i) Cr(L- or D-ala)$_2$(L-leu)]. These complexes were obtained during heating, in spite of using the bisleucinato chromium(III) complexes, [Cr(L-leu)$_2$(NCS)(OH$_2$)], as the starting material.

It should also be noted that the reactions are stereospecific; that is, the $(+)_{546}$- and $(-)_{546}$-isomers were obtained with L- and D-alanine respectively.

ii) [Cr(L- or D-ala)(L-leu)$_2$]. These complexes were obtained from the filtrate. It should be noted that the reactions are also stereospecific and that the optical purity of the product, $(+)_{546}$-[Cr(L- or D-ala)(L-leu)$_2$], increases with a rise in the standing temperature of the filtrate.

The optical resolution of DL-alanine based on the different reactivities of [Cr(L-leu)$_2$(NCS)(OH$_2$)] for L- and D-alanine has been undertaken, the results will be requested in a future report.

The numerical data of the absorption spectra and the CD spectra of the mixed complexes obtained during heating and after standing using DL-alanine are listed in Table 2. The CD curve of the mixed complex obtained during heating is also shown in Fig. 1. A comparison with the CD curves of the mixed complexes obtained using L- and DL-alanine shows that the CD curves and the $\Delta\varepsilon$ values of these complexes are similar to each other. Therefore, in the case of DL-alanine, the mixed complex obtained during heating may be $(+)_{546}$-[Cr(L-ala)$_2$(L-leu)].

In addition, compared with the mixed complexes obtained using D- and DL-alanine, the $\Delta\varepsilon$ values of these complexes obtained after standing are also similar to each other at each temperature. Therefore, in the case of DL-alanine, the mixed complexes which were obtained after standing at each temperature may be [Cr(D-ala)(L-leu)$_2$]. The optical resolution of DL-alanine may be possible through the reaction.

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