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Stereoselectivity in Mixed Tris-Type Cobalt(III) Complexes with Glycine and L-Aspartic Acid*1

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The reaction of the carbonatobis(glycinato)cobaltate(III) with L-aspartate in the presence of active charcoal led to the stereoselective formation of tris(glycinato-L-aspartato) complexes. By means of ion-exchange chromatography and fractional precipitation, four optically-active complexes, *mer*-*Λ*- and *fac*-*Λ*-$[Co(gly)_{3-n}(L\text{-}asp)_n]^{n-}$ ($n=1,2$), have been isolated, and they have been characterized by means of their absorption and circular dichroism spectra. Furthermore, the percent compositions of the geometrical isomers for the complexes ($n=1,2,3$) in the reaction mixture and also of *Λ*- (or *Δ*-) isomers for each geometrical isomer have been estimated using the spectral data. A marked stereoselectivity (>90%) has been found in the *fac*-*Λ*-isomers, while an appreciable selectivity (*ca.* 70%) has been found for the *mer* isomers. These stereoselectivities have been explained in terms of an enhanced stability through hydrogen bonding between the *β*-carboxylate group in the coodinated L-aspartate and the amino group in the adjacent ligand.

When optically-active ligands are combined with metal ions to make a source of dissymmetry at the central metal, the resulting diastereoisomers are usually unequal in amount. This stereoselectivity has been known for such asymmetric ligands as 1,2-diamines and amino acids. In the case of diamine

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complexes, the stereoselectivity has been attributed to the interactions of the puckered chelate rings with each other.[1] On the other hand, in the case of aminoacidato complexes two factors have been considered in connection with the selectivity. One factor comes from the presence of bulky substituents in the ligands; the absence of the *mer*-Λ-isomer of the tris(L-prolinato)cobalt(III) complex can thus be explained.[2] The other factor is due to the interaction of the polar substituents in the aminoacidato ligand with the other polar site of the adjacent ligand. The stereoselective formation of Λ-(+)-$[Co(en)_2(L\text{-glut})]^+$ relative to the Δ-isomer, for example, has thus been interpreted.[3],*2 Indeed, an X-ray analysis of the Λ-isomer has shown the existence of hydrogen bonding between the γ-carboxylate group of the L-glutamate and the amino group of the ethylenediamine chelate.[3,4]

Previously, we reported the preparation of tris-type cobalt(III) complexes with different kinds of amino acids (*i. e.*, glycine, L- or D-alanine, and L-valine).[5] In the present work, the preparation of tris-type mixed complexes with glycinato and L-aspartato ligands was attempted in order to investigate the stereoselective effect of the coordinated L-aspartate ion on the complex formation.

In the course of this study, we succeeded in the spontaneous resolution of the potassium carbonatobis(glycinato)cobaltate(III) which had been used in the above preparation as the starting material.

Experimental

Preparations. Crystals (6.4 g, 0.02 mol) of potassium carbonatobis(glycinato)cobaltate(III) prepared by a previously-described method[5] were dissolved in 100 m*l* of water, and the 5.4 g of L-aspartic acid (0.04 mol) and 2.4 g of potassium hydroxide (0.04 mol) were added to the solution. After adding 2 g of active charcoal, the solution was stirred at 40—50°C for an hour; the color of the solution was thus changed from violet to red-violet. After the removal of the active charcoal and a small amount of a precipitated material by filtration, the solution was adjusted to a pH of about 6 with 6N acetic acid. A portion of this solution was added to an ion-exchange column (diameter, 3.5 cm; height of resin, 30 cm) containing 100—200 mesh Dowex 1×8 resin in chloride form. When the column was swept with water, the *mer* and *fac* isomers of the tris(glycinato) complex were eluted. Then, the column was treated with a 0.1M aqueous solution of calcium chloride at the rate of about 0.3 m*l*/min. After prolonged elution, six bands were separated; they were alternately violet and red in color. Each band was collected in fractions, and the absorption and circular dichroism spectra were measured with each fraction. Strong Cotton-effect peaks were observed, with a negative sign for the red bands and a positive one for the violet bands, in the first absorption-band region. This suggests that the stereoselective formation of either Λ or Δ isomers has occurred in these complexes. The fractions are conveniently labeled as E-1, E-2, ·····, up to E-6, according to the order of elution. The chromatographic separation was repeated a number of times in order to store up the same fractions. The stored solutions were concentrated to small volumes under reduced pressure. When ethanol was added to the concentrate, the calcium salt of the desired complex was precipitated as a crude material. This was dissolved in a little water, and then the solution was acidified with 6N hydrochloric acid. After a while, the complex precipitated as the hydrogen compound in place of the calcium salt. Recrystallization was performed by dissolving the compound in slightly alkaline water and by then acidifying it with diluted hydrochloric acid. This recrystallization procedure was repeated several times until the resulting complex showed no change in the intensity of its CD peak.

Formation Ratios. Since only one diastereomer could be isolated for each geometrical isomer, we conveniently assumed that the Λ and Δ isomers of a complex have the same ε and $\Delta\varepsilon$ values, but with the opposite sign, in their first absorption-band region. On the basis of this assumption, the relative concentrations of the six fractions and the formation ratios of the Λ and Δ isomers were determined spectrophotometrically using the ε and $\Delta\varepsilon$ values of the crystallized complexes. In order to ascertain the effect of the reaction time upon the formation ratios, we employed 5-hour and 10-hour reactions in addition to the usual one-hour reaction.

Spontaneous Resolution. When a supersaturated aqueous solution of potassium carbonatobis(glycinato)-cobaltate(III) was left to stand at room temperature, big crystals (*ca.* 4 mm^2) were separated out. Observing these crystals under a microscope, we were able to select two forms of the crystals which could not be superimposed. The aqueous solution of each piece of these forms gave an $\Delta\varepsilon$ value of the same magnitude, but with the opposite sign (*i. e.*, $\Delta\varepsilon_{max}=\pm 3.2$ in the first band region).

Measurements. The absorption spectra were measured with a Hitachi Perkin-Elmer Model 139 UV-VIS spectrophotometer, while the circular dichroism spectra were recorded on a JASCO Model ORD/UV-5 spectrophotometer with a CD attachment, using 60% perchloric acid as the solvent. The proton magnetic resonance spectra in deuterium oxide were recorded on a JEOL Model C-60H spectrometer, using tetramethylsilane as the internal reference.

Results and Discussion

Preparation. In a previous paper,[5] we reported that the reaction of the carbonatobis(glycinato) complex with L-valine gave the bis(glycinato)L-

1) E. J. Corey and J. C. Bailar, Jr., *J. Amer. Chem. Soc.*, **81**, 2620 (1959).

2) R. G. Denning and T. S. Piper, *Inorg. Chem.*, **5**, 1056 (1966).

3) J. H. Dunlop, R. D. Gillard and N. C. Payne, *J. Chem. Soc., A*, **1967**, 1469.

*2 The representation of the absolute configuration, Δ and Λ refers to L and D in the original paper.[3]

4) J. H. Dunlop, R. D. Gillard, N. C. Payne and G. B. Robertson, *Chem. Commun.*, **1967**, 874.

5) M. Shibata, H. Nishikawa and Y. Nishida, *Inorg. Chem.*, **7**, 9 (1968).

TABLE 1. ELEMENTAL ANALYSES, ABSORPTION SPECTRA AND CD SPECTRA OF THE COMPLEXES PREPARED

Label	Complex		Elemental Anal % N	C	H	Band I ν_{max}	Band I ε_{max}	Band II ν_{max}	Band II ε_{max}	CD ν	CD $\Delta\varepsilon_{max}$
E-1	*mer*-*Λ*-[Co(gly)$_2$L-aspH]·H_2O	Found	11.72	26.65	3.93	56.1	112	80.4	161	56.7	+3.13
		Calcd	11.77	26.90	4.51					82.4	−0.73
E-2	*fac*-*Δ*-[Co(gly)$_2$L-aspH]·H_2O	Found	11.37	27.19	4.42	57.9	160	80.0	132	56.0	−1.34
		Calcd	11.77	26.90	4.51					82.2	+0.48
E-3	*mer*-*Λ*-[Co gly(L-aspH)$_2$]·2.5H_2O	Found	9.41	27.41	4.43	56.1	151	80.4	171	56.7	+3.00
		Calcd	9.50	27.16	4.79					82.2	−0.50
E-4	*fac*-*Δ*-[Co gly(L-aspH)$_2$]·2H_2O	Found	10.00	27.50	4.29	57.9	171	80.0	142	56.0	−1.41
		Calcd	9.70	27.73	4.16					82.2	+0.45

all ν: 10^{13} sec^{-1}

valinato complex predominantly. In this work, however, the reaction of the bis(glycinato) complex with L-aspartate gave at the same time a series of complexes represented by the general formula of $[Co(gly)_{3-n}(L\text{-asp})_n]^{n-}$ (n=0,1,2,3). Such a reaction may be the result of the presence of active charcoal in the system.

Characterization of the Complexes. The results of the elemental analyses of the isolated complexes are summarized in Table 1. From the results and the elution order, it is considered that the complexes obtained from the E-1 and E-2 bands are geometrical isomers of bis(glycinato)L-aspartatocobaltate(III), and that the complexes from E-3 and E-4 are those of glycinatobis(L-aspartato)cobaltate(III). Figure 1 shows the absorption spectra of the bis(glycinato) complex from E-1 and E-2. Since the bis(aspartato) complexes have spectra similar to those of the bis(glycinato) complexes, their spectra are omitted. The absorption spectrum of the violet complex obtained from E-1 (and E-3) showed a splitting of the first absorption band, whereas the red complex from E-2 (and E-4) showed no splitting. From these features in the spectra, the geometrical structures of the violet and red complexes could be identified as the *mer* and *fac* forms respectively.[6] The numerical data on the spectra are given in Table 1.

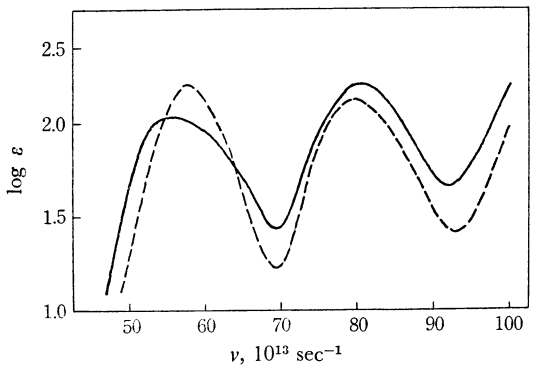

Fig. 1. Absorption spectra of [Co(gly)$_2$ L-aspH]·H_2O.
——: *mer*(from E-1) ------: *fac*(from E-2)

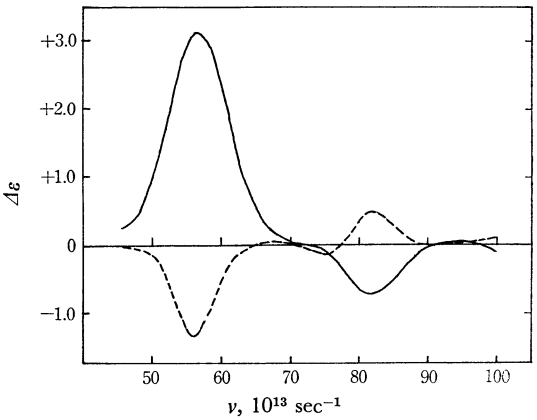

Fig. 2. CD spectra of [Co(gly)$_2$ L-aspH]·H_2O.
——: *mer* ------: *fac*

The CD spectra for the bis(glycinato) complexes are shown in Fig. 2. The spectra are similar in shape to those of the known tris(L-aminoacidato) complexes.[7] It is well known that the absolute configuration for a *fac* isomer of the tris(aminoacidato) complex can be related to that for the tris(ethylenediamine) cobalt(III) complex,[8] whereas the configuration of the corresponding *mer* isomer can be related to that for *mer*-tris(L-alaninato)-cobalt(III).[9] On this basis, the present *fac* isomer, exhibiting a dominant negative peak in the first-absorption-band region, should be identified as the *Δ* isomer, and the *mer* isomer with a dominant positive peak, as the *Λ* isomer.

For the tris-type complex containing two kinds

6) Y. Shimura and R. Tsuchida, This Bulletin, **29**, 311 (1956).

7) B. E. Douglas and S. Yamada, *Inorg. Chem.*, **4**, 1561 (1965); J. H. Dunlop and R. D. Gillard, *J. Chem. Soc.*, **1965**, 6531.

8) K. Nakatsu, M. Shiro, Y. Saito and H. Kuroya, This Bulletin, **30**, 158 (1957).

9) M. G. B. Drew, J. H. Dunlop, R. D. Gillard and D. Rogers, *Chem. Commun.*, **1966**, 42.

of aminoacidato ligands, four geometrical isomers are possible. One of them is the *fac* form, while the other three isomers belong to the *mer* form. It was experimentally found that the eluted solution of the E-3 band contains at least two geometrical-*mer* isomers; when the dominant CD peak was measured for successively-collected fractions of the band, the intensity and sign changed as follows; $+76 \rightarrow +54 \rightarrow +24 \rightarrow +4 \rightarrow -8 \rightarrow +2 \rightarrow +20$ (where the values are given by an arbitrary scale).

For all the complexes isolated, powdered crystals were obtained. On crystallization, the *mer* complexes precipitated as voluminous materials. The *Λ* isomers of the *mer* form were less soluble than the corresponding *Δ* isomers, which were not isolated because of their high solubility. On the the other hand, *fac-Λ* complexes precipitated readily, and they were less soluble in the bis(glycinato) complex, and more soluble in the bis(aspartato) complex, than the corresponding *Λ* isomers, which were not isolated because of their minute quantities.

Stereoselectivity. From the experiments on the formation ratios, we estimated the percent compositions of the *mer* and *fac* isomers and also the percent compositions of the *Λ* (or *Δ*) isomer predominantly formed for each geometrical isomer. The results are given in Tables 2 and 3. Since it is assumed that the ε and $|\Delta\varepsilon|$ values for a *mer* or a *fac* complex are the same with both the *Λ* and *Δ* isomers, — since, that is, the vicinal effects of the L-aspartate ion are disregarded, the results obtained are not very exact, but they do seem to be useful for estimating the stereoselectivity. For the tris(L-aspartato) complexes, the results were obtained from the data previously reported.[10]

The stereoselective formation of one diastereoisomer was markedly found in the *fac-Λ* isomers of the bis(glycianato), bis(L-aspartato), and tris-(L-aspartato) complexes. That is, the percent compositions of the isomers exceeded 90% in most cases. On the other hand, the selective formation for the *mer* isomers was appreciably found in their *Λ* isomers; the percent compositions of the *Λ* isomers ranged from 61% to 77% for a 1-hour reaction.

Table 2. Percent compositions of the reaction mixture

Complex / Reaction time (hr)	$Co(gly)_2asp^-$		$Cogly(asp)_2^{2-}$		$Co(asp)_3^{3-}$	
	mer %	*fac* %	*mer* %	*fac* %	*mer* %	*fac* %
1	17	15	22	30	6	10
5	17	14	23	32	6	8
10	13	10	21	31	8	17

Table 3. Percent compositions of *Δ* or *Λ* isomers

Complex / Reaction time (hr)	$Co(gly)_2asp^-$		$Cogly(asp)_2^{2-}$		$Co(asp)_3^{3-}$	
	mer *Λ*%	*fac* *Δ*%	*mer* *Λ*%	*fac* *Δ*%	*mer* *Λ*%	*fac* *Δ*%
1	61	89	73	95	77	95
5	59	83	72	95	78	95
10	57	82	69	95	72	95

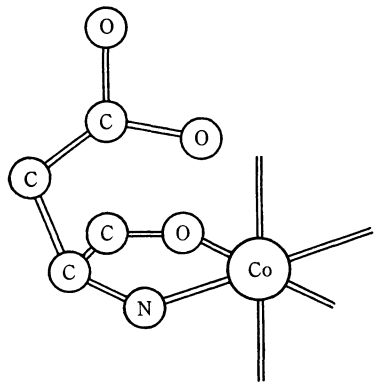

Fig. 3. The molecular model of coordinated L-aspartate.

When the molecular model for the chelation of a L-aspartate ion as a bidentate ligand is constructed, the *β*-carboxylate group of the aspartato ligand can be directed to the adjacent site of coordination, as is shown in Fig. 3. If the site is occupied by an amino group of the another aminoacidate ion, the *β*-carboxylate group is likely to interact with the amino group through hydrogen bonding in a manner similar to that found in the *Λ*(+)-L-glutamatobis(ethylenediamine)cobalt (III) complex.[3,4] If the site is occupied with a carboxylate group of the second ligand, both of the carboxylate groups will repel each other. The *fac-Λ* isomers have the possibility of such hydrogen bonding equal to the number of the chelated aspartato ligand. On the other hand, the *fac-Λ* isomers produce only the repulsion structures. Thus, the highly stereoselective formation of the *fac-Λ* isomers can be attributed to the possibility of such a hydrogen bonding. In the *mer*-bis(aspartato) complexes, the hydrogen bonding is possible for the both the *Δ* and *Λ* isomers, but the *Λ* isomer is favoured in the number of the possible hydrogen bonding. In this way, the preferential formation of the *mer-Λ* complex can be explained.

As may be seen in Table 2, the reaction time has an effect on the amounts of the products; one hour's reaction gives about 32% of the bis(glycinato) complex and about 16% of the tris(aspartato) complex in addition to 52% of the main product, while ten hour's reaction gives about 23% of the bis-(glycinato) and 25% of the tris(aspartato) complex. Such an increase in the tris(aspartato) complex

10) M. Shibata, H. Nishikawa and K. Hosaka, This Bulletin, **40**, 236 (1967).

with the reaction time can also be explained as the stereoselective effect of the L-aspartato ligand through the number of the possible hydrogen bonding.

However, in the bis- or tris(aspartato) complex the reason why the *fac* form is formed in an amount greater than that of the *mer* form cannot be explained by the possible hydrogen bonding, for its number is the same for both forms and, conversely, the *mer* form has more possible isomers than the *fac* form. The reason is suggested by the fact that, in the bis(glycinato) complex, the *mer* form is present in a greater amount than the *fac* form. As is well known, the *mer*-Λ-tris(L-prolinato)cobalt(III) isomer cannot exist because of the collision of the substituents with a cyclic structure.[2] Such a collision has also been observed in the *mer*-Λ-tris(L-leucinato) complex by means of the PMR spectrum.[2] For similar reasons, the complexes containing more than two aspartate ions appear to be more stable in the *fac*-Λ form, where the mutual repulsion in β-carboxyl groups is almost negligible. In the *mer* form, this repulsion is fairly large, especially in the Λ isomers. In our laboratory, concurrently with this study, the mixed complexes with L-aspartic acid and alanine were investigated. In these complexes, the *fac*/*mer* ratios were larger than in the present case, because of the addition of a methyl group; it must be noted that even in the complex containing one aspartate ion the *fac* form is more stable than the *mer* form.

Spontaneous Resolution. As far as we know, three examples have been reported of the spontaneous resolution of cobalt(III) complexes.[11] They are $K_3[Co(C_2O_4)_3]\cdot 3H_2O$, $[CoC_2O_4(en)_2]Cl\cdot 4H_2O$, and K[Co(trimethylenediaminetetraacetato)]$\cdot 2H_2O$. We are now able to show another example with $K[CoCO_3(gly)_2]\cdot 2H_2O$.*3 For this complex, three geometrical isomers, namely, *trans*(N), C_2-*cis*(N), and C_1-*cis*(N), are possible. However, the circular dichroism spectrum of the complex concerned (Fig. 4) was similar, in shape, to that of the known C_1-*cis*(N)$[CoC_2O_4(gly)_2]^-$;[12] moreover, the PMR spectrum of the present complex showed a pattern similar to that of the C_1-*cis*(N) oxalato complex, namely, two resonance lines due to the CH_2 group at 3.35, 3.51 ppm. Therefore, we can identify the present complex as the C_1-*cis*(N) isomer.[13]

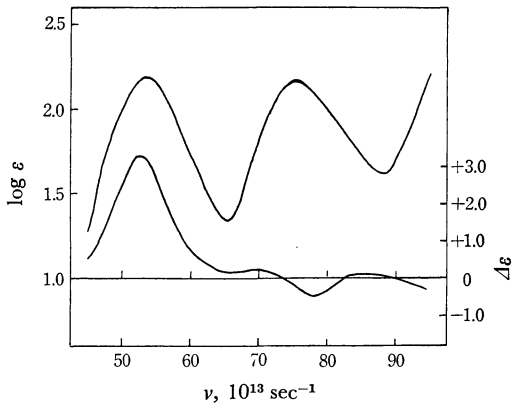

Fig. 4. Absorption and CD specta of $K[CoCO_3(gly)_2]\cdot 2H_2O$.

11) F. M. Jaeger and W. Thomas, *Proc. Acad. Sci. Amsterdam*, **21**, 693 (1919). Y. Igarashi, Y. Yoshikawa and K. Yamazaki, Proceedings of the 21st Annual Meeting of the Chemical Society of Japan, Osaka, April, 1968, p. 1102; H. Ogino, M. Takahashi and N. Tanaka, Proceedings of the 18th Symposium on Coordination Chemistry, Kyoto, October, 1968, p. 9.

*3 In Ref. 5 this complex was reported as mono hydrate.

12) N. Matsuoka, J. Hidaka and Y. Shimura, *Inorg. Chem.*, **9**, 719 (1970).

13) N. Matsuoka, J. Hidaka and Y. Shimura, This Bulletin, **40**, 1863 (1967).