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Stereoselectivity in Mixed Tris-type Complexes of Cobalt(III) with Glycine and L-Glutamic Acid[1]

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The following ten complexes have been isolated from a reaction mixture of the $[CoCO_3(gly)_2]^-$ ion and L-glutamate in the presence of active charcoal: *mer*-[Co(gly)$_2$L-glutH] (two isomers), *mer*-Cogly(L-glutH)$_2$], *mer*-Λ-[Co(L-glutH)$_3$], *fac*-Λ and Δ-[Co(gly)$_2$(L-glutH], *fac*-Λ and Δ-[Cogly(L-glutH)$_2$], and *fac*-Λ and Δ-[Co(L-glutH)$_3$]. These complexes have been characterized by various spectral data. The Δ/Λ ratios in the *fac* isomers have been estimated to be ca. 60/40, 68/32, and 75/25 for the bis(glycinato), bis(L–glutamato) and tris(L–glutamato) complexes respectively, while no appreciable stereoselectivity has been found in the corresponding *mer* isomers.

Several works on the stereoselectivity in mixed-ligand complexes of cobalt(III) containing L-aspartic acid as a ligand have been made in our laboratory; the complexes studied were of the tris(glycinato-L-aspartato),[2] tris(L-or D-alaninato-L-aspartato),[3] tris-(l-propylenediamine-L-aspartato)[4] and tris(ethylenediamine-L-aspartato)[5] series. Through these works, it has been found that the stereoselectivity observed can be explained in terms of the favorable interaction of the dangling β-carboxylate group in the chelated L-aspartate ion with the amino group in the adjacent chelated ligand.

In the present work, L-glutamic acid (L-glutH$_2$), with a γ-carboxyl group, was taken in order to make a comparison with previous works. That is, a series of tris(glycinato-L-glutamato) complexes, $[Co(gly)_{3-n}(\text{L-glut})_n]^{n-}$ ($n=1, 2, 3$), have been prepared and their diastereoisomers have been isolated. On the basis of the absorption, the circular dichroism, and the proton magnetic resonance spectral data, the isolated isomers have been characterized; then the degree of the stereoselectivity has been evaluated on the basis of the spectral data of the characterized isomers.

By the way, Gillard et al. have recently reported a more detailed study[6] than the previous one[7] on the reaction of L-glutamic acid with the $[CoCO_3(en)_2]^+$ ion.

Experimental

Preparations. The preparative reaction and the chromatographic separation were done similarly to the ways

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[1] Presented at the 21st Symposium on Coordination Chemistry, Nagoya, October, 1971.

[2] K. Kawasaki, J. Yoshi, and M, Shibata, This Bulletin, 43, 3819 (1970).

[3] T. Matsuda, T. Okumoto, and M. Shibata, *ibid.*, accepted for publication.

[4] Y. Kojima and M. Shibata, *Inorg. Chem.*, **10**, 2382 (1971).

[5] Y. Kojima and M. Shibata, presented at the 21st Symposium on Coordination Chemistry, Nagoya, October, 1971.

[6] R. D. Gillard, R. Maskill, and A. Pasini, *J. Chem. Soc., A*, **1971**, 2268.

[7] J. H. Dunlop, R. D. Gillard, and N. C. Payne, *ibid.*, **1967**, 1469.

described in the previous work[2]; potassium carbonatobis(glycinato)cobaltate(III) (6.4 g, 0.02 mol) was used as the starting material. The L-glutamic acid (5.9 g, 0.04 mol) and sodium hydroxide (1.6 g, 0.04 mol) used were of a reagent grade. Dowex 1-X8 resin in the chloride form was used for the chromatographic separation, and an aqueous solution of calcium chloride (0.05 M) was used as the eluting solution.

When chromatographed on a column of the resin, the reaction mixture finally gave six bands colored alternatively violet and red. These bands were separately collected in fractions labelled from E-1 to E-6 according to the elution order. By careful elution, the first band was further separated into two bands, which were then collected in fractions labelled Nos. 1 and 2. Each fraction, stored up to a certain amount, was concentrated under reduced pressure; ethanol was then added to the concentrate to precipitate the desired complex as its calcium salt. This crude salt was dissolved in a minimum amount of water, and then the solution was acidified with 6 *N* hydrochloric acid in order to convert the calcium salt into the less soluble hydrogen compound. From each fraction corresponding to the red bands (E-2, E-4, E-6), a pair of diastereoisomers (Δ and Λ) was obtained by means of the solubility difference. As for the other fractions, those corresponding to the violet bands (E-1, E-3, E-5), only the E-5 fraction gave one isomer of the diastereomeric pair in the course of crystallization, while the other fractions gave mixtures of the diastereoisomers. The compounds were purified by dissolving them in slightly alkalined water and by then acidifying the solutions with diluted hydrochloric acid. However, one isomer of the pair in E-4 was purified from a large amount of hot water, because it was sparingly soluble in water. For all of the optically-pure compounds, the purification procedure was repeated until the main CD peak of the compound showed a constant intensity ($\Delta\varepsilon$ value).

The results of the elemental analyses of the isolated compounds will be shown below (Table 1).

Formation Ratios. A similar but smaller-scale reaction was carried out; the starting complex (1.71 g, 0.005 mol), L-glutamic acid (1.47 g, 0.01 mol), sodium hydroxide (0.40 g, 0.01 mol), and active charcoal (0.5 g) were used. The temperature in the reaction was kept at *ca.* 60°C, but the reaction time was varied—0.5, 1 and 3 hr. Each reaction mixture, under different conditions, was chromatographed on a small column in a way similar to that described above. From the spectral data of the fractions, the percent compositions among the six bands were evaluated. Moreover, the percent compositions of the Δ isomers in the red bands were calculated on the basis of the spectral data of the isolated diastereomers.

Similar experiments were also carried out with the reaction times of 2 and 5 hr without sodium hydroxide.

Measurements. The absorption spectra were measured with a Hitachi Perkin-Elmer Model 139 UV-VIS spectrophotometer. The circular dichroism spectra were recorded on a JASCO Model ORD/UV-5 spectropolarimeter. The proton magnetic resonance spectra were all measured in deuterium oxide containing an equivalent Na_2CO_3, with a JEOL Model C-60H spectrometer using sodium 3-(trimethylsilyl)-1-propanesulfonate as the internal reference.

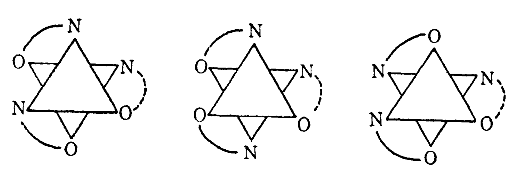
Results and Discussion

Characterization of the Isomers. It was apparent, from the absorption spectra and the elution order, that both types of bands, those colored violet and those colored red, consisted of *mer* and *fac* isomers in the *tris*(glycinato-L-glutamato) series, $[Co(gly)_{3-n}(L\text{-}glut)_n]^{n-}$ ($n=1, 2, 3$); A total of ten compounds were crystallized from the fraction. The six compounds obtained from the E-2, E-4, and E-6 fractions were pairs of diastereoisomers of the *fac* complexes. The compound obtained from E-5 was the Λ isomer of *mer*-$[Co(L\text{-}glut)_3]^{3-}$, while the corresponding Δ isomer was not isolated, although the existence of the species

Table 1. Elemental analysis and absorption spectral data[a] of the isolated complexes

Label	Complex	Elemental Anal. %[b]			Band I		Band II	
		C	N	H	ν[c]	ε	ν[c]	ε
E-1	*mer*-$[Co(gly)_2L\text{-}glutH]\cdot H_2O$ (No. 1)	29.23 (29.12)	11.60 (11.32)	4.78 (4.90)	55.6	111	80.7	156
	mer-$[Co(gly)_2L\text{-}glutH]\cdot 2H_2O$ (No. 2)	27.79 (27.77)	10.80 (10.80)	5.00 (5.19)	56.1	110	80.7	168
E-2	*fac*-Λ-$[Co(gly)_2L\text{-}glutH]$	30.44 (30.60)	11.90 (11.90)	4.95 (4.58)	57.4	163	80.0	146
	fac-Δ-$[Co(gly)_2L\text{-}glutH]$	30.38 (30.60)	11.87 (11.90)	4.70 (4.58)	57.6	158	80.0	134
E-3	*mer*-$[Cogly(L\text{-}glutH)_2]\cdot 2H_2O$	31.70 (31.24)	9.10 (9.11)	5.37 (5.25)	56.7	106	80.4	153
E-4	*fac*-Λ-$Ca[Cogly(L\text{-}glut)_2]\cdot 4H_2O$	26.92 (26.91)	10.03 (10.07)	4.81 (4.80)	57.6	176	80.0	160
	fac-Δ-$[Cogly(L\text{-}glutH)_2]$	33.64 (33.89)	9.85 (9.88)	4.84 (4.51)	57.8	170	80.0	139
E-5	*mer*-Λ-$[Co(L\text{-}glutH)_3]$	36.51 (36.22)	8.58 (8.45)	4.99 (4.87)	56.4	107	80.4	169
E-6	*fac*-Λ-$[Co(L\text{-}glutH)_3]$	35.92 (36.22)	8.49 (8.45)	5.26 (4.83)	57.6	183	80.0	169
	fac-Δ-$[Co(L\text{-}glutH)_3]\cdot 0.5H_2O$	35.92 (35.57)	8.49 (8.30)	5.26 (4.99)	57.8	185	80.0	146

a) Measured in 60% perchloric acid. b) ( ): calcd. c) All ν: 10^{13} sec^{-1}.



cis(N) *cis*(O) *trans*(N) *cis*(O) *cis*(N) *trans*(O)

Fig. 1. Possible geometrical isomers.

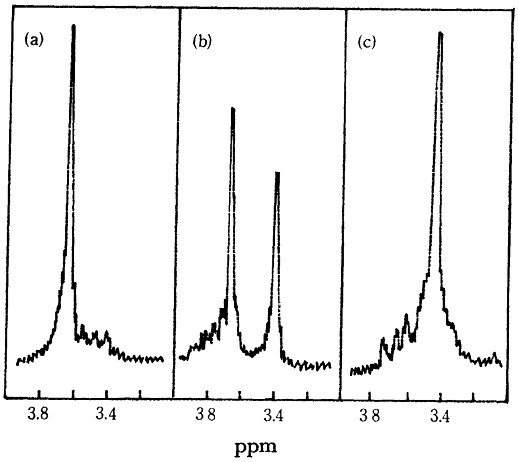


Fig. 2. PMR spectra of [Co(gly)$_2$L-glut]$^-$ (3∼4 ppm region).
a) *mer* (No. 1) b) *mer* (No. 2) c) *fac*

had been evidenced by the CD spectral change in the process of crystallization. The compound obtained from the No. 1 fraction of E–1 was a mixture of the Λ and Δ isomers of the *mer*-[Co(gly)$_2$L-glut]$^-$ complex, while the compound obtained from No. 2 was the Λ isomer contaminated with a small amount of the Δ isomer. The compound obtained from the E–3 fraction was also a mixture of the paired isomers of *mer*-[Cogly(L-glut)$_2$]$^{2-}$. The results of the elemental analyses and the absorption spectral data in 60% perchloric acid are summarized in Table 1.

Structure of mer *Isomers.* In general, the *mer* form of a tris-chelated complex with two kinds of α-aminoacidates has three possible geometrical isomers concerned with the arrangement of two identical ligands (Fig. 1). In the previous works, at least two isomers have been found to exist in the *mer*-[Cogly(L-asp)$_2$]$^{2-2)}$ amd *mer*-[CoL-ala(L-asp)$_2$]$^{2-3)}$ complexes. The spectra of the present *mer*-[Co(gly)$_2$-L-glut]$^-$ complexes are shown in Fig. 2. The CH$_2$ resonance of the glycinate rings is observed in the 3.3∼3.7 ppm region as a single line for the compound obtained from the No. 1 fraction, while it is observed as two lines of the compound obtained from No. 2. The weak lines near the CH$_2$ resonance are due to the CH resonance of the glutamate ring.

Denning and Piper[8] have reported the PMR spectra of the *mer*-[Co(L-ala)$_3$] and *mer*-[Co(L-leu)$_3$] complexes; these spectra show only two sets of doublets, with the ratio of 1 : 2, in the CH$_3$ resonance region; this fact can be related to the near equivalence of the two chelated rings with respect to the pseudo-three fold axis compared to the third ring. If analogous consideration is made of the present *mer* mixed complexes by disregarding the side group (—CH$_2$CH$_2$COOH) of the chelated glutamate, the two glycinate rings in the *cis*(N)*cis*(O) isomer seem to be near equivalent and can be expected to show a single CH$_2$ resonance line. For the remaining two isomers, two resonance lines would be expected. Thus, the complex isolated from the No. 1 fraction can tentatively be identified as the *cis*(N)*cis*(O) isomer, and the other one, obtained from No. 2, as either the *trans*(N)*cis*(O) or the *cis*(N)-*trans*(O) isomer. The above supposition seems to be realistic judging from the evidence that the CH$_2$ resonance of the Λ and Δ mixture of *fac*-[Co(gly)$_2$L-glut]$^-$ exhibited only one peak, indicating little influence of the side group of the chelated glutamate (Fig. 2, (c)).

CD Spectra. The additivity rule of the vicinal effects on the CD spectra has been reported for several cobalt(III) complexes.[9] Figure 3 shows the CD spectra of the six *fac* compounds in 60% perchloric acid. The spectra for the Λ and Δ isomers are not mirror images of each other and change in a regular way with the number of the chelated L-glutamate because of the vicinal effect of the ligand. Figure 4 shows the vicinal curves of the three *fac* complexes and also the configurational curve of the tris-(L-glutamato) complex, all of which were calculated from the observed spectra of the pairs of Λ and Δ isomers. The configurational curves of the bis(glycinato) and bis(L-glutamato) complexes accord with that of the tris(L-glutamato) complex. The magnitude of the vicinal effects obtained for each complex is estimated to be 1 : 2 : 3 in proportion to the number fo the chelated glutamato ligand. This proves not only the additivity between the vicinal and configurational effects, but also the additivity within the vicinal effects themselves.

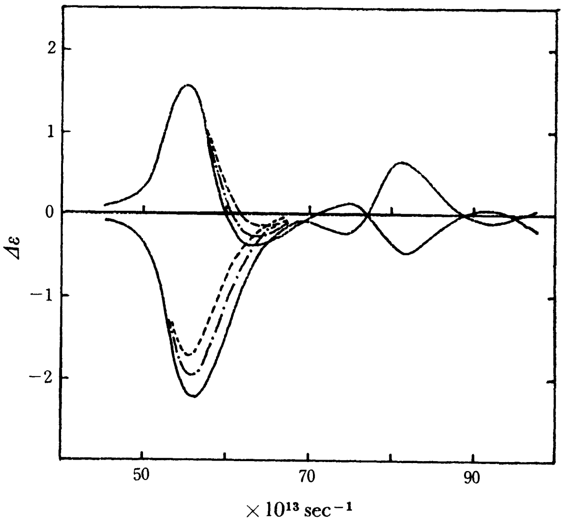


Fig. 3. CD spectra of *fac*-[Co(gly)$_{3-n}$(L-glut H)$_n$] in 60% HClO$_4$.
----: $n=1$, —·—: $n=2$, ——: $n=3$

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

[9] For example, B. E. Douglas and S. Yamada, *ibid.*, **4**, 1561 (1965).

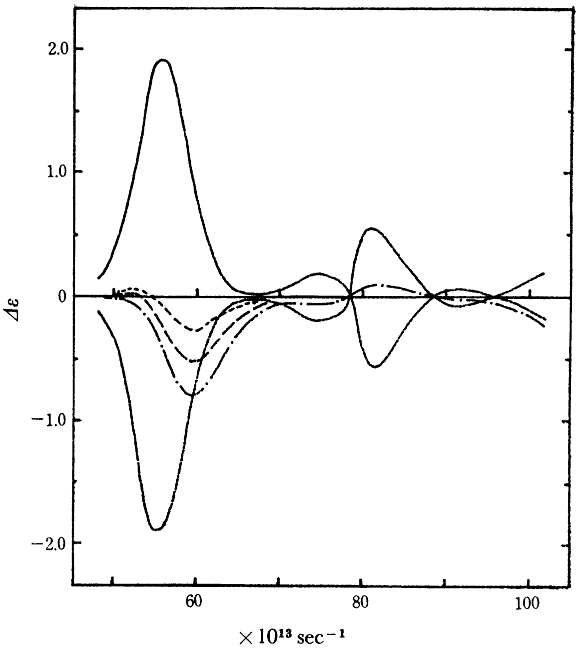

Fig. 4. Vicinal and configurational curves for CD spectra of *fac*-$[Co(gly)_{3-n}(L\text{-}glutH)_n]$.
Vicinal curve; ----: $n=1$, ——: $n=2$, —·—: $n=3$
Configurational curve; ——: $n=3$

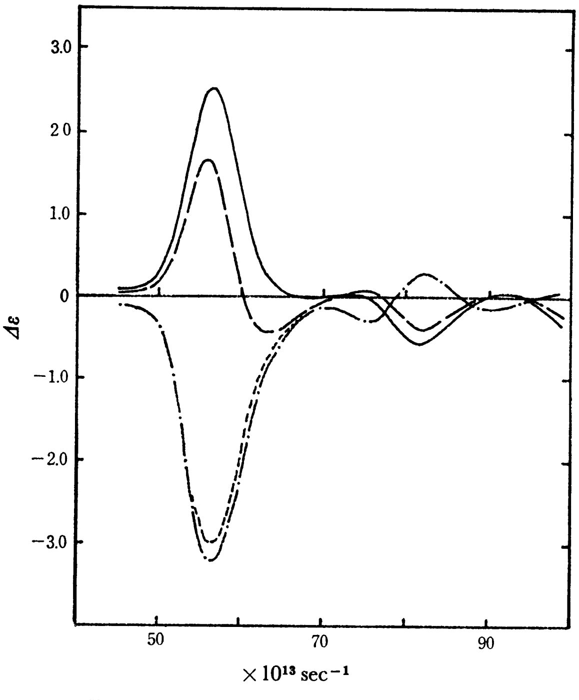

Fig. 5. CD spectra of *fac*-$[Co(L\text{-}glutH)_3]$.
——, —·—: in 0.1 N NaOH aq. soln.
----, ----: in 0.5 N Na_3PO_4 aq. soln.

Figure 5 shows the CD spectra of *fac*-$[Co(L\text{-}glut)_3]^{3-}$ measured in 0.1 N sodium hydroxide and 0.5 N trisodium phosphate solutions. The spectrum of the Λ isomer in the sodium hydroxide solution shows a single peak with a positive sign in the first absorption band region. When the same sample is measured in a trisodium phosphate solution, the small negative peak appears on the shorter wavelength side and the positive peak decreases in its intensity to a large extent. The spectra of the Δ isomer, however, do not show such a large difference between the above two solvents. A similar effect on the CD spectrum by the phosphate ion was observed for Λ-$[Co(en)_3]^{3+}$ and Λ-$[Co(\mathit{l}\text{-}pn)_3]^{3+}$ and was studied in detail by Mason *et al.*10) The reason for such an effect on the CD spectrum in our case seems to be that it is hard for the phosphate ion to interact with the amino groups in the Δ isomer by the repulsion with the γ-carboxylate groups, since the chelated glutamate ring seems to be near-planar in the isomers concerned. The spectrum of the Λ isomer measured in the trisodium phosphate solution very similar to that in 60% perchloric acid, implying that the latter medium interacts with the complex as the phosphate ion.

Figure 6 shows the CD spectra of the *mer*-Λ-$[Co(L\text{-}glut)_3]^{3-}$ in 60% perchloric acid, 0.1 N sodium hydroxide, and 0.5 N trisodium phosphate solutions. The spectra in an alkaline solution are not influenced very much by the presence of the phosphate ion. The similarity of the spectra in the perchloric acid and trisodium phosphate solutions was not observed for this isomer. The *mer* arrangement of the amino groups seems to inhibit the outer-sphere complexation.

Stereoselectivity. Figure 7 shows the CD spectra in the first absorption band region for the E–1, E–3, and E–5 fractions. Each spectrum exhibits a rather weak Cotton effect curve similar to the vicinal curve for such a complex as *mer*-$[Co(L\text{-}ala)_3]$.9) This indicates that the stereoselective formation of one diastereoisomer has scarcely occurred for the *mer* isomers. (By the way, the corresponding spectra for the *mer* fractions of the L-aspartato complexes showed strong Cotton effect curves, indicating the stereoselective formation of the Λ isomers.)2)

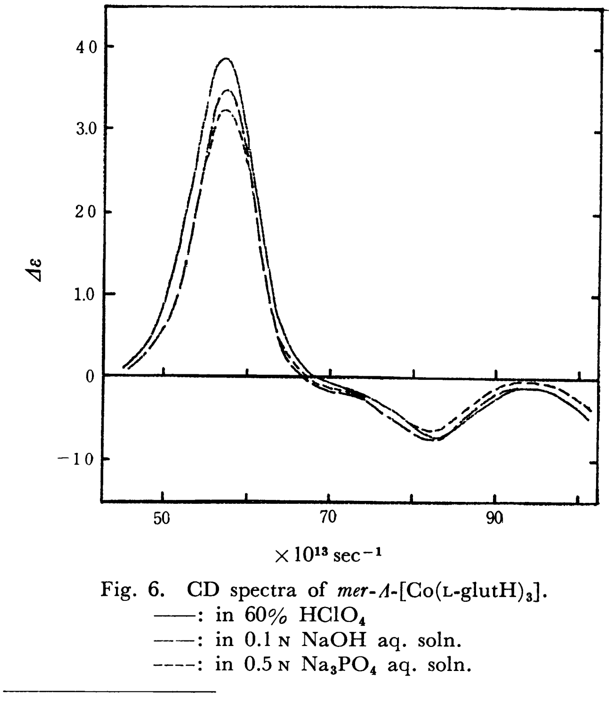

Fig. 6. CD spectra of *mer*-Λ-$[Co(L\text{-}glutH)_3]$.
——: in 60% $HClO_4$
——: in 0.1 N NaOH aq. soln.
----: in 0.5 N Na_3PO_4 aq. soln.

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10) R. Larsson, S. F. Mason, and B. J. Norman, *J. Chem. Soc.*, *A*, **1966**, 301; S. F. Mason and B. J. Norman, *ibid.*, **1966**, 307.

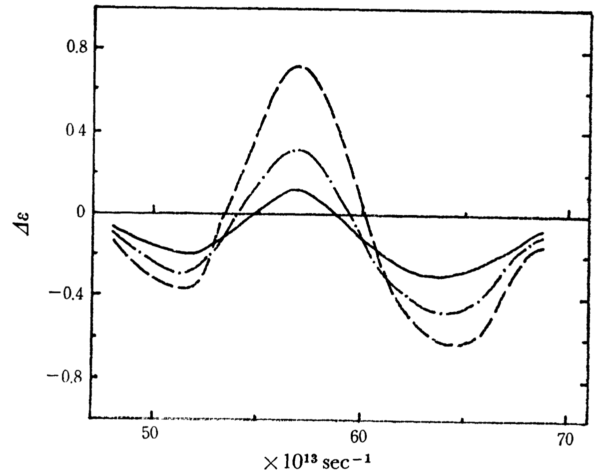

Fig. 7. CD spectra of *mer* fractions.
——: E-1, —·—: E-3, ----: E-5

The percent compositions of the Δ isomers in the E-2, E-4, and E-6 fractions are given in Table 2, together with the data on the corresponding fractions of the L-aspartato complexes.²⁾ The results in both sets of data show the preferential formation of the Δ isomers, but the degree of the selectivity in the L-glutamato complexes is considerably less than that in the L-aspartato complexes.

TABLE 2. PERCENT COMPOSITIONS OF Δ ISOMERS FOR *fac* FORMS

Reaction time (hr)	Complexes E-2 $[Co(gly)_2L\text{-}glut]^-$	 E-4 $[Cogly(L\text{-}glut)_2]^{2-}$	 E-6 $[Co(L\text{-}glut)_3]^{3-}$
0.5	60%	67%	74%
1	60	68	75
3	60	68	75
2ᵃ⁾	59	66	69
5ᵃ⁾	50	50	50
	$[Co(gly)_2L\text{-}asp]^-$	$[Cogly(L\text{-}asp)_2]^{2-}$	$[Co(L\text{-}asp)_3]^{3-}$
1	89	95	95

a) These two reactions were performed at acidic condition (pH *ca.* 6). The others were all performed at pH *ca.* 10.

The stereoselectivity in the L-aspartato complexes has been interpreted in terms of an enhanced stability through hydrogen-bonding between the β-carboxylate group of the coordinated L-aspartate ion and the amino group in the adjacent ligand.²⁾ By the same interpretation, the weaker stereoselectivity in the L-glutamato complexes may be said to be due to the lower ability of the γ-carboxylate group of the coordinated L-glutamato ion to interact with the adjacent group. Indeed, there are some cobalt(III) complexes containing the L-aspartate ion as a terdentate ligand,¹¹⁾ but no such glutamato complexes have yet been found. All of several attempts to make bis(L-glutamato)cobaltate(III) were unsuccessful.

The percent compositions of the *mer* and *fac* isomers in the reaction mixture are given in Table 3. Similar data²⁾ on the related complexes are also cited in the table.

TABLE 3. PERCENT COMPOSITIONS OF THE REACTION MIXTURE

Reaction time (hr)	Complexes $[Co(gly)_2L\text{-}glut]^-$ *mer*	 *fac*	 $[Cogly(L\text{-}glut)_2]^{2-}$ *mer*	 *fac*	 $[Co(L\text{-}glut)_3]^{3-}$ *mer*	 *fac*
1	22%	16%	26%	20%	10%	5%
	Complexes $[Co(gly)_2L\text{-}asp]^-$ *mer*	 *fac*	 $[Cogly(L\text{-}asp)_2]^{2-}$ *mer*	 *fac*	 $[Co(L\text{-}asp)_3]^{3-}$ *mer*	 *fac*
1	17%	15%	22%	30%	6%	10%

In the present complexes, more of the *mer* isomers are formed than the *fac* isomers, whereas more *fac* isomers are formed than the *mer* isomers in the *tris*- and bis(L-aspartato) complexes. The larger formation of the *fac* isomer in the *tris*(L-aspartato) complex can be attributed to the possible hydrogen bonding. That is, the amounts formed increased in the order of *fac*-Λ< *mer*-Λ<*mer*-Δ<*fac*-Δ; this order agrees with the order of the number of the possible hydrogen bonding for for these isomers (their numbers are 0, 1, 2 and 3). This is not true for the isomers of the tris(L-glutamato) complexes, because their amounts increased in the order of *fac*-Λ<*fac*-Δ<*mer*-Δ≃*mer*-Λ. The formation ratio of each *fac*-Δ isomer against the Λ isomer was kept constant at various reaction times when the reaction mixture had been prepared as an alkaline solution with sodium hydroxide (pH∼10). On the other hand, with the reaction mixture without sodium hydroxide (pH∼6), the formation ratio was estimated to be nearly 1.0 for the 5-hour reaction. That is, the stereoselectivity disappeared when the reaction was prolonged under such acidic conditions. This fact seems to suggest that the γ-carboxylate groups of the chelated glutamates protonate partially in an acidic medium and are less able to form hydrogen bonds with the adjacent groups. Thus, it may be concluded that the polar interaction of the dangling (β- or γ-) carboxylate groups with adjacent coordinated groups plays an important part in the stereoselectivity in complexes containing optically-active aspartic or glutamic acid. The lower selectivity in the L-glutamato complexes may be responsible for the longer side group ($-CH_2CH_2COO^-$).

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11) J. I. Legg and D. W. Cooke, *J. Amer. Chem. Soc.*, **89**, 6854 (1967); K. Hosaka, H. Nishikawa, and M. Shibata, This Bulletin, **42**, 277 (1969); S. Yamaka, J. Hidaka, and B. E. Douglas, *Inorg. Chem.*, **10**, 2187 (1971).