The Stereochemistry and Reactivity of Metal-Schiff Base Complexes. II. High Stereoselectivity in (1*S*,2*S*)-*N*,*N*′-1,2-Cyclohexylenebis-(salicylideneaminato)(sal$_2$-(*S*,*S*)-chxn) Cobalt(III) Complexes with Amino Acids and the Optical Resolution of Amino Acids with Cobalt(III)-sal$_2$-(*S*,*S*)-chxn*

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A series of mixed ligand cobalt(III)–Schiff base complexes with the general formula of [Co(sal$_2$-(*S*,*S*)-chxn)(aa)] (aa=gly$^-$, L- and D-ala$^-$, L- and D-val$^-$, L- and D-leu$^-$, L- and D-thr$^-$, or L- and D-trp$^-$) were newly prepared from [Co(sal$_2$-(*S*,*S*)-chxn)] and amino acids by air oxidation. All the complexes were found to take, stereoselectively, the *Λ-cis-β*$_1$(*fac*)-structure, irrespective of the configuration of the amino acids. On the other hand, the reactions of [Co(sal$_2$-(*S*,*S*)-chxn)] with an excess of DL-amino acids in open air gave [Co(sal$_2$-(*S*,*S*)-chxn) (aa)], in which L-amino acids were selectively coordinated except for proline. These stereospecificities were found from the optical-purity measurement of the unreacted amino acids which had been separated from the reaction solutions by extracting the formed complex with chloroform. The configuration and the optical purities of the unreacted amino acids recovered from 1:2 reaction solutions (complex: DL-amino acid) were as follows: ala, (D, 6—10%); leu, (D, 6—8%); met, (D, 6—8%); ser, (D, 10—12%); thr, (D, 27—30%); asp, (D, 16—18%); glu, (D, 6—8%); phe, (D, 29—31%); trp, (D, 41—43%); pro, (L, 48—50%). These stereoselectivities and stereospecificities were explained in terms of the thermodynamic origin and the stereochemical requirement of the complexes.

In recent papers,[1,2] the stereoselectivity in cobalt(III)–Schiff base complexes containing L-amino acids, [Co(sal$_2$en)(L-aa)] and [Co(7,7′-Me-sal$_2$en)(L-aa)], has been reported on. In these complexes, the stereoselectivity was thermodynamic in origin and was well explained in terms of the intramolecular steric repulsion between the alkyl groups of the coordinated amino acids and the H–C=N or CH$_3$–C=N groups of the Schiff base ligands. In this paper, we wish to report on another type of stereoselectivity which comes from a chiral Schiff base ligand in cobalt(III)-sal$_2$-(*S*,*S*)-chxn complexes with amino acids. Also to be reported is a stereospecificity of the cobalt(III)-sal$_2$-(*S*,*S*)-chxn complex to L-amino acids. The study is very interesting because the stereospecificity is thermodynamic in origin and is related to the optical resolution of amino acids with a metal complex[3–13] or to the problem of chiral recognition in metal-coenzyme.[14–19]

Experimental

Preparation of the Complexes. *1)* [*Co(sal$_2$-(S,S)-chxn)*]: This complex was prepared by the method described in Ref. 20 using (1*S*,2*S*)-*N*,*N*′-1,2-cyclohexylenebis(salicylideneamine). The optically active cyclohexanediamine used for the preparation of the optically active Schiff base ligand was resolved by a modification of the literature method.[21] A solution of *d*-tartaric acid (150 g) in 250 ml of water was cooled to about 10 °C. To this solution we then cautiously added 57 g of 1,2-cyclohexanediamine (Tokyo Kasei Co.) in small batches with cooling and stirring, followed by cooling in a refrigerator at about 0 °C for a day. A white powder-like compound was precipitated from the cold solution by scratching the wall of the beaker and subsequently separated by filtration. The white precipitate was the (+)$_D$-component and was recrystallized from a minimum amount of hot water to show a constant optical rotation (5—6 times), $[\alpha]_D$= +27.0°. Yield, 12.5 g. Found: C, 38.68; H, 6.52; N, 6.47%. Calcd for $C_6H_{16}N_2(C_4H_5O_6)_2 \cdot H_2O$: C, 38.89; H, 6.53; N, 6.48%. The hydrochloride of the (+)$_D$-component, which was obtained by the usual procedure,[21] showed an $[\alpha]_D$ of +16.0° (lit,[21] +15.8°).

The (−)$_D$-component was obtained as white needles or plates by the slow concentration of the filtrate at room temperature. It was recrystallized from a minimum amount of hot water several times to show a constant optical rotation, $[\alpha]_D$=−12.1° (lit,[22] −12°). Yield, about 7.0 g. Found: C, 44.75; H, 7.65; N, 10.49%. Calcd for $C_6H_{16}N_2(C_4H_4O_6) \cdot 1/4H_2O$: C, 44.69; H, 7.69; N, 10.42%. The hydrochloride showed $[\alpha]_D$ of −16.0°.

The absolute configuration, (1*S*, 2*S*), has been determined for (+)$_D$-chxn by Marumo *et al.* from the X-ray crystal analysis of (−)$_D$-$[Co((+)\text{-chxn})_3]Cl_3 \cdot 5H_2O$.[23]

2) [*Co(sal$_2$-(S,S)-chxn)(aa)*]: Since the preparative method is almost the same for all the complexes, only a representative procedure will be described here. The amino acid (1.5×10^{-3} mol) dissolved in 35 ml of water was added to a suspension of [Co(sal$_2$-(*S*,*S*)-chxn)] (0.5 g, 1.3×10^{-3} mol) in 45 ml of methanol. The mixture was stirred vigorously in open air for about 30 min at 60 °C. By this procedure, the complex was dissolved to give green solution. After cooling to room temperature, the solution was concentrated to about 35 ml at room temperature. Chloroform (about 50 ml) was added to extract the formed complex, and the crude product was obtained by evaporating off the chloroform to dryness. It was then recrystallized from methanol (complexes of L-ala, L-thr, D-thr, L-trp, and D-trp) or reprecipitated from chloroform (complexes of gly, D-ala, L-val, D-val, L-leu, and D-leu) by evaporating to dryness. The yields were 80—90%. These complexes can also be prepared from a mixture of a large excess of amino acid (about 1×10^{-2} mol) in 100 ml of water and [Co(sal$_2$-(*S*,*S*)-chxn)(aa)] (1×10^{-3} mol) in 50 ml of methanol, followed by a treatment similar to the method mentioned above. The compounds were identified by their PMR spectra, and their yields were 80—90%. The analytical data are listed in Table 1.

Optical Resolution of Amino Acids. The method for the optical resolution of amino acids is similar for all the amino acids, and so only a representative procedure will be given

* A part of this study was reported in *Chem. Lett.*, **1976**, 745.

Table 1. Elemental analysis data

Complex	C (%) Found(Calcd)	H (%) Found(Calcd)	N (%) Found(Calcd)
[Co(sal$_2$-(*S*,*S*)-chxn)(gly)]·H_2O	56.29(56.06)	5.66(5.56)	8.73(8.91)
[Co(sal$_2$-(*S*,*S*)-chxn)(L-ala)]·4.5H_2O	50.31(50.37)	6.42(6.43)	7.68(7.66)
[Co(sal$_2$-(*S*,*S*)-chxn)(D-ala)]·$CHCl_3$	48.65(48.37)	4.48(4.57)	7.11(7.05)
[Co(sal$_2$-(*S*,*S*)-chxn)(L-val)]·0.5$CHCl_3$·H_2O	53.39(53.44)	5.67(5.72)	7.23(7.33)
[Co(sal$_2$-(*S*,*S*)-chxn)(D-val)]·0.5$CHCl_3$·H_2O	53.68(53.44)	5.64(5.72)	7.22(7.33)
[Co(sal$_2$-(*S*,*S*)-chxn)(L-leu)]·0.5$CHCl_3$	55.68(55.92)	5.96(5.76)	7.24(7.33)
[Co(sal$_2$-(*S*,*S*)-chxn)(D-leu)]·0.5$CHCl_3$	55.75(55.92)	5.81(5.76)	7.32(7.33)
[Co(sal$_2$-(*S*,*S*)-chxn)(L-thr)]·H_2O	57.61(57.72)	5.52(5.65)	8.30(8.41)
[Co(sal$_2$-(*S*,*S*)-chxn)(D-thr)]·H_2O	57.92(57.72)	5.54(5.65)	8.39(8.41)
[Co(sal$_2$-(*S*,*S*)-chxn)(L-trp)]·3.5H_2O	57.60(57.67)	5.83(5.93)	8.64(8.68)
[Co(sal$_2$-(*S*,*S*)-chxn)(D-trp)]·4H_2O	56.92(56.88)	5.92(6.01)	8.66(8.56)

here. The molar ratio of the reactants is 1: 2 (Complex: DL-amino acid). DL-Amino acid (2.6×10^{-3} mol), dissolved in 40 ml of water, was added to a suspension of [Co(sal$_2$-(*S*,*S*)-chxn)] (0.5 g, 1.3×10^{-3} mol) in 60 ml of methanol. The mixture was then stirred vigorously for 30 min at about 60 °C. After cooling, the green complex was extracted into chloroform (50 ml, twice), and the water layer was concentrated to near dryness. The white precipitate thus obtained was washed with methanol; the yields were 90—100% (a half of the used amino acid corresponds to the yield of 100%). The white precipitate in each case was confirmed to be the corresponding amino acid by a study of its IR spectrum. The opical purity of the recovered amino acids was determined by using the method described in Ref. 24.

Measurements. The IR spectra were recorded as KBr pellets with a Hitachi EPI-S2 spectrophotometer. The electronic Absorption spectra were measured with a Hitachi EPS-3 spectrophotometer at 25 °C. The CD spectra were recorded with a JASCO J-20 Automatic Recording Spectropolarimeter at room temperature. The optical rotation at 435 nm was measured with a JASCO DIP-180 Automatic Polarimeter at 25 °C. The PMR spectra were measured with a Hitachi R-20 spectrometer (60 MHz) at 35 °C in CD_3OD using TMS as the internal reference.

Results and Discussion

Stereoselectivity. The data for the electronic absorption spectra (AB) and the circular dichroism spectra (CD) are summarized in Table 2, while some representative AB and CD spectra are shown in Fig. 1 (and Fig. 1 in *Chem. Lett.*, **1976**, 745). The PMR spectral data are listed in Table 3, while some representative PMR spectra are shown in Fig. 2 (and Fig. 2 in *Chem. Lett.*, **1976**, 745.)

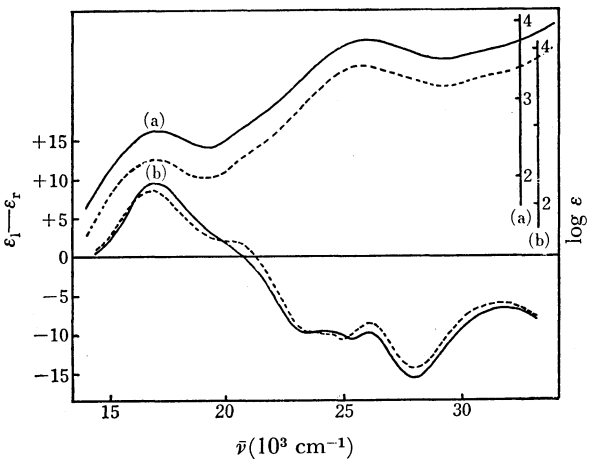

Fig. 1. AB and CD spectra of *Λ*-[Co(sal$_2$-(*S*,*S*)-chxn)-(L-val)] (——) and *Λ*-[Co(sal$_2$-(*S*,*S*)-chxn)(D-val)] (……) in MeOH.

All the complexes exhibit AB and CD spectra which are quite similar to one another. Thus, it is suggested that all the complexes prefer to take the same geometrical structure. All the complexes show CD intensities in the first absorption region (16000—21000 cm^{-1}) as strong as those for optically pure isomers of [Co(sal$_2$en)-(aa)].[2] Thus, it is also suggested that all the complexes prefer to take the same optical form. These speculations are strongly supported by the PMR spectra. All the complexes show almost the same PMR signal for the coordinated sal$_2$-(*S*,*S*)-chxn. Moreover, the PMR signals of the alkyl groups of the coordinated amino acids consist of peaks which correspond to only one isomer. Therefore, it is clear from these data that the

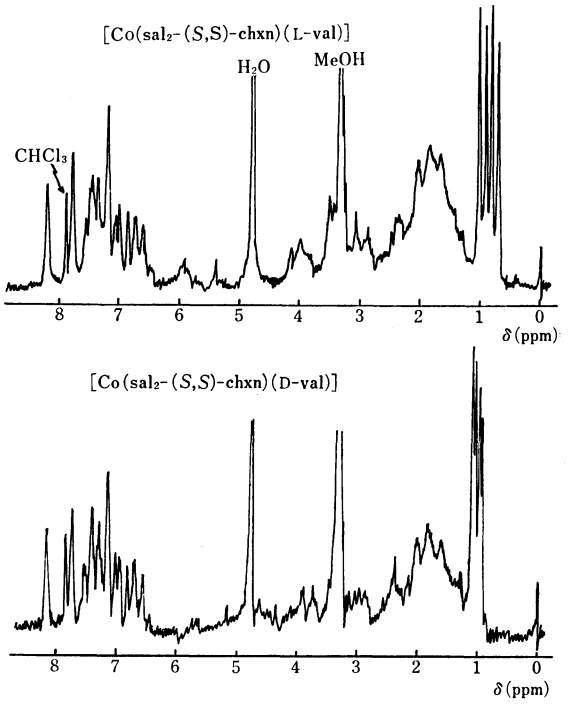

Fig. 2. PMR Spectra of representative complexes in CD_3OD.

TABLE 2. AB AND CD SPECTRAL DATA FOR [Co(sal$_2$-(*S*,*S*)-chxn)(aa)] IN METHANOL
(Wave number are in 10^3 cm^{-1})

Amino acid (aa)	AB (log ε_{max})	CD ($\Delta\varepsilon_{ext}$)	mino acid (aa)	AB (log ε_{max})	CD ($\Delta\varepsilon_{ext}$)
Gly	16.95(2.56)	16.95(+8.35)	D-Leu	16.95(2.59)	16.81(+8.68)
	20.83(2.58)[a]	20.00(+1.01)		21.28(2.74)[a]	20.62(+1.65)
	25.97(3.73)	23.64(−8.33)		25.97(3.88)	23.64(−9.55)
		25.00(−7.81)			25.00(−9.42)
		28.17(−12.94)			28.17(−13.28)
L-Ala	17.09(2.58)	16.95(+10.66)	L-Thr	17.09(2.62)	16.65(+10.82)
	21.28(2.73)[a]	20.00(+1.30)		21.28(2.83)[a]	20.00(+1.87)
	25.97(3.74)	23.64(−10.86)		25.97(3.86)	23.42(−10.95)
		25.00(−10.86)			25.32(−10.93)
		28.17(−15.90)			28.17(−16.50)
D-Ala	17.09(2.64)	16.95(+8.44)	D-Thr	16.95(2.56)	16.81(+9.96)
	21.28(2.72)[a]	20.62(+1.48)		21.28(2.79)[a]	20.62(+2.58)
	25.97(3.81)	23.64(−8.82)		25.97(3.76)	23.64(−10.44)
		25.00(−8.88)			25.32(−9.56)
		28.17(−13.31)			28.17(−15.22)
L-Val	17.09(2.62)	16.95(+9.50)	L-Trp	17.09(2.60)	16.95(+10.62)
	21.28(2.76)[a]	20.00(+2.00)		23.81(3.46)[a]	20.00(+2.31)
	25.97(3.78)	23.26(−9.50)		25.97(3.84)	23.42(−10.00)
		25.32(−10.23)			25.32(−9.28)
		28.17(−15.32)			28.17(−14.20)
D-Val	17.09(2.60)	16.95(+8.53)	D-Trp	16.95(2.56)	16.81(+8.46)
	21.28(2.73)[a]	20.63(+2.10)		22.22(2.98)[a]	20.00(+1.82)
	25.97(3.79)	23.64(−9.33)		25.97(3.87)	23.64(−8.30)
		25.00(−10.37)			25.00(−7.82)
		28.17(−13.98)			28.17(−11.55)
L-Leu	17.09(2.58)	16.95(+8.98)			
	21.28(2.70)[a]	20.00(+1.65)			
	25.97(3.88)	23.64(−9.46)			
		25.00(−9.27)			
		28.17(−13.48)			

a) Shoulder.

complexes exist as only one diastereoisomer in methanol. As will be mentioned later, six diastereomers are possible for each complex: *Λ*- and *Δ-cis-*β_1, *Λ*- and *Δ-cis-*β_2, and *Λ*- and *Δ-cis-*α. However, all the complexes utilize only one diastereoisomer, and their structures are similar to one another whether the coordinated amino acid is L or D. Thus, it may be concluded that 1) the stereoselectivity in the [Co(sal$_2$-(*S*,*S*)-chxn)(aa)] complex is complete, and 2) the stereoselectivity of the coordinated sal$_2$-(*S*,*S*)-chxn is great enough to assume only one optical form.

Although some differences in CD strengths are observed between the complexes with L- and D-amino acids, this is not due to the poor stereoselectivity but to the vicinal effect of the coordinated amino acids. Since the CD strengths in these Schiff base complexes are 2—3 times greater than those in the usual amino acidato cobalt(III) complexes,[25-28] the vicinal effect may also be somewhat stronger in these complexes. Quite a strong vicinal effect has also been observed for [Co(tfac$_2$en)-(L-aa)] (tfac$_2$en=dianion of *N*,*N'*-ethylenebis(trifluoroacetylacetoneamine); the results will be reported elsewhere.

All the complexes show no time-dependence on their CD and PMR spectra in methanol. Thus, the isomerization reaction such as seen in [Co(sal$_2$en)(L-aa)] and [Co(7,7'-Me-sal$_2$en)(L-aa)] may not occur in these sal$_2$-(*S*,*S*)-chxn-complexes.[2] However, these complexes are substitution-labile for the coordinated amino acid. That is, as has been described in the Experimental section, the reaction of these complexes with an excess of another amino acid (aa'H) proceeds comparatively rapidly to give [Co(sal$_2$-(*S*,*S*)-chxn)(aa')] with a retention of the configuration. These facts mean that the stereoselectivity of sal$_2$-(*S*,*S*)-chxn-complexes is so high that no conversion of the configuration of the coordinated Schiff base ligand is observed. Since the stereoselectivity in substitution-labile complexes can usually be ascribed to thermodynamic origins,[11-13] the stereoselectivity observed here can also be thought to be thermodynamic in origin.

Structure of the Complexes. All the complexes isolated show ν(COO$^-$) at 1625—1630 cm^{-1}, suggesting the coordination of the carboxylate group of the amino acidato ligand to the central cabolt(III) ion.[29] The elemental analysis suggests that all the amino acids act as bidentate ligands. Since the PMR signal of the H–C=N group of the sal$_2$-(*S*,*S*)-chxn ligand is split into

Table 3. PMR Spectral data for [Co(sal$_2$-(*S*,*S*)-chxn)(aa)] in CD_3OD (δ, ppm)

Amino acid (aa)	sal$_2$-(*S*,*S*)-chxn			CH_3 of amino acid[c]
	HC=N[c]	ϕ-protons	chxn[b]	
Gly	8.19(1) 7.72(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	
L-Ala	8.19(1) 7.70(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.37(1.5) 1.25(1.5) } (doublet)
D-Ala[a]	8.18(1) 7.70(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.56(1.5) 1.44(1.5) } (doublet)
L-Val[a]	8.20(1) 7.77(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.00(1.5) 0.88(1.5) } (doublet) 0.80(1.5) 0.68(1.5) } (doublet)
D-Val[a]	8.20(1) 7.77(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.09(1.5) 0.97(1.5) } (doublet) 1.05(1.5) 0.83(1.5) } (doublet)
L-Leu[a]	8.17(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	0.99(1.5) 0.91(1.5) } (doublet) 0.96(1.5) 0.88(1.5) } (doublet)
D-Leu[a]	8.17(1) 7.71(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.04(1.5) 0.95(1.5) } (doublet) 0.97(1.5) 0.88(1.5) } (doublet)
L-Thr	8.23(1) 7.77(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.24(1.5) 1.12(1.5) } (doublet)
D-Thr	8.22(1) 7.77(1)	7.5—6.5 (multiplet)	2.3—1.3 (multiplet)	1.34(1.5) 1.22(1.5) } (doublet)
L-Trp	8.10(1)[d] 7.55(1)[d]	7.5—6.5 (multiplet)	2.0—1.0 (multiplet)	
D-Trp	8.20(1) 7.70(1)	7.5—6.5 (multiplet)	2.0—1.0 (multiplet)	

a) This mcoplex shows a $CHCl_3$ signal at 7.87 ppm. b) Broad multiplet. c) The number of protons is in parentheses. d) The high-field shift of this peak is perhaps due to the anisotropic effect of the phenyl ring.

two peaks of equal intensity, the *cis*-α- and *cis*-β-structures are thought to be possible. However, the *cis*-α-structure is thought to be quite unstable, and such a complex has not yet been reported in cobalt(III)–Schiff base complexes.[30,31] On the other hand, the *cis*-β-structure is well known.[30-34] Since the stereoselectivity in these complexes is thermodymanic in origin, as has been mentioned above, the thermodynamically stable *cis*-β-structure is confidently assigned to the complexes. It is well known that (*S*,*S*)-chxn and its derivatives take the δ-conformation exclusively.[35-37] This is due to the extraordinary stability of the chair form of the cyclohexane ring. Molecular models indicate that the δ-conformation persists in sal$_2$-(*S*,*S*)-chxn and that the Λ-configuration is strain-free in its complex with the *cis*-β form. Therefore, the Λ-configuration is confidently assigned to all the complexes. As will be discussed later, [Co(sal$_2$-(*S*,*S*)-chxn)(L-aa)] is more thermodynamically stable than [Co(sal$_2$-(*S*,*S*)-chxn)-(D-aa)]. This is mainly due to the intramolecular steric repulsion between the alkyl group of the coordinated amino acid and the H–C=N group of the Schiff base ligand. This repulsion is larger in the D-aa-complex than in the L-aa-complex. Molecular models show that the steric repulsion is larger in the Λ_D-*cis*-β_1(*fac*) isomer than in the Λ_L-*cis*-β_1(*fac*) isomer. However, the Λ_L-*cis*-β_2(*mer*) isomer displays somewhat a larger steric repulsion than the Λ_D-*cis*-β_2(*mer*) isomer. Thus, the *cis*-β_1(*fac*)-structure shown in Fig. 3 may be assigned to all the complexes.

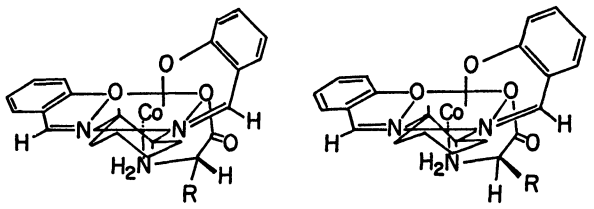

Fig. 3. The proposed structure of [Co(sal$_2$-(*S*,*S*)-chxn)-(aa)].

Stereospecificity. In order to study the stereospecificity of the complexes toward L- or D-amino acids, we examined the reactions of [Co(sal$_2$-(*S*,*S*)-chxn)] with various racemic amino acids in open air. The molar ratio in the reaction was maintained at 1:2 (complex: DL-amino acid). The stereospecificity was estimated from the optical purity of the unreacted amino acid which was recovered from the reaction solution by extracting the formed complex with chloroform, followed by the concentration of the amino-acid solution. The optical purities of the unreacted amino acids are sum-

TABLE 4. OPTICAL PURITY OF UNREACTED AMINO ACIDS WHICH WERE RECOVERED FROM THE REACTION SOLUTIONS OF [Co(sal$_2$-(*S*,*S*)-chxn)] AND DL-AMINO ACIDS IN A 1 : 2 MOLAR RATIO

Amino acid	Configuration of unreacted amino acid	Optical purity (%)	Amino acid	Configuration of unreacted amino acid	Optical purity (%)
Ala	D(R)	6—10	Asp	D(R)	16—18
Val	D(R)	6—8	Glu	D(R)	6—8
Leu	D(R)	6—8	Phe	D(R)	29—31
Met	D(R)	6—8	Trp	D(R)	41—43
Ser	D(R)	10—12	Pro	L(S)	48—50
Thr	D(R)	27—30			

marized in Table 4. Since the reaction is stoichiometric, it is written as follows:

$$2[\text{Co(sal}_2\text{-}(S,S)\text{-chxn)}] + 4\text{aaH} + 0.5\text{O}_2 \longrightarrow 2[\text{Co(sal}_2\text{-}(S,S)\text{-chxn)(aa)}] + 2\text{aaH} + \text{H}_2\text{O}. \quad (1)$$

Moreover, since all the complexes are substitution-labile toward the coordinated amino acids, the following equilibrium is also thought to be established in solution:

$$[\text{Co(sal}_2\text{-}(S,S)\text{-chxn)(L-aa)}] + \text{D-aaH} \rightleftarrows [\text{Co(sal}_2\text{-}(S,S)\text{-chxn)(D-aa)}] + \text{L-aaH}. \quad (2)$$

Here, we must consider the possibility of the racemization of amino acids or the assymetric transfer of the coordinated amino acids, but these processes were not observed under our experimental conditions. Therefore, the results in Table 4 indicate that Equilibrium 2 tends to lie toward the left side. Thus, it may be concluded that the cobalt(III)-sal$_2$-(*S*,*S*)-chxn-complex favors L-amino acids more than D-amino acids, with the exception of proline. Since the existence of Equilibrium 2 means that the stereospecificity is thermodynamic in origin, it may be concluded that the L-aa-complex is thermodynamically more stable than the D-aa-complex, again with the exception of proline. In this case, it is known that the stereoselective behavior of proline is markedly different from that of the other amino acids.[1,2]

The stereospecificity increases in the order, ala$\sim$met$\sim$leu$\sim$val$\sim$glu$<$ser$<$asp$<$thr$\lesssim$phe$<$trp$<$pro. This order parallels the increasing order of the stereoselectivity in the [Co(sal$_2$en)(L-aa)] complex and also coincides with the increasing order of the steric crowding of the alkyl group of the amino acid.[2] Therefore, an intramolecular steric repulsion between the alkyl group and the H–C=N group of the Schiff base ligand, such as seen in the [Co(sal$_2$en)(L-aa)] complex,[2] exists in each complex, and it may be larger in the Λ_D-isomer than in the Λ_L-isomer. This is the reason why the L-amino acid is selectively coordinated in the complex. In the case of proline, the molecular model indicates that the steric repulsion is larger in the Λ_L-isomer than in the Λ_D-isomer.

Variation of the Molar Ratio (DL-Amino Acid/Complex) in the Reaction. Figure 4 shows the plots of the optical purity of unreacted amino acid *versus* the molar ratio (m/n) in the reaction of n mol of a complex with $2m$ mol of DL-amino acid. In this figure, the solid lines show the calculated values, and the circles, the observed values. The calculation was carried out by using Eqs. 3 and 4 as derived below. Here, K is the equilibrium constant of Reaction 2 and is equal to

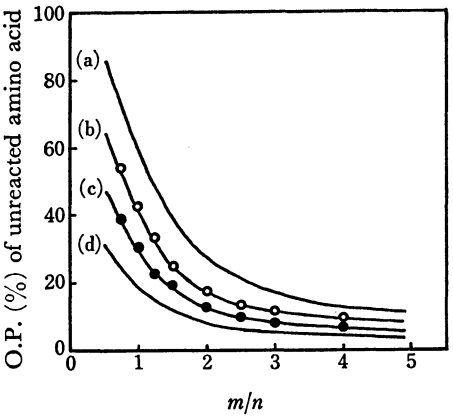

Fig. 4. A plot of optical purity (O.P.) of unreacted amino acid and molar ratio (m/n) in the reaction of n mol of complex with $2m$ mol of DL-amino acid. (a), (b), (c), and (d) are the calculated curve for K=20, K=6.0, K=3.4, and K=2, respectively. ○ and ● are the observed values for tryptophan (○) and phenylalanine (●).

K_L/K_D ($K_L>K_D$ in sal$_2$-(*S*,*S*)-chxn-complex), where K_L and K_D are the stability constants written as follows:

$$K_L = [\text{Co(Y)(L-aa)}]/[\text{Co(Y)}][\text{L-aa}],$$
$$K_D = [\text{Co(Y)(D-aa)}]/[\text{Co(Y)}][\text{D-aa}].$$

Co(Y) indicates the Co(sal$_2$-(*S*,*S*)-chxn)-complex, and the brackets stand for the concentration.

When the reaction of n mol of the complex with $2m$ mol of DL-amino acid ($2m>n$) is considered, the optical purity of the unreacted amino acid is written as follows:

$$\text{O.P. (\%)} = \{[\text{D-aa}]_f - [\text{L-aa}]_f\}/\{[\text{D-aa}]_f + [\text{L-aa}]_f\} \times 100.$$

where $[\text{D-aa}]_f$ and $[\text{L-aa}]_f$ are the concentrations of free D- and L-amino acids respectively. Since the complex formation is quantitative, and if we can neglect the concentration of free complex, [Co(Y)], the O.P.(%) can be written as follows:

$$\text{O.P. (\%)} = \{[\text{D-aa}]_f - (2m-n-[\text{D-aa}]_f)\}/\{[\text{D-aa}]_f + (2m-n-[\text{D-aa}]_f)\} \times 100, \quad (3)$$

where

$$[\text{D-aa}]_f = \{-(3m-n-mK+nK) + [(3m-n-mK+nK)^2 - 4(mn-2m^2)(K-1)]^{1/2}\} \times [2(K-1)]^{-1}. \quad (4)$$

Thus, if K is known, we can estimate the O.P.(%) of the unreacted amino acid by using Eqs. 3 and 4. In Fig. 4, we selected K arbitrarily (K=2 or 20) or as fitted to the

observed values (K=3.4 for phe and K=6.0 for trp).

From these results, it may be seen that the observed values fit the calculated curves quite well at all the reaction molar ratios; the K-values for phe and trp are quite reliable. These K-values are close to the thermodynamic stereoselectivity (Λ_L-*cis*-β_1 isomer/Δ_L-*cis*-β_1 isomer) of the Co(sal$_2$en)-complexes with L-phe and L-trp, respectively (about 4 for phe and 8 for trp).[2] Here, the Λ_L-*cis*-β_1 isomer/Δ_L-*cis*-β_1 isomer ratio is equal to the Λ_L-*cis*-β_1 isomer/Λ_D-*cis*-β_1 isomer ratio; it corresponds to the relative stability constant between the complex with L-aa and that with D-aa. Therefore, these results give strong support for the thermodynamic origin of the stereospecificity.

Finally, it should be pointed out that, although the optical purity at $2m/n$=2 is not very high, it becomes higher as m becomes smaller, and that the use of a chloroform-soluble, non-electrolyte complex is one of the advantages of our method of optical resolution of amino acid, as it provides for the easy separation of the unreacted amino acid and the formed complex by solvent extraction.

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