The Stereochemistry and Reactivity of Metal-Schiff Base Complexes. III. The Kinetic and Thermodynamic Stereoselectivities in the Formation of *N,N'*-Ethylenebis(α-methylsalicylideneaminato)cobalt(III) Complexes with L-Proline, Hydroxy-L-proline, and *allo*-Hydroxy-L-proline

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Under air-oxidation conditions, the reaction of [Co(α-Me-sal$_2$en)] with L-aaH, where α-Me-sal$_2$en represents the dianion of *N,N'*-ethylenebis(α-methylsalicylideneamine) and where L-aaH denotes L-proline, hydroxy-L-proline, or *allo*-hydroxy-L-proline, proceeded rapidly to yield *Λ-cis*-β_2-[Co(α-Me-sal$_2$en)(L-aa)] stereoselectively, followed by the slow isomerization of the *Λ-cis*-β_2-isomer thus formed to give the corresponding *Δ-cis*-β_2-isomer in a yield of almost 100% under equilibrium conditions. The complexes thus formed were isolated and characterized by the use of their absorption, circular dichroism, and ^{1}H-NMR spectra. The preferential formation of the *Λ-cis*-β_2-isomer in the initial reaction was found to be kinetic in origin. The kinetic stereoselectivity was determined to be 87% for L-proline, 56% for hydroxy-L-proline, and 23% for *allo*-hydroxy-L-proline by the measurement of the rotation at 435 nm of the reaction solutions. On the other hand, no kinetic differentiation was observed for the formation of the similar *cis*-β_2-complexes with L-alanine, L-valine, L-methionine, L-phenylalanine, L-tryptophan, *N*-benzyl-L-alanine, and *N*-methyl-L-alanine. On the basis of these data, the mechanism of the initial complexation was discussed. The high thermodynamic stereoselectivity for *Δ-cis*-β_2-isomer was explained in terms of the intramolecular steric interaction between the pyrrolidine ring of the coordinated L-aa and the distorted α-Me-sal$_2$en ligand in the complex.

The asymmetric reaction of metal complexes with chiral amino acid is an attractive problem, and many studies have been directed toward the stereoselectivity or stereospecificity of cobalt(III)–amino acid complexes. However, almost all of the asymmetric reactions reported have been those for the first-order[1-6] or second-order[7] transformations of the diastereoisomers thus formed. For the asymmetric reaction under kinetically controlled conditions, there are few studies, and no kinetic differentiation has been conclusively demonstrated for the formation of the diastereoisomers of cobalt(III) complexes containing chiral amino acid. A kinetic stereoselective formation of *Λ*-[Co(L-glu)(en)$_2$]$^+$ from racemic-[Co(CO_3)(en)$_2$]$^+$ and L-glutamic acid had been proposed by Gillard and his co-workers,[8-11] but subsequently disproven.[12,13] Kinetic differentiation has been claimed in the complexation of racemic-[Co(CO_3)(en)$_2$]$^+$ with the *N*-terminus of chiral peptides,[14] but no evidence has been presented to preclude a thermodynamic equilibrium upon the hydrolysis of the peptide linkage to produce *Λ*- and *Δ*-[Co(L-amino acidato)(en)$_2$]$^{2+}$. Little stereospecificity was found in the synthesis of β_2-[Co(L-pro)(trien)]$^{2+}$ from β-[Co(OH)(H_2O)(trien)]$^{2+}$ and L-proline under kinetically controlled conditions.[15,16] The selective formation of *Λ*-β_2-[Co(L-ala)(tetramine)]$^{2+}$ by the decarboxylation of the α-methyl-α-amino-malonato ligand (AMM) bound to the *Λ*-β_2-Co(tetramine)-complex should be kinetic in origin,[17,18] but it is a kind of ligand reaction of the coordinated AMM and not the direct complexation of chiral amino acid.

On the other hand, we have recently found that the reaction of [Co(α-Me-sal$_2$en)] with L-proline produces, stereoselectively, *Λ-cis*-β_2-[Co(α-Me-sal$_2$en)(L-pro)] under air-oxidation conditions, followed by the slow isomerization of the *Λ-cis*-β_2-isomer to give the corresponding *Δ-cis*-β_2-isomer in a high stereoselectivity (almost 100% at the equilibrium conditions).[19,20] This reaction is very interesting because 1) the preferential formation of the *Λ*-β_2-isomer in the initial reaction seems to be kinetic in origin, and 2) the stereoselectivity for the final product, the *Δ*-β_2-isomer, is quite high as compared with that for cobalt(III)-tetramine complexes with L-proline.[15,21-24] In this paper, the initial complexations between [Co(α-Me-sal$_2$en)] and various L-amino acids[25] are studied in detail, and the kinetic stereoselectivity in the formation of *Λ*- and *Δ-cis*-β_2-isomers of their complexes will be discussed, together with the formation mechanism. The high stereoselectivity for the *Δ*-β_2-isomer of the L-pro-complex will also be discussed from the stereochemical point of view.

Experimental

The Isolation of the Reaction Products. The starting material, [Co(α-Me-sal$_2$en)], was prepared by the method of Bigotto *et al.*[26]

(1) [Co(α-Me-sal$_2$en)(L-pro)]: In a previous communication,[19] methanol was used as the solvent for the reaction between [Co(α-Me-sal$_2$en)] and L-proline; however, in the present study a mixture of chloroform, methanol, and water was used as the solvent. This is mainly done to increase the solubilty of the reactants. L-Proline (1.4 g, 0.012 mol), in a mixed solvent of methanol (20 cm^3) and water (2 cm^3), was added to a chloroform solution (200 cm^3) of [Co(α-Me-sal$_2$en)] (3.7 g, 0.01 mol). The solution was stirred in the open air for about 15 min, until the color of the solution became green. The solution was then filtered to eliminate a trace amount of a brownish by-product.

(a) $(-)_{435}$-Product(2 : 1 Mixture of Λ- *and* Δ-cis-β_2-*Isomers)*: The green filtrate was concentrated as soon as possible to near dryness at room temperature. The green powder thus obtained was washed with a mixture of ether and methanol (9 : 1) and then air-dried. Yield, about 4.9 g (96%). Found:

C, 54.46; H, 6.29; N, 8.20%. Calcd for $CoC_{23}H_{26}N_3O_4 \cdot 2H_2O$: C, 54.87; H, 6.01; N, 8.34%. $[M]_{435} = -10700$ °m mol^{-1} dm^3 in chloroform. When the green product was dissolved in chloroform and the solution was concentrated to near dryness, a green powder with a $[M]_{435}$ value of $-10700°$ was obtained. Found: C, 54.35; H, 6.39; N, 8.25%. However, when this product was slowly recrystallized from methanol, green crystals with a plus rotation were obtained. Found: C, 54.72; H, 5.83; N, 8.31%. $[M]_{435} = +30500°$ in chloroform.

(b) $(\pm)_{435}$-Product (1 : 1 Mixture of Λ- *and* Δ-cis-β_2-*Isomers)*: The green filtrate obtained above was stirred for a further 3—4 h and then slowly concentrated to a small volume at room temperature. The green powder so obtained was washed with a mixture of ether and methanol (9 : 1) and then air-dried. Yield, about 4.5 g. Found: C, 54.98; H, 5.89; N, 8.33%. Calcd for $CoC_{23}H_{26}N_3O_4 \cdot 2H_2O$: C, 54.87; H, 6.01; N, 8.34%. $[M]_{435} = -600°$ in chloroform. The $(\pm)_{435}$-product was sometimes obtained in the form of no-crystalline water, and the latter was scarcely soluble in various solvents. Found: C, 58.89; H, 5.74; N, 8.85%. Calcd for $CoC_{23}H_{26}N_3O_4$: C, 59.10; H, 5.61; N, 8.99%. When the soluble $(\pm)_{435}$-product was reprecipitated from chloroform by reducing the solution to near dryness, a green powder with $[M]_{435}$ value of $-600°$ (in chloroform) was obtained. However, when it was recrystallized from methanol, green crystals with a plus rotation ($[M]_{435} = +30500°$) were isolated.

*(c) $(+)_{435}$-Product (*Δ-cis-β_2-*Isomer)*: The green filtrate obtained above was warmed for 1 d at about 40 °C, and then it was concentrated to a small volume. Green crystals with a plus rotation were thus obtained in about a 90% yield. Found: C, 54.98; H, 6.15; N, 8.51%. Calcd for $CoC_{23}H_{26}N_3O_4 \cdot 2H_2O$: C, 54.87; H, 6.01; N, 8.34%. $[M]_{435} = +30500°$ in chloroform.

*(2) [Co(α-Me-sal$_2$en)(HO-*L*-pro)]*: Hydroxy-L-proline (0.8 g, 6.1×10^{-3} mol), in a mixed solvent of water (3 cm^3) and methanol (25 cm^3), was added to a chloroform solution (150 cm^3) of [Co(α-Me-sal$_2$en)] (1.85 g, 5.0×10^{-3} mol). The solution was stirred in the open air for about 13 min. After a trace amount of hydroxy-L-proline had then been filtered off, the filtrate was concentrated to dryness as soon as possible at room temperature. A green powder (about 2.5 g) was thus obtained and was treated as follows.

(a) $(-)_{435}$-Product (3 : 2 Mixture of Λ- *and* Δ-cis-β_2-*Isomers)*: The green powder (2.5 g) was partially dissolved in chloroform (70 cm^3), and the chloroform-soluble component was evaporated to dryness at room temperature. The green powder thus obtained was washed with ether and air-dried. Yield, about 0.3 g. Found: C, 52.92, H, 5.69; N, 7.92%. Calcd for $CoC_{23}H_{26}N_3O_5 \cdot 2H_2O$: C, 53.18; H, 5.82; N, 8.09%. $[M]_{435} = -7500°$ in chloroform.

(b) $(\pm)_{435}$-Product (1 : 1 Mixture of Λ- *and* Δ-cis-β_2-*Isomers)*: The green powder (2.5 g) was dissolved in methanol (about 100 cm^3), and an equal volume of water was added. The solution was concentrated as soon as possible to a small volume at room temperature. Green crystals with a small rotation ($[M]_{435} = -700°$ in chloroform) were thus obtained in about a 70% yield. Found: C, 54.30; H, 5.91; N, 8.10%. Calcd for $CoC_{23}H_{26}N_3O_5 \cdot 1.5H_2O$: C, 54.12; H, 5.73; N, 8.23%.

*(c) $(+)_{435}$-Product (*Δ-cis-β_2-*Isomer)*: The green powder (2.5 g) was dissolved in 200 cm^3 of methanol, and then water (20 cm^3) was added. The solution was heated at about 60 °C for 1 h, and then it was allowed to stand at room temperature for 1 d. Green crystals with a plus rotation ($[M]_{435} = +34000°$ in chloroform) were thus obtained in about an 80% yield. Found: C, 54.36; H, 5.90; N, 7.99%. Calcd for $CoC_{23}H_{26}N_3O_5 \cdot 1.5H_2O$: C, 54.12; H, 5.73; N, 8.23%.

*(3) [Co(α-Me-sal$_2$en)(*allo-*HO-*L*-pro)]*: *(a) $(\pm)_{435}$-Product (1 : 1 Mixture of* Λ- *and* Δ-cis-β_2-*Isomers)*: [Co(α-Me-sal$_2$en)] (0.7 g, 1.9×10^{-3} mol) was partially dissolved in chloroform (50 cm^3), and then *allo*-hydroxy-L-proline (0.25 g, 1.9×10^{-3} mol) in a mixed solvent of water (2 cm^3) and methanol (5 cm^3) was added. The mixture was stirred vigorously in the open air for about 15 min. After a trace amount of unreacted materials had been filtered off, the green solution was reduced as soon as possible nearly to dryness at room temperature. The green powder thus obtained was washed with ether and air-dried. Yield, about 0.9 g. Found: C, 50.80; H, 5.91; N, 7.65%. Calcd for $CoC_{23}H_{26}N_3O_5 \cdot 3.5H_2O$: C, 50.55; H, 6.09; N, 7.79%. $[M]_{435} = +600°$ in chloroform.

*(b) $(+)_{435}$-Product (*Δ-cis-β_2-*Isomer)*: The $(\pm)_{435}$-product (0.5 g) obtained above was dissolved in methanol (100 cm^3) and then the solution was slowly concentrated to a small volume. Green crystals with a plus rotation ($[M]_{435} = +48000°$ in chloroform) were thus obtained in about a 70% yield. Found: C, 55.05; H, 5.58; N, 8.19%. Calcd for $CoC_{23}H_{26}N_3O_5 \cdot H_2O$: C, 55.09; H, 5.63; N, 8.38%.

Measurements. The electronic absorption spectra were recorded with a Hitachi EPS-3 Spectrophotometer at 23 °C. The CD spectra were measured 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 23 °C. The PMR spectra were recorded with a Hitachi R-20 Spectrometer (60 MHz) at 35 °C, using TMS as the internal reference. The solution for the measurement of the kinetic stereoselectivity was prepared as follows: an amino acid (5.5×10^{-5} mol) was dissolved in a mixed solvent (6 cm^3) of methanol and water (11 : 1 in volume), and this solution was added to a freshly prepared chloroform solution of [Co(α-Me-sal$_2$en)] (2.5×10^{-3} mol dm^{-3}, 20 cm^3). The solution was made up to 50 cm^3 with chloroform as soon as possible and stirred in the open air for 1 or 2 min. After this, the rotation at 435 nm and the absorption at 595 nm of the solution were measured.

Results and Discussion

The Isolation and Properties of the Reaction Products. When [Co(α-Me-sal$_2$en)] (orange in color) was allowed to react with L-proline under air-oxidation conditions, the reaction solution immediately became green in color and exhibited a minus rotation at 435 nm. After this, the absorption spectrum of the green solution scarcely varied any more; however, the rotation at 435 nm slowly increased to show a plus rotation under the equilibrium conditions. The time dependence of the absorption at 595 nm and the mutarotation at 435 nm for the reaction solution are shown in Fig. 1. In order to get informations about the above phenomena, the isolation of the reaction products was attempted. As has been mentioned in the Experimental section, depending upon the reaction time, three green complexes with different rotations could be isolated from the solution: the initial product with a minus rotation at 435 nm (represented by $(-)_{435}$-product), the second with almost no rotation ($(\pm)_{435}$-product), and the final product with a plus rotation ($(+)_{435}$-product). They all had the same composition, corresponding to [Co(α-Me-sal$_2$en)(pro)]$\cdot 2H_2O$.

Also from the reaction solutions of [Co(α-Me-sal$_2$en)] with hydroxy-L-proline and *allo*-hydroxy-L-proline, similar products were obtained. Since the properties

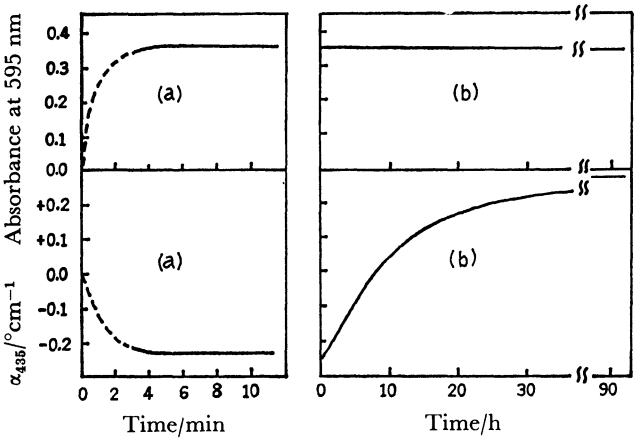

Fig. 1. The time dependences of the absorption (595 nm) and the rotation (435 nm) of the reaction solution between [Co(α-Me-sal$_2$en)] (1.0×10^{-3} M) and L-proline (1.1×10^{-3} M) in the mixed solvent of $CHCl_3$, CH_3OH, and H_2O (88: 11: 1 in volume).
Cell length: 1.0 cm, (a): those for the initial reaction solution, (b): those for full time.

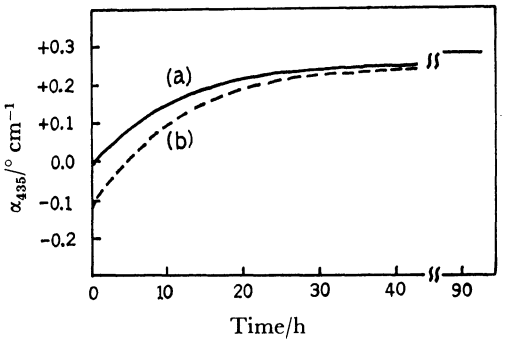

Fig. 2. The mutarotation of [Co(α-Me-sal$_2$en)(L-pro)] complex (1.0×10^{-3} M) in the mixed solvent of $CHCl_3$, CH_3OH, and H_2O (88: 11: 1 in volume).
Cell length: 1.0 cm, (a) (——): $(\pm)_{435}$-product, (b) (------): $(-)_{435}$-product.

of the L-pro-, HO-L-pro-, and *allo*-HO-L-pro-complexes resemble each other quite closely, the L-pro-complex will be used here for an example.

Both the $(-)_{435}$- and $(\pm)_{435}$-products of the L-pro-complex exhibited mutarotation in methanol or in a mixed solvent containing methanol, to show plus rotations under the equilibrium conditions, although the $(+)_{435}$-product showed no observable mutarotation. The mutarotation curves for both the $(-)_{435}$- and $(\pm)_{435}$-products are shown in Fig. 2. From both the equilibrated solutions, the $(+)_{435}$-product was isolated. As may be seen in Fig. 2, the mutarotation curves for both products are quite similar: the plots of $\ln(\alpha_\infty-\alpha_t)$ *vs.* the time for both mutarotation curves give straight lines with the same slope. Accordingly, it is clear that the $(-)_{435}$-product isomerizes to the $(+)_{435}$-product by way of the $(\pm)_{435}$-product. Since the mutarotation curve for the reaction solution of [Co(α-Me-sal$_2$en)] with L-proline in Fig. 1 closely resembles that for the $(-)_{435}$-product in Fig. 2, it can be concluded that the reaction between [Co(α-Me-sal$_2$en)] and L-proline produces $(-)_{435}$-[Co(α-Me-sal$_2$en)(L-pro)] preferentially, followed by its isomerization to give the corresponding $(+)_{435}$-isomer.

The rates of mutarotation for the $(-)_{435}$- and $(\pm)_{435}$-products depend strongly on the nature of the solvent: the rate is comparatively fast in methanol, but it is quite slow in chloroform. Therefore, the molar rotations of the $(-)_{435}$- and $(\pm)_{435}$-products scarcely varied between before and after their recrystallizations from chloroform.

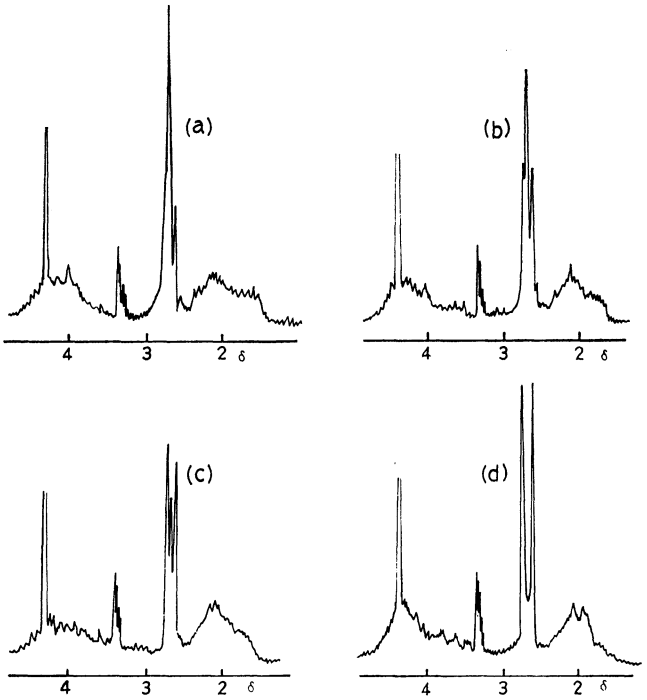

Fig. 3. The ^{1}H-NMR spectra of [Co(α-Me-sal$_2$en)-(L-pro)] complex in the mixed solvent of $CDCl_3$ and CD_3OD (4 : 1) at 35 °C.
(a): $(-)_{435}$-product, (b): $(\pm)_{435}$-product, (d): $(+)_{435}$-product. The ^{1}H-NMR spectra of $(-)_{435}$- and $(\pm)_{435}$-products exhibit time dependence. Those for $(-)_{435}$-product about 40 min and 240 min after dissolution correspond to (b) and (c), respectively, and that at the equilibrium conditions to (d). The ^{1}H-NMR spectra for $(\pm)_{435}$-product about 180 min after dissolution and at the equilibrium conditions correspond to (c) and (d), respectively.

Figure 3 shows the ^{1}H-NMR spectra of the isolated L-procomplexes soon after dissolution. The numerical data are listed in Table 1. The ^{1}H-NMR spectra of the $(-)_{435}$- and $(\pm)_{435}$-products each exhibited a clear time dependence in the methyl signal of the coordinated α-Me-sal$_2$en ligand, and each ^{1}H-NMR spectrum at the equilibrium conditions coincided with that of the $(+)_{435}$-product. However, the $(+)_{435}$-product showed no observable time dependence in its ^{1}H-NMR spectrum. From the time dependence of the methyl signal, the central peak at 2.76 ppm can safely be ascribed to $(-)_{435}$-[Co(α-Me-sal$_2$en)(L-pro)], and the two peaks with an equal intensity at 2.72 and 2.82 ppm, to $(+)_{435}$-[Co(α-Me-sal$_2$en)(L-pro)]. No other shoulders or peaks were observed in the methyl signal. These facts clearly

Table 1. ^{1}H-NMR spectral data for [Co(α-Me-sal$_2$en)((L-aa)][a] (δ)

L-aa and solvent	Products	ϕ-Protons[b]	$-CH_2-CH_2-$[b]	$-CH_3$[c]		$-CH_2-$[b] (Pyrrolidine ring)
L-pro $CDCl_3+CD_3OD$[d] (4 : 1)	$(-)_{435}$-	6.5—7.7	3.5—4.5	2.71 2.81	(doublet) [1 : 1]	1.6—2.4
				2.76	[4]	
	$(\pm)_{435}$-	6.5—7.7	3.5—4.5	2.72 2.82	(doublet) [1 : 1]	1.6—2.4
				2.77	[2]	
	$(+)_{435}$-	6.5—7.7	3.5—4.5	2.72 2.82	(doublet) [1 : 1]	1.6—2.4
HO-L-pro DMSO-d_6+$CDCl_3$[e] +CD_3OD (3 : 1 : 1)	$(-)_{435}$-	6.4—7.8	3.5—4.6	2.68 2.75	(doublet) [1 : 1]	1.7—2.4
				2.75	[3]	
	$(\pm)_{435}$-	6.4—7.8	3.5—4.6	2.68 2.75	(doublet) [1 : 1]	1.7—2.4
				2.75	[2]	
	$(+)_{435}$-	6.4—7.8	3.5—4.4	2.68 2.75	(doublet) [1 : 1]	1.7—2.4
allo-HO-L-pro $CDCl_3$+DMSO-d_6[f] +CD_3OD (6 : 2 : 1)	$(\pm)_{435}$-	6.5—7.7	3.5—4.5	2.70 2.72	(doublet) [1 : 1]	1.8—2.5
				2.70 2.76	(doublet) [1 : 1]	
	$(+)_{435}$-	6.5—7.7	3.5—4.4	2.70 2.76	(doublet) [1 : 1]	1.9—2.4

a) The data are those soon after dissolution. b) Multiplet. c) [ ] represents the relative peak area. d) Signals of the solvent: MeOH (3.32 ppm), HDO (4.20 ppm), $CHCl_3$ (7.45 ppm). e) Signals of the solvent: DMSO (2.55), MeOH (3.23), HDO (4.11), $CHCl_3$ (overlap with ϕ-protons). f) Signals of the solvent: DMSO (2.59), MeOH (3.30), HDO (3.85), $CHCl_3$ (7.75).

Table 2. Isomer ratios for the isolated products

Complex	Products	Λ-β_2-Isomer : Δ-β_2-Isomer
[Co(α-Me-sal$_2$en)-(L-pro)]	$(-)_{435}$-	6.6 : 3.3
	$(\pm)_{435}$-	5 : 5
	$(+)_{435}$-	0 : 10
[Co(α-Me-sal$_2$en)-(HO-L-pro)]	$(-)_{435}$-	6 : 4
	$(\pm)_{435}$-	5 : 5
	$(+)_{435}$-	0 : 10
[Co(α-Me-sal$_2$en)-(*allo*-HO-L-pro)]	$(\pm)_{435}$-	5 : 5
	$(+)_{435}$-	0 : 10

indicate that only two species are involved in the isomerization of the $(-)_{435}$- and $(\pm)_{435}$-products.

From the relative peak area of the methyl signal in the ^{1}H-NMR spectra of the isolated products soon after dissolution, the existing ratio between $(-)_{435}$- and $(+)_{435}$-isomers in each product can be estimated; the values are listed in Table 2. In the case of the L-pro-complex, it becomes clear that the $(-)_{435}$- and $(\pm)_{435}$-products are 2 : 1 and 1 : 1 mixtures of $(-)_{435}$- and $(+)_{435}$-[Co(α-Me-sal$_2$en)(L-pro)] respectively, but the $(+)_{435}$-product is the pure $(+)_{435}$-isomer of [Co(α-Me-sal$_2$en)(L-pro)]. Since the $(+)_{435}$-product shows no time dependence in its ^{1}H-NMR spectrum, its thermodynamic stereoselectivity can be concluded to be almost 100%.

Similar results have also been obtained for the HO-L-pro- and *allo*-HO-L-pro-complexes.

The Structure and the Thermodynamic Stereoselectivity of the Complexes. The electronic absorption (AB) and the circular dichroism (CD) spectra of the L-pro-complexes are shown in Fig. 4. The numerical data are listed in Table 3. The CD spectra of the $(-)_{435}$- and $(\pm)_{435}$-products for the L-proline varied gradually in methanol or in a mixed solvent containing methanol, and their CD spectra under the equilibrium conditions coincided with the CD spectrum of the $(+)_{435}$-product, although the variation in their AB spectra was negligibly small. Further, as may be seen in Fig. 4, an isosbestic point is observed at 21.4 k cm^{-1} in their CD spectra. These facts strongly support that only two species, $(-)_{435}$- and $(+)_{435}$-isomers of [Co(α-Me-sal$_2$en)(L-pro)], are involved in the mutarotation of the L-pro-complex. The CD spectrum of the $(+)_{435}$-product showed no observable time dependence.

The AB spectrum of the $(-)_{435}$-product closely resembles that of the $(+)_{435}$-product, and the CD spectrum of the $(-)_{435}$-product is quite similar to that of the $(+)_{435}$-product, except for the reversed CD sign. Therefore, it seems that the $(-)_{435}$- and $(+)_{435}$-isomers take the same geometrical structure with respect to the coordinated atoms. The AB and CD spectra of the $(+)_{435}$-product closely resemble those of $(-)_{435}$-Λ-*cis*-β_2-[Co(α-Me-sal$_2$en)(L-ileu)]·1.5H$_2$O,[3,20] except for the reversed CD sign. Accordingly, the Λ-*cis*-β_2-structure can be assigned to the $(+)_{435}$-isomer of [Co(α-Me-sal$_2$en)(L-pro)], and the Λ-*cis*-β_2-structure, to the $(-)_{435}$-isomer.

Similar results have also been obtained for the HO-L-pro- and *allo*-HO-L-pro-complexes.

Generally, the stereoselectivity under the equilibrium conditions is thermodynamic in origin. The Co(α-Me-sal$_2$en)-complexes with L-pro, HO-L-pro, and *allo*-HO-

TABLE 3. ABSORPTION AND CD SPECTRAL DATA[a)]

Complex	Products	Absorption $\tilde{\nu}/10^3$ cm^{-1} (log ε)	CD $\tilde{\nu}/10^3$ cm^{-1} ($\Delta\varepsilon$)
[Co(α-Me-sal$_2$en)-(L-pro)]	$(-)_{435}$-	16.7(2.55) 26.4(3.78)	16.3(+3.52), 19.2(+1.38) 22.7(−2.80), 24.1(−3.31) 25.3(−3.83), 30.8(−3.19)
	$(\pm)_{435}$-	16.7(2.54) 26.4(3.77)	14.3(+0.07), 15.8(−0.27) 17.8(+0.32), 21.2(−0.94) 23.0(+0.28), 24.5(−1.33) 27.2(+2.80), 29.4(−0.20) 31.0(+0.47)
	$(+)_{435}$-	16.7(2.54) 26.4(3.76)	16.3(−9.99). 19.2(−4.15) 23.2(+10.2), 27.2(+17.9) 30.8(+8.84)
[Co(α-Me-sal$_2$en)-(HO-L-pro)]	$(-)_{435}$-	16.8(2.58) 26.7(3.83)	16.6(+4.21), 18.5(+2.20) 22.7(−3.47), 25.6(−4.44) 30.3(−3.74)
	$(\pm)_{435}$-	16.8(2.59) 26.7(3.84)	16.9(+1.58), 18.5(+1.29) 21.7(−1.05), 24.9(−3.11) 27.4(+1.90), 30.3(−1.59)
	$(+)_{435}$-	16.9(2.57) 26.7(3.84)	16.3(−11.8), 19.2(−4.53) 23.3(+12.8), 27.2(+21.3) 30.8(+10.1)
[Co(α-Me-sal$_2$en)-(*allo*-HO-L-pro)]	$(\pm)_{435}$-	16.8(2.62) 26.9(3.78)	14.6(+0.22), 16.2(−0.67) 17.7(+0.29), 20.5(−1.72) 23.6(+0.41), 25.5(−0.71) 27.4(+1.40), 31.4(+0.71)
	$(+)_{435}$-	16.9(2.63) 27.1(3.85)	16.3(−15.4), 19.7(−8.08) 23.5(+15.2), 27.3(+22.6) 31.1(+13.9)

a) Soon after dissolution in a mixed solvent of $CHCl_3$+MeOH+H_2O (88 : 11 : 1 in volume).

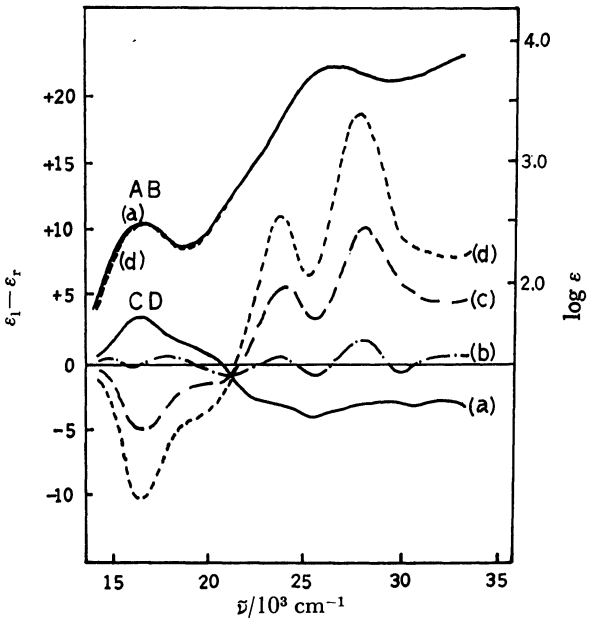

Fig. 4. The AB and CD spectra of [Co(α-Me-sal$_2$en)-(L-pro)] complex in the mixed solvent of $CHCl_3$, CH_3OH, and H_2O (88: 11: 1 in volume) at room temperature.
(a) (——): $(-)_{435}$-product, (b) (-·-·-): $(\pm)_{435}$-product, (d) (------): $(+)_{435}$-product. The CD spectra of $(-)_{435}$- and $(\pm)_{435}$-products exhibit time dependence. Those for $(-)_{435}$-product about 4 and 16 h after dissolution correspond to (b) and (c), respectively, and that at the equilibrium conditions to (d). The CD spectra for $(\pm)_{435}$-product about 12 h after dissolution and at the equilibrium conditions correspond to (c) and (d), respectively.

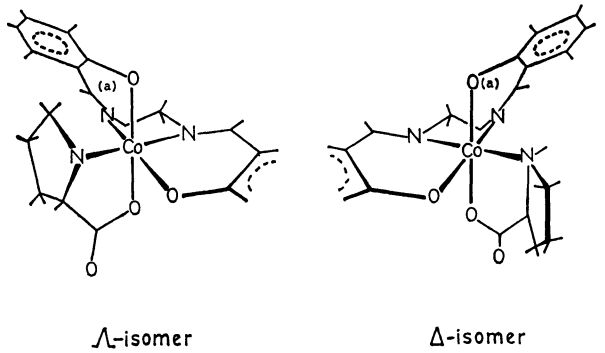

Fig. 5. The steric structure of *Λ-cis-*β_2- and *Δ-cis-*β_2-isomers of [Co(α-Me-sal$_2$en)(L-pro)] complex.

L-pro take the *Δ-cis-*β_2-structure almost always under the equilibrium conditions, as has been mentioned above. This implies that the *Δ-cis-*β_2-isomer is more stable than the corresponding *Λ-cis-*β_2-isomer at about 11.3 kJ mol^{-1} ($-\Delta G$ value of 1 : 100 equilibrium mixture) or more in each complex. On the other hand, in the cases of $[Co(en)_2(L\text{-pro})]^{2+}$ and β_2-$[Co(trien)(L\text{-pro})]^{2+}$, although they favor the *Δ*-configuration, the ratio between the *Δ*- and *Λ*-isomers under the equilibrium conditions is about 3 : 1 ($\Delta G = -2.7$ kJ mol^{-1}) in both complexes. From these facts, it can be said that the stereoselectivity of the Co(α-Me-sal$_2$en)-complexes is much higher than that of the Co(tetramine)-complexes. This high thermodynamic stereoselectivity of the Co(α-Me-sal$_2$en)-complexes comes from the characteristic steric structure of the coordinated α-Me-sal$_2$en ligand. As is shown in Fig. 5, when it takes the *cis-β*-configuration, a chelate ring (a) inclines toward the

side of the coordinated amino acid about 30° from the N–Co–O plane of (a).[3,20] In the case of the L-pro-complex, the molecular model suggests that this inclination of the chelate ring (a) brings about an extreme steric closeness (1.4—1.6 Å) between the distorted chelate ring (a) and the pyrrolidine ring of the L-proline when it has the *Λ-cis-*β_2-structure. However, when it has the *Δ-cis-*β_2-structure, there is no abnormal closeness between them. In the case of the *Λ-cis-*β_2-structure, the pyrrolidine ring somewhat approaches the two phenolic oxygen atoms of α-Me-sal$_2$en (about 2.5 Å), but the steric repulsion in the *Λ-cis-*β_2-structure seems to be much weaker than that between the pyrrolidine ring and the chelate ring (a) in the *Λ-cis-*β_2-structure. Thus, the *Δ-cis-*β_2-structure may be favored under equilibrium conditions.

In the cases of the HO-L-pro- and *allo*-HO-L-pro-complexes, their molecular models indicate that the hydroxy group on each pyrrolidine ring brings about no intramolecular steric interaction with the coordinated α-Me-sal$_2$en ligand, whether it has the *Λ-* or *Δ-cis-*β_2-structure. Therefore, they may also favor the *Δ-cis-*β_2-structure almost always, as is observed in the L-pro-complex.

Kinetic Stereoselectivity. In spite of the thermodynamic advantage of the *Λ-cis-*β_2-structure, the initial reaction between [Co(α-Me-sal$_2$en)] and L-proline produced the thermally unstable *Λ-cis-*β_2-isomer of [Co(α-Me-sal$_2$en)(L-pro)] preferentially. This fact can be explained only when the kinetic advantage in the formation of *Λ-cis-*β_2-isomer is considered. In fact, it has been observed in another of our experiments that the formation rate of *Λ-cis-*β_2-[Co(sal$_2$-(*S*,*S*)-chxn)(L-pro)] from [Co(sal$_2$-(*S*,*S*)-chxn)] and L-proline is much faster than that of *Δ-cis-*β_2-[Co(sal$_2$-(*R*,*R*)-chxn)(L-pro)] from [Co(sal$_2$-(*R*,*R*)-chxn)] and L-proline, where sal$_2$chxn represents the dianion of *N*,*N*′-1,2-cyclohexylenebis(salicylideneamine).[4,27] Hence, the initial formation of the *Λ-cis-*β_2-isomer for the Co(α-Me-sal$_2$en)-complex can be regarded as a kinetically controlled reaction. Here, the initial complexations between [Co(α-Me-sal$_2$en)] and various L-amino acids were studied in detail in order to estimate the values of the kinetic stereoselectivity for their reactions. In order to follow the initial reactions, a mixture of chloroform, methanol, and water (88 : 11 : 1 in volume) was used as the solvent. This solvent is used mainly because it will increase the solubiltiy of the reactants, but also partly because it will slow the isomerization rate of the formed complexes. Since the manner of the reactions is quite similar for all the amino acids investigated here, the reactions with L-proline and L-phenylalanine will be given as examples.

Figure 6 shows the absorption spectra of the complexes before and after the reaction. Figure 7 shows the time dependence of the absorbance at 595 nm and the mutarotation at 435 nm of the reaction solution with L-phenylalanine; those for L-proline are shown in Fig. 1. In each case, the absorbance became constant within a few minutes after the initiation of the reaction, and the absorption spectra a few minutes after the initiation of the reaction closely resembled those under equilibrium

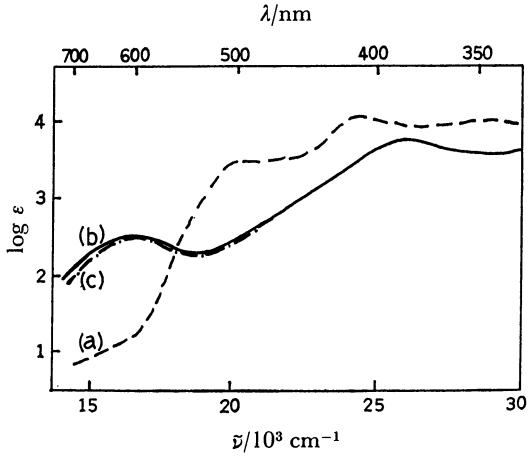

Fig. 6. The absorption spectra of [Co(α-Me-sal$_2$en)] in chloroform (1.0×10^{-3} M) and of the reaction solution between [Co(α-Me-sal$_2$en)] (1.0×10^{-3} M) and L-proline (1.1×10^{-3} M) in the mixed solvent of $CHCl_3$, CH_3OH, and H_2O (88: 11: 1 in volume).
(a): [Co(α-Me-sal$_2$en)], (b): few min after initiation of the reaction, (c) : at the equilibrium conditions.

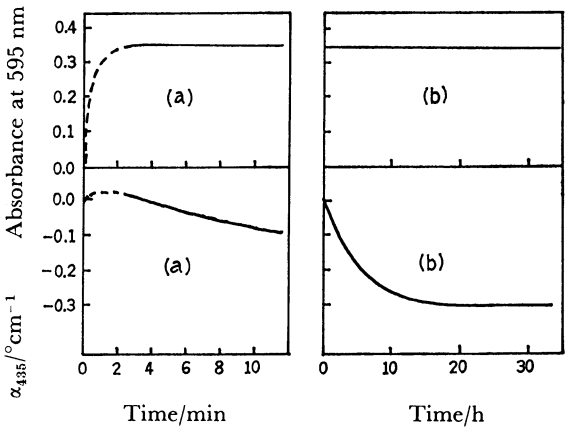

Fig. 7. The time dependences of the absorption (595 nm) and the rotation (435 nm) of the reaction solution between [Co(α-Me-sal$_2$en)] (1.0×10^{-3} M) and L-phenylalanine (1.1×10^{-3} M) in the same solvent with that in Fig. 1.
(a) : Those for the initial reaction solution, (b) : those for full time.

conditions. Further, the absorption spectrum under equilibrium conditions coincided with that of the corresponding complex, *cis-*β_2-[Co(α-Me-sal$_2$en)(L-pro)] or *cis-*β_2-[Co(α-Me-sal$_2$en)(L-phe)].[3,20] From these facts, it is concluded that the complexation of [Co(α-Me-sal$_2$en)] with L-amino acid proceeds quite rapidly under air-oxidation conditions to form *cis-*β_2-[Co(α-Me-sal$_2$en)-(L-aa)] quantitatively.

The plots of $\ln|\alpha_\infty-\alpha_t|$ *vs.* the time for each mutarotation gave a straight line, and the slope coincided with the observed isomerization rate constant between the *Λ-* and *Λ-cis-*β_2-isomers of the corresponding complex (see Table 4). Accordingly, the mutarotation of each reaction solution can safely be ascribed to the isomerization of the *cis-*β_2-complex formed between the *Λ-* and *Δ-*isomers. As is shown in Fig. 7 and Table 4, the

TABLE 4. THE ROTATION OF REACTION SOLUTIONS OF [Co(α-Me-sal$_2$en)] WITH L-AMINO ACIDS AND THAT OF THE ISOLATED COMPLEXES, [Co(α-Me-sal$_2$en)(L-aa)][a]

Amino acid[25]	Reaction solution[b]			Isolated complex[c]		
	α_{435} (°cm^{-1}) (soon after reaction)	α_{435} (°cm^{-1}) (at equilibrium conditions)	k_{obsd} (s^{-1})	α_{435} (°cm^{-1}) (soon after dissolution)	α_{435} (°cm^{-1}) (at equilibrium conditions)	k_{obsd} (s^{-1})
L-ala	+0.011	−0.086	6.2×10^{-4}	+0.013[d]	−0.085	6.1×10^{-4}[g]
L-val	+0.016	−0.160	6.9×10^{-4}	+0.011[d]	−0.165	6.8×10^{-4}[g]
L-ileu	+0.028	−0.148	7.0×10^{-4}	−0.425[e]	−0.153	
L-met	0.000	−0.089	7.7×10^{-4}	−0.416[e]	−0.088	
L-phe	+0.018	−0.310	5.6×10^{-4}	+0.020[d]	−0.312	5.8×10^{-4}[g]
L-trp	+0.008	−0.349	6.3×10^{-4}	−0.510[e]	−0.352	
N-benzyl-L-ala	+0.016	−0.363	3.2×10^{-4}		−0.364[f]	
N-methyl-L-ala	−0.038	−0.355	1.2×10^{-5}		−0.355[f]	
L-pro	−0.235	+0.275	2.2×10^{-5}	−0.006[d]	+0.285	2.2×10^{-5}[h]
HO-L-pro	−0.185	+0.330	2.0×10^{-5}	−0.007[d]	+0.335	2.0×10^{-5}[h]
allo-HO-L-pro	−0.110	+0.485	6.1×10^{-5}	+0.006[d]	+0.480	6.2×10^{-5}[h]

a) Rotations with a 1 cm cell at 23 °C in a mixed solvent of $CHCl_3+CH_3OH+H_2O$ (88 : 11 : 1 in volume). b) The concentration of [Co(α-Me-sal$_2$en)]$=1.0\times10^{-3}$ mol dm^{-3}; the concentration of L-aaH$=1.1\times10^{-3}$ mol dm^{-3}. c) The concentration of the complex$=1.0\times10^{-3}$ mol dm^{-3}. d) 1 : 1 mixture of *Λ*- and *Δ*-*cis*-β_2-isomers.[3] e) *Λ*-*cis*-β_2-isomer. f) Unpublished data. g) Observed isomerization rate from *Δ*- to *Λ*-*cis*-β_2-isomers. h) Observed isomerization rate from *Λ*- to *Δ*-*cis*-β_2-isomers.

initial rotation of the reaction solution for L-phenylalanine is very small, and it is nearly identical with that of the 1 : 1 mixture of *Λ*- and *Δ*-*cis*-β_2-[Co(α-Me-sal$_2$en)(L-phe)]. Therefore, it is concluded, for L-phenylalanine, that the formation ratio between the *Λ*- and *Δ*-*cis*-β_2-isomers in the initial complexation is about 1 : 1; the kinetic stereoselectivity is estimated to be nearly zero. Similar results have also been obtained for L-ala, L-val, L-met, L-ileu, and L-trp. In the cases of *N*-benzyl-L-ala and *N*-methyl-L-ala, since the rotations of their initial reaction solutions are also very small, their kinetic stereoselectivities are both estimated to be almost zero, although four *cis*-β_2-isomers are possible in the *N*-alkyl-amino acidato complex.

On the other hand, in the cases of L-pro, HO-L-pro, and *allo*-HO-L-pro, each reaction solution initially exhibited a large minus rotation. Since the rotations of the free amino acids were negligibly small under the experimental conditions employed (1×10^{-3} mol dm^{-3}), it is clear that the large minus rotation of each reaction solution comes from the $(-)_{435}$-isomer of the formed complex. Generally, the vicinal effect of the coordinated chiral amino acid is additive in nature. In the cases of the L-pro-, HO-L-pro-, and *allo*-HO-L-pro-complexes, it can be regarded that the rotation of each $(\pm)_{435}$-product corresponds to the vicinal effect of each L-amino acid, because the $(\pm)_{435}$-product is a 1 : 1 mixture of the *Λ*- and *Δ*-*cis*-β_2-isomers of the corresponding L-amino acidato complex. Therefore, the kinetic stereoselectivity for these complexes can be estimated by the use of the following equation:

$$\{([\Lambda]-[\Delta])/([\Lambda]+[\Delta])\}\times100(\%) = |([M]^{A}_{435}-[M]^{B}_{435})/([M]^{C}_{435}-[M]^{B}_{435})|\times100$$

where $[\Lambda]$ and $[\Delta]$ represent the concentrations of the *Λ*- and *Δ*-*cis*-β_2-isomers of the formed complex respectively; $[M]^{A}_{435}$ and $[M]^{C}_{435}$ represent the molar rotations at 435 nm of the complexes in the initial reaction solution (A) and in the equilibrium reaction solution (C) respectively, $[M]^{C}_{435}$ corresponds to the molar rotation of the $(+)_{435}$-isomer, and $[M]^{B}_{435}$ indicates the molar rotation of the $(\pm)_{435}$-product. The estimated values are listed in Table 5. Figure 8 shows the CD spectra for the reaction solutions of L-pro and *allo*-HO-L-pro. From these CD spectra, it is confirmed that: 1) the CD spectrum for the initial reaction solution of L-pro and that for the $(+)_{435}$-*Λ*-*cis*-β_2-isomer of the L-pro-complex are almost mirror images of each other; 2) the *Λ*-*cis*-β_2-isomer is formed with a high kinetic stereoselectivity; 3) the CD-intensity of the initial reaction solution for *allo*-HO-L-pro is much smaller than that for L-pro, while the kinetic stereoselectivity for the *allo*-HO-L-pro-complex is much lower than that for L-pro-complex, and 4) the CD spectrum of the reaction solution under equilibrium conditions coincides with that of the $(+)_{435}$-isomer of the corresponding isolated complex.

TABLE 5. KINETIC STEREOSELECTIVITY IN THE FORMATION OF *Λ*- AND *Δ*-*cis*-β_2-[Co(α-Me-sal$_2$en)(L-aa)]

Amino acid[25]	$([\Lambda]-[\Delta])/([\Lambda]+[\Delta])\times100(\%)$
L-ala, L-val, L-met L-ileu, L-phe, L-trp	≈0
N-benzyl-L-ala, *N*-methyl-L-ala	≈0
L-pro	87
HO-L-pro	56
allo-HO-L-pro	23

From these results and discussion, it can be concluded that 1) the kinetic differentiation in the formation of the *Λ*- and *Δ*-*cis*-β_2-diastereoisomers is characteristic of

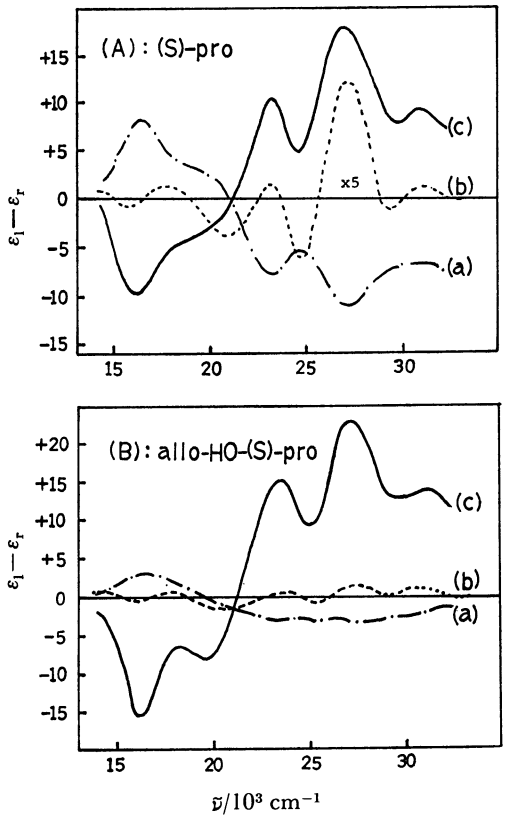

Fig. 8. The CD spectra of the reaction solutions of [Co(α-Me-sal$_2$en)] with L-proline (A) and *allo*-OH-L-proline (B) in the same solvent with that in Fig. 1. The reaction molar ratio=1 : 1.1.
(a) : Soon after reaction, (c) : at the equilibrium conditions, (b) : the CD spectrum of the corresponding $(\pm)_{435}$-product, which corresponds to the vicinal effect of the coordinated L-proline or *allo*-HO-L-proline.

the amino acids with a pyrrolidine ring, but 2) the kinetic stereoselectivity decreases in the order of: L-pro>HO-L-pro>*allo*-HO-L-pro.

The Reaction Mechanism. As has been mentioned above, the reaction between [Co(α-Me-sal$_2$en)] and L-amino acid under air-oxidation conditions proceeded quite rapidly to form *cis*-β_2-[Co(α-Me-sal$_2$en)(L-aa)] quantitatively. However, no reaction occurred under nitrogen. When the L-amino acid neutralized with LiOH was used, the formation of [Co(α-Me-sal$_2$en)-(L-aa)] was rather slow. Further, the rate of the air oxidation of [Co(α-Me-sal$_2$en)] was quite slow in the absence of L-amino acid. On the other hand, it is well known that the planar Co(II)–Schiff base complexes adsorp O_2 to give [Co(Schiff base)(O_2)] or [Co(Schiff base)]$_2O_2$.[28,29] Further, in the presence of a base, *trans*-[Co(Schiff base)(O_2)(Base)][30,31] and *trans*-[Co(Schiff base)(Base)$_2$]$^{+}$[26,32] are formed. Thus, the formation reaction of [Co(α-Me-sal$_2$en)(L-aa)] from [Co(α-Me-sal$_2$en)] and L-aaH by air-oxidation can be thought to proceed as follows:

$$[\text{Co}(\alpha\text{-Me-sal}_2\text{en})] + O_2 + {}^{-}\text{OOC-CHR-NH}_3^{+} \longrightarrow \textit{trans}\text{-}[\text{Co}(\alpha\text{-Me-sal}_2\text{en})(O_2)(\text{OOC-CHR-NH}_3^{+})] \quad (1)$$

$$\textit{trans}\text{-}[\text{Co}(\alpha\text{-Me-sal}_2\text{en})(O_2)(\text{OOC-CHR-NH}_3^{+})] \longrightarrow \textit{cis}\text{-}\beta_2\text{-}[\text{Co}(\alpha\text{-Me-sal}_2\text{en})(\text{OOC}\diagdown\!\diagup\text{NH}_2\text{CHR})] + HO_2. \quad (2)$$

The first reaction (1) is the formation of the O_2-adduct in the presence of amino acid. Since the amino acid exists as a zwitter-ion in solution, here it may coordinate to cobalt, with its carboxylato group as a unidentate ligand. The second reaction (2) is the chelation of the unidentate amino acid, which includes the deprotonation from the ammonium group of amino acid and the subsequent coordination of the amino group to the central cobalt ion, with the departure of O_2 from the O_2-adduct as O_2^- or HO_2.

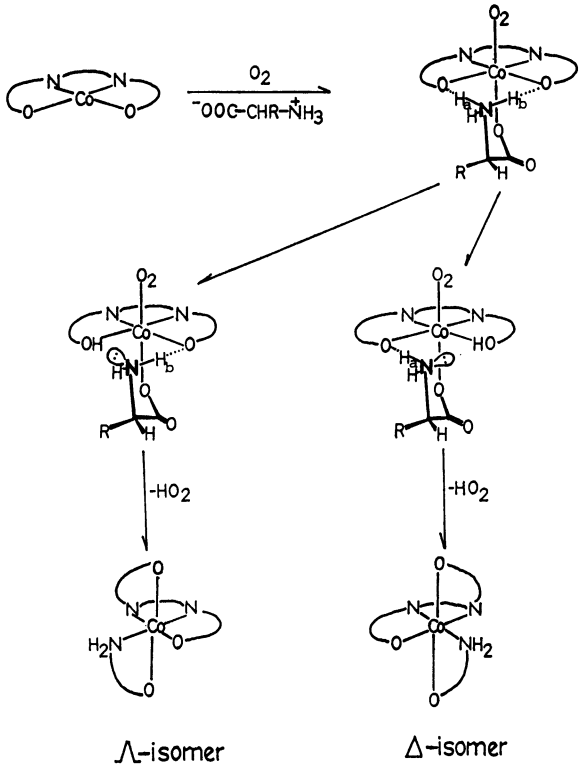

Fig. 9. The proposed reaction mechanism for the formation of *cis*-β_2-[Co(α-Me-sal$_2$en)(L-aa)] complex from [Co(α-Me-sal$_2$en)] and L-aaH under air-oxidation conditions.

In the intermediate, [Co(α-Me-sal$_2$en)(O_2)(OOC-CHR-NH_3^+)], the ammonium group of the amino acid has a positive charge and the phenolic oxygen atoms of the coordinated α-Me-sal$_2$en ligand have a negative charge. Thus, a hydrogen bonding can be expected to exist between them. Further, it has been reported recently that the phenolic oxygen atoms act as proton acceptors.[33] Accordingly, the deprotonation in Reaction (2) may take place by the transfer of one of the protons on the ammonium group to one of the phenolic oxygen atoms through the hydrogen bonding. A plausible reaction mechanism is shown in Fig. 9. In order to explain the kinetic stereoselectivities for various amino acids in Table 5, it is assumed in this mechanism that, when H_a in Fig. 9 is deprotonated, the *Λ-cis*-β_2-isomer is

produced, but when H_b is deprotonated, the *Δ-cis-*β_2-isomer is formed.

In the cases of such amino acids as L-ala, L-phe, and L-ileu, the molecular models indicate that the two protons, H_a and H_b, are sterically equivalent in the intermediate, [Co(α-Me-sal$_2$en)(O_2)(OOC–CHR–NH_3^+)]. This corresponds to the finding that the probability of the deprotonation of H_a and H_b is 50 : 50; the formation ratio between *Λ-* and *Δ-cis-*β_2-isomers is 1 : 1. In fact, as may be seen in Table 5, the kinetic stereoselectivity for such amino acids complexes as L-ala, L-phe, and L-ileu is nearly zero.

In the case of L-pro, the two protons are not equivalent, because L-proline can coordinate as a chelating ligand only when the configuration of the nitrogen atom is in the (*S*)-form. That is, only the deprotonation of H_a is effective in the chelation of L-proline. Therefore, the *Λ-cis-*β_2-isomer may be formed preferentially in the case of the L-pro-complex. On the other hand, in the case of HO-L-pro, because of the equatorial orientation of the hydroxyl group, the conformation of the pyrrolidine ring is not the same as that of L-pro. Hence, the intermediate of the HO–L-pro-complex is not able to take the same hydrogen-bonding structure as that of the L-pro-complex. The most plausible hydrogen bonding in the HO-L-pro-complex is shown in Fig. 10, together with that of the L-pro-complex. In the case of the HO-L-pro-complex, the proton, H_a in Fig. 10, can transfer either of the two phenolic oxygen atoms. Thus, the kinetic stereoselectivity becomes lower than that for the L-pro-complex. In the case of *allo*-HO-L-pro, as is shown in Fig. 11, since an intramolecular hydrogen bonding between the hydroxyl group and the carboxylato group is possible, its pyrrolidine ring takes the same conformation as that for the HO-L-pro-complex. Therefore, the kinetic stereoselectivity for the *allo*-HO-L-pro-complex may become much lower than that for the L-pro-complex.

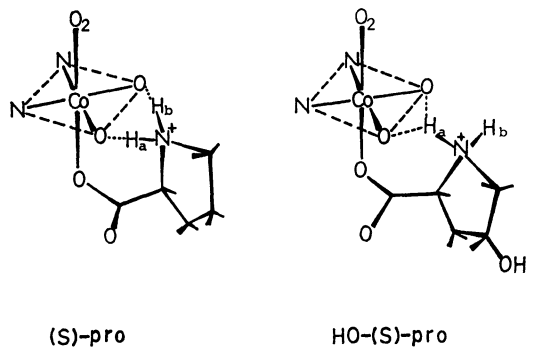

Fig. 10. The hydrogen bonding structure of the reaction intermediates for L-proline and HO-L-proline.

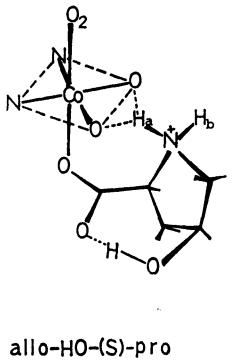

Fig. 11. The proposed structure of the reaction intermediate for *allo*-HO-L-proline.

Regarding the isomerization mechanism between *Λ-* and *Δ-cis-*β_2-isomers, a study is now underway; we have already obtained the reliable experimental result that the isomerization proceeds through a five-coordinated intermediate, [Co(α-Me-sal$_2$en)(OOC–CHR–NH_2)]. This study will be reported in the near future.

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References

1) M. Saburi, S. Yoshikawa, and M. Shibata, "The Coordination Stereochemistry of Octahedron," Kagaku Sosetsu, **13**, Gakkai Shuppan Center, pp. 109 and 134 (1976). Other references are cited therein.

2) H. Takenaka and M. Shibata, *Bull. Chem. Soc. Jpn.*, **49**, 2133 (1976).

3) Y. Fujii, T. Isago, M. Sano, N. Yanagibashi, S. Hirasawa, and S. Takahashi, *Bull. Chem. Soc. Jpn.*, **49**, 3509 (1976).

4) Y. Fujii, M. Sano, and Y. Nakano, *Bull. Chem. Soc. Jpn.*, **50**, 2609 (1977).

5) S. Yoshikawa, M. Saburi, and M. Yamaguchi, *Pure Appl. Chem.*, **50**, 915 (1978); M. Yamaguchi, S. Yamamatsu, T. Furusawa, S. Yano, M. Saburi, and S. Yoshikawa, *Inorg. Chem.*, **19**, 2010 (1980).

6) M. Okabayashi, K. Igi, and J. Hidaka, *Bull. Chem. Soc. Jpn.*, **52**, 753 (1979).

7) R. C. Job and T. C. Bruice, *J. Am. Chem. Soc.*, **100**, 5089 (1978).

8) J. H. Dunlop, R. D. Gillard, N. C. Payne, and G. B. Robertson, *J. Chem. Soc., Chem. Commun.*, **1966**, 784.

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

10) R. D. Gillard, N. C. Payne, and G. B. Robertson, *J. Chem. Soc., A*, **1970**, 2579.

11) R. D. Gillard, R. Maskill, and A. Pasini, *J. Chem. Soc., A*, **1971**, 2268.

12) J. I. Legg and J. Steele, *Inorg. Chem.*, **10**, 2177 (1971).

13) D. A. Buckingham, J. Dekkers, A. M. Sargeson, and L. G. Marzilli, *Inorg. Chem.*, **12**, 1207 (1973).

14) D. E. Allen and R. D. Gillard, *J. Chem. Soc., Chem. Commun.*, **1967**, 1091.

15) D. A. Buckingham, I. E. Maxwell, and A. M. Sargeson, *J. Chem. Soc., Chem. Commun.*, **1969**. 581.

16) D. A. Buckingham, L. G. Marzilli, I. E. Maxwell, A. M. Sargeson, and H. C. Freeman, *J. Chem. Soc., Chem. Commun.*, **1969**, 583; D. A. Buckingham, I. E. Maxwell, A. M. Sargeson, and M. R. Snow, *J. Am. Chem. Soc.*, **92**, 3617 (1970).

17) R. G. Asperger and C. F. Liu, *Inorg. Chem.*, **6**, 796 (1967).

18) R. C. Job and J. C. Bruice, *J. Am. Chem. Soc.*, **96**, 809 (1974).

19) Y. Fujii, T. Isago, and M. Sano, *Chem. Lett.*, **1975**, 1299.

20) In previous papers,[3,4,19] the *cis*-β_1-structure was assigned tentatively to the [Co(Schiff base)(amino acid)] complex; however, it has been found recently, in our X-ray study for $(-)_{435}$-[Co(α-Me-sal$_2$en)(L-ileu)]·1.5H_2O, that the complex takes the *cis*-β_2-structure: Y. Kushi, R. Tamura, M. Kuramoto, T. Yoshizawa, H. Yoneda, and Y. Fujii, *J. Chem. Soc., Chem. Commun.*, **1978**, 266. Since the CD spectrum of the complex in solution is identical with that in the solid state, the *cis*-β_2-structure can be assigned also to the complex in solution.

21) M. Saburi, M. Homma, and S. Yoshikawa, *Inorg. Chem.*, **8**, 367 (1969).

22) C. T. Lin and B. E. Douglas, *Inorg. Chem. Acta*, **4**, 3 (1970).

23) M. H. Ghandehari, T. N. Anderson, D. R. Boone, and H. Eyring, *J. Am. Chem. Soc.*, **92**, 6466 (1970).

24) D. A. Buckingham, J. Dekkers, A. M. Sargeson, and M. Wein, *Inorg. Chem.*, **12**, 2019 (1973).

25) In this paper, the following abbreviations are used: L-ala=L-alanine, L-val=L-valine, L-met=L-methionine, L-ileu=L-isoleucine, L-phe=L-phenylalanine, L-trp=L-tryptophan, L-pro=L-proline, HO-L-pro=hydroxy-L-proline, *allo*-HO-L-pro=*allo*-hydroxy-L-proliue, N-benzyl-L-ala=*N*-benzyl-L-alanine, and *N*-methyl-L-ala=*N*-methyl-L-alanine.

26) A. Biggoto, G. Costa, G. Mestroni, G. Pellizer, A. Puxeddu, E. Reisenhofer, L. Stefani, and G. Tauzher, *Inorg. Chem. Acta Reviews*, **4**, 41 (1970).

27) Will be published elsewhere.

28) H. Ogino and K. Ogino, "Coordination Chemistry of Metalloenzymes," Nankodo, Tokyo (1974), p. 55.

29) A. Nishinaga, "Bioinorganic Chemistry," Kagakudojin, Kyoto (1974), p. 179.

30) G. Amiconi, M. Brunori, E. Autonini, G. Tauzer, and G. Costa, *Nature*, **228**, 549 (1970).

31) A. L. Crumbliss and F. Basolo, *J. Am. Chem. Soc.*, **92**, 55 (1970).

32) Y. Fujii, A. Osawa, Y. Furukawa, F. Ebina, and S. Takahashi, *Bull. Chem. Soc. Jpn.*, **45**, 2459 (1972).

33) J. R. Thornback and G. Wilkinson, *J. Chem. Soc., Dalton Trans.*, **1978**, 110.