The Stereochemistry and Reactivity of Metal-Schiff Base Complexes. VI. The Kinetics and Mechanism of Isomerization between Δ_L-β_2- and Λ_L-β_2-Diastereoisomers of *N,N'*-Ethylenebis(α-methylsalicylideneaminato)cobalt(III) Complexes with L-Amino Acid

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The kinetics for isomerization between Δ_L-β_2- and Λ_L-β_2-diastereoisomers of [Co(α-Me-sal$_2$en)(L-aa)], where L-aa represents L-phe, L-met, L-ile, L-pro, *N*-Bz–L-ala, and *N*-Me–L-ala, were studied in methanol. The activation enthalpies (ΔH^*/kJ mol^{-1}) and the activation entropies (ΔS^*/J K^{-1} mol^{-1}) from the Δ_L-β_2-isomer (unstable form) to the Λ_L-β_2-isomer (stable form) were determined to be 86.6 and −9.6 for L-phe, 92.5 and +6.7 for L-met, 87.5 and −8.0 for L-ile, 100.4 and +28.0 for *N*-Bz–L-ala, and 102.9 and +18.4 for *N*-Me–L-ala, respectively. For L-pro-complex, the Δ_L-β_2-isomer is the stable form, and the enthalpy and entropy for isomerization from Λ_L-β_2- to Δ_L-β_2-isomers were 96.2 and 0.0. The isomerization was catalyzed by acids but not by bases, and was much faster than the substitution of coordinated L-amino acid. The H–D exchange of N–H proton of *N*-Me–L-ala-complex proceeded with almost the same rate as the isomerization. The isomerization showed strong solvent dependency; it was fast in a hydrogen-bonding solvent, but was quite slow in a weak- or nonhydrogen-bonding solvent. On the basis of these facts, proton-assisted and/or hydrogen-bonding solvent-assisted intramolecular mechanism *via* an intermediate is proposed, in which the Schiff base takes a planar configuration and the amino acid coordinates as a unidentate ligand with its carboxylate group.

Many studies have been directed toward the synthesis and the first order asymmetric transformation of Co(N$_4$)-complexes with a chiral amino acid, where (N$_4$) denotes a tetramine ligand such as (en)$_2$ and trien.[1–4] However, there are only a few studies for detailed isomerization mechanism among the diastereoisomers of these complexes.[5,6] This may be due to the inertness of Co(N$_4$)-complexes: charcoal is usually needed as a catalyst to promote the isomerization. On the other hand, we have recently found that cobalt(III) complexes containing a sal$_2$en-type Schiff base and L-amino acid, β_2-[Co(Schiff base)(L-aa)], easily isomerize in methanol to establish the equilibrium between Δ_L-β_2- and Λ_L-β_2-isomers.[7–12] This reaction is very interesting because the isomerization is quite fast as compared with that of Co(N$_4$)-complexes.

In order to elucidate the isomerization mechanism and the origin of the isomerization lability of cobalt(III)–Schiff base complexes, the isomerization kinetics for β_2-[Co(α-Me-sal$_2$en)(L-aa)] was studied.[13]

Experimental

Materials. The complex β_2-[Co(α-Me-sal$_2$en)(L-aa)] was prepared as previously reported.[7,9,10] The 1 : 1 mixture of Δ_L- and Λ_L-β_2-isomers of L-met-complex was obtained by the addition of a large excess of water to the methanol solution (*ca.* 1 M, 1 M = 1 mol dm^{-3}) of Λ_L-β_2-[Co(α-Me-sal$_2$en)(L-met)].[7] Found: C, 53.32; H, 5.78; N, 8.01%. Calcd for $CoC_{23}H_{28}N_3O_4S \cdot H_2O$: C, 53.18; H, 5.82; N, 8.09%. $[M]^{25}_{435} = +600°$ (soon after dissolution in methanol, $c = 1.0 \times 10^{-3}$ M). $[M]^{25}_{435} = -15400°$ (under equilibrium conditions in methanol). ^{1}H NMR: δ 2.67 (6H, S, CH_3–C=N), δ 1.85, 1.75 (3H, two S with equal intensity, –S–CH_3) (soon after dissolution in $CDCl_3$ + CD_3OD (8 : 1 in volume)).

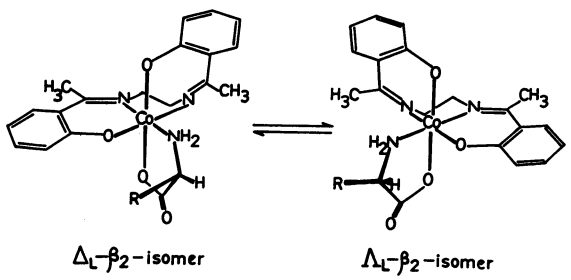

Fig. 1. Structures of two isomers of β_2-[Co(α-Me-sal$_2$en)-(L-aa)].

Reagent grade organic solvents were used after distillation. The other chemicals were reagent grade and used without further purification.

Kinetic Procedure. The complexes (2.5×10^{-5} mol) were dissolved in a given solvent (25 cm^3) at a given temperature, and, whenever necessary, other reagents were added. The mutarotation at 435 nm of the solutions was measured with 1 cm cell by the use of a thermostated cell-holder (the deviation of the solution temperature = ±0.1 °C). When the mutarotation was very slow, the solutions were placed in a thermostat bath, and picked up one by one at proper intervales. The rate constant was calculated from the slope of plots of $\ln(a_\infty - a_t)$ *vs.* time, where a_∞ and a_t are the optical rotations under the equilibrium conditions and at time *t*, respectively (see Appendix).

Measurements. The optical rotation at 435 nm was measured on a JASCO DIP-140 Polarimeter. The electronic absorption and circular dichroism spectra were recorded on a Hitachi 200-10 Spectrometer and a JASCO J-20 Spectropolarimeter, respectively. The ^{1}H NMR spectra were measured on a Hitachi R-20 Spectrometer.

Results and Discussion

The Kinetics of Isomerization of β_2-[Co(α-Me-sal$_2$en)(L-aa)] in Methanol. The isomerization rate of β_2-[Co(Schiff base)(L-aa)] complexes has been observed to depend strongly on the kind of the Schiff base ligand.[14] For *N,N'*-ethylenebis(4-phenyl-4-oxo-2-butaniminato) or *N,N'*-ethylenebis(α-phenyl-5-methylsalicylideneaminato), the isomerization is too fast to be

TABLE 1. ISOMERIC RATIOS AND ISOMERIZATION RATE CONSTANTS OF β_2-[Co(α-Me-sal$_2$en) (L-aa)]

L-aa	Temp/°C	Isomeric ratio ([Λ_L]/[Δ_L])		Rate constant in methanol		
		In crystals	In methanol	k_{obsd}/s^{-1} d)	k_{+1}/s^{-1}	k_{-1}/s^{-1}
L-phe	15		5.56	4.28×10^{-4}	3.63×10^{-4}	6.52×10^{-5}
	25	1	4.80	1.56×10^{-3}	1.29×10^{-3}	2.69×10^{-4}
	35		4.59	4.98×10^{-3}	4.09×10^{-3}	8.91×10^{-4}
L-met	25	1	1.65	1.37×10^{-3}	8.53×10^{-4}	5.17×10^{-4}
L-met	15		1.78	3.50×10^{-4}	2.24×10^{-4}	1.26×10^{-4}
	25	a)	1.65	1.36×10^{-3}	8.47×10^{-4}	5.13×10^{-4}
	35		1.58	4.80×10^{-3}	2.94×10^{-3}	1.86×10^{-3}
L-ile	15		2.78	4.21×10^{-4}	3.10×10^{-4}	1.11×10^{-4}
	25	a)	2.55	1.53×10^{-3}	1.10×10^{-3}	4.30×10^{-4}
	35		2.41	4.98×10^{-3}	3.52×10^{-3}	1.46×10^{-3}
L-por	25		b)	9.05×10^{-5}		9.05×10^{-5}
	35	1	b)	3.18×10^{-4}		3.18×10^{-4}
	45		b)	1.11×10^{-3}		1.11×10^{-3}
N-Bz-L-ala	25		c)	4.40×10^{-4}	4.40×10^{-4}	
	35	2	c)	1.80×10^{-3}	1.80×10^{-3}	
	45		c)	6.00×10^{-3}	6.00×10^{-3}	
N-Me-L-ala	25	a)	27.6	5.37×10^{-5}	5.18×10^{-5}	1.88×10^{-6}
N-Me-L-ala	25		27.6	5.36×10^{-5}	5.17×10^{-5}	1.90×10^{-6}
	35	1	24.4	2.33×10^{-4}	2.24×10^{-4}	9.10×10^{-6}
	48		22.9	1.14×10^{-3}	1.09×10^{-3}	4.77×10^{-5}

a) Pure Λ_L-isomer. b) Λ_L-isomer is almost 100%. c) Λ_L-isomer is almost 100%. d) Standard deviations are ±0.03.

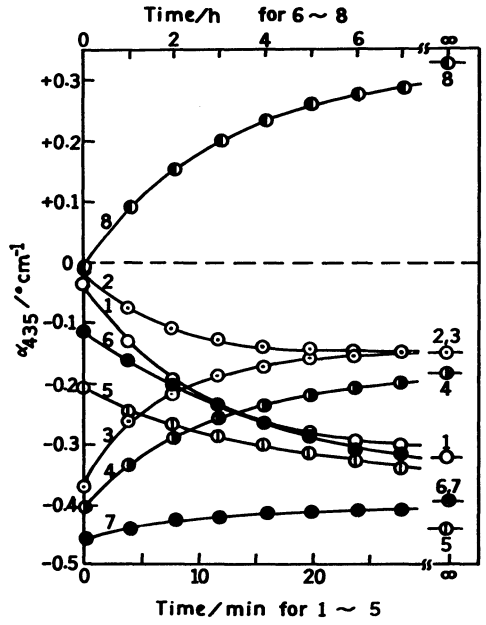

Fig. 2. Mutarotations of β_2-[Co(α-Me-sal$_2$en)(L-aa)] in methanol at 25 °C.
Complex concentration = 1.0×10^{-3} M. Cell length = 1.0 cm. 1: L-phe, 2: L-met (1 : 1 mixture), 3: L-met (pure Λ_L-β_2-isomer), 4: L-ile, 5: *N*-Bz-L-ala, 6: *N*-Me-L-ala (1 : 1 mixture), 7: *N*-Me-L-ala (pure Λ_L-β_2-isomer), 8: L-pro.

followed with a polarimeter at 25 °C in methanol, but for *N*,*N*'-ethylenebis(5, 5, 5-trifluoro-4-oxo-2-pentaniminato), the reaction is very slow. Since the Co(α-Me-sal$_2$en)-complex isomerizes with a suitable rate for rotational measurements, it was selected as the representative complex in this work.

The isomeric ratios of the complexes in the solid state are listed in Table 1. The complexes β_2-[Co(α-Me-sal$_2$en)(L-aa)] are isolated usually as the 1 : 1 mixture of Δ_L- and Λ_L-isomers or as the pure Λ_L-isomer. This is mainly due to the solubilities of the complexes. When the complexes were dissolved in methanol (Fig. 2), the solutions exhibited a mutarotation with a minus sign at 435 nm under the equilibrium conditions except for L-pro-complex. For L-pro-complex, the rotation has a plus sign. As has been reported previously,[7,9,10] during the mutarotation the absorption spectra do not show any obvious change, whereas the CD spectra an isosbestic point at about 470 nm. On the basis of the AB, CD, and ^{1}H NMR spectral studies and the X-ray analysis,[8,11] the following facts has been verified: 1) the mutarotation corresponds to the isomerization between $(+)_{435}$-Δ_L-β_2- and $(-)_{435}$-Λ_L-β_2-diastereoisomers, and neither decomposition nor the other reaction occurs in methanol; 2) the Λ_L-β_2-isomer predominates under the equilibrium conditions except for the L-pro-complex, for which the Λ_L-β_2-isomer is predominant.

In Fig. 2 both the 1 : 1 mixture and the pure Λ_L-β_2-isomer of the L-met-complex reached to the same optical rotation under the equilibrium conditions of mutarotation. A similar behaviour to the L-met-complex was observed for the *N*-Me-L-ala-complex. These facts clearly indicate that the present isomerization reaction belongs to a reversible one. In Fig. 3 the plots of $\ln(\alpha_\infty - \alpha_t)$ *vs.* time gave a straight line up to at least 90% completion of the isomerization, and the slopes were found to be independent of the complex concentration. Hence, the rate formula is expressed as follows:

$$\text{Rate} = k_{obsd}[\text{complex}], \quad (1)$$

Table 2. Activation parameters of isomerization of β_2-[α-Me-sal$_2$en) (L-aa)] in methanol

L-aa	pK_{a_1}	pK_{a_2}	$\Delta H^{\ddagger}$ (k_{+1}) kJ mol^{-1}	$\Delta S^{\ddagger}$ (k_{+1}) J K^{-1} mol^{-1}	$\Delta H^{\ddagger}$ (k_{-1}) kJ mol^{-1}	$\Delta S^{\ddagger}$ (k_{-1}) J K^{-1} mol^{-1}
L-phe	2.21	9.18	86.6±3.3	−9.6±11.1	94.1±4.2	+2.5±14.6
L-met	2.28	9.34	92.5±5.9	+6.7±12.6	96.7±5.0	+15.1±10.5
L-ile	2.32	9.76	87.5±3.3	−8.0±11.0	92.5±4.2	+1.3±14.2
N-Bz-L-ala			100.4±8.3	+28.0±21.6		
N-Me-L-ala	2.18[a]	10.02[a]	102.9±6.7	+18.4±15.9	109.2±6.7	+12.1±15.9
L-pro	2.02	10.52			96.2±5.0	0.0±10.9

a) Value of *N*-methylglycine.

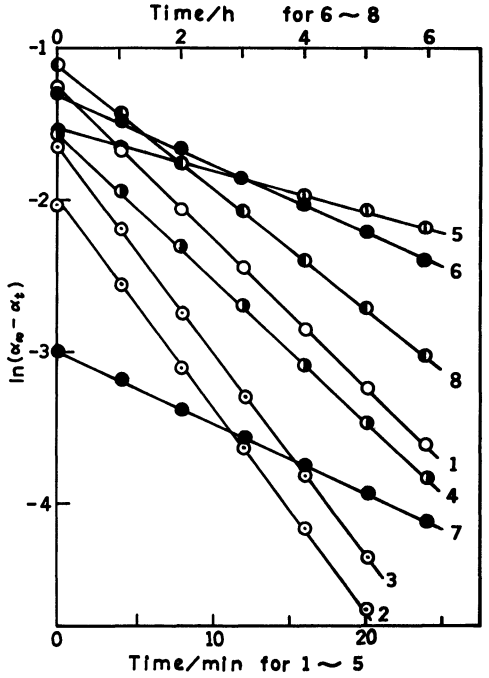

Fig. 3. Plots of ln ($\alpha_\infty - \alpha_t$) *vs.* time for mutarotations of β_2-[Co(α-Me-sal$_2$en)(L-aa)] in methanol at 25 °C.
1: L-phe, 2: L-met (1 : 1 mixture), 3: L-met (pure Λ_L-β_2-isomer), 4: L-ile, 5: *N*-Bz-L-ala, 6: *N*-Me-L-ala (1 : 1 mixture), 7: *N*-Me-L-ala (pure Λ_L-β_2-isomer), 8: L-pro.

where k_{obsd} represents the observed first order rate constant. The k_{obsd} values are summarized in Table 1. When the isomerization rate constant from Λ_L- to Λ_L-β_2-isomers is written as k_{+1}, and that from Λ_L- to Δ_L-β_2-isomers as k_{-1}, the k_{obsd} value is related to k_{+1} and k_{-1} by Eq. 2 as is shown in Appendix:

$$k_{obsd} = [(K+1)/K]k_{+1} = (K+1)k_{-1}, \quad (2)$$

where K denotes the isomeric ratio between Λ_L- and Δ_L-β_2-isomers, $K=[\Lambda_L\text{-}\beta_2\text{-isomer}]/[\Delta_L\text{-}\beta_2\text{-isomer}]$, under the equilibrium conditions. Equation 2 was confirmed from the fact that the k_{obsd} values for the 1 : 1 mixture and the pure Λ_L-β_2-isomer are identical in the cases of the L-met- and *N*-Me-L-ala-complexes. The K values were estimated from the CD intensity of the complexes as previously reported.[12] The K values and the k_{+1}, k_{-1} values thus obtained are summarized in Table 1.

The activation parameters were calculated from the temperature dependence of k_{+1} and k_{-1} values, and are given in Table 2. Table 2 indicates that 1) the activation enthalpy becomes generally large when the pK_{a_2} value of L-amino acid is large, and 2) the activation entropies of all the complexes are very small with plus or minus sign, suggesting similar isomerization mechanisms.

Effects of Water, Salts, Acids, Bases, and Amino Acids on the Isomerization in Methanol. The water content of the methanol solution gave no significant effect on the observed isomerization rates of all the complexes in the range from 1×10^{-3} to 1×10^{-1} M (complex concentration$=1\times10^{-3}$ M). However, when a large excess of water (5 M) was added to the methanol solution, the isomerization became somewhat faster (about 15%). This is due to the faster isomerization in water than in methanol (*vide infra*). $NaClO_4$ and CH_3COONa also gave no effect on the isomerization rates in the range from 1×10^{-3} to 2×10^{-1} M. This fact indicates that effects of the ionic strength is negligibly small.

The relationship between acetic acid concentration and the observed isomerization rate is illustrated in Fig. 4. The diagrams are linear at least up to 3×10^{-1} M of acetic acid for L-phe-, L-met-, L-ile-, and L-pro-complexes, and up to 3×10^{-2} M of acetic acid for *N*-Bz-L-ala- and *N*-Me-L-ala-complexes. The intercepts coincided with the k_{obsd} value in the absence of acetic acid. Hence, the k_{obsd} is expressed by

$$k_{obsd} = k_{obsd}^{MeOH} + k_{obsd}^{AcH}[CH_3COOH]. \quad (3)$$

The values of k_{obsd}^{AcH} are listed in Table 3. Acetic acid is a weak protic acid, and its catalytic effect on the isomerization is linear to the acetic acid concentration as observed above. Thus, the effect may be caused by the action of the acetic acid molecules.

When a large excess of acetic acid was added, the partial decomposition of the complexes occurred. The decomposition was confirmed from the changes of optical rotation and absorption spectra. Since the plots of $\ln(\alpha_\infty - \alpha_t)$ *vs.* time for the partial decomposition give a linear relation, the observed decomposition rates are listed in Table 3. The degree of decomposition increases in the folllowing order:

L-phe < L-pro = L-met < L-ile < *N*-Bz-L-ala < *N*-Me-L-ala.

In the presence of trichloroacetic acid, all the complexes isomerized quite rapidly, followed by decomposition to produce brown complexes with the loss of optical rotation, even in 1×10^{-2} M. The isomerization was too fast to follow. The decomposition rates are summarized in Table 3. Since trichloroacetic acid is a strong protic acid, its effect may be due to proton. In fact, the isomerization and decomposition were very fast

TABLE 3. VALUES OF k_{obsd}^{AcH}, ACID-BASE DECOMPOSITION RATES, AND SUBSTITUTION RATES OF AMINO ACIDS OF β_2-[Co(α-Me-sal$_2$en) (L-aa)] IN METHANOL AT 25 °C

L-aa	k_{obsd}^{AcH} / M^{-1} s^{-1}	Observed decomposition rate constants/s^{-1}				Substitution rate constants/s^{-1} with phenylalanine[b] (2×10^{-2} M)
		CH_3COOH (1 M)	Cl_3CCOOH (1×10^{-2} M)	KOH (1 M)	Pyridine (1 M)	
L-phe	2.30×10^{-2}	4.9×10^{-3} (10%)[a]	9.3×10^{-3}	6.8×10^{-4}	2.5×10^{-5}	1.0×10^{-6}
L-met	1.38×10^{-2}	2.2×10^{-2} (13%)[a]	2.2×10^{-2}	1.3×10^{-3}	2.4×10^{-5}	2.0×10^{-6}
L-ile	1.11×10^{-2}	1.3×10^{-2} (20%)[a]	1.9×10^{-2}	7.9×10^{-4}	8.3×10^{-4}	2.3×10^{-6}
N-Bz-L-ala	4.75×10^{-3}	6.1×10^{-4} (35%)[a]	3.1×10^{-3}	2.3×10^{-5}	1.1×10^{-5}	7.5×10^{-6}
N-Me-L-ala	2.36×10^{-2}	1.3×10^{-3} (42%)[a]	7.8×10^{-3}	4.7×10^{-4}	1.7×10^{-5}	2.7×10^{-6}
L-pro	8.05×10^{-3}	3.5×10^{-4} (12%)[a]	1.7×10^{-3}	3.1×10^{-5}	1.4×10^{-5}	4.4×10^{-7} (45%)[c]

a) Degree of decomoposition. b) Observed value. c) Partial substitution.

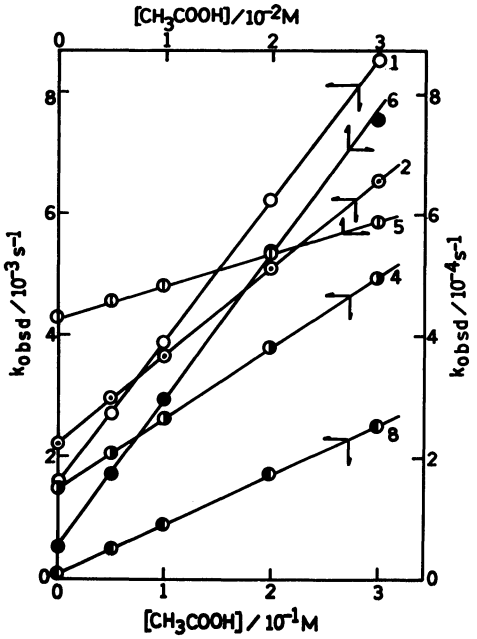

Fig. 4. Influence of acetic acid in methanol at 25 °C. 1: L-phe, 2: L-met (1 : 1 mixture), 4: L-ile, 5: *N*-Bz-L-ala, 6: *N*-Me-L-ala (1 : 1 mixture), 8: L-pro.

in the presence of HCl as well.

Bases such as KOH and pyridine gave no catalytic effect on the isomerization for KOH 1×10^{-3}—1×10^{-2} M, and for pyridine 1×10^{-3}—5×10^{-2} M except for *N*-Bz-L-ala- and *N*-Me-L-ala-complexes. For *N*-alkyl-L-ala-complexes partial decomposition occurred even in a low concentration of a base (*ca.* 2×10^{-3} M of the base). When a large excess of bases was added, all the complexes except for the L-pro-complex decomposed to form *trans*-[Co(α-Me-sal$_2$en)(base)$_2$]$^{\pm n}$. For the L-pro-complex only partial decomposition occurred, which was confirmed by the loss of optical rotation and spectral change. Since the plots of $\ln(a_\infty - a_t)$ *vs.* time gave a linear relation, the estimated decomposition rates are listed in Table 3.

The sensitivity of the base decomposition was observed to increase in the following order of amino acids:

L-pro < L-phe < L-met < L-ile < *N*-Bz-L-ala < *N*-Me-L-ala.

This order is almost the same as that for the decomposition under the acidic conditions.

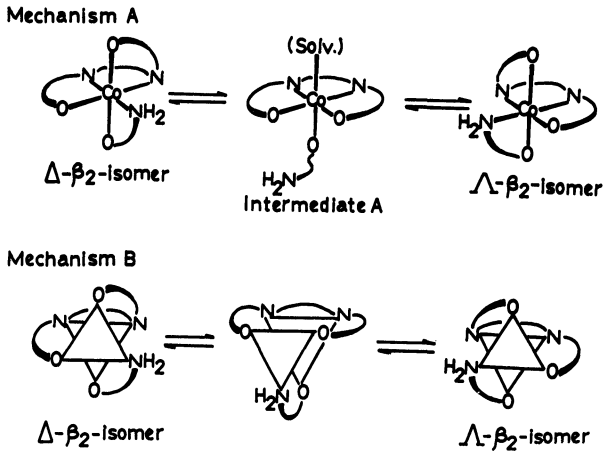

Fig. 5. Sterically possible isomerization mechanisms.

Free amino acids such as phenylalanine and proline gave no significant effect on the isomerization of all the complexes. However, when the complex solutions containing free amino acids were allowed to stand for a long time, substitution of the coordinated amino acidate ion occurred. Since the plots of $\ln(a_\infty - a_t)$ *vs.* time for the substitution with D-phenylalanine (L-phenylalanine in the case of L-pro-complex) gave a linear relation, the observed substitution rate can be estimated, and the first order rate constants observed are listed in Table 3. The substitution is much slower than the isomerization in all the complexes, indicating that the isomerization proceeds *via* an intramolecular mechanism.

From these results, it can be pointed out that the intramolecular isomerization mechanism of all the complexes should be quite similar because of their similar properties.

Isomerization Mechanism. A β_2-[Co(Schiff base)-(L-aa)] complex is composed of one quadridentate and one bidentate ligands. Hence, its intramolecular isomerization is sterically restricted as compared with that of tris(bidentate) complexes. Molecular models indicate that only two mechanisms in Fig. 5 are sterically possible, and a bond breaking mechanism between cobalt(III) and a carboxylate group of the amino acidate is sterically impossible. Mechanism **A** in Fig. 5 is a Co–N bond breaking mechanism with an intermediate in which the quadridentate Schiff base takes a planar configuration, and the amino acidate coordinates as a unidentate ligand with its carboxylate group. Mecha-

Table 4. Isomerization rates and H-D exchange rates of β_2-[Co(α-Me-sal$_2$en) (*N*-Me-L-ala)] in the mixed solvent of methanol and chloroform (1:4 in volume) at 35 °C

Isomer ratio of starting complex	Isomerization			H-D Exchange
	k_{obsd}/s^{-1}	k_{+1}/s^{-1}	k_{-1}/s^{-1}	k_{obsd}[a)]$/s^{-1}$
1:1 mixture of Δ_L- and Λ_L-isomers	1.10×10^{-4}	1.06×10^{-4}	4.33×10^{-6}	$(1.0\pm0.3)\times10^{-4}$
Pure Λ_L-isomer				$(4.3\pm0.2)\times10^{-6}$

a) Value in $CD_3OD+CDCl_3$ (1:4).

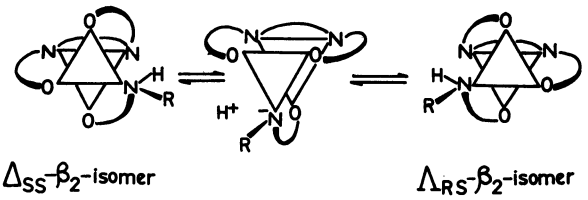

Fig. 6. *R-S* inversion of an asymmetric nitrogen atom in the twist mechanism.

nism **B** is a twist mechanism without a Co^{III}–ligand bond breaking. Since the activation enthalpy is correlated with pK_{a_2} value of the amino acid and the ionic strength effect on the isomerization is negligibly small, the Co–O bond breaking mechanism can safely be omitted, but it is quite difficult to distinguish between Mechanisms **A** and **B**.

In the case of *N*-alkyl–L-ala-complexes, however, Mechanism **B** is unlikely, because, 1) the *N*-alkyl–L-ala-complexes have an asymmetric nitrogen atom at the amino group.*** Therefore, not only the inversion between Δ- and Λ-configurations but also the inversion between *R*- and *S*-configurations of the asymmetric nitrogen atom are required in the isomerization between Δ_{SS}- and Λ_{RS}-β_2-isomers;[15] 2) the *R–S* inversion is impossible in Mechanism **B** without deprotonation of an N–H proton (Fig. 6).

If the deprotonation occurs during the isomerization, the H–D exchange rate of the N–H proton should be 10^2—10^3 times or more faster than the isomerization rate in Mechanism **B**.[16] On the other hand, in Mechanism **A**, the H–D exchange rate is expected to be comparable to the isomerization rate of the complex, because Mechanism **A** involves an intermediate in which the amino group is free from the cobalt(III) ion, and the H–D exchange rate of a free amino group is usually very fast. On the basis of these expectations, the H–D exchange rates for the *N*-Me–L-ala-complex were measured. Since the complex was hardly soluble in CD_3OD, a mixed solvent of CD_3OD and $CDCl_3$ (1 : 4 in volume) was used. The ^1H NMR spectral variation was shown in Fig. 5 of Ref. 10, and the ln-plots are shown in Fig. 7. The diagrams are linear up to at least 40% completion of the H–D exchange for the 1 : 1 mixture of Δ_{SS}- and Λ_{RS}-β_2-isomers and up to at least 80% completion for the pure Λ_{RS}-β_2-isomer. The first order H–D exchange rate constants thus obtained

*** The $(+)_{435}$-isomer of *N*-alkyl–L-ala-complexes used here corresponds to the Δ_{SS}-β_2-isomer, and the $(-)_{435}$-isomer to the Λ_{RS}-β_2-isomer.[10,15]

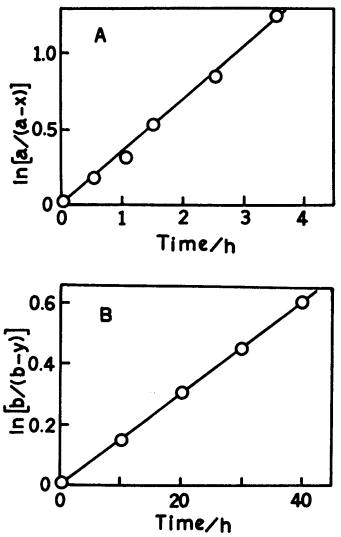

Fig. 7. ln-plots for H–D exchange of *N*-Me–L-ala-complex in mixed solvent of CD_3OD and $CDCl_3$ (1 : 4 in volume) at 35 °C.
A=1 : 1 mixture. B=Pure Λ_L-β_2-isomer. a=Initial concentration of Δ_L-β_2-isomer. x=Concentration of deuterated isomer at time *t*. b=Initial concentration of Λ_L-β_2-isomer. y=Concentration of deuterated isomer at time *t*.

are listed in Table 4. The isomerization rate constants in the mixed solvent of CH_3OH and $CHCl_3$ (1 : 4 in volume) were estimated from the mutarotation at 435 nm of the complex, and are given in Table 4.

Table 4 indicates that 1) the H–D exchange rate for the 1 : 1 mixture is almost the same as the isomerization rate (k_{+1}) from Δ_{SS}- to Λ_{RS}-β_2-isomers; 2) the H–D exchange rate for the pure Λ_{RS}-β_2-isomer is almost identical with the isomerization rate (k_{-1}) from Λ_{RS}- to Δ_{SS}-β_2-isomers. Thus, it can be concluded that Mechanism **A** is most probable as the isomerization mechanism of the *N*-Me–L-ala-complex. Since there is no reason that other amino acidato complexes take a different isomerization mechanism from that of the *N*-Me–L-ala-complex, all the complexes investigated here are concluded to isomerize *via* Mechanism **A**.

It has been observed that the formation of β_2-[Co(α-Me-sal$_2$en)(L-aa)] complexes from *trans*-[Co(α-Me-sal$_2$en)(O_2)] and L-amino acid proceeds *via* an intermediate similar to **A** in Fig. 5, and it is much faster than the isomerization of β_2-[Co(α-Me-sal$_2$en)(L-aa)].[9] These facts suggest that the formation of Δ_L- and Λ_L-β_2-isomers from Intermediate **A** in Fig. 5 is much faster than the isomerization. Accordingly, the rate deter-

TABLE 5. OBSERVED ISOMERIZATION RATES (k_{obsd}/s^{-1}) IN VARIOUS SOLVENTS AT 23.5 °C

L-aa-Complex	CH_3COOH[b]	H_2O	*m*-cresol	MeOH	EtOH	*n*-PrOH
L-ile	2.0×10^{-2}	5.0×10^{-3}	3.8×10^{-3}	1.2×10^{-3}	5.2×10^{-4}	4.4×10^{-4}
(λ/nm)[a]	(579)	(587)	(587)	(584)	(582)	(580)
L-phe	2.0×10^{-2}	3.1×10^{-3}[c]	4.6×10^{-3}	1.4×10^{-3}	1.1×10^{-3}	3.8×10^{-4}
(λ/nm)[a]	(578)	(585)[c]	(587)	(583)	(582)	(580)
L-aa-complex	*n*-BuOH	*i*-BuOH	*s*-BuOH	Aniline	Acetone, DMF, DMSO, THF, 1,4-Dioxane, Pyridine	
L-ile	4.4×10^{-4}	2.3×10^{-4}	7.3×10^{-5}	1.8×10^{-5}	Very slow	
(λ/nm)[a]	(580)	(580)	(578)	(577)	(575—570)	
L-phe	2.3×10^{-4}	2.5×10^{-4}	1.5×10^{-4}	2.3×10^{-5}	Very slow	
(λ/nm)[a]	(580)	(580)	(577)	(576)	(577—574)	

a) First absorption maximum. b) A small amount of decomposition of complex occurred in CH_3COOH. c) Value in mixed solvent of H_2O and MeOH (2:3 in volume).

mining step of the isomerization is thought to be the formation process of *trans*-Intermediate **A** from Δ_L- and Λ_L-β_2-isomers.

Effect of Solvents on the Isomerization. In order to get further information, isomerizations in various solvents were investigated. The k_{obsd} values for the representative complexes are summarized in Table 5. From these measurements, the following tendencies were found: 1) the isomerization becomes faster in the following order of solvents: acetone, DMF, DMSO, THF, 1,4-dioxane, pyridine<aniline<BuOH<PrOH <EtOH<MeOH < *o*-cresol < H_2O < CH_3COOH; 2) the isomerization in acetone, DMF, DMSO, THF, 1,4-dioxane, and pyridine is quite slow or no isomerization occurs; 3) no decomposition of the complex occurred in pyridine and aniline, although the decomposition of the complex occurred in the mixed solvents of methanol and pyridine or aniline.

The isomerization is faster in the solvents having a hydrogen bonding proton than in weak- or nonhydrogen bonding solvents. Thus, hydrogen bonding solvents clearly assist the isomerization. As has been observed previously,[12] the hydrogen bonding occurs mainly at the phenolic oxygen atoms of a Schiff base ligand, and when the hydrogen bonding is stronger, the first absorption band of the complexes shifts to the lower energy side. This shift is caused by the lowering of the coordination ability of phenolic oxygen atoms due to the hydrogen bonding. A similar shift of the first absorption band was also observed in the present study, and when the shift was larger, the isomerization was faster. Therefore, it can be concluded that 1) the hydrogen bonding at the phenolic oxygen atoms of the Schiff base ligand assists the isomerization, and 2) the stronger the hydrogen bonding is, the more labile the isomerization is.

For the formation of Intermediate **A** in Fig. 5 from Δ_L- and Λ_L-β_2-isomers, not only the bond breaking between the cobalt(III) atom and the amino group of amino acidate ion but also the rearrengement of the coordinated Schiff base ligand from β- to *trans*-configurations is needed. And, for the rearrangement of the Schiff base ligand, a loosening of the Co^{III}–phenolic oxygen bond is necessary. Since the hydrogen bonding solvents are thought to act to make the Co^{III}–phenolic oxygen bond more loose, their effects may be to assist rearrengement of the Schiff base ligand. We think that the catalytic effect of protic acid should be similar to that of hydrogen bonding solvents, because it has been known that the protonation occurs at the phenolic oxygen atoms.[17]

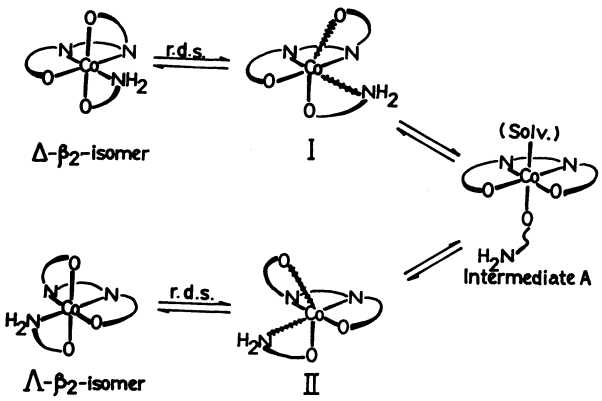

Fig. 8. Proposed isomerization mechanism.

On the basis of these results and above discussion, we propose an isomerization mechanism shown in Fig. 8. In Fig. 8, we assummed that 1) the rate controlling step is the formation of activated complexes **I** and **II**, and 2) the activated complexes take a structure in which two bonds, that between cobalt(III) and the amino group, and that between cobalt(III) and one of the phenolic oxygen atoms, are stretched.

The authors wish to express their deep thanks to Professor J. C. Bailar Jr., of University of Illinois for his encouragement.

Appendix

Derivation of the Rate Equation. When the isomerization rate constant from Δ_L- to Λ_L-isomers is written as k_{+1} and that from Λ_L- to Δ_L-isomers as k_{-1}, they can be expressed as follows:

$$k_{+1} = ([\Lambda_L]_\infty/at)\ln\{[\Lambda_L]_\infty/([\Lambda_L]_\infty-[\Lambda_L]_t\}, \quad (1)$$

$$k_{-1} = ([\Delta_L]_\infty/at)\ln\{[\Delta_L]_\infty/([\Delta_L]_\infty-[\Delta_L]_t)\}, \quad (2)$$

where, $[\Lambda_L]_t$, $[\Delta_L]_t$ and $[\Lambda_L]_\infty$, $[\Delta_L]_\infty$ represent the concentrations of Λ_L- and Δ_L-isomers at the time t, and at the equilibrium conditions, respectively, and a denotes the total complex

concentration. When the molar rotations of Λ_L- and Δ_L-isomers are expressed by $[M]_{\Lambda L}$ and $[M]_{\Delta L}$, respectively, the observed rotation (α_t) at the time t can be written as follows:

$$\begin{aligned}\alpha_t &= [M]_{\Lambda L}[\Lambda_L]_t d + [M]_{\Delta L}[\Delta_L]_t d \\ &= ([M]_{\Lambda L}-[M]_{\Delta L})[\Lambda_L]_t d + [M]_{\Delta L} ad \\ &= ([M]_{\Delta L}-[M]_{\Lambda L})[\Delta_L]_t d + [M]_{\Lambda L} ad, \end{aligned} \quad (3)$$

where, d is the cell length.

From Eq. 3, the following relations can be derived:

$$[\Lambda_L]_t = (\alpha_t-[M]_{\Delta L} ad)/([M]_{\Lambda L}-[M]_{\Delta L})d, \quad (4)$$

$$[\Delta_L]_t = (\alpha_t-[M]_{\Lambda L} ad)/([M]_{\Delta L}-[M]_{\Lambda L})d. \quad (5)$$

Similarly, $[\Lambda_L]_\infty$ and $[\Delta_L]_\infty$ can be written as follows:

$$[\Lambda_L]_\infty = (\alpha_\infty-[M]_{\Delta L} ad)/([M]_{\Lambda L}-[M]_{\Delta L})d, \quad (6)$$

$$[\Delta_L]_\infty = (\alpha_\infty-[M]_{\Lambda L} ad)/([M]_{\Delta L}-[M]_{\Lambda L})d. \quad (7)$$

When the isomeric ratio under the equilibrium conditions is expressed by

$$K = [\Lambda_L]_\infty/[\Delta_L]_\infty = k_{+1}/k_{-1}, \quad (8)$$

k_{+1} and k_{-1} in Eqs. 1 and 2 can be written as follows by the use of relations in Eqs. 4—8:

$$\begin{aligned} k_{+1} &= [K/(K+1)t] \\ &\times \ln\{[K/(K+1)]([M]_{\Lambda L}-[M]_{\Delta L})ad/(\alpha_\infty-\alpha_t)\}, \end{aligned} \quad (9)$$

$$\begin{aligned} k_{-1} &= [1/(K+1)t] \\ &\times \ln\{[1/(K+1)]([M]_{\Delta L}-[M]_{\Lambda L})ad/(\alpha_\infty-\alpha_t)\}. \end{aligned} \quad (10)$$

By transforming the Eqs. 9 and 10, Eqs. 11 and 12 are obtained:

$$\begin{aligned} \ln(\alpha_\infty-\alpha_t) &= -[(K+1)/K]k_{+1}t \\ &+ \ln\{[K/(K+1)]([M]_{\Lambda L}-[M]_{\Delta L})ad\}, \end{aligned} \quad (11)$$

$$\begin{aligned} \ln(\alpha_\infty-\alpha_t) &= -(K+1)k_{-1}t \\ &+ \ln\{[1/(K+1)]([M]_{\Delta L}-[M]_{\Lambda L})ad\}. \end{aligned} \quad (12)$$

When the values of $-[(K+1)/K]k_{+1}$ and $-(K+1)k_{-1}$ are designated as $k^{\Delta\to\Lambda}_{obsd}$ and $k^{\Lambda\to\Delta}_{obsd}$, respectively, the following relationship can be derived by the use of Eq. 8:

$$k^{\Delta\to\Lambda}_{obsd} = -[(K+1)/K]k_{+1} = -(K+1)k_{-1} = k^{\Lambda\to\Delta}_{obsd}. \quad (13)$$

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13) The following abbreviations are used: *N*-Bz-L-ala=*N*-benzyl-L-alaninate, *N*-Me-L-ala=*N*-methyl-L-alaninate, α-Me-sal$_2$en=*N*,*N*′-ethylenebis(α-methylsalicylideneamine) dianion.

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15) In the notation of Λ_{RS}- and Δ_{SS}-isomers, the first sufix (*R* or *S*) represents the configuration of the asymmetric nitrogen atom of the coordinated *N*-alkyl amino acid, and the second sufix (*S*) denotes that of the asymmetric carbon atom of the amino acid.

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