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The Stereochemistry and Reactivity of Metal-Schiff Base Complexes. IV. The Stereoselectivity of *N*,*N*′-Ethylenebis(α-methylsalicylideneaminato)-cobalt(III) Complexes with *N*-Benzyl-L-alanine, *N*-Methyl-L-alanine, and *N*-Benzyl-*N*-Methyl-L-alanine, and the Stereospecificity of (1*S*, 2*S*)-*N*,*N*′-1,2-Cyclohexylenebis(salicylideneaminato)-cobalt(III) Complexes toward *N*-Benzyl-L-alanine

Yuki Fujii,* Makoto Matsufuru, Akira Saito, and Sakiko Tsuchiya

Department of Chemistry, Faculty of Science, Ibaraki University Bunkyo-cho, Mito, Ibaraki 310

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Cobalt(III) complexes containing *N*-alkyl-L-alanine and a Schiff base ligand, β_2-[Co(α-Me-sal$_2$en)(*N*-R-L-ala)] (where α-Me-sal$_2$en represents the dianion of *N*,*N*′-ethylenebis(α-methylsalicylideneamine) and *N*-R-L-ala denotes the anion of titled amino acids), have been prepared. They were characterized by the use of the absorption, circular dichroism, and ^{1}H NMR spectra of the complexes. They showed quite high stereoselectivity for Λ_{RS}-β_2-configuration: 93% for *N*-methyl-L-alanine, and almost 100% for *N*-benzyl-L-alanine and *N*-benzyl-*N*-methyl-L-alanine. The similar β_2-Co(sal$_2$-(*S*,*S*)-chxn) complexes with *N*-benzyl-L- and *N*-benzyl-D-alanines, where sal$_2$-(*S*,*S*)-chxn represents the dianion of (1*S*,2*S*)-*N*,*N*′-1,2-cyclohexylenebis(salicylideneamine), have been synthesized to investigate the stereospecificity of the complex toward *N*-benzyl-L-alanine. It was found that Co(sal$_2$-(*S*,*S*)-chxn) complex reacts with *N*-benzyl-L-alanine in a high stereospecificity (93—94% at the 1:2 reaction molar ratio between the complex and racemic *N*-benzylalanine, and almost 100% at the 1:100 molar ratio). The above phenomena were explained in terms of the thermodynamic selectivity of the complexes.

The steric control of the diastereoisomers of metal complexes is one of the interesting subjects in the stereochemistry of coordination compounds. Many studies have been directed toward the stereoselectivity or stereospecificity of Co(N$_4$) complexes with a chiral amino acid,[1] where (N$_4$) denotes a tetramine ligand such as (en)$_2$ or trien. However, the stereoselectivity of the [Co(N$_4$)(aa)]$^{2+}$ complexes is not so high. For examples, the isomeric ratio of the diastereoisomers, Λ/Δ, at the equilibrium conditions is about 50/50 in [Co(en)$_2$(L-ala)]$^{2+}$,[2] 37/63 in [Co(en)$_2$(L-val)]$^{2+}$,[2] 33/67 in β_2-[Co(trien)(L-pro)]$^{2+}$,[3] and 18/82 in β_2-[Co(pyht)(L-ala)]$^{2+}$.[4] In the case of Co(N$_4$) complexes with *N*-alkyl-L-amino acid, the stereoselectivity is higher than the corresponding L-amino acidato complex; but the Λ/Δ ratio is 80/20, 60/40, or 90/10 in [Co(en)$_2$(*N*-Me-L-ala)]$^{2+}$,[5] β_2-[Co(trien)(*N*-Me-L-ala)]$^{2+}$,[6] or β_2-[Co(2(*S*)10(*S*)-Me$_2$-2,3,2-tet)(*N*-Me-L-ala)]$^{2+}$ [7] respectively.[8]

We have recently found that the stereoselectivity of cobalt(III)–Schiff base complexes with a chiral amino acid, β_2-[Co(Schiff base)(L-aa)], is much higher than that of the corresponding Co(N$_4$) complexes: Λ/Δ is 67/33 in the L-ala complex, 90/10 in the L-phe complex, and about 0/100 in the L-pro complex.[9,10] It is most interesting that the stereoselectivity of the L-pro complex reaches almost 100%. This quite high stereoselectivity of the L-pro complex comes from the strong intramolecular steric repulsion between the Schiff base ligand and the pyrrolidine ring, a kind of *N*-alkyl group, of L-proline. Therefore, in the Co(III)–Schiff base system, it can be expected that the *N*-alkyl amino acidato complex may show quite high stereoselectivity.

In this paper, the preparation and the stereoselectivity of Co(α-Me-sal$_2$en) complexes with *N*-methyl-L-alanine, *N*-benzyl-L-alanine, and *N*-benzyl-*N*-methyl-L-alanine will be studied to establish a quite high steric control of the diastereoisomers of amino acidato cobalt(III) complexes. The optical resolution of amino acids[11] will be used to study the stereospecificity of Co(sal$_2$-(*S*,*S*)-chxn) complex toward *N*-benzyl-L-alanine.

Experimental

Preparation of the Complexes. [Co(α-Me-sal$_2$en)] was prepared by the method of Bigotto *et al.*[12] [Co(sal$_2$-(*S*,*S*)-chxn)] was prepared by the method described in Ref. 13. (1*S*,2*S*)-1,2-Cyclohexanediamine was resolved by the method reported in Ref. 13. *N*-Alkyl amino acids were prepared by the method of Quitt *et al.*[14]

[*Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)*]. *1:1 Mixture of Λ_{RS}- and Δ_{SS}-β_2-Isomers (Complex I)*: *N*-Benzyl-L-alanine (2.1 g, 1.2×10^{-2} mol) in a mixed solvent of water (20 cm^3) and methanol (130 cm^3) was added to a slurry of [Co(α-Me-sal$_2$en)] (3.8 g, 1.1×10^{-2} mol) in chloroform (250 cm^3). The mixture was stirred vigorously in the open air for about 7 min until the color of the solution became green. After a trace amount of unreacted [Co(α-Me-sal$_2$en)] had then been filtered off, water (about 500 cm^3) was added to the filtrate; then the water-soluble component was extracted into water (twice). The chloroform layer was filtered, and petroleum ether (about 2 dm^3) was added to the filtrate to give a green powder. Since the reaction product is labile in isomerization in solution, the above procedure should be carried out as quickly as possible. When the procedure took about 15 min, the green precipitate thus obtained showed the molar rotation at 435 nm of -1.95×10^4° ($c=1.0\times10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution), which corresponds to a 1:2 mixture of Δ_{SS}- and Λ_{RS}-β_2-isomers of [Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)]. Yield, about 4.0 g. Found: C, 62.27; H, 5.61; N, 7.77%. Calcd for $CoC_{28}H_{30}N_3O_4\cdot0.5H_2O$: C, 62.22; H, 5.78; N, 7.77%. The 1:1 mixture was obtained by treating the 1:2 mixture as follows. The 1:2 mixture (0.4 g) was dissolved in chloroform (20 cm^3), and acetone (30 cm^3) was added to it. The solution was concentrated to a small volume with a rotary vacuum evaporator at about 40 °C. The green powder thus obtained was washed with acetone and dried under vacuum. Yield, about 0.2 g. Found: C, 59.30; H,

5.36; N, 7.36%. Calcd for $CoC_{28}H_{30}N_3O_4 \cdot 0.5H_2O \cdot 0.5\ CHCl_3$: C, 59.49; H, 5.52; N, 7.37%. $[M]_{435} = -2.50 \times 10^{3°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution).

Λ_{RS}-β_2-Isomer (Complex II): Method A. One gram of the green powder ($[M]_{435} = -1.95 \times 10^{4°}$) obtained above was dissolved in the mixed solvent of chloroform (30 cm^3) and methanol (30 cm^3). The solution was slowly concentrated to a small volume at room temperature to give green crystals in about an 85% yield. Found: C, 51.48; H, 5.13; N, 6.26%. Calcd for $CoC_{28}H_{30}N_3O_4 \cdot 1.5H_2O \cdot CHCl_3$: C, 51.38; H, 5.05; N, 6.20%. $[M]_{435} = -4.38 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform soon after dissolution).

Method B. *N*-Benzyl-L-alanine (2.1 g, 1.2×10^{-2} mol) in a mixed solvent of water (20 cm^3) and methanol (130 cm^3) was added to the slurry of [Co(α-Me-sal$_2$en)] (3.8 g, 1.1×10^{-2} mol) in chloroform (175 cm^3). The mixture was stirred vigorously in the open air for 2 h. After a trace amount of brownish by-product had been filtered off, the filtrate was slowly concentrated to a small volume. The green crystals thus obtained were recrystallized from a mixed solvent of chloroform and methanol (1:1 in volume). Yield, about 4.2 g. Found: C, 51.67; H, 5.06; N, 6.32%. Calcd for $CoC_{28}H_{30}N_3O_4 \cdot 1.5H_2O \cdot CHCl_3$: C, 51.38; H, 5.06; N, 6.20%. $[M]_{435} = -4.38 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution). When the complex was recrystallized from methanol and water, green crystals without any crystalline chloroform were obtained. Found: C, 58.36; H, 6.10; N, 7.29%. Calcd for $CoC_{28}H_{30}N_3O_4 \cdot 2.5H_2O$: C, 58.33; H, 6.12; N, 7.29%. $[M]_{435} = -4.38 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution).

[Co(α-Me-sal$_2$en)(N-Me-L-ala)]. 1:1 Mixture of Λ_{RS}-β_2-Isomer and Δ-β_2-Isomers (Complex III): *N*-Methyl-L-alanine (1.3 g, 1.2×10^{-2} mol) in a mixed solvent of water (10 cm^3) and methanol (100 cm^3) was added to the slurry of [Co(α-Me-sal$_2$en)] (3.7 g, 1.1×10^{-2} mol) in chloroform (250 cm^3). The mixture was stirred vigorously in the open air for about 10 min, until the solution became green. After a trace amount of unreacted [Co(α-Me-sal$_2$en)] had been filtered off, water (500 cm^3) was added to the filtrate to extract the water-soluble component into water (twice). The chloroform layer thus obtained was filtered, and petroleum ether (about 2 dm^3) was added to the filtrate to give green powder in about a 3.5 g yield. It was dried under vacuum. When this procedure took about 20 min, the green product thus obtained showed $[M]_{435}$ of $-1.44 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution), which corresponds to the 1:2 mixture of Δ- and Λ_{RS}-β_2-isomers. The 1:1 mixture was obtained by the following procedure. The green powder (0.8 g) obtained above was dissolved in chloroform (20 cm^3), and acetone (20 cm^3) was added to it. When the solution was concentrated to a small volume with a rotary vacuum evaporator at about 40 °C, the 1:1 mixture was precipitated as a green powder in about a 40% yield. Found: C, 56.47; H, 5.82; N, 8.95%. Calcd for $CoC_{22}H_{26}N_3O_4 \cdot 0.5H_2O$: C, 56.90; H, 5.86; N, 9.05%. $[M]_{435} = -6.1 \times 10^{3°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution).

Λ_{RS}-β_2-Isomer (Complex IV): One gram of the green powder obtained above (the 1:2 mixture of Δ- and Λ_{RS}-β_2-isomers) was dissolved in a mixed solvent of chloroform (10 cm^3) and methanol (30 cm^3), and the solution was warmed at about 50 °C for 7 h. When petroleum ether (about 300 cm^3) was added to the solution, the Λ_{RS}-β_2-isomer was precipitated as a green powder in about an 80% yield. It was dried under vacuum. Found: C, 56.64; H, 5.91; N, 8.82%. Calcd for $CoC_{22}H_{26}N_3O_4 \cdot 0.5H_2O$: C, 56.90; H, 5.86; N, 9.05%. $[M]_{435} = -4.15 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution).

When the 1:2 mixture obtained above was recrystallized from a mixed solvent of methanol and water, green crystals with $[M]_{435}$ of $-2.40 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform, soon after dissolution) were isolated in an 85% yield. The product corresponds to the 1:4 mixture of Δ- and Λ_{RS}-β_2-isomers. Found: C, 56.72; H, 5.99; N, 8.93%. Calcd for $CoC_{22}H_{26}N_3O_4 \cdot 0.5H_2O$: C, 56.90; H, 5.86; N, 9.05%.

Λ_{RS}-β_2-[Co(α-Me-sal$_2$en)(N-Bz,Me-L-ala)] (Complex V). This complex was prepared by a method similar to that employed for the preparation of Λ_{RS}-β_2-[Co(α-Me-sal$_2$en)-(*N*-Bz-L-ala)] (Complex II), as mentioned above (Method B). When the complex was recrystallized from methanol and water, it was obtained as a green powder in about a 70% yield. Found: C, 60.61; H, 6.22; N, 7.15%. Calcd for $CoC_{29}H_{32}N_3O_4 \cdot 1.5H_2O$: C, 60.84; H, 6.16; N, 7.34%. $[M]_{435} = -4.12 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; chloroform).

Λ_{RS}-β_2-[Co(sal$_2$-(S,S)-chxn)(N-Bz-L-ala)] (Complex VI). *N*-Benzyl-L-alanine (0.27 g, 1.5×10^{-3} mol) in a mixed solvent of water (10 cm^3) and methanol (20 cm^3) was added to a slurry of [Co(sal$_2$-(*S,S*)-chxn)] (0.5 g, 1.3×10^{-3} mol) in methanol (40 cm^3). The mixture was stirred vigorously in the open air for about 1 h to give a green solution. When the green solution was concentrated to a small volume, green crystals were obtained in about an 0.6 g yield. They were recrystallized from methanol. Found: C, 60.70; H, 6.21; N, 7.18%. Calcd for $CoC_{30}H_{32}N_3O_4 \cdot 2H_2O$: C, 60.71; H, 6.11; N, 7.08%. $[M]_{435} = -3.94 \times 10^{4°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; methanol).

1:1.5 Mixture of Δ-$_{RS}$ and Λ_{RR}-β_2-[Co(sal$_2$-(S,S)-chxn)(N-Bz-D-ala)] (Complex VII). This complex was prepared by a method similar to that employed for the preparation of Complex VI. It was obtained as a green powder in about a 70% yield. Found: C, 60.56; H, 6.18; N, 7.27%. Calcd for $CoC_{30}H_{32}N_3O_4 \cdot 2H_2O$: C, 60.71; H, 6.18; N, 7.08%. $[M]_{435} = -8.6 \times 10^{3°}$ ($c = 1.0 \times 10^{-3}$ mol dm^{-3}; methanol).

The Optical Resolution of N-Benzylalanine with [Co(sal$_2$-(S,S)-chxn)]. Racemic *N*-benzylalanine (0.47 g, 2.64×10^{-3} mol) in water (20 cm^3) was added to the slurry of [Co(sal$_2$-(*S,S*)-chxn)] (0.5 g, 1.32×10^{-3} mol) in methanol (100 cm^3). The mixture was stirred in the open air for about 1 h. To the resulting green solution, chloroform (250 cm^3) and water (250 cm^3) were added, and the mixture was shaken for about 5 min. The chloroform layer (A) and the water layer (B) were separated with a separatory funnel. Water (150 cm^3) was added to the chloroform layer (A), and a residual trace amount of *N*-benzylalanine was extracted into the water layer (C). Then, chloroform (150 cm^3) was added to the water layer (B), and a residual trace amount of green complex was extracted into chloroform layer (D). The water solutions (B) and (C) were mixed together, and the resulting mixture was evaporated to dryness. A white precipitate was obtained in about an 0.23 g (98%) yield. The precipitate was confirmed to be *N*-benzylalanine from its ^{1}H NMR spectrum and the elemental analysis. The optical purity of the *N*-benzylalanine was determined to be 93% (D-form) by the method of Ref. 15.

The chloroform solutions (A) and (D) were combined and the mixture was evaporated to dryness. The green powder thus obtained was washed with water. This green powder was then partially dissolved in a mixed solvent of methanol (50 cm^3) and water (100 cm^3), $NaBH_4$ (0.05 g, 1.32×10^{-3} mol) was added to the mixture. The mixture

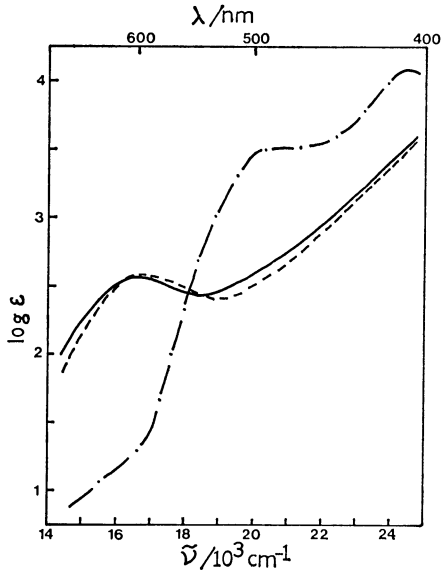

Fig. 1. The absorption spectrum of [Co(α-Me-sal$_2$en)] in $CHCl_3$ under nitrogen (—·—·), and those for the reaction solution of [Co(α-Me-sal$_2$en)] (1.0×10^{-3} mol dm^{-3}) and *N*-benzyl-L-alanine (1.1×10^{-3} mol dm^{-3}) in a mixed solvent of $CHCl_3$ and CH_3OH (4:1) under the air-oxidation conditions. (——): Soon after reaction, (----): at the equilibrium conditions.

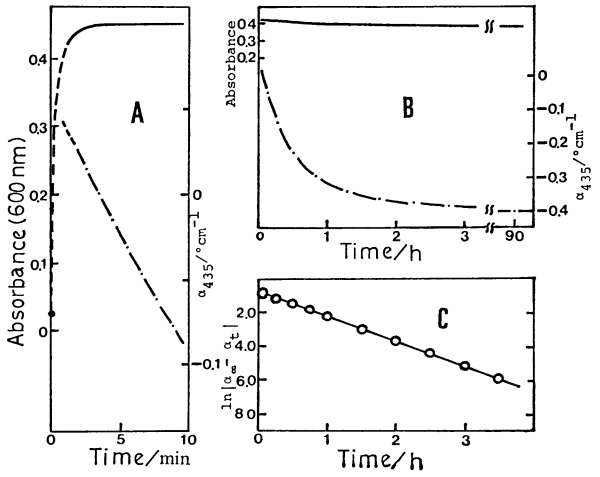

Fig. 2. The time dependences of the absorbance at 600 nm (——) and the rotation at 435 nm (—·—·) for the reaction solution of [Co(α-Me-sal$_2$en)] (1.0×10^{-3} mol dm^{-3}) and *N*-benzyl-L-alanine (1.1×10^{-3} mol dm^{-3}) in a mixed solvent of $CHCl_3$ and CH_3OH (4:1) under the air-oxidation conditions at 35 °C. Cell length = 1.0 cm.
A: Those for the initial reaction, B: those for the full reaction, C plot of $\ln|\alpha_\infty-\alpha_t|$ *vs.* the time.

was stirred vigorously for about 15 min until an orange precipitate of [Co(sal$_2$-(*S*,*S*)-chxn)] appeared. The precipitate was filtered, and water (250 cm^3) and chloroform (250 cm^3) were then added to the filtrate to extract a trace amount of orange complex into the chloroform. The pH of the water solution was adjusted to about 7 with dil HCl, and then the solution was evaporated to dryness to give a white powder. Methanol (150 cm^3) was added to the white precipitate to extract *N*-benzylalanine into methanol. When the methanol solution was concentrated to a small volume, a white precipitate was obtained in about an 0.24 g yield. The precipitate was confirmed to be *N*-benzylalanine, contaminated by a small amount of H_3BO_3 from the ^{1}H NMR spectrum and the elemental analysis. No further purification was attempted. The optical purity of the *N*-benzylalanine was 94% (L-form).[15]

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-140 Digital Polarimeter. The ^{1}H NMR spectra were recorded with a Hitachi R-20 Spectrometer (60 MHz) using TMS as the internal reference at 35 °C.

Results and Discussion

The Reaction of [Co(α-Me-sal$_2$en)] with N-*Alkyl*-L-*alanine, and the Preparation and Properties of* β_2-*[Co(α-Me-sal$_2$en)(*N-*R*-L-*ala)] Complexes.* *1)* β_2-*[Co(α-Me-sal$_2$en)(*N-*Bz*-L-*ala)]*: Figure 1 shows the absorption spectrum of [Co(α-Me-sal$_2$en)] and that of the reaction solution of [Co(α-Me-sal$_2$en)] and *N*-benzyl-L-alanine under air-oxidation conditions. Figure 2 shows the time dependences of the absorbance at 600 nm and the rotation at 435 nm for the reaction solution. The absorbance at 600 nm becomes almost constant within a few minutes after the initiation of the reaction, and the absorption spectrum soon after reaction closely resembles that at the equilibrium conditions. Further, the absorption spectra are very similar to those of the β_2-[Co(α-Me-sal$_2$en)(L-aa)].[8,9,16] Accordingly, it seems that the complexation between [Co(α-Me-sal$_2$en)] and *N*-benzyl-L-alanine proceeds quite rapidly to form β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)]. On the other hand, the rotation at 435 nm of the reaction solution shows a small plus value soon after reaction, but it changes gradually to show a large minus value at the equilibrium conditions. The plot of $\ln|\alpha_\infty-\alpha_t|$ *vs.* the time for the mutarotation gives a straight line, as is shown in Fig. 2. These facts indicate that the reaction produces a mixture of two species: $(+)_{435}$- and $(-)_{435}$-isomers of β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)] complex, and then the $(+)_{435}$-isomer thus formed isomerizes slowly to the $(-)_{435}$-isomer. In fact, as has been mentioned in the Experimental section, from the initial reaction solution, a green powder with a small minus rotation at 435 nm (represented as Complex I) was isolated. From the equilibrium solution, green crystals with a large minus rotation at 435 nm (Complex II) were isolated. Both complexes had the same composition that corresponding to [Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)], and their absorption spectra resemble not only each other but also those of the reaction solution mentioned above. Further, the mutarotation curve for Complex I was very similar to that for the reaction solution: the slopes of the plots of $\ln|\alpha_\infty-\alpha_t|$ *vs.* the time for both mutarotations were the same. Therefore, it can be concluded that [Co(α-Me-sal$_2$en)] reacts with *N*-benzyl-L-alanine quite rapidly to form a mixture of the $(+)_{435}$- and $(-)_{435}$-isomers of β_2-[Co(α-Me-sal$_2$en)-

Table 1. The ^{1}H NMR spectral data of the complexes (δ)[a),d)]

Complex	C-CH_3[c)]	N-CH_3	CH_3-C=N	Others
I[b)]	0.70, 0.82 [1.5]; 1.29, 1.41 [1.5]		2.73 [3]; 2.82 [3]	4.0(HDO), 4.1(multiplet of N-C$\underline{H}_2$-ϕ), 3.8—4.6 (broad multiplet of N-CH_2-CH_2-N), 6.4—7.8 (multiplet of phenyl protons)
II[b)]	0.70, 0.82 [3]		2.73 [3]; 2.82 [3]	4.0(HDO), 4.1(multiplet of N-C$\underline{H}_2$-ϕ), 3.8—4.6 (broad multiplet of N-CH_2-CH_2-N), 6.4—7.8 (multiplet of phenyl protons)
III[b)]	1.32, 1.44 [1.5]; 1.39, 1.51 [1.5]	2.15, 2.24 [3][c)]	2.68 [3]; 2.77 [3]	4.1(HDO), 3.6—4.7(broad multiplet of N-CH_2-CH_2-N), 6.5—7.7(multiplet of phenyl protons)
IV[b)]	1.32, 1.44 [3]	2.15, 2.24 [3][c)]	2.68 [3]; 2.77 [3]	4.1(HDO), 3.6—4.7(broad multiplet of N-CH_2-CH_2-N), 6.5—7.7(multiplet of phenyl protons)
V	0.40, 0.51 [3]	2.15 [3]	2.66 [3]; 2.79 [3]	4.1(HDO), 3.5—4.7(broad multiplet of N-CH_2-CH_2-N), 6.5—7.7(multiplet of phenyl protons)
VI	0.83, 0.92 [3]		7.85 [1]; 8.05 [1] (H-C=N)	1.5—2.3(multiplet of C_6H_{10}), 4.1(HDO), 3.4—3.7 (C$\underline{H}_2$-ϕ), 6.5—7.7(multiplet of phenyl protons)
VII	1.12, 1.24 [1.8]; 1.35, 1.48 [1.2]		7.79 [2] (H-C=N)	1.5—2.3(multiplet of C_6H_{10}), 4.1(HDO), 3.37 (C$\underline{H}_2$-ϕ), 6.5—7.7(multiplet of phenyl protons)

a) Solvent = $CD_3OD + CDCl_3$ (1 : 4). b) Soon after dissolution. c) Doublet. d) [ ] represents relative peak area.

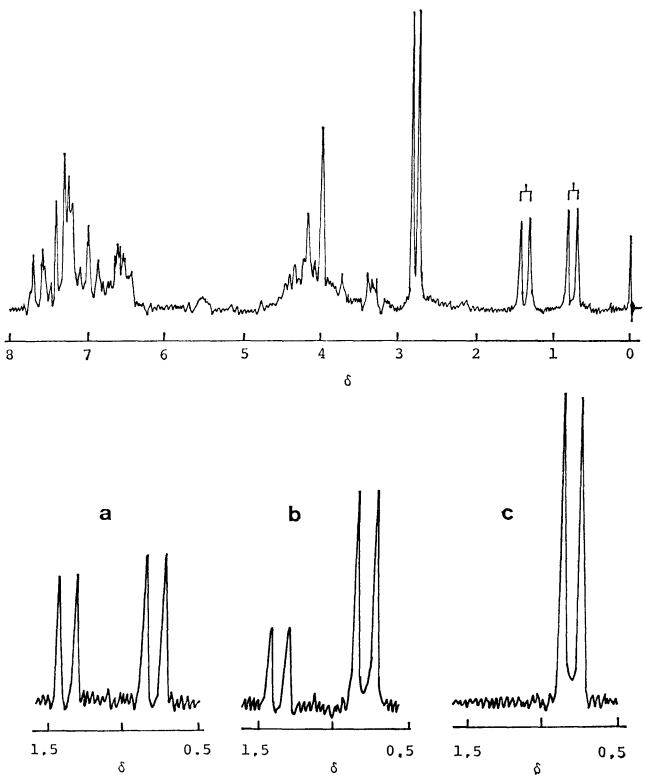

Fig. 3. The ^{1}H NMR spectrum of Complex I (1:1 mixture of Δ_{SS}- and Λ_{RS}-β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)]) in a mixed solvent of $CDCl_3$ and CD_3OD (4:1) soon after dissolution.
a, b, and c are the time dependences of C-CH_3 signal of the coordinated *N*-benzyl-L-alaninate.
a: About 3 min after dissolution, b: about 10 min after, c: at the equilibrium conditions.

(*N*-Bz-L-ala)] complex, and the $(+)_{435}$-isomer thus formed isomerizes slowly to the $(-)_{435}$-isomer. It has already been shown that β_2-Co(α-Me-sal$_2$en) complexes with L-amino acids are labile in isomerization between Δ- and Λ-configurations.[8,9] On the other hand, no mutarotation was observed for Complex II.

Figure 3 shows the ^{1}H NMR spectra of the *N*-Bz-L-ala complexes. The numerical data are listed in Table 1. The ^{1}H NMR spectrum of Complex I exhibited a time dependence in its methyl signal of the coordinated *N*-benzyl-L-alaninato ligand, and that of the complex at the equilibrium conditions coincided with that of Complex II. The methyl signal of Complex I soon after dissolution consists of two doublets at 0.77 and 1.35 ppm (center of the doublet) with the relative intensity ratio of about 1:1. Complex II shows only one doublet at 0.77 ppm. No other peaks or shoulders were observed for the methyl signal. These facts strongly support the assertion that only two species, the $(+)_{435}$- and $(-)_{435}$-isomers, are involved in the mutarotation of Complex I. From the ^{1}H NMR spectra, it can be concluded that 1) Complex I is the 1:1 mixture of the $(+)_{435}$- and $(-)_{435}$-isomers of β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)], 2) Complex II is the pure $(-)_{435}$-isomer of the *N*-Bz-L-ala complex, and 3) the stereoselectivity at the equilibrium conditions of the *N*-Bz-L-ala complex is almost 100%. As will be mentioned later, the Λ_{RS}-β_2-structure is assigned to the $(-)_{435}$-isomer, and the Δ_{SS}-β_2-structure to the $(+)_{435}$-isomer. Here, it should be noted that 1) the formation of both $(+)_{435}$- and $(-)_{435}$-isomers in the initial reaction between [Co(α-Me-sal$_2$en)] and *N*-benzyl-L-alanine can be regarded as kinetic in origin,[9] 2) the isolation of the 1:1 mixture of $(+)_{435}$- and $(-)_{435}$-isomers from the solution of the 1:2 mixture may be due to the lower solubility

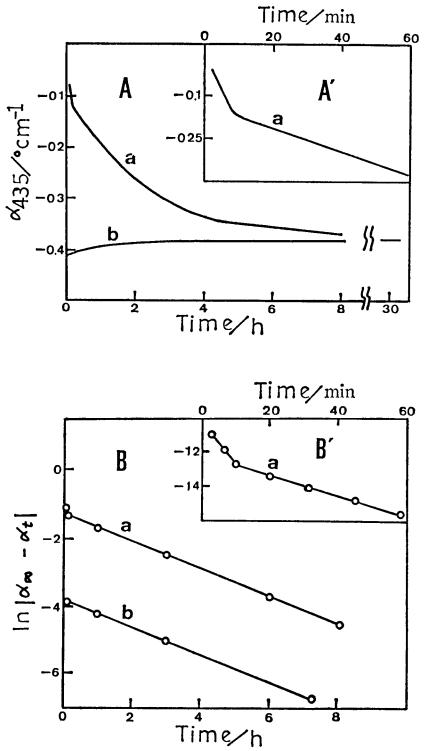

Fig. 4. The mutarotation (A) and the plot of ln|$\alpha_\infty - \alpha_t$| *vs.* the time (B).
A′ and B′ show those of the initial reaction solution.
a: The reaction solution of [Co(α-Me-sal$_2$en)] (1.0×10^{-3} mol dm^{-3}) with *N*-methyl-L-alanine (1.1×10^{-3} mol dm^{-3}) in a mixed solvent of $CHCl_3$ and CH_3OH (4:1) under the air-oxidation conditions at 35 °C,
b: Complex IV (Δ_{RS}-β_2-[Co(α-Me-sal$_2$en)(*N*-Me-L-ala)]) (1.0×10^{-3} mol dm^{-3}) in the same conditions as a.

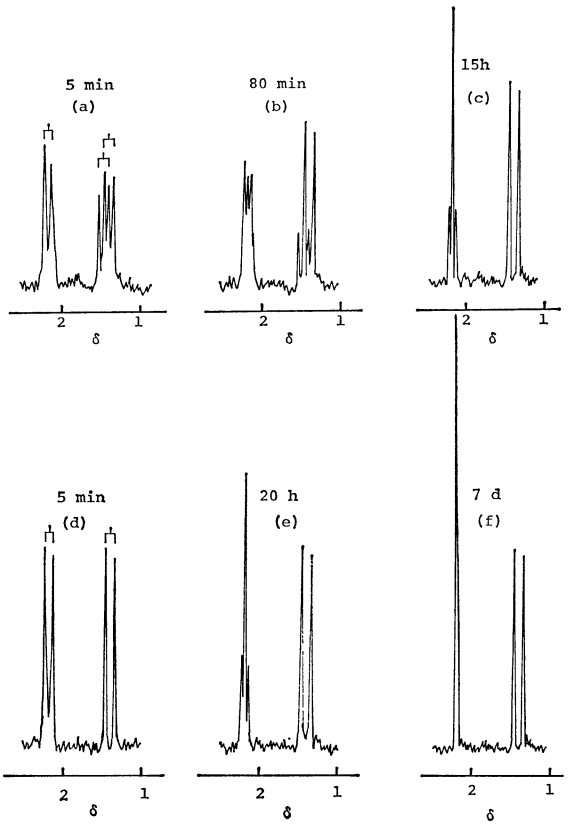

Fig. 5. The ^{1}H NMR spectra of β_2-[Co(α-Me-sal$_2$en)-(*N*-Me-L-ala)] complexes in a mixed solvent of $CDCl_3$ and CD_3OD (4:1).
(a), (b), (c), and (f) are the time dependences of N–CH_3 and C–CH_3 signals of the coordinated *N*-methyl-L-alaninate for Complex III. (d), (e), and (f) are those for Complex IV.

of the 1:1 mixture as compared with the solubility of the 1:2 mixture, and 3) the preference of the $(-)_{435}$-isomer at the equilibrium conditions should come from a thermodynamic origin. The thermodynamic stereoselectivity of the *N*-Bz-L-ala complex will be mentioned later in detail.

*2) β_2-[Co(α-Me-sal$_2$en)(*N*-Me-L-ala)]*: In the reaction for [Co(α-Me-sal$_2$en)] and *N*-methyl-L-alanine, the absorption spectra of the reaction solution soon after reaction and at the equilibrium conditions resembled each other quite closely, and they were very similar to those for β_2-[Co(α-Me-sal$_2$en)(L-aa)]. The absorbance at 600 nm of the reaction solution became almost a constant within a few minutes after initiation of the reaction: the complexation is very fast. The rotation at 435 nm of the reaction solution changed gradually to show a large minus rotation at the equilibrium conditions. These spectral and rotational properties of the *N*-Me-L-ala complex are very similar to those of the *N*-Bz-L-ala complex. However, as is shown in Fig. 4, the plot of ln|$\alpha_\infty - \alpha_t$| *vs.* the time for the mutarotation gives two straight lines crossing at about $t=10$ min. A quite similar mutarotation was observed for Complex III, which was isolated from the initial reaction solution between [Co(α-Me-sal$_2$en)] and *N*-methyl-L-alanine. These facts indicate that three species at least, two $(+)_{435}$-isomers and one $(-)_{435}$-isomer of β_2-[Co(α-Me-sal$_2$en)(*N*-Me-L-ala)] complex, are involved in the mutarotation, and one of the two $(+)_{435}$-isomers isomerizes much faster to the $(-)_{435}$-isomer than the other $(+)_{435}$-isomer does. As mentioned later, four diastereoisomers are thought to be available for the β_2-[Co(α-Me-sal$_2$en)(*N*-Me-L-ala)] complex; their relative stability is as follows: Δ_{RS}->Δ_{SS}->Δ_{RS}->Δ_{SS}-isomers. Therefore, the $(+)_{435}$-isomer, which isomerizes first, may correspond to the less stable Δ_{RS}-isomer, and the other $(+)_{435}$-isomer may correspond to the Δ_{SS}-isomer.

As is shown in Fig. 4, Complex IV also exhibits a mutarotation; it has a smaller minus rotation at the equilibrium conditions than that soon after dissolution, although the degree of the mutarotation is very small. This fact indicates that the stereoselectivity of the *N*-Me-L-ala complex is less than 100%.

Figure 5 shows the ^{1}H NMR spectra of Complexes III and IV. The ^{1}H NMR spectrum of Complex III exhibited a time dependence in the *C*-methyl signal of the coordinated *N*-methyl-L-alaninato ligand. The methyl signal of Complex III soon after dissolution consists of two doublets at 1.34 and 1.55 ppm (center of the doublet) with the relative intensity of about 1:1. At the equilibrium conditions, only one doublet at 1.34 ppm is observed, and the ^{1}H NMR

Table 2. The isomeric ratio of β_2-[Co(α-Me-sal$_2$en)(*N*-R-L-ala)] at the equilibrium conditions[a)]

N-R-L-ala	Λ_{RS}-Isomer/Λ_{SS}-Isomer	Stereoselectivity
N-Bz-L-ala	≈100/≈0	≈100%
N-Me-L-ala	96.5/3.5	93%
N-Bz,Me-L-ala	≈100/0	≈100%

a) Solvent = $CH_3OH + CHCl_3$ (1 : 4 in volume), Temp = 35 °C.

spectrum is identical with that for Complex IV. Complex IV showed no observable time dependence in its ^{1}H NMR spectrum, except that the *N*-methyl signal became a singlet due to the H-D exchange of N–H proton on the *N*-methyl-L-alaninato ligand with deuterium of the solvent. Such ^{1}H NMR spectral behavior suggests that 1) Complex III is the 1:1 mixture of two species of isomer of [Co(α-Me-sal$_2$en)(*N*-Me-L-ala)] complex, 2) Complex IV is the pure $(-)_{435}$-isomer of the *N*-Me-L-ala complex, and 3) the stereoselectivity at the equilibrium conditions of the *N*-Me-L-ala complex is almost 100%. However, the above suggestions 1) and 3) somewhat disagree with the results obtained from the rotational measurements for the *N*-Me-L-ala complexes mentioned above. The disagreement in suggestion 1) may come from the overlap of peaks in the ^{1}H NMR spectrum, low sensitivity of the ^{1}H NMR spectrum as compared with the rotational measurement, or the rapid isomerization of one of the two $(+)_{435}$-isomers to the $(-)_{435}$-isomer in the course of the ^{1}H NMR spectral measurement for Complex III. The discrepancy in suggestion 3) should come from the low sensitivity of the ^{1}H NMR spectrum as compared with that of the rotational measurement. Here, the stereoselectivity at the equilibrium conditions of the *N*-Me-L-ala complex was estimated by the use of the following equation:

$$\text{Stereoselectivity } (\%) = [M]^{B}_{435}/[M]^{A}_{435} \times 100,$$

where $[M]^{A}_{435}$ and $[M]^{B}_{435}$ denote the molar rotations at 435 nm of Complex IV soon after dissolution (A) and at the equilibrium conditions (B) respectively. The estimated stereoselectivity is listed in Table 2.

*3) β_2-[Co(α-Me-sal$_2$en)(*N*-Bz,Me-L-ala)]*: The absorbance at 600 nm of the reaction solution between [Co(α-Me-sal$_2$en)] and *N*-benzyl-*N*-methyl-L-alanine became a constant value within a few minutes after the start of the reaction: the complexation of *N*-benzyl-*N*-methyl-L-alanine is quite fast, as are those of *N*-benzyl-L-alanine and *N*-methyl-L-alanine. Unlike the above two amino acids, however, the reaction solution of *N*-benzyl-*N*-methyl-L-alanine showed a large minus rotation at 435 nm from the beginning of the reaction, and no mutarotation was observed. The rotation of free *N*-benzyl-*N*-methyl-L-alanine itself is negligibly small at 435 nm under the experimental conditions employed ($c = 1.0 \times 10^{-3}$ mol dm^{-3}). These facts indicate that only the $(-)_{435}$-isomer of β_2-[Co(α-Me-sal$_2$en)(*N*-Bz,Me-L-ala)] complex is produced by the formation reaction, and that the other isomers are not produced. As mentioned later, the other isomers may be too unstable to be produced. In fact, only the $(-)_{435}$-isomer (Complex V) was isolated from the reaction solution. Complex V itself is not so stable; thus, it decomposes at a higher temperature in methanol.

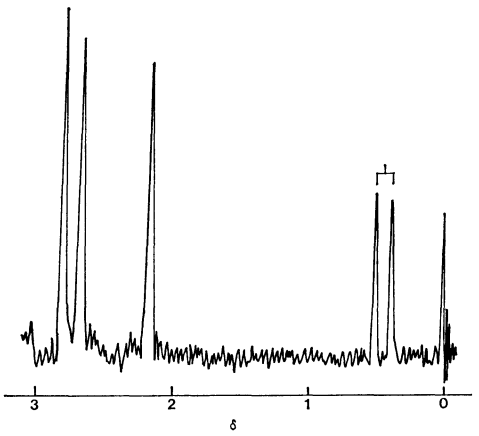

Fig. 6. The ^{1}H NMR spectrum of Λ_{RS}-β_2-[Co(α-Me-sal$_2$en)(*N*-Bz,Me-L-ala)] in $CDCl_3 + CD_3OD$ (4:1).

Figure 6 shows the ^{1}H NMR spectrum of Complex V. The ^{1}H NMR spectrum corresponds to that of the only species of isomer, and no time dependence is observed. Since Complex V exhibits no mutarotation at 435 nm and no time dependence in its ^{1}H NMR spectrum, the stereoselectivity under the equilibrium conditions is estimated to be almost 100%.

The Structure and the Stereoselectivity of β_2-[Co(α-Me-sal$_2$en)(N-R-L-ala)] Complexes. 1) The Structure of the Complexes: The electronic absorption (AB) and the circular dichroism (CD) spectra of the isolated Complexes I—V are shown in Fig. 7. The CD spectra of Complexes I, III, and IV exhibited mutarotations The CD spectrum of Complex I gradually increased in its intensity, and that of Complex I at the equilibrium conditions corresponded to that of Complex II. The CD spectrum of Complex III gradually increased in its intensity, whereas that of Complex IV slowly decreased in its intensity, and the CD spectra of both Complexes at the equilibrium conditions coincided with each other. Further, the AB spectrum of Complex I soon after dissolution was very similar to that at the equilibrium conditions, and the AB spectrum at the equilibrium conditions coincided with that of Complex II. For Complexes III and IV, each AB spectrum soon after dissolution was very similar to that at the equilibrium conditions; AB spectra of both Complexes at the equilibrium conditions were the same.

Since the AB spectra of all the complexes isolated here resemble each other quite closely, it can be assumed that the geometrical structure with respect to the coordinated atoms is the same for all the complexes. The CD spectra of Complexes II, IV, and V, which correspond to the pure $(-)_{435}$-isomer of each *N*-R-L-ala complex, are very similar to that of $(-)_{435}$-Λ-β_2-[Co(α-Me-sal$_2$en)(L-ileu)].[8,16] Therefore, the Λ-β_2-structure can be assigned to the $(-)_{435}$-isomers. Figure 8 shows the vicinal effect of the coordinated *N*-R-L-ala in Complexes II, IV, and V. The vicinal effect was calculated by the use of the

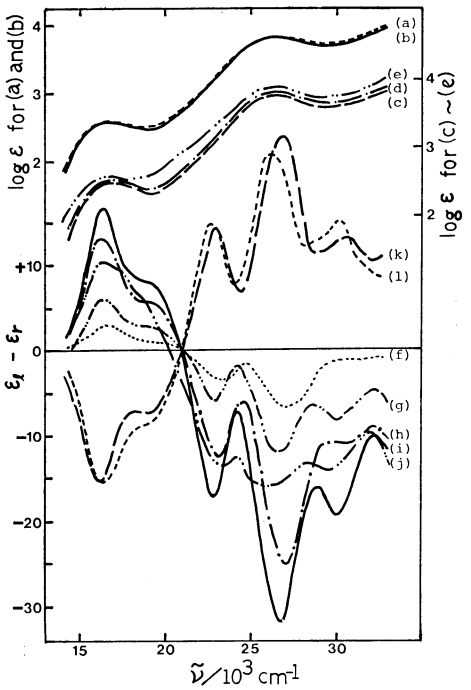

Fig. 7. AB and CD spectra of the complexes in a mixed solvent of $CHCl_3$ and CH_3OH (4:1).
(a): Complex I soon after dissolution, (b): Complex II, (c): Complex III soon after dissolution, (d): Complex IV soon after dissolution, (e) Complex V, (f): CD spectrum of Complex III at the isomeric ratio of 1:2 (Δ_{SS}-:Δ_{RS}-isomers), (g): Complex I at the isomeric ratio of 1:2 (Δ_{SS}-:Δ_{RS}-isomers), (h): Complex IV soon after dissolution, (i): Complex II, (j): Complex V, (k): the estimated CD spectrum of Δ_{SS}-β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)], and (l): the estimated CD spectrum of Δ_{SS}-β_2-[Co(α-Me-sal$_2$en)(*N*-Me-L-ala)].

following equation:[17]

$$\text{CD(vicinal) in } (-)_{435}\text{-isomer} = \text{CD}^{\text{A}} - 3(\text{CD}^{\text{B}} - \text{CD}^{\text{C}}), \quad (1)$$

where CD^A represents the CD for the pure $(-)_{435}$-isomer of β_2-[Co(α-Me-sal$_2$en)(*N*-R-L-ala)], and CD^B and CD^C represent the CD's of the 1:2 (B) and 1:1 (C) mixtures of Δ- and Δ-β_2-[Co(α-Me-sal$_2$en)(L-ala)][8,16] respectively. The vicinal effects of all the *N*-R-L-ala closely resemble each other; they are very similar to that of the L-pro complex,[9] except for the reversed CD sign. It is well known that L-proline can chelate to metal ion with *N(S)C(S)*-configuration, and that the vicinal effect of the asymmetric coordinated atom is much larger than that of the asymmetric atom far from the metal ion. Thus, *N(R)C(S)*-configuration can safely be assigned to the coordinated *N*-R-L-ala in Complexes II, IV, and V. The X-ray study for Complex II is now going on, and we have recently confirmed that Complex II takes the Δ_{RS}-β_2-structure.[18]

The estimated CD curves for the $(+)_{435}$-isomers of the *N*-Me-L-ala and *N*-Bz-L-ala complexes, which exist in the course of the isomerization of Complexes I and III, are shown in Fig. 7. These CD curves were calculated by the use of the following equation:

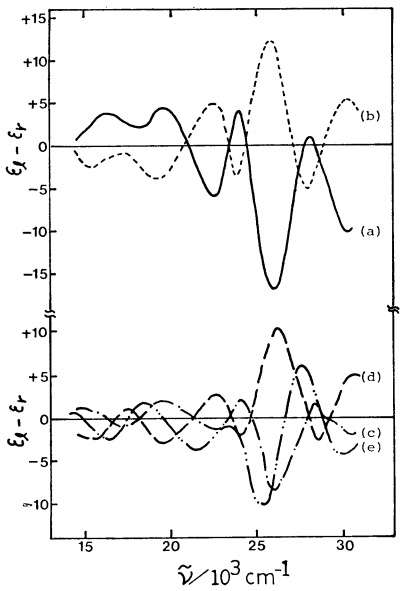

Fig. 8. The vicinal CD of the complexes.
(a) and (b) are those for Δ_{RS}- and Δ_{SS}-β_2-isomers of *N*-Bz-L-ala-complex respectively, (c) and (d) are those for Δ_{RS}- and Δ_{SS}-β_2-isomers of *N*-Me-L-ala-complex respectively, and (e) is the vicinal CD for Δ_{RS}-β_2-isomer of *N*-Bz,Me-L-ala-complex.

$$\text{CD}((+)_{435}\text{-isomer}) = 3\text{CD}^{\text{D}} - 2\text{CD}^{\text{A}}, \quad (2)$$

where CD^D represents the CD of the 1:2 mixture of the $(+)_{435}$- and $(-)_{435}$-isomers of the *N*-R-L-ala complex. The CD spectra could be measured in the course of the isomerization of the 1:1 mixture (Complexes I and III).[19] CD^A denotes the CD of the pure $(-)_{435}$-isomer of the *N*-R-L-ala complex. It is observed that the estimated CD curves for the $(+)_{435}$-isomers are almost mirror images of the CD spectra of the $(-)_{435}$-isomers. Thus, the Δ-β_2-structure can be assigned to the $(+)_{435}$-isomers. The vicinal effect of the *N*-R-L-ala in the $(+)_{435}$-isomers is shown in Fig. 8. The vicinal CD was calculated by the use of the following equation:

$$\text{CD(vicinal) in } (+)_{435}\text{-isomer} = \text{CD}^{\text{E}} - 3(\text{CD}^{\text{B}} - \text{CD}^{\text{C}}), \quad (3)$$

where CD^B and CD^C have been described above, and CD^E denotes the CD of the pure $(+)_{435}$-isomer. Since the vicinal effect is almost a mirror image of that of the corresponding *N*-R-L-ala in the $(-)_{435}$-isomers, the *N(S)C(S)*-configuration can be assigned to the *N*-R-L-ala in the $(+)_{435}$-isomers.

From these results and discussion, it can be concluded that the $(-)_{435}$-isomers of *N*-R-L-ala complex (Complexes II, IV, and V) take the Δ_{RS}-β_2-structure, whereas the $(+)_{435}$-isomer of the *N*-Bz-L-ala complex and one of the two $(+)_{435}$-isomers of the *N*-Me-L-ala complex, which isomerizes more slowly, take the Δ_{SS}-β_2-structure.

2) The Stereoselectivity: The stereoselectivity at the equilibrium conditions of *N*-R-L-ala complex is listed in Table 2. A quite high stereoselectivity can be established in the Co(Schiff base) complexes of *N*-R-L-ala, and the stereoselectivity is much higher than

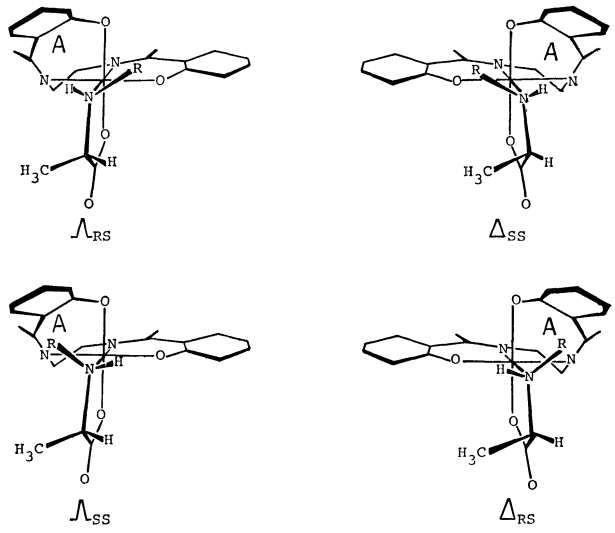

Fig. 9. Structure of four diastereoisomers of β_2-[Co(α-Me-sal$_2$en)(*N*-R-L-ala)].

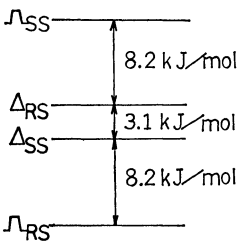

Fig.10. The relative energy difference among four diastereoisomers of *N*-Me-L-ala-complex.

that of Co(trien) complexes. Since the stereoselectivity under the equilibrium conditions can be regarded as thermodynamic in origin, the sterochemical reason why there is a large difference in the thermodynamic stability among the diastereoisomers of Co(Schiff base) complexes is developed as follows.

(a) N-*Me*-L-*ala Complex*: The possible four β_2-isomers are shown in Fig. 9. It is characteristic of a tetradentate Schiff base ligand with β-configuration that the chelate ring (A) in Fig. 9 inclines toward the side of the coordinated amino acid about 30° from the N–Co–O plane of (A). In the cases of Λ_{RS}- and Λ_{SS}-β_2-isomers, the molecular models indicate that the inclination of the chelate ring (A) brings about an extreme steric closeness (1.2—1.4 Å) between the distored chelate ring (A) and the *N*-methyl group of the coordinated amino acid. However, in the cases of Λ_{RS}- and Δ_{SS}-β_2-isomers, there is no abnormal steric closeness between them. In the cases of Λ_{RS}- and Δ_{SS}-β_2-isomers, the *N*-methyl group somewhat approaches to the two phenolic oxygen atoms of α-Me-sal$_2$en ligand (about 2.3 Å), but the steric repulsion seems to be much weaker than that between the chelate ring (A) and the *N*-methyl group in the Δ_{RS}- and Λ_{SS}-β_2-isomers. Thus, it can be assumed that Λ_{RS}- and Δ_{SS}-β_2-isomers are much more stable than Δ_{RS}- and Λ_{SS}-β_2-isomers. In the case of L-pro complex, it has been reported that the Δ_{SS}-β_2-isomer is more stable than the Λ_{SS}-β_2-isomer at about 11.3 kJ mol^{-1} or more.[9]

On the other hand, the conformational relationship between the *N*-methyl and *C*-methyl groups of the *N*-methyl-L-alaninato ligand is staggered (*trans*) in the Λ_{RS}- and Δ_{RS}-β_2-isomers, but it is nearly eclipsed (*cis*) in the Λ_{SS}- and Δ_{SS}-β_2-isomers. And, staggered is more stable than eclipsed. In the case of Co(α-Me-sal$_2$en) complex with *N*-methyl-L-alanine, the energy difference is estimated to be about 8.2 kJ mol^{-1} from the isomeric ratio, Λ_{RS}-isomer/Λ_{SS}-isomer, at the equilibrium conditions, and it is clearly smaller than the steric repulsion energy difference, 11.3 kJ mol^{-1}, between the Schiff base ligand and the *N*-methyl group mentioned above.

Consideration of the above two factors, which are though to contribute greatly to the stability of the diastereoisomers, allows the relative stability among the four isomers to be estimated to be Λ_{RS}->Δ_{SS}->Δ_{RS}->Λ_{SS}-β_2-isomers. The estimated energy differences among the four isomers are shown in Fig. 10.

In the cases of Co(trien) and Co((3*S*,8*S*)-dimetrien) complexes with *N*-methyl-L-alanine,[1,6] the isomeric ratio at the equilibrium conditions is Λ_{RS}-:Δ_{SS}-:Δ_{RS}-isomers=about 60:20:20 and about 85:11:4 respectively. On the other hand, in the case of the Co(α-Me-sal$_2$en) complex, the isomeric ratio at the equilibrium conditions is Λ_{RS}-:Δ_{SS}-isomers=96.5:3.5. The difference in the stereoselectivity between the Co(N$_4$) and Co(Schiff base) complexes seems to come from the following steric reasons: 1) the steric interaction between *N*-methyl group and the tetradentate ligand is much stronger in a Co(Schiff base) complex than a Co(N$_4$) complex, so that Δ_{RS}- and Λ_{SS}-isomers are too unstable to exist at the equilibrium conditions in the case of the Co(Schiff base)-system. 2) In order to decrease the steric closeness between *N*-methyl and *C*-methyl groups in the *N(S)C(S)*-configuration, the chelate ring of *N*-methyl-L-alanine in Co(trien) complex takes a nearly puckered conformation.[20] However, in the case of Co(Schiff base) complex, when the chelate ring takes this nearly puckered conformation, the *N*-methyl group comes close to one of the phenolic oxygen atoms of the Schiff base ligand. Thus, the energy difference between Λ_{RS}- and Δ_{SS}-isomers is much larger in the Co(Schiff base)-system than in the Co(N$_4$)-system.

(b) N-*Bz*-L-*ala Complex*: The steric crowding brough about by a *N*-benzyl group is much larger than that by a *N*-methyl group. Accordingly, the steric interaction between the *N*-alkyl group and the chelate ring (A) in Fig. 9 is much stronger in the *N*-Bz-L-ala complex than in the *N*-Me-L-ala complex, when they take Δ_{RS}- and Λ_{SS}-β_2-configurations. The Δ_{RS}- and Λ_{SS}-isomers of the *N*-Bz-L-ala complex are thus thought to be more unstable than those of the *N*-Me-L-ala complex. Further, the *cis* interaction between the *N*-alkyl group and the *C*-methyl group of the chelated amino acid in the *N(S)C(S)*-configuration is also much stronger in the *N*-Bz-L-ala complex than in the *N*-Me-L-ala complex. Thus, in the case of *N*-Bz-L-ala complex, only the Λ_{RS}-β_2-isomer is favored stereoselectively under the equilibrium conditions.

(c) N-*Bz*,*Me*-L-*ala Complex*: From the strong steric

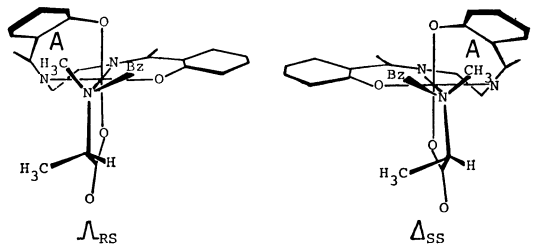

Fig.11. The steric structure of Λ_{RS}- and Δ_{SS}-β_2-isomers of *N*-Bz,Me-L-ala-complex.

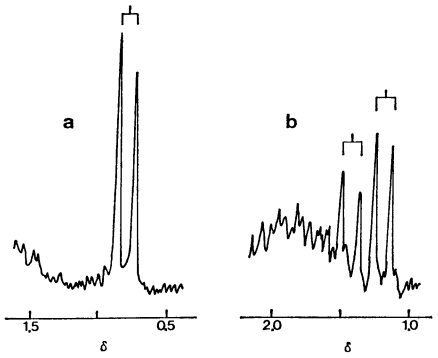

Fig.12. The ^{1}H NMR spectra of Co(sal$_2$-(*S*,*S*)-chxn)-complexes in a mixed solvent of $CDCl_3$ and CD_3OD (4:1).
a: Λ_{RS}-β_2-[Co(sal$_2$-(*S*,*S*)-chxn)(*N*-Bz-L-ala)], b: a mixture of Λ_{RR}- and Δ_{SR}-β_2-isomers of [Co(sal$_2$-(*S*,*S*)-chxn)(*N*-Bz-D-ala)].

intereaction between the *N*-benzyl group and the distored chelate ring (A), the Δ_{RS}- and Λ_{SS}-β_2-isomers of the *N*-Bz,Me-L-ala complex are though to be relatively unstable as compared with the Λ_{RS}- and Δ_{SS}-isomers of the complex. Further, as shown in Fig. 11, even when the complex takes Λ_{RS}- and Δ_{SS}-configurations, the strong steric repulsion between the *N*-methyl group and the chelate ring (A) is inevitable: the *N*-Bz,Me-L-ala complex is thought to be more unstable than the *N*-Me-L-ala and *N*-Bz-L-ala complexes. In fact, Complex V decomposes at a higher temperature. The *cis* interaction between *N*-alkyl group and *C*-methyl group is also inevitable in the case of the *N*-Bz,Me-L-ala complex. However, the *cis* interaction between *N*-methyl group and *C*-methyl group in the Λ_{RS}-configuration is weaker than that between *N*-benzyl group and *C*-methyl group in the Δ_{SS}-configuration. Thus, the *N*-Bz,Me-L-ala complex takes the Λ_{RS}-β_2-structure stereoselectively.

Stereospecificity of Co(sal$_2$-(S,S)-chxn) Complex. It has been reported that a Co(sal$_2$-(*S*,*S*)-chxn) complex assumes the Λ-β_2-structure excusively when it reacts with amino acids such as L- and D-alanines and L- and D-valines.[11] Accordingly, it can be expected that the Co(sal$_2$-(*S*,*S*)-chxn) complex produces a complex containing *N*-benxyl-L-alanine stereospecifically, when it is allowed to react with racemic *N*-benzylalanine, because the Co(α-Me-sal$_2$en) complex with *N*-benzyl-L-alanine, which is similar, shows almost 100% stereoselectivity for the Λ_{RS}-β_2-configuration, as has been mentioned above.

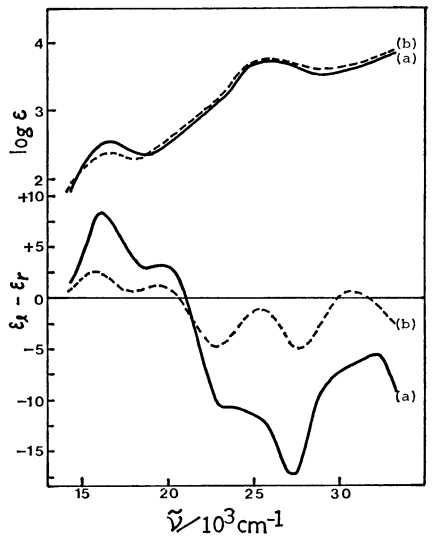

Fig.13. AB and CD spectra of Co(sal$_2$-(*S*,*S*)-chxn)-complexes in the same solvent as that in Fig. 7.
a: *N*-Bz-L-ala, b: *N*-Bz-D-ala.

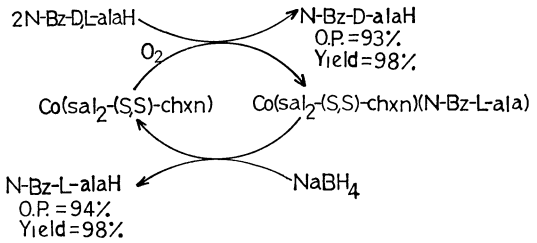

Fig.14. The scheme for the optical resolution of *N*-benzylalanine with Co(sal$_2$-(*S*,*S*)-chxn)-complex.
The optical purity shown in this figure is the value when the reaction molar ratio between [Co(sal$_2$-(*S*,*S*)-chxn)] and racemic *N*-benzylalanine is 1:2.

Figure 12 shows the ^{1}H NMR spectra of the Co-(sal$_2$-(*S*,*S*)-chxn) complexes with *N*-Bz-L-ala and *N*-Bz-D-ala. From the *C*-methyl signals of the coordinated *N*-benzyl amino acids, it is clear that the *N*-Bz-L-ala complex (Complex VI) exists as only one species of isomer but the *N*-Bz-D-ala complex (Complex VII) exists as a mixture of two species of isomer at about 1:1.5 isomeric ratio.

Figure 13 shows the AB and CD spectra of the complexes. Since the AB and CD spectra of the *N*-Bz-L-ala complex are very similar to those of $(-)_{435}$-Λ-β_2-[Co(α-Me-sal$_2$en)(L-ileu)],[8,16] the Λ_{RS}-β_2-structure can be assigned to it. In the case of the *N*-Bz-D-ala complex, the AB and CD spectra are also similar to those of $(-)_{435}$-Λ-β_2-[Co(α-Me-sal$_2$en)(L-ileu)]; however, the CD intensity is much smaller than that of the *N*-Bz-L-ala complex. The molecular model of Co(sal$_2$-(*S*,*S*)-chxn) complexes suggests that the sal$_2$-(*S*,*S*)-chxn moiety can take Λ-β-configuration as well as Λ-β-form, although the strain energy is much larger in Λ-β-configuration. Therefore, the *N*-Bz-D-ala complex may be a mixture of Λ_{RR}-β_2- and Δ_{SR}-β_2-isomers with the isomeric ratio of about 1.5:1.

The formation of the Δ_{SR}-β_2-isomer was not expected. It is expected that the Δ_{SR}-β_2-isomer will be more unstable than the Λ_{RR}-β_2-isomer and the Λ_{RR}-

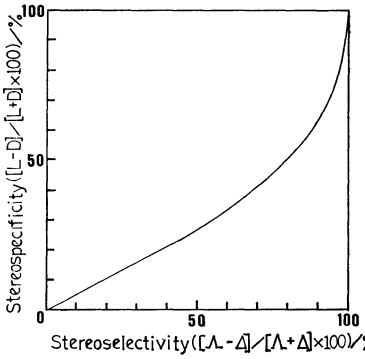

Fig.15. The estimated relationship between stereoselectivity of Co(α-Me-sal$_2$en)-complex and stereospecificity in the reaction of [Co(sal$_2$-(*S*,*S*)-chxn)] with racemic amino acid (the molar ratio=1:2).

β_2-isomer will be much more unstable than the Λ_{RS}-β_2-isomer of *N*-Bz-L-ala complex. Thus, our initial expectations may still be satisfied.

In order to estimate the stereospecificity of the Co(sal$_2$-(*S*,*S*)-chxn) complex toward *N*-benzyl-L-alanine, we examined the reaction of [Co(sal$_2$-(*S*,*S*)-chxn)] and racemic *N*-benzylalanine at 1:2 reaction molar ratio under the air-oxidation conditions. The reaction scheme is shown in Fig. 14. The detailed experimental procedure is described in the Experimental section. Two points should be noted; 1) no racemization of *N*-benzylalanine is observed in the employed experimental conditions, and 2) the recovered [Co(sal$_2$-(*S*,*S*)-chxn)] can be used repeatedly.

From the optical purity of the isolated *N*-benzylalanine, it can be concluded that *N*-benzyl-L-alanine coordinates to the Co(sal$_2$-(*S*,*S*)-chxn) complex in a high stereospecificity (93—94%). However, the stereospecificity did not reach 100%. Figure 15 shows the relationship between the stereoselectivity for Δ- and Λ-isomers in the Co(α-Me-sal$_2$en) complex and the stereospecificity in the reaction of similar Co(sal$_2$-(*S*,*S*)-chxn) complex with a racemic amino acid at 1:2 reaction molar ratio. The relationship was calculated by the use of Equations (3) and (4) in Ref. 11. This figure indicates that the higher the stereoselectivity, the higher the stereospecificity, but their values are not the same. For example, when the stereoselectivity is 98%, the stereosepecificity is 82%. and when it is 99.7%, the stereospecificity is 93%. From these calculations, it is estimated that the stereoselectivity of β_2-[Co(α-Me-sal$_2$en)(*N*-Bz-L-ala)] is not complete but it may reach about 99.7%.

It should be noted that when the reaction molar ratio between [Co(sal$_2$-(*S*,*S*)-chxn)] and racemic *N*-benzylalanine was 1:100, the optical purity of the *N*-benzylalanine recovered from the produced complex was almost 100% (L-form).

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References

1) M. Saburi and S. Yoshikawa, "Chemistry of Octahedral Complexes," Kagaku Sosetsu, Gakkai Shuppan Center, Tokyo (1976), Vol. 13, p. 109.
2) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Am. Chem. Soc.*, **89**, 5133 (1967).
3) M. H. Ghandehari, T. N. Anderson, D. R. Boone, and H. Eyring, *J. Am. Chem. Soc.*, **92**, 6466 (1970).
4) The data cited here is the isomeric ratio between Λ_L- and Λ_D-isomers: M. Yamaguchi, S. Yamamatsu, T. Furusawa, S. Yano, M. Saburi, and S. Yoshikawa, *Inorg. Chem.*, **19**, 2010 (1980).
5) D. A. Buckingham, J. Dekkers, A. M. Sargeson, and M. Wein, *Inorg. Chem.*, **12**, 2019 (1973).
6) D. A. Buckingham, I. E. Maxwell, and A. M. Sargeson, *Inorg. Chem.*, **9**, 2663 (1970).
7) M. Yamaguchi, S. Yano, M. Saburi, and S. Yoshikawa, *Bull. Chem. Soc. Jpn.*, **53**, 691 (1980).
8) Y. Fujii, T. Isago, M. Sano, N. Yanagibashi, S. Hirasawa, and S. Takahashi, *Bull. Chem. Soc. Jpn.*, **49**, 3509 (1976).
9) Y. Fujii, K. Shiono, K. Ezuka, and T. Isago, *Bull. Chem. Soc. Jpn.*, **53**, 3537 (1980).
10) The following abbreviations are used: *N*-Bz-L-ala=anion of *N*-benzyl-L-alanine, *N*-Me-L-ala=anion of *N*-methyl-L-alanine, *N*-Bz,Me-L-ala=anion of *N*-benzyl-*N*-methyl-L-alanine, *L*-ala=anion of L-alanine, L-val=anion of L-valine, L-ileu=anion of L-isoleucine, L-phe=anion of L-phenylalanine, L-pro=anion of L-proline. In the notations used in this paper: Λ_{RS}, Δ_{SS}, Δ_{RS}, and Λ_{SS}, the first suffix (R or S) represents the configuration of the asymmetric nitrogen atom of the coordinated *N*-alkyl amino acid, and the second suffix (S) denotes that of the asymmetric carbon atom of the amino acid.
11) Y. Fujii, M. Sano, and Y. Nakano, *Bull. Chem. Soc. Jpn.*, **50**, 2609 (1977).
12) A Biggoto, G. Costa, G. Mestroni, G. Pellizer, A. Puxeddu, E. Reisenhofer, L. Stefani, and T. Tauzer, *Inorg. Chem. Acta, Reviews*, **4**, 41 (1970).
13) H. Aoi, M. Ishimori, S. Yoshikawa, and T. Tsuruta, *J. Organomet. Chem.*, **85**, 241 (1975).
14) P. Quitt, J. Hellerbach, and K. Vogler, *Helv. Chim. Acta*, **46**, 327 (1963).
15) Y. Fujii, S. Hirasawa, and S. Takahashi, *Chem. Lett.*, **1976**, 817.
16) In previous paper,[8,11] the β_1-structure was assigned tentatively to the [Co(Schiff base)(amino acid)] complexes; however, it has been found recently, in our X-ray study for $(-)_{435}$-[Co(α-Me-sal$_2$en)(L-ileu)]·1.5H$_2$O, that the complex has the β_2-structure: K. Kushi, R. Tamura, M. Kuramoto, T. Yoshizawa, H. Yoneda, and Y. Fujii, *J. Chem. Soc., Chem. Commun.*, **1978**, 266.
17) $3(CD^B - CD^C)$ corresponds to the configurational effect in the β_2-[Co(α-Me-sal$_2$en)(L-ala)] complex.
18) Will be published elsewhere.
19) In the case of the *N*-Me-L-ala complex, Complex I contains three isomers: two $(+)_{435}$-isomers and one $(-)_{435}$-isomer. However, one of the two $(+)_{435}$-isomers isomerizes quite rapidly. Thus, the contribution of one of the two $(+)_{435}$-isomers to the CD intensity at the isomeric ratio of 1:2 between $(+)_{435}$- and $(-)_{435}$-isomers can be neglected.
20) B. F. Anderson, D. A. Buckingham, G. J. Gainsford, G. B. Robertson, and A. M. Sargeson, *Inorg. Chem.*, **14**, 1658 (1975).