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Stereochemical Studies of *N*-Methyl-(*S*)-alaninatocobalt(III) Complexes with Chiral Tetramines. II.[1] Cobalt(III)-*N*-Methyl-(*S*)- and (*R*)-alaninate-*N*,*N*′-Bis(β-aminoethyl)-1(*R*), 2(*R*)-diaminocyclohexane Systems

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The preparation and structural assignments of *N*-methyl-(*S*)- and -(*R*)-alaninatocobalt(III) complexes with *N*,*N*′-bis(β-aminoethyl)-1(*R*),2(*R*)-diaminocyclohexane (abbreviated as (*R*)-baetchxn) are described. The Λ-β_2-(*SSR*) isomer has been obtained for Co(*N*-Me-(*S*)-ala)((*R*)-baetchxn)$^{2+}$ ion. The two isomers, which have been found for the Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion under equilibrium condition at pH 7, are assigned as the Λ-β_2(*SSR*) and Λ-β_2(*SSS*) configurations, taking into account the stereospecific coordination of the (*R*)-baetchxn. The stereoisomerism of Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion is also discussed. The structures of two species observed in the PMR measurements of Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion and assigned to Λ-β_2(*SSR*) and Λ-β_2-(*SSS*) configurations, respectively, are determined, based on the chemical shifts of α-methine protons of *N*-methylalaninate moieties.

The presence of three diastereoisomers has been proved for the β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion (*N*-Me-(*S*)-ala=*N*-methyl-(*S*)-alaninate ion). These isomers were assigned to the Λ-β_2(*SSR*) Δ-β_2(*RRS*), and Δ-β_2-(*RSS*) configurations by Buckingham and coworkers.[2,3] In a previous report, we examined the adequacy of these assignments by the use of 5(*S*)-methyl-1,4,7,10-tetraazadecane (abbreviated as 5(*S*)-metrien) in place of trien. The 5(*S*)-metrien, one of chiral trien derivatives, coordinates stereospecifically with the Δ-*cis*-β(*RR*) configuration.

The two diastereoisomers of the Δ-β_2-Co(*N*-Me-(*S*)-ala)(5(*S*)-metrien)$^{2+}$ ion detected by the proton magnetic resonance (PMR) measurements were assigned to the Δ-β_2(*RRS*) and Δ-β_2(*RRR*) configurations. Further, the remarkable similarities observed between the PMR and circular dichroism (CD) behaviors of the Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ and Δ-β_2-Co(*N*-Me(*S*)-ala)(5-(*S*)-metrien)$^{2+}$ isomers in equilibria in neutral aqueous solution (pH 6.5—7.0) led to the conclusion that one of the Δ-β_2 isomers of the trien complex has the (*RRR*) configuration, instead of the (*RSS*) configuration.[1] This conclusion interpreted consistently the difference of stabilities between the Δ-β_2(*RRS*) and Δ-β_2-(*RSS*) configurations of Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion expected from a strain energy minimization study (the former is 3.2 kcal/mol in favor of the latter).[2]

However, it is difficult to neglect completely the possibility of the inversion at the "planar" secondary N atom for the 5(*S*)-metrien complexes. *N*,*N*′-Bis(β-aminoethyl)-1(*R*),2(*R*)-diaminocyclohexane (abbreviated as (*R*)-baetchxn) is one of chiral trien derivatives, which has been demonstrated to adopt stereospecifically the Λ-*cis*-β(*SS*) configuration upon coordination. Further, it is significant that for the coordinated (*R*)-baetchxn there is no possibility of conformational inversion with respect to the central diamine linkage, since the 1(*R*),2(*R*)-diaminocyclohexane moiety takes solely the λ conformation due to its cyclic structure. The conformational inversion at the central diamine linkage is necessary for the isomerization from the Λ-β(*SS*) to Λ-β(*SR*) configuration. In order to confirm the conclusions on the Δ-β_2-Co(*N*-Me-(*S*)-ala)(5(*S*)-metrien)$^{2+}$ complexes, *N*-Me-(*S*)- and *N*-Me-(*R*)-ala (*N*-Me-(*R*)-ala=*N*-methyl-(*R*)-alaninate ion) complexes with (*R*)-baetchxn have been examined, the results of which will be reported in this paper.

Experimental

N-Methyl-(*S*)-alanine and *N*-Methyl-(*R*)-alanine were prepared by the method of Quitt, Hellerbach, and Vogler,[5] using (*S*)- and (*R*)-alanine, respectively, as the starting amino acids. Commercially available 1,2-diaminocyclohexane (Tokyo Kasei Kogyo) was resolved with *d*-tartaric acid, according to the method of Asperger and Liu.[6] *N*,*N*′-Bis(β-aminoethyl)-1(*R*),2(*R*)-diaminocyclohexane was prepared as follows.

N,N′-*Bis(chloroacetyl)-1*(R),*2*(R)*-diaminocyclohexane.* 1(*R*),2(*R*)-diaminocyclohexane dihydrochloride (14.0) was dissolved in 150 ml of water, containing 18 g of sodium hydroxide. Tothis solution cooled in an ice bath to 10°C was added a solution of chloroacetyl chloride (22.6 g) in benzene (80 ml) drop by drop with vigorous stirring by means of a blender. After the addition had been completed, the stirring was continued for 10 more min. The resultant white solid mass was filtered off, and washed with water. Yield, 28 g. The crude product was recrystallized from methanol by adding ether. Found: C, 44.71; H, 5.98; N, 11.11%. Calcd for $C_{10}H_{16}N_2O_2Cl_2$: C, 44.29; H, 5.95; N, 10.33%.

N,N′-*Bis(glycyl)-1*(R),*2*(R)*-diaminocyclohexane Dihydrochloride.* *N*,*N*′-Bis(chloroacetyl)-1(*R*),2(*R*)-diaminocyclohexane (14.0 g) dissolved in 200 ml of hot methanol was mixed with 300 ml of aqueous ammonia (28%) and ammonium carbonate (50 g). The mixture was left to stand at room temperature for 7 days, and the resultant solution was evaporated to dryness on a rotary evaporator under reduced pressure. The white precipitates, which remained, were collected, washed with ethanol and ether, and dried under vaccuum. Yield, 12.0 g. The crude product was recrystallized from methanol–ethanol mixture (1:2). Found: C, 39.83; H, 7.24; N, 18.73%. Calcd for $C_{10}H_{22}N_4O_2Cl_2$: C, 39.35; H, 7.27; N, 18.36%.

N,N′-*Bis(β-aminoethyl)-1*(R),*2*(R)*-diaminocyclohexane Tetrahydrochloride.* To a suspension of lithium aluminium hydride (10.8 g) in anhydrous tetrahydrofuran (250 ml) was added *N*,*N*′-bis(glycyl)-1(*R*),2(*R*)-diaminocyclohexane dihydrochloride (14.0 g) in small portions. The mixture was then stirred and heated under reflux for 24 hr, and cooled to room temperature. The subsequent treatments were the same as those described in a previous paper.[4)]

Λ-cis-β-Dichloro (N,N′-bis (β-aminoethyl) - 1 (R), 2 (R) - diaminocyclohexane) cobalt (III) Chloride Hemihydrate (Λ-cis-β-[CoCl$_2$*((R)-baetchxn)]Cl·0.5H*$_2$*O)* was also prepared according to the method reported previously.[4)]

Λ-β$_2$*(SSR)-[Co(N-Me-(S)-ala)((R)-baetchxn)](ClO*$_4$*)*$_2$. *Λ-cis-β*-[CoCl$_2$((*R*)-baetchxn)]Cl·0.5H$_2$O (1.15 g) was dissolved in 5 ml of water, followed by 0.126 g of LiOH·H$_2$O. To the solution were added 0.31 g of *N*-methyl-(*S*)-alanine and 0.5 g of active charcoal, successively. The solution was then warmed to 70 °C on a water bath for 30 min. The active charcoal was filtered off and washed with a small volume of water. The filtrate and washings were combined and concentrated to a volume of 2 ml on a water bath below 70 °C. Then, 1.5 g of solid LiClO$_4$ were added, and cooled in an ice bath for 2 hr. The orange-red crystals, which separated, were collected, washed with cold water and ethanol, and air-dried. Yield, 1.30 g. The product was recrystallized from hot water. Found: C, 27.83; H, 5.80; N, 12.77%. Calcd for [Co(C$_{10}$H$_{24}$N$_4$)(C$_4$H$_8$NO$_2$)](ClO$_4$)$_2$: C, 27.42; H, 5.98; N, 12.97%.

Λ-β$_2$*-[Co(N-Me-(R)-ala)((R)-baetchxn)]I*$_2$*, A Mixture of Λ-β*$_2$*(SSR) and Λ-β*$_2$*(SSS) Isomeres.* *Λ-cis-β*-[CoCl$_2$((*R*)-baetchxn)]Cl·0.5H$_2$O (0.57 g) was dissolved in 5 ml of water, followed by 0.063 g of LiOH·H$_2$O. The solution was warmed to 70 °C on a water bath, and 0.155 g of *N*-methyl-(*R*)-alanine and 0.2 g of active charcoal were added, successively. The resultant solution was warmed to 70°C for 15 min. The active charcoal was then filtered off, and washed with a small volume of water. The filtrate and washings were combined and concentrated to a volume of 3 ml on a water bath below 60 °C. To the solution were added 0.7 g of NaI dissolved in a minimum volume of water, and cooled in an ice bath overnight. The red crystals, which separated, were collected, washed with dilute NaI solution and ethanol, and air-dried. Yield, 0.52 g. Found: C, 27.85; H, 5.38; N, 10.83%. Calcd for [Co(C$_{10}$H$_{24}$N$_4$)(C$_4$H$_8$NO$_2$)]I$_2$: C, 27.33; H, 5.24; N, 11.39%.

Λ-β$_2$*(SSR)-[Co(N-Me-(R)-ala)((R)-baetchxn)](ZnCl*$_4$*)*. The filtrate obtained after the removal of active charcoal as described above was concentrated to a volume of 7 ml on a water bath below 60 °C. The solution was, then, diluted with 20 ml of ethanol, and 1.5 g of NaI dissolved in a minimum volume of water was added. The solution was cooled in an ice bath overnight, and the orange-rad crystals, which appeared, were filtered off, washed with ethanol, and air-dried. Yield, 1.27 g. This compound, which contains the ethanol of crystallization, was added in 10 ml of 0.1 M HCl, containing an excess amounts of freshly prepared AgCl. All the contents were mixed thoroughly until the complexes dissolved completely. Silver salts were filtered off, and washed well with water. The filtrate and washings were combined, and zinc chloride (1.4 g) was added, followed by 1 ml of concentrated HCl. The resultant solution was cooled in a refrigerator overnight, and the orange crystals, which appeared, were collected, washed with cold water and ethanol, and air-dried. Yield, 0.65 g. A further crop of crystals was obtained from the filtrate after the concentration. Found: C, 28.72; H, 5.58; N, 12.05%. Calcd for [Co(C$_4$H$_8$NO$_2$)(C$_{10}$H$_{24}$N$_4$)](ZnCl$_4$): C, 29.57; H, 5.67: N, 12.32%.

Measurements. Visible absorption spectra were measured with a Shimadzu MPS-50L recording spectrophotometer. Circular dichroism curves were obtained with a JASCO J-20 automatic recording spectropolarimeter. 100-MHz proton magnetic resonance spectra were obtained using a JEOL PS-100 spectrometer using sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an internal standard reference. For the PMR measurements, perchlorate salt (about 50 mg sample) suspended in the solvent (0.01 M DCl or D$_2$O, 0.5—0.7 ml) was treated with twice the molar amounts of tetraphenylarsonium chloride. The white precipitates were removed by filtration, and the filtrate was employed for PMR measurement. Iodide salts (about 60 mg samples) suspended in the solvent (0.5—0.7 ml) were treated with twice the molar amounts of silver nitrate. The precipitated AgI were removed by filtration, and the PMR spectra of the filtrates were recorded.

60 MHz PMR spectra were obtained with a Hitachi R-20B spectrometer.

Results and Discussion

The 100 MHz PMR spectra of the Co(*N*-Me-(*S*)-ala)((*R*)-baetchxn)$^{2+}$ ion, obtained in 0.01 N DCl and D$_2$O solutions, are shown in Fig. 1(a) and (b), respectively. In 0.01 M DCl, the deuterium exchange of *N*-bonded protons is retarded sufficiently so that the *N*-methyl proton signal is observed as the doublet at 2.58 ppm (standard, DSS). In D$_2$O solution, the *N*-bonded protons have exchanged with solvent D$_2$O, and the *N*-methyl signal has collapsed to a singlet. In both spectra ((a) and (b)), the C-methyl signals were observed as the single doublet at 1.50 ppm. It is apparent from these observations that the Co(*N*-Me-(*S*)-ala)((*R*)-baetchxn)$^{2+}$ ion is composed of the single species. Further, the PMR spectrum obtained in 0.01 N DCl (Fig. 1(a)) corresponds well to that of the *Λ-β*$_2$(*SSR*)-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion reported earlier,[2)] except that complicated broad peaks are found in 1.0—2.0 and 2.0—2.5 ppm regions for the (*R*)-baetchxn complex. These broad peaks should be ascribed to the signals for protons of the cyclohexane ring of (*R*)-baetchxn.

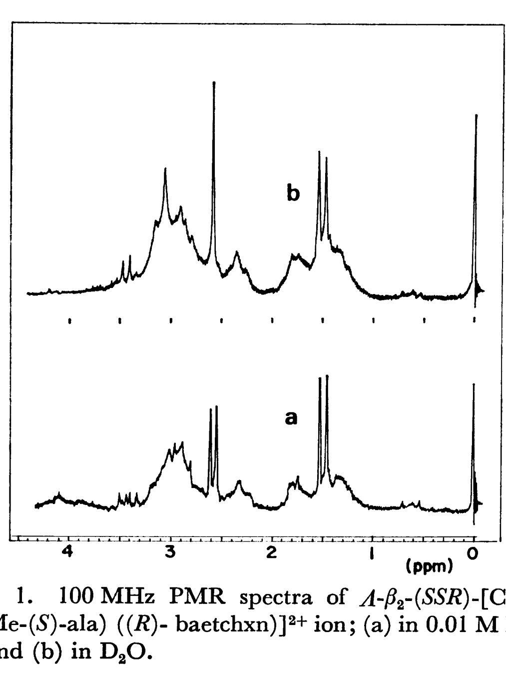

Fig. 1. 100 MHz PMR spectra of *Λ-β*$_2$-(*SSR*)-[Co(*N*-Me-(*S*)-ala) ((*R*)- baetchxn)]$^{2+}$ ion; (a) in 0.01 M DCl, and (b) in D$_2$O.

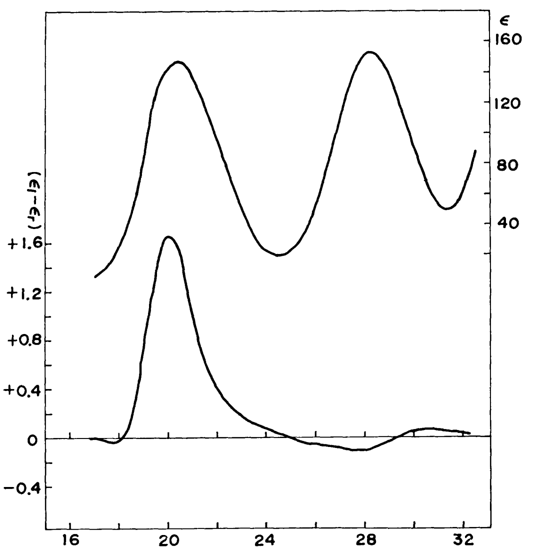

Fig. 2. Visible absorption and CD spectra of Λ-β_2-(*SSR*)-[Co(*N*-Me-(*S*)-ala) ((*R*)-baetchxn)]$^{2+}$ ion.

The Co(*N*-Me-(*S*)-ala)((R)-baetchxn)$^{2+}$ ion shows the visible absorption and CD spectra shown in Fig. 2. These curves resembles closely to the corresponding curves of the Λ-β_2(*SSR*) isomers of Co(*N*-Me-(*S*)-ala)-(trien)$^{2+}$ and Co(*N*-Me-(*S*)-ala)(5(*R*)-metrien)$^{2+}$ ions. Therefore, the present (*R*)-baetchxn complex can be assigned to the Λ-β_2(*SSR*)(*S*)[3] configuration.

It was found previously that the Δ-β_2-Co(*N*-Me-(*S*)-ala)(5(*S*)-metrien)$^{2+}$ complex arised in the single species as the iodide, whereas the same complex ion gave rise to a mixture of two isomeric forms as the perchlorate.[1] Similarly, the Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion could be isolated in the pure state as the iodide form.[2] On these bases, we tried to obtain the Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion, which should appear in the Λ-β_2 configuration and in the enantiomeric relation to the above Δ-β_2 isomers with *N*-Me-(*S*)-ala group, as the iodide form.

However, [Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)]I$_2$ isolated from an aqueous solution, was found to be an isomeric mixture of two species, though the complex ions had the Λ absolute configuration as expected. The PMR spectra of this complex obtained in 0.01 M DCl and D_2O solutions are shown in Fig. 3(a) and (b), respectively. The spectrum in 0.01 M DCl shows two *N*-methyl doublets at 2.40 and 2.57 ppm, indicating the presence of two isomers in the crystalline state. The *C*-methyl signals, which appeared as three peaks in the vicinity of 1.5 ppm, can be regarded as an overlap of two doublets.

It was found unexpectedly that one of the isomers of Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion crystallized out from an aqueous ethanol in the single isomeric form. The PMR spectrum of this orange-red needle-like crystals measured in 0.01 M DCl is shown in Fig. 3(c). This spectrum exhibits only one doublet for the *N*-methyl signal (2.40 ppm). The *C*-methyl signal is also observed as the single double (1.43 ppm). These findings indicate that the present complex is largely composed of the single species. Furthermore, the presence of ethanol in the crystal is obviously demonstrated by the triplet and quartet centered at 1.14 and 3.60 ppm, respectively. However, the elemental analysis data for this complex could not provide any sufficient results. Hence, we turned this compound to the tetrachlorozincate salt, which gave the consistent analysis data.

The PMR spectrum of the above complex obtained in 0.01 M DCl (Fig. 3(d)) was found to be identical with that shown in Fig. 3(c), except for the signals of ethanol appeared additionally in the latter case. The spectrum of this complex obtained in D_2O was also identical with that of Fig. 3(b). The PMR spectral changes caused by the variation of the pH of solvent

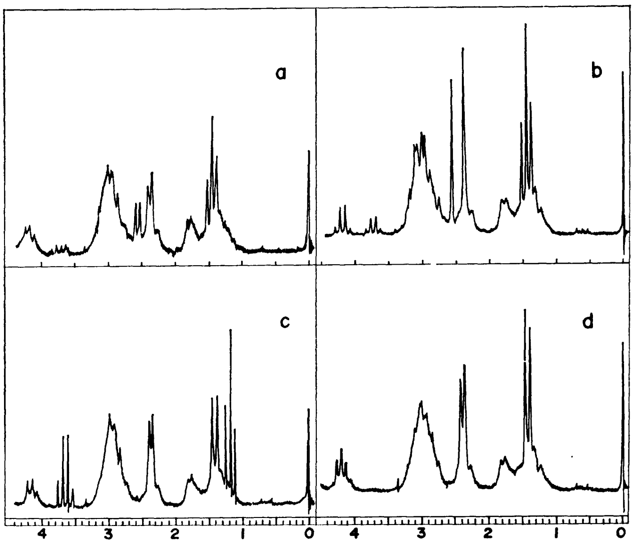

Fig. 3. 100 MHz PMR spectra of Λ-β_2-[Co(*N*-Me-(*R*)-ala) ((*R*) baetchxn)]$^{2+}$ ion; (a) Λ-β_2-(*SSR*)+Λ-β_2-(*SSS*) in 0.01 M DCl, (b) Λ-β_2-(*SSR*)+Λ-β_2-(*SSS*) in D_2O (pD=6.8), (c) Λ-β_2-(*SSR*) containing ethanol in 0.01M DCl, (d) Λ-β_2-(*SSR*), ($ZnCl_4$) salt in 0.01 M DCl.

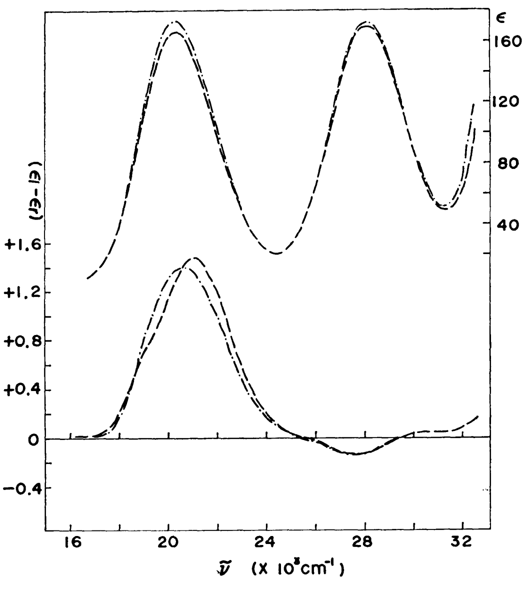

Fig. 4. Visible absorption and CD spectra of Λ-β_2-[Co-(*N*-Me-(*R*)-ala)-((*R*)-baetchxn)] ($ZnCl_4$) in 0.1 M $HClO_4$ (----), and in H_2O (pH 7) (—•—•).

are analogous to those observed for the Δ-β_2-[Co(*N*-Me-(*S*)-ala)(trien)]I_2[2] and for the Δ-β_2-[Co(*N*-Me-(*S*)-ala)(5(*S*)-metrien)]I_2. Corresponding to these PMR changes, the visible absorption and CD spectral changes were noticed for the trien and 5(*S*)-metrien complexes in acidic and neutral aqueous solutions. The CD and visible absorption curves of Λ-β_2-[Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)]($ZnCl_4$) also changed in a similar way through the variation of the solvents, as shown in Fig. 4.

Buckingham and coworkers have supposed that the isomerization of the isolated Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion at pH 6.5—7.0 may be caused by the inversion at an asymmetric secondary N center, and that two possibilities exist for scuh isomerization; inversion at the *N*-methyl group or at the "planar" secondary N center of β-trien skeleton. The latter possibility has been adopted by Buckingham *et al.*, and the equilibrium between the Δ-β_2-(*RRS*)(*S*) and Δ-β_2-(*RSS*)(*S*) configurations has been postulated.[2]

In the case of (*R*)-baetchxn complex with Λ-β configuration, the possibility of the conformational inversion of the central chelate ring can be thoroughly excluded, since the conformation of the 1(*R*),2(*R*)-diaminocyclohexane chelate ring is solely restricted in the λ-*gauche* form. Hence, the possibility of the inversion at the "planar" secondary N center which must accompany the conformational inversion of the central chelate ring can also be ruled out for the (*R*)-baetchxn complex. Therefore, the two isomers observed for the Λ-β_2-Co(*N*-Me(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion should be arisen from a source of asymmetry other than the "planar" secondary N center of trien moiety. The inversion at the *N*-methyl group can be regarded as the relevant origin of the isomerization mentioned above. Consequently, the two species detected in the PMR spectrum (Fig. 3(b)) should be assigned to the Λ-β_2(*SSR*)(*R*) and Λ-β_2(*SSS*)(*R*) configurations.

The complex ions, Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ and Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$, are in the enantiomeric relation with regard to every chiral center: the absolute configuration around the Co(III) ion, those of the secondary N centers of trien skeleton and of *N*-methyl groups, and those of the asymmetric α-C atom of *N*-methylalanine moiety. Therefore, the stereoisomerism noticed for the restricted Λ-β(*SS*) framework of (*R*)-baetchxn complexes must be applicable to the Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion, even though the possibility of the inversion at the "planar" secondary N center would be retained for the trien complex.

The PMR spectrum of Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion (Fig. 3(b)) indicates that the relative intensities of *N*-methyl signals of the Λ-β_2(*SSR*)(*R*) fand Λ-β_2(*SSS*)(*R*) isomers are approximately equal. This means that these isomers have the comparable stabilities with each other. The Δ-β_2(*RRS*) and Δ-β_2(*RRR*) isomers of Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion must also have the nearly equal stabilities, even if the other isomer, Δ-β_2(*RSS*) form, would be sufficiently stable in comparison with the Δ-β_2(*RRS*) form, as expected by Buckingham *et al.*[2] In practice, however, only two species have been detected in the PMR spectrum of the Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion equilibrated at pH 7.[2] Further, the PMR spectral features of these isomers are entirely analogous to those of the Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion, especially in the regions of the *N*-methyl and *C*-methyl signals. Accordingly, the two detectable species of Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion should be assigned as the (*RRS*) and (*RRR*) isomers, instead of the (*RSS*) isomer. This conclusion is in accordance with that obtained in a previous paper, using the 5(*S*)-metrien.[1]

It has been considered to be difficult to make individual structural assignments for the two isomers of Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ ion.[2] We have tentatively assigned these isomers to the Δ-β_2(*RRS*) and Δ-β_2-(*RRR*) configurations, respectively, on the ground of the chemical shifts of *N*-methyl groups of the two isomers. To make sure these assignments, we have examined the PMR spectra of Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ isomers, and obtained interesting findings.

In the spectrum of Fig. 3(b), two small quartets are observed at 3.73 and 4.19 ppm. These signals can be assigned to the methine protons of *N*-Me-(*R*)-ala moieties of the Λ-β_2(*SSR*) and Λ-β_2(*SSS*) isomers, respectively. For the corresponding *N*-Me-(*S*)-ala complex ion, the methine quartet is detected at 3.44 ppm in the spectrum of Fig. 1(b), though the same signal can not be recognized in Fig. 1(a) due probably to the overlap of N–H resonance. Similarly, it is rather difficult to find definitely the methine quartet in the spectrum of Fig. 3(a) because of the appearance of broad N–H peaks in the region of 4.0—4.5 ppm.

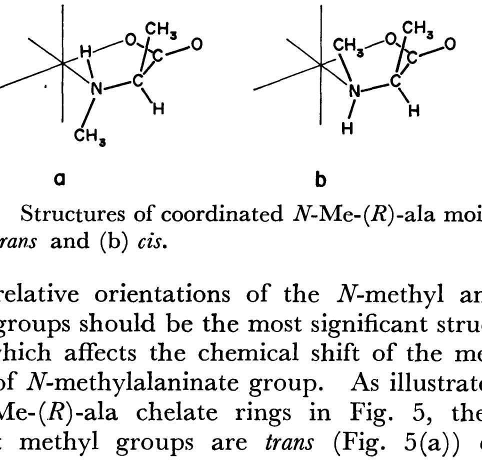

Fig. 5. Structures of coordinated *N*-Me-(*R*)-ala moiety; (a) *trans* and (b) *cis*.

The relative orientations of the *N*-methyl and C-methyl groups should be the most significant structural factor which affects the chemical shift of the methine proton of *N*-methylalaninate group. As illustrated for the *N*-Me-(*R*)-ala chelate rings in Fig. 5, the two adjacent methyl groups are *trans* (Fig. 5(a)) or *cis* (Fig. 5(b)) to each other. In the *trans* form, the *N*-methyl is *cis* with respect to the methine proton, and, therefore, the methine should be strongly affected by the magnetic anisotropy of the C–N bond of the *N*-methyl group. It is anticipated that the C–N bond anisotropy will appear in a similar manner as that for the C–C single bond, and that the methine proton in the *trans* form (Fig. 5(a)) will show the high-field shift compared to the methine in the *cis* form (Fig. 5(b)), because the C–N bond anisotropy should no longer have any significant effects to the methine proton in the latter case.

The *N*- and *C*-methyl groups are in the *trans* con-

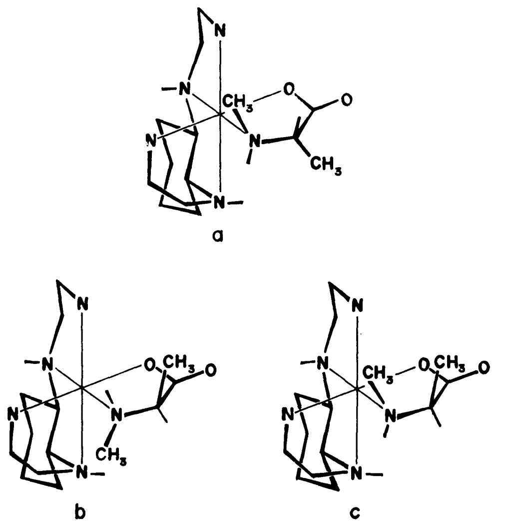

Fig. 6. Structures of (*R*)-baetchxn complexes: (a) Λ-β_2-(*SSR*)(*S*), (b) Λ-β_2-(*SSS*)(*R*), and (c) Λ-β_2-(*SSR*)(*R*).

figuration for the Λ-β_2(*SSR*)(*S*) and Λ-β_2(*SSS*)(*R*) isomers, while these are *cis* in the Λ-β_2(*SSR*)(*R*) isomer of the (*R*)-baetchxn complexs, as shown in Fig. 6(a)—(c). The methine resonance of Λ-β_2(*SSR*)(*S*) isomer, with the *trans* configuration, is found at 3.44 ppm as described previously. Taking account of the C–N bond anisotropy, the quartets observed at 3.73 and 4.19 ppm in Fig. 3(b) should be assigned to the *trans* and the *cis* configuration, or to the Λ-β_2(*SSS*)(*R*) and the Λ-β_2-(*SSR*)(*R*) configuration, respectively.

It was found that the Λ-Co((*S*)-ala)(en)$_2{}^{2+}$ and -Co-((*R*)-ala)(en)$_2{}^{2+}$ ions ((*S*)-ala and (*R*)-ala=(*S*)- and (*R*)-alaninate) show their methine quartets at about 3.98 and 4.15 ppm, respectively.[7,8] Both these complexes are free from the C–N bond anisotropy under consideration. It is interesting to note that the chemical shifts of methine protons of the (*R*)-ala complex coincide well with that of the Λ-β_2(*SSR*)-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion (4.19 ppm), in which there are no influences of the C–N anisotropy. The difference of the chemical shifts (0.17 ppm) between the above (*S*)- and (*R*)-alanine complexes should be ascribed to the difference of the absolute configuration of the α-C atom of alaniate group. The methine signal of the Λ-β_2-(*SSS*)(*R*) isomer, having the *trans* configuration with respect to the *N*- and C-methyl groups, appeared in the higher field relative to that of the Λ-β_2(*SSR*)(*R*) isomer with the *cis* configuration, but in the lower field than that of the Λ-β_2(*SSR*)(*S*) isomer with the *trans* configuration. The difference in the chemical shifts of the methine signals between the (*SSR*)(*S*) and (*SSS*)(*R*) isomers (0.29 ppm), both of which take the *trans* configuration with regard to the *C*- and *N*-methyl groups, seem to be analogous to that found in the above alanine complexes.[7,8]

The determination of the *C*-methyl groups of Λ-β_2-(*SSR*) and Λ-β_2(*SSS*) isomers of Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion has been achieved by the spin-decoupling method. Since a 60 MHz spectrometer has been employed for these measurements, the two *C*-methyl signals have appeared separately as two doublets as shown in Fig. 7. The irradiation of the quartet at 4.19 ppm has caused the collapse of the doublet in the higher field (1.43 ppm) to the singlet, and the irradiation of the quartet at 3.73 ppm has produced the collapse of the doublet at 1.51 ppm to the singlet, as indicated in Fig. 7. From these results, the isolated isomer of the Λ-β_2-Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)$^{2+}$ ion which shows the *C*-methyl doublet at 1.43 ppm (Fig. 3(d)) can be decided as the (*SSR*)(*R*) configuration. The PMR spectral data of the (*R*)-baetchxn and related complexes are summarized in Table 1.

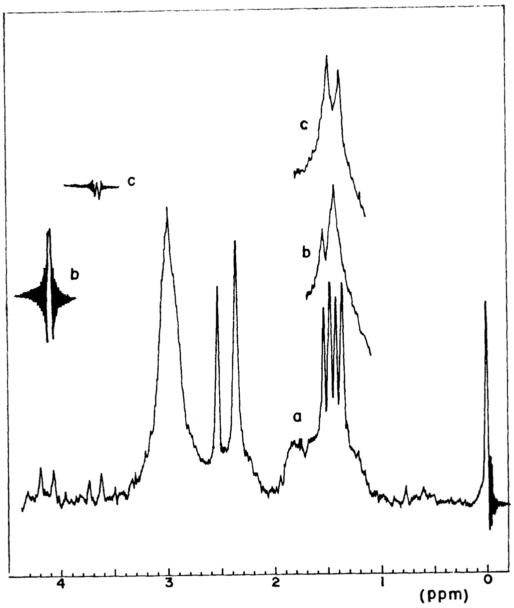

Fig. 7. 60 MHz PMR spectra of mixture of Λ-β_2-(*SSR*)- and Λ-β_2-(*SSS*)-[Co(*N*-Me-(*R*)-ala)((*R*)-baetchxn)]$^{2+}$ ion; (a) in D_2O, (b) the spectrum irradiated at 4.19 ppm, (c) the spectrum irradiated at 3.73 ppm.

TABLE 1. ASSIGNMENTS OF PROTON RESONANCE SHIFTS[a] OF *N*-METHYLALANINE MOIETIES

	C–CH$_3$	N–CH$_3$	C–H
Λ-β_2(*SSR*)-Co(*N*-Me-(*S*)-ala)-((*R*)-baetchxn)$^{2+}$	1.50	2.58	3.44
Λ-β_2(*SSR*)-Co(*N*-Me-(*R*)-ala)-((*R*)-baetchxn)$^{2+}$	1.43	2.40	4.19
Λ-β_2(*SSS*)-Co(*N*-Me-(*R*)-ala)-((*R*)-baetchxn)$^{2+}$	1.51	2.57	3.73
Λ-β_2(*SSR*)-Co(*N*-Me-(*S*)-ala)-(5(*R*)-metrien)$^{2+}$	1.53	2.61	3.52[b]
Δ-β_2(*RRS*)-Co(*N*-Me-(*S*)-ala)-(5-(*S*)-metrien)$^{2+}$	1.42	2.38	4.06
Δ-β_2(*RRR*)-Co(*N*-Me-(*S*)-ala)-(5(*S*)-metrien)$^{2+}$	1.50	2.58	3.80[b]
Co(*N*-Me-(*S*)-laa)(NH$_3$)$_4{}^{2+}$	1.48	2.48	3.54
Λ-Co(*N*-Me-(*S*)-ala)(en)$_2{}^{2+}$	1.49	2.53	3.55

a) ppm from DSS. b) Determined by the spin decoupling method, using a 60 MHz spectrometer.

No attention has been turned to the methine signals of the *N*-methylalanine group in former studies.[1,2] This may be due to the fact that the complicated methylene (and methine) proton signals of trien,[2] 5(*R*)- or 5(*S*)-metrien,[1] which appear in the region of 3.3—

3.8 ppm, obscure the methine quartets in question. However, one of the methine quartets is clearly noticed at 4.06 ppm in the PMR spectrum of the Δ-β_2-Co(*N*-Me-(*S*)-ala)(5(*S*)-metrien)$^{2+}$ isomers in D_2O.[1] The corresponding quartet can be acknowledged in the PMR spectrum of the Δ-β_2-Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ isomers reported by Buckingham *et al.*[2] We have sought the hidden methine signals of 5(*R*)- and 5(*S*)-metrien complexes by the decoupling method. The most appropriate position of the irradiation which produces the collapse of the *C*-methyl doublet to a singlet has been determined as the center of the methine signal. The data are given in Table 1. The assignments of the two isomers of Δ-β_2-Co(*N*-Me-(*S*)-ala)-(5(*S*)-metrien)$^{2+}$ ion is consistent with those made from the chemical shifts of the *N*-methyl group in a previous paper.[1] The same arguments should be applicable to the Co(*N*-Me-(*S*)-ala)(trien)$^{2+}$ system, though the adequecy has not been examined in this study.

References

1) Part I. M. Saburi, M. Homma, and S. Yoshikawa, *Inorg. Chem.*, **12**, 1250 (1973).

2) D. A. Buckingham, I. E. Maxwell, and A. M. Sargeson, *ibid.*, **9**, 2663 (1970).

3) Nomenclature: The *RS* representations of the asymmetric N atoms of trien and its derivatives and of *N*-methylalanine and the asymmetric α-C atoms of amino acids follow that by Buckingham *et al.* *cf.* Ref. (2). The use of β,β_1 and β_2 follows that used by L. G. Marzilli, and D. A. Buckingham, *Inorg. Chem.*, **6**, 1042 (1967). The absolute configuration about the cobalt(III) center is indicated by the prefix Λ or Δ: *Inorg. Chem.*, **9**, 1 (1970).

4) M. Goto, M. Saburi, and S. Yoshikawa, *Inorg. Chem.*, **8**, 358 (1969).

5) P. Quitt, J. Hellerbach, and K. Vogler, *Helv. Chim. Acta*, **46**, 327 (1963).

6) R. G. Asperger and C. F. Liu, *Inorg. Chem.*, **4**, 1492 (1965).

7) D. A. Buckingham, L. Durham, and A. M. Sargeson, *Aust. J. Chem.*, **20**, 257 (1967).

8) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **89**, 5133 (1967).