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Cobalt(III) Complexes Containing an Aldonic Acid

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Stable complexes of the type $[Co(aldonato)(en)_2]^+$, where en is ethylenediamine and aldonato is the diacid anion of D-gluconic acid or L-mannonic acid, were prepared by the reaction of aldonic acid lactones with *rac*-$[Co(CO_3)(en)_2]^+$. Two diastereomers (Δ and Λ) have been separated by ion-exchange chromatography from each of the aldonato complexes. These complexes were characterized by NMR, electronic absorption, and circular dichroism spectra. The structures of all four complexes were found to have an aldonato ligand which coordinates bidentately through an oxygen atom of the carboxylato group and an oxygen atom of the deprotonated hydroxyl group on C(2).

It has been widely known for a long time that aldonic acids form stable complexes with metal ions.[1)] Especially, gluconic acid and its salts have been used extensively as sequestering agents for metal ions in alkaline media. Numerous industrial applications have been reported.[2)] These ligands have many functional groups which can bind to metal ions. However little has been reported on the coordination chemistry of aldonic acid complexes. Several crystal structures of aldonic acid salts have been reported,[3)] but only two of the transition metal aldonic acid complexes, those are lead gluconate[4)] and manganese gluconate,[5)] have been clarified. Both complexes are polymer, in which the gluconato ligands bridge two metals. Because of the lability of these metal complexes, it seems that these complexes have no fixed chelate in solution.

Accordingly, substitution inert cobalt(III) complexes are suitable to study the coordination behavior of these ligands. It is interesting to examine the coordination behavior of metal complexes of the C-2 epimers, gluconic acid and mannonic acid, since the chelate ring formation via hydroxyl group on C(2) atom is expected.

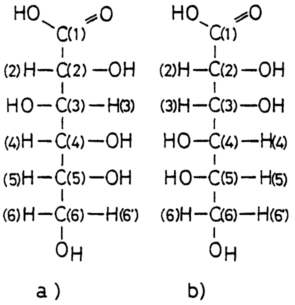

Fig. 1. Structure of (a) D-gluconic and (b) L-mannonic acid.

We report the first successful isolation of several Co(III) complexes of D-gluconic acid and L-mannonic acid (Fig. 1), and the coordination geometry of the complexes were studied by visible-UV absorption, CD, and NMR spectra as a part of our study to investigate sugar transition metal complexes.[6)]

Experimental

Materials, Measurements and Analyses. D-Glucono-1,5-lactone and L-manno-1,4-lactone were purchased from Tokyo Kasei Kogyo and Sigma Co., respectively.

^{1}H NMR spectra were recorded on a JEOL GX-400 spectrometer using 2,2-dimethyl-1-propanol as an internal reference. ^{13}C NMR spectra were obtained on this instrument or JNM-PFT-100 spectrometer using tetramethylsilane as an external reference.

Visible-UV absorption spectra were obtained with a HITACHI model 340 spectrophotometer. Circular dichroism spectra were measured with a JASCO J-500 spectropolarimeter.

Preparation of Δ and Λ-[Co(D-gluconato)(en)$_2$]ClO$_4$·H$_2$O. *Caution!* These perchlorate salts are stable under the experimental conditions as described below. However these complexes are potentially explosive, so that these materials should be handled with great care.

Aldonic acid complexes were prepared by a method analogous to that reported for the lactic acid complexes.[7,8)] 1.38 g of $[Co(CO_3)(en)_2]Cl$[9)] was dissolved in 10 mL of water, 0.89 g of D-glucono-1,5-lactone was added. The solution was heated to 90 °C and refluxed on a steam bath for 4 h. After cooling, the solution was diluted with water (500 mL) and poured onto a column of SP-Sephadex C25 gel (Na$^+$ form; 4×30 cm). The column was washed with water (1 L), and the adsorbed products were eluted with 0.05 M sodium perchlorate solution (1 M=1 mol dm^{-3}). A red band of unipositive charged complexes was eluted, this was made of a mixture of two isomers. Sodium perchlorate was partially removed from the red eluted solution by a Sephadex G-10 gel permiation chromatography, then the solution collected were separated again by Dowex 50W X-8 resin (Na$^+$ form; 3×60 cm) with 0.25 M NaH_2PO_4–0.25 M Na_2HPO_4 buffer solution. It was impossible to separate two isomers with one pass through the column, so that the isomers were separated by recycled elution using a peristaltic tube pump. After the complete separation in the resin, each band was eluted with 0.1 M sodium perchlorate. Sodium perchlorate was removed

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from each of the separated red solution by passing three times through a Sephadex G-10 gel column (3.5X50 cm). Each red liquor was evaporated under reduced pressure to a syrup, this was dissolved in a small amount of water, then ethanol was added to incipient turbidity. The solution was kept in a refrigerator. Λ-[Co(D-gluconato)(en)$_2$]ClO$_4$·H$_2$O (**1**) was obtained as a little hygroscopic reddish powder (100 mg) from the latter fractions of the Dowex eluents, and Δ-[Co(D-gluconato)(en)$_2$]ClO$_4$·H$_2$O (**2**) was obtained as red needles (180 mg) from the former fractions. Anal. Found for Λ-isomer: **1**: C, 24.61; H, 5.73; N, 11.48; Cl, 7.27%, for Δ-isomer **2**: C, 24.48; H, 5.50; N, 11.08; Cl, 6.97%. Calcd for CoC$_{10}$H$_{28}$O$_{12}$N$_4$Cl: C, 24.47; H, 5.75; N, 11.42; Cl, 7.22%.

Preparation of Δ and Λ-[Co(L-mannonato)(en)$_2$]ClO$_4$·H$_2$O. These complexes were prepared from [Co(CO$_3$)(en)$_2$]Cl and L-manno-1,4-lactone by the above mentioned procedure. The Λ-isomer **3** (160 mg) was also obtained from the latter fractions separated by a Dowex 50W X-8 cation-exchange column chromatography, and the Δ isomer **4** (130 mg) was obtained from the former fractions. Both of the isomers were isolated as somewhat hygroscopic red powder. Anal. Found for Λ-isomer **3**: C, 24.05; H, 5.35; N, 10.94; Cl, 7.83%, for Δ-isomer **4**: C, 23.63; H, 5.08; N, 10.59; Cl, 6.29%. Calcd. for CoC$_{10}$H$_{28}$O$_{12}$N$_4$Cl: C, 24.47; H, 5.75; N, 11.42; Cl, 7.22%.

Results and Discussions

Isolation of Aldonic Acid Complexes. Aldonic acid complexes were prepared by the reaction of [Co(CO$_3$)(en)$_2$]Cl complex with aldonic acid lactones. In an aqueous solution, D-glucono-1,5-lactone and L-manno-1,4-lactone, which were used in this study, were known to have the equilibrium between the lactones and acid forms.[10] When D-glucono-1,5-lactone was used, two +1 charged red complexes (complex **1** and **2**) were separated from the reaction mixture by ion exchange chromatography, both of these complexes were isolated as perchlorate salts. When L-manno-1,4-lactone was used, two red complexes **3** and **4** were also obtained.

Analytical results indicated that all these complexes obtained have one dinegative charged aldonato ligand, two ethylenediamine ligands, a perchlorate counter anion, and a solvated water molecule. Two isomers were obtained for both the aldonic acid complexes. These isomers are found to be Δ and Λ isomers whose absolute configurations were determined by CD spectra as described later.

UV-Visible Absorption Spectra. The absorption and CD spectra for the series of complexes are shown in Fig. 2, and their spectral data are presented in Table 1. These absorption spectra all show two peaks in the d-d transition region. The band positions and the intensities of the absorption spectra for these complexes are nearly identical. Each lowest energy peak shows a symmetrical curve without any shoulder in the first absorption region, which is characteristic for

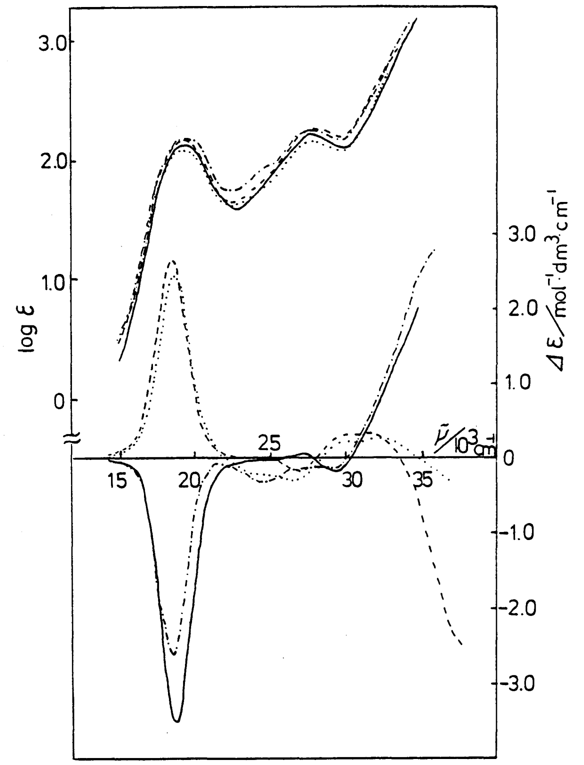

Fig. 2. Electronic absorption and circular dichroism spectra of aldonato complexes. (——) Δ-[Co(D-gluconato)(en)$_2$]$^+$, (----) Λ-[Co(D-gluconato)(en)$_2$]$^+$, (-·-·-) Δ-[Co(L-mannonato)(en)$_2$]$^+$, and (------) Λ-[Co(L-mannonato)(en)$_2$]$^+$.

Table 1. Electronic Absorption and CD Spectra

Complex	Abs max/10^3 cm^{-1} (log ε)	CD max/10^{3}cm^{-1} ($\Delta\varepsilon$/mol^{-1}dm^{3}cm^{-1})
Λ-[Co(D-gluconato)(en)$_2$]ClO$_4$·H$_2$O	19.4(2.13)	18.6(+2.64)
	28.1(2.24)	27.0(−0.19) 31.6(+0.30)
Δ-[Co(D-gluconato)(en)$_2$]ClO$_4$·H$_2$O	19.4(2.11)	18.7(−3.53)
	28.0(2.20)	26.9(+0.075) 29.2(−0.21)
Λ-[Co(L-mannonato)(en)$_2$]ClO$_4$·H$_2$O	19.4(2.05)	18.7(+2.42)
	28.0(2.12)	26.7(−0.30) 32.9(+0.24)
Δ-[Co(L-mannonato)(en)$_2$]ClO$_4$·H$_2$O	19.4(2.19)	18.5(−2.61)
	28.0(2.24)	24.8(−0.30) 28.6(−0.12)
Λ-[Co((*R*)-lactato)(en)$_2$]Cl$_2$·H$_2$O[a)]	19.4(2.12)	19.2(+2.37)
	27.8(2.14)	24.7(−0.67) 30.0(+0.064)
Λ-[Co(D-tartrato)(en)$_2$]Cl[b)]	19.7(2.07)	19.0(+1.79)
	28.3(2.14)	27.5(−0.13)

a) From Ref. 7. b) From Ref. 12.

Table 2. ^{13}C NMR Data for Aldonato Complexes. (ppm from TMS ext.)

Complex	Carbon atom of aldonato				Carbon atom of diamine	
	C1	C2	C3-5	C6		
Λ-[Co(D-gluconato)(en)$_2$]$^{2+}$	191.5	82.5	75.3	63.9	46.4	46.1
			72.2		44.3	43.9
			70.8			
Δ-[Co(D-gluconato)(en)$_2$]$^{2+}$	191.1	82.6	75.6	63.8	46.6	46.1
			72.2		44.6	44.5
			70.4			
Λ-[Co(L-mannonato)(en)$_2$]$^{2+}$	192.0	81.7	74.6	64.3	46.5	46.4
			73.4		44.7	44.6
			72.6			
Δ-[Co(L-mannonato)(en)$_2$]$^{2+}$	191.6	81.2	74.5	64.0	46.4	46.2
			72.8		44.9	44.5
			72.5			

the *cis*(*O*-*O*)-[CoN$_4$O$_2$] type.[11] The spectral results for Λ-[Co((*R*)-lactato)(en)$_2$]$^+$[7] and Δ-[Co(L-tartrato)(en)$_2$]$^+$[12] are also shown in Table 1. The similarity of band maxima and molar absorption coefficients of these aldonato complexes to those of lactato or tartrato complexes supports that the aldonic acids coordinate to cobalt atom through a carboxylato group and a deprotonated hydroxyl group of the aldonato ligand.

NMR Spectra and Coordination Structures. The ^{13}C NMR spectral data of these complexes together with those of sodium aldonate are given in Table 2. Because ^{1}H and ^{13}C NMR spectra of these complexes resemble each other, the following discussion applies equally to all of the complexes. The ^{13}C NMR spectra of these complexes show ten signals. The higher-field four signals and the lower-field six signals can be ascribed to the two ethylenediamine units and to the aldonic acid unit, respectively. The coordination points of the aldonato ligand were determined from these NMR data.

As a typical example, we deal with Λ-[Co(D-gluconato)(en)$_2$]ClO$_4\cdot$H$_2$O (**1**). The complete ^{1}H decoupled ^{13}C NMR spectrum of **1** in the range of 60—200 ppm is shown in Fig. 3. The C(1) and C(6) carbons of aldonato ligands were easily assigned by using non ^{1}H decoupling with NOE measurement. The C(2) carbon centered at about δ 82 was assigned by using selective decoupling methods as described below.

The ^{1}H NMR spectral data of the gluconato units of these complexes are tabulated in Table 3. A doublet at about δ 4.2 could be assigned to the H2 proton on C(2) atom. All other peaks were assigned by using double resonance techniques. In the ^{13}C NMR spectra, a selective irradiation of the proton resonance at about δ 4.2 gave one singlet peak at about δ 82. Accordingly, the ^{13}C signal at about δ 82 was assigned to C(2) atom.

Both C(1) and C(2) carbons shift clearly to the lower-field in comparison with those of sodium gluconate (Fig. 3). These low-field shift of the carbon nuclei may be caused by the coordination of the adjacent oxygen atom to the cobalt atom. In fact, we observed the similar low-field shift of ^{13}C signal for cobalt(III) complexes.[13]

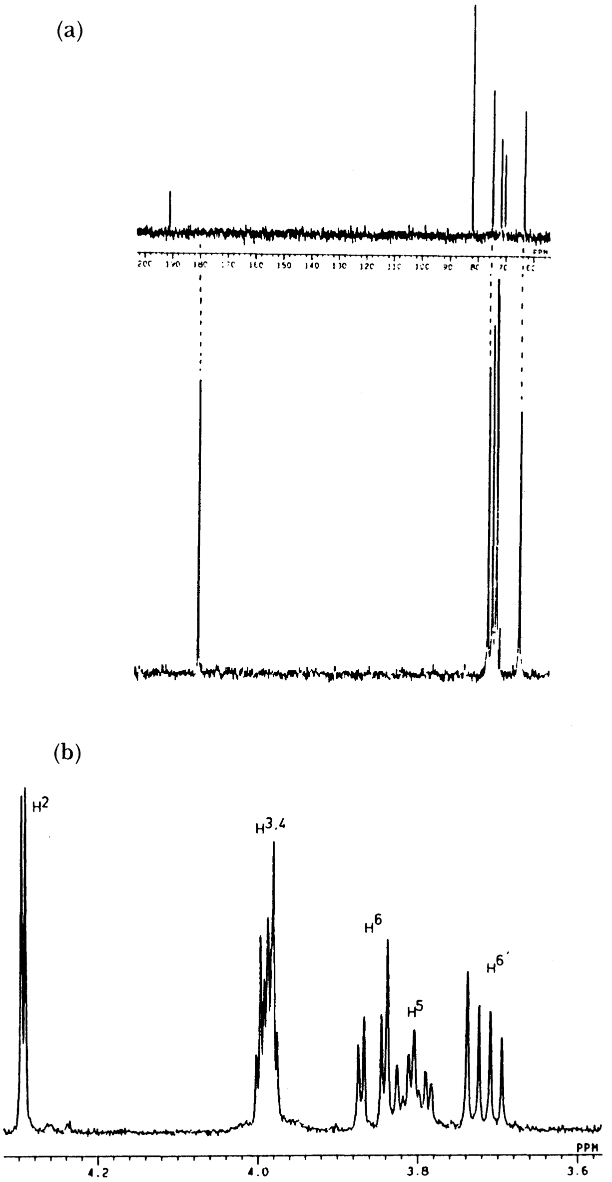

Fig. 3. (a) Upper, ^{13}C NMR spectrum of Λ-[Co(D-gluconato)(en)$_2$]$^+$ (60—200 ppm region). Lower, ^{13}C NMR spectrum of sodium D-gluconate. (b) ^{1}H NMR of Λ-[Co(D-gluconato)(en)$_2$]$^+$ (3.7—4.3 ppm). All spectra were obtained in D$_2$O solution.

Table 3. ^{1}H NMR Data for Aldonato Complexes

Complex	Chemical shift values (ppm)					
	H2	H3	H4	H5	H6	H6′
Λ-[Co(D-gluconato)(en)$_2$]$^{2+}$	4.30	3.98	4.00	3.80	3.72	3.86
Δ-[Co(D-gluconato)(en)$_2$]$^{2+}$	4.24	3.97	4.00	3.82	3.72	3.85
Λ-[Co(L-mannonato)(en)$_2$]$^{2+}$	4.21	4.06	3.93	3.78	3.71	3.86
Δ-[Co(L-mannonato)(en)$_2$]$^{2+}$	4.27	4.02	3.89	3.78	3.71	3.86

	Coupling constant/Hz					
	$J_{\mathrm{H2,3}}$	$J_{\mathrm{H3,4}}$	$J_{\mathrm{H4,5}}$	$J_{\mathrm{H5,6}}$	$J_{\mathrm{H5,6'}}$	$J_{\mathrm{H6,6'}}$
Λ-[Co(D-gluconato)(en)$_2$]$^{2+}$	1.8	2.0	a)	5.8	2.8	11.5
Δ-[Co(D-gluconato)(en)$_2$]$^{2+}$	1.5	2.4	7.6	5.8	2.8	11.3
Λ-[Co(L-mannonato)(en)$_2$]$^{2+}$	3.0	2.4	7.6	6.3	2.7	11.6
Δ-[Co(L-mannonato)(en)$_2$]$^{2+}$	3.0	2.6	6.4	6.1	2.5	9.0

a) Cannot determined due to the overlapping of the peaks.

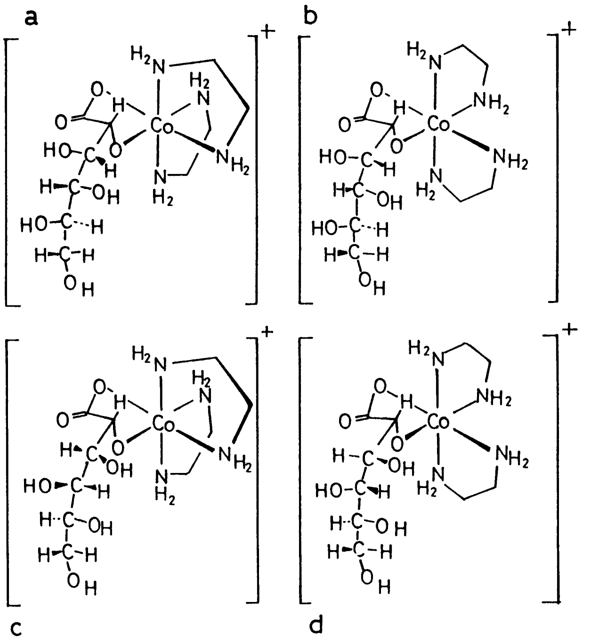

Fig. 4. Structures of (a) Λ-[Co(D-gluconato)(en)$_2$]$^+$, (b) Δ-[Co(D-gluconato)(en)$_2$]$^+$, (c) Λ-[Co(L-mannonato)(en)$_2$]$^+$, and (d) Δ-[Co(L-mannonato)-(en)$_2$]$^+$ ions.

From the above arguments we concluded that aldonato ligands coordinate to the cobalt at two points through the carboxylato oxygen atom and through the deprotonated hydroxyl oxygen atom on C(2) forming a five-membered chelate ring. The same discussions can be done for all of the other aldonato complexes (**2**, **3**, and **4**), their structures are shown in Fig. 4. No other complexes except these complexes containing five-membered aldonato chelate were detectable on the +1 charged reaction products. This fact points out that five-membered chelate formation is the most favorable coordination of the aldonato ligands.

Some interesting information concerning the conformation of the aldonato ligands can be drawn from the NMR J_{HH} coupling constant values. The values $J_{\mathrm{H4,5}}$ and $J_{\mathrm{H5,6}}$ are comparatively large, but $J_{\mathrm{H2,3}}$ and $J_{\mathrm{H3,4}}$ are small, so that it is deduced that the conformation of the carbon skeleton of aldonato ligands is not completely flexible, but it is somewhat fixed even in aqueous solution. There are no significant differences between the coupling constants of the gluconato complexes and the mannonato complexes except some differences in $J_{\mathrm{H2,3}}$ values. This difference is reasonable because gluconato and mannonato ligands can originally be regarded as C(2) epimer, and only H2-H3 relative configuration is different between those ligands (see Fig. 1).

Circular Dichroism Spectra and Stereochemistry of the Complexes. Two diastereomers can be obtained from each of these aldonato complexes. The CD spectra in the first d-d absorption region of the two isomers give nearly mirror image curves. For both the D-gluconato and L-mannonato complexes, the compounds in the former eluted fractions from the Dowex cation exchange column are assigned to Δ isomers because these complexes have a minus CD peak in the region, on the other hand, those in the latter eluted fractions are assigned to Λ isomers.[14]

It is well-known that the contributions to the optical activity from the configurational and vicinal effects are essentially additive in considering the CD spectra of the octahedral metal complexes.[15] The vicinal effect ($\Delta\varepsilon(R)$ or $\Delta\varepsilon(S)$) includes the conformational effect of the chelate rings (δ or λ) and the effect induced from the asymmetric centers (R or S) in the ligand. The following relationships will then hold: $\Delta\varepsilon(\Lambda)=1/2[\Delta\varepsilon(\Lambda R)-\Delta\varepsilon(\Delta R)]$ and $\Delta\varepsilon(R)=1/2[\Delta\varepsilon(\Lambda R)+\Delta\varepsilon(\Delta R)]$, where $\Delta\varepsilon(R)$ is the CD contribution due to the vicinal effect of the coordinated (R) chelate such as (R)-amino acids, (R)-hydroxy acids, or (R)-aldonic acids and $\Delta\varepsilon(\Lambda)$ is the contribution of Λ configuration. In general, the configurational effect is much greater than the vicinal effect in cobalt complexes. But, Kipp and Haines, however, reported that the CD spectra of Λ-[Co((R)-lactato)(en)$_2$]$^+$ and its Δ isomer are not mirror image, so the vicinal effect of the hydroxy acid ligand is more intense than would be expected from comparison with similar amino acid complexes.[7)]

In our aldonato complexes, however, the calculated configurational contribution to the circular dichroism $\Delta\varepsilon(\Lambda)$ is much greater than the vicinal contribution, $\Delta\varepsilon(R)$. In fact, $\Delta\varepsilon(\Lambda)$ are 3.1 for D-gluconato complexes and 2.5 for L-mannonato complexes and $\Delta\varepsilon(R)$ are 0.4 for D-gluconato complexes and 0.1 for L-mannonato complexes, respectively. Accordingly, the configurational effect is the main effect in these aldonato complexes as observed for other related complexes containing amino acids.

The formation ratio of Δ and Λ diastereomers of these aldonato complexes was determined on the basis of their absorption strength.

Λ : Δ (complex **1**: complex **2**), was determined to 52 : 48 for D-gluconato complexes and complex **3** : complex **4** was 67 : 33 for L-mannonato complexes. It is well-known that only a small stereoselectivity was observed in the preparation of $[Co(en)_2(\text{L-amino acidato})]^{2+}$ in comparison with $[Co(en)_2(\text{chiral diamine})]^{3+}$.[16)] The hydroxy acid ligand seems to give a nearly planer five membered chelate ring as well as the amino acid. Therefore, the stereoselectivity of the aldonato complexes due to the conformational preferences is not expected so much. The isomers ratio (Λ : Δ) for the gluconato complexes is, indeed, nearly 50 : 50. However, small stereoselectivity was observed in the formation of the mannonato complexes. Accordingly, it is suspected that small stereoselectivity is given by the interaction between the hydroxylmethylene chain of the mannonato ligand and diamine ligands.

It is well-known that chiral amino acid ligands in the complex such as $[Co(ala)(en)_2]^+$ (ala=L- or D-alaninato) are easily epimerized in mild alkaline solution (pH 9—10).[17)] The stability of these aldonato complexes in alkaline solution were monitored by CD measurement. The CD spectral curves of all these complexes do not change after heating at 40 °C even in 0.1 M Na_2CO_3 solution (pH 12). Thus, α-proton of aldonato chelate is found to be remarkably inactive in comparison with that of amino acid chelate. Since in the first stage of base catalyzed epimerization OH^- ions would smoothly attack to complexes which have large positive charges, one of the reasons of the stability is suspected to be more negative charge of the aldonato ligands than amino acid ligands.

Conclusion

Both Δ and Λ-$[Co(aldonato)(en)_2]^{2+}$ complexes containing five-membered aldonato chelate were obtained from the reaction between aldonic acid lactones and *rac*-$[Co(CO_3)(en)_2]^+$. Some stereoselectivity between the diastereomers (Δ and Λ) is observed although it is relatively low. α-Protons of these aldonato chelates are remarkably inactive in alkaline solution in comparison with the $[Co(\text{amino acidato})(en)_2]^{2+}$ complexes.

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