Geometrical and Optical Isomers of Diethylenetriaminemonoacetato(ethylenediamine)cobalt(III) Ion and their Isomerism

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Abstract

Two isomers of the complex ion in the title were obtained and each isomer was resolved chromatographically into its antipodes. The two isomers with their isomer proportion of 27.9 and 72.1% in the equilibrium mixture were assigned to α and β(*mer*-N) isomers, respectively, of three possible geometrical isomers, from the measurements of their absorption, circular dichroism, and NMR spectra.

Preference of the β(*mer*-N) to the isomer and very poor yield of an expected β(*fac*-N) isomer were confirmed by conformational analyses carried out for each structure of the isomers of Λ configuration, with possible configurations around nitrogen atoms and conformations of chelate rings. They gave minimized total strain energies of 43.13, 44.24, and 52.63 kJ/mol for the Λ-*R*,*R*(en:λ) structure of a β(*mer*-N) isomer, the Λ-*S*,*R*(δ,δ) structure of an α isomer, and a Λ-*R*,*S*(λ,λ) structure of a β(*fac*-N) isomer, respectively.

From the results, configurations and conformations of the enantiomers of the resolved β(*mer*-N) and its isomers were deduced. An unfound isomer, β(*fac*-N) isomer, is thought to be very unstable; it would exist as less than 2% of the amount of β(*mer*-N) isomer, even if it were present in the reaction mixture.

Introduction

The complex ion in the title, $[Co(dtma)(en)]^{2+}$ (dtma = diethylenetriaminemonoacetato, or formally 8-amino-3,6-diazaoctanato) possesses three possible geometrical isomers, as shown in Fig. 1a. Each of the β-isomers has two possible isomers due to asymmetric centers at the secondary nitrogen atoms. For the α-isomer, however, such an isomerism is not available because configurations around the secondary nitrogen atoms are fixed by chelation.

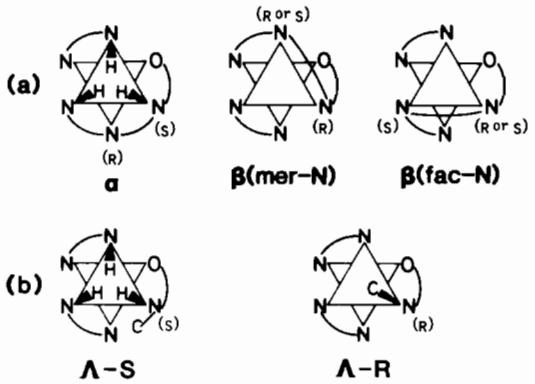

Fig. 1. Schematic structures of the possible isomers of (a): Λ-$[Co(dtma)(en)]^{2+}$ and (b): Λ-$[Co(sar)(en)_2]^{2+}$.

Cobalt(III) complexes with tetradentate ligands have been studied, first by Collman *et al.* [1] and then by others [2–6]. They reported that complexes of the type $[Co(AA)(dtma)]^{n+}$ (AA = bidentate ligand) were isolated mostly as β(*mer*-N) isomers. No other possible isomers including optical ones have been obtained so far.

Previously we isolated all four of the possible isomers of the bis(ethylenediamine)sarcosinatocobalt(III) ion, $[Co(sar)(en)_2]^{2+}$, and studied their stereoselectivity [7]. Figure 1b shows two isomers of Λ configurations, where *R* and *S* are configurations around the asymmetric nitrogen atom. The structures of the Λ-α and Λ-β isomers of $[Co(dtma)(en)]^{2+}$ seem to resemble those of the Λ-*S* and Λ-*R* isomers of $[Co(sar)(en)_2]^{2+}$, respectively.

The ratio of the Λ-*S* isomer to the Λ-*R* isomer on equilibration was 15/85. The lower stability of Λ-*S* can be ascribed to increased non-bonded interaction due to access of the N-methyl group of the sarcosinato ligand to the adjacent ethylenediamine ligand. Thus, in the present complex containing the dtma ligand, in which the methyl group of sarcosinato is linked to a nitrogen atom of en through another methylene group, the strain due to non-bonded inter-

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action would be decreased, and an isomer ratio of Λ-α to Λ-β higher than 15/85 is expected for [Co(dtma)(en)]$^{2+}$.

In the present study, we intended to obtain all the possible isomers of the complex in the pure optically active form. The isolated isomers are characterized and assigned to each structure, and the formation ratio at equilibrium determined experimentally is compared with the difference in the calculated total strain energy obtained from the conformational analysis of each isomer.

Experimental

Preparation of Diethylenetriaminemonoacetato(ethylenediamine)cobalt(III)iodide ([Co(dtma)(en)]I_2) and Column-chromatographic Separation of the Isomers

Into the suspension of [$CoCl_2$(dtma)] (20 g) [1] in 150 ml of water were added 25 g of 20% ethylenediamine aqueous solution and 2 g of activated charcoal. The mixture was heated at 60 °C for about 6 h with stirring. Charcoal and insoluble materials were filtered off. From half of the filtrate, the iodide salt of the complex was precipitated by adding an excess of sodium iodide. The iodide of the complex was recrystallized from alcoholic water (EtOH–H_2O). *Anal.* Found: C, 17.96; H, 4.23; N, 13.13. Calc. for $C_8H_{22}N_5O_2CoI_2$: C, 18.03; H, 4.16; N, 13.14%.

The rest of the filtrate was chromatographed on an SP-Sephadex column (φ 3.0 × 84 cm or 1.7 × 76 cm) with a 0.12 M Na_2SO_4 solution as eluant. The elution gave two orange-colored bands well separated from each other, besides pink–red and yellow–brown colored bands of univalent and tervalent complex cations which were eluted much faster and slower, respectively, than those above.

Each complex included in the two orange bands, denoted by **A** and **B** in order of effluence, was obtained as a chloride salt by a method similar to that described previously [7]. The complex chlorides of both **A** and **B** complexes were confirmed to be [Co(dtma)(en)]Cl_2 from their elemental analyses. *Anal.* Found, (**A**): C, 27.44; H, 6.69; N, 19.11 (**B**): C, 27.23; H, 6.21; N, 19.78. Calc. for $C_8H_{22}N_5O_2$-$CoCl_2$: C, 27.43; H, 6.33; N, 20.00%.

Equilibration

About 0.1 g of the chloride or iodide of each complex was dissolved in 20 ml of water with or without Na_2SO_4 (0.12 M), adjusted to pH *ca.* 9 with NaOH. After the addition of activated charcoal (0.1 g), the mixture was incubated at 60 °C for one day with constant stirring. The activated charcoal was then filtered off, and aliquots of the filtrate were subjected to column-chromatography using an aqueous 0.12 M Na_2SO_4 solution as eluant.

Each solution gave two orange bands corresponding to the **A** and **B** complexes. Each eluate from the **A** and **B** bands was collected. The contents of the **A** and **B** complexes were determined by measurement of the optical density of the solutions.

Chromatographic Resolution

Each of the **A** and **B** complexes was chromatographed again on an SP-Sephadex column (φ 3.0 × 84 cm) with a 0.12 M $Na_2[Sb_2(L\text{-}C_4H_2O_6)_2]$ solution as eluant. The elution of the **A** isomer gave two well-separated bands denoted by **A-1** and **A-2** in order of effluence, while that of the **B** isomer resulted in no appreciable separation. For the separation of the **B** isomer, a recycling chromatographic technique [8] was employed under the same conditions as above. After seven cycles, two bands were sufficiently separated. These isomers are hereafter denoted by **B-1** and **B-2**, in a manner similar to those of the **A** isomer. The concentration ratio of isomer **1** to isomer **2** was 1.0 in the case of either **A** or **B**.

Each isomer was obtained as the chloride salt from the corresponding eluate using a method similar to that described above. All four isomers (**A-1**, **A-2**, **B-1**, and **B-2**) were optically active and their circular dichroism (CD) spectra show that **A-1** and **A-2** are enantiomeric, as are **B-1** and **B-2**.

Deuteration

Glycinate methylene protons in the **A** and **B** isomer were deuterated by heating each isomer in a dilute DCl(D_2O) solution according to the method of Gailey *et al.* [9] with a slight modification.

A typical procedure is as follows. The chloride salt of the **A** or **B** isomer was dissolved in 2 ml of D_2O and the solution was slowly evaporated to dryness over P_2O_5 under reduced pressure. The residue was dissolved in 2 ml of 0.8 M DCl, and the solution was sealed in a glass tube and heated at *ca.* 90 °C for 4 days in an oil bath. The ^{13}C NMR spectrum of the solution was directly measured.

Preparation of [Co(dtma)(^{15}N, ^{15}N-en)]$^{2+}$

0.45 g of ^{15}N-enriched ethylenediamine hydrochloride, $^{15}NH_2CH_2CH_2{}^{15}NH_2 \cdot 2HCl$: ^{15}N isotopic content *ca.* 27%, was dissolved in 10 ml of H_2O and the pH of the solution was adjusted to *ca.* 9 with NaOH. The solution was added to the suspension of [$CoCl_2$(dtma)] (0.91 g) and activated charcoal (0.1 g) in 40 ml of water. The mixture was heated at about 60 °C for one hour with stirring. After filtration, the filtrate was chromatographed on an SP-Sephadex column using a 0.12 M Na_2SO_4 solution as eluant.

The **A** and **B** isomers containing ^{15}N-enriched ethylenediamine were obtained separately as 0.5 M HCl solutions by the method described previously [7].

Physical Measurements

Absorption (AB) spectra were recorded on a Shimadzu UV200 spectrophotometer, and circular dichroism spectra on a JASCO J-20 Automatic Recording Spectropolarimeter. ^{13}C and ^{15}N NMR spectra were obtained with a JEOL JNM FX-60 spectrometer at a probe temperature of 35 °C. Dioxane and a D_2O solution of $Na^{15}NO_3$ in a coaxial inner tube were used as external references of ^{13}C and ^{15}N NMR signals, respectively.

Conformational Analysis

Strain-energy minimization calculations were carried out by employing a modification of the MM2 computer program. The bond-stretching force constants were obtained from the table of Snow [10] and angle-bending and torsional force constants were adopted from those of DeHayes and Busch [11]. When the force constants were not available from these sources, they were adopted or estimated from the original MM2. Before the present calculations, strain-energy minimization was performed for $[Co(edta)]^-$, and some equilibrium bond distances were adjusted so that the structure would better fit that obtained by the X-ray method [12].

Results and Discussion

Equilibration of the Isomers of $[Co(dtma)(en)]^{2+}$ Ion

When either the **A** or the **B** isomer in a weakly basic solution was incubated at 60 °C in the presence of activated charcoal, the equilibrium mixture contained both **A** and **B** in the ratio of about 28/72, the same as the ratio in the reaction mixture (Table I). This means that the **A** and **B** isomers isomerize reversibly to each other, and the latter is more stable than the former in aqueous solutions. No difference was found in the isomer ratio between the chloride and iodide salt solutions after equilibration. However, the sulfate salt solution or addition of sulfate ions to the iodide salt solution caused a significant increase in the content of the **A** isomer in the equilibrium mixture, e.g., up to 35% in a 0.2 M sodium sulfate solution. Such an increase is considered to show that the **A** isomer has a larger tendency to form ion-pairs with sulfate ions than does the **B** isomer [7]. This suggests that the **A** isomer would be an α isomer in which three hydrogens of N–H bonds are oriented in parallel at one face of the octahedron.

Chromatographic Behavior and Resolution

The **A** isomer is eluted faster and resolved more easily with a 0.12 M $Na_2[Sb_2(L\text{-}C_4H_2O_6)_2]$ solution on an SP-Sephadex column than the **B** isomer. The latter requires seven recyclings of chromatography for a sufficient resolution. Greater selectivity for $[Sb_2(L\text{-}C_4H_2O_6)_2]^{2-}$ ions is found between the enantiomers of the **A** isomer which forms a more stable ion-pair with a sulfate ion. Furthermore, the **A** isomer can also be resolved with a sodium L-tartrate solution as eluant. These facts provide additional evidence for the assignment of the **A** isomer as an α isomer with the same orientation mentioned in the previous section.

Absorption (AB) and Circular Dichroism (CD) Spectra

Figure 2 shows AB and CD spectra of the resolved isomers in the region of the first and second absorption bands. From the enantiomeric CD spectra of **A-1** and **A-2** and of **B-1** and **B-2**, only those of **A-1** and **B-2** are shown in the figure. They are considered to have Λ configuration because they have dominant CD peaks with positive signs at the longer wavelengths. The first absorption band of the **A** isomer is shifted toward the longer wavelength, compared with that of the **B** isomer. Such a shift may be due to the larger splitting of the absorption band of the former. These spectra are comparable to the spectra of Λ-$[Co(sar)(en)_2]^{2+}$ [7]. The CD spectrum of the **A-1** isomer particularly resembles that of the Λ-*S* isomer of $[Co(sar)(en)_2]^{2+}$ except for their different intensities. Therefore, it may be concluded that the **A** isomer is an α isomer and, accordingly, the **A-1** isomer can be assigned to that

TABLE I. Equilibrium Isomer Distributions for $[Co(dtma)(en)]^{2+}$ Salt at 60 °C

Isomer (salt)[a]	Solution	Formation (%)		Formation ratio A/B
		A	B	
Reaction mixture*		27.8	72.2	0.385
B (iodide)	H_2O	27.3	72.7	0.376
A (chloride)	H_2O	28.1	71.9	0.390
B (chloride)	H_2O	28.3	71.7	0.395
B (sulfate)	H_2O	32.5	67.5	0.482
B (iodide)	0.2 M Na_2SO_4	35.1	64.9	0.540

[a]Starting substance for equilibration except in the case of *.

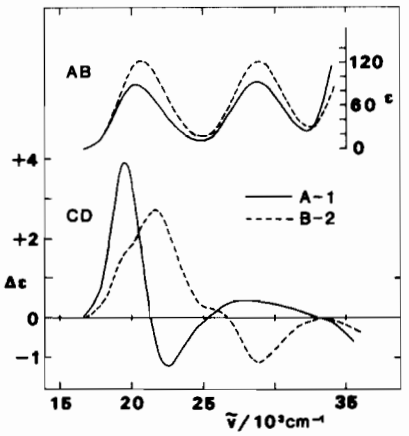

Fig. 2. AB and CD spectra of the resolved isomers. (——): **A-1**; (- - -): **B-2**. Intensity of CD spectrum of **B-2** is doubled.

of a Λ-α-*S*,*R* configuration, while the **B** isomer is one of the β isomers (see conformational analysis below).

Carbon-13 and Nitrogen-15 NMR Spectra and Assignment of the Signals

Figure 3 shows the positions and intensities of $^{13}C\{^1H\}$ NMR signals of the **A** and **B** isomers. The spectrum of the **A** isomer has a signal of two-fold intensity in the higher field. The weak signal at the lowest field of each spectrum is that of the carboxylate group. The spectra of deuterated and ^{15}N(en)-enriched **B** isomers are compared with that of the normal one in Fig. 4. In the ^{15}N(en)-enriched complex, two signals of ethylenediamine carbon nuclei are expected to be doublets due to coupling with the ^{15}N nucleus adjacent to each carbon nucleus. Thus, the two signals in the higher field are readily assigned to the en-carbon nuclei.

Protons of α-methylene of amino carboxylato complexes are known to be exchangeable with deuterons [9]. A signal of the deuterated methylene carbon is broadened by coupling with the deuteron. Therefore, the signal which disappeared in spectrum C is assigned to that of a glycinate methylene carbon, and the adjacent slightly broadened signal is of a γ-methylene carbon to a carboxyl group. The signals of the **A** isomer are similarly assigned. The assignments to each carbon are shown in Fig. 3. Among the unassigned signals in the **A** isomer, the one showing incidental degeneracy with an en carbon signal at the highest field may be assigned to the methylene carbon adjacent to the amino group on the basis of its structural similarity to a methylene carbon of en. The separation in the spectrum between the signals of two methylene carbon nuclei of ethylenediamine is much larger for the **B** isomer than for the **A** isomer.

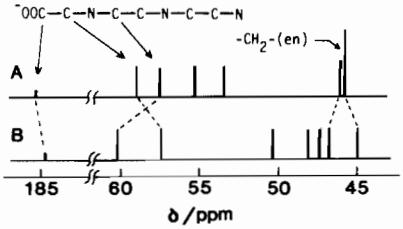

Fig. 3. Positions and intensities of $^{13}C\{^1H\}$ NMR signals of the **A** and **B** isomers.

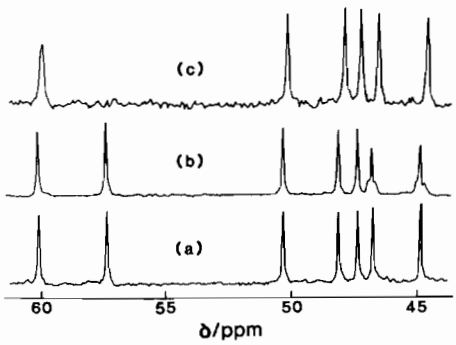

Fig. 4. $^{13}C\{^1H\}$ NMR spectra of the **B** isomer of $[Co(dtma)(en)]^{2+}$. (a): normal; (b): ^{15}N(en)-enriched; (c): deuterated (see text).

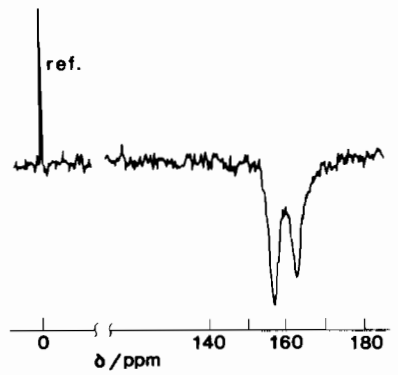

Fig. 5. $^{15}N\{^1H\}$ NMR spectrum of the ^{15}N(en)-enriched **B** isomer with δ values to higher field, using $Na^{15}NO_3$ as an external reference.

Chemical shifts of ^1H, ^{13}C, and ^{15}N nuclei are known to be considerably influenced by ligands in the *trans* position [13, 14]. This suggests that the **B** isomer is a β(*mer*-N) isomer, where one carbon atom of the en ring is *trans* to the oxygen atom and the other is in a *cis* position; both of the en carbon atoms are *cis* to the oxygen atom in both the α and the β(*fac*-N) isomer. This assignment is also supported by $^{15}N\{^1H\}$ NMR spectrum of the **B** isomer with the ^{15}N-enriched en ligand (Fig. 5). The spectrum shows two well-separated peaks attributable to two nitrogen nuclei of ethylenediamine. The signal in

TABLE II. Total Strain Energy of Possible Isomers of $[Co(dtma)(en)]^{2+}$ (in kJ/mol)

Isomer	Configuration (Conformation)			
α	Λ-*S*,*R*[a](δ,δ)[b] 44.24	Λ-*S*,*R*(δ,λ) 49.18	Λ-*S*,*R*(λ,δ) 53.82	Λ-*S*,*R*(λ,λ) 54.88
β(*fac*-N)	Λ-*R*,*S*(δ,δ) 62.33	Λ-*R*,*S*(δ,λ) 65.22	Λ-*R*,*S*(λ,δ) 55.58	Λ-*R*,*S*(λ,λ) 52.63
	Λ-*S*,*S*(δ,δ) 61.10	Λ-*S*,*S*(δ,λ) 70.50	Λ-*S*,*S*(λ,δ) 58.17	Λ-*S*,*S*(λ,λ) 57.02
β(*mer*-N)	Λ-*R*,*R*(en:δ) 43.36	Λ-*R*,*R*(en:λ) 43.13	Λ-*R*,*S*(en:δ) 52.65	Λ-*R*,*S*(en:λ) 50.27

[a]A pair of *R* and *S* notations refer to the configurations of the nitrogen atoms at the 3- and 6-positions of dtma. [b]A pair of δ and λ notations refer to the conformations of the chelate ring containing the nitrogen atoms at the 6- and 9-positions of dtma and of ethylenediamine.

the higher field would be due to the nitrogen *trans* to the oxygen atom, and another signal due to the nitrogen *cis* to it.

Conformational Analysis

In order to further confirm the structures of the isomers obtained, conformational analysis was carried out about the possible isomers (Fig. 1). Table II shows the calculated strain energy of the energy-minimized structures. Among the α isomers, the Λ-*S*,*R*(δ,δ) or Δ-*R*,*S*(λ,λ) structure is the most stable. Therefore, the isolated isomers, **A-1** and **A-2** are assigned to the Λ-*S*,*R*(δ,δ) and Δ-*R*,*S*(λ,λ) configurations, respectively, in accordance with that speculated from their CD spectra. Similarly, it can be concluded that the **B-1** and **B-2** isomers have the β(*mer*-N)-Δ-*S*,*S* and -Λ-*R*,*R* configurations, respectively. Since, in these isomers, the conformational change (δ or λ) of ethylenediamine is not sensitive to their strain energies, the conformations may be easily interchanged in an aqueous solution.

At equilibrium in an aqueous solution in the presence of activated charcoal at 60 °C, only two geometrical isomers could be detected, α isomer (28%) and β(*mer*-N) isomer (72%). The preferential formation of the β(*mer*-N) isomer is compatible with the results shown in Table II. If the third isomer, β(*fac*-N) exists in the equilibrium mixture, the content will be less than 2%.

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