Trifunctional Amino Acid Cobalt(III) Complexes of N,N'-Diethylethylenediamine-N,N'-di-α-butyrato Ligand

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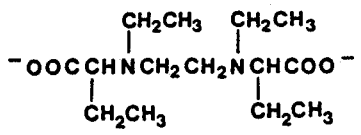
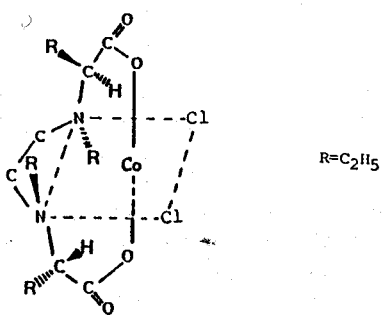
Cobalt(III) complexes of trifunctional amino acid and N,N'-diethylethylenediamine-N,N'-di-α-butyrate(deedba), *s-cis*-[Co(deedba)(L-aa)] (L-aa=S-methyl-L-cysteine, L-aspartic acid, L-glutamic acid) have been prepared from the reaction between the *s-cis*-[Co(deedba)(Cl_2)]$^-$ complex and the corresponding amino acid. The amino acids have been found to coordinate through the amine and carboxylate groups. The S-methyl-L-cystene is coordinated not by the sulfur donor atom, but by the nitrogen and oxgen donor atoms, and the L-aspartic and L-glutamic acids are coordinated to the cobalt(III) ion *via* formation of the five-membered glycinate chelate ring. Relatively small optical activity shown by the complexes is due to the chiral center present in the amino acids.

Introduction

The metal complexes of the linear flexible tetradentate ligands of the type ONNO in the donor atom array such as edda (ethylenediamine-N,N'-diacetic acid, $HOOCCH_2NHCH_2CH_2NHCH_2COOH$) have been studied by a number of workers.[1~8] Recently, we have prepared a novel ONNO-type tetradentate ligand, N,N'-diethylethylenediamine-N,N'-di-α-butyrate (deedba), and the *s-cis* isomer of the dichloro cobalt(III) complex of deedba,[9] *s-cis*-[Co(deedba)Cl_2]$^-$ (Figure 1). The deedba cobalt(III) complexes of the trifunctional amino acids such as S-methyl-L-cysteine (L-smc), L-aspartic acid (L-asp), and L-glutamic acid (L-glu) are of particular interest because only two of the three fuctional groups present in those amino acids can bine to the cobalt(III) complexes of deedba. S-methyl-L-cystein, L-aspartic acid, and L-glutamic acid can, when coordinated to a metal ion, form a five-, six-, seven-, or even eightmembered (L-glu) chelate ring depending on the mode of coordination. A trifunctional amino acid ligand offers an additional interesting question as to which functional groups are utilized in chelation. There are three possible modes of chelation when L-smc reacts with [Co(deedba)Cl_2]$^-$ as shown in Figure 2: N, S chelation (I), S, O chelation(II), and N, O chelation(III). In the *s-cis*-[Co(deedba)(L-aa)] complex (L-aa=L-asp or L-glu), there are also three possible geometric isomers resulting from the different modes of coordination of the amino acids (Figure 3). Although the trifunctional amino acids have been observed to coordinate to a metal ion mostly through the -NH_2 and -COO^- group,[10~12] we have undertaken to study the chelate systems of the cobalt(III) complexes containing the deedba and the trifunctional amino acids of L-smc, L-asp, and L-glu.



N,N'-diethylethylenediamine-N,N'-di-α-butyrate (deedba)



R=C_2H_5

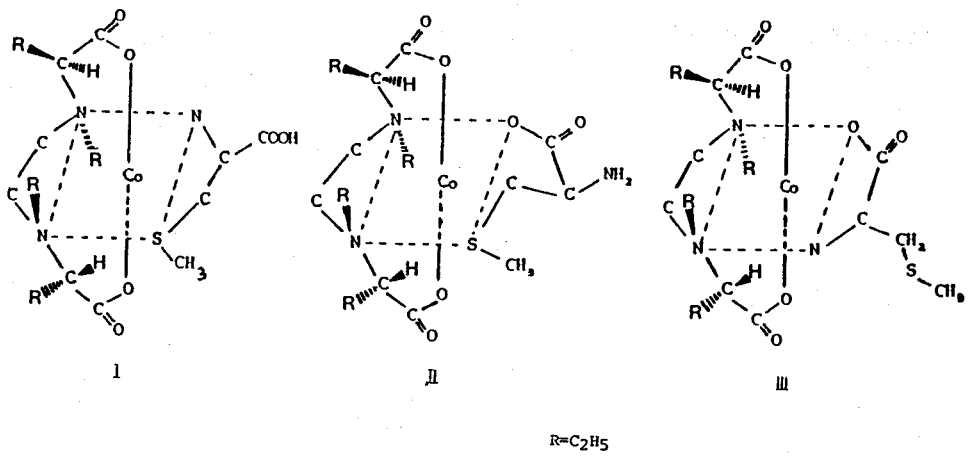
Figure 1. Structures of deedba ligand and *s-cis*-[Co(deedba)(Cl_2)]$^-$ complex.

Experimental

L-Aspartic acid (Aldrich), L-glutamic acid (Aldrich), and S-methyl-L-cysteine (Nutritional Biochemicals) were used without further purification. Dowex 50W-X4 cation exchange resin (200-400 mesh, H^+ form) was used after purification to separate the metal complex isomers prepared in this work. Electronic absorption and infrared spectra were recorded on a Shimadzu UV-240 double Beam Spectrometer and a Shimadzu IR 435 Spectrometer, respectively. Pmr spectra were measured with a 270 MHz JEOL GSX-270 Spectrometer and a 80 MHz Varian FT-80A spectrometer. Cicular Dichroism spectra were obtained from a JASCO J-550C Automatic Recording Spectropolaimeter. Elemental analyses were performed by Micro-Tech Analytical Lab., Skokie, Illinois, USA.

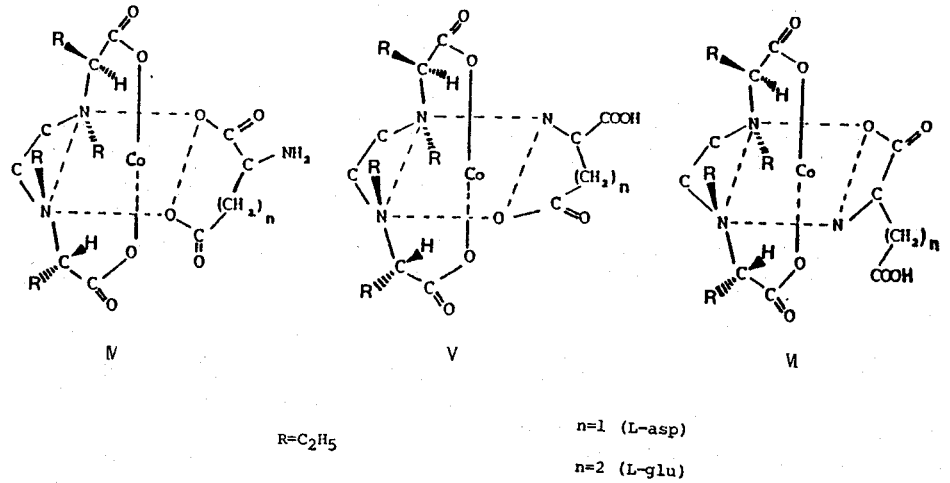
Preparation of Barium N,N'-diethylethylenediamine-N,N'-di-a-butyrate(Badeedba) and *s-cis*-hydrogen Dichloro(N,N'-diethylethylenediamine-N,N'-di-α-butyrato) cobaltate(III), *s-cis*-H[Co(deedba)Cl_2]. The synthesis of the deedba ligand and the *s-cis*-H[Co(deedba)Cl_2] complex has been described previously.[9]

Preparation of *S-cis*-N,N'-diethylethylenediamine-N,N'-di-α-butyrate)(S-methyl-L-cysteinato)cobalt(III), *s-cis*-[Co(deedba)(L-smc)]. 1.3 g (3 mmol) of *s-cis*-H[Co(deedba)Cl_2] was dissolved in 40 mL of water and heated for 20 min at 60 ℃. 0.4 g (3 mmol) of S-methyl-L-cysteine was added to this solution and the pH of the solution was adjusted to 8.0 with 1 N NaOH. 0.1 g of active carbon was



R=C_2H_5

Figure 2. The geometrical isomers of [Co(deedba)(L-smc)] complex.



R=C_2H_5 n=1 (L-asp) n=2 (L-glu)

Figure 3. The geometrical isomers of [Co(deedba)(L-aa)] where aa is aspartic or glutamic acid.

added to this solution and the reaction mixture was refluxed for 8 hrs at 60 ℃ while stirring with a mechanical stirrer. The reaction mixture was filtered and the residues were washed with hot water. The combined filtrate and washings were concentrated to 5 mL, which was admitted to a column packed with Dowex 50W-X4 cation exchange resin (200-400 mesh, H^+ form). One fraction was detected by elution with water. The violet band was collected and concentrated to obtain the violet soild product, which was vacuum dried. Yield: 0.15 g (11%). Anal. Calcd. for $CoC_{18}H_{33}O_6N_3S$: C, 45.19; H, 6.95; N, 8.78. Found; C, 45.22; H, 6.88; N, 8.16.

Preparation of *S-cis*-N,N′-diethylethylenediamine-N,N′-di-α-butyrato(L-aspartato)cobalt(III) chloride, *s-cis*-[Co(deedba)(L-asp)]. This was prepared *via* the same method as that used to prepare *s-cis*-[Co(deedba)(L-smc)] using 1.1 g (2.5 mol) of *s-cis*-H[Co(deedba)Cl_2] and 0.3 g (2.5 mol) of L-aspartic acid. Yield: 0.3 g (26%), Anal. Calcd. for $CoC_{18}H_{30}O_8N_3 \cdot 0.5H_2O$: C, 42.61; H, 5.96; N, 8.28. Found: C, 42.92; H, 5.88; N, 8.16.

Preparation of *S-cis*-N,N′-diethylethylenediamine-N,N′-di-α-butyrato(L-glutamato)cobalt(III), *s-cis*-[Co (deedba)(L-glu)]. This was prepared *via* the same method as that used to prepare *s-cis*-[Co(deedba)(L-smc)] using L-glutamic acid (0.45 g, 3 mmol) in place of L-smc. Yield: 0.3 g (21%). Anal Calcd for $CoC_{19}H_{32}O_8N_3H_2O$: C, 43.02; H, 6.08; N, 7.92. Found: C, 43.01; H, 5.86; N, 7.71.

Results and Discussion

The trifunctional amino acid cobalt(III) complexes of deedba have been prepared from the substitution reactions between the *s-cis*-[Co(deedba)Cl_2]$^-$ complex and each of the amino acids used here, S-methyl-L-cysteine, L-aspartic acid and L-glutamic acid. Each of these reactions has yielded only one product, *s-cis*-[Co(deedba)(L-aa)] complex. Table 1 shows the COO stretching frequencies for the deedba ligand and the complexes prepared in this work. While the ligand shows the free -COOH group at 1590 cm^{-1}, the *s-cis*-[Co (deedba)(L-smc)] complex indicates the coordinated -COO^- at 1640 cm^{-1}. Accordingly, the structure I is ruled out due to the siginficant shift of the COO mode (Figure 2).[13]

The electronic absorption spectra are particularly helpful in distinguishing the coordinating donor atoms of N, O, and S. In the visible spectrum of [Co(deedba)(L-smc)] (Figure 4) the d-d transition occurs at 538 and 365 nm. The band at the longer wavelength is due to the transition $A_{1g} \rightarrow T_{2g}(O_h)$.

Table 1. The COO Antisymmetric Stretching Frequencise of the *s-cis*-[Co(deedba)(L-aa)] Complexes

Compound	as COO (cm^{-1})	
deedba	1590[a]	
s-cis-[Co(deedba)(L-smc)]	1640	
s-cis-[Co(deedba)(L-asp)]	1640	1720[a]
s-cis-[Co(deedba)(L-glu)]	1640	1720[a]

[a]Uncoordinated COO stretching band.

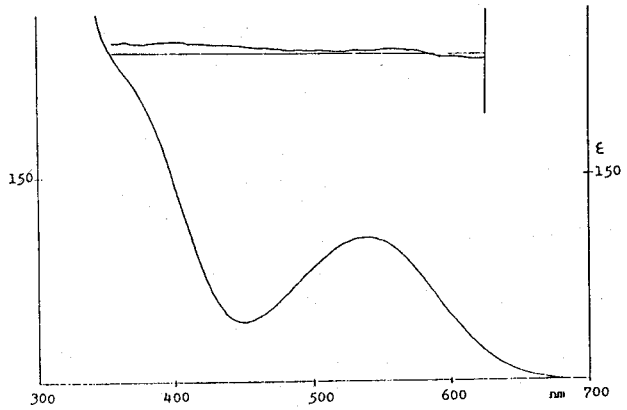


Figure 4. CD and Electronic absorption spectra of *s-cis-mer*-[Co (deedba)(L-smc)].

If and S atom is coordinated, the visible spectrum of either $[CoN_3O_2S]$ or $[CoN_2O_3S]$ (structure II in Figure 2) would have shown the d-d transitions at much longer wavelengths (~600 nm) than those observed in this work, reflecting the relative positions of the groups in the spectrochemical series $-S^- <$ amine $< -CO^{2-}$. Therefore, the Structure II in Figure 2 is eleminated, and in the [Co(deedba)(L-smc)] complex the coordination of the S-methyl-L-cysteine ligand takes place through the amine and carboxylate groups (Structure III) to give the meridional N, O chelation.

In the pmr spectrum of the *s-cis-mer*-[Co(deedba)(L-smc)] complex (Figure 5), the methyl protons at the sulfur atom should be shown as a singlet near 1.9 ppm, the β-methylene protons and the α-carbon proton of L-smc at 2.7 and 3.4 ppm, respectively, although these peaks are somewhat complicated due to the protons in the N-ethyl, and the C-ethyl groups of the deedba ligand shown at near 1.1 ppm as two triplets.

In the *s-cis*-[Co(deedba)(L-aa)] complexes (L-L=L-asp or L-glu), the Structure IV (Figure 3) would not occur in reality because of the excessively large chelate ring to be formed by those amino acids. The Structure V involves a chelate ring formed by the amino group and the non-α-carboxylate group, while the structure VI has a chelate ring formed by the amino acid and the α-carboxylate groups.

Infrared spectra of both the *s-cis*-[Co(deedba)(L-asp)] and *s-cis*-[Co(deedba)(L-glu)] complexes show the uncoordinated -COOH at 1720 cm^{-1} and the coordinated $-COO^-$ at 1640 cm^{-1}, indicating the fact that the complexes prepared in this work have either the Strucure V or the Structure VI. In the case of the L-glutamic acid complex, *s-cis*-[Co(deedba)(L-

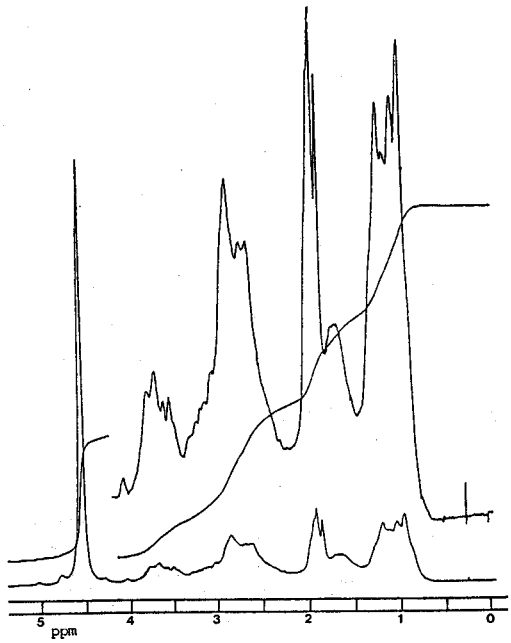


Figure 5. PMR Spectrum of *s-cis-mer*-[Co(deedba)(L-smc)].

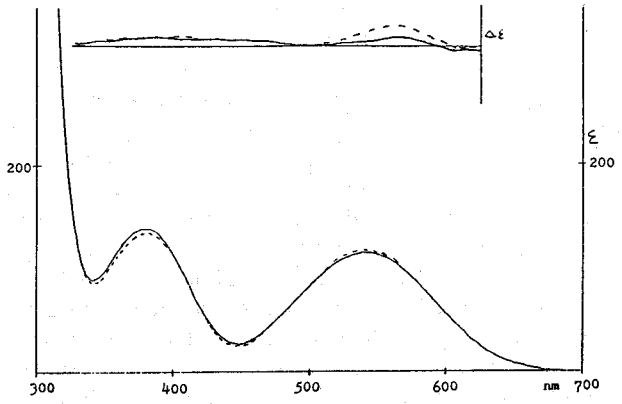


Figure 6. CD and Electronic absorption spectra of *s-cis-mer*-[Co (deedba)(L-glu)] (—) and *s-cis-mer*-[Co(deedba)(L-asp)] (---).

glu)], the structure V can be eliminated, for the glutamato chelate ring would involve a seven membered ring, which would be much more unstable than the five-membered chelate ring of the structure VI. The *s-cis*-[Co(deedba)(L-glu)] complex is, therefore, expected to take the Structure VI, and, as a matter of fact, the glutamic and aspartic acids are known to coordinate *via* the five-membered chelate ring.[10,12] The electronic absorption spectra for the L-asp and L-glu complexes (Figure 6) are not particularly helpful in distinguishing the structures because the Structures V and VI are of the same CoN_3O_3 type. The pmr spectra of the complexes prepared in this work, however, give some evidence for the existenced of a five-memebered chelating in the complex for structure VI.

In the pmr spectrum of the *s-cis*-[Co(deedba)(L-asp)] complex (Figure 7) the terminal methyl protons in the N-ethyl and C-ethyl groups of the deedba ligand are shown at near 1.1 ppm. The β-methylene protons of the L-asp are shown

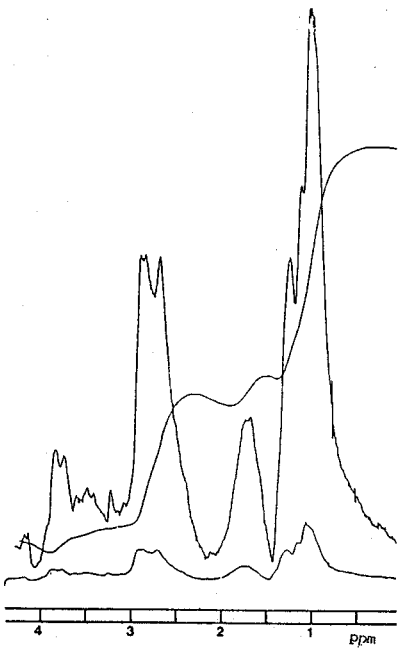


Figure 7. PMR Spectrum of *s-cis-mer*-[Co(deedba)(L-asp)].

at 2.7 ppm along with the methylene protons between the two nitogen donor atoms of the deedba ligand. The proton of L-asp and the α-protons in the R ring (outside chelating of deedba) are shown in the 3.3-4.0 region. A similar spectral behavior was also observed for $[Co(NH_3)_4(L\text{-asp})]^{2+}$ as a model for assigning the more complex spectra.[10] The pmr spectrum of *s-cis*-[Co(deedba)(L-glu)] complex shows the same pattern as observed for the *s-cis*-[Co(deedba)(L-asp)] complex. The similarity in the chemical shifts of the terminal methyl protons of the deedba ligand in the complexes of L-smc, L-asp, and L-glu are resulted from the protons being in the same chemical environment in those complexes as would be expected, if the complexes have a five membered chelate ring. Our assignment that *s-cis*-[Co(deedba)(L-asp)] and *s-cis*-[Co(deedba)(L-glu)] complexes have the Structure VI is substantiated by the observation that the glutamic and aspartic acids are coordianted exclusively *via* the five-memberd glycinate ring in the [Co(tmdda)(L-glu)] and [Co(tmdda)(L-asp)] complexes.[10,12]

The *s-cis*-$[Co(deedba)Cl_2]^-$ complex used as a starting material has been obtained as a racemic mixture. The CD curves (Figures 4 and 6) show relatively small optical activity for the complexes prepared in this work. Although the L-amino acids take the λ chelate ring conformation exclusively when coordinated to a metal ion,[16,17] the overall optical activity of the amino acid complexes of [Co(deedba)(L-aa)] are diminished because of the racemic nature of the dichloro $[Co(deedba)Cl_2]^-$ complex from which the amino acid complexes are prepared. The optical activity shown in Figures 4 and 6 should, therefore, be due to the contribution from the chiral center present in the amino acids rather than the contribution from the amino acid chelate ring conformation.

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