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Proton Magnetic Resonance Spectra of L- or D-Aspartato (L-2,4-diaminobutyrato)cobalt(III) Complexes

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Three diastereomeric isomers of the L-aspartato(L-2,4-diaminobutyrato)cobalt(III) and two of the D-aspartato (L-2,4-diaminobutyrato)cobalt(III), $Co(N)_3(O)_3$ type were prepared and isolated. The isomers were characterized by their electronic absorption and proton magnetic resonance spectra. Their PMR spectra indicate that the carbon proton adjacent to the coordinated N atom resonates at a higher magnetic field when O atom occupies the site *trans* to the N atom than when N atom occupies the same place.

The preparation and characterization of cobalt(III) complexes containing optically active amino acids which are potentially tridentate ligands have been reported for those with L-2,4-diaminobutyrate ion (L-2,4-dba),[1)] D- or L-2,3-diaminopropionate ion (D- or L-2,3-dpa),[2)] L-aspartate ion (L-asp)[3,4)] and L-histidinate ion (L-his).[5)]

However, the assignments are tentative except for that for $[Co(L\text{-}2,3\text{-}dpa)_2]^+$, the exact geometries of which have been determined on the basis of an X-ray diffraction study of one of the *cis* O isomers.[6)] An alternative proposal has been given for the isomers for $[Co(L\text{-}asp)_2]^-$.[7)] The complexes of bis(L-aspartato)-cobaltate(III) and L-aspartato(iminodiacetato)cobaltate(III) belong to the $[Co(N)_2(O)_4]$ type, and the complexes of bis(L-2,4-diaminobutyrato)cobalt(III) and bis(histidinato)cobalt(III) to the $[Co(N)_4(O)_2]$ type. The aim of the present study was to prepare the mixed complexes [Co(L- or D-asp)(L-2,4-dba)] of the $[Co(N)_3(O)_3]$ type.

Experimental

L-2,4-Diaminobutyric acid was prepared from L-glutamic acid by the Schmidt reaction.[8)] All the other materials were of reagent grade.

Three Isomers of [Co(L-asp)(L-2,4-dba)]. To a hot solution (*ca.* 70 °C) containing 1.33 g (0.01 mol) of L-aspartic acid and 1.55 g (0.01 mol) of L-2,4-diaminobutyric acid monohydrochloride in 50 ml of water were added 3.6 g (0.01 mol) of freshly prepared $Na_3[Co(CO_3)_3]\cdot 3H_2O$ and 1 g of activated charcoal. The mixture was stirred on a boiling water bath for *ca.* 30 min. The mixture was then filtered and the charcoal was carefully washed with hot water. The washings and filtrate were combined and concentrated to *ca.* 20 ml on a rotary evaporator at about 40 °C and kept in a refrigerator overnight. Violet powder crystals which appeared were filtered off, washed with a small amount of water and air-dried. The filtrate was passed through a column (3.0×30 cm) containing strong acid cation exchange resin in a hydrogen form (Dowex 50 w×8, 25—50 mesh) and successively through a colum (3.0×30 cm) containing strong base anion exchange resin in a hydroxide form (Dowex 21 k, 25—50 mesh). When water was passed through the column a non-charged complex flowed out. The eluate was concentrated to 10—20 ml. Chromatographic separation was then carried through a column (3.0×110 cm) containing strong acid cation exchange resin in a sodium form (Dowex 50w×8, 100—200 mesh). The adsorbed band was eluted with water at a rate of 0.4 ml/min. Three colored bands, violet (L1), redish violet(L2) and red (L3) were eluted in succession. The three eluates were collected separately and evaporated to dryness in a vacuum desiccator. Each crude product was dissolved in water and reprecipitated with ethanol. Since the amount of L3 was very small. The following alternative method was tried. To a solution containing 1.33 g (0.01 mol) of L-aspartic acid, 1.55 g (0.01 mol) of L-2,4-diaminobutyric acid and 1.0 g (0.025 mol) of NaOH in 30 ml of water were added 2.4 g (0.01 mol) of $CoCl_2\cdot 6H_2O$, 5 ml of 10% of hydrogen peroxide and 1 g of activated charcoal. The mixture was stirred on a boiling water bath for 30 min. Treatment of the reaction was the same as above. By this method the L3 isomer was obtained in a relatively higher yield.

Two Isomers of [Co(D-asp)(L-2,4-dba)]. The isomers were obtained by a similar method to that described above. One of the two meridional isomers was not obtaind. Two isomers were separated and are referred to as D1 and D2 by elution order. Found: (L1) C, 29.55; H, 5.14; N, 12.84%. (L3) C, 29.77; H, 5.15; N, 12.99%. Calcd for $CoC_8H_{14}O_6N_3\cdot 1H_2O$: C, 29.54; H, 4.97; N, 12.92%. Found: (L2) C, 30.38; H, 4.63; N, 13.18%. (D1) C, 29.55; H, 5.23; N, 13.22%. Calcd for $CoC_8H_{14}O_6N_3\cdot 0.5H_2O$: C, 30.39; H, 4.02; N, 13.29%. Found: (D2) C, 28.81; H, 5.78; N, 12.21%. Calcd for $CoC_8H_{14}O_6N_3\cdot 1.5H_2O$: C, 28.75; H, 5.13; N, 12.57%.

Measurements. The electronic absorption spectra were measured with a JASCO ORD-UV-5 spectrometer, proton magnetic resonance(PMR) spectra (100 MHz) in D_2O with a JEOL PS 100 spectrometer. Sodium 2,3-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal reference.

Results and Discussion

The possible isomers of [Co(L- or D-asp)(L-2,4-dba)] complexes are shown in Fig. 1. They are denoted by L- or D-series with respect to the asp used. Both series of mixed complexes are composed of two meridional and one facial about $[Co(N)_3(O)_3]$. The two L-*mer* isomers are denoted by L-*trans*O_5 *cis*N_5 (oxygen and nitrogen atoms of the five-membered chelate rings are respectively *trans* and *cis* with each other) and L-*cis*O_5 *trans*N_5. The three [Co(L-asp)(L-2,4-dba)] isomers (L-*trans*O_5 *cis*N_5, L-*fac*, L-*cis*O_5 *trans*N_5) seem to be generated at 120° intervals by an imaginary twist of one coordinated ligand relative to the other about an axis passing through the two ligand occupied triangular faces of the cobalt(III) coordination octahedron. The same kind of relationship exists for the three isomers containing D-aspartate ion.

Separation of the two mixed complexes was accomplished by chromatography on a cation exchange

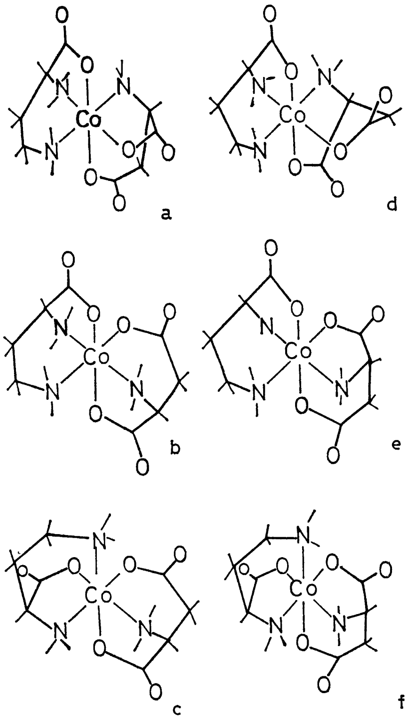

Fig. 1. The six possible geometrical isomers of the [Co(L- or D-asp)(L-2,4-dba)].
a: D-*cis*O_5 *cis*N_5, b: D-*trans*O_5 *trans*N_5, c: D-*fac*, d: L-*trans*O_5 *cis*N_5, e: L-*cis*O_5 *trans*N_5, f: L-*fac*.

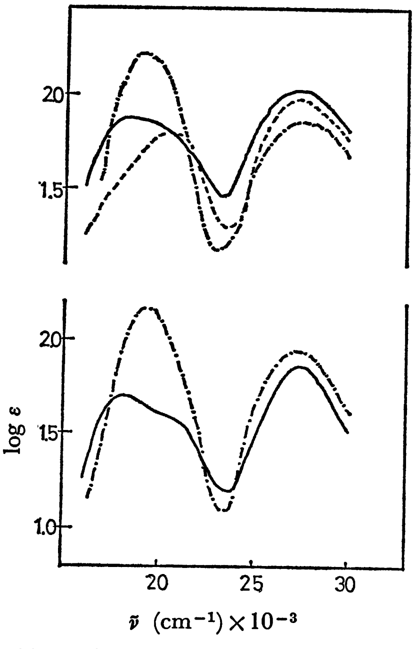

Fig. 2. Absorption spectra of the five isomers of the [Co(L- or D-asp)(L-2,4-dba)].
upper ——, L1; ----, L2; -·-·- L3, lower ——, D1; -·-·- D2.

resin column. Since the complexes exhibit electronic absorption spectra which agree with the crystal field considerations for *mer* and *fac* isomers (Fig. 2), it is possible to assign the *mer* geometry to L1, L2 and D1, and *fac* geometry to L3 and D2.

Assignment of Isomers. It is of significance to

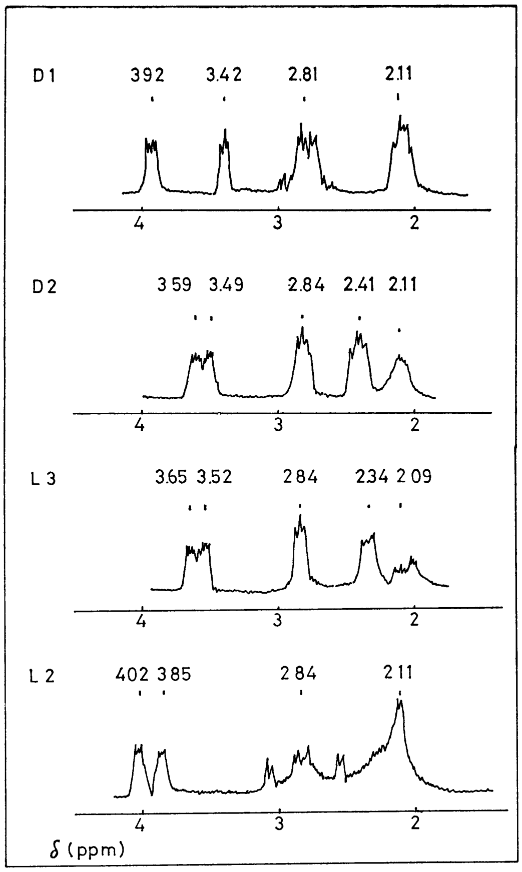

Fig. 3. PMR spectra of the four isomers of the [Co(L- or D-asp)(L-2,4-dba)].

determine the configuration of the *mer* isomers (L1, L2 and D1). Proton magnetic resonance spectra for the four isomers of the [Co(L- or D-asp)(L-2,4-dba)] in D_2O solution are given in Fig. 3. L1 is sparingly soluble in water, and L2, L3, D1 and D2 are soluble in D_2O sufficient for PMR measurements. L1, L3, D1 and D2 are soluble in trifluoroacetic acid, but not L2. Since the PMR specturm of L1 in trifluoroacetic acid resembles that of D1 in the same solvent, the spatial distribution of the ligand atoms (especially N or O atoms) seems to be analogous to that of D1. There is a similarity between the spectra of L3 and D2 in trifluoroacetic acid. The six mixed isomers have C_1 symmetry (Fig. 1). The PMR spectra are thus expected to consist of one ABX pattern due to the CH_2CH moiety of L- or D-asp and one ABMNX pattern due to the CH_2CH_2CH moiety of L-2,4-dba. In order to determine all the resonance lines of these protons, spin decoupling technique was used.

The peak at 2.11 (Fig. 3) can be assigned to the β-methylene protons of L-2,4-dba because of their magnetic shielding and electronegativities. Irradiation of this peak changes the multiplets at *ca.* 3.4—3.5 for D1, D2 and L3 and at *ca.* 3.8 for L2 to a singlet. This indicated that the signals at 3.4—3.5 for D1, D2 and L3 and at *ca.* 3.8 for L2 are attributed to the methine proton of L-2,4-dba moieties. Irradiation of the peak at *ca.* 2.8 makes the lowest field multiplets reduce to a singlet in all the complexes. Thus the lowest field

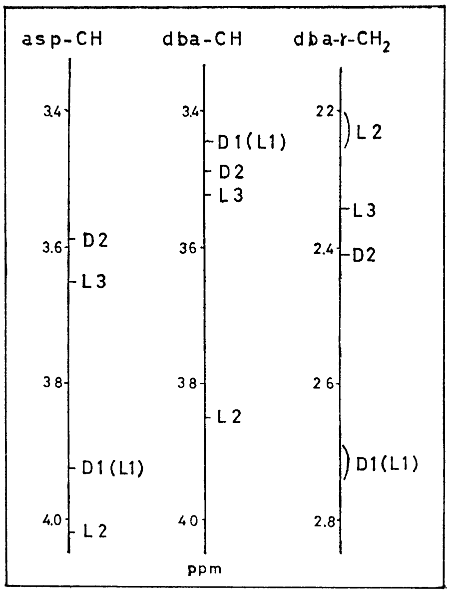

Fig. 4. The distribution of the proton chemical shifts of the [Co(L- or D-asp)(L-2,4-dba)] isomers.

resonance in all of the four spectra should be assigned to the methine proton of aspartic acid and the peak at *ca.* 2.8 to the methylene protons of aspartic acid. Chemical shifts of D1, D2, L2 and L3 are shown in Fig. 4.

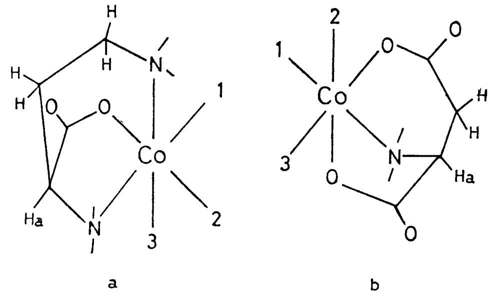

Fig. 5. The relation of the Ha proton chemical shifts and the sites of the other ligand.

The proton resonance peaks of the α-proton of the coordinated asp can be classified into two groups, as can also the chemical shifts of the α-proton and γ-protons of the L-2,4-dba. Although molecular model consideration suggests that the asp and L-2,4-dba coordinated may take several types of conformation, the direction of the C–H bond of α-carbon of both ligands does not seem to change. On the other hand, the difference in conformation of the six-membered chelate ring of L-2,4-dba coordinated seriously affects the orientation of the C–H bonds of γ-carbon, which may give rise to some change in the chemical shifts of γ-carbon protons. As a whole the PMR spectrum of D2 resembles that of L3 (Fig. 3) suggesting that the origin which differentiates the chemical shifts of the α-carbon protons of L-2,4-dba and L- or D-asp into the two magnetic field regions can be ascribed to the effects of the other ligands present, and not to the conformational changes of its own. The bicyclo chelate ring system formed by the coordination of each ligand is common in all six isomers. Because of the identical chelate ring systems, the coupling constant scheme between the eight carbon protons (OOC–CH$_2$–$\underset{|\atop \mathrm{NH_2}}{\mathrm{CHCOO}}$ and H$_2$NCH$_2$–CH$_2$–$\underset{|\atop \mathrm{NH_2}}{\mathrm{CHCOO}}$) in each ligand ring system may be closely resemble each other in the six cases. The geometrical isomers would then reveal themselves mostly in different chemical shifts of the eight carbon-bounded protons in individual cases of the same asp and L-2,4-dba. Different spectra for L2 and L3 and, for D1 and D2 have virtually been observed. For the sake of convenience the three coordination sites occupied by L- or D-asp, situated opposite to the fixed L-2,4-dba, are numbered as indicated in Fig. 5a. For the D2 and L3 isomers the three sites in the order 1,2,3 of the L-2,4-dba are occupied by oxygen, nitrogen and oxygen atoms, respectively (Fig. 5a), while those of the asp are occupied by oxygen, nitrogen and nitrogen atoms, respectively (Fig. 5b). The chemical shift of Ha proton of L-2,4-dba (Fig. 5a) is affected by:[9] 1) the polarity of the amine group due to the polarization of the metal ion induced by the ligand atom of site 1, 2) that of the carboxylate group due to the polarization of the metal ion induced by the ligand atom of site 2, and 3) magnetic anisotropic effects due to site 3. When the chemical shifts of the α-carbon proton of the L-2,4-dba of the complex D2 and L3 are governed by 1), the O atom which occupies site 1 gives rise to a higher field shift of the α-carbon proton of the L-2,4-dba. If this relation holds in the other cases (that is, whenever the O atom occupies site 1 (Fig. 5a), the α-carbon proton adjacent to the N atom *trans* to site 1 resonates at a higher field than when N atom occupies it), the chemical shift of the α-carbon proton of the L-2,4-dba of the D1 isomer which also lies in the higher field suggests that site 1 of D1 is occupied by the O atom. Thus, the isomer is assigned to D-*cis*O$_5$ *cis*N$_5$ configuration. The chemical shift of the α-carbon proton of the L-2,4-dba of the L2 isomer which lies in the lower field causes the isomer to be assigned to the L-*cis*O$_5$ *trans*N$_5$ configuration, as well. The chemical shift of the α-carbon proton of the L- or D-asp of the L3 and D2 isomer belongs to the higher field group, and site 1 corresponding to these protons should be occupied by the O atom. The chemical shift of the α-carbon proton of the D- or L-asp of the D1 and L2 isomers lies in the lower field, which indicates that site 1 corresponding to these protons is certainly occupied by the N atom. A similar relationship between the chemical shift of the γ-carbon protons of the L-2,4-dba and the atom of the site 1 holds as well (Fig. 4). The relation between PMR chemical shifts of each isomer and the corresponding atom in site 1 is given in Table 1. In the case of sites 2 and 3 no simple explanation for the distinct classification of chemical shifts into two categories of magnetic field region can be given. Thus situation 1) seems to influence the chemical shifts in this case most favorably. The above consideration is in line with the study by Buckingham *et al.*[10] and Clifton and Pratt[11] for pentaammine cobalt(III) complexes [Co(NH$_3$)$_5$X]$^{n+}$. The PMR spectra of this series show two NH$_3$ reso-

TABLE 1. RELATIONSHIP BETWEEN CARBON PROTONS OF EACH ISOMER AND THE ATOM OCCUPYING THE CORRESPONDING SITE 1

	asp-CH	dba-CH	dba-γ-CH_2
D-*cis*O_5*cis*-N_5	N	O	N
D-*fac*	O	O	O
D-*trans*O_5*trans*N_5	N	N	O
L-*trans*O_5*cis*N_5	N	O	N
L-*fac*	O	O	O
L-*cis*O_5*trans*N_5	N	N	O

nances with a 12 : 3 intensity ratio, the intense band being in the lower field. The 12 equivalent protons belong to the NH_3 groups *cis* to the ligand X and the 3 to the *trans* NH_3 group. Clifton and Pratt[11] suggested that the *cis* protons may have been shifted to a lower field than the *trans*, since the polarity of the *trans* ammine group from the metal ion was reduced by ligand X. Our results are regarded as an extension of the above consideration on the reduced polarity of ammine nitrogen atom to that of the carbon proton adjacent to the ammine group. In order to ascertain whether the method of assignment holds for other complex systems or not, the chemical shifts of the PMR spectra of the $[Co(L\text{-}asp)_2]^-$,[4] $[Co(L\text{-}asp)(ida)]^-$ [12] and $[Co(L\text{-}2,4\text{-}dba)_2]^+$ complexes (Fig. 6) were investigated. The PMR spectra of the $[Co(L\text{-}2,3\text{-}dpa)_2]^+$ complexes were similar to those of the $[Co(L\text{-}2,4\text{-}dba)_2]^+$ complexes except for the peaks due to the β-carbon protons of the L-2,4-dba. The atom (O or N) in parentheses is the atom occupying site 1 (Fig. 6). Since the chemical shift of the γ-carbon protons of the L-2,4-dba coordinated was not distinct, the whole peaks are shown. The geometry of the F isomer of the $[Co(L\text{-}asp)_2]^-$ was *trans* N on the basis of the absorption spectrum. The S and L isomers have *cis* N geometries. The chemical shift of the α-carbon proton of L-asp of the F isomer lies in the lower field, which is in line with the fact that site 1 of this complex is occupied by the N atom. The chemical shift of α-carbon protons of the L-asp of the S and L isomers lies in a higher field in accordance with the fact that their site 1 was occupied by oxygen atom. This agrees with the trend found here. The same situation holds in the case of the $[Co(L\text{-}asp)(ida)]^-$ isomers. However the two *cis* N isomres cannot be distinguished from each other. In the $[Co(L\text{-}2,4\text{-}dba)_2]^+$ complexes, each isomer has been assigned by comparing the PMR spectra of $[Co(L\text{-}2,4\text{-}dba)_2]^+$ with those of $[Co(L\text{-}2,3\text{-}dpa)_2]^+$, assignments of which were based on X-ray analysis. The α isomer of the complex $[Co(L\text{-}2,4\text{-}dba)_2]^+$ has the *trans*O geometry and the β and γ isomers the *cis*O geometries. It has not been possible to assign the two *cis*O isomers so far to the *cis,trans,cis* (the isomers were named by considering the spatial relationship of first the two donor oxygens, then the two α-nitrogens, and finally the two γ nitrogens.) or the *cis,cis,trans* geometries without using the analogies of the PMR spectra of the corresponding complexes $[Co(L\text{-}2,3\text{-}dpa)_2]^+$. Applying the trend we found to this system, we find that since α-proton of the L-2,4-dba of the γ-isomer resonates in a higher field and that of α and β isomers in a lower field, site 1 of the γ isomer should be occupied by an O atom and that of α and of β by N atoms. The same relationship holds between the γ-protons of L-2,4-dba and the corresponding site 1. We can thus assign the β and γ isomers to the *cis,trans,cis* and *cis,cis,trans* geometries respectively. These assignments agree well with the result by Freeman and Liu.[1] For the $[Co(N)_4(O)_2]$ systems, the two *cis*O isomers can be distinguished by comparing their PMR spectra. For the $[Co(N)_3(O)_3]$ system the two meridional isomers are also distinguishable.

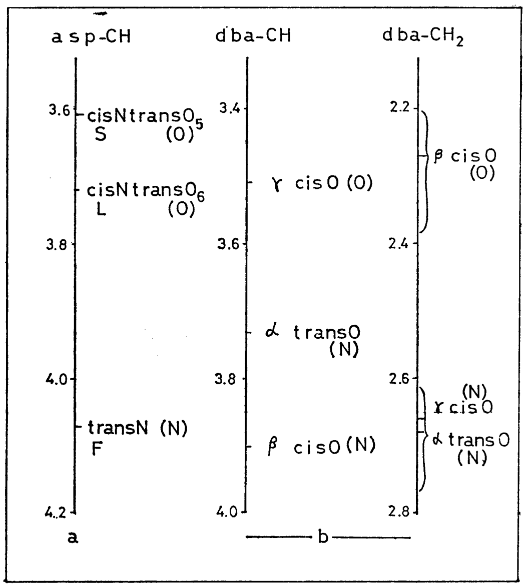

Fig. 6. The distribution of the chemical shifts of the $[Co(L\text{-}asp)_2]^-$ isomers (F=first elute, S=second elute, L=last elute) and the $[Co(L\text{-}2,4\text{-}dba)_2]^+$ (α=first elute, β=second elute, γ=last elute).

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