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# Preparation and Isomerization of Isomers of the L- or D-Aspartato(L-histidinato)cobalt(III) Complex

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The six isomers of the [Co(L- or D-asp)(L-his)] complex (asp = aspartate ion and his = histidinate ion) have been prepared and the isomerization studied in the absence of any catalyst. The equilibrium mole fractions of these isomers in water has been found for L-*trans*$O_5$*cis*$N_5$, L-*cis*$O_5$*trans*$N_5$, L-*fac*, to be 0.53, 0.06, and 0.41, respectively, those for D-*cis*$O_5$*cis*$N_5$, D-*trans*$O_5$*trans*$N_5$, and D-*fac* to be 0.48, 0.01, and 0.51 respectively. The indication is that the relative positions of the six coordinated atoms around a cobalt atom cause these unequal isomer concentration ratios. The isomerisms are dealt with by means of a network of first order reversible reactions and the absolute values of the rate constants at 80 °C have been determined.

In a previous work,[1] the isomerzation of D-aspartato(L-2,4-diaminobutyrato)cobalt(III), [Co(D-asp)(L-2,4-dba)] was studied in the presence of active carbon. The relative rate constants of the isomerization and the mole fractions of the isomers at equilibrium were determined. However, those of the [Co(L-asp)(L-2,4-dba)] complex could not be determined on account of their low solubilities. In this paper, the preparation and the isomerization of the isomers of the D- or L-aspartato(L-histidinato)cobalt(III) complex are presented. All isomers are soluble in water.

## Experimental

*Preparation of [Co(L- or D-asp)(L-his)].* To a solution of $CoCl_2\cdot6H_2O$ (2.4 g) in water (20 cm$^3$) containing 10% $H_2O_2$ (5 cm$^3$) was added an aqueous solution containing L-aspartic acid (1.33 g), L-histidine (1.55 g), and NaOH (0.95 g). The pH of this mixed solution became *ca.* 7. The solution was stirred for 24 h at 30 °C, concentrated to about 20 cm$^3$ and passed through a column (30 mm$\phi$ $\times$ 700 mm) containing a strong acid cation exchange resin (Dowex 50WX8, Na$^+$ form). By slowly washing the column with water, five bands were distinguished, the last three bands corresponding to the isomers of the [Co(L-asp)(L-his)] complex. The three fractions were violet (H1), brick red (H2), and red violet (H3) in that order of elution. In order to separate the bands of H1 and H2 precisely, the fractions were circulated several times in the column using a quantitative micropump. The three fractions were evaporated to dryness below 30 °C by a rotatory evaporator. The isomers of the [Co(D-asp)(L-his)] complex were similarly prepared using D-asp insted of L-asp. The three fractions were violet (I1), brick red (I2), and red violet (I3) in that order of elution. Found: (H1) C, 30.66; H, 4.95; N, 13.80%. Calcd for $CoC_{10}H_{13}O_6N_4\cdot3H_2O$: C, 30.21; H, 4.81; N, 14.01%. Found: (I2) C, 35.08; H, 3.87; N, 16.63%. Calcd for $CoC_{10}H_{13}O_6N_4\cdot0.5H_2O$: C, 34.95; H, 3.81; N, 16.31%. Found: (H2) C, 33.01; H, 3.81; N, 14.81%. (H3) C, 32.65; H, 4.15; N, 15.00%. (I1) C, 32.81; H, 4.18; N, 15.40%. (I3) C, 32.35; H, 4.25; N, 14.89%. Calcd for $CoC_{10}H_{13}O_6N_4\cdot1.5H_2O$: C, 32.41; H, 4.35; N, 14.89%.

The method of isomerization for the [Co(L- or D-asp)(L-his)] complex was similar to that described in a previous paper.[1] Since the H1(I1), H2(I2), and H3(I3) isomers could be easily separated by means of high speed liquid chromatography (column contained a strong cation exchange resin, TSK LS-212 Toyo Soda Ind., Na$^+$ form), the concentrations of these isomers were determined with a UV spectrophotometer (at 254 nm) by comparison with the peak height of a known concentration of isomer.

## Results and Discussion

*Characterrization.* Figure 1 shows the possible isomers of the [Co(L- or D-asp)(L-his)] complex. 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 the chromophore $[Co(N)_3(O)_3]$. The isomers are denoted by considering the 5-membered glycinato N and O atoms. The two mer isomers for the L-series are denoted by L-*trans*$O_5$ *cis*$N_5$ and L-*cis*$O_5$ *trans*$N_5$. Similarly the three isomers of [Co(D-asp)(L-his)] are designated

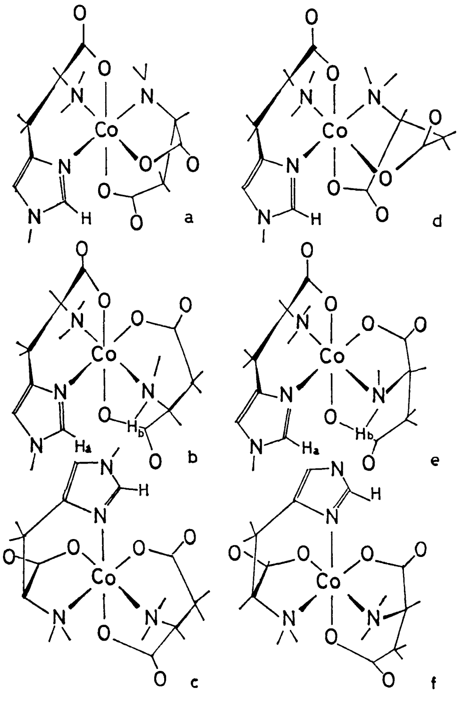

Fig. 1. The six possible geometrical isomers of the [Co(L- or D-asp)(L-his)] complex, a; *cis*$O_5$*cis*$N_5$, b; *trans*$O_5$*trans*$N_5$, c; D-*fac*, d; *trans*$O_5$*cis*$N_5$, e; *cis*$O_5$-*trans*$N_5$, and f; L-*fac*.

by D-*cis*$O_5$*cis*$N_5$, D-*trans*$O_5$*trans*$N_5$, and D-*fac*. Figures 2a and 3a show the electronic absorption spectra.

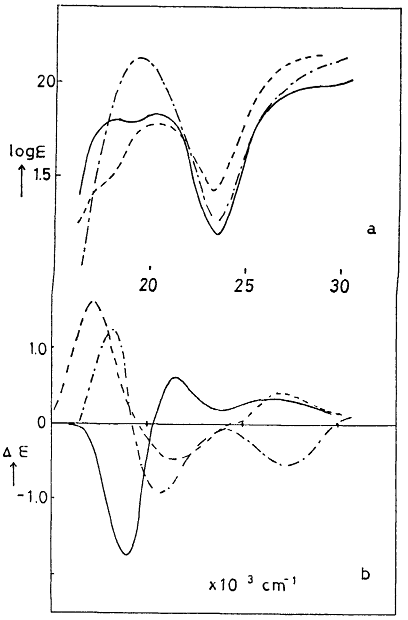

Fig. 2. Absorption (upper) and CD (lower) spectra of [Co(L-asp)(L-his)]. H1 (——), H2 (----), and H3 (——).

Table 1 shows the numerical data for the electronic absorption spectra of [Co(L- or D-asp)(L-his)], together with those for the isomers of [Co(L- or D-asp)(L-2,4-dba)].[1] The absorption spectra of the [Co(L- or D-asp)(L-his)] complexes were similar to those for [Co(L- or D-asp)(L-2,4-dba)]. The ligand L-2,4-dba differs from the histidine only in that it contains the $NH_2$–$CH_2$-group in the position occupied by the imidazole group in histidine. The charge transfer bands which tail into the visible region in the spectra of the [Co(L- or D-asp)(L-his)] complexes are absent in the [Co(L- or D-asp)(L-2,4-dba)] complexes. When the elution order and the similarity of the visible absorption spectra between [Co(L- or D-asp)(L-his)] and [Co(L- or D-asp)(L-2,4-dba)] are taken into account, the isomers H1, H2, and H3 are tentatively assigned as L-*trans*$O_5$*cis*$N_5$, L-*cis*$O_5$*trans*$N_5$, and L-*fac*. The isomers I1, I2, and I3 are also assigned as *D-cis*$O_5$*cis*$N_5$, D-*trans*$O_5$*trans*$N_5$, and D-*fac* in the same manner. Figures 2b and 3b show the CD spectra of the six isomers of [Co(asp)(his)]. The CD spectrum for a specific isomer *e.g.* the first eluate of the [Co(L- or D-asp)-(L-his)] complex is quite similar to that for the isomer being eluted in the same order *e.g.* the first eluate of the [Co(L- or D-asp)(L-2,4-dba)] complex. Both isomers may have the same configuration as shown in Fig. 1. However, the coordination of the L-his in place of L-2,4-dba for the [Co(L- or D-asp)(L-2,4-

TABLE 1. ABSORPTION AND CD SPECTRAL DATA OF [Co(L- OR D-asp)(L-his)]

| Complex | I band |  |  |  | II band |  |  |  |
|---|---|---|---|---|---|---|---|---|
|  | Absorption |  | CD |  | Absorption |  | CD |  |
|  | $\tilde{\nu}_{max}$ [a] | log ε | $\tilde{\nu}_{max}$ | Δε | $\tilde{\nu}_{max}$ | log ε | $\tilde{\nu}_{max}$ | Δε |
| L-*trans*$O_5$*cis*$N_5$ | 18.0 | 1.78 | 18.9 | −1.70 | 27.5 | 1.99 | 27.5 | 0.40 |
|  | (18.2)[b] | (1.92) | (18.7) | (−2.50) | (27.2) | (2.05) | (27.2) | (0.96) |
|  | 20.2 | 1.83 | 21.5 | 0.60 |  |  |  |  |
|  | (20.0) | (1.92) | (21.8) | (0.80) |  |  |  |  |
| L-*cis*$O_5$*trans*$N_5$ | 17.2 | 1.78 | 17.2 | 1.55 | *ca.* 28 | 2.15 | 27.2 | 0.45 |
|  | (16.7) | (1.44) | (17.5) | (2.28) | (27.2) | (1.99) | (26.8) | (0.33) |
|  | 20.4 | 1.78 | 21.5 | −0.50 |  |  |  |  |
|  | (20.4) | (1.97) | (19.8) | (−0.20) |  |  |  |  |
| L-*fac* | 19.5 | 2.12 | 18.2 | 1.20 | *ca.* 27 | 2.05 | 27.6 | −0.53 |
|  | (19.3) | (2.23) | (18.2) | (1.48) | (27.3) | (1.90) | (*ca.* 27) | (−0.11) |
|  |  |  | 20.6 | −0.90 |  |  |  |  |
|  |  |  | (20.6) | (−0.56) |  |  |  |  |
| D-*cis*$O_5$*cis*$N_5$ | 18.2 | 1.85 | 18.4 | −1.45 | 27.5 | 2.01 | 26.5 | 0.25 |
|  | (18.3) | (1.75) | (18.4) | (−2.80) | (27.3) | (1.88) | (27.8) | (0.80) |
|  | 21.2 | 1.65 | 21.2 | 0.95 |  |  |  |  |
|  | (20.8) | (1.55) | (21.3) | (1.08) |  |  |  |  |
| D-*trans*$O_5$*trans*$N_5$ | 17.0 | 1.20 | 19.9 | 1.50 | 27.5 | 2.00 | 27.7 | 0.55 |
|  | (16.8) | (1.38) | (16.7) | (2.75) | (27.4) | (1.73) | (28.0) | (0.26) |
|  | 20.8 | 1.68 | 20.3 | −1.55 |  |  |  |  |
|  | (20.5) | (1.75) | (19.5) | (−2.25) |  |  | (24.8) | (0.10) |
| D-*fac* | 19.5 | 2.20 | 18.4 | 0.90 | 27.5 | 2.02 | 27.4 | −0.45 |
|  | (19.3) | (2.13) | (16.7) | (0.10) | (27.2) | (1.95) | (28.0) | (−0.20) |
|  |  |  | 20.6 | −0.55 |  |  |  |  |
|  |  |  | (19.8) | (−0.40) |  |  |  |  |

a) Wave numbers are given in $10^3$ cm$^{-1}$.

b) The figures in the parentheses denote the data for [Co(L- or D-asp)(L-2,4-dba)].

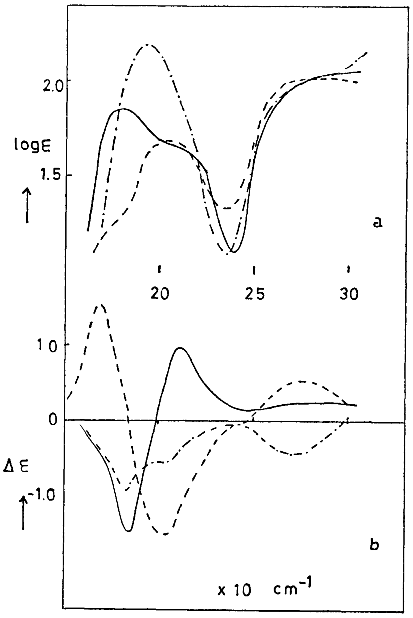

Fig. 3. Absorption (upper) and CD (lower) spectra of [Co(D-asp)(L-his)]. I1 (——), I2 (----), and I3 (—–—).

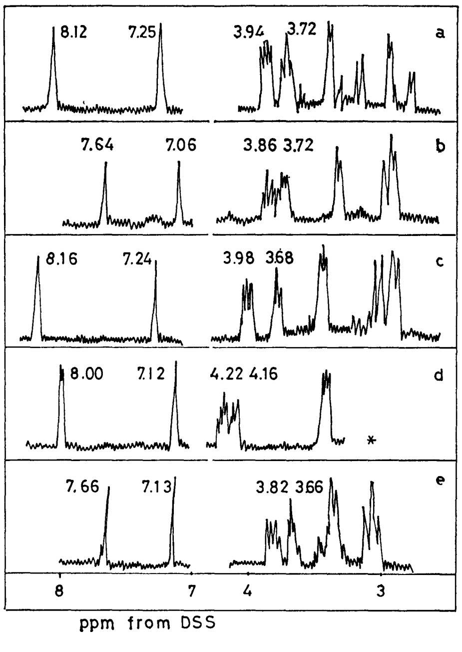

Fig. 4. PMR spectra of a; H1, b; H3, c; I1, d; I2, and e; I3.

dba)] complex decreases the magnitude of the CD peaks of the four mer isomers in the first absorption band region. It is interesting that the CD spectrum for the H1 isomer resembles that for the I1 isomer in spite of the coordination of the enantiomeric ligand.

*PMR Spectra.* Figure 4 shows the PMR spectra of the five isomers. The spectrum of I2 could not be obtained because of its low solubility. The L-his has the patterns of ABX and AX and the L- or D-asp that of AX only. The peaks near $\delta$ 8.0 ppm for the five PMR spectra are ascribed to the 2-protons of imidazole and the peaks near $\delta$ 7 ppm to the 5-protons of imidazole having a higher electronegativity than that for the 2-proton. The peaks at *ca.* 3.4 ppm are due to the methylene protons of asp and the peaks higher than those to the methylene protons of L-his. The peaks at *ca.* $\delta$ 4.2—3.6 ppm are assigned to those of the methine protons for L-his and L- or D-asp. The distribution of all the peaks for the five isomers agree with the prediction based on the empirical rule as developed by the authors.[2] Consequently H1, H2, and H3 were assigned as *trans*$O_5$*cis*$N_5$, *cis*$O_5$*trans*$N_5$, and L-*fac*, and I1, I2, and I3 as *cis*$O_5$*cis*$N_5$, *trans*$O_5$*trans*$N_5$, and *D-fac*, respectively.

*Isomerization of the Isomers of [Co(L- or D-asp)(L-his)].* All the isomers of [Co(L- or D-asp)(L-his)] isomerized in water without any catalyst. Figure 5 shows a series of chromatograms corresponding to the change in concentration of each isomer due to the isomerization of H3. Each isomer can be separated from the mixture by high speed liquid chromatography. The TSK-212 resin is eminently suitable for the separation of the isomers of a complex with no charge. Since no concentration loss of the complex due to other reactions was found within experimental error, it was possible to treat the concentration of the complex as constant throughout the experiment and so network analysis[3] is available for this reaction. The system of differrential equations representing the behavior of the system is shown as follows:

$$\mathrm{d}a_1/\mathrm{d}t = -(k_{12}+k_{13})a_1 + k_{21}a_2 + k_{31}a_3,$$

$$\mathrm{d}a_2/\mathrm{d}t = k_{12}a_1 - (k_{23}+k_{21})a_2 + k_{32}a_3,$$

$$\mathrm{d}a_3/\mathrm{d}t = k_{13}a_1 + k_{23}a_2 - (k_{31}+k_{32})a_3,$$

where $a_1$, $a_2$, and $a_3$ are the molar fractions of H1(I1), H2(I2), and H3(I3), respectively. The rate constant of the reaction, for which the notation of the H$i$(I$i$)-($i$=1,2,3) isomer is transformed into H$j$(I$j$), is represented by $k_{ij}$. This analysis was applicable for obtaining the relative value of the rate constant ($k_{ij}'$). In order to obtain absolute values ($k_{ij}$), the relative rate constans are substituted in a certain differential equation, for example,

$$\mathrm{d}a_2/\mathrm{d}t = k[k_{12}'a_1-(k_{23}'+k_{21}')a_2+k_{32}'a_3],$$

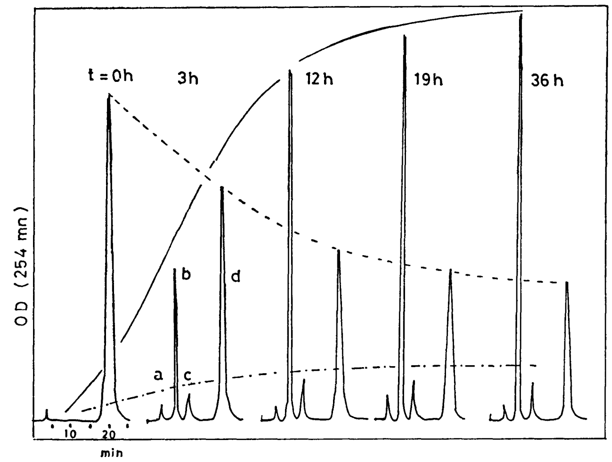

Fig. 5. High speed liquid chromatograms indicating the isomerization of the H2 isomer. a: Marker, b: H1(I1), c: H2(I1), and d: H3(I3).

where $k$ is the ratio $(k_{12}/k_{12}')$. All the $k_{ij}$ of H*i* and I*i* systems are shown in Fig. 6. In the case of the H*i* system, the values of the rate constants decrease in the order $k_{23}>k_{31},k_{13},k_{21}>k_{12},k_{32}$. Figure 7 shows the experimentally observed compositions for isomerization. The molar fractions at equilibrium are as follows; H1(0.53), H2(0.06), and H3(0.41). The free energy differences at 25 °C are as follows: $\Delta G_{12}=G(\text{H1})-G(\text{H2})=-RT\ln(53/6)=-5.40$ kJ/mol and $\Delta G_{23}=RT\ln(41/6)=4.76$ kJ/mol. In case of the I*i* system, the values of the rate constants decrease in the order $k_{23}\gg k_{13},k_{31}>k_{21},k_{32}>k_{12}$. This order closely resembles the H*i* system. The molar fractions at equilibrium are as follows: I1(0.48), I2(0.01), and I3(0.51). The free energy differences at 25 °C are as follows: $\Delta G_{12}'=G'(\text{I1})-G'(\text{I2})=-RT\ln(0.48/0.01)=-9.74$ kJ/mol and $\Delta G_{23}'=RT\ln(0.51/0.01)=9.74$ kJ/mol. In both systems each isomer may have only a little steric hindrance and hydrogen bonding between the coordinated his and asp. The fact that the molar fractions are in the order $transO_5cisN_5>\text{L-}fac\gg cisO_5transN_5$ for [Co(L-asp)(L-his)], and $\text{D-}fac\approx cisO_5cisN_5\gg transO_5\text{-}transN_5$ for [Co(D-asp)(L-his)] suggests the existance of a common effect determining the molar fractions. Firstly the $transN_5$ isomers must be less stable than the $cisN_5$ isomers in both systems and secondly the $transO_5$ isomers are a little less stable than the $cisO_5$ isomers between mer isomers. In the case of the iosmerization of [Co(D-asp)(L-2,4-dba)], the molar fraction of the $transO_5transN_5$ isomer at equilibrium was the smallest of the three, although the molar distribution for the fac isomer was smaller than that for $cisO_5cisN_5$ ($cisO_5cisN_5$, $transO_5transN_5$, $fac=0.68$, 0.11, 0.21).[1] Recently, investigations of the *trans* effect for the cobalt(III) complex containing S-bonded sulfite ligands have been reported.[4] In cobalt(III) chemistry, S-bonded sulfite produces a specific and dramatic labilization of the ligands situated in the *trans* position. This electronic effect which is transmitted through the bonds may apply in this our study, *i.e.* it is suggested that the two α-nitrogen atoms avoid the *trans* position around a Co(III).

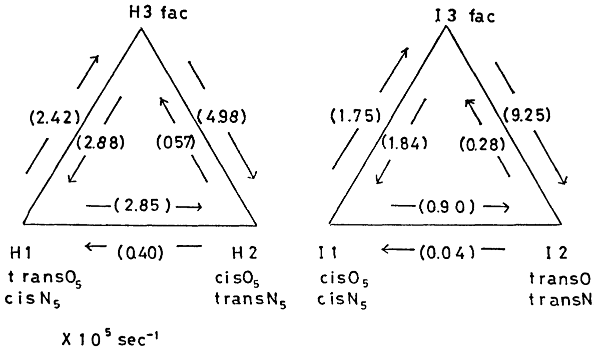

Fig. 6. Rate constants of the isomerization at 80 °C.

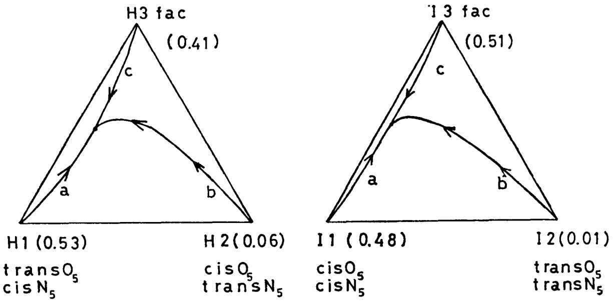

Fig. 7. Experimentally observed compositions for the isomerization at 80 °C. a: From H1(I1), b: from H2(I2), and c: from H3(I3).

## References

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