BIOINORGANIC APPROACH TO THE CYTOCHROME OXIDASE ACTIVE SITE.  STRONGLY
SPIN-COUPLED COPPER(II)-IRON(III) HETERO-METAL BINUCLEAR COMPLEXES[1]

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Copper(II)-iron(III) binuclear complexes, $CuFe(fsaR)Cl \cdot nH_2O$, with
N,N'-bis(3-carboxysalicylidene)alkanediamines ($H_4fsaR$) were prepared
and characterized.  Cryomagnetic measurements indicated a considerably
strong antiferromagnetic spin-exchange interaction operating between
the metal ions.  The exchange integrals (ca. -50 $cm^{-1}$) are the largest
among the copper(II)-iron(III) complexes so far reported, and hence
the complexes  mimic the cytochrome oxidase active center.

Cytochrome oxidase is the terminal oxidation-reduction enzyme in mitochondrial
respiration.[2]  Recent ESR,[2] MCD,[3] and magnetic susceptibility[4,5] investigations
have suggested the presence of a strongly spin-coupled copper(II)-iron(III)(s=5/2)
system at the cytochrome $a_3$ active site, where the metal ions are presumed to be
bridged by imidazolate group.[2]  However, no synthetic copper(II)-iron(III) complex
with the imidazolate bridge has been obtained.  In spite of the increasing interests
in spin-exchange interaction between copper(II) and iron(III) ions, copper(II)-
iron(III) complexes so far obtained showed practically no spin-exchange interaction
between the metal ions.[6-9]
In this study we report the first example of copper(II)-iron(III) complexes
displaying a strong antiferromagnetic spin-spin coupling between the metal ions.
The ligands used for preparing the complexes are the 2:1 type Schiff bases which were
obtained by reacting 3-formylsalicylic acid with ethylenediamine, 1,2-propylenediamine,
2,3-butanediamine, 1,2-cyclohexanediamine, or o-phenylenediamine, the ligands being
abbreviated as $H_4fsaen$, $H_4fsapn$, $H_4fsabn$, $H_4fsach$, and $H_4fsaph$, respectively.
Mononuclear copper(II) complexes, $Cu(H_2fsaR)$ (R=en, pn, bn, ch, ph), were prepared
by the method described previously.[10]  The synthetic methods of the copper(II)-
iron(III) complexes, $CuFe(fsaR)Cl \cdot nH_2O$, are nearly the same, and are exemplified by
$CuFe(fsaen)Cl \cdot 2 \cdot 5H_2O$.  To a suspension of $Cu(H_2fsaen) \cdot \frac{1}{2}H_2O$ (86 mg) in absolute
methanol (70 ml) was added $FeCl_3$ (36 mg).  The mixture was stirred at ca. 50°C and
to this was added triethylamine (50 mg).  A reddish purple solution thus formed was
filtered and left stand overnight to give purplish brown prisms.  $NiFe(fsaR)Cl \cdot nH_2O$,
which will serve for examining the magnetic properties of $CuFe(fsaR)Cl \cdot nH_2O$, were
also prepared in the same way.  Elemental analyses of $CuFe(fsaR)Cl \cdot nH_2O$ and
$NiFe(fsaR)Cl \cdot nH_2O$ are given in Table 1.
Infrared spectra of $CuFe(fsaR)Cl \cdot nH_2O$ and $NiFe(fsaR)Cl \cdot nH_2O$ display a strong
band around 1550 $cm^{-1}$, attributable to the coordinated carboxylate group.  Electronic

Table 1. ELEMENTAL ANALYSES OF COMPLEXES

| | Found(%) | | | Calcd(%) | | |
|---|---|---|---|---|---|---|
| | C | H | N | C | H | N |
| CuFe(fsaen)Cl·2.5H$_2$O | 39.27 | 3.21 | 4.96 | 39.15 | 3.10 | 5.07 |
| CuFe(fsapn)Cl·2.5H$_2$O | 40.19 | 3.38 | 4.88 | 40.30 | 3.38 | 4.95 |
| CuFe(fsabn)Cl.4H$_2$O | 39.28 | 4.25 | 4.41 | 39.43 | 4.30 | 4.60 |
| CuFe(fsach)Cl·3.5H$_2$O | 42.37 | 4.03 | 4.49 | 42.32 | 4.04 | 4.49 |
| CuFe(fsaph)Cl·H$_2$O | 46.18 | 3.04 | 4.79 | 46.10 | 2.46 | 4.89 |
| NiFe(fsaen)cl·H$_2$O | 42.20 | 3.14 | 5.24 | 41.55 | 2.71 | 5.38 |
| NiFe(fsapn)Cl·2H$_2$O | 41.61 | 3.16 | 5.38 | 41.32 | 3.28 | 5.07 |
| NiFe(fsabn)Cl·0.5H$_2$O | 44.39 | 3.68 | 4.91 | 44.37 | 3.54 | 5.17 |
| NiFe(fsach)Cl·2H$_2$O | 44.46 | 3.97 | 4.61 | 44.61 | 3.74 | 4.72 |
| NiFe(fsaph)Cl·3.5H$_2$O | 42.84 | 2.90 | 4.60 | 43.08 | 3.12 | 4.57 |

spectra of the complexes were measured by reflection on a powder sample. The spectra of CuFe(fsaR)Cl·nH$_2$O are similar to each other and show absorption bands in the region 19,000-21,000 cm$^{-1}$. It is known that the copper(II) ion coordinated to the O$_4$-donating site shows a d-d band near 13,500 cm$^{-1}$.[10] Since no such a band was observed for CuFe(fsaR)Cl·nH$_2$O, we may conclude that the copper(II) ion is bonded to the N$_2$O$_2$-donating site and the iron(III) ion to the O$_4$-site (Fig. 1). It is noticed that CuFe(fsaR)Cl·nH$_2$O bears a marked spectral resemblance to Cu(H$_2$fsaR).[10] It is likely that the iron(III) is in high-spin state and hence shows no spin-allowed d-d transition bands. Electronic spectra of NiFe(fsaR)Cl·nH$_2$O resemble each other. In Ni$_2$(fsaR)·nH$_2$O and CuNi(fsaR)·nH$_2$O,[10-12] the nickel(II) ion bonded to the O$_4$-donating site has an octahedral structure with two water molecules at the apical positions and exhibits d-d bands at 9,500 and 15,000 cm$^{-1}$. Since no absorption is observed in the region 6,000-18,000 cm$^{-1}$ for NiFe(fsaR)Cl·nH$_2$O, we may conclude that these complexes also possess the binuclear skeleton shown in Fig. 1.

Magnetic moments of CuFe(fsaR)Cl·nH$_2$O were measured in the temperature range 80-300K (Table 2). Temperature-dependences of magnetic moments indicate spin-spin coupling between the metal ions. Based on the Heisenberg model ($\mathcal{H}=-2Js_1s_2$), two spin states, s=2 and 3, are brought about by spin-spin coupling between copper(II)(s=1/2) and iron(III)(s=5/2) ions. The energy separation between the s=2 ground state and the s=3 excited state is given by -6J (J being the exchange integral). By applying the Van Vleck equation, the susceptibility for the (s=1/2)-(s=5/2) system is given by the equation,

$$\chi_M = \frac{Ng^2\beta^2}{kT} \cdot \frac{5\exp(-6J/kT) + 14}{5\exp(-6J/kT) + 7} + N\alpha \ ,$$

where each symbol has its usual meaning.
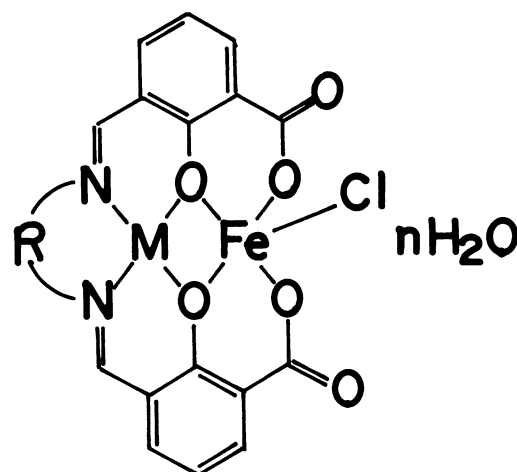


M(II)=Cu(II), Ni(II)

Fig. 1. Structure of complexes.

Table 2. TEMPERATURE VARIATIONS OF MAGNETIC SUSCEPTIBILITIES AND MAGNETIC MOMENTS OF $CuFe(fsaR)Cl \cdot nH_2O$.

| R=en | | | R=pn | | | R=bn | | | R=ch | | | R=ph | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T(K) | $\chi_M \times 10^6$ | $\mu_{eff}$ | T(K) | $\chi_M \times 10^6$ | $\mu_{eff}$ | T(K) | $\chi_M \times 10^6$ | $\mu_{eff}$ | T(K) | $\chi_M \times 10^6$ | $\mu_{eff}$ | T(K) | $\chi_M \times 10^6$ | $\mu_{eff}$ |
| 103.5 | 28148 | 4.83 | 87.4 | 31258 | 4.67 | 87.4 | 32803 | 4.79 | 83.4 | 32200 | 4.63 | 81.7 | 32888 | 4.64 |
| 108.4 | 27142 | 4.85 | 100.9 | 27394 | 4.70 | 95.7 | 30066 | 4.80 | 94.0 | 29113 | 4.68 | 98.3 | 27911 | 4.68 |
| 122.5 | 24578 | 4.91 | 118.8 | 23432 | 4.72 | 108.4 | 25853 | 4.73 | 108.4 | 25853 | 4.73 | 113.2 | 24832 | 4.74 |
| 135.4 | 22830 | 4.97 | 133.8 | 21345 | 4.78 | 122.5 | 24294 | 4.88 | 122.5 | 23410 | 4.79 | 127.7 | 22456 | 4.79 |
| 149.4 | 21126 | 5.02 | 151.0 | 19358 | 4.84 | 135.4 | 22570 | 4.94 | 136.2 | 21770 | 4.87 | 142.8 | 20710 | 4.86 |
| 162.7 | 19825 | 5.08 | 163.1 | 18294 | 4.89 | 149.4 | 20787 | 4.98 | 150.1 | 20142 | 4.92 | 157.1 | 19393 | 4.94 |
| 176.8 | 18502 | 5.11 | 178.5 | 16790 | 4.90 | 164.5 | 19169 | 5.02 | 163.4 | 18991 | 4.98 | 171.6 | 18226 | 5.00 |
| 190.2 | 17425 | 5.15 | 192.9 | 16188 | 5.00 | 178.5 | 18095 | 5.08 | 176.2 | 17998 | 5.04 | 186.3 | 17216 | 5.06 |
| 203.0 | 16745 | 5.21 | 209.5 | 15395 | 5.08 | 193.5 | 17000 | 5.13 | 191.9 | 16865 | 5.09 | 200.8 | 16396 | 5.13 |
| 216.7 | 16030 | 5.27 | 225.2 | 14392 | 5.09 | 207.7 | 16242 | 5.19 | 206.1 | 16089 | 5.15 | 215.2 | 15554 | 5.17 |
| 229.9 | 15308 | 5.31 | 240.4 | 13870 | 5.16 | 222.6 | 15338 | 5.23 | 219.6 | 15433 | 5.21 | 229.9 | 14962 | 5.25 |
| 243.9 | 14691 | 5.35 | 254.7 | 13238 | 5.19 | 237.0 | 14612 | 5.26 | 234.2 | 14794 | 5.25 | 245.3 | 14422 | 5.32 |
| 257.3 | 14042 | 5.38 | 268.6 | 12737 | 5.23 | 252.1 | 14045 | 5.32 | 248.6 | 14210 | 5.32 | 260.5 | 13791 | 5.36 |
| 270.4 | 13594 | 5.42 | 281.6 | 12255 | 5.25 | 266.6 | 13389 | 5.34 | 263.2 | 13661 | 5.36 | 276.0 | 13266 | 5.41 |
| 284.3 | 13026 | 5.44 | 295.7 | 11884 | 5.30 | 280.6 | 12962 | 5.39 | 278.6 | 13098 | 5.40 | 291.7 | 12770 | 5.46 |
| 297.8 | 12572 | 5.47 | | | | 295.4 | 12459 | 5.43 | 294.9 | 12594 | 5.44 | | | |

Magnetic susceptibilities of $CuFe(fsaR)Cl \cdot nH_2O$ can be interpreted by the equation given above. A typical example of the best fit between the experimental and the theoretical susceptibilities is given in Fig. 2. The exchange integrals determined for other complexes, assuming g=2.0 and Nα=0, are as follows: J=-64 cm$^{-1}$ for $CuFe(fsapn)Cl \cdot$ 2.5H$_2$O, -52 cm$^{-1}$ for $CuFe(fsabn)Cl \cdot 4H_2O$, -48 cm$^{-1}$ for $CuFe(fsach)Cl \cdot 3.5H_2O$, and -48 cm$^{-1}$ for $CuFe(fsaph) \cdot H_2O$. Powder ESR spectra (X-band at 77.4K) of $CuFe(fsaR)Cl \cdot nH_2O$ showed a very broad band in the region 500-4000 gauss (=10$^{-4}$T), owing to the short relaxation time due to spin-exchange interaction.

The magnetic moments of $CuFe(fsaR)Cl \cdot nH_2O$ near liquid nitrogen temperature are lower than 4.90 BM, the spin-only value expected for the fully spin-coupled (s=1/2)-(s=5/2) system. In order to elucidate this, magnetic susceptibilities of $NiFe(fsaR)Cl \cdot nH_2O$ were measured in the range 80-300K. The room temperature magnetic moments fall in the range 5.85-5.94 BM, typical for high-spin iron(III) complexes. However, the moments decrease considerably with lowering of temperature to 5.32-5.55 BM near liquid nitrogen temperature. Zero-field splitting of the iron(III)(s=5/2) state seems to be the major contribution to the decrease in magnetic moment. Similar zero-field splitting may occur in $CuFe(fsaR)Cl \cdot nH_2O$ and this should be responsible for the slight deviation of magnetic susceptibility from the theoretical curve at low temperature.

Since we neglect the zero-field splitting and temperature-independent paramagnetism, the exchange integrals evaluated for $CuFe(fsaR)Cl \cdot nH_2O$ are approximate values. However, those effects seem much smaller than the spin-spin coupling. Hence, we may conclude that a fairly strong antiferromagnetic spin-exchange interaction (J∼-50 cm$^{-1}$) operates in the complexes. The present complexes are the strongest in antiferromagnetic spin-spin coupling among the copper(II)-iron(III) complexes so far reported and mimic the cytochrome s$_3$ active center.
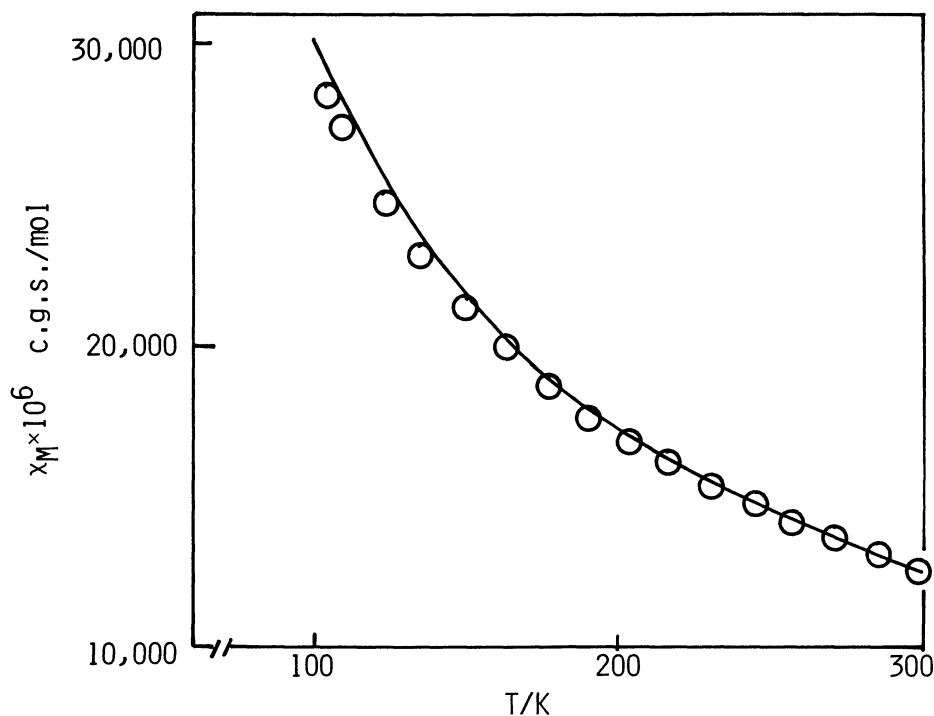
Fig. 2.  Temperature variation of magnetic susceptibility
of CuFe(fsaen)Cl·2.5H$_2$O.  Solid curve is drawn on the
basis of the theoretical susceptibility expression using
parameters, J=-50 cm$^{-1}$, g=2.0 and N$\alpha$=0.

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