CHEMISTRY LETTERS, pp. 1281-1284, 1980. © The Chemical Society of Japan 1980

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

Hisashi OKAWA,* Wakako KANDA, and Sigeo KIDA
Department of Chemistry, Faculty of Science, Kyushu University 33,
Hakozaki, Higashiku, Fukuoka 812

Copper(II)-iron(III) binuclear complexes, CuFe(fsaR)Cl·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 susceptibility4,5) 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·nH_2O, are nearly the same, and are exemplified by CuFe(fsaen)Cl·2·5H_2O. To a suspension of Cu(H_2fsaen)·$\frac{1}{2}H_2O$ (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·nH_2O, which will serve for examining the magnetic properties of CuFe(fsaR)Cl·nH_2O, were also prepared in the same way. Elemental analyses of CuFe(fsaR)Cl·nH_2O and NiFe(fsaR)Cl·nH_2O are given in Table 1.

Infrared spectra of CuFe(fsaR)Cl·nH_2O and NiFe(fsaR)Cl·nH_2O display a strong band around 1550 cm^{-1}, attributable to the coordinated carboxylate group. Electronic

Table 1. ELEMENTAL ANALYSES OF COMPLEXES

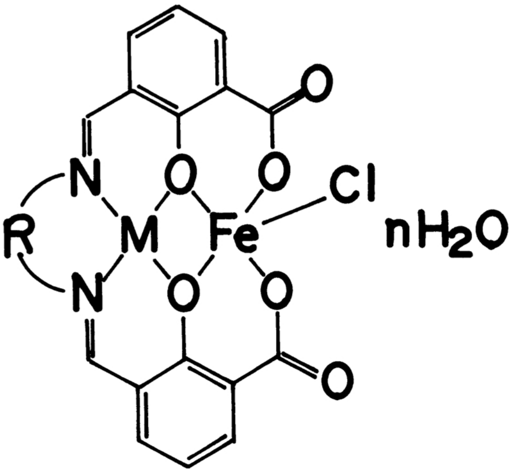
	Found(%)			Calcd(%)		
	C	H	N	C	H	N
CuFe(fsaen)Cl·2.5H_2O	39.27	3.21	4.96	39.15	3.10	5.07
CuFe(fsapn)Cl·2.5H_2O	40.19	3.38	4.88	40.30	3.38	4.95
CuFe(fsabn)Cl.4H_2O	39.28	4.25	4.41	39.43	4.30	4.60
CuFe(fsach)Cl·3.5H_2O	42.37	4.03	4.49	42.32	4.04	4.49
CuFe(fsaph)Cl·H_2O	46.18	3.04	4.79	46.10	2.46	4.89
NiFe(fsaen)cl·H_2O	42.20	3.14	5.24	41.55	2.71	5.38
NiFe(fsapn)Cl·2H_2O	41.61	3.16	5.38	41.32	3.28	5.07
NiFe(fsabn)Cl·0.5H_2O	44.39	3.68	4.91	44.37	3.54	5.17
NiFe(fsach)Cl·2H_2O	44.46	3.97	4.61	44.61	3.74	4.72
NiFe(fsaph)Cl·3.5H_2O	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_2O 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_2O, we may conclude that the copper(II) ion is bonded to the N_2O_2-donating site and the iron(III) ion to the O_4-site (Fig. 1). It is noticed that CuFe(fsaR)Cl·nH_2O bears a marked spectral resemblance to Cu(H_2fsaR).[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_2O resemble each other. In Ni_2(fsaR)·nH_2O and CuNi(fsaR)·nH_2O,[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_2O, we may conclude that these complexes also possess the binuclear skeleton shown in Fig. 1.

Magnetic moments of CuFe(fsaR)Cl·nH_2O 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,

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

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)	$\chi_M\times10^6$	μ_{eff}	T(K)	$\chi_M\times10^6$	μ_{eff}	T(K)	$\chi_M\times10^6$	μ_{eff}	T(K)	$\chi_M\times10^6$	μ_{eff}	T(K)	$\chi_M\times10^6$	μ_{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 $N\alpha=0$, are as follows: $J=-64\ cm^{-1}$ for $CuFe(fsapn)Cl\cdot 2.5H_2O$, $-52\ cm^{-1}$ 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 ($J\sim-50\ cm^{-1}$) 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.

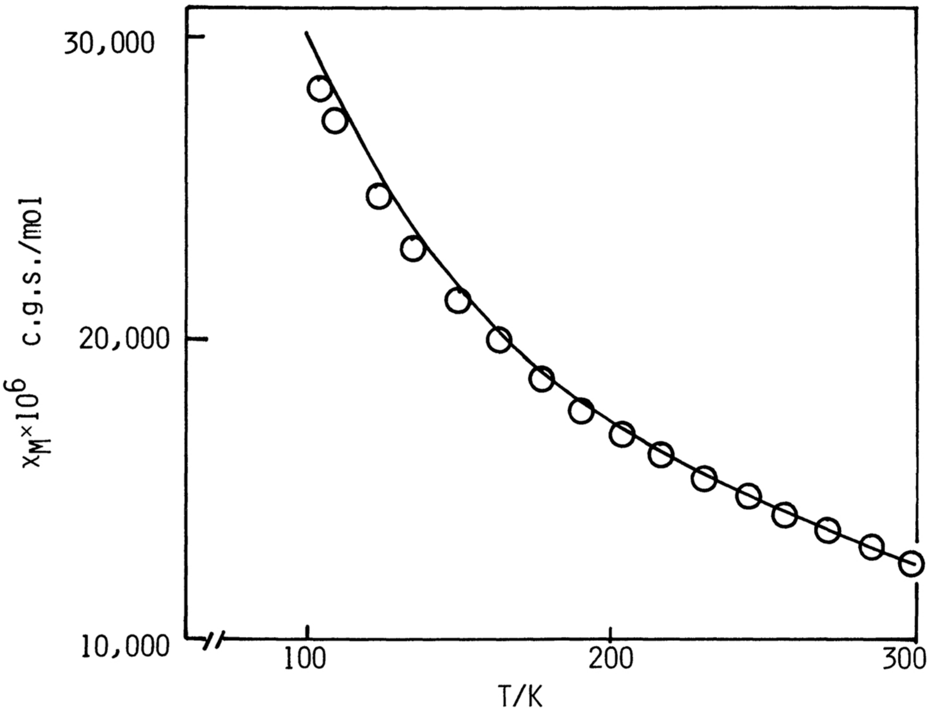


Fig. 2. Temperature variation of magnetic susceptibility of CuFe(fsaen)Cl·$2.5H_2O$. Solid curve is drawn on the basis of the theoretical susceptibility expression using parameters, $J=-50$ cm^{-1}, $g=2.0$ and $N\alpha=0$.

References

1) Binuclear Metal Complexes. XXXVI. Part XXXV: M. Mikuriya, H. Okawa, and S. Kida, Bull. Chem. Soc. Jpn., in press.

2) G. Palmer, G. T. Babcock, and L. E. Vickery, Proc. Nat. Acad. Sci., U.S.A., 73, 2206 (1976).

3) G. T. Babcock, L. E. Vickery, and G. Palmer, J. Biol. Chem., 251, 7907 (1976).

4) M. F. Tweedle, L. J. Wilson, L. Gardia-Iniguez, G. T. Babcock, and G. Palmer, J. Biol. Chem., 253, 8065 (1978).

5) T. H. Moss, E. Shapiro, T. E. King, H. Beinert, and C. Hartell, J. Biol. Chem., 253, 8072 (1978).

6) M. Vidali, G. Rizzardi, P. A. Vigato, U. Cassellato, S. Kida, and H. Okawa, Inorg. Chim. Acta, 34, 19 (1979).

7) M. J. Gunter, L. N. Mander, G. M. McLaughlin, K. S. Murray, K. J. Berry, P. E. Clark, and D. A. Buckingham, J. Am. Chem. Soc., 102, 1470 (1980).

8) R. H. Petty and L. J. Wilson, J. Chem. Soc., Chem. Comm., 1978, 483.

9) T. Prosperi and A. A. G. Tomlinson, J. Chem. Soc., Chem. Comm., 1979, 196.

10) M. Tanaka, M. Kitaoka, H. Okawa, and S. Kida, Bull. Chem. Soc. Jpn., 49, 2469 (1976).

11) H. Okawa, M. Tanaka, and S. Kida, Chem. Lett., 1974, 987.

12) N. Torihara, H. Okawa, and S. Kida, Inorg. Chim. Acta, 26, 97 (1976).

(Received August 14, 1980)