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Five-coordinate Copper(II) Complexes with a Thio Group as Type II Copper Models

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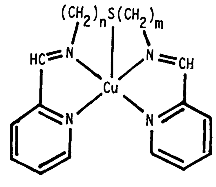
Five-coordinate copper(II) complexes with a thio group were synthesized as non-blue copper(II) models by reactions of copper(II) perchlorate and condensation products of 2-pyridinecarbaldehyde or salicylaldehyde and bis(2-aminoethyl) sulfide or 2-aminoethyl 3-aminopropyl sulfide. In the complexes where thio group is coordinated to copper(II) at an equatorial position, the ESR spin Hamiltonian parameters $g_{//}$ and $A_{//}$ prominently decreased, and charge transfer bands due to sulfur to copper appeared at 300—350 nm and occasionally at 400—500 nm. On the other hand, complexes with a thio group at an axial position afforded slightly smaller $A_{//}$ values and charge transfer bands with lower intensity in the similar regions. The biological significance of a sulfur donation to non-blue copper(II) has been discussed.

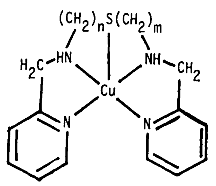
Among the three types of copper ions found in copperproteins the "non-blue" (type II) copper displays no remarkable properties as "blue"(type I) copper or "ESR-nondetectable"(type III) copper. The associated ESR parameters of the type II coppers are similar to those of common tetragonal copper(II) complexes: $-A_{//}$ values are in the range of 15—20($\times 10^{-4}$) cm^{-1} and $g_{//}$ values are of 2.2—2.3. The visible absorption spectra arising from type II copper have also been considered to be the same with those of low molecular weight copper(II) complexes,[1] although they are often obscured by the type I and III coppers in multi-copper oxidases such as laccase, ceruloplasmin, and ascorbate oxidases. Having no conspicuous properties, the type II copper has thus been unfamiliar compared with coppers of the other types.

However, non-blue coppers in galactose oxidase[2] and amine oxidase[3] have been convinced to be in the environment of square-pyramid based on their d-d absorption spectra. Although there are only limited data on the protein ligands around type II copper, coordination of 2 to 4 imidazolyl groups and some oxygens has been reasonably proposed. Of special interest is the suggestion that a thio group is possibly coordinated to type II copper in galactose oxidase[4,5] and amine oxidase.[3] Here we report spectral properties of five-coordinate copper complexes with a thio group in an equatorial or an axial position as non-blue copper models.

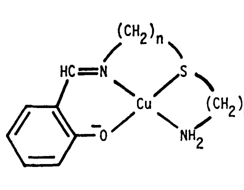
In this work, several quinquedentate ligands with a thio group were synthesized by condensation of bis(2-aminoethyl) sulfide (abbreviated as aes) or 2-aminoethyl 3-aminopropyl sulfide(aps) and 2-pyridinecarbaldehyde(pca) or salicylaldehyde(sal). Copper(II) complexes of these sulfur-containing ligands were prepared and the effects of sulfur coordination at an equatorial or an axial position on absorption and ESR spectra were comparatively studied.



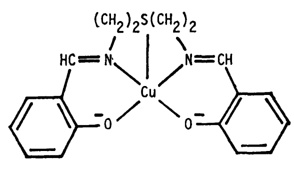
n=2, m=3 Cu(pca=aps=pca)
n=2, n=2 Cu(pca=aes=pca)



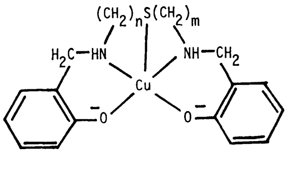
n=2, m=3 Cu(pca-aps-pca)
n=2, n=2 Cu(pca-aes-pca)



n=2, m=3 or n=3, m=2
Cu(sal=aps)



Cu(sap=aes=sal)



n=2, m=3 Cu(sal-aps-sal)
n=2, n=2 Cu(sal-aes-sal)

Experimental

Materials. Copper(II) perchlorate hexahydrate and salicylaldehyde were purchased from Nakarai Chemicals Ltd., *N*-(2-bromoethyl)phthalimide from Wako Chemicals Ltd., *N*-(3-bromopropyl)phthalimide from Aldrich, and 2-pyridinecarbaldehyde was obtained from Merck AG and distilled. All other reagents used were of the highest grade commercially available.

Preparation of Complexes. Cu(pca=aps=pca): Sulfur-containing diamine, aps, was prepared according to Amundsen *et al.*[6] To this was added twice amounts of pca in aqueous ethanol to give the 2 : 1 pca : aps Schiff base, which was treated with Cu(ClO$_4$)$_2$·6H$_2$O, and was allowed to stand at room temperature. Blue crystals were isolated as perchlorate, and was recrystallized from H$_2$O–EtOH. Found: C, 35.79; H, 3.48; N, 9.81%. Calcd for CuC$_{17}$H$_{20}$N$_4$S(ClO$_4$)$_2$: C, 35.52; H, 3.51; N, 9.75%.

Cu(pca=aes=pca), Cu(sal=aps) and Cu(sal=aes=sal): These complexes were synthesized by the same method as Cu(pca=aps=pca). Found: C, 34.43; H, 3.44; N, 10.35%. Calcd for CuC$_{16}$H$_{18}$N$_4$S(ClO$_4$)$_2$(Cu(pca=aes=pca)): C, 34.26; H, 3.23; N, 9.99%. Found: C, 35.79; H. 4.17; N, 6.95%. Calcd for CuC$_{12}$H$_{17}$N$_2$OS(ClO$_4$) (Cu(sal=aps)): C, 36.00; H, 4.28; N, 7.00%. Found: C, 42.94; H, 3.90; N, 5.62%. Calcd for CuC$_{18}$H$_{18}$N$_2$O$_2$S·2H$_2$O·2/3 NaClO$_4$ (Cu(sal=aes=sal)) C, 42.59; H, 4.37: N, 5.62%. The results of elemental analysis for Cu(sal=aes=sal) was only explainable by assuming the presence of some coprecipitated $NaClO_4$, which was hardly removed. The product was, however, used for the spectroscopic and ESR measurements without further treatment, since there was no fear of serious effect.

Cu(pca=aps=pca): The condensed product of pca and aps in ethanol was reduced with $NaBH_4$ untill the yellow color of the Schiff base faded out, and the excess of $NaBH_4$ was treated with HCl. After filtration, the filtrate was mixed with $Cu(ClO_4)_2\cdot 6H_2O$ to give blue crystals. Recrystallization was performed once from aqueous ethanol. Found: C, 27.90; H, 4.16; N, 7.52%. Calcd for $CuC_{17}H_{24}N_4S(ClO_4)_2\cdot 7H_2O$: C, 27.64; H, 4.23; N, 7.58%.

Cu(pca-aes-pca), Cu(sal=aps=sal), and Cu(sal=aes=pca): These complexes were prepared by the same method as described for Cu(pca=aps=pca). Found: C, 33.58; H, 3.96; N, 9.84%. Calcd for $CuC_{16}H_{22}N_4S(ClO_4)_2$(Cu(pca=aes=pca)): C, 34.02; H, 3.93; N, 9.92%. Found: C, 45.53; H, 5.42; N, 5.52%. Calcd for $CuC_{17}H_{24}N_2O_2S\cdot 2H_2O\cdot 1/2NaClO_4$(Cu-(sal=aps=sal)): 45.16; H, 5.59; N, 5.55%. Found: C, 37.49; H, 4.06; N, 4.98%. Calcd for $CuC_{18}H_{22}N_2O_2S\cdot 2H_2O\cdot NaClO_4$(Cu(sal=aes=sal)): C, 37.17; H, 4.51; N, 4.82%.

Spectral Measurements and Instruments. Absorption spectra were recorded on 1 cm- or 1 mm-path length cell in the range 260—1100 nm with a Hitachi 323 spectrophotometer at room temperature. Electron spin resonance (ESR) spectra of copper complexes were recorded using a JEOL JES-FE1X instrument at 77 K. Magnetic field was calibrated on a Mn(II) in MnO(ΔH_{3-4}=8.69 mT) and g values were calibrated based on Li-TCNQ(g=2.0025). *N,N*-dimethylformamide was used as solvent.

Results

Absorption spectra of pca-containing complexes exhibited the splitted d-d bands, indicating the successful formations of five-coordinate complexes. Charge transfer bands arising from thio group appeared at 315—340 nm in most cases (Fig. 1). Although the complex Cu(pca=aes=pca) did not exhibit an apparent peak in this region, molar absorptivity of this complex was observed to be five times larger than those of the complexes which have no sulfide ligand (*i.e.* Cu(pca=pda=pca), where pda represents 1,5-pentanediamine). Another charge transfer peak was observed at 462 nm, though it was not certain whether or not the peak arose from charge transfer of thio group to copper. This was because of the fact that pca Schiff base complexes devoid of thio group occasionally exhibited a peak in this region.

ESR parameters and absorption spectral data of each complex are tabulated in Table 1. Cu(pca=aps=pca), Cu(pca-aps-pca), and Cu(pca-aes-pca) have similar spin Hamiltonian parameters: $g_{//}$ values are in the range 2.17—2.21 and $-A_{//}$ values of 16.7—17.1($\times 10^{-4}$) cm^{-1}. The prominently lowered $g_{//}$ values and $-A_{//}$ values indicate that the electron density around the copper(II) ion is appreciably reduced because of the sulfur donation in an equatorial position, since these complexes are five coordinate as clearly indicated in the splitting of d-d bands. On the other hand, Cu(pca=aes=pca) exhibited a larger $g_{//}$ value, suggesting a formation of entirely different donor setting around the copper(II) ion. The weaker contribution of sulfur donation on ESR spectrum seems to be due to the binding of the soft group at an apical position.[7] The

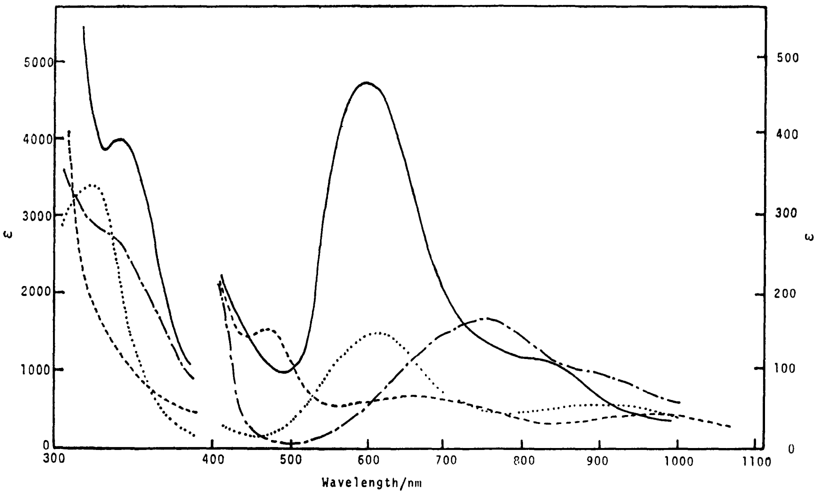


Fig. 1. Absorption spectra of Cu(pca=aps=pca) (——) Cu(pca=aps=pca) (—•—), Cu(pca=aes=pca) (------), and Cu(pca=aes=pca)(······).

Table 1. ESR parameters and absorption spectral data for the copper(II) complexes

Complex	ESR parameters			Absorption spectral data λ_{max}/nm, ε		
	$g_{//}$	$g_{\perp}$	$\frac{-A_{//}\times 10^4}{cm^{-1}}$	CT band	d-d band	
Cu(pca=aps=pca)	2.17	2.08	17.1	343 (4000)	604 (437)	830 (114)
Cu(pca-aps-pca)	2.20	2.06	17.0	335 (2730)	737 (163)	920 (98)
Cu(pca=aes=pca)	2.27	2.06	16.9	462 (153)	665 (69)	995 (43)
Cu(pca-aes-pca)	2.21	2.06	16.7	315 (3350)	610 (142)	870 (58)

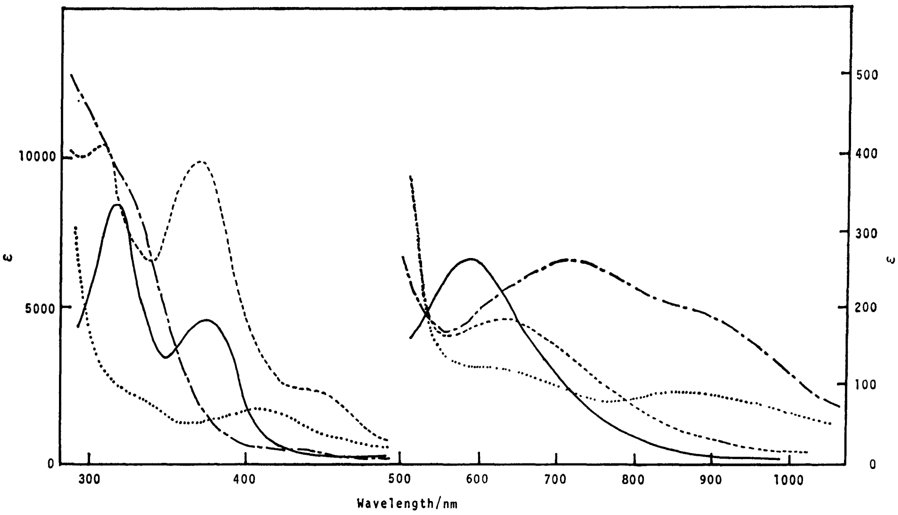


Fig. 2. Absorption spectra of Cu(sal=aps) (——), Cu(sal=aps=sal) (—·—), Cu(sal=aes=sal) (------), and Cu(sal=aes=sal) (······).

obscured charge transfer band around 350 nm also would favor this interpretation. Copper(II) complex of the Schiff base of salicylaldehyde and aps, Cu(sal=aps=sal), was not isolated as quinquedentate complex but was as a quadridentate planar complex Cu(sal=aps) which contained N_2OS donor set, in spite of being employed twice amount of sal for preparation. The complex exhibited a symmetrical sharp d-d absorption at 584 nm and a charge transfer band at 316 nm (Fig. 2). In line with this, the use of *N*-(2-aminoethyl)-3-aminopropylamine(aea) in place of aps also gave highly square planar quadridentate complex, Cu(sal=aea). The symmetrical d-d absorption appeared in a similar region at 563 nm, but no peak was found in 300—400 nm, indicating that the peaks appeared in this region in figures are charge transfer bands due to sulfur group to copper. In contrast with the above, the reduced Schiff base complex, Cu(sal=aps=sal) afforded the quinquedentate form, exhibiting the splitted d-d bands at 720 and 910 nm. The absorption bands at 320 (shoulder) and 440 nm might be the sulfur to copper(II) charge transfer bands. The former would be attributed to $S(\sigma)\rightarrow Cu$ and the latter to $S(\pi)\rightarrow Cu$.[8] Although Cu(sal=aes=sal) did not exhibit the clearly splitted d-d bands, the rather broader d-d band would imply a formation of square-pyramidal copper(II) complex. Charge transfer bands were clearly observed at 304 and 450 nm. The reduced Schiff base complex, Cu(sal=aes=sal), also gave distinctly splitted d-d bands at 600 and 865 nm and charge transfer bands at *ca.* 330 and 405 nm.

The effect of coordination of the thio group in an equatorial position has been recognized in the smaller $-A_{//}$ values (Table 2). The pronounced instance is the difference in the $-A_{//}$ values of 17.9 and 19.8($\times 10^{-4}$) cm^{-1} for Cu(sal=aps) and Cu(sal=aea), respectively. The similar coordination effect of the thio group can be realized also in the pair Cu(sal=aes=sal) and Cu(sal=aes=sal). The $-A_{//}$ value for Cu(sal=aes=sal) increases *ca.* 1×10^{-4} cm^{-1}, suggesting that the thio group occupies an axial position in this complex similarly to the case of Cu(pca=aes=pca).

Discussion

Of eight complexes, which were tried to prepare in this work, quinquedentate complexes with N_4S or N_2O_2S donor set were isolated and characterized to display apparently splitted d-d transition bands or a broader d-d absorption band. Charge transfer bands of sulfur to copper were disclosed to appear at 300—350 nm and occasionally at 400—500 nm. The band at 300—350 nm was very clear when the sulfur occupies an equatorial position. As for the reason it may be considered that p(σ) orbital of sulfur and $d_{x^2-y^2}$ orbital of copper(II) well overlap each other, hence strong charge transfer will occur between these orbitals. On the other hand, overlapping of p(π) and $d_{x^2-y^2}$ orbitals can be attributed only through a torsion of these orbitals. Accordingly, the band at 400—500 nm is occasionally

TABLE 2. ESR PARAMETERS AND ABSORPTION SPECTRAL DATA FOR THE COPPER (II) COMPLEXES

Complex	ESR parameters			Absorption spectral data λ_{max}/nm, ε			
	$g_{//}$	$g_{\perp}$	$-A_{//}\times 10^4$ cm^{-1}	CT band		d-d band	
Cu(sal=aps)	2.20	2.05	17.9	316(8740)		584(176)	
Cu(sal=aps=sal)	2.20	2.05	18.1	320_{sh}(9390)	440(426)	720(250)	910(173)
Cu(sal=aes=sal)	2.21	2.06	17.8	304(10200)	450(2260)	639(184)	
Cu(sal=aes=sal)	2.23	2.05	18.7	330(2170)	405(1750)	600(126)	865(92)

absent itself or is not very clear even if it appeared. When the sulfur atom binds copper(II) at an axial position, charge transfer from sulfur to copper might be permitted between either p(π) and $d_{x^2-y^2}$ or p(σ) and d_{z^2} orbitals. These transitions might appear at 330—350 nm and possibly even at 405—460 nm. The difference in the position of sulfur donor sensitively affects the ESR spin Hamiltonian parameters. When the sulfur occupies an equatorial position, both $g_{//}$ and $-A_{//}$ values will appreciably decrease, because the covalent character of Cu–S bond may weaken the electron density of central metal ion.9) On the other hand, binding of sulfur at an axial position only lowers $-A_{//}$ value a little as compared with those of ordinary tetragonal copper(II) complexes. The parameter, $g_{//}$, does not seem sensitively reflect the sulfur donation in the axial position. The similar effect of soft donor ligation at an axial position of copper(II) has been reported in some cases.7,8)

The d-d absorptions of non-blue coppers including those of multi-copper oxidases have been observed in the region of 600—1000 nm.10–13) The presence of charge transfer bands at 314 and 450 nm has been reported for galactose oxidase2) and in the range 300—500 nm for amine oxidase.3) In addition, non-blue coppers of multi-copper oxidases have been considered to have a close relation to the absorptions in the regions.10–13) These bands, even though not all of them, can be attributed to the charge transfer bands of sulfur to copper as described above. Some investigators reported that a SH group participates in the catalytic cycle of galactose oxidase14) and amine oxidase,15) although it is not certain whether or not the SH groups are coordinated to copper. If a sulfido group is coordinated to copper(II) ion, it must occupy an axial position, since the ESR parameters of non-blue coppers in enzymes do not suggest the binding of the SH group in an equatorial position. ESR parameters, $g_{//}$ and $-A_{//}$, of non-blue coppers were reported as 2.27 and 18.7×10^{-4} cm^{-1}, 2.29 and 16.9×10^{-4} cm^{-1}, 2.25 and 19×10^{-4} cm^{-1}, 2.21 and 20×10^{-4} cm^{-1}, and 2.22 and 19×10^{-4} cm^{-1} for galactose oxidase, amine oxidase, ceruloplasmine, ascorbate oxidase and laccase, respectively.17)

The non-blue coppers are not considered to alter the valence state in the course of the catalytic cycles differing from blue coppers, though Hamilton *et al.*18) considered bivalent state of copper is not active in galactose oxidase. At any rate, coordination chemistry of non-blue coppers does not seem favorable to the alteration of valence state of copper(II).19,20) The axial sulfur, if it really exists, might be considered to supply electrons *via* copper(II) ion to molecular oxygen.

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