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Remote Substituent Effects in Pyrrole-2-carboxaldiminate Complexes of Copper(II)

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A number of copper(II) bis chelates with anions of pyrrole-2-carboxaldehyde Schiff bases have been synthesized. The amine substituents are phenyl moieties, which themselves bear in the para position a series of substituents, ranging from the electron-withdrawing nitro group to the relatively electron-releasing dimethylamino group. Investigation of the $\text{Cu}^{\text{II}}-\text{Cu}^{\text{I}}$ redox potentials shows that electron-withdrawing groups increase the stability of copper(I) relative to copper(II). There are correlations among $E_{1/2}$, the basicity of the precursor anilines, and the Taft parameter, σ° , of the ring substituent, the plot of $nFE_{1/2}/2.3RT$ vs. $2\sigma^{\circ}$ having a slope of +1.28. ESR spectroscopy shows the complexes to have essentially square-planar geometry. The response of the redox potential and the insensitivity of the ESR parameters to the ring substituents are discussed in relationship to structural properties of protein-bound copper.

Introduction

Determination of the relationships which exist between the functional properties of copper proteins and the structural characteristics of their active sites has been the goal of a considerable amount of research effort in recent years. As almost all cuproproteins function by electron-transfer processes, there has been renewed interest centered on the redox-related chemistry of copper.¹⁻³ Spectroscopic techniques (particularly electron spin resonance) have yielded a considerable body of data for cuproproteins, but the interpretation of such data in terms of structural descriptions is still in its infancy. In addition, the degree to which the redox potential of a copper protein reflects its active site structure is imperfectly understood, and it is desirable to determine the relative sensitivities of various spectroscopic properties (ESR, for example) and chemical indices, such as redox potential, to the structural characteristics in and near the protein's active site. We have been investigating the relationships which exist among the spectroscopic, thermodynamic, and static structural properties of mononuclear^{3,4} and binuclear⁵ copper moieties and report here on the relative sensitivities of certain of these properties to the effect of remote substituents in a series of square-planar mononuclear copper chelates of the type depicted in Figure 1.

There have been only a small number of systematic studies of the redox properties of interrelated copper(II) complexes.^{2,3,6-8} The redox chemistry of the $\text{Cu}^{\text{II}}-\text{Cu}^{\text{I}}$ couple at equivalent degrees of complexation has often been deduced from thermodynamic cycles involving determination of formation constants for the cuprous and cupric states and the reduction potential of the aqueous couple.⁵ Application of voltammetric and polarographic techniques directly to the $\text{Cu}^{\text{II}}-\text{L}_n$ system offers considerable advantages with regard to solvent choice and removal of the necessity for synthesis of oxygen-sensitive copper(I) systems, while the results obtained still relate to the relative affinities of copper(II) and copper(I) for the given ligand system.

Experimental Section⁹

UV-visible absorption spectra were obtained on Cary-14 or 17D spectrophotometers, mass spectra from a Varian MAT-4B instrument operating at 70 eV, and ESR spectra on a Varian E-3 X-band spectrometer, calibrated with DPPH and an NMR probe. Proton NMR spectra were obtained on Varian T-60 and XL-100 instruments; chemical shifts are referred to internal Me_4Si .

Electrochemistry was performed in a three-electrode cell at 25.0 ± 0.2 °C, using as counterelectrode a platinum wire coil and as reference electrode a Ag/AgClO_4 (0.01 M), TEAP (0.1 M), CH_3CN half-cell, the potential of which we have measured to be 0.30 V positive of the SCE, both in $\text{CH}_3\text{CN}/\text{TEAP}$ at 25 °C. The working electrode was a mercury/gold amalgam/gold electrode disk (0.289 ± 0.001 cm², prepared by coating the clean gold surface with triply distilled mercury)

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or a platinum disk electrode (0.300 ± 0.001 cm²). These electrodes are part of a Beckman RDE assembly and were used for RDE polarography and (nonrotated) for cyclic voltammetry. The potentiostat was a PAR-173 instrument, incorporating a PAR-176 i/E converter. Voltammograms were recorded with an X-Y recorder or a storage oscilloscope.

Acetonitrile was distilled off P_4O_{10} under nitrogen, while polarographic grade tetraethylammonium perchlorate (G. F. Smith Chemical Co.) was dried in vacuo over P_4O_{10} before use. Solutions added to the electrochemical cell were purged of oxygen by bubbling nitrogen or argon, saturated with solvent, and then blanketed with the same gas during the experiments. Other solvents used were ACS reagent grade, as were the metal salts. Pyrrole-2-carboxaldehyde (Aldrich Chemical Co. and Eastman Kodak Co.) was used as supplied, as were the anilines (BDH, MCB, Aldrich, Eastman Kodak, K & K), while triethylamine (Eastman Kodak) was distilled off phthalic anhydride before being used for syntheses.

Synthetic Procedures

The Schiff bases *N'*-*p*-tolylpyrrole-2-carboxaldimine and *N'*-(*p*-dimethylaminophenyl)pyrrole-2-carboxaldimine were prepared by refluxing equimolar (20 mmol) quantities of *p*-toluidine and *N,N*-dimethyl-*p*-phenylenediamine, respectively, with pyrrole-2-carboxaldehyde, in ethanol (40 mL) and a drop of acetic acid, for 1 h. The solvent volume was reduced by vacuum evaporation, and the products were filtered off, recrystallized from ethanol, and dried in vacuo over P_4O_{10} . Yields were ca. 50%.

The chelates of copper(II) with the pyrrole-2-carboxaldimines having methyl, phenyl, and 2,6-dimethylphenyl as imine substituents were prepared as described previously.^{3,10} Although a number of variations of this procedure were used for synthesis of the other compounds reported herein, the most generally effective method was found to be as follows. To hot methanol (40–100 mL) was added copper(II) acetate hydrate (1.0 g, 5.0 mmol), pyrrole-2-carboxaldehyde (1.0 g, 10.5 mmol), and the appropriate substituted aniline (15 mmol). The mixture was brought to reflux, triethylamine (1.1 g, 11 mmol) was added, and refluxing was continued until product precipitated. This required several hours for the less basic amines, while with those more basic ($\text{p}K_a > \text{ca. } 4$), aqueous copper(II) acetate could be used, and the reaction was considerably faster. Product precipitation was completed, if necessary, by evaporation of solvent or addition of water. The product was filtered off, dried, recrystallized, and dried in vacuo over P_4O_{10} . Yields overall were generally 60–80%, but lower for the *p*-nitrophenyl derivative.

Analyses for C, H, and N (performed by Mr. P. Borda at the University of British Columbia) are given in Table I, together with other analytical properties and physical characteristics of the compounds.

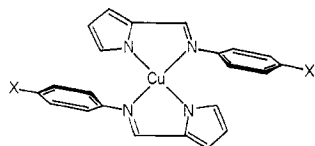
Results and Discussion

Synthesis and Characterization. In general, longer reaction times and lower yields were associated with the synthesis of chelates derived from the less basic anilines, and this very likely arises from the weaker nucleophilicity of such species toward both coordinated or noncoordinated aldehyde. Among the complexes prepared, the two solvates formed, namely, $\text{Cu}(\text{P2A-Ph-NMe}_2)_2 \cdot \text{CH}_3\text{CN}$ and $\text{Cu}(\text{P2A-Ph-Ph})_2 \cdot \text{C}_6\text{H}_6$, have ample precedent in coordination chemistry.¹¹

Table I. Analytical Properties of the Compounds

ion coordinated	precursor amine	recrystn solvent	appearance	mp, °C	% C		% H		% N	
					calcd	found	calcd	found	calcd	found
H ⁺	<i>p</i> -toluidine	ethanol	cream prisms	99	78.2	78.1	6.57	6.64	15.2	15.3
H ⁺	<i>N,N</i> -dimethyl- <i>p</i> -phenylenediamine	ethanol	orange-brown crystals	139	73.2	72.9	7.09	7.00	19.7	19.8
Zn ²⁺	<i>p</i> -toluidine	acetonitrile	yellow needles	260 dec	66.8	67.0	5.14	4.98	13.0	13.1
Zn ²⁺	<i>N,N</i> -dimethyl- <i>p</i> -phenylenediamine	acetonitrile	orange crystals	247 dec	63.7	63.9	5.76	5.72	17.2	17.4
Ni ²⁺	<i>N,N</i> -dimethyl- <i>p</i> -phenylenediamine	toluene	deep red-brown crystals	>260	64.6	64.8	5.84	6.00	17.4	17.2
Cu ²⁺	<i>p</i> -toluidine	benzene	shiny black crystals	194	67.1	67.2	5.13	5.30	13.1	13.1
Cu ²⁺	<i>p</i> -anisidine	benzene	shiny black crystals	198	62.4	62.7	4.76	5.00	12.1	11.9
Cu ²⁺	<i>p</i> -iodoaniline	chloroform	brown crystals	185	40.5	40.3	2.45	2.60	8.58	8.66
Cu ²⁺	<i>p</i> -bromoaniline	chloroform	shiny black crystals	178	47.2	47.0	2.86	3.00	10.0	10.1
Cu ²⁺	<i>p</i> -chloroaniline	chloroform	feathery brown needles	184.5	56.1	56.3	3.39	3.49	12.0	11.9
Cu ²⁺	<i>p</i> -fluoroaniline	chloroform	black prisms	204.5	60.4	60.1	3.66	3.60	12.8	13.1
Cu ²⁺	<i>p</i> -nitroaniline	dichloromethane	iridescent black crystals	215 dec	53.7	53.2	3.28	3.19	17.1	17.1
Cu ²⁺	<i>p</i> -aminoacetophenone	2-methoxyethanol	shiny black crystals	200	64.3	64.1	4.56	4.60	11.5	11.4
Cu ²⁺	<i>N,N</i> -dimethyl- <i>p</i> -phenylenediamine	acetonitrile	shiny black crystals	182	63.6	63.9	5.87	6.27	18.5	18.5 ^a
Cu ²⁺	<i>p</i> -aminobenzotrifluoride	benzene	fine black needles	205	63.9	63.7	5.74	5.79	17.3	17.4 ^b
Cu ²⁺	<i>p</i> -aminobiphenyl	benzene	brown, polycrystalline	206	53.6	53.6	2.97	3.16	10.4	10.8
Cu ²⁺	ethyl <i>p</i> -aminobenzoate	ethanol	greenish brown prisms	178.5	73.8	73.7	4.70	4.62	10.1	10.4 ^b
Cu ²⁺	mesidine ^d	benzene	shiny black crystals	227	61.6	61.1	4.80	4.64	10.3	10.3
Cu ²⁺	4-bromo-2,6-dimethylaniline	benzene	black crystals	207.5	69.3	69.1	6.21	6.34	11.5	11.7
					51.0	51.0	3.91	3.89	9.13	9.03

^a CH₃CN solvate. ^b After drying at 125 °C (0.05 mmHg). ^c Benzene solvate. ^d 2,4,6-Trimethylaniline.

Figure 1. Representative M(P2A-Ph-X)₂ species.

The mass spectra of the complexes all exhibited strong peaks at *m/e* values corresponding to Cu(P2A-Ph-X)₂⁺. In addition, a considerable fraction of the copper appeared in species of the type Cu₂(P2A-Ph-X)₂⁺, as was observed previously³ for Cu(P2A-alkyl)₂ compounds.

Square-planar complexes of the type Cu(P2A-alkyl)₂ in weakly coordinating or noncoordinating solvents exhibit an absorption envelope in the visible region of the spectrum, which can be deconvoluted into two bands, near 500 and 650 nm.³ In the complexes Cu(P2A-Ph-X)₂, usually only the longer wavelength transition can be discerned as a shoulder, as the shorter wavelength region is dominated in all these deeply colored complexes by intense ligand-based absorption, adequately exemplified by Figure 2 and Table II.

For this study, it was preferable to use a weakly coordinating solvent, in order to minimize any effect on the redox properties of the chelates, brought about by variations among them in the strength of axial ligation by a strong donor. Cu(P2A-CH₃)₂ was thus used as a model system to compare the donor properties of various solvents toward the copper(II) center; its d-d transitions are less obscured by the tail of the UV absorption and shift greatly to longer wavelength in strongly coordinating solvents. In addition to toluene (λ_{max} 480 nm) and acetonitrile (λ_{max} 501 nm), DMF (λ_{max} 505 nm), dichloromethane (λ_{max} 510 nm), 2-methoxyethanol (λ_{max} 510 nm), nitromethane (λ_{max} 510 nm), and acetone (λ_{max} 515 nm) appeared to be weak perturbants relative to pyridine (λ_{max} 650 nm).

The carboxaldimine proton, located near δ 8.2 in the NMR spectra of the protonated Schiff bases and their zinc chelates (X = NMe₂, CH₃), is strongly shielded by the nickel ion and shifted to δ 4–6; the pyrrole α proton is also shifted upfield.¹⁰ However, generally narrow line widths are otherwise observed, and this, together with the presence of the strong 450-nm

Table II. Principal Electronic Absorption Bands^a

coordinated ion	phenyl para substituent	λ, nm	ε, L mol ⁻¹ cm ⁻¹
H ⁺	NMe ₂	325	22 200
Zn ²⁺	NMe ₂	371	44 000
Ni ²⁺	NMe ₂	367	32 100
		450 ^b	4 400
Cu ²⁺	NMe ₂	383	38 600
Cu ²⁺	NO ₂ ^c	410	50 200
		670 ^b	210

^a In acetonitrile solution. ^b Shoulder; ε at quoted λ. ^c In dichloromethane solution.

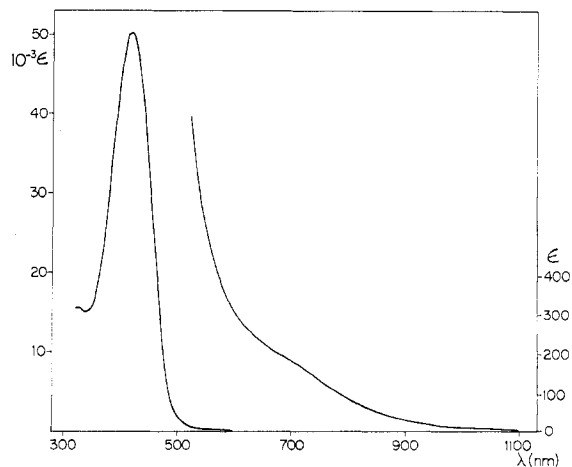


Figure 2. Electronic absorption spectrum of Cu(P2A-Ph-NO₂)₂ in dichloromethane solution. The left- and right-hand ordinate scales refer to the left- and right-hand curves of the spectrum.

ligand field band in Ni(P2A-Ph-NMe₂)₂, shows the nickel(II) chelates to be predominantly square planar and diamagnetic in acetonitrile and halocarbon solutions.

Redox and ESR Properties of the Compounds. Acetonitrile was chosen as the solvent for electrochemistry, as it gave voltammograms relatively free of problems associated with adsorption and slow electrode kinetics or following reactions.

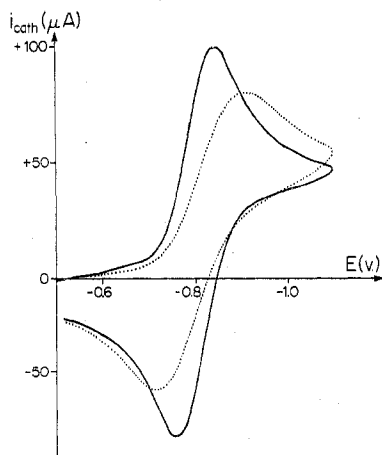


Figure 3. Cyclic voltammograms of 1.38 mM $\text{Cu}(\text{P2A-Ph-OCH}_3)_2$ in 0.1 M TEAP/ CH_3CN at mercury (solid line) and platinum (broken line) electrodes. The former yields $D = 7.4 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ at 25 °C. The scan rate was 0.10 V s^{-1} , and E 's are vs. Ag^+/Ag nonaqueous reference electrode.

Table III. Redox Properties of the Compounds

compd	para substituent	aniline $\text{p}K_a^a$	$-E_{1/2}^b$, V, $\text{Cu}^{\text{II}}/\text{I}$	σ^c
1	NO_2	1.05	0.62	+0.82
2	COCH_3	2.19	0.70	+0.46
3	COOC_2H_5	2.38	0.69	+0.46
4	CF_3	2.57	0.69	+0.54 ^d
5	Cl	3.81	0.72	+0.27
6	Br	3.91	0.73	+0.26
7	I	3.78	0.73	+0.27
8	F	4.52	0.75	+0.17
9	C_6H_5	4.27	0.75	-0.01 ^d
10	H	4.61	0.76	0.00
11	CH_3	5.07	0.78	-0.15
12	OCH_3	5.29	0.80	-0.12
13	$\text{N}(\text{CH}_3)_2$	6.2 ^e	0.84	-0.44

^a H. A. Sober, Ed., "Handbook of Biochemistry", 2nd ed, CRC Press, Cleveland, Ohio, 1973, p J-207. ^b $\pm 10 \text{ mV}$ vs. a nonaqueous Ag^+/Ag reference electrode. ^c L. P. Hammett, "Physical Organic Chemistry", 2nd ed, McGraw-Hill, New York, N.Y., 1970, p 356. ^d σ_{para} values: T. H. Lowry and K. S. Richardson, "Mechanism and Theory in Organic Chemistry", Harper and Row, New York, N.Y., 1976, p 63. ^e Estimated, ± 0.1 , from data given in A. Albert and E. P. Serjeant, "Ionisation Constants of Acids and Bases", Methuen, London, 1962, p 147.

Figure 3 shows the typical voltammetric response for these complexes in the potential region of interest. Voltammetry at a platinum electrode gave results complicated by electrode kinetics at the scan rates ($35\text{--}1000 \text{ mV s}^{-1}$) used, whereas a mercury electrode yielded more directly interpretable data. When corrected for iR drop, the peak potential separations (60 mV) are those expected for reversible one-electron redox processes,¹² except for the case of $\text{Cu}(\text{P2A-Ph-NO}_2)_2$.

The cathodic peak current functions ($i_{\text{pc}}/c\nu^{1/2}$) are similar to those observed at this electrode for systems well characterized as $n = 1^{2,3}$ and lead to diffusion coefficient values in the range $(6\text{--}10) \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ for $n = 1$. In addition, these redox processes are in the vicinity where it has been established^{2,3} that the reaction $\text{Cu}(\text{II}) + e^- \rightleftharpoons \text{Cu}(\text{I})$ occurs in these systems; so for the above reasons, we assign the reductions of copper(II) complexes to the above process in the range -0.5 to -1.0 V . (Table III). As expected on this basis, neither of the chelates $\text{Zn}(\text{P2A-Ph-CH}_3)_2$ nor $\text{Zn}(\text{P2A-Ph-NMe}_2)_2$ shows any reduction process at potentials more positive than -2.2 V in $\text{CH}_3\text{CN}/\text{TEAP}$.

Rotating mercury electrode polarography evidences that $\text{Ni}(\text{P2A-Ph-NMe}_2)_2$ is reduced at $E_{1/2} = -1.58 \text{ V}$ in the same

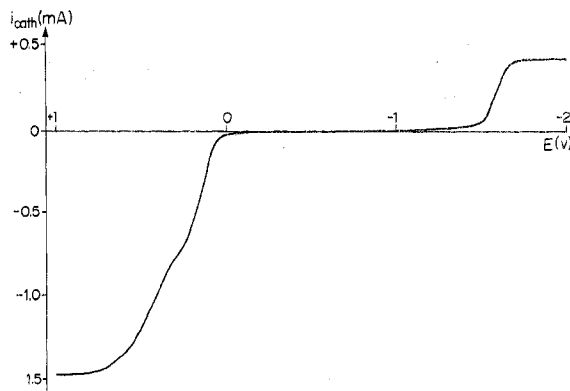


Figure 4. RDE polarogram of 1.26 mM $\text{Ni}(\text{P2A-Ph-NMe}_2)_2$ in 0.1 M TEAP/10:1 $\text{CH}_3\text{CN-CH}_2\text{Cl}_2$ at 25 °C. From -0.5 V , the anodic scan is at an RPE and the cathodic scan at a mercury surface, yielding $D = 1.1 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$. The data are vs. a nonaqueous Ag^+/Ag reference electrode.

solvent (Figure 4). The limiting current observed is consistent with a one-electron process, but cyclic voltammetry shows it to be quite irreversible, unlike some other nickel(II) chelates we have studied, including $\text{Ni}(\text{P2A}_2\text{-prn})$.^{3,13}

The copper(II), nickel(II), and zinc(II) complexes with P2A-Ph-NMe_2^- as ligands are all oxidizable at the RPE a few hundred millivolts positive vs. the Ag^+/Ag reference half-cell in $\text{CH}_3\text{CN}/\text{TEAP}$ (Figure 4). Two equivalent oxidation processes are observed, poorly resolved in rotating electrode polarograms. In each case, the first of these is associated with a limiting current, the magnitude of which ($i_L/c\nu^{1/2} = \text{ca. } 40 \mu\text{A M}^{-1} \text{ rad}^{-1/2} \text{ s}^{1/2}$) is twice that observed for the $n = 1$ reduction ($i_L/c\nu = \text{ca. } 20 \mu\text{A mM}^{-1} \text{ rad}^{-1/2} \text{ s}^{1/2}$) of $\text{Cu}(\text{P2A-Ph-NMe}_2)_2$, and is, therefore, due to a two-electron oxidation step. $\text{Zn}(\text{P2A-Ph-CH}_3)_2$ also exhibits these oxidation processes, which are irreversible (cyclic voltammetry, 100 mV s^{-1}) in all four cases. Hence, they are likely not due to the simple reversible $n = 1$ oxidations which *p*-phenylenediamines undergo¹⁴ but are probably associated with oxidation of the imine moiety. Both $E_{1/2}$ and $i_{\text{pc}}/c\nu^{1/2}$ for $\text{Cu}(\text{P2A-Ph-NMe}_2)_2$ were independent of concentration over the range $0.1\text{--}2.5 \text{ mM}$, indicating the unlikelihood that significant self-association (dimerization) occurs in these $\text{Cu}(\text{P2A-Ph-X})_2$ chelates in acetonitrile. In addition, we have not observed for toluene solutions any $g = 4$ ($\Delta M_s = 2$) resonances of the type usually associated with dimeric species, which in any case usually form via a ligand donor atom acting as a bridge between two metals, which is most unlikely here.

James and Williams⁶ have demonstrated the dependence of the $\text{Cu}^{\text{II}}\text{--Cu}^{\text{I}}$ redox potential on the electronic effects of remote substituents on chelating ligands. They proposed a linear relationship between E_1 and ligand $\text{p}K_a$ for substituted 2,2'-bipyridyls, increasing σ -donor power stabilizing copper(II) relative to copper(I).

As the redox potential is also sensitive to the stereochemical properties of the metal ion,^{2,3} particularly via crystal field effects for copper(II), it is necessary to compare inductive effects within constant geometry about the copper(II) ion. As intense ligand-based ($\pi\text{--}\pi^*$, $n\text{--}\pi^*$) transitions obscure the d-d bands in most of the compounds of Figure 1, electronic absorption spectroscopy is not useful for deducing the copper(II) stereochemistry. However, the ESR spectra of CuN_4 centers are quite responsive to changes in geometry away from tetragonal.³ The ESR spectrum of $\text{Cu}(\text{P2A-mesityl})_2$ is shown in Figure 5. The ^{14}N superhyperfine coupling was in general less resolved in the simpler $\text{Cu}(\text{P2A-Ph-X})_2$ species. Representative ESR parameters are given in Table IV. For the phenyl-substituted pyrrole-2-carboxaldiminate copper(II) complexes, the values observed for g_{\parallel} and $|A_{\parallel}|$ in particular

Table IV. ESR Parameters for Selected Compounds

imine substituent	solvent	$10^4 A_{\parallel} $, cm ⁻¹	g_{\parallel}	g_0^a	g_{\perp}	$10^4 A_{\perp} $, cm ⁻¹
methyl ^b	toluene	181	2.197	2.102	2.055	65
<i>tert</i> -butyl ^b	toluene	108	2.267	2.134	2.068	14
phenyl	toluene	176	2.201			
<i>p</i> -nitrophenyl	toluene	174	2.203			
<i>p</i> -(trifluoromethyl)-phenyl	toluene	176	2.204			
<i>p</i> -(dimethylamino)-phenyl	CH ₃ CN/CH ₃ NO ₂ ^c	165	2.238			
<i>p</i> -(dimethylamino)-phenyl	toluene	176	2.199			
2,4,6-trimethyl-phenyl	CH ₃ CN/CH ₃ NO ₂	169	2.231			
2,4,6-trimethyl-phenyl	toluene	189	2.187	2.096	2.051	69
4-bromo-2,6-dimethyl-phenyl	CH ₃ CN/CH ₃ NO ₂	171	2.212			
4-bromo-2,6-dimethyl-phenyl	toluene	190	2.189			

^a Computed using $g_0 = (g_{\parallel} + 2g_{\perp})/3$ with $g_{\parallel} \pm 0.002$ and $g_{\perp} \pm 0.005$. ^b From ref 3. ^c 50% v/v.

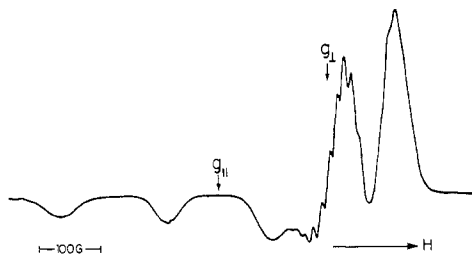


Figure 5. X-Band ESR spectrum of Cu(P2A-mesityl)₂ in toluene glass at 77 K.

evidence square-planar coordination geometry for the CuN₄ moiety, comparable with that pertaining to Cu(P2A-CH₃)₂³ and contrasting with a pseudotetrahedral structure, as in that of Cu(P2A-*t*-Bu)₂,¹⁵ which shows a greatly reduced value of $|A_{\parallel}|$ and a markedly larger g_{\parallel} value. In fact, the spectrum of Cu(P2A-Ph-NO₂)₂ is almost superimposable with even that of Cu(P2A-Ph-NMe₂)₂. Although g_{\parallel} is known to increase as the electron-withdrawing power of a ligand substituent increases,¹⁶ the consonant variation observed in g_{\parallel} within the series Cu(P2a-Ph-X)₂ is only of the same magnitude as the experimental error. Therefore, despite the fact that the above two species represent opposite extremes in terms of the inductive effect of the phenyl ring substituent, the ESR parameters g_{\parallel} and $|A_{\parallel}|$, which relate to electron density in the CuN₄ plane, are relatively insensitive to para substitution in these ligands' aryl groups. Ortho methylation does appear to change g_{\parallel} and $|A_{\parallel}|$ significantly in the expected directions, however, while the effect of a potentially coordinating solvent component (acetonitrile vs. toluene) is essentially independent of the para substituent.

In contrast, the reduction potentials are quite responsive to the inductive properties of the phenyl ring's para substituent, replacement of NMe₂ by CF₃ raising the Cu^{II}-Cu^I reduction potential by 150 mV. There is a close correlation ($r = 0.982$) between the $E_{1/2}$ value of the bis(*N'*-arylpyrrole-2-carboxaldiminato)copper(II) chelate and the pK_a of the aniline precursors to the Schiff base; clearly the aqueous solution basicity of the aniline toward a proton is translated smoothly into σ -donor power at the imine nitrogen. The $E_{1/2}$ vs. pK_a data may be fitted to a straight line (Figure 6) although this need not necessarily hold.¹⁷ The linear free-energy relationship represented by this result may be formalized (Figure 7) by plotting $nFE_{1/2}/2.303RT$ vs. $2\sigma^{\circ}$ where σ° is the Taft substituent parameter. There seems little justification in resorting to σ values which would take into account resonance through stabilization differences between the two copper redox states. Indeed, molecular models show steric hindrances which suggest coplanarity of the (imine) phenyl group with the pyrrole-2-carboxaldimine framework to be unlikely (Figure 1). Linear correlations between $E_{1/2}$ and σ have been observed for multiple redox equilibria in similarly substituted metal

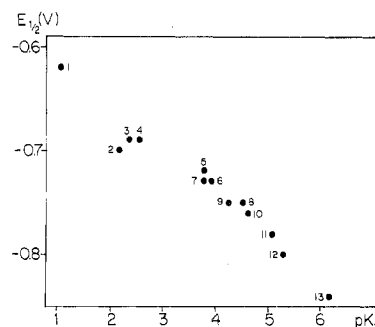


Figure 6. Plot of $E_{1/2}$ vs. pK_a of precursor aniline for Cu(P2A-Ph-X)₂ species.

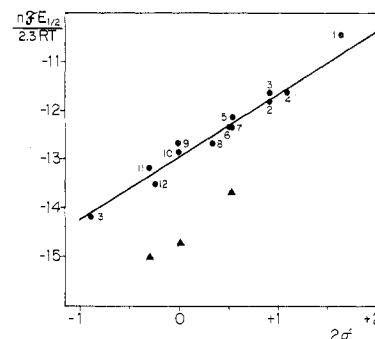


Figure 7. Plot of $nFE_{1/2}/2.3RT$ vs. $2\sigma^{\circ}$ for Cu(P2A-Ph-X)₂ species (circles) and for three complexes (triangles) with 2,6-dimethyl-4-substituted-phenylimine moieties.

complexes of tetraphenylporphyrins, excluding the *p*-NMe₂ case.¹⁸⁻²¹ For this Cu^{II}-Cu^I redox reaction, Taft σ° values for the para substituents correlate quite linearly with the $E_{1/2}$ values for the Cu^{II}-Cu^I couple. The plot in Figure 7 yields a value for the reaction constant, ρ , of 1.28 ± 0.17 (or 0.076 ± 0.010 V in a plot of $E_{1/2}$ vs. $2\sigma^{\circ}$). The data for the *p*-nitro-substituted species has been omitted from the least-squares fit of the line, as the reduction wave has poorly reproducible reversibility, although the $E_{1/2}$ value obtained fits the regression adequately well.

This ρ value is comparable with values observed for the effect of phenyl-ring substitution on the redox potentials of porphyrin and metal-based processes in metal *meso*-tetraphenylporphyrin complexes,¹⁹⁻²¹ that is, where the substituent is separated by five to eight conjugable bonds from the reaction site, as in the pyrrole-2-carboxaldiminates. The present case appears to be the only one yet for which an extensive $E_{1/2}$ vs. σ correlation has been found to be satisfactory for a copper chelate system.²² The E_f data for the Cu^{II}-Cu^I system ligated with 4,4'-disubstituted-2,2'-bipyridyls do not correlate as well with σ values ($r = 0.89$ for $E_{1/2}$ vs. $4\sigma_{\text{para}}$) although the E_f - pK_a plot was linear.⁶

Figure 7 also contains data for three compounds synthesized from 4-substituted-2,6-dimethylanilines, namely, the bis-(pyrrole-2-carboxaldiminato)copper(II) species with Br, H, and CH₃ as the (phenyl) 4'-substituent, for which the $E_{1/2}$ values are -0.81, -0.87, and -0.89, respectively. The potentials are all more negative (by ca. 100 mV) than for the species without methyl groups ortho to the aniline nitrogen, and this lowering of $E_{1/2}$ must be partially accounted for by the electron-releasing effect of these ortho methyl groups, in agreement with the ESR results.

Results of the type presented here further demonstrate that the redox potential of a copper(II) site is quite sensitive to the electrostatic inductive effects of substituents at centers remote from the metal ion. Similar dependence of redox potential on ligand substituents has been demonstrated recently by Bossu et al.⁸ for the peptide-ligated copper(III)-copper(II) couple. Clearly, the E° of a Cu^{II}-Cu^I couple bound, for example, at the active site of a copper protein can, in effect, be "fine tuned" to the optimum value required for catalytic activity by both stereochemical and inductive effects. Tetrahedral distortion of a square copper(II) system systematically moves the reduction potential to more positive values,³ while again, with a given set of donor atoms, the reduction potential will change according to the α substituent of a coordinated peptide and to the presence of interactions of the ligands with charged groups. The replacement of the proton by zinc(II) on an imidazole coordinated to the copper(II) in bovine superoxide dismutase provides an extreme example of the latter as a remote aromatic substitution in a copper protein structure.²³

The lack of sensitivity of the ESR spectra to substitutions which markedly affect the potential of the Cu^{II}-Cu^I couple is noteworthy in itself. For example, although the azurins from *P. aeruginosa* and *P. denitrificans* have quite similar ESR parameters (g_{\parallel} , $|A_{\parallel}|$, g_{\perp}), their reduction potentials near pH 7 differ by 80 mV.²⁴ It, therefore, seems reasonable that conclusions regarding the structural properties of protein copper binding sites (i.e., geometry and ligands) as deduced from spectroscopic and crystallographic studies of a limited number of copper proteins may be extended at the very least to protein copper with similar ESR parameters, regardless of variations of the order of ± 100 mV among the redox potentials of the proteins. These results also suggest, that while the redox potential of a metalloprotein is indicative of the nature of a metal's coordination environment, it is likely to be sensitive enough to influences outside the first coordination sphere so as not to be valuable as a detailed diagnostic criterion for the coordination sphere.

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Registry No. HP2A-Ph-CH₃, 14479-37-9; HP2A-Ph-N(CH₃)₂, 66562-68-3; Zn(P2A-Ph-CH₃)₂, 66562-92-3; Zn(P2A-Ph-N(CH₃)₂)₂, 66562-99-0; Ni(P2A-Ph-N(CH₃)₂)₂, 66563-00-6; Cu(P2A-Ph-CH₃)₂, 15490-11-6; Cu(P2A-Ph-OCH₃)₂, 66563-01-7; Cu(P2A-Ph-I)₂, 66562-93-4; Cu(P2A-Ph-Br)₂, 66562-94-5; Cu(P2A-Ph-Cl)₂, 66562-95-6; Cu(P2A-Ph-F)₂, 66562-96-7; Cu(P2A-Ph-NO₂)₂, 66562-97-8; Cu(P2A-Ph-COCH₃)₂, 66562-98-9; Cu(P2A-Ph-N(CH₃)₂)₂, 66563-03-9; Cu(P2A-Ph-CF₃)₂, 66563-02-8; Cu(P2A-Ph-Ph)₂, 66563-04-0; Cu(P2A-Ph-COOC₂H₅)₂, 66563-05-1; Cu(P2A-Ph-2,4,6-(CH₃)₃)₂, 66609-89-0; Cu(P2A-Ph-4-Br-2,6-(CH₃)₂)₂, 66563-06-2; Cu(P2A-Ph)₂, 15170-41-9; Cu(P2A-Ph-NO₂)₂, 66563-07-3; Cu(P2A-Ph-COCH₃)₂, 66563-08-4; Cu(P2A-Ph-COOC₂H₅)₂, 66563-09-5; Cu(P2A-Ph-CF₃)₂, 66563-12-0; Cu(P2A-Ph-Cl)₂, 66563-13-1; Cu(P2A-Ph-Br)₂, 66563-14-2; Cu(P2A-Ph-I)₂, 66563-15-3; Cu(P2A-Ph-F)₂, 66563-16-4; Cu(P2A-Ph-C₆H₅)₂, 66563-17-5; Cu(P2A-Ph)₂, 66563-18-6; Cu(P2A-Ph-CH₃)₂, 66563-19-7; Cu(P2A-Ph-OCH₃)₂, 66563-10-8; Cu(P2A-Ph-N(CH₃)₂)₂, 66563-11-9.

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- (9) Abbreviations: DPPH, diphenylpicrylhydrazyl radical; TEAP, tetraethylammonium perchlorate; RDE, rotating disk electrode; RPE, rotating platinum electrode; Ph, phenyl; ESR, electron spin resonance; NMR, nuclear magnetic resonance; SCE, saturated calomel electrode; NMe₂, dimethylamino group; prn, trimethylene group.
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Rate of Inversion of Sulfur in Cobalt(III)-Thioether Complexes

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The synthesis and characterization of several isomers of cobalt(III)-tren complexes containing (*R*)-cysteine, cysteamine, and their S-methylated derivatives as ligands are described. It is shown that the rate of sulfur inversion in the S-bonded thioether-cobalt(III) complexes is slow ($k_i < 10$ s⁻¹) on the NMR time scale at 25 °C but it exceeds 0.1 s⁻¹.

Introduction

It was recently demonstrated that sulfenates (RSO⁻) S-bonded to octahedral cobalt(III) do not readily invert about

sulfur¹ and are analogous to free sulfoxides (RR'SO) in this respect (Figure 1). Thioethers (RR'S) like sulfenates are rendered chiral on coordination and it is known that the