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Synthesis, Spectroscopic and Redox Behaviour of some Copper(II) and Copper(I) Biomimetic Complexes

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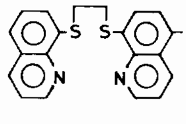
Abstract

Copper complexes with acyclic ligands have been synthesized with a chelate unit of the composition CuN_xS_y. In the electronic spectra of copper(II) complexes a highly intensive charge-transfer band $nS \rightarrow d_{x^2-y^2}$ (Cu^{2+}) occurs within the range 620–720 nm. Corresponding copper(I) complexes were prepared by electrochemical reduction and characterized by electron spectroscopy. Values of the redox potential ($E_{1/2}$) of the $CuL^{2+/+}$ pair as well as those of the rate constant of the electrode reaction (k_{sh}) were obtained by cyclic voltammetry on a platinum electrode in acetonitrile. The behaviour of the complexes as new models of 'blue' copper proteins is discussed.

Introduction

Regardless of the fact that the first 'blue' copper proteins were isolated from organisms nearly 30 years ago [1], the structure of the active centres of these biooxidants has not been fully explained until now. At present it is assumed that the unusual properties of these proteins are conditioned mainly by the coordination of cysteine or methionine sulphur atoms to the copper(II) ions [2]. Biomodelling with the help of copper(II) coordination compounds with sulphur-containing ligands is used at present to explain the structural details of the coordination unit of proteins containing copper of type 1 their abnormally high intensity absorption bands at *ca.* 600 nm ($\epsilon = 2000–8000\ M^{-1}\ cm^{-1}$) and the positive values of the redox potentials (0.4–0.8 V). In the literature such models are described with mercapto ligands [3–6] as well as with ligands containing thio-ether groups [3, 4, 7–9].

The aim of this paper is the synthesis, spectral and electrochemical studies of some models of active centres of 'blue' copper proteins. Copper complexes with polydentate derivatives of 8-mercaptoquinoline (L1 to L5) were chosen as models.



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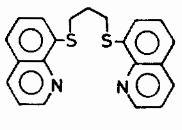

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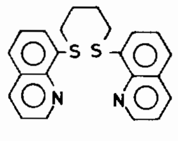

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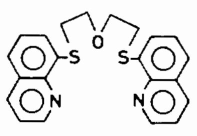

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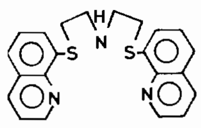

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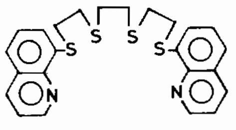

L5

Experimental

The sodium salt of 8-mercaptoquinoline (Biolar, U.S.S.R.) and 1,5-dibromo-3-azapentane hydrobromide (Aldrich) were used without further purification. 1,2-Dibromethane, 1,3-dibromopropane and 1,4-dibromobutane (Aldrich) were distilled prior to synthesis. 1,8-Dichloro-3,6-dithiaoctane was synthesized as described earlier [10]. Acetonitrile for spectral and electrochemical studies was dried over P_2O_5 and distilled with CaH_2.

The copper complexes with L1 and L2 were prepared analogously [11]; complexes with L3, L4 and L5, respectively, were synthesized *in situ* without prior preparation of ligands by the addition of an equimolar amount of $Cu(ClO_4)_2 \cdot 6H_2O$ to the reaction mixture of 8-mercaptoquinoline and the corresponding α,ω-dihalogeno derivative in ethanol at room temperature [12]. The complexes were recrystallized from an acetonitrile–ethanol mixture (1:1).

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The electronic spectra were recorded on a Specord M 40 spectrophotometer (Zeiss, Jena). The electrochemical measurements were made with a Polarographic analyzer PA 2 (Laboratorní přístroje, Praha) with a three-electrode arrangement. The working electrode used was a platinum disc electrode (surface area 1.15 mm^2), sealed in soft glass. The reference electrode consisted of a Calomel electrode with aqueous 4 M LiCl and with a salt bridge filled with 0.1 M $LiClO_4$ in acetonitrile. The auxiliary electrode was a wide-surface platinum electrode. The scan rate was changed within the interval 10 to 500 mV/s. The diffusion coefficients were determined chronoamperometrically.

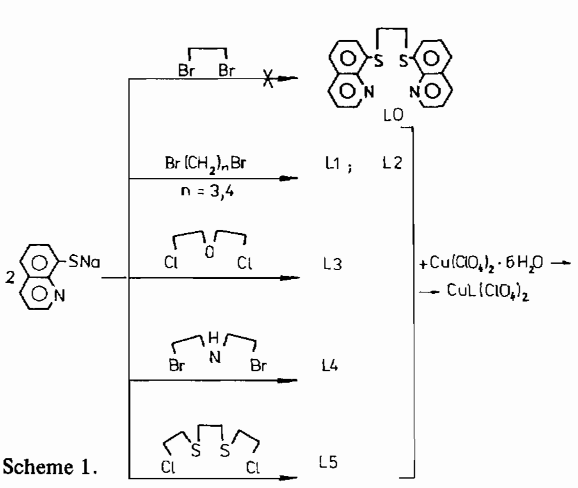
Coulometric measurements as well as preparatory electrolysis were made with a coulometric analyzer OH-404 (Radelkis, Budapest). The working electrode consisted of double circular platinum net placed parallel to a frit separating the anodic from the cathodic compartment of the electrolytic cell. An extensive graphite electrode was used as auxiliary electrode. The reference electrode was the same as in the voltammetric measurements. The base electrolyte used was 0.1 M $LiClO_4$ and the inert gas used was argon saturated with acetonitrile vapour.

Results

Synthesis

The synthesis reactions are given in Scheme 1. The ligands L1 and L2 were prepared as solid individual compounds; L3 and L5 were obtained as oils which were not purified further. Efforts to prepare the L0 ligand as well as the complex of this according to the above-mentioned scheme were not successful due to the alternative reaction of quaternization of the nitrogen atoms of quinoline [11, 12]. The synthesized compounds were characterized by elemental analysis (Table I).

The copper(I) complexes were prepared by preparatory electrolysis of the CuL^{2+} acetonitrile solutions at potentials 0.25 V more negative than the redox potentials of $CuL^{2+/+}$. For the electrolysis the charge used corresponded to the one-electron reduction of CuL^{2+}.



Scheme 1.

Electronic Spectra

The electronic spectra were measured in acetonitrile solutions of CuL^{2+} and CuL^+, respectively. Table II gives the maxima of the absorption bands (λ_{max}) as well as the corresponding values of the coefficients of extinction (ϵ). From the data it follows that copper(II) complexes with the ligands studied show one band in the visible part of the spectrum within the range 630–640 nm, except for $CuL3^{2+}$ where the shift of the absorption band towards the higher wavelength 720 nm was observed. The ϵ values were 200–440 M^{-1} cm^{-1} which are atypical for most copper complexes absorbing within this range. Within the ultraviolet region all complexes possessed a broad absorption band within the range 300–320 nm which is split into a doublet with maxima at 305 and 315 nm, respectively.

The CuL^{2+} reduction to CuL^+ is connected with marked changes in the electronic spectra. In the visible region the band disappears within the range 630–640 nm and within the UV range the band is widespread at 300 nm and, except for $CuL3^+$, the band with a maximum at 260 nm is observed ($\epsilon \sim$ 16 000–44 000 M^{-1} cm^{-1}).

Electrochemical Study

The cyclic voltammograms of the studied copper(II) complexes show the quasi-reversible character of

TABLE I. Elemental Analysis Data

Compound	Found (%)					Calculated (%)				
	C	H	N	S	Cu	C	H	N	S	Cu
L2	70.23	5.18	7.37	17.14		70.18	5.31	7.44	17.07	
$CuL2(ClO_4)_2$	40.67	3.07	4.48	10.15	9.90	41.33	3.13	4.38	10.05	9.94
$CuL3(ClO_4)_2$	40.20	2.91	4.05	9.91	9.89	40.32	3.05	4.28	9.81	9.70
$CuL4(ClO_4)_2$	40.07	3.20	6.58	9.62	9.73	40.39	3.21	6.43	9.82	9.71
$CuL5(ClO_4)_2$	39.03	3.19	3.98	17.76	8.57	39.40	3.28	3.83	17.58	8.69

TABLE II. Electronic Spectra in Acetonitrile

Compound	λ_{max} (nm)	ϵ (M^{-1} cm^{-1})	
$CuL1(ClO_4)_2$	305 (18000)	315 (18000)	630 (300)
$CuL2(ClO_4)_2$	308 (16800)	318 (16800)	640 (330)
$CuL3(ClO_4)_2$	305 (13600)	315 (13600)	720 (440)
$CuL4(ClO_4)_2$	305 (17200)	315 (16400)	620 (290)
$CuL5(ClO_4)_2$	305 (12200)	315 (12000)	630 (200)
$CuL1(ClO_4)$	255 (16000)		
$CuL2(ClO_4)$	258 (24800)	310 broad (13800)	
$CuL3(ClO_4)$		295 broad (22000)	318 sh (17000)
$CuL4(ClO_4)$	255 (14000)	290 (16800)	315 sh (10800)
$CuL5(ClO_4)$	258 (44000)	300 broad (13800)	
L1	255 (27000)		
L2	255 (38000)		

the redox process. The difference in potentials of the cathodic and anodic peaks (ΔE_p) is 80–200 mV at the polarization rates 20–500 mV s^{-1}. The ratio of the anodic and cathodic peak currents ($i_{p,a}/i_{p,c}$) is in all cases near one. From the ΔE_p dependence on the polarization rate, the values of the rate constants of the electrode reaction (k_{sh}) were determined. These values are summarized in Table III together with $E_{1/2} = (E_{pc} + E_{pa})/2$ values as well as the diffusion coefficients D, determined chronoamperometrically.

The coulometric study confirmed the one-electron character of the reduction of all CuL^{2+}. The reoxidation of CuL^+, made at potentials more positive by 0.2 V than E_{pa}, required a charge equal to that consumed for the CuL^{2+} reduction; this confirms the redox stability of both forms of the complexes in acetonitrile and the one-electron character of the redox changes.

Chemical Reactivity

The reduction of $CuL1^{2+}$–$CuL5^{2+}$ in acetonitrile by biosubstrates like NADH, NADPH, FADH, glutathione, cysteine and ascorbic acid was studied. The products of chemical reduction are the corresponding CuL^+ complexes. The spectrophotometric titration confirmed the one-electron stoichiometry of the redox reactions which may be expressed by the equation

$$CuL^{2+} + HSt \longrightarrow CuL^+ + St + H^+$$

(where St = substrate)

It has been found that if the acetonitrile CuL^{2+} solutions are left to stand for several months the formation of CuL^+ complexes proceeds. These are relatively inert to oxidation by air oxygen; they are, however, easily oxidized electrochemically to the initial CuL^{2+} complexes.

Discussion

Synthesis

During synthesis of the compounds, it was observed that the pure ligand could not be obtained from the reaction mixture in the case when the carbon chain of the α,ω-halogeno derivative consists of two atoms (1,2-dibromo-ethane, 1,5-dichloro-3-oxopentane, 1,5-dibromo-3-azapentane and 1,8-dichloro-3,6-dithiaoctane). In the case of the dihalogen derivatives containing a polyatomic carbon chain (1,3-dibromopropane and 1,4-dibromobutane) the reaction is smooth. This phenomenon can be explained by the higher reactivity of β-halogen derivatives in nucleophilic substitutions which leads to the greater formation of quaternized products of 8-mercaptoquinoline. The formation of these products makes the separation of the reaction mixtures more difficult and the ligands L3 to L5 were thus not prepared in a pure state.

TABLE III. Electrochemical Data in Acetonitrile[a]

Complex	$E_{1/2}$ (V)	ΔE_p (V)	$10^4 \times k_{s,h}$ (cm s^{-1})	$10^6 \times D$ (cm^2 s^{-1})
$CuL1(ClO_4)_2$	0.400	0.120	2.5	4.4
$CuL2(ClO_4)_2$	0.660	0.080	7.4	1.4
$CuL3(ClO_4)_2$	0.435	0.100	4.4	2.0
$CuL4(ClO_4)_2$	0.480	0.110	4.6	3.3
$CuL5(ClO_4)_2$	0.530	0.100	4.8	2.8

[a] Supporting electrolyte = 0.1 M $LiClO_4$; platinum electrode used as a working electrode; $E_{1/2}$ *vs.* SCE (4 M LiCl); ΔE_p values for scan rate of 50 mV s^{-1}.

The $CuL(ClO_4)_2$ complexes were prepared in ethanolic medium at room temperature. The increased formation of copper(I) complexes during the synthesis at higher temperature (over 60 °C) can be ascribed to the redox reaction of copper(II) complexes with the ethanol.

Electronic Spectra

A typical feature of the spectra of the copper(II) complexes studied is the intensive absorption band within the range 620–720 nm. High values of the extinction coefficient ϵ within this range are characteristic for coordination compounds of copper(II) with sulphur-donor ligands, including cyclic and acyclic complexes of the type $CuN_xS_y^{2+}$ [3, 4, 13]. The absorption band may be assigned as that of a charge-transfer band from non-bonding orbitals of the sulphur atom to the singly occupied $d_{x^2-y^2}$ orbital of the copper(II) ion, $nS \rightarrow d_{x^2-y^2}$ (Cu^{2+}). More detailed assignement of this band is the object of discussion at present [3, 4]. The more marked shift of the absorption band in the case of $CuL3^{2+}$ may be explained by axial coordination of the oxygen atom leading to a change in geometry of the chelate unit. The low extinction coefficient of $CuL5^{2+}$ containing the maximum number of donor sulphur atoms (4) is connected with a strong deformation of the chelate unit owing to which the overlap of the orbitals of the sulphur atoms and the copper(II) $d_{x^2-y^2}$ orbital is less. A similar phenomenon was described in the case of the complex with a chelate knot $CuS_3N_2^{2+}$ [3].

The consequence of the reduction of copper(II) complexes is the loss of the above-mentioned absorption band. This is, at the same time, further proof that the $d_{x^2-y^2}$ orbital is fully occupied in the case of Cu(I) and the charge transfer from sulphur orbitals is thus not possible.

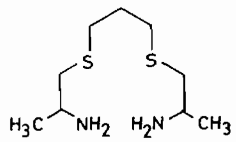
Two absorption maxima recorded in $CuL1^{2+}$ up to $CuL5^{2+}$ complexes in the ultraviolet region may be [3] ascribed to the transition of $S \rightarrow d_{x^2-y^2}$ (Cu^{2+}). The shift of the maxima towards the lower wavelengths compared with the compounds described in ref. 3 is connected with the change of energy of the orbitals of sulphur atoms bonded to the aromatic rings of quinoline. In the reduced complexes the discussed band is broader and in the case of some complexes it is also more intensive, which shows the greater inclination of Cu(I) towards coordination by sulphur atoms.

In the spectra of CuL^{2+} the highly intensive band is absent at *ca.* 250 nm at which it is observed in free ligands, in the S-substituted 8-mercaptoquinolines [14] as well as in CuL^+ complexes. This band refers to the nitrogen donor atoms of quinoline. It is known that the coordination of nitrogen atoms with Cu(II) leads to a shift of the charge-transfer band towards shorter wavelengths. The considerable shift of the band of the present complexes outside the usually studied part of the spectrum may be explained by the connection of the orbitals of the nitrogen atoms to the conjugated system of quinoline. In the case of CuL^+ complexes, the discussed band appears again which shows the weak tendency of nitrogen towards Cu(I) coordination.

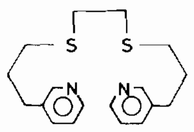
Electrochemical Behaviour

Positive values of potentials of $CuL^{2+/+}$ pairs as well as the adsorption of sulphur-containing compounds were obtained with the use of platinum as a working electrode in voltammetric measurements. All CuL^{2+} complexes are, on this electrode in acetonitrile, subject to a quasi-reversible one-electron reduction which was confirmed by the E_p, $i_{p,a}/i_{p,c}$ values as well as the electrolytic charge values. The value $\Delta E_p = 65$ mV was determined for the ferrocenium/ferrocene pair in the check of the properties of the working electrode. The data in Table III show the same trend of changes in rate constant (k_{sh}) and in $E_{1/2}$ values. The greatest $E_{1/2}$ value was found for the complex with the ligand L2. The construction of molecular models of complexes confirms that the tetrahedral structure of the chelate unit CuN_2S_2 is realized most easily only in the case of CuL2 which causes an easier reduction of copper(II) to copper(I) and offers maximum gain in free Gibbs energy. The least positive $E_{1/2}$ value was observed for the $CuL1^{2+}$ complex, the donor set of which possesses the lowest mobility among the synthesized complexes and for which the formation of even a deformed tetrahedral structure is linked with great steric difficulties. Thus the geometrical structure of the chelate unit influences in an important way the values of the redox potentials (thermodynamic parameter) as well as the rate of the electrode reaction (kinetic parameter).

The measured $E_{1/2}$ values are substantially higher than the redox potentials of most copper(II) macrocyclic complexes with N_2S_2 in the same solvent [13], and are higher than those of the complex with the acyclic ligand L6 for which $E_{1/2} = -0.06$ V [7].



L6



L7

It is interesting that the value of $E_{1/2}$ of the $CuL7^{2+}$ complex is 0.38 V [7] which is relatively near to the $E_{1/2}$ values of the complexes studied by us. The increase in the redox potential is evidently connected with the introduction of pyridine or quinoline nitrogen atoms having π-acceptor ability which stabilizes copper(I).

Chemical Reactivity

Preliminary attempts to study the reactions of $CuL1^{2+}$ to $CuL5^{2+}$ complexes have shown that these are effective one-electron oxidizing agents of biosubstrates. The stability of the copper(I) oxidation state in the studied complexes deserves attention compared to macrocyclic compounds of the type CuN_2S_2 [15]. In contrast to the latter the copper(I) complexes studied by us are not subject to fast oxidation by air oxygen. This may be explained by the presence of quinoline rings with a π-delocalized system of electrons, the consequence of which is the stabilization of $CuN_xS_y^+$.

An interesting property of $CuL1^{2+}$ to $CuL5^{2+}$ complexes is the self-reduction of these if the solutions are left to stand. A similar phenomenon was observed in some 'blue' copper proteins like azurine [16] and plastocyanine [17].

Comparison with Natural Systems

The $CuN_xS_y^{2+}$ complexes, synthesized and studied in the present work, are structural analogues of active centres of 'blue' copper proteins, as the chelate units of these have identical structures. Besides this, absorption bands at *ca.* 600 nm have been observed in the electronic spectra of systems such as proteins of type 1 Cu. The lower values of the extinction coefficients in the case of model compounds may be explained by the solvolysis characteristic for copper(II) complexes with sulphur-donor ligands in the medium of coordinating solvents [3, 7]. This reaction leads to the inclusion of sulphur with solvent in the coordination sphere, to the formation of the so-called 'dangling' sulphur, and to the decrease in extinction coefficients of the charge-transfer bands. The copper(II) complexes described possess high values of redox potential which lie within the range of the potentials of 'blue' copper proteins.

Besides this, the electron-transport properties of the centre of type 1 Cu are modelled by the reactivity of the studied complexes in the oxidation of biosubstrates. Similarly to the 'blue' copper proteins the synthesized complexes are subject to self-reduction in solution.

In the present work new thiaazachelate complexes of copper were thus prepared and characterized spectroscopically, electrochemically, as well as chemically. They represent structural and functional models of 'blue' copper proteins.

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