# Electrochemical and spectroelectrochemical study of copper complexes with 1,10-phenanthrolines

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## Abstract

The redox behaviour of a series of copper(II) complexes with different phenanthrolines (1:2 metal to ligand) in dimethylformamide solvent is reported. Cyclic voltammetry, controlled potential coulometry and spectroelectrochemistry in the visible region have been used. Accurate values for the formal potential of the copper(II)/copper(I) couples could be computed by spectroelectrochemistry, also in those cases in which the systems are poorly reversible. Two further reductions lead to neutral and anionic copper species, respectively. The nature of the substituents on the phenanthroline ligands has been found to affect strongly the redox potential of the former couples, while a less marked influence on the latter ones has been evidenced. On the other hand, differences in the ligands induce very different kinetic stability of the copper complexes formed in the more cathodic processes.

## Introduction

Attention has been devoted to copper complexes with nitrogen ligands as possible antineoplastic substances. Their pharmacological activity [1, 2] has been tentatively ascribed to the capability of the metal in the +1 oxidation state to induce cleavage of DNA of neoplastic cells through the formation of hydroxyl radicals from hydrogen peroxide. This requires that the copper(II) complexes are reducible in the biological environment in order to generate the copper(I) active form. It is hence particularly important to assign accurate values to the redox potential of the copper(II)–copper(I) couple in similar complexes, as well as to identify the factors that affect this thermodynamic parameter. As an additional reason for being interested in the electrochemistry of this class of compounds, phenanthroline ligands seem particularly suitable for stabilizing low valent copper complexes [3–6]; our aim is hence also that of better defining the stability of similar compounds [3–5, 7].

In a previous article we have reported on the electrochemical behaviour of copper complexes with 1,10-phenanthroline, 2,9-dimethyl-1,10-phenanthroline and 4,7-dimethyl-1,10-phenanthroline, both with a 1:1 and

a 1:2 metal to ligand stoichiometry [5]. We subsequently extended our study to ternary complexes in which one phenanthroline ligand was substituted by two cinnamate anions [8]. Our findings are consistent with the results of recent studies on similar complexes, bearing particularly bulky substituents in 2 and 9 positions of the phenanthroline ring [3, 4, 6]. As an additional part of our studies on this class of compounds, we report here on the electrochemical and spectroelectrochemical behaviour of a wide series of binary copper complexes with differently substituted phenanthrolines, with 1:2 metal to ligand ratio, being interested in all aspects of their cathodic behaviour.

## Experimental

### Materials

The following ligands were used: 1,10-phenanthroline (phen), 2,9-dimethyl-1,10-phenanthroline (dmp), 4,7-dimethyl-1,10-phenanthroline (4,7-dmp), 5,6-dimethyl-1,10-phenanthroline (5,6-dmp), 3,4,7,8-tetramethyl-1,10-phenanthroline (tmp), 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (bcp), 4,7-diphenyl-1,10-phenanthroline (4,7-dpp), 5-methyl-1,10-phenanthroline (mphen), 5-nitro-1,10-phenanthroline (nphen) and 5-chloro-1,10-phenanthroline (cphen). Scheme 1 presents

Scheme 1.
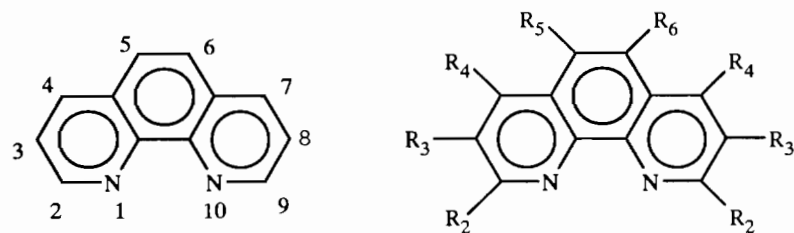
| Ligand | R_2 | R_3 | R_4 | R_5 | R_6 |
|---|---|---|---|---|---|
| phen | H | H | H | H | H |
| dmp | CH_3 | H | H | H | H |
| 4,7-dmp | H | H | CH_3 | H | H |
| 5,6-dmp | H | H | H | CH_3 | CH_3 |
| tmp | H | CH_3 | CH_3 | H | H |
| bcp | CH_3 | H | C_6H_5 | H | H |
| 4,7-dpp | H | H | C_6H_5 | H | H |
| mphen | H | H | H | CH_3 | H |
| nphen | H | H | H | NO_2 | H |
| cphen | H | H | H | Cl | H |

a formulation of the listed molecules. All these compounds were from Aldrich. Dimethylformamide (DMF) (Aldrich, anhydrous, 99 + %, Gold Label, water < 0.005%, packaged under nitrogen) was used as solvent in all electrochemical tests, without further purification. Tetraethylammonium tetrafluoroborate (Fluka) supporting electrolyte was dried overnight at 50 °C under reduced pressure before use.

*Preparation of the copper complexes*

The synthesis of the complexes studied was carried out according to the literature [9], by adding a methanol solution of $Cu(NO_3)_2 \cdot 5H_2O$ (0.5 mmol in 1 ml) to a methanol solution of the proper phenanthroline (1 mmol in 3–5 ml). After magnetic stirring, powdered precipitates separated, that were dried under vacuum. Elemental analyses, conductivity measurements at $5 \times 10^{-4}$ M concentration in DMF, and magnetic susceptibilities at room temperature resulted in agreement with the formulation $CuL_2(NO_3)_2 \cdot xH_2O$, where $x$ is different for the different compounds. Thermal gravimetry showed that the loss of water molecules from the hydrated complexes is complete at 70 °C, except for $Cu(tmp)_2(NO_3)_2 \cdot H_2O$, when the temperature should be increased up to 125 °C. These findings suggested the way to dry the products before submitting them to electrochemical tests.

*Electrochemical and spectroelectrochemical measurements*

An Amel System 5000 computerized instrument was used as a potential waveform generator, a potentiostat and a coulometer in all the electrochemical experiments. The relevant responses were recorded on an Amel model 863 XY recorder. Cyclic voltammetric and controlled potential coulometric tests were all carried out in an H-shaped cell. Working and auxiliary electrode compartments were separated from each other by a sintered glass disk in the exhaustive electrolyses, working and auxiliary electrodes being a platinum gauze and a mercury pool, respectively. In the cyclic voltammetric experiments the working electrode was a platinum disk of 2 mm diameter and the platinum gauze was used as the auxiliary electrode. Tests were also performed on a mercury electrode, prepared by covering a gold disk, with the aim of studying possible dependence of the charge transfer kinetics on the electrode material. However, the data obtained were not conclusive, also due to adsorptions on the electrode surface that many of the compounds studied undergo. The reference electrode was in any case an aqueous saturated calomel electrode (SCE), connected to the working electrode compartment by a salt bridge containing the same solvent medium. The measurements were performed at room temperature and the solutions were de-aerated by bubbling 99.999% pure argon through.

In the spectroelectrochemical experiments in the visible region an optically transparent thin layer elec-

trode (OTTLE) cell [10] was used. The working electrode was a gold minigrid (100 l.p.i.) sandwiched between two microscope slides, 0.1 mm Teflon spacers fixing the path length. The two microscope slides were held together by an epoxy glue which decomposes in DMF slowly enough not to pollute the solution during the experiment. In order to reduce the uncompensated ohmic drop that, due to the relatively high resistance present in this cell assembly, leads to different potential values along the grid, 0.5–1.0 M supporting electrolyte concentrations were used. The spectra were obtained with a Hewlett-Packard model 8452A diode array spectrophotometer, controlled by a Hewlett-Packard Vectra QS/165 computer. In these experiments the spectra were recorded under potentiostatic conditions: a staircase potential waveform was applied to the minigrid working electrode, the potential step being of 20 mV and the step time ranging from 300 to 600 s. The scan was centered at an estimate of $E°$ performed by low-scan rate ($1.0$ mV s$^{-1}$) cyclic voltammetry carried out in the same cell. The longest times were necessary to attain redox equilibrium in the cases of particularly slow electron transfer. A screen was then used to allow the beam only to cross the central region of the grid, since diffusion at upper and lower edges, altering the local composition of the solution, prevents the system from reaching equilibrium conditions in those regions. The spectra of the oxidized and reduced forms were recorded by polarizing the minigrid at potential values 300 mV anodic and cathodic with respect to rough estimates of $E°$, respectively. The absorbance of the oxidized form at $\lambda_{max}$ of the reduced species was indistinguishable from the background value under our experimental conditions, so that the ratio between the concentrations of oxidized and reduced forms could be expressed as a function of the absorbances of exhaustively reduced solutions and of solutions with a composition conditioned by the redox equilibrium at the working potential. The plot of the logarithm of these ratios versus the relevant potential value (Nernst's plot) accounted for a linear dependence and allowed the evaluation of the formal potential of the redox couple [10]. The tests were performed at a temperature of $25 \pm 0.2$ °C.

Elemental analysis of Cu, C, H and N was used to identify the fine powder present in the solution after electrolysis at the second cathodic process as metal copper.

## Results and discussion

The cyclic voltammetric curves reported in Figs. 1 and 2 are representative of the voltammetric behaviour of the class of compounds studied. Three subsequent
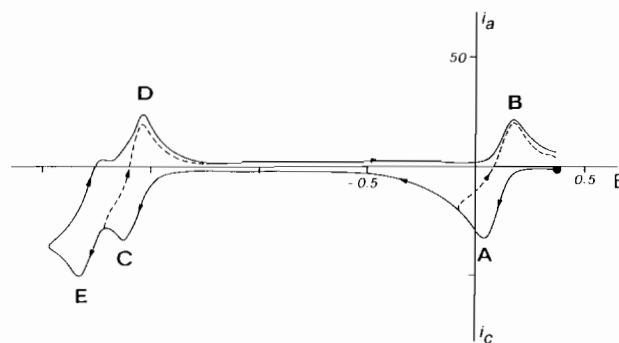


Fig. 1. Cyclic voltammetric curves recorded on $4 \times 10^{-3}$ M [Cu(5,6-dmp)$_2$](NO$_3$)$_2$, 0.1 M tetraethylammonium tetrafluoroborate, DMF solution. Pt working electrode; $E$, in V, is referred to SCE; $i$ in $\mu$A; 0.2 V s$^{-1}$ potential scan rate; ● starting potential for the cathodic scan.
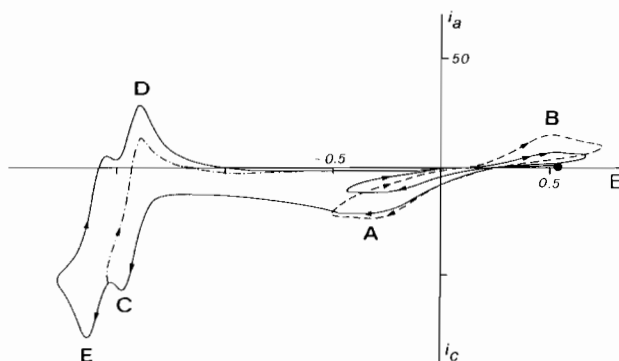


Fig. 2. Cyclic voltammetric curves recorded on $4 \times 10^{-3}$ M [Cu(4,7-dpp)$_2$](NO$_3$)$_2$, 0.1 M tetraethylammonium tetrafluoroborate, DMF solution. Experimental conditions as in Fig. 1.

cathodic processes are evidenced: by comparison with current–potential curves recorded separately on solutions of ligand and of copper ions [5], they can be ascribed to subsequent redox processes involving the copper complex. The reduction of the relevant free ligand is also recorded: it occurs at even more negative potentials, in most cases quite close to the reduction of the solvent medium, and is not shown in the Figures. Differences are noted for the cphen and nphen derivatives. In the case of the complex with cphen, neither a backward peak directly associated to C nor a cathodic peak corresponding to E are clearly detectable at 0.2 V s$^{-1}$. As to the nphen derivative, the C–D system is recorded at much less negative potentials than for the other complexes, quite close to the values at which the relevant free ligand is electroactive. An additional reduction is evidenced at the same potentials at which the free ligand is also further reducible ($E_{p,c} = -1.70$ V at 0.2 V s$^{-1}$ scan rate).

As regards the first cathodic process (system A–B), a very different reversibility degree is found for the different complexes, depending on the nature and position of the substituents on the phenanthroline rings.

The separation between cathodic and anodic peak potentials, that can be taken as a measure of the electrode reversibility of the redox couple involved, ranges from 60 mV (reversible charge transfer) for the case of the dmp complex to more than 700 mV for the 4,7-dpp and nphen derivatives, at a potential scan rate of 0.2 V s$^{-1}$, see Fig. 2. Controlled potential coulometries at potentials of the first cathodic response in all cases involve the consumption of one electron per molecule of electroactive substance. The same peak systems are recorded by cyclic voltammetric tests on the reduced solutions, and the starting copper(II) complexes are quantitatively regenerated by one-electron exhaustive reoxidation at peak A. In those cases in which high irreversibility affects the electrode charge transfer, the responses are also very broad and poorly reproducible, so much so that the evaluation of proper peak potentials is rather approximated, if even possible. As a consequence, the computation of $E_{1/2}^{r}$ as the half-sum of anodic and cathodic peak potentials, which is often a good experimental estimate of the standard potential of the redox couple involved in the peak system [11], is possible only with a large approximation for the 4,7-dmp and nphen derivatives, and definitely unreliable for the complex with 4,7-dpp ligand. On the other hand, very accurate formal potential values $(E^{\circ\prime})$ can be obtained by spectroelectrochemical experiments performed following the procedure outlined in 'Experimental', even in those cases in which the charge transfer is affected by high irreversibility. The wavelengths of maximum absorbance of the different copper(I) complexes under our experimental conditions, i.e. the wavelength values at which the data to use in the Nernst's plot are drawn out, are reported in Table 1. A detailed analysis of the spectra recorded on the solutions of the different compounds is beyond the scope of the present work; they have been however extensively discussed elsewhere for some of the com-

pounds we are dealing with [12] and the absorptions can be in all cases ascribed to MLCT. As an example of how the spectroelectrochemical tests are performed in order to compute the $E^{\circ\prime}$ values, Fig. 3 reports a thin-layer cyclic voltammogram recorded on a solution of the tmp derivative, together with the sequence of spectra recorded during a cathodic staircase potential ramp on the same solution. The computed $E^{\circ\prime}$ values for the different complexes studied are also listed in Table 1. The indicated uncertainties take into account the differences between the plots obtained in a cathodic potential scan, i.e. by reducing the copper(II), and in an anodic sweep, i.e. by oxidizing the copper(I) complexes solutions, as well as the distribution of the experimental points around the best regression lines, i.e. the standard deviation of the regression. It is clear from the data reported in Table 1 that electronic effects of the substituents on the phenanthroline ring influence significantly the redox potential of the copper(II)–copper(I) couple. It is however also evident that a major role is played by possible steric effects; in particular, the formal potentials of both the compounds bearing substituents in 2 and 9 positions undergo a marked shift towards positive values. This finding can be explained by a destabilization of the copper(II) complex due to distortion towards tetrahedral coordination [5, 13]. Copper(I) complexes are stabilized at the same time, thanks to the capability of copper(I) to form tetrahedral bonds with $4s4p^3$ orbitals [14].

Further reductions of the complexes (peaks C and E in Figs. 1 and 2) likely have ligand-based character: the $d^{10}$ electronic configuration of the metal centre and the nature of the transition ascribed to the absorption in the visible region suggest that the LUMO is basically an orbital of the ligand both as to the first reduction – peak C, a first ligand molecule involved – and as to the second cathodic process – peak E, the second ligand unit involved. Table 1 reports estimates of the

TABLE 1. Redox potentials of the copper complexes and of the free ligands; $\lambda_{max}$ for the copper(I) species

| Ligand | $E^{\circ\prime}$ [CuL$_2$]$^{2+}$/[CuL$_2$]$^+$ (mV vs. SCE) | $E_{1/2}^{r}$ [CuL$_2$]$^+$/[CuL$_2$] (V vs. SCE) | $\lambda_{max}$ [CuL$_2$]$^+$ (nm) | $E_{1/2}^{r}$ L/L$^-$ (V vs. SCE) |
|---|---|---|---|---|
| phen | $80 \pm 3$ | $-1.53$ | 442 | $-2.00$ |
| dmp | $581 \pm 3$ | $-1.60$ | 458 | $-2.10$ |
| 4,7-dmp | $14 \pm 3$ | $-1.70$ | 440 | $-2.07$ |
| 5,6-dmp | $53 \pm 7$ | $-1.58$ | 446 | $-2.09$ |
| tmp | $18 \pm 2$ | $-1.76$ | 430 | $-2.20^a$ |
| bcp | $593 \pm 5$ | $-1.51$ | 478 | $-1.99$ |
| 4,7-dpp | $83 \pm 3$ | $-1.42$ | 460 | $-1.88$ |
| mphen | $82 \pm 5$ | $-1.55$ | 442 | $-2.04$ |
| nphen | $147 \pm 2$ | $-0.64$ | 452 | $-0.85$ |
| cphen | $141 \pm 3$ | $-1.45^a$ | 444 | $-1.82^a$ |

$E_{1/2}^{r}$ L/L$^-$ values are given with an approximation of $\pm 0.05$ V.  $^a$No directly associated backward peak detectable: $E_{p,c}$ (0.2 V s$^{-1}$) is given.
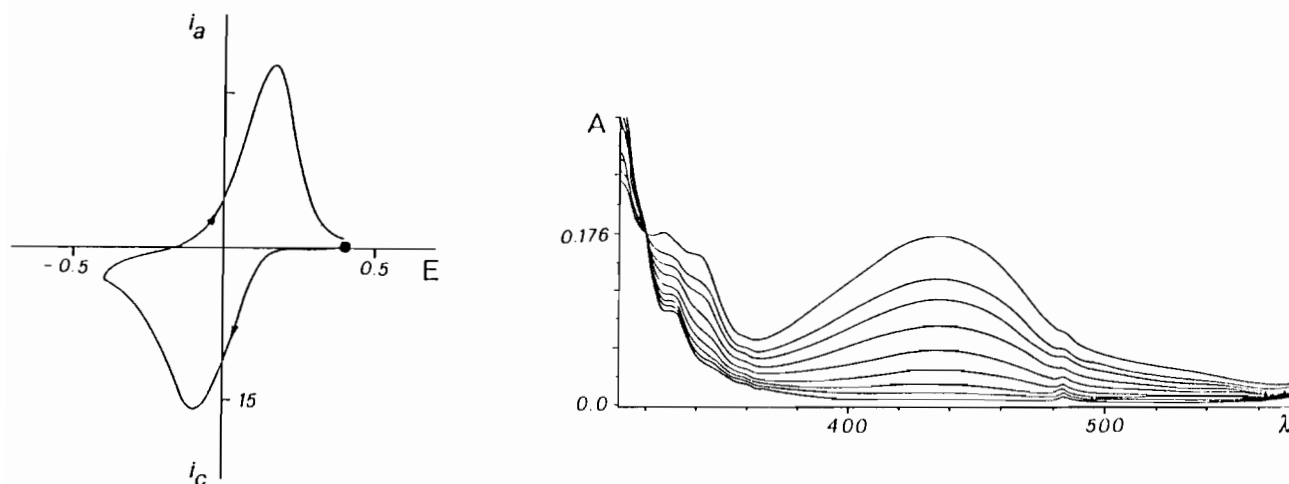
Fig. 3. Cyclic voltammogram (1.0 mV s$^{-1}$ scan rate) recorded in OTTLE cell on $2.3 \times 10^{-3}$ M [Cu(tmp)$_2$](NO$_3$)$_2$, 0.5 M tetraethylammonium tetrafluoroborate, DMF solution, together with absorption spectra in the visible region recorded in the same cell under potentiostatic conditions; uncompensated $iR$ drop is present. Working potentials of 300; 100; 80; 60; 40; 0; $-20$; $-220$ mV vs. SCE at increasing absorbance. $A$ in arbitrary units; $\lambda$ in nm.

standard potential of the redox couples involved in the peak system corresponding to C–D in Figs. 1 and 2. The experimental approximation of the standard potential is in this case the 'reversible half-wave potential', $E^r_{1/2}$, evaluated on responses recorded at a potential scan rate high enough for the backward to forward peak current ratio to be close to unity, i.e. to make the charge transfer unaffected by any coupled irreversible chemical reaction on the time scale of the voltammetric test. For the sake of comparison, $E^r_{1/2}$ or $E_{p,c}$ values for the reduction of the relevant free ligands are also reported. The listed potential values for the ligands are to be intended, in general, simply as rough estimates of the potentials at which the ligands undergo reduction. The electrode charge transfer is quasi-reversible and is followed by an irreversible chemical reaction, with a rate that depends strongly on the nature of the substituents. Hence, the non-reversible character of the charge transfer causes the forward cathodic peak to shift cathodically, often merging into the solvent reduction, as the potential scan rate is increased with the aim of preventing the homogeneous coupled chemical reaction from occurring significantly on the time scale of the experiment. The definition of the mechanism of the cathodic reduction of the ligands, as well as a precise evaluation of the relevant $E^r_{1/2}$ is not, of course, an aim of this work.

Coulometric tests at potentials of the peak corresponding to C show that this further reduction also involves one electron per molecule, for all the complexes studied except for the cphen derivative: for this complex two electrons per molecule are spent. As to the nphen derivative, the closeness of the potentials at which complex and free ligand are reduced causes the coulometric results to be strongly dependent on the exact value of the working potential. One electron per molecule of electrolyzed species is only consumed at a potential anodic to the peak potential value for the reduction of the complex: the number of exchanged electrons increases when working at more cathodic potentials.

By cyclic voltammetric tests at different potential scan rates, on the basis of the values of the ratio between backward (D) and forward (C) peak currents, the following scale of relative stability can be deduced for the complexes primarily electrogenerated at peak C, on varying the nature of the ligand: bcp ≃ nphen > dmp ≃ 4,7-dpp > phen ≃ 4,7-dmp ≃ 5,6-dmp ≃ mphen > tmp. The availability of data for a wide series of derivatives allows us to give a more correct interpretation also to the results reported by us in a previous paper [5]. At the end of the electrolyses a fine powder is in part suspended in the solution and in part deposited on the walls of the cell and on the platinum gauze; after polishing, this is bright brown in colour. In all cases but those of the bcp and nphen derivatives, no anodic process can be evidenced at less anodic potentials than those at which oxidation of metal copper takes place. By oxidizing the platinum gauze in a fresh solution at these potentials ($\simeq +0.3$ V) copper(II) ions are formed and, on the other hand, by anodizing a different, clean platinum gauze dipped inside the reduced solution, the suspension progressively disappears and the starting copper(II) complexes are regenerated to an extent corresponding to the number of Coulombs spent in the latter reoxidation. Furthermore, the sum of the Coulombs spent in the two anodic electrolyses is equal to the number of Coulombs used in the overall reduction (two moles of electrons per one mole of starting complex). The suspension, when

filtered off and analyzed, is shown to consist of pure metal copper. On the other hand, in the cases of the bcp and nphen derivatives, in cyclic voltammograms recorded at the end of the reduction at the peak corresponding to C, the D–C peak system is present: peak D is recorded as the forward peak in an anodic scan starting at the electrolysis potential and peak C is detected as the directly associated backward response. The height of this peak system is about 15% with respect to that recorded on the starting solution; it lowers progressively and the peaks are no longer detectable 2 to 3 h after completion of the electrolysis. Accordingly, reoxidizing the reduced solutions at potentials of the peak corresponding to D just after the end of the cathodic reduction, about 10% of the Coulombs corresponding to a one-electron process are collected and the copper(I) complex is regenerated to an equivalent yield. The results of all these tests fit well with the voltammetric data and are consistent with a reduction mechanism in which the copper(I) complexes are reduced in part to electrodeposited metal copper and in part to complexes of formally zerovalent metal. These last compounds are short-lived, significantly stable on a time scale longer than that of voltammetric tests only in the cases of the bcp and nphen derivatives: they decompose to metal copper and free ligand in the bulk of the solution, at a rate depending on the nature of the ligand. In particular. for the bcp and nphen derivatives the decomposition is slow enough to allow the detection of significant amounts of complex at the end of the exhaustive reduction. In this connection, it must be also noticed that, in voltammetric curves recorded on solutions exhaustively reduced at peak C, the height of the peak corresponding to E in Fig. 1 parallels that of D, i.e. it is undetectable in all cases except for the bcp and nphen derivatives. This strongly suggests that peak E has to be attributed to further reduction of the formally zerovalent metal complexes [3]; the possibility of reducing a similar compound can be accounted for by the presence of two molecules of ligand in the complex. It is noteworthy that at high enough potential scan rate a backward anodic peak is directly associated to E. On the basis of the height of this peak on varying the ligand, the same scale of relative stability reported above for the neutral $CuL_2$ species could be ascertained for the further reduced, very labile $CuL_2^-$ complexes.

A peculiar behaviour is proper of the cphen derivative, since the copper(I) complex is reduced directly via a two-electron process. Voltammetric and coulometric data relative to this compound are consistent with a fast decomposition of the primarily formed reduced species to metal copper, to free ligand and to other organic species derived from the radical anion of the ligand, likely 1,10-phenanthroline and chloride ions [15]. It is hence not surprising that, after reoxidizing copper metal inside the reduced solution, the voltammetric behaviour cannot be easily interpreted, since copper(II) ions formed in the presence of different ligands that are capable of complexing the metal ions.

## Acknowledgements

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