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Cu(II) and Ni(II)-1,10-phenanthroline-5,6-dione-amino acid ternary complexes exhibiting pH-sensitive redox properties

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Syntheses, and electrochemical properties of two novel complexes, [Cu(phendio)(L-Phe)(H_2O)](ClO_4)·H_2O (1) and [Ni(phendio)(Gly)(H_2O)](ClO_4)·H_2O (2) (where phendio = 1,10-phenanthroline-5,6-dione, L-Phe = L-phenylalanine, Gly = glycine), are reported. Single-crystal X-ray diffraction results of (1) suggest that this complex structure belongs to the orthorhombic crystal system. The electrochemical properties of free phendio and these complexes in phosphate buffer solutions in a pH range between 2 and 9 have been investigated using cyclic voltammetry. The redox potential of these compounds is strongly dependent on the proton concentration in the range of −0.3–0.4 V vs SCE (saturated calomel reference electrode). Phendiol reacts by the reduction of the quinone species to the semiquinone anion followed by reduction to the fully reduced dianion. At pH lower than 4 and higher than 4, reduction of phendio proceeds via $2e^-/3H^+$ and $2e^-/2H^+$ processes. For complexes (1) and (2), being modulated by the coordinated amino acid, the reduction of the phendio ligand proceeds via $2e^-/2H^+$ and $2e^-/H^+$ processes, respectively. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: 1,10-phenanthroline-5,6-dione; amino acid; nickel(II); copper(II); cyclic voltammetry

INTRODUCTION

Cytochrome *c* oxidase (CcO) is the terminal *trans*-membrane enzyme of the respiratory electron transport chain of aerobic organisms; it converts atmospheric oxygen into water and couples the oxygen reduction reaction to proton pumping across the membrane.[1–4] The pumping of protons results in the creation of an electrochemical proton gradient which subsequently drives ATP synthesis.[5] The proton pumping across the membrane must work against both electric and pH gradients. The reduction of O_2 to $2H_2O$ in the catalytic centre of the enzyme is recognized to provide energy for the process;[1–4] however, the exact mechanism of the coupling between the redox chemistry and the uphill proton translocation is poorly understood. Much has been learned since the structure of the enzyme was solved,[6,7] but the key residues involved in redox-coupled proton activity still remain unidentified. Although there has been much interest in the mechanism of proton pumping in cytochrome c oxidase, there have been few studies on the mechanism of proton pumping using model compounds. Herein we outline a proposal for a simple artificial redox-linked proton pump gate. 1,10-Phenanthroline-5,6-dione (phendio) ligand could be an interesting candidate for modelling proton pumping since its quinone moiety is a redox active species easily reduced to semiquinone and catecholate[8] and exhibiting pH-dependent responses. In this context, we focused on the development of ternary copper(II) and nickel(II) complexes of 1,10-phenanthroline-5,6-dione with amino acids [Cu(phendio)(L-Phe)(H_2O)](ClO_4)·H_2O (**1**) and [Ni(phendio)(Gly)(H_2O)](ClO_4)·H_2O (**2**) and investigated their electrochemical properties. The selection of amino acids as the second ligand in the complexes may increase the biocompatibility of these complexes.

EXPERIMENTAL

Material and measurements

L-Phe was purchased from Aldrich. The other reagents were obtained from Tianjin Guangfu Chemical Reagent Company

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and used without further purification. All the reagents used were analytical reagent grade. CHN analyses were carried out on a Perkin-Elemer analyser at the Institute of Elemento-Organic Chemistry, Nankai University.

Infrared spectra were measured on a Bruker Vector 22 FT-IR instrument in the region of 4000–400 cm^{-1} in KBr pellets.

UV–vis spectra were measured in the range 190–1400 nm using a Jasco V-570 spectrophotometer. Samples were prepared by dissolving the isolated title complexes in dimethyl sulfoxide, the concentrations being adjusted at 4 or 0.06 mM ($1\ M = 1\ mol\ dm^{-3}$) with respect to Cu (II) or Ni(II).

Electrochemistry

Cyclic voltammetry measurements were performed on a BAS Epsilon Electrochemical Workstation. All samples were purged with nitrogen prior to measurements. Sample solutions of 7 ml volume were mixed in 10 ml vials. A standard three-electrode system consisting of glassy carbon working electrode, platinum-wire auxiliary electrode and a saturated calomel reference electrode (SCE) was used. The voltage scan rate during the CV measurements was 100 mV/s. Acidic solutions in a pH range between 2 and 4 were adjusted by mixing 0.1 mol dm^{-3} $HClO_4$ and 0.1 mol dm^{-3} NaH_2PO_4 solutions. The phosphate buffer solutions in a pH range between 4 and 9 were prepared using 0.1 mol dm^{-3} NaH_2PO_4, 0.1 mol dm^{-3} Na_2HPO_4 and 0.1 mol dm^{-3} Na_3PO_4 solutions. The pH measurements were carried out using a WTW-315i pH meter (Wissenchaftlich-Technische Werkstätten Instruments Inc.).

X-ray crystallography

A green single crystal of $[Cu(phendio)(L\text{-}Phe)(H_2O)](ClO_4)\cdot H_2O$ with approximate dimensions of 0.42 × 0.27 × 0.06 mm was mounted on a glass fibre. Determination of the unit cell and data collection were performed using MoKa radiation ($\lambda = 0.71073P$) on a Bruker SMART 1000 diffractometer equipped with a CCD camera. The $\omega - \phi$ scan technique was employed.[9] Crystal parameters and structure refinements for the complex are summarized in Table 1. Selected bond lengths and angles are listed in Table 2. The structure was solved primarily by direct methods and secondly by Fourier difference techniques and refined using the full-matrix least-squares method. The computations were performed with the SHELXL-97 program.[10,11] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were set in calculated positions and refined as riding atoms with a common fixed isotropic thermal parameter.

Table 1. Crystal data and structure refinement for $[Cu(phendio)(L\text{-}Phe)(H_2O)](ClO_4)\cdot H_2O$

Empirical formula	$C_{21}\ H_{20}\ Cl\ Cu\ N_3\ O_{10}$
Formula weight	573.39
T (K)	293(2)
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
a (Å)	7.8114(16)
b (Å)	11.963(2)
c (Å)	25.375(5)
α (deg)	90.000°
β (deg)	90.000°
γ (deg)	90.000°
V ($Å^3$)	2371.2(8)
Z	4
Calculated density (mg m^{-3})	1.606
Absorption coefficient (mm^{-1})	1.096
F(000)	1172
θ range for data collection(deg)	1.88–25.02
Limiting indices	$-9 \le h \le 9$ $-14 \le k \le 12$ $-29 \le l \le 30$
Reflections collected/unique	13 374/4193 ($R_{int} = 0.0375$)
Absorption correction	Semi-empirical from equivalents
Data/restraints/parameters	4193/6/326
Goodness-of-fit on F^2	1.066
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0496$, $wR_2 = 0.1340$
R indices (all data)	$R_1 = 0.0644$, $wR_2 = 0.1440$
Largest difference peak and hole (e.A^{-3})	0.939, −0.622

Table 2. Selected bond lengths (Å) and angles (deg)

Cu(1)–O(2)	1.935(3)	O(2)–Cu(1)–N(1)	83.72(17)
Cu(1)–N(1)	1.980(5)	O(2)–Cu(1)–N(3)	91.71(15)
Cu(1)–N(3)	1.993(4)	N(1)–Cu(1)–N(3)	166.6(2)
Cu(1)–N(2)	2.019(4)	O(2)–Cu(1)–N(2)	168.32(16)
Cu(1)–O(3)	2.207(4)	N(1)–Cu(1)–N(2)	101.28(17)
O(1)–C(9)	1.220(6)	N(3)–Cu(1)–N(2)	81.04(16)
O(2)–C(9)	1.281(6)	O(2)–Cu(1)–O(3)	94.98(16)
O(4)–C(14)	1.210(6)	N(1)–Cu(1)–O(3)	101.24(18)
O(5)–C(15)	1.208(6)	N(3)–Cu(1)–O(3)	91.73(16)
N(1)–C(8)	1.481(6)	N(2)–Cu(1)–O(3)	94.39(16)

General procedure for the synthesis of complexes (1) and (2)

1,10-Phenanthroline-5,6-dione was prepared according to the literature method.[12] $[Cu(phendio)(L\text{-}Phe)(H_2O)](ClO_4)\cdot H_2O$ (**1**), a ternary copper(II) complex, was prepared by mixing a 10 ml methanolic solution of $Cu(ClO_4)_2\cdot 6H_2O$ (185 mg, 0.5 mmol), L-Phenylalanine (82.5 mg, 0.5 mmol) and 0.07 ml (0.5 mmol) triethylamine with heating and stirring under aerobic conditions for 30 min, 1,10-phenanthroline-5,6-dione

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(105 mg, 0.5 mmol) in methanolic solution (10 ml) was added, and then the solution was stirred for about 3 h at room temperature. Green blocky single crystals suitable for X-ray diffraction were obtained on slow evaporation of a methanolic solution of the complex. Yield: 83%. Calculated for $C_{21}H_{20}ClCuN_3O_{10}$ (%): C 44.0; H 3.52; N 7.33. Found (%): C 44.6; H 3.50; N 7.28. IR (KBr, cm^{-1}): 1704s, 1646s, 1580s, 1489m, 1432s, 1390m, 1355w, 1306m, 1087vs, 852w, 754w, 731m, 706w, 624 m cm^{-1} (vs, very strong; s, strong; m, medium; w, weak).

$[Ni(phendio)(Gly)(H_2O)](ClO_4){\cdot}H_2O$ (**2**) was synthesized by the procedure described for (**1**) above except that $Ni(ClO_4)_2{\cdot}6H_2O$ and glycine were used in place of $Cu(ClO_4)_2{\cdot}6H_2O$ and L-Phenylalanine, respectively. The carmine precipitate was filtered off and washed twice with 15 ml methanol and 15 ml water. Yield: 71%. Calculated for $C_{15}H_{16}ClN_3NiO_{10}$ (%): C 36.58; H 3.27; N 8.53. Found (%): C 36.47; H 3.40; N 8.48. IR (KBr, cm^{-1}): 1700s, 1622s, 1577s, 1480m, 1429s, 1384m, 1302m, 1092vs, 816w, 732m, 710w, 625 m cm^{-1} (vs, very strong; s, strong; m, medium; w, weak).

Caution! Perchlorate salts of metal complexes containing organic ligands are potentially explosive. Only small quantity of material should be prepared and handled with suitable safety measures.

RESULTS AND DISCUSSION

The metal complexes were characterized by IR, UV–visible and x-ray structural analyses. The electrochemical properties of free phendio and the title complexes in aqueous solutions at various pH values were investigated.

Spectroscopic studies

The IR spectra of these complexes show asymmetric $\nu_{as}(COO^-)$ and symmetric stretching vibrations $\nu_s(COO^-)$ of 1646 and 1390 cm^{-1},[13] respectively. The difference between $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$ stretching frequencies is greater than 200 cm^{-1}, which indicates that the carboxylate groups are coordinated to the metal ion in a monodenate fashion.[14] A strong band at 1704 cm^{-1}, is assigned to $\nu_s(C=O)$ of the 1,10-phenanthroline-5,6-dione. The very strong bands at 1087 cm^{-1} have been assigned to $\nu(Cl{-}O)$ of perchlorate anions. The electronic absorption spectrum of $[Cu(phendio)(\text{L-Phe})(H_2O)](ClO_4){\cdot}H_2O$ in dimethyl sulfoxide solution presents two absorption bands, in which the intense band at 320 nm ($\varepsilon = 5.25 \times 10^4$ $dm^3\ mol^{-1}\ cm^{-1}$) can be attributed to the $\pi-\pi^*$ transitions of the coordinated phendio ligand, and the broad and weak absorption band at 617 nm ($\varepsilon = 183.5$ $dm^3\ mol^{-1}\ cm^{-1}$) to the d–d transition of the central Cu^{2+} ion. The spectra of the complex $[Ni(phendio)(Gly)(H_2O)](ClO_4){\cdot}H_2O$ exhibits a strong peak at about 305 nm ($\varepsilon = 2.65 \times 10^4$ $dm^3\ mol^{-1}\ cm^{-1}$), which is assignable to $\pi-\pi^*$ transitions in the phendio chromophore and a broad band near 730 nm ($\varepsilon = 222$ $dm^3\ mol^{-1}\ cm^{-1}$) to a d–d transition of Ni(II).

X-ray structural characterization

The perspective view of $[Cu(phendio)(\text{L-Phe})(H_2O)](ClO_4){\cdot}H_2O$ is shown in Fig. 1. The key bond lengths and angles are summarized in Table 2. In the complex, the copper(II) ion is coordinated in a distorted square pyramidal geometry through the carboxylate oxygen O(2) and the amino nitrogen N(1) atoms of L-Phenylalanine and two N atoms of the 1,10-phenanthroline-5,6-dione in the basal plane and a water molecule in the apical position. The four equatorial donor atoms are nearly coplanar, while the copper atom lies above the plane by 0.1978 Å toward the axial oxygen. Bond angles around copper in the square plane are influenced by the bite of the ligands, so that the values 81.04(16)° for N(3)–Cu(1)–N(2) and 83.72(17)° for O(2)–Cu(1)–N(1) are 'compressed', while those for O(2)–Cu(1)–N(3) and N(1)–Cu(1)–N(2) are 91.71(15) and 101.28(17)°, respectively. The values of copper–oxygen and copper–nitrogen bonds are in agreement with those in the literature for similar geometries.[14] As is usual, the copper–O(3) distance of 2.207(4) Å is significantly longer than those in the square base; the angles involving O(3) are in the range 91.73(16)–101.24(18), showing some distortion. Bond distances and angles in the L-Phe ligand are as expected and similar to those in previously reported structures.[15]

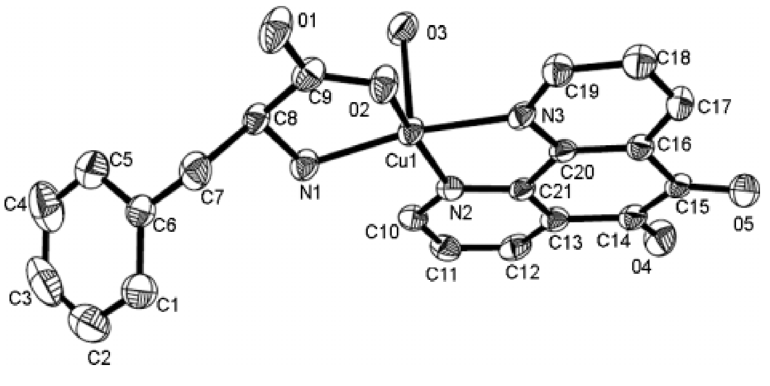

Figure 1. ORTEP diagram of the complex $[Cu(phendio)(\text{L-Phe})(H_2O)](ClO_4){\cdot}H_2O$.

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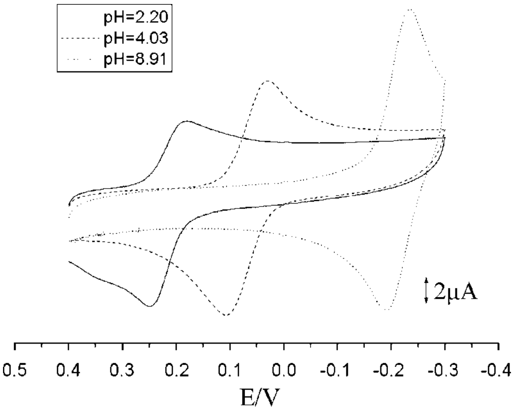


Figure 2. Cyclic voltammograms of phendio in 0.1 mol dm^{-3} phosphate buffer solutions at several pH values.

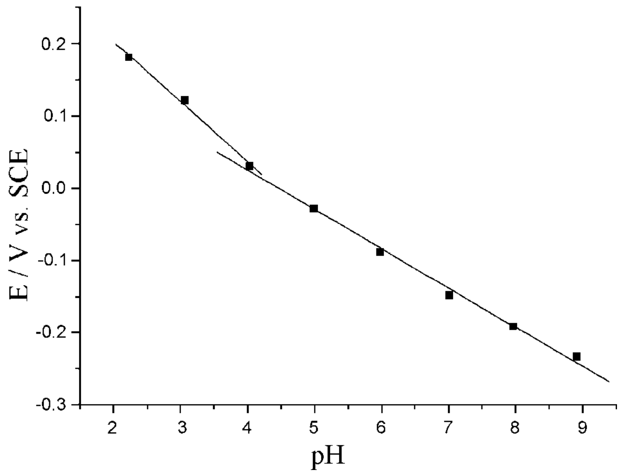
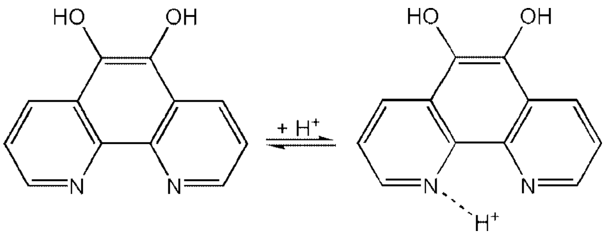


Figure 3. Plots of E_c (vs SCE) vs pH for the reduction of phendio.

Cyclic voltammetric studies

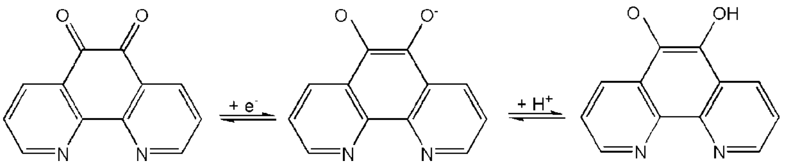
In order to facilitate the electrochemical assignment of the metal–phendio complexes, the electrochemistry of the free phendio will be briefly discussed. It should be mentioned that the cyclic voltammogram for the free ligand was obtained under the same conditions as that employed in the study of its complexes. Figure 2 shows the cyclic voltammogram of phendio in different pH phosphate buffer solutions. The voltammograms exhibit a couple of redox peaks, but the peak potential is shifted to the more negative values as pH increases, and studies at $\text{pH} > 9$ are made difficult by the base-catalysed decomposition of phendio, which produces 4,5-diazafluorenone. The broad anodic and cathodic wave at low pH value are interpreted as the overlapping of the two closely successive (quinone/semiquinone) and (semiquinone/catecholate) redox couples [equations (1) and (2)].[8] This assumption, supported by their peak potentials, was irrespective of the scan rates. It should be noticed that the ΔE_p of ~42 mV was obtained at a high pH value, which is attributed to reduction of the quinone species to the semiquinone anion followed by reduction to the fully reduced dianion at the same potential.[16]

Figure 3 shows the plot of E_c values of free phendio against pH. There is a breakpoint at ca. pH 4, and the slopes of the plot below pH 4 and above pH 4 were determined graphically as ca. −83 and −54 mV/pH, respectively. The slopes in the plot indicate that the reduction of the phendio occurs via $2e^-/3H^+$ and $2e^-/2H^+$ processes.[17] In accordance with this, quinone molecules undergo two one-electron reductions in H_2O to give catecholate analogues and simultaneously combine one or two protons [equations (1) and (2)]. In the range of pH 2–4, the pyridine nitrogen site of phendio was protonated [equation (3)].[18]

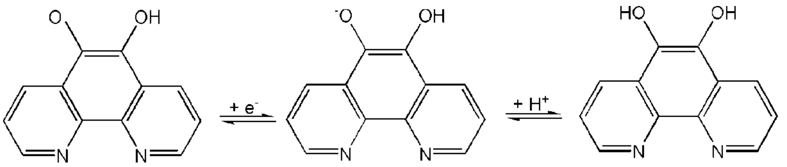


(3)

The electrochemical properties of [Cu(phendio)(L-Phe)(H_2O)](ClO_4) · H_2O (**1**) and [Ni(phendio)(Gly)(H_2O)](ClO_4)



(1)



(2)

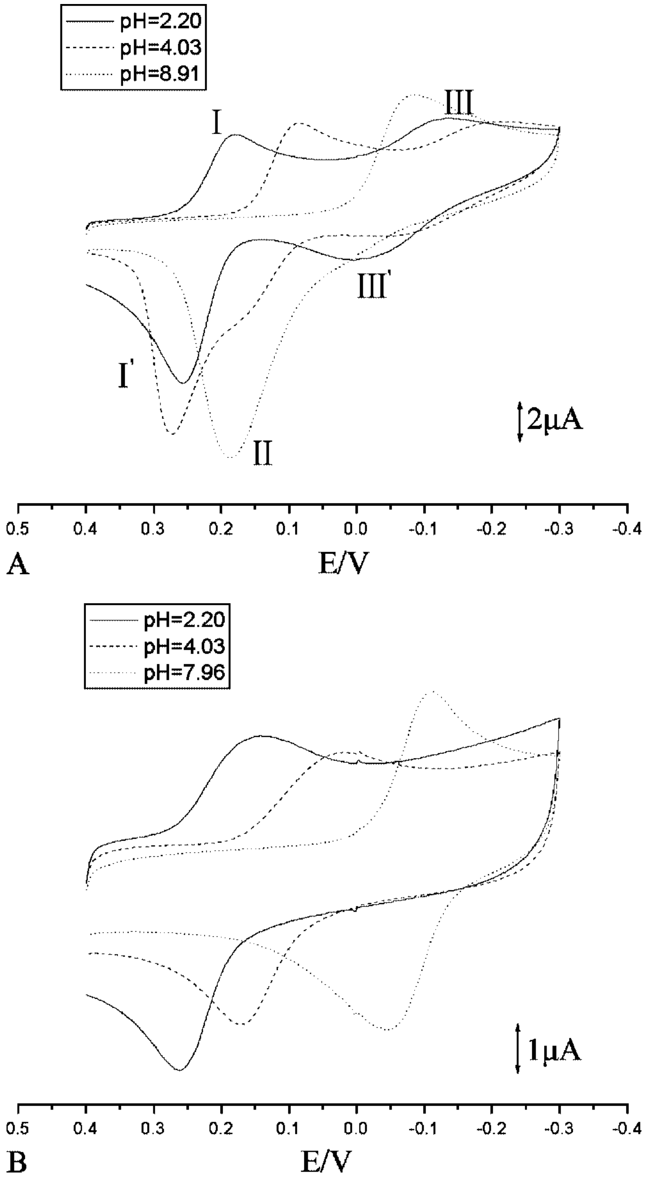


Figure 4. Cyclic voltammograms of (A) ([Cu(phendio)(L-Phe)$(H_2O)](ClO_4)\cdot H_2O$ and (B) [Ni(phendio)(Gly)$(H_2O)](ClO_4)\cdot H_2O$ in 0.1 mol dm^{-3} phosphate buffer solutions at several pH values.

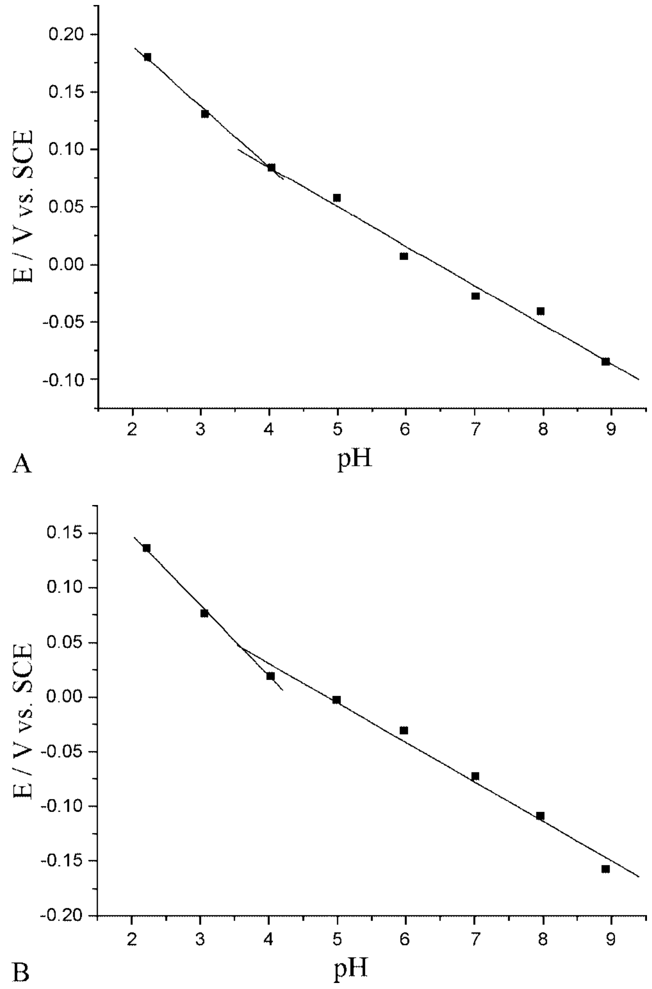


Figure 5. Plots of E_c (vs SCE) vs pH for the reduction of (A) ([Cu(phendio)(L-Phe)$(H_2O)](ClO_4)\cdot H_2O$ and (B) [Ni(phendio)(Gly)$(H_2O)](ClO_4)\cdot H_2O$.

$\cdot H_2O$ (**2**) at a glassy carbon electrode were investigated using cyclic voltammetry in aqueous solutions having pH values between 2 and 9. As shown in Fig. 4(A), the cyclic voltammogram of (**1**) at pH 2.2 exhibits a pair of waves with $E_a = 0$ V (III′) and $E_c = -0.13$ V (III) vs SCE; $\Delta E_p = 130$ mV (where E_a and E_c are the anodic and cathodic peak potentials, and ΔE_p is the potential separation between the peaks), attributed to redox processes centred on the metal (Cu^{II}/Cu^{I}). An increase in pH promotes the disappearance of this pair of waves. Analogous to the phendio system, a pair of waves with $E_a = 0.25$ V (I′) and $E_c = 0.18$ V (I), $\Delta E_p = 70$ mV can be assigned to the two one-electron redox of coordinated phendio. The electrochemical response is sensitive to the pH, and the waves shift to more negative potentials as the pH is increased. If the pH is raised to 7.01, cathodic peak **I** moves to -0.03 V and becomes irreversible. In addition, an anodic wave appears at 0.2 V (II), which can be assigned to the metal-centred oxidation. In acidic medium, there is an overlap of anodic peaks of $Cu^{II/III}$ and phendio ligand. The cyclic voltammograms of [Ni(phendio)(Gly)$(H_2O)](ClO_4)\cdot H_2O$ (**2**) [see Fig. 4(B)] show only one redox couple assigned to the ligand-centred reduction/oxidation processes and an increase of pH is associated with a decrease in the wave couple potentials.

There is one breakpoint at ca. pH 4 in the plot of E_c of the ligand-centred redox potentials of **1** against pH [Fig. 5(A)]. The slopes of the plot of E_c of [Cu(phendio)(L-Phe)$(H_2O)](ClO_4)\cdot H_2O$ at pH lower than 4 and higher than pH 4 were roughly -52 and -34 mV/pH, respectively, which indicate that the reduction of the phendio ligand proceeded via the $2e^-/2H^+$ and $2e^-/H^+$ processes. The electrochemical behaviour of [Ni(phendio)(Gly)$(H_2O)](ClO_4)\cdot H_2O$ (**2**) [see

Fig. 5(B)] is similar to that of complex **1**. By comparing the slopes of complexes **1** and **2** with those of phendio, the distinct behaviour of the complexes vs the free ligand is apparent. The most plausible explanation for this obvious difference concerns the influence of the coordinated amino acid in that the amido group can combine protons. In accordance with this, the proton dissociation constants for the NH_2 group of glycine and phenylalanine ($pK_{b,Gly} = 9.58$, $pK_{b,Phe} = 9.09$)[19] are larger than that of coordinated phendiol (6,6, phendiol = 1,10-phenanthroline-5,6-diol).[20] In addition, the number of protons integrated with coordinated phendio is dependent on pH.

CONCLUSION

Two novel proton pump model complexes, $[Cu(phendio)(L\text{-}Phe)(H_2O)](ClO_4)\cdot H_2O$ (**1**) and $[Ni(phendio)(Gly)(H_2O)](ClO_4)\cdot H_2O$ (**2**), have been synthesized and characterized. The crystal structure of $[Cu(phendio)(L\text{-}Phe)(H_2O)](ClO_4)\cdot H_2O$ shows that the copper(II) ion is coordinated in a distorted square pyramidal geometry. The electrochemical properties of these complexes are pH-dependent and the reduction of coordinated phendio proceeded via the $2e^-/2H^+$($pH < 4$) and $2e^-/H^+$($pH > 4$) processes, being modulated by the amino acid ligands through combining protons on the NH_2 groups. This behaviour could be an advantage for research into the mechanism of proton pumps.

Acknowledgements

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