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Preparation and Spectral, Magnetic, and Electrochemical Characterization of a Flexible Phenoxo-Bridged Binuclear Copper(II) Complex

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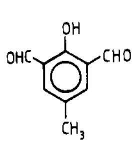
The preparation of a pentadentate binucleating ligand, 2,6-bis((salicylideneamino)methyl)-4-methylphenol, is described together with the corresponding pyrazolate-bridged copper(II) complex, Cu_2L. Spectroscopic evidence suggests square-planar coordination of the copper ions, and the magnetic data when fitted to the Bleaney–Bowers equation give an exchange coupling ($2J$) of -457 ± 5 cm^{-1}. The complex has unusual stereochemical flexibility, which enables reactions coupled with reduction to be considered in some detail. The electrochemical reduction of the complex Cu_2L has been examined at mercury and platinum electrodes. Two overall one-electron-reduction steps are observed, which appear to be $Cu_2L + e^- \rightleftharpoons [Cu_2L]^-$ and $[Cu_2L]^- + e^- \rightleftharpoons [Cu_2L]^{2-}$. However, there are considerable differences in the electrochemical behavior of the compound at the two electrodes and the temperature dependence is not consistent with the commonly employed one-electron reversible or quasi-reversible theoretical models. Rather, a more complex reaction scheme in which a structural change accompanies the charge transfer in addition to the reaction $[Cu_2L]^{2-} + Cu_2L \rightleftharpoons 2[Cu_2L]^-$ is needed to provide a rational explanation of the data. The stereochemical and/or magnetic changes accompanying electron transfer may have relevance to electron transfer in molecules of biological importance.

Introduction

Binuclear complexes containing copper(II) centers have been the subject of continuing intensive investigation because of their relevance as structural models for the active sites in the dioxygen-binding protein hemocyanin and various multicopper oxidases.[2] EXAFS studies[3] have indicated that each copper ion in oxyhemocyanin is coordinated to two histidine nitrogen atoms. Although the identity of the endogenous group in this protein has not been unambiguously determined, it is generally considered to be an –OR bridge provided by a hydroxide,[4] tyrosinyl,[5,6] seryl, or threonyl ligand.[7,8] A number of model compounds have been reported that are based on a phenoxide endogenous bridge.[9–22] The pentadentate binucleating ligands pioneered by Robson,[9–17] and later reported by Kida and Okawa,[18–22] are derived from 2-hydroxy-5-methylisophthalaldehyde (1) and are capable of bridging two copper atoms in the presence of an exogenous ligand (X), e.g. 2.



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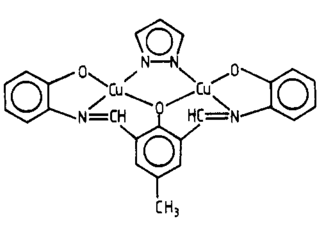

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In a more recent development the binuclear copper(II) complex 3 has been reported,[23a] which contains a heptadentate binucleating ligand derived from 2,6-bis(chloromethyl)-*p*-cresol and bis[2-(1-pyrazolyl)ethyl]amine. A closely related complex has been prepared that has an exogenous peroxide bridge.[23b,c] The isolation of such compounds gives strong support to the use of these ligand systems as models for hemocyanin.

In conjunction with our investigations on binuclear copper(II) complexes based on 1,3-diaminopropan-2-ol and 1,5-diaminopentan-3-ol[8,24] (4), an aromatic analogue, 2,6-bis(aminomethyl)-4-methylphenol dihydrochloride (5), was prepared. The pentadentate Schiff base ligand forms the complex 6, related to 2 but with an increase in stereochemical flexibility in the inner chelate rings due to the presence of the methylene linkage.

Importantly, the presence of the aromatic ring confers a degree of rigidity around the endogenous bridging site not encountered in the aliphatic analogues 4. This paper describes the synthesis of the ligand backbone (5) together with the synthesis and characterization of 6, including the magnetic and electrochemical properties to ascertain the importance of the introduction of stereochemical flexibility.

The detailed electrochemical behavior of the binuclear copper(II) species is of particular interest in view of the redox properties of the binuclear copper protein type 3 centers. The strongly antiferromagnetically coupled copper pairs in the type 3 centers frequently appear to undergo two cooperative one-electron transfers at the same potential. However, as shown in the case of *Rhus vernicifera* laccase, half-reduction of the type

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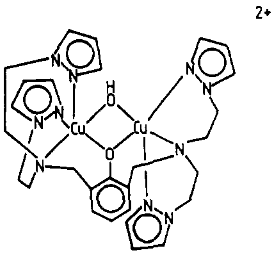

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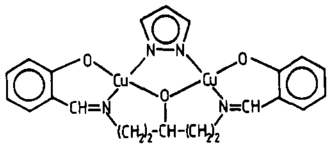

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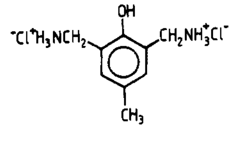

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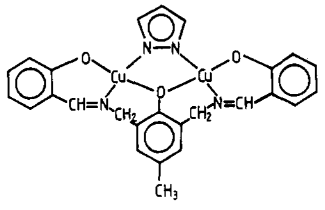
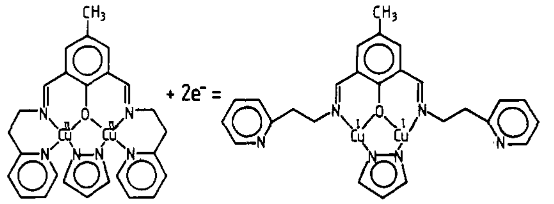


6

3 copper pair can occur in the absence of a type 2 copper or in the presence of the reduced state of the type 2 copper.[25]

A range of redox behavior related to that of the proteins has been noted in electrochemical studies of binuclear copper complexes.[26-35] In some situations structural changes can take place, at the coordinated copper centers, during the two-electron redox processes as illustrated[30] by the proposed reaction



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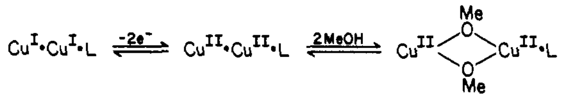
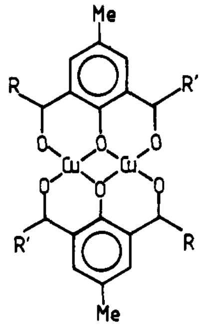
The nearly diamagnetic triketonate binuclear copper(II) complexes have been shown to exhibit two reversible one-electron transfers at the same potential.[36-38]

Similarly, a macrocyclic binuclear copper(II) complex with no apparent magnetic interactions between the two copper ions was shown to have two electrochemically reversible, one-electron charge-transfer steps at nearly identical potentials.[39] The oxidation of a binuclear copper(I) complex has also shown two one-electron charge-transfer steps but accompanied by a chemical reaction, either subsequent to each step (ECEC mechanism) or subsequent to the net two-electron transfer (EEC mechanism). Both charge-transfer processes appear to occur at the same potential, and the reaction for the EEC case is postulated to occur as follows:[40]



$$\mathrm{Cu^{I}{\cdot}Cu^{I}{\cdot}L} \underset{}{\overset{-2e^-}{\rightleftharpoons}} \mathrm{Cu^{II}{\cdot}Cu^{II}{\cdot}L} \overset{2\,\mathrm{MeOH}}{\rightleftharpoons} \mathrm{Cu^{II}(\mu\text{-}OMe)_2Cu^{II}{\cdot}L}$$

A series of closely related phenoxide-bridged binuclear copper(II) complexes (**9**) has also shown two apparently sequential one-electron charge-transfer reactions at the same potential.[32]



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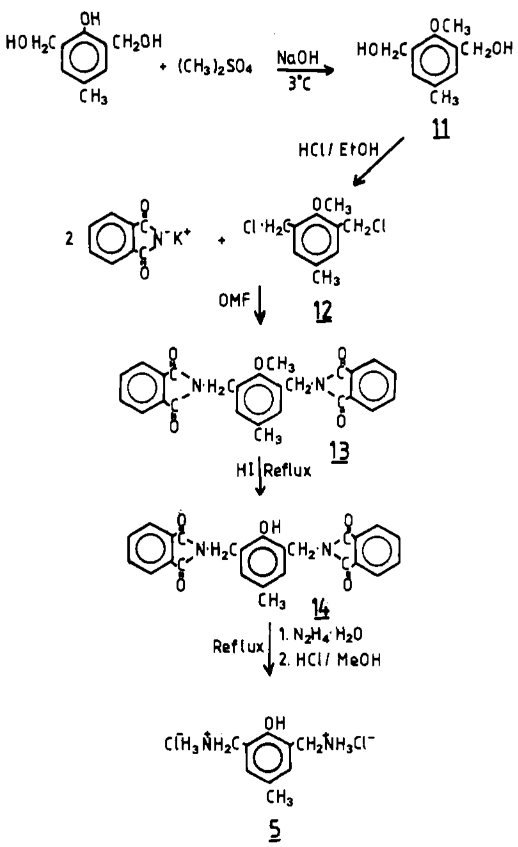
The electrode reaction was found to be dependent on the nature of the R group, varying from the simple Nernstian behavior to an EC type reaction.

A second group of binuclear copper(II) complexes shows two readily discernible one-electron charge-transfer processes. In general, the two processes follow different mechanisms with the

Scheme I



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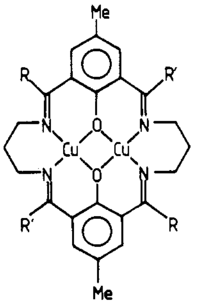
first step having a greater probability of being electrochemically reversible than the second. The phenoxide-bridged macrocyclic complexes **10**, examined by Gagne,[27,29] Nag,[33] and Hendrickson,[34] are examples of this class and exhibit two one-electron charge-transfer steps with a separation of ca. 0.35–0.8 V. The behavior of the first couple $Cu^{II}Cu^{II}L + e^- \rightarrow Cu^{II}Cu^{I}L$ was found to be near-Nernstian, while Nag reported that the second couple appeared to involve adsorption at the hanging-mercury-drop electrode.[33] Like compounds **3**, **4**, and **7**, complex **6**, which is of interest in this work, also has the advantage of accommodating an exogenous bridge, thereby more closely resembling the type 3 met forms. The electrochemistry may therefore be expected to show some similarity to this class of binuclear complex. However, the stereochemical flexibility inherent in **6** may be expected to produce rather different redox and other behavior. In particular, kinetic steps accompanying electron transfer may be relatively rapid and more apparent than is the case with other complexes previously examined. This aspect is of considerable interest in the present work.



10

Experimental Section

Preparation of Compounds. Synthesis of 2,6-Bis(aminomethyl)-4-methylphenol Dihydrochloride (5). The sequence of steps for the preparation of **5** from 2,6-bis(hydroxymethyl)-4-methylphenol[41] is shown in Scheme I.

2,6-Bis(hydroxymethyl)-4-methylanisole (11). 2,6-Bis(hydroxymethyl)-4-methylphenol (20 g, 0.12 mol) was dissolved in 2.5% aqueous sodium hydroxide solution (200 cm^3, 0.125 mol) and cooled to 3 °C. Dimethyl sulfate (12 cm^3, 0.127 mol) was added slowly to the stirred solution over 0.3 h. When the addition was complete, the reaction mixture was maintained at 3 °C for a further 0.75 h and then it was allowed to warm slowly to ambient temperature. The thick white precipitate that formed was allowed to stand overnight before the mixture was extracted with warm chloroform (3 × 100 cm^3). The combined extracts were dried over anhydrous magnesium sulfate, and after filtration the filtrate was evaporated to dryness on a rotary evaporator: yield 15.3 g (70%); mp 103–104.5 °C after recrystallization from petroleum ether (90–110 °C). ^{1}H NMR: δ 2.3 (s, CH_3); 3.8 (s, OCH_3); 4.7 (s, CH_2); 7.1 (s, phenyl).

2,6-Bis(chloromethyl)-4-methylanisole (12). Compound **11** (20 g, 0.11 mol) was dissolved in ethanol and heated at 50–60 °C while dry hydrogen chloride gas was bubbled through the solution until uptake of the gas was complete. The solution was evaporated on a rotary evaporator to give a white solid, yield 24.1 g (100%). The product may be recrystallized from ethanol or petroleum ether; mp 58 °C. ^{1}H NMR: δ 2.3 (s, CH_3); 3.9 (s, OCH_3); 4.7 (s, CH_2); 7.1 (s, phenyl).

2,6-Bis(phthalimidomethyl)-4-methylanisole (13). Compound **12** (12.1 g, 0.055 mol) was added in small portions to a stirred suspension of potassium phthalimide (22.5 g, 0.121 mol) in dimethylformamide (200 cm^3). The mixture was stirred for 2 days at approximately 50 °C. A 500-mL amount of chloroform was then added after cooling, and the mixture was washed with 4% aqueous sodium hydroxide (200 cm^3) and then water. The organic layer after being dried over anhydrous magnesium sulfate was filtered and evaporated to dryness on a rotary evaporator; yield 19 g (78%). ^{1}H NMR: δ 2.2 (s, CH_3); 4.0 (s, OCH_3); 4.9 (s, CH_2); 6.9 (s, phenyl); 7.8 (m, phthaloyl).

2,6-Bis(phthalimidomethyl)-4-methylphenol (14). Hydriodic acid (80 cm^3) freshly distilled from red phosphorus was stirred while compound **13** (19 g, 0.043 mol) was added. The stirred mixture was heated at reflux for 4.5 h, cooled to room temperature, and then extracted with chloroform (3 × 100 cm^3). The combined extracts were washed with water (2 × 100 cm^3) and sodium thiosulfate solution until the iodine coloration disappeared. The chloroform solution, having been dried over anhydrous magnesium sulfate, was filtered, and the filtrate was evaporated to dryness in a rotary evaporator and finally dried under vacuum (0.01 mmHg); yield 16.3 g (89%). ^{1}H NMR: δ 2.2 (s, CH_3); 4.8 (s, CH_2); 7.0 (s, phenyl); 7.8 (m, phthaloyl).

2,6-Bis(aminomethyl)-4-methylphenol Dihydrochloride (5). A mixture containing methanol (200 cm^3), compound **14** (16.3 g, 0.038 mol), and hydrazine hydrate (4.2 g, 0.084 mol) was refluxed for 2.5 h, after which water (100 cm^3) was added and the methanol was removed on a rotary evaporator. After the addition of hydrochloric acid (100 cm^3) the mixture was refluxed for 2 h, cooled in ice, and filtered. The residue was washed with water. The filtrate and washings were combined and evaporated to dryness on a rotary evaporator. The residue was dissolved in ethanol (150 cm^3), and the addition of diethyl ether (150 cm^3) precipitated a white solid, which was washed with ethanol/ether and dried in vacuo; yield 6.5 g of monohydrate (67%). Anal. Calcd for $C_9H_{18}Cl_2N_2O_2$: C, 42.04; H, 7.05; N, 10.89; O, 12.44; Cl, 27.57. Found: C, 41.97; H, 6.97; N, 11.05; O, 12.24; Cl, 27.68. ^{1}H NMR (in D_2O): δ 2.3 (s, CH_3); 4.2 (s, CH_2); 7.2 (s, phenyl).

Preparation of 2,6-Bis((salicylideneamino)methyl)-4-methylphenol. Potassium hydroxide (0.34 g, 0.006 mol) in methanol (10 cm^3) was added to **5** (0.72 g, 0.003 mol) in methanol (20 cm^3). After 0.15 h the mixture was filtered into salicylaldehyde (0.73 g, 0.006 mol) in methanol (40 cm^3). The yellow precipitate that formed was filtered after 0.5 h, washed with methanol, and dried in vacuo: yield 0.75 g (69%); mp 192.5–193 °C after recrystallization from chloroform. Anal. Calcd for $C_{23}H_{23.5}N_2O_{3.75}$: C, 71.21; H, 6.11; N, 7.22; O, 15.47. Found: C, 71.02; H, 5.90; N, 7.18; O, 15.4.

Preparation of Compound 6. To 2,6-bis((salicylideneamino)-methyl)-4-methylphenol (1.6 g, 0.0041 mol) suspended in methanol was added potassium hydroxide (0.96 g, 0.017 mol) in methanol (15 cm^3) to give a clear yellow solution. Pyrazole (0.4 g, 0.006 mol) in methanol (15 cm^3) was added to the above solution, and then the mixture was added slowly to a stirred solution of copper(II) perchlorate hexahydrate (3.17 g, 0.0086 mol) in methanol (20 cm^3) to give a green precipitate. The mixture was allowed to stand for 1 h, and then it was heated at 60 °C for 0.5 h and reduced in volume to 20 cm^3. The mixture was extracted with chloroform (200 cm^3), and the extract was washed with water (40 cm^3). The chloroform layer was separated, dried over anhydrous magnesium sulfate, reduced in volume to 150 cm^3, and then allowed to stand in an open beaker at room temperature for 48 h. The resulting green precipitate was collected by filtration, washed with chloroform, and air-dried; yield 0.3 g. After the addition of acetonitrile (20 cm^3) to the warmed filtrate, the solution was allowed to evaporate overnight to yield a further 0.19 g of product. These isolations and subsequent similar treatment of the filtrate gave a total yield of 0.62 g. The compound was recrystallized from chloroform/acetonitrile. Anal. Calcd for $C_{26}H_{22}N_4O_3Cu_2$: C, 55.22; H, 3.92; N, 9.91; Cu, 22.47. Found: C, 55.11; H, 3.98; N, 10.05; Cu, 23.15.

Measurements. Microanalyses were performed by Bernhardt Analytical Laboratories, Elbach, West Germany. Copper content was determined on a Varian Model AA275 atomic absorption spectrophotometer. Infrared spectra were recorded on a Perkin-Elmer Model 457 spectrometer as KBr disks. ^{1}H NMR spectra of $CDCl_3$ solutions were recorded on a Perkin-Elmer Model R32 (90-MHz) spectrometer. Chemical shifts are in ppm relative to internal Me_4Si. Electronic spectra were measured with a Cary Model 17 spectrophotometer. The magnetic susceptibility measurements were determined at 26 points over the temperature range 4.2–300 K with a Faraday balance.

Electrochemical measurements were carried out with a PAR Model 170 electrochemical system with a three-electrode configuration. Solutions were 2×10^{-3} M with 0.1 M tetraethylammonium perchlorate (supporting electrolyte) in dimethylformamide (10 cm^3). Positive-feedback circuitry was used to minimize *iR* drop. The solvent was purified (from BDH AnalaR grade dimethylformamide) by drying over molecular sieves (3A) for 48 h. It was then decanted, allowed to stand over barium oxide (24 h), decanted, and twice distilled in vacuo at 60 °C in the absence of light. The distillate was stored under oxygen-free nitrogen at 4 °C. All subsequent manipulations were done under dried argon.

Results and Discussion

Synthesis and Magnetic Properties. The building unit for the pentadentate binucleating ligand described in this paper is 2,6-bis(aminomethyl)-4-methylphenol dihydrochloride (**5**). An effective synthesis of this compound is illustrated in Scheme I. Each step in the synthesis gives a high yield, and **5** can be obtained in pure form. The Schiff base ligand formed by the reaction of **5**

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Table I. Dc Polarographic Reduction of Compound **6**[a]

drop time, s	$E_{1/2}(1)$, V (vs. SCE)	$E_{3/4}(1) - E_{1/4}(1)$, mV	slope (1),[b] mV	$i_d(1)$, μA	$E_{1/2}(2)$, V (vs. SCE)	$E_{3/4}(2) - E_{1/4}(2)$, mV	slope (2),[b] mV	$i_d(2)$, μA
0.5	−0.783	53	59	5.8	−1.046	53	59	5.6
1.0	−0.783	57	62	6.8	−1.046	53	57	6.8
2.0	−0.790	57	65	8.2	−1.018	47	51	7.5

[a] Conditions: supporting electrolyte 0.1 M Et_4NClO_4 in DMF; 21 ± 2 °C. [b] Reciprocal slope of plot of $i/(i_d - i)$ vs. E.

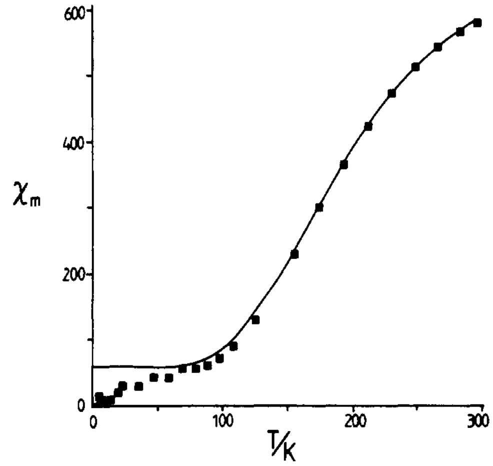

Figure 1. Temperature-dependent magnetic susceptibility (per Cu) of compound **6**. The solid line is that calculated from the parameters given in the text.

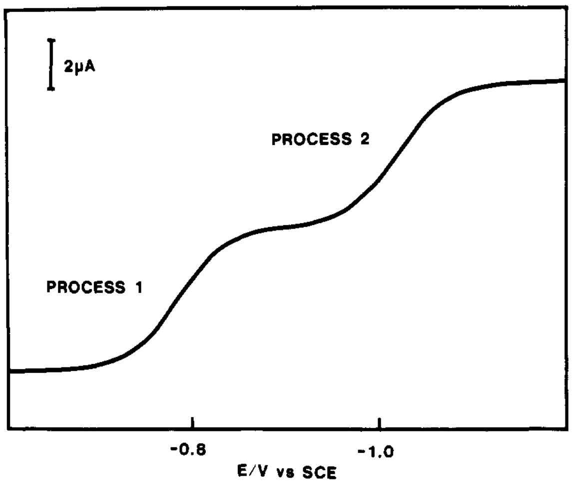

Figure 2. Dc polarogram for reduction of 2 × 10^{-3} M **6** in DMF (0.1 M Et_4NClO_4) at 20 °C (drop time 0.5 s).

with salicylaldehyde gives a pentadentate ligand that is able to coordinate two copper(II) ions in the binucleated species (**6**). The pyrazolato anion is introduced as an exogenous bridging unit, and chemical analysis, together with the properties of the complex, indicates that the binucleated species has an endogenous phenoxo bridging oxygen.

The infrared spectrum of **6** shows an absorption band at 1632 cm^{-1} compared with 1640 cm^{-1} for the free ligand and is assigned to $\nu(C{=}N)$. The electronic spectrum contains an absorption maximum in the solid state at 560 nm with a shoulder at 605 nm, while in chloroform solution an absorption maximum occurs (ϵ = 603) at 612 nm which is consistent with square-planar coordination of the copper(II) centers.[8,13,42]

The magnetic susceptibility of the complex between 4.2 and 300 K (Figure 1) is compatible with a strongly antiferromagnetically coupled Cu^{2+}–Cu^{2+} pair with the molar susceptibility, χ (per molecule), at 300 K being only ca. 600 × 10^{-6} cm^3 mol^{-1} and decreasing to almost zero at ca. 100 K. The small values observed in the low-temperature region lead to some scatter in the data. It is notable that there is no evidence of any paramagnetic impurity, which often occurs in such systems.[8]

Except for small deviations at low temperatures the data can be fitted to the spin Hamiltonian $-2JS_1 \cdot S_2$. The best-fit parameters to the Bleaney–Bowers equation[43] are $g = 2.20 \pm 0.02$, $2J = -457 \pm 5$ cm^{-1}, and $N\alpha = 60 \times 10^{-6}$ cm^3 mol^{-1} per Cu. The $2J$ value for exchange between the two copper(II) ions may be compared to the value found for the compound **2** ($2J = -460$ cm^{-1}, $g = 2.1$, $N\alpha = 90 \times 10^{-5}$ cm^3 mol^{-1} per Cu).[17] It appears that structural changes in the endogenous bridging units in **2** and the present compound **6**, which has a somewhat more flexible backbone, have made a negligible difference to the overall magnetic interactions of the copper(II) ions. On the other hand, a much stronger interaction occurs in **4**, which is found to be diamagnetic.[24] We have recently discussed in some detail the magnetic–structural correlations in complexes of the present kind.[8,24]

Electrochemistry. (a) Dc Polarography. The dc polarogram of compound **6** (in DMF at 21 °C with 0.1 M Et_4NClO_4 as the supporting electrolyte) consists of two well-separated reduction waves (Figure 2). Comparison with the limiting current per unit concentration for the known one-electron diffusion-controlled reduction $Na^+ + e^- \rightleftharpoons Na(Hg)$ suggests that each reduction involves a one-electron transfer.

With use of a drop time of 0.5 s, for the first reduction process $E_{1/2}(1)$ was found to be −0.783 V while for the second process $E_{1/2}(2) = -1.046$ V. When the drop time is increased to 2.0 s, $E_{1/2}(1) = -0.790$ V and $E_{1/2}(2) = -1.018$ V. In general, as the drop time becomes longer, $E_{1/2}(1)$ becomes slightly more negative while $E_{1/2}(2)$ becomes significantly more positive. At a drop time of 0.5 s, the slope of the plot of E vs. log $[i/(i_d - i)]$ (E = potential, i = current, i_d = diffusion-controlled limiting current), for both processes, is 59 ± 2 mV whereas at the longer drop time of 2 s the slope for the first wave increases to 65 ± 2 mV while that of the second process decreases to 51 ± 2 mV. DC polarographic data are summarized in Table I.

All the data imply that both processes are close to reversible, but some departure from the single uncomplicated charge-transfer steps

$$Cu_2L + e^- \xrightleftharpoons{E_{1/2}(1),\ k_s(1)} Cu_2L^- \qquad (1)$$

$$Cu_2L^- + e^- \xrightleftharpoons{E_{1/2}(2),\ k_s(2)} Cu_2L^{2-} \qquad (2)$$

is evident. $k_s(n)$ is the heterogeneous charge-transfer rate constant for process n, and the charge-transfer coefficient α has been omitted here and elsewhere for clarity of presentation.

In other work these processes have been generally treated as simple electron-transfer steps.[27,34,35] Clearly the present data cannot be fitted exactly to this model at least under polarographic conditions. This was also indicated by other techniques that were also used to examine the reduction processes.

(b) Cyclic Voltammetry at a Hanging-Mercury-Drop Electrode. Cyclic voltammetry of compound **6**, at a hanging-mercury-drop electrode (HMDE) at 21 °C, again shows two very well-defined reduction processes (Figure 3). Data at various scan rates and temperatures are summarized in Table II.

Some unusual features emerge from these data. The ratio of the reduction current (i_p^{red}) for the forward scan to the oxidation current for the reverse scan (i_p^{ox}) is close to unity for both reduction steps, as expected for a chemically reversible process. For process 1 at both +20 and −23 °C, $\Delta E_p(1)$ is close to the theoretically

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Table II. Cyclic Voltammetry Data for the Reduction of 2×10^{-3} M **6** at the HMDE[a]

scan rate, mV s^{-1}	E_p^{red}, V (vs. SCE)	E_p^{ox}, V (vs. SCE)	ΔE_p, mV	i_p^{red}/i_p^{ox}	i_p^{red}, μA	$i_p^{red}v^{-1/2}$, μA $mV^{-1/2}$ $s^{-1/2}$
			Process 1, 20 °C			
200	−0.830	−0.752	78	1.1[b]	9.5	0.67
100	−0.825	−0.760	65	1.2[b]	6.0	0.60
50	−0.823	−0.757	66	1.0[b]	4.6	0.65
20	−0.823	−0.760	63	0.9[b]	3.0	0.67
10[c]	−0.823	−0.757	66	0.9[b]	2.3	0.73
			Process 2, 20 °C			
500	−1.095	−0.982	113	1.01	13.5	0.60
200	−1.080	−0.978	102	1.20	9.0	0.64
100	−1.087	−0.973	114	1.26	6.0	0.60
50	−1.077	−0.978	99	1.10	4.6	0.65
20	−1.068	−0.990	78	1.06	3.0	0.67
10[c]	−1.063	−0.990	73	1.01	2.3	0.73
			Process 1, −23 °C			
500	−0.863	−0.778	75	1.08[b]		
100	−0.847	−0.775	72	1.05[b]	6.4	0.64
50	−0.842	−0.779	63	1.08[b]	4.3	0.61
20	−0.840	−0.782	58	1.08[b]	2.8	0.63
10	−0.839	−0.787	52	1.03[b]	2.0	0.63
			Process 2, −23 °C			
500	−1.130	−0.960	170	1.14	11.0	0.49
200	−1.087	−0.972	115	1.18	7.3	0.52
100	−1.070	−0.975	95	1.19	5.2	0.52
50	−1.054	−0.978	76	1.17	4.0	0.57
20	−1.050	−0.985	65	1.16	2.6	0.58
10	−1.050	−0.993	57	0.98	2.0	0.63

[a] Supporting electrolyte 0.1 M Et_4NClO_4 in DMF. [b] Estimated from peak heights to an extrapolated base line; in all other cases the Nicholson equation[56] was used. [c] Data obtained at this scan rate are subject to depletion effects.

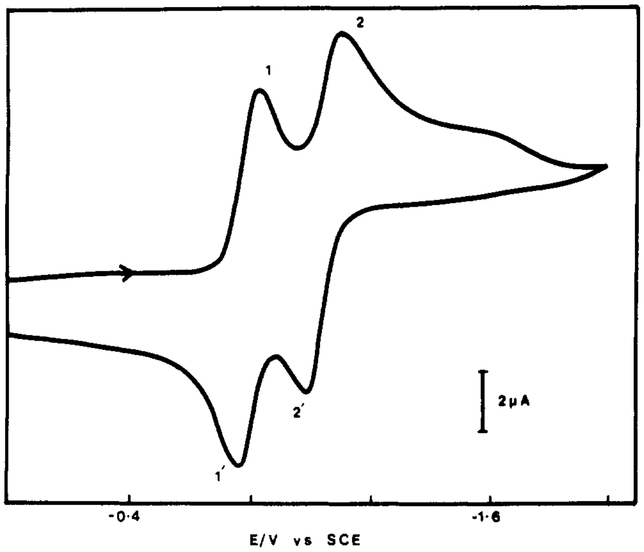

Figure 3. Cyclic voltammetric reduction of 2×10^{-3} M compound **6** in DMF (0.1 M Et_4NClO_4) at the hanging-mercury-drop electrode at 20 °C (scan rate 100 mV s^{-1}).

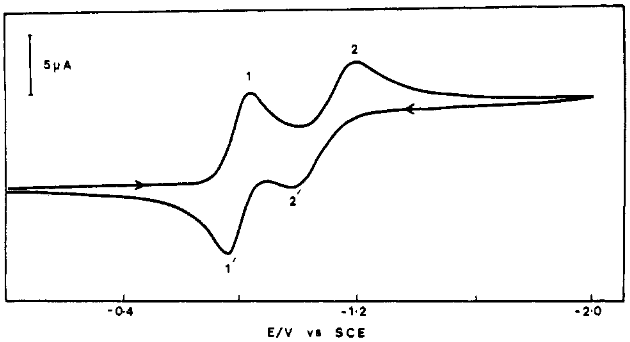

Figure 4. Cyclic voltammetric reduction of 2×10^{-3} M compound **6** in DMF (0.1 M Et_4NClO_4) at a platinum electrode at 20 °C (scan rate 20 mV s^{-1}).

predicted value for an electrochemically reversible process, at the scan rates examined. Process 2 has some resemblance to a quasi-reversible one-electron reduction at 20 °C. However, at −23 °C, $\Delta E_p(2)$ is actually less than $\Delta E_p(2)$ at 20 °C for scan rates less than 100 mV s^{-1}, a feature that cannot be explained if slow electron transfer is the rate-determining step even after allowing for the RT/nF factor. A decrease in the rate of electron transfer is expected at lower temperatures, and if a single quasi-reversible model were appropriate, ΔE_p must be greater at −23 °C than at 20 °C for all scan rates. The data cannot be fitted by a simple slow-electron-transfer model.

As in the dc polarography, departure from Nernstian behavior is evident under a number of conditions. The two redox processes seem to be mutually interactive as was established from the polarographic data. That is, the product(s) of the first reduction step contributes to the second process in a manner not explicable in terms of two single charge-transfer steps.

(c) Cyclic Voltammetry at a Platinum Electrode. In addition to an irreversible oxidation process, with a peak potential at +1.3 V, two reduction processes (Figure 4) are observed in the cyclic voltammograms of **6** at a platinum electrode (Table III). The contrast to the data at the mercury electrodes is significant. Process 2 actually appears chemically reversible at slow scan rates but not at high scan rates. The data imply that the heterogeneous charge-transfer rate constant is appreciably slower at the platinum electrode than at the mercury electrode, but again the quasi-reversible model does not fit the data at the platinum electrode.

(d) Implications of the Electrochemical Data. Rationalization of the electrochemical data can be made by assuming that (i) a structural change accompanies the charge-transfer step, (ii) the reaction $Cu_2L^{2-} + Cu_2L \rightleftharpoons 2Cu_2L^-$ is important, (iii) $k_s(Hg) \gg k_s(Pt)$, and (iv) Cu_2L^{2-} is inherently unstable, but at the mercury electrode weak adsorption stabilizes this product.

Spectroscopic and magnetic data indicate that Cu_2L contains planar Cu(II) moieties that are coplanar with each other. After electron transfer Cu_2L^- could rearrange to produce an alternative structural form. The ligand is considered to be able to introduce substantial flexibility into the system as noted in the Introduction.

Table III. Cyclic Voltammetry Data for the Reduction of 2×10^{-3} M **6** at a Platinum Electrode[a]

scan rate, mV s^{-1}	E_p^{red}, V (vs. SCE)	E_p^{ox}, V (vs. SCE)	ΔE_p, mV	i_p^{red}/i_p^{ox}	i_p^{red}, μA	$i_p^{red}v^{-1/2}$, μA mV$^{-1/2}$ s$^{-1/2}$
			Process 1, 20 °C			
500	−0.879	−0.730	149	1.04	32	1.43
200	−0.853	−0.738	115	1.03	21	1.48
100	−0.850	−0.740	110	1.00	16	1.60
50	−0.838	−0.746	92	1.06	10.7	1.51
20	−0.835	−0.753	82	1.02	7	1.57
10[b]	−0.832	−0.755	77	0.95	5	1.58
			Process 2, 20 °C			
500	−1.290				20	0.89
200	−1.260				14	0.99
100	−1.230				10	1.00
50	−1.213				7.5	1.06
20	−1.195	−0.973	222	1.19	5.5	1.23
10[b]	−1.165	−1.000	170	0.90	4.2	1.33
			Process 1, −23 °C			
500	−0.962	−0.686	276	1.02	19	0.85
200	−0.923	−0.710	213	0.99	13	0.92
100	−0.906	−0.727	179	1.06	9	0.90
50	−0.883	−0.746	137	0.93	7.3	1.03
20	−0.865	−0.753	112	0.87	4.6	1.03
10[b]	−0.862	−0.763	99	0.80	3.6	1.14
			Process 2, −23 °C			
500	−1.360					
200	−1.332					
100	−1.360					
50	−1.300					
20	−1.243	−1.020	223	0.90	3.5	0.78
10[b]	−1.265	−1.037	228	0.82	3.0	0.95

[a] Supporting electrolyte 0.1 M Et_4NClO_4 in DMF. [b] Data obtained at this scan rate are subject to depletion effects.

An extreme rearrangement would be one in which the Cu^I ion would assume a tetrahedral or trigonal geometry such as that favored by a related compound,[30] **8**. Structural rearrangements have been noted in the mixed-valence macrocyclic compound[44] **10**. Although many combinations are possible, it is convenient to consider the problem as though there exist two possible forms of Cu_2L^-, α-Cu_2L^- and β-Cu_2L^-, where α is the planar configuration and β an unknown configuration and α- and β-forms may be magnetically inequivalent. With this structural representation, process 1 may now be written in its simplest form:

$$\begin{tikzcd}
\alpha\text{-}Cu_2L + e^- \arrow[r, shift left, "E^\circ(1\alpha),\ k_s(1\alpha)"] \arrow[d, shift right, "k_1"'] & \alpha\text{-}[Cu_2L]^- \arrow[l, shift left] \arrow[d, shift right, "k_2"'] \\
\beta\text{-}Cu_2L + e^- \arrow[r, shift left, "E^\circ(1\beta),\ k_s(1\beta)"] \arrow[u, shift right, "k_{-1}"'] & \beta\text{-}[Cu_2L]^- \arrow[l, shift left] \arrow[u, shift right, "k_{-2}"']
\end{tikzcd} \qquad (1)$$

In this reaction scheme $E^\circ(1\alpha)$ and $E^\circ(1\beta)$ represent the standard potentials of the appropriate redox couples and are similar to each other and $k_s(1\alpha)$ and $k_s(1\beta)$ represent the heterogeneous charge-transfer rate constants at $E^\circ(1\alpha)$ and $E^\circ(1\beta)$, respectively (the charge-transfer coefficient has been omitted for clarity); k_1, k_{-1}, k_2, and k_{-2} represent the homogeneous isomerization rate constants. The theory and implications for this class of reaction have been considered recently[45,46] and explain the data much more satisfactorily than the

$$Cu_2L + e^- \underset{}{\overset{E^\circ,\ k_s}{\rightleftharpoons}} [Cu_2L]^-$$

model, which has generally been considered in studies of this kind. In the square scheme the possible reaction

$$\beta\text{-}Cu_2L^- + \alpha\text{-}Cu_2L \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \alpha\text{-}Cu_2L^- + \beta\text{-}Cu_2L$$

is also allowed thermodynamically and could contribute to the overall scheme. However, cross redox reactions of this kind will be excluded from the present discussions.

If the first reduction is considered as above, the second process may be defined as

$$\begin{tikzcd}
\alpha\text{-}[Cu_2L]^- + e^- \arrow[r, shift left, "E^\circ(2\alpha),\ k_s(2\alpha)"] \arrow[d, shift right, "k_4"'] & \alpha\text{-}[Cu_2L]^{2-} \arrow[l, shift left] \arrow[d, shift right, "k_5"'] \\
\beta\text{-}[Cu_2L]^- + e^- \arrow[r, shift left, "E^\circ(2\beta),\ k_s(2\beta)"] \arrow[u, shift right, "k_{-4}"'] & \beta\text{-}[Cu_2L]^{2-} \arrow[l, shift left] \arrow[u, shift right, "k_{-5}"']
\end{tikzcd} \qquad (2)$$

The opposite effect on $E_{1/2}(1)$ and $E_{1/2}(2)$, with increase in drop time and temperature dependence can be explained by this mechanism.

Smith et al.[47,48] have demonstrated that if the two processes

$$A + e^- \overset{E^\circ(3),\ k_s(3)}{\rightleftharpoons} A^- \qquad (3)$$

$$B + e^- \overset{E^\circ(4),\ k_s(4)}{\rightleftharpoons} B^- \qquad (4)$$

exist, then the reaction $B^- + A \rightleftharpoons A^- + B$ will have the effect of making the more negative process (4) appear to be more reversible than if this step did not occur. The extent of influence depends on $k_s(2)$. This theory has been applied to some inorganic systems.[49,50] The data in this work are entirely consistent with the occurrence of the process

$$\alpha\text{- and/or } \beta\text{-}[Cu_2L]^{2-} +$$
$$\alpha\text{- and/or } \beta\text{-}[Cu_2L] \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} 2(\alpha\text{- and/or } \beta\text{-}[Cu_2L]^-) \qquad (5)$$

The apparently greater reversibility of process 2 at the platinum

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electrode at slow scan rates may be attributed to this reaction. At slow scan rates more time is available for the cross reaction (5) to occur.

The above electrochemical study leads to the conclusion that the reduction of Cu_2L produces kinetically labile species. Unfortunately, the $[Cu_2L]^-$ and $[Cu_2L]^{2-}$ species appear to be too reactive to isolate and characterize by controlled-potential electrolysis, as decomposition occurs in the longer time scale experiments. The difference in $E_{1/2}(1)$ and $E_{1/2}(2)$ is clearly less than that for **10**.[27] However, the half-reduced form of this compound is relatively stable and shows an ESR signal for the mixed-valence species consistent with the electron being delocalized between the metal ions at ambient temperature but localized on one metal ion at 77 K.[27] The localized/delocalized electron configuration could conceivably be important in this work as indicated in the electrochemical data and may represent the α and β forms of the Cu_2L^- complexes.

Long and Hendrickson[34] found that while some of this class of compounds gave a seven-line ESR signal at ambient temperature, others gave a four-line signal consistent with a localized electron. In addition, the differential pulse voltammogram of one of the binuclear copper(II) compounds showed a reduction process intermediate to the two main processes.[34] This compound was among those showing electron localization at ambient temperature. Similarly Drago et al.[35] examined the electrochemistry of a binuclear complex related to **2** but with an ethoxide exogenous bridge (X). When it was electrolyzed to the half-reduced state, a four-line ESR signal was observed at ambient temperature as in the frozen state. These observations coupled with our work are consistent with the existence of processes of dynamic isomerization with rate and equilibrium constants of significant variability highly dependent on the ligand structure.

X-ray photoelectron spectroscopy by Gagne et al.[51] and finally a crystal structure determination[44] have revealed the presence of the genuine mixed-oxidation-state center $Cu^+\cdot Cu^{2+}$, in the solid state, rather than a delocalized structure for compound **10**. The mechanism for electron delocalization is probably through dynamic isomerization as described in this work. The contribution from the magnetic exchange coupling was evaluated to be 6 mV[31] for the singlet–triplet energy separation ($2J$) of $-586\ cm^{-1}$. This magnitude in potential is consistent with the electrochemical behavior described above. It has also been recently observed that minor conformational changes associated with related binuclear copper(II) complexes do occur and give rise to significant differences in exchange coupling[52] and consequently a small change in the reduction potential. Thus, the structural change proposed in this work may be associated with isomerization, resulting in a spin change of the kind described above. In conclusion, the present work demonstrates that a much closer examination of the electrochemical data is required to determine whether models based on simple electron charge-transfer steps are appropriate. In the present example this is clearly not the case. Further studies are required to ascertain whether other binuclear complexes exhibit similar electrochemical behavior. Clearly, the flexibility of the binuclear complex is important in determining the reversibility or otherwise of the reduction processes as are other structural features.[25–39,53–55]

Although the redox processes reported here occur at potentials that are more negative than those in the type 3 sites in copper proteins, the model compound **6**, like many other similar phenoxide-bridged copper(II) complexes, is capable of acting as a two-electron center. Consequently, these model compounds contribute to the better understanding of the possible stereochemical interactions of the type 3 copper compounds associated with electron transfer.

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Registry No. **5**, 96705-28-1; **6**, 96689-03-1; **11**, 6327-85-1; **12**, 34920-23-5; **13**, 96689-00-8; **14**, 96689-01-9; $[Cu_2L]^-$, 96689-04-2; $[Cu_2L]^{2-}$, 96689-05-3; 2,6-bis(hydroxymethyl)-4-methylphenol, 91-04-3; 2,6-bis((salicylideneamino)methyl)-4-methylphenol, 96689-02-0.

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Stability Constant and Reaction Mechanisms of the Nickel(II)–Tripeptide Complex of α-Aminoisobutyric Acid

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The $Ni^{II}(H_{-2}Aib_3)^-$ complex (Aib is the α-aminoisobutyryl residue) is unusually stable and is relatively sluggish in its reactions with acid and with cyanide ion. The β_{1-21} stability constant (for Ni^{2+} and $L^- \rightleftarrows Ni(H_{-2}L)^- + 2H^+$) is $10^{-9.65}$ M, which is 1500 times larger for L = Aib_3 than for L = G_3 (G is the glycyl residue). The rate of acid dissociation for $Ni^{II}(H_{-2}Aib_3)^-$ is 3400–390000 times slower than for the G_3 complex. Cyanide ion reacts rapidly to form $Ni^{II}(H_{-2}Aib_3)(CN)^{2-}$, which then has a $[CN^-]^2$ dependence to give $Ni(CN)_4^{2-}$. The third-order rate constant is 13 $M^{-2}\ s^{-1}$, which is 100 times smaller than for the corresponding reactions with the G_3 complex. The stability and kinetic effects of $Ni^{II}(H_{-2}Aib_3)^-$ are attributed, in large part, to the increase in the nickel–N(peptide) bond strength due to the α-carbon methyl groups.

Introduction

The α-aminoisobutyryl (Aib) residue is present in peptides that act as microbial antibiotics.[1–3] The presence of adjacent Aib residues in peptides restricts their conformation, due to steric effects of the two methyl groups on the α-carbons.[4,5] The absence of hydrogens on the α-carbons is important in the stabilization of Aib_3 complexes of copper(III) and nickel(III).[6] These tripeptide complexes are relatively slow to undergo self-redox decomposition.[6]

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