Blue Copper Models. Spectroscopic and Electrochemical Studies of Copper(II) Complexes with New Ligand Systems containing Sulphur and Nitrogen Donor Atoms

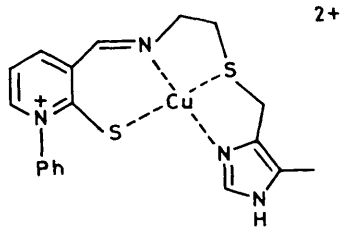
Luigi Casella, Michele Gullotti, Alessandro Pintar, Fiorella Pinciroli, and Roberto Viganò
Dipartimento di Chimica Inorganica e Metallorganica, Centro CNR, Università di Milano, 20133 Milano, Italy
Piero Zanello
Dipartimento di Chimica, Università di Siena, 53100 Siena, Italy

A series of new polyfunctional ligands derived from the condensation of 1-isopropyl- or 1-phenyl-3-formyl-2(1*H*)-pyridinethione with aminoalkylthioalkylbenzimidazoles having alkyl chains of various lengths between the donor atoms and the corresponding copper(II) complexes have been synthesized and spectroscopically characterized. The complexes show marked structural variations according to the length of the alkyl chains of the ligands, square planar, square pyramidal, trigonal bipyramidal, and distorted five-co-ordinate, and for one complex a wider range of distorted structures, including four- and five-co-ordinate, is accessible depending on the solvent and physical state. Electrochemistry in non-aqueous solvents indicates that the copper(II) complexes undergo a quasi-reversible one-electron reduction at markedly positive potentials, in the range from +0.23 to 0.35 V *vs.* saturated calomel electrode. The complete chemical reversibility of the Cu^{II}–Cu^{I} redox change has been tested by controlled-potential electrolysis. The five-co-ordinate complexes exhibit reduction potentials ≈0.1 V higher than the square-planar complexes, independently of their actual geometry, square pyramidal, trigonal bipyramidal, or intermediate between these.

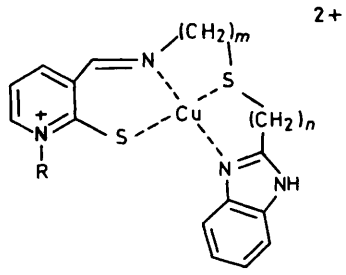
The search for synthetic models for the Type 1 active sites of copper proteins must tackle the problem of the intrinsic redox instability of copper(II)–thiolate bonding with respect to copper(I) and disulphide. This is evident in a number of recent studies on copper(II)–aliphatic thiolate complexes,[1–3] and will become even more serious as distortion of the copper(II) chromophore from tetragonal to pseudo-tetrahedral stereochemistry is introduced into the system, better to mimic the 'blue' sites in the proteins,[4] since it is known that such an arrangement thermodynamically favours access to the copper(I) oxidation state. One way which is usually followed in model chemistry to obtain redox-stable systems is to replace the easily oxidizable aliphatic thiols with aromatic[5–8] or heterocyclic[9–11] thiols, or with alkyl dithiocarboxylates.[12]

The copper(II) complex (**1**) was recently prepared[13] with the ligand derived from the condensation of 3-formyl-1-phenyl-2(1*H*)-pyridinethione, and an aminothiaimidazole compound which is an intermediate in the synthesis of the antiulcer drug cimetidine. Although this complex exhibited the common square-planar stereochemistry, the ligand system was of some interest because of the pyridinium thiolate nature of one of the sulphur donors and the non-symmetric collection of donor atoms. We thought that by appropriate modification of such a ligand it would be possible to obtain complexes with spectral properties of more relevance in the context of blue copper biomimetic chemistry. The series of copper(II) complexes that we report here, (**2**), is derived from the ligands resulting from the condensation of formylpyridinethiones with a group of aminoalkylthioalkylbenzimidazoles, containing carbon chains of variable length between the donor atoms. For synthetic reasons, the imidazole nucleus of (**1**) has been replaced with the parent, but more easily accessible, benzimidazole nucleus in (**2**).

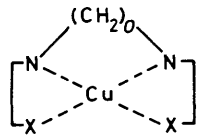
The main scope of the present investigation is to establish a relationship between the size of the fused chelate ring system in complexes (**2**), which is determined by the length of the carbon chains, and the stereochemistry of the resulting metal complex, since it is known for copper(II) complexes of type (**A**), with a symmetric distribution of the donor atoms in CuN_4,[14] CuN_2O_2,[15] and CuN_2S_2[12b,14c,16] cores, that an increase in the length *o* of the carbon chain can produce significant distortion of the copper chromophore from square planar toward pseudo-tetrahedral. Consequently, we also expect that the length of the



(**1**)



	R	*m*	*n*
(**2a**)	Ph	2	2
(**2b**)	Ph	2	1
(**2c**)	Ph	3	1
(**2d**)	Ph	4	1
(**2e**)	Pr^i	2	2
(**2f**)	Pr^i	2	1
(**2g**)	Pr^i	3	1
(**2h**)	Pr^i	4	1



(A) X = N, O, S

chains *m* and *n* affects to some extent the redox potential of the relevant copper(II)–copper(I) couples.

Experimental

Physical Measurements.—Elemental analyses (C, H, and N) were by the microanalytical laboratory of the University of Milano; copper analyses were made by atomic absorption spectrometry. Infrared spectra were recorded on a Nicolet MX-1E FT-IR instrument, with a standard resolution of 2.0 cm^{-1}, electronic spectra on a Perkin-Elmer Lambda-5 spectrophotometer. Proton n.m.r. spectra were obtained at 80 or 200 MHz on a Bruker WP-80 or AC-200 FT spectrometer, respectively; all chemical shift data are downfield from $SiMe_4$. E.s.r. spectra were obtained at *X*-band frequencies on a Varian E-109 instrument and were calibrated with diphenylpicrylhydrazyl. Conductivity measurements were performed on 10^{-3} mol dm^{-3} acetonitrile solutions of the complexes using an Amel model 133 conductivity meter. Magnetic susceptibilities of solid samples were measured at 295 K by the Faraday technique on a Cahn 1000 electrobalance. Cyclic voltammetry was performed in a three-electrode cell having a platinum working electrode surrounded by a platinum-spiral counter electrode, and the aqueous saturated calomel reference electrode (s.c.e.) mounted with a Luggin capillary. A BAS 100A Electrochemical Analyzer was used as polarizing unit. Controlled-potential coulometric tests were performed in a H-shaped cell with anodic and cathodic compartments separated by a sintered glass disc. The working macroelectrode was a platinum gauze; a mercury pool was used as counter electrode. An Amel model 551 potentiostat with an associated coulometer (Amel model 558 integrator), was employed. In all electrochemical tests, the temperature was controlled at 20 ± 0.1 °C.

Reagents and Preparations.—All reagents were of the highest grade commercially available and were used as received. 3-Formyl-1-phenyl-2-(1*H*)-pyridinethione was prepared from the sodium salt of glutacondialdehyde (pent-2-enedial)[17] and phenyl isothiocyanate according to a published procedure.[18] 3-Formyl-1-isopropyl-2(1*H*)-pyridinethione was a generous gift from Dr. Jan Becher (Odense University, Denmark). 2-(2′-Chloroethyl)benzimidazole[19] and 2-mercaptomethylbenzimidazole hydrochloride[20] were prepared with slight variations of the original procedures. For the preparation of some of the phthalimidoalkanethiols we followed the route described earlier to obtain one of the members of this series of compounds.[21]

2-(2′-*Chloroethyl*)*benzimidazole.* 1,2-Diaminobenzene (10.8 g) and β-chloropropionic acid (16.2 g) were refluxed in 4 mol dm^{-3} hydrochloric acid (100 cm^3) for 1 h. The green solution was diluted with water (100 cm^3), cooled in an ice-bath, and neutralized by dropwise addition of 6 mol dm^{-3} ammonia with vigorous stirring. The white precipitate of the benzimidazole was collected by filtration, washed with small amounts of cold water, and dried under vacuum over P_2O_5 (yield 48%). This product is unstable[19] and it was thus used as such immediately after preparation.

N-(2-*Mercaptoethyl*)*phthalimide.* A mixture of cysteamine (2-aminoethanethiol) hydrochloride (11.6 g), sodium acetate (23.0 g), and phthalic anhydride (16.5 g) in glacial acetic acid (150 cm^3) was refluxed overnight with stirring. Then it was cooled, evaporated to dryness under vacuum, treated with aqueous sodium carbonate solution, and extracted several times with chloroform. The combined organic extracts were concentrated to a small volume under vacuum and cold diethyl ether was added to the residue. The white solid precipitate was filtered off, washed with diethyl dether, and dried (yield 80%). I.r. (Nujol mull): 2 555w [ν(SH)]; 1 770m, 1 730s,br [ν(C=O)], and 715s cm^{-1} [δ(CH)]. ^1H N.m.r. ($CDCl_3$): δ 7.6—7.9 (m, 4 H, Ph), 3.86 (t, 2 H, NCH_2), 2.6—3.0 (m, 2 H, SCH_2), and 1.42 (t, 1 H, SH).

2-[2′-(*Benzimidazol-2″-yl*)*ethylthio*]*ethylamine dihydrochloride.* An equimolar mixture of *N*-(2-mercaptoethyl)-phthalimide (30 mmol) and metallic sodium was refluxed in dry tetrahydrofuran (thf) (100 cm^3) under nitrogen for 1 h. Solid 2-(2′-chloroethyl)benzimidazole (48 mmol) was added to the mixture after cooling and this was heated again at reflux temperature overnight. The solvent was evaporated to dryness under vacuum and the residue was treated with chloroform. The precipitate of sodium chloride was filtered off and the filtrate was concentrated and chromatographed on Al_2O_3 by elution with chloroform. After removal of a band of unreacted mercaptoethylphthalimide and a minor band due to an impurity, the band of the product was collected and concentrated to a small volume. Diethyl ether was added to complete precipitation of the phthalimide derivative of the required amine (yield 25%). I.r. (Nujol mull): 1 770m, 1 701s [ν(C=O)], 735m and 713m cm^{-1} [δ(CH)]. ^1H N.m.r. ($CDCl_3$): δ 10 (br, 1 H, NH), 7.0—8.0 (m, 8 H, Ph), 3.97 (t, 2 H, NCH_2), 3.0—3.4 (m, 4 H, SCH_2CH_2C), and 2.94 (t, 2 H, S–CH_2–benzimidazole).

The phthalimide derivative (6 mmol), hydrazine dihydrochloride (6 mmol), and potassium hydroxide (12 mmol) were refluxed in absolute ethanol (100 cm^3) for 40 h. After the mixture had cooled, the precipitate of phthalohydrazide was filtered off and the filtrate was evaporated to dryness. The residue was treated with 12 mol dm^{-3} hydrochloric acid (30 cm^3) and refluxed for 17 h. Then the solution was evaporated to dryness under vacuum. The residue was treated with ethanol and re-evaporated to dryness; then it was dissolved in ethanol and the product was precipitated by addition of diethyl ether, filtered off and dried under vacuum (yield 65%) (Found: C, 44.20; H, 5.80; N, 14.60. Calc. for $C_{11}H_{15}N_3S{\cdot}2HCl$: C, 44.90; H, 5.80; N, 14.30%). ^1H N.m.r. (D_2O): δ 7.2—7.6 (m, 4 H, Ph) and 2.8—3.5 (m, 8 H, CH_2).

2-(*Benzimidazol-2′-ylmethylthio*)*ethylamine dihydrochloride.* A mixture of *N*-(2-mercaptoethyl)phthalimide (20 mmol), 2-chloromethylbenzimidazole (20 mmol), methanolic 1 mol dm^{-3} sodium hydroxide (20 cm^3), and absolute ethanol (100 cm^3) was stirred under nitrogen for 15 min and concentrated to half volume under vacuum. Then it was refluxed overnight under nitrogen. After cooling, dichloromethane (50 cm^3) was added, and the mixture subsequently left to stand in a refrigerator for several hours. The precipitate of sodium chloride was filtered off and the filtrate was evaporated to dryness under vacuum. The residue was dissolved in the minimum amount of a chloroform and chromatographed on an alumina column ($CHCl_3$). After removal of a band of unreacted starting product, the band of the phthalimide derivative of the amine was concentrated to a small volume and precipitated with diethyl ether (yield 50%). I.r. (Nujol mull): 1 768m, 1 707s [ν(C=O)], 733m and 718m cm^{-1} [δ(CH)]. ^1H N.m.r. ($CDCl_3$): δ 10.4 (br, 1 H, NH), 7.0—8.0 (m, 8 H, Ph), 4.13 (s, 2 H, CH_2–benzimidazole), 3.86 (t, 2 H, NCH_2), and 2.88 (t, 2 H, CCH_2S).

A mixture of this phthalimide derivative (10 mmol), hydrazine dihydrochloride (10 mmol), and potassium hydroxide (20 mmol) in absolute ethanol (60 cm^3) was refluxed for 11 h. After the mixture had cooled, the white precipitate was filtered off and the solution evaporated to dryness. The residue was treated with 12 mol dm^{-3} hydrochloric acid (30 cm^3) and the mixture was

refluxed overnight. After concentration of the solution to less than half volume, the white precipitate formed on cooling was filtered off. The filtrate was evaporated to dryness under vacuum and the oily residue was treated several times with ethanol and evaporated to dryness until a solid residue was obtained. This was treated with a small amount of absolute ethanol and with diethyl ether. The product was collected by filtration and dried under vacuum (yield 80%) (Found: C, 40.55; H, 5.90; N, 13.85. Calc. for $C_{10}H_{13}N_3S\cdot 2HCl\cdot H_2O$: C, 40.25; H, 5.75; N, 14.10%). ^{1}H N.m.r. (D_2O): δ 7.3—7.9 (m, 4 H, Ph), 4.28 (s, 2 H, CH_2–benzimidazole), 3.2—3.4 (m, 2 H, NCH_2), and 2.8—3.1 (m, 2 H, SCH_2C).

N-(3-*Mercaptopropyl*)*phthalimide*. A solution of metallic sodium (25.7 mmol) in absolute ethanol (100 cm^3) was saturated with hydrogen sulphide in an ice-bath. To this mixture a solution of *N*-(3-bromopropyl)phthalimide (20 mmol) in cold dimethylformamide (dmf) (25 cm^3) was added with stirring. After 15 min the solution was allowed to reach room temperature and then was gently heated to 100 °C in an oil-bath kept at constant temperature for 1 h. Then the solution was cooled and cold water (100 cm^3) was added. The oil separated subsequently crystallized. The white solid was filtered off and recrystallized from ethanol (yield 70%). I.r. (Nujol mull): 2 550m [ν(SH)], 1 763m, 1 698vs,br [ν(C=O)], and 719s cm^{-1} [δ(CH)]. ^{1}H N.m.r. ($CDCl_3$): δ 7.4—8.0 (m, 4 H, Ph), 3.68 (t, 2 H, NCH_2), 2.37 (≈q, 2 H, CH_2S), 1.82 (m, 2 H, CCH_2C), and 1.43 (≈t, 1 H, SH).

N-(4-*Mercaptobutyl*)*phthalimide*. This compound was prepared as described above from *N*-(4-bromobutyl)-phthalimide (yield 75%). I.r. (Nujol mull): 2 551m [ν(SH)], 1 764m, 1 698vs,br [ν(C=O)], and 721s cm^{-1} [δ(CH)]. ^{1}H N.m.r. ($CDCl_3$): δ 7.4—8.0 (m, 4 H, Ph), 3.70 (≈t, 2 H, N–CH_2), 2.50 (m, 2 H, CH_2S), and 1.2—2.1 (m, 5 H, CCH_2CH_2C + SH).

2-*Mercaptomethylbenzimidazole hydrochloride*. 1,2-Diaminobenzene (25 mmol) and mercaptoacetic acid (30 mmol) were refluxed in 6 mol dm^{-3} hydrochloric acid (40 cm^3) for about 40 h. The resulting green solution was concentrated to about 15 cm^3 under vacuum and cooled. The white precipitate thus formed was collected by filtration, crystallized from ethanol–diethyl ether, and dried under vacuum (yield 70%) (Found: C, 47.60; H, 4.60; N, 13.85. Calc. for $C_8H_8N_2S\cdot HCl$: C, 47.90; H, 4.50; N, 13.95%). ^{1}H N.m.r. (D_2O): δ 7.1 (≈s, 4 H, Ph) and 3.83 (s, 2 H, CH_2).

3-(*Benzimidazol-2′-ylmethylthio*)*propylamine dihydrochloride*. To a solution of metallic sodium (32 mmol) in absolute ethanol (150 cm^3) was added 2-mercaptomethylbenzimidazole hydrochloride (16 mmol) under nitrogen. *N*-(3-Bromopropyl)-phthalimide (16 mmol) was added and the resulting mixture was refluxed for 18 h under a nitrogen atmosphere. Then this was evaporated to dryness and the residue was treated with dichloromethane. The inorganic salt was filtered off and the filtrate was concentrated to a small volume and chromatographed on alumina ($CHCl_3$). After elution of a minor band of unreacted bromopropylphthalimide, the band of the phthalimide derivative of the amine was collected, concentrated to a small volume, and precipitated by addition of diethyl ether. The white solid was filtered off and dried (yield 85%). I.r. (Nujol mull): 1 769m, 1 703vs [ν(C=O)], 738m and 717m cm^{-1} [δ(CH)]. ^{1}H N.m.r. ($CDCl_3$): δ 10.5 (br, 1 H, NH), 7.0—7.9 (m, 8 H, Ph), 4.00 (s, 2 H, CH_2–benzimidazole), 3.75 (t, 2 H, NCH_2), 2.57 (t, 2 H, CCH_2S), and 1.91 (qnt, 2 H, CCH_2C).

The phthalimide derivative (11.4 mmol), hydrazine dihydrochloride (11.4 mmol), and potassium hydroxide (22.8 mmol) were refluxed in absolute ethanol (100 cm^3) for 4 d. After cooling in a refrigerator, dichloromethane (80 cm^3) was added and the white precipitate was filtered off. The filtrate was evaporated to dryness and the residue was refluxed in 6 mol dm^{-3} hydrochloric acid (70 cm^3) for 16 h. On cooling in a refrigerator a white precipitate formed; this was filtered off and the solution evaporated to dryness. The residue was treated several times with absolute ethanol and evaporated to dryness until a solid was obtained (yield 85%) (Found: C, 44.30; H, 5.80; N, 14.40. Calc. for $C_{11}H_{15}N_3S\cdot 2HCl$: C, 44.90; H, 5.80; N, 14.30%). ^{1}H N.m.r. (D_2O): δ 7.3—7.8 (m, 4 H, Ph), 4.21 (s, 2 H, CH_2–benzimidazole), 3.08 (t, 2 H, NCH_2), 2.70 (t, 2 H, CCH_2S), and 1.95 (≈qnt, 2 H CCH_2C).

4-(*Benzimidazol-2′-ylmethylthio*)*butylamine dihydrochloride*. The phthalimide derivative of this amine was prepared following the same procedure as for the corresponding propylamine derivative (yield 75%). I.r. (Nujol mull): 1 768m, 1 704vs [ν(C=O)], 738m and 716m cm^{-1} [δ(CH)]. ^{1}H N.m.r. ($CDCl_3$): δ 10.9 (br, 1 H, NH), 7.0—7.9 (m, 8 H, Ph), 3.98 (s, 2 H, CH_2–benzimidazole), 3.53 (t, 2 H, NCH_2), 2.54 (t, 2 H, CCH_2S), and 1.3—1.9 (m, 4 H, CCH_2CH_2C). It was decomposed by treatment with hydrazine dihydrochloride and potassium hydroxide in refluxing ethanol as described above. The dihydrochloride salt of the butylamine was obtained in 68% yield (Found: C, 43.85; H, 6.35; N, 13.00. Calc. for $C_{12}H_{17}N_3S\cdot 2HCl\cdot H_2O$: C, 44.15; H, 6.50; N, 12.90%). ^{1}H N.m.r. (D_2O): δ 7.3—7.8 (m, 4 H, Ph), 4.24 (s, 2 H, CH_2–benzimidazole), 2.97 (≈t, 2 H, NCH_2), 2.67 (≈t, 2 H, CCH_2S), and 1.5—1.9 (m, 4 H, CCH_2CH_2C).

Preparation of Copper(II) *Complexes*.—The copper(II) complexes (**2**) were prepared according to the following procedure. The aminoalkylthioalkylbenzimidazole dihydrochloride (1 mmol) was converted into the neutral compound by treatment with the appropriate amount of methanolic 1 mol dm^{-3} sodium hydroxide in ethanol–dichloromethane (1 : 3). The precipitate of sodium chloride was filtered off and the solvent was rotary-evaporated. The resulting oil was treated with the 3-formylpyridinethione derivative (1 mmol) and refluxed in absolute ethanol (30 cm^3) for 0.5 h. Copper(II) perchlorate hexahydrate (1 mmol), dissolved in a small amount of ethanol, was rapidly added to the ice-cooled solution of the Schiff base. The resulting dark green or brownish green precipitate was immediately filtered off, washed with small amounts of cold absolute ethanol, and dried under vacuum.

Complex (**2f**) (Found: C, 35.90; H, 3.85; Cu, 9.90; N, 8.55. Calc. for $C_{19}H_{22}Cl_2CuN_4O_8S_2$: C, 36.05; H, 3.50; Cu, 10.00; N, 8.85%). I.r. (Nujol mull): 1 646m [ν(C=N)], 1 618m, 1 563m [ν(ring)], 1 100vs,br, 620s [ν(ClO_4)], 801m, 748m, and 721w cm^{-1} [δ(CH)]. Λ_M = 230 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.80 μ_B.

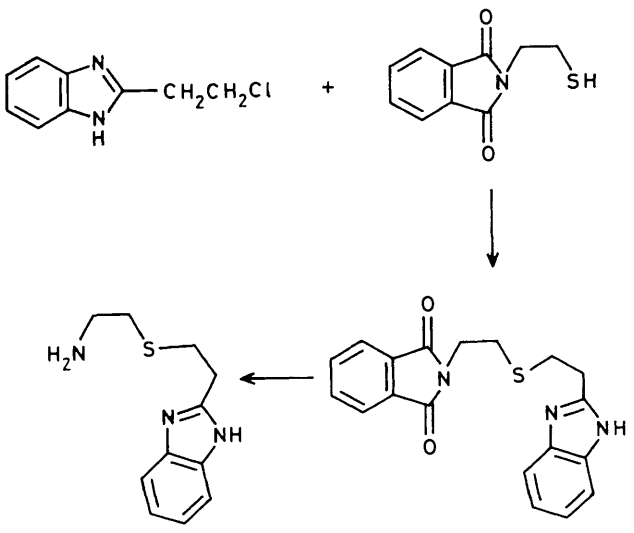
Complex (**2e**) (Found: C, 37.55; H, 3.95; Cu, 10.0; N, 8.90. Calc. for $C_{20}H_{24}Cl_2CuN_4O_8S_2$: C, 37.15; H, 3.75; Cu, 9.80; N, 8.65%). I.r. (Nujol mull): 1 645m [ν(C=N)]; 1 621w, 1 599m, 1 561m [ν(ring)]; 1 095vs,br, 624s [ν(ClO_4)], 802m, 753m, and 724m cm^{-1} [δ(CH)]. Λ_M = 227 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.75 μ_B.

Complex (**2g**) (Found: C, 37.40; H, 3.55; Cu, 9.70; N, 8.45. Calc. for $C_{20}H_{24}Cl_2CuN_4O_8S_2$: C, 37.15; H, 3.75; Cu, 9.80; N, 8.65%). I.r. (Nujol mull): 1 638m [ν(C=N)], 1 594m, 1 565m [ν(ring)], 1 095vs,br, 622s [ν(ClO_4)], 805m, 758m, and 720m cm^{-1} [δ(CH)]. Λ_M = 225 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.88 μ_B.

Complex (**2h**) (Found: C, 38.55; H, 4.10; Cu, 9.50; N, 8.30. Calc. $C_{21}H_{26}Cl_2CuN_4O_8S_2$: C, 38.15; H, 3.95; Cu, 9.60; N, 8.50%). I.r. (Nujol mull): 1 640m [ν(C=N)], 1 599m, 1 562m [ν(ring)], 1 100vs,br, 621s [ν(ClO_4)], 806w, 752m, and 722m cm^{-1} [δ(CH)]. Λ_M = 226 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.75 μ_B.

Complex (**2b**) (Found: C, 39.90; H, 3.15; Cu, 9.30; N, 8.40. Calc. for $C_{22}H_{20}Cl_2CuN_4O_8S_2$: C, 39.60; H, 3.00; Cu, 9.50; N, 8.40%). I.r. (Nujol mull): 1 643m [ν(C=N)], 1 592m, 1 559m [ν(ring)], 1 095vs,br, 622s [ν(ClO_4)], 804w, 762m, 720m, and 696m cm^{-1} [δ(CH)]. Λ_M = 239 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.96 μ_B.

Complex (**2a**) (Found: C, 40.60; H, 3.60; Cu, 9.60; N, 8.35. Calc. for $C_{23}H_{22}Cl_2CuN_4O_8S_2$: C, 40.55; H, 3.25; Cu, 9.30; N, 8.25%). I.r. (Nujol mull): 1 646m [ν(C=N)], 1 595m, 1 558m



Scheme 1.

[ν(ring)], 1 100vs,br, 622s [ν(ClO_4)], 806w, 764m, 720m, and 697m cm^{-1} [δ(CH)]. Λ_M = 250 S cm^2 mol^{-1}; $\mu_{eff.}$ = 2.00 μ_B.

Complex (**2c**) (Found: C, 40.90; H, 3.30; Cu, 9.10; N, 8.55. Calc. for $C_{23}H_{22}Cl_2CuN_4O_8S_2$: C, 40.55; H, 3.25; Cu, 9.30; N, 8.25%). I.r. (Nujol mull): 1 645m [ν(C=N)], 1 617m, 1 590m, 1 559m [ν(ring)], 1 100vs,br, 623s [ν(ClO_4)], 803w, 764m, 722m, and 698m cm^{-1} [δ(CH)]. Λ_M = 225 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.80 μ_B.

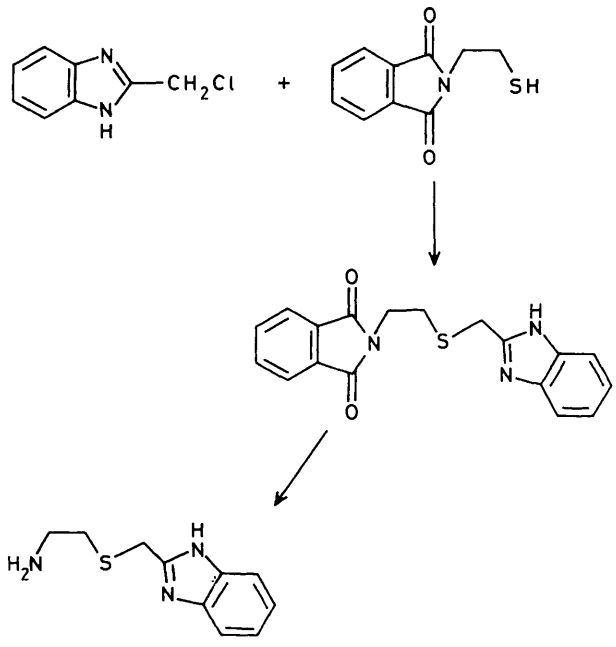
Complex (**2d**) (Found: C, 42.00; H, 3.85; Cu, 9.00; N, 7.95; Calc. for $C_{24}H_{24}Cl_2CuN_4O_8S_2$: C, 41.45; H, 3.50; Cu, 9.10; N, 8.05%). I.r. (Nujol mull): 1 638m [ν(C=N)], 1 592m, 1 555m, [ν(ring)], 1 100vs,br, 623s [ν(ClO_4)], 802w, 764m, 721m, and 698m cm^{-1} [δ(CH)]. Λ_M = 220 S cm^2 mol^{-1}; $\mu_{eff.}$ = 1.98 μ_B.

The zinc(II) analogue, (**3h**), of complex (**2h**) was prepared similarly (Found: C, 37.80; H, 4.25; N, 8.70. Calc. for $C_{21}H_{26}Cl_2N_4O_8S_2Zn$: C, 38.05; H, 3.95; N, 8.45%). I.r. (Nujol mull): 1 660m, 1 645m [ν(C=N)], 1 620 (sh), 1 550m [ν(ring)], 1 100vs,br, 620m [ν(ClO_4)], 855w, 790w, 740m, and 700w cm^{-1} [δ(CH)]. Λ_M = 225 S cm^2 mol^{-1}.

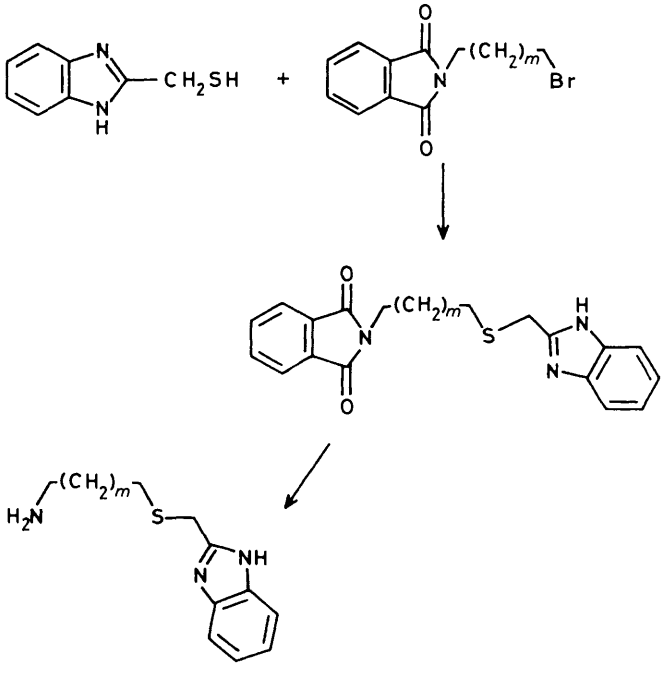
Results and Discussion

Ligand Design and Characterization.—Our main effort has been to develop a synthetic route to polyfunctional ligands that in some way could simulate the donor sets of the Type 1 copper sites and allow for the possibility of further refinement in ligand structure within an established synthetic frame. A structural requisite to be satisfied by the ligands was the incorporation of the thioether sulphur donor in an internal position of the chain, to circumvent the reluctance of thioethers to co-ordinate to Cu^{II}, while the use of quadridentate chelating ligands was expected to overcome the kinetic lability of Cu^{II}. Imines ligands were thus designed to provide a basis to investigate in some systematic way the structural elements to be included in order to obtain reliable model complexes for the protein blue copper sites. The flexibility in ligand design enables one to introduce carbon chain residues of variable length and structure between the donor atoms of the aminoalkylthioalkylbenzimidazoles; however, only linear residues were used in the present systems. Further progress toward a synthetic Type 1 copper analogue will involve replacement of the heterocyclic thiolate residue of (**2**) with a suitably substituted aliphatic thiol.

The syntheses of the various aminoalkylthioalkylbenzimidazoles were carried out according to Schemes 1—3. These routes, involving thioether bond formation in the last step and



Scheme 2.



Scheme 3. m = 3 or 4

use of preformed benzimidazole derivatives, were found more convenient than the alternatives involving synthesis of the benzimidazole nucleus by Phillips condensation in the last step, which were employed, for instance, in the syntheses of symmetrical benzimidazole thioether ligands.[22,23] 3-(Benzimidazol-2′-ylmethylthio)propylamine and 4-(benzimidazol-2′-ylmethylthio)butylamine dihydrochlorides were also synthesized according to Scheme 2, from the corresponding *N*-(mercaptoalkyl)phthalimides and 2-chloromethylbenzimidazole, but the yields were remarkably lower and the purification procedure more elaborate than those involved in Scheme 3. However, in general we did not try to optimize yields and operations for the

Table 1. Electronic spectra of metal complexes in acetonitrile solution

Complex	$\lambda_{max.}$/nm (ε/dm^3 mol^{-1} cm^{-1})					
(2b)	272 (12 500) 810 (sh) (220)	279 (11 000)	328 (7 000)	382 (8 700)	420 (sh) (3 800)	605 (560)
(2a)	270 (12 100)	278 (10 400)	324 (8 800)	384 (9 700)	425 (sh) (4 000)	585 (580)
(2c)	270 (sh) (13 800) 840 (250)	279 (sh) (12 100)	327 (9 200)	375 (7 400)	455 (sh) (2 300)	600 (sh) (170)
(2d)	272 (12 650)	279 (12 500)	325 (9 800)	380 (sh) (6 700)	460 (sh) (1 850)	765br (260)
(2f)	273 (15 000) 800 (sh) (100)	280 (14 000)	325 (5 800)	363 (5 600)	400 (sh) (2 600)	625 (220)
(2e)	271 (11 100)	278 (10 500)	320 (7 300)	373 (7 100)	450 (sh) (2 000)	580 (sh) (400)
(2g)	273 (12 900)	280 (12 400)	321 (8 300)	370 (sh) (5 400)	440 (sh) (2 100)	850 (200)
(2h)	270 (11 100) 830 (sh) (300)	278 (10 300)	321 (8 600)	366 (7 100)	450 (sh) (1 200)	720 (400)
(3h)	273 (sh) (9 800)	278 (10 000)	316 (6 700)	355 (4 500)		

Table 2. E.s.r. spectra of copper(II) complexes in frozen solutions[a]

Complex	$g_{\|}$	$g_{\perp}$	$10^4\|A_{\|}\|$/cm^{-1}	$10^4\|A_{\perp}\|$/cm^{-1}
(2b)	2.210	2.07	163	
(2a)	2.166	2.05	174	
(2c)	1.981	2.160		116
(2d)	2.236	2.06	145	
(2f)	2.185	2.07	168	
(2e)	2.162	2.05	172	
(2g)	1.980	2.163		114
(2h)	2.186[b]	2.06[b]	133[b]	

[a] Recorded in acetonitrile–chloroform solution at −150 °C. [b] $g_{\|} = g_1$; $g_{\perp} = g_2, g_3$; $A_{\|} = A_1$.

preparations. A single member of the aminoalkylthioalkylbenzimidazoles with more than one carbon atom separating the thioether sulphur from the benzimidazole ring was synthesized because from the properties of the resulting copper(II) complexes (**2a**) and (**2e**) it became clear that further lengthening of this part of the ligand chain was of no utility.

The condensation between the aminoalkylthioalkylbenzimidazoles and formylpyridinethiones occurs readily and completely. In a few instances we isolated the resulting imines; their spectral properties are very similar to those of the free ligand of complex (**1**),[13] with additional features due to the presence of benzimidazole rather than imidazole nuclei (near-u.v. electronic bands at 270—280 nm, proton n.m.r. signals between δ 7.0 and 8.0). Upon complex formation the iminepyridinethione ligands assume pyridinium thiolate character, as was clearly evidenced by the spectroscopic properties of the copper(I) and zinc(II) complexes corresponding to (**1**).[13] This behaviour is confirmed here in the 1-isopropyl-substituted pyridinethione series by the zinc(II) complex (**3h**).

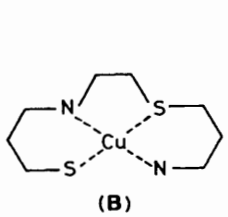
Spectroscopic Properties of Copper(II) Complexes.—The copper(II) complexes (**2**) were routinely prepared as perchlorate salts in view of the extremely weak co-ordinating ability of this anion, especially in solution. Their i.r. spectra displayed characteristic imine ν(C=N) bands in the range 1 638—1 646 cm^{-1} and broad, unresolved, bands near 1 100 cm^{-1} indicative of unco-ordinated perchlorate. Magnetic susceptibility measurements, solution conductivity data, and e.s.r. spectra are clearly indicative of mononuclear copper(II) species.

The electronic spectra of the complexes are summarized in Table 1. The main contribution to these spectra in the near-u.v. region is due to intraligand transitions within the conjugated imine chromophore of the pyridinium thiolate form of the ligands, as discussed previously for (**1**)[13] and it is exemplified here by the spectrum of the zinc complex (**3h**). Besides the ligand absorptions, additional contributions due to ligand-to-metal charge-transfer (l.m.c.t.) transitions from filled orbitals on the donor groups to the copper(II) *d* vacancy are expected to occur down to 450 nm. The tentative assignment of the various l.m.c.t. transitions has been given previously for complex (**1**)[13] and will not be detailed further here since the ligand donor groups are practically identical, though some minor changes within the present series of complexes may occur as a consequence of the variation in metal geometry determined by changes in the length of the alkyl chains *m* and *n*.

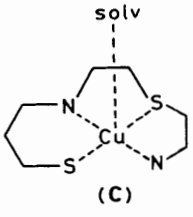
Deductions about the main structural features of the complexes in solution can be made on the basis of their electronic (*d–d* band envelope) and e.s.r. spectra. Both types of spectra show significant differences in the two parallel series of complexes as a function of fragments $(CH_2)_m$ and $(CH_2)_n$ and are clearly indicative of the geometric arrangement around the metal dictated by these chains. The nature of the substituent R on the pyridine nitrogen atom of the ligand apparently has a minor effect except, possibly, for its size.

The complexes (**2a**) and (**2e**) exhibit a single, somewhat broadened, *d–d* band near 600 nm which is typical for square-planar complexes (weak axial interaction). The e.s.r. spectra of these complexes recorded in frozen solution are of the axial type and also indicative of nearly tetragonal stereochemistry ($g_{\|} > g_{\perp}$, large $A_{\|}$ values, Table 2). On the other hand, the visible spectra of the two complexes with smaller chelate ring near the benzimidazole nucleus, (**2b**) and (**2f**), display two partially resolved *d–d* bands, near 600 and 800 nm, the first of which has higher intensity. These spectra are typical for five-co-ordinate, square-pyramidal geometries[24] and have been observed many times for copper(II) complexes with polydentate ligands including thioether functionalities (see, *e.g.*, refs. 6*b*. 14*c*, 22*b*, and 23*c*). The e.s.r. spectra are still of axial type and indicate a $d_{x^2-y^2}$ ground state ($g_{\|} > g_{\perp} > 2.0$), suggesting that the dominant tetragonal stereochemistry is maintained in frozen solution. The existence of some significant axial interaction by a co-ordinating group in the complexes with 6-5-5 chelate ring type is confirmed by the e.s.r. data, since the increase in $g_{\|}$ and the decrease in $|A_{\|}|$ values with respect to the parameters observed for the corresponding complexes with 6-5-6 chelate ring type is in line with what is expected when the axial interaction becomes stronger.[25]

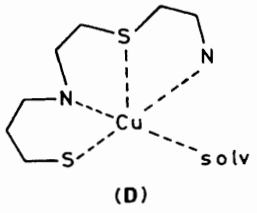
A comparison with the spectral data (*d–d* bands and e.s.r. parameters) of complex (**1**)[13] (6-5-5 chelate ring type) shows that these are almost coincident with those of (**2a**) and (**2e**) [6-5-6 chelate ring type, square-planar structure (**B**)]. The different behaviour of (**2b**) and (**2f**) (6-5-5 chelate ring type) can



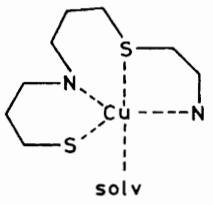
(B)



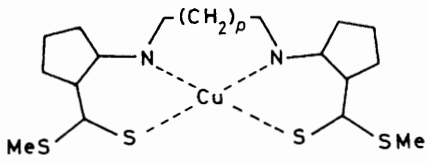
(C)



(D)



(E)



(F)

be accounted for by considering that in a planar structure the aromatic ring of the benzimidazole residue [absent in (**1**)] would come in too close a contact to the substituent in position 1 of the pyridine ring, for the small size of the five-membered ring. Therefore, to minimize such interaction it is likely that the ligand is forced to assume the bent structures (**C**) or (**D**) in the systems with 6-5-5 chelate ring arrangement, leaving a solvent molecule (solv) free to bind to the metal. Some solvent dependence of the absorption and e.s.r. spectra and previous results on copper(II)–bispyridylthioether complexes[14c] suggest that structure (**D**) with an axial thioether group and basal solvent co-ordination is favoured for these systems. In the case of (**2a**) and (**2e**) the steric problem is less serious because the benzimidazole residue is part of a six-membered chelate ring, which is larger and more flexible, thus allowing a more convenient orientation of the aromatic ring.

The spectra of the compounds with three-carbon-atom chains between the imine and thioether groups, (**2c**) and (**2g**) (6-6-5 chelate ring type) are surprisingly different from the previous ones. Both the room-temperature *d–d* spectra and the frozen-solution e.s.r. spectra are clearly indicative of trigonal-bipyramidal species (d_{z^2} ground state): $\lambda_{max.} > 800$ nm, $g_\perp > g_\parallel \approx 2.0$.[24d,26] The donor group of the ligand occupying an axial position is quite certainly the thioether group since it is the weakest donor and is included in the flexible part of the ligand chain. Extending the length of the bridge between the imine and thioether groups has apparently the effect of increasing the dihedral angle between the planes N(imine)–Cu–S and S–Cu–N(imidazole), thus changing the structure of the equatorial core of the complex from tetragonal (**D**) to trigonal (**E**).

Some further changes in the properties of the complexes occur when a fourth methylene bridge between the imine and thioether groups is included in the ligands. In particular, the copper(II) systems with 6-7-5 chelate rings exhibit marked redox instability in solution. This problem exists to some extent also for the complexes with (benzimidazolylmethylthio)propylamine residues but for (**2d**) it becomes rather serious because complete reduction of Cu^{II} occurs in times of the order of a few minutes in acetonitrile solution at room temperature. This process can be monitored spectroscopically by the decrease in intensity of the absorption band in the range 350—400 nm, which largely comprises l.m.c.t. transitions to Cu^{II},[13] and the *d–d* bands; but no isosbestic points are observed, indicating the occurrence of complex reactions. The redox instability is somewhat lower in solvents with lower ability to stabilize Cu^{I} and did not prevent isolation of the complexes in reasonably pure form, by performing the synthesis at low temperature.

The pair of complexes (**2d**) and (**2h**) is the only one for which some non-negligible spectral difference can be attributed to the type of substituent R on the pyridinium ring. The low-energy absorption spectrum of the former complex comprises a very broad absorption band, encompassing the *d–d* transitions, which extends from about 600 to 900 nm, with $\lambda_{max.}$ near 760 nm. This somewhat unusual spectrum is likely to result from the presence of several isomeric structures of the complex in equilibrium in solution. The frozen-solution e.s.r. spectrum is, however, much simpler, since it shows a single species, indicating that only a narrow range of structures is allowed in the frozen state. A typical axial spectrum with $g_\parallel > g_\perp$ is observed, with partially resolved structure (≈ 15 G, 1.5×10^{-3} T) in the perpendicular component of the signal, probably due to super-hyperfine coupling with the nitrogen donors of the ligand. The $A_\parallel$ value (0.0145 cm^{-1}) is markedly lower than for the other complexes with tetragonal stereochemistry in the series, indicating that significant distortion toward a pseudo-tetrahedral arrangement occurs in the present case. This $A_\parallel$ value is actually the same as that found for the copper(II) diamino-dithiocarboxylate complex (**F**) ($p = 4$), for which the *X*-ray crystal structure is available,[12b] and compares with those of other pseudo-tetrahedral CuN_2S_2 complexes of type (**A**).[10,11b] It is noteworthy that the $g_\parallel$ values found for all these latter systems (2.14—2.17) are much lower than that of (**2d**). This difference is due to the neutral charge carried by the above CuN_2S_2 complexes, while the $g_\parallel$ value observed for (**2d**) is approximately in the range found for dipositive copper(II)–bisthioether complexes.[6b,14c,22b,23]

The *d–d* spectrum of complex (**2h**) is better defined; two component bands are partially resolved, with $\lambda_{max.}$ at 720 nm and a shoulder at lower energy. This spectrum differs from both those of (**2f**) and (**2g**), which can be assumed as typical for the two limiting five-co-ordinate geometries, indicating that a distorted structure must be present in the complex with 6-7-5 chelate ring type. This interpretation is supported by the appearance of the frozen-solution e.s.r. spectrum of the complex, which is clearly rhombic in nature. The small value of the hyperfine coupling constant at lowest field ($A_1 = 0.0133$ cm^{-1}) and the considerably broadened (but unresolved) high-field component of the signal are typical signatures of e.s.r. spectra of five-co-ordinate complexes with geometry intermediate between square pyramidal and trigonal bipyramidal.[27] We note that the hyperfine coupling observed here is one of the lowest found for copper(II) complexes with sulphur-containing ligands.

Thus the behaviour of the copper(II) complexes with 6-7-5 chelate rings shows that when the alkyl chain between the imine and thioether donors in (**2**) becomes too long it is no longer possible for the sulphur atom to bond axially as in (**D**) or (**E**). The co-ordination set of the complex is forced into a distorted structure, two variants of which are depicted as (**G**) and (**H**).

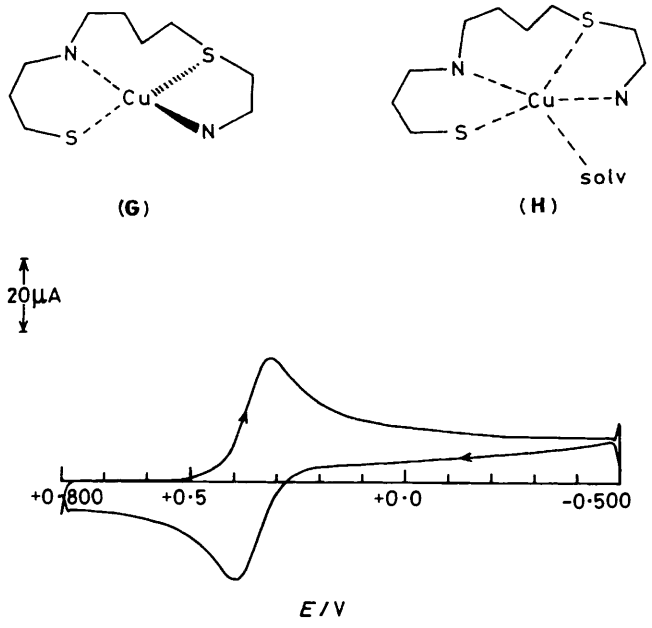


Figure 1. Cyclic voltammogram recorded at a platinum electrode in an acetonitrile solution containing complex (**2f**) (2.0×10^{-3} mol dm^{-3}) and $[NEt_4]ClO_4$ (0.1 mol dm^{-3}); scan rate 0.2 V s^{-1}

Both types of structures are accessible, due to the flexibility of the alkyl chain of the ligand carrying the thioether group, with a preference for (**H**) when there is little hindrance to the approach of a solvent molecule to the metal.

Electrochemistry.—The redox behaviour of the copper(II) complexes was preliminarily examined by cyclic voltammetry. Figure 1 shows the cyclic voltammetric response exhibited by complex (**2f**) in a deareated acetonitrile solution. One reduction peak occurs in the potential range from +0.8 to −0.5 V, with a directly associated reoxidation peak in the reverse scan. Controlled-potential coulometry at 0.0 V indicates that this reduction process involves the consumption of one electron per molecule of starting copper(II) complex.

Analysis of the cyclic voltammetric responses with scan rates varying from 0.02 to 51.2 V s^{-1} showed the following features; the anodic-to-cathodic peak current ratio (i_{pa}/i_{pc}) is constantly equal to 1; the difference between the potential of the anodic peak and that of the cathodic peak (ΔE_p) gradually increases from 72 to 428 mV; the ratio between the cathodic peak current and the square root of the scan rate ($i_{pc}v^{-\frac{1}{2}}$) is practically constant. All these data are diagnostic[28] for a simple quasi-reversible one-electron charge transfer. The average of the potentials of the cathodic and anodic peaks can be assumed as a good estimate of the formal electrode potential for the Cu^{II}–Cu^{I} couple which is +0.35 V *vs.* s.c.e. Under the same experimental conditions the ferrocenium–ferrocene reference couple is located at +0.38 V. Qualitatively similar results were obtained for the complexes (**2a**), (**2b**), and (**2e**).

The chemical reversibility of the Cu^{II}–Cu^{I} electron transfer in these four complexes has been tested by controlled-potential coulometry. After exhaustive one-electron electrolysis at 0.0 V, all the complexes exhibited cyclic voltammograms completely coincident with the starting ones, except for the inversion of response, which corresponds to an oxidation process. As a consequence of one-electron reduction, the complexes with (benzimidazolylmethylthio)ethylamine residues turn from green to yellowish maroon, while those with (benzimidazolylethylthio)ethylamine residues turn to reddish maroon. Exhaustive one-electron reoxidations at +0.7 V fully regenerate the starting green copper(II) complexes.

Table 3. Redox potentials (in V *vs.* s.c.e.) for the cathodic electron transfers of the copper(II) complexes in different solvents

	MeCN			dmf	
Complex	$E^{o\prime}$ (Cu^{II}–Cu^{I})	$\Delta E_p{}^a$/mV	$E_p{}^b$ (Cu^{I}–Cu^{0})	$E^{o\prime}$ (Cu^{II}–Cu^{I})	$\Delta E_p{}^a$/mV
(**2b**)	+0.34	118	−1.40	+0.34	160
(**2a**)	+0.24	108	−1.30	+0.24	102
(**2c**)	+0.35	127	−0.70	+0.32	147
(**2d**)				+0.33	200
(**2f**)	+0.35	80	−0.84	+0.33	140
(**2e**)	+0.23	122	−1.30	+0.24	160
(**2g**)	+0.33	100	−0.90	+0.30	96
(**2h**)				+0.34	250

[a] Measured at 0.2 V s^{-1}. [b] Peak potential at 0.2 V s^{-1} for irreversible processes.

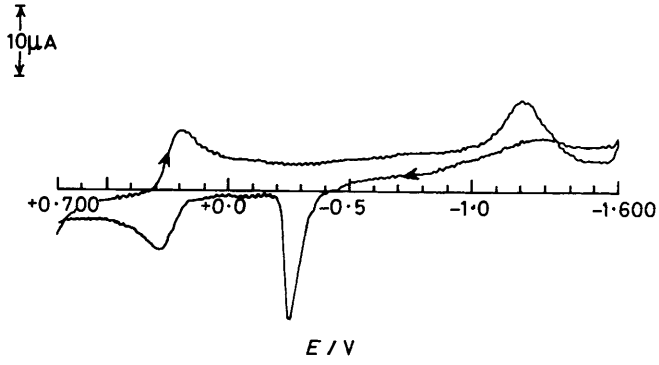


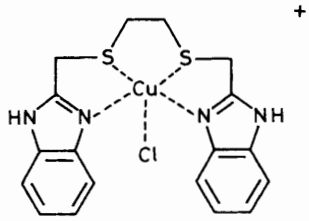
Figure 2. Cyclic voltammogram recorded at a platinum electrode in an acetonitrile solution containing complex (**2e**) (2.2×10^{-3} mol dm^{-3}) and $[NEt_4]ClO_4$ (0.1 mol dm^{-3}); scan rate 0.02 V s^{-1}

The electrochemistry of the complexes containing (benzimidazolylmethylthio)propylamine residues is less straightforward, since their acetonitrile solutions are stable only for a few minutes, so preventing macroelectrolysis tests. However, in cyclic voltammetry the $i_{pc}/(C_o v^{\frac{1}{2}})$ ratio for the cathodic response recorded immediately after the dissolution of the copper(II) complexes is comparable with those previously described for the Cu^{II}–Cu^{I} redox process, indicating also in this case the occurrence of an one-electron reduction.

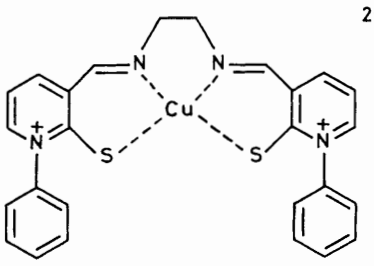
Finally, the complexes with (benzimidazolylmethylthio)-butylamine were quite intractable from the electrochemical viewpoint in acetonitrile solution because of the irreproducibility of the relevant responses likely due to rapid decomposition. It was however possible to obtain reliable cyclic voltammetric data for the Cu^{II}–Cu^{I} redox change in dimethylformamide solution, where the complexes are slightly longer lived.

All the copper(II) complexes exhibit a second cathodic step, attributable to the Cu^{I}–Cu^{0} redox change, lacking a directly associated response in the reverse scan because of the rapid demetallation following this second electron transfer. This is confirmed by the appearance of the characteristic stripping peak in the reverse scan due to the reoxidation of electrodeposited copper metal to free copper(I) ion, as shown in Figure 2 for complex (**2e**). An irreversible oxidation process is present at about +1.5 V for all the complexes. Comparison with the behaviour of the zinc complex (**3h**) allows this to be attributed to a ligand-centred process.

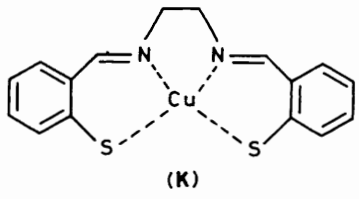
Table 3 summarizes the electrode potentials for the reduction



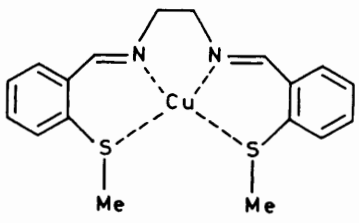
(I)



(J)



(K)



(L)

of the copper(II) complexes in acetonitrile and dimethylformamide solutions, together with the parameter ΔE_p at a constant scan rate for the Cu^{II}–Cu^{I} electron transfer; this can be assumed as a rough index of the degree of departure from electrochemical reversibility, considering that for a purely reversible one-electron charge transfer $\Delta E_p = 59$ mV is expected. It is likely that the quasi-reversibility of the electrode process is largely due to the stereochemical changes accompanying the Cu^{II}–Cu^{I} redox step, rather than to an intrinsic aspect of the heterogeneous charge transfer. In general, the change of solvent from acetonitrile to dimethylformamide appreciably reduces the degree of reversibility of the Cu^{II}–Cu^{I} reduction. In addition, there is no unequivocal trend in the apparent reorganizational barrier for the two groups of compounds. This confirms the well known difficulty in drawing quantitative conclusions on the structural rearrangements accompanying electron transfers based only on ΔE_p.[29] However, also the actual value of the thermodynamic parameter $E^{\circ\prime}$ is correlated to the stereochemical reorganization occurring during the reduction from copper(II) to copper(I).[14a] Assuming that in all cases the final copper(I) geometry is pseudo-tetrahedral, we can speculate that the highest structural barrier is experienced by the square-planar copper(II) compounds containing (benzimidazolylethylthio)ethylamine residues, whereas the reduction of all five-co-ordinate complexes, with (benzimidazolylmethylthio)-ethylamine, -propylamine, or -butylamine * residues, involves roughly the same reorganizational energy. In agreement with the spectral data, the nature (aliphatic or aromatic) of the substituent on the pyridine nitrogen atom does not affect appreciably the reduction potentials. This suggests no electronic conjugation of these groups with the CuN_2S_2 moiety.

Among the relatively high number of mononuclear copper(II) complexes having a N_2S_2 donor set studied electrochemically,[6b,9,14c,30] two can be correlated to the present series, (**I**) and (**J**). In acetonitrile the Cu^{II}–Cu^{I} redox change for (**I**) occurs at $E^{\circ\prime} = +0.37$ V,[30a] whereas that of (**J**) occurs at $E^{\circ\prime} = -0.17$ V[31] (in agreement with the value of -0.22 V found in dmf solution).[9] Complex (**I**) is five-co-ordinate and contains two thioether linkages, which markedly raise the reduction potential of the Cu^{II}–Cu^{I} couple,[6b,14c] while (**J**) is square planar and exhibits a reduction potential intermediate between those of the parent salicylaldimine complexes containing aromatic thiolates, (**K**) (-0.83 V),[30a] and thioether residues, (**L**) ($+0.42$ V).[6b] This shows that the pyridinium thiolate sulphur donor gives a contribution to the reduction potential of the Cu^{II}–Cu^{I} couple which is half-way between those of the thiolate and thioether sulphur. The main contributions to the relatively high redox potential of complexes (**2**) come, therefore, from their positive charge and the presence of a thioether sulphur donor, but also the benzimidazole and pyridinium thiolate groups are likely to contribute to the elevation of $E^{\circ\prime}$, since they can exert effective withdrawal of electron density from the metal through the extended π system.

Conclusions

The present investigation reports copper(II) complexes with new polyfunctional, non-symmetrical ligand molecules carrying N,S donor atoms which try to simulate the donor environment of the protein blue sites. Variations in the length of the carbon chains between the donor atoms produce remarkable changes in the structure of the complexes, as is clearly evidenced by their spectroscopic properties, and some significant distortion from regular geometries results for systems with 6-7-5 chelate rings. The redox potentials of the complexes are generally high, but they are clearly different for square-planar and five-co-ordinate complexes, the latter gaining a positive contribution of ≈ 0.1 V to $E^{\circ\prime}$ from geometric factors.[14b] It is interesting that the $E^{\circ\prime}$ values lie in the middle of the range spanned by the Type 1 sites of copper proteins (from $+0.18$ to $+0.78$ V *vs.* standard hydrogen electrode).[32]

The properties of complexes (**2**) suggest that further progress toward realistic models for the copper blue sites may be achieved with ligand systems containing (benzimidazolylmethylthio)butylamine residues, perhaps with more rigidity in the four-atom chain between the amino and thioether donors, condensed with aliphatic carbonyl thiols suitably substituted by bulky groups, in order sterically to hinder the intermolecular contact which is generally responsible for disulphide formation in synthetic copper(II) thiolate complexes. The synthesis of such carbonyl thiol compounds is in progress in our laboratory.

Acknowledgements

The authors thank the Italian Ministry of Education for financial support, M. Bonfà for recording n.m.r. spectra, and M. S. Franzoni for the magnetic susceptibilities.

* The electronic spectra of complexes (**2d**) and (**2h**) in dmf solution are quite similar, displaying a low-energy *d*–*d* band at 760—770 nm ($\varepsilon \approx 200$ dm^3 mol^{-1} cm^{-1}). The frozen-solution e.s.r. spectra of the two complexes in the same solvent are also very similar, but both show the presence of more than one species.

References

1 J. S. Thompson, T. J. Marks, and J. A. Ibers, *Proc. Natl. Acad. Sci. USA*, 1977, **74**, 3114; *J. Am. Chem. Soc.*, 1979, **101**, 4180; J. S. Thompson, J. L. Zitzmann, T. J. Marks, and J. A. Ibers, *Inorg. Chim. Acta*, 1980, **46**, L101.

2 J. M. Downes, J. Whelan, and B. Bosnich, *Inorg. Chem.*, 1981, **20**, 1081; J. Whelan and B. Bosnich, *ibid.*, 1986, **25**, 3671.

3 P. K. Bharadwaj, J. A. Potenza, and H. J. Schugar, *J. Am. Chem. Soc.*, 1986, **108**, 1351; E. John, P. K. Bharadwaj, J. A. Potenza, and H. J. Schugar, *Inorg. Chem.*, 1986, **25**, 3065.

4 P. M. Colman, H. C. Freeman, J. M. Guss, M. Murata, V. A. Norris, J. A. M. Ramshaw, and M. P. Venkatappa, *Nature (London)*, 1978, **272**, 319; E. T. Adman, R. E. Stenkamp, L. C. Sieker, and L. H. Jensen, *J. Mol. Biol.*, 1978, **123**, 35; E. T. Adman and L. H. Jensen, *Isr. J. Chem.*, 1981, **21**, 8; G. E. Norris, B. F. Anderson, and E. N. Baker, *J. Am. Chem. Soc.*, 1986, **108**, 2784.

5 J. L. Hughey IV, T. G. Fawcett, S. M. Rudich, R. A. Lalancette, J. A. Potenza, and H. J. Schugar, *J. Am. Chem. Soc.*, 1979, **101**, 2617.

6 (*a*) A. W. Addison and E. Sinn, *Inorg. Chem.*, 1983, **22**, 1225; (*b*) A. W. Addison, T. N. Rao, and E. Sinn, *ibid.*, 1984, **23**, 1957.

7 O. P. Anderson, C. M. Perkins, and K. K. Brito, *Inorg. Chem.*, 1983, **22**, 1267.

8 M. F. Corrigan, K. S. Murray, B. O. West, and J. R. Pilbrow, *Aust. J. Chem.*, 1977, **30**, 2455.

9 J. Becher, D. J. Brockway, K. S. Murray, P. J. Newman, and H. Toftlund, *Inorg. Chem.*, 1982, **21**, 1791.

10 P. Beardwood and J. F. Gibson, *J. Chem. Soc., Chem. Commun.*, 1983, 1099.

11 (*a*) J. Becher, H. Toftlund, and P. H. Olesen, *J. Chem. Soc., Chem. Commun.*, 1983, 740; (*b*) O. P. Anderson, J. Becher, H. Frydendahl, L. F. Taylor, and H. Toftlund, *ibid.*, 1986, 699; (*c*) H. Toftlund, J. Becher, P. H. Olesen, and J. Z. Pedersen, *Isr. J. Chem.*, 1985, **25**, 56; (*d*) J. Becher, H. Toftlund, P. H. Olesen, and H. Nissen, *Inorg. Chim. Acta*, 1985, **103**, 167.

12 (*a*) R. D. Bereman, M. R. Churchill, and G. Shields, *Inorg. Chem.*, 1979, **18**, 3117; (*b*) R. D. Bereman, G. D. Shields, J. Bordner, and J. R. Dorfman, *ibid.*, 1981, **20**, 2165.

13 L. Casella, *Inorg. Chem.*, 1984, **23**, 2782, 4781.

14 (*a*) H. Yokoi and A. W. Addison, *Inorg. Chem.*, 1977, **16**, 1341; (*b*) A. W. Addison, in 'Copper Coordination Chemistry: Biochemical and Inorganic Perspectives,' eds. K. D. Karlin and J. Zubieta, Adenine Press, New York, 1983, p. 109; (*c*) D. E. Nikles, M. J. Powers, and F. L. Urbach, *Inorg. Chem.*, 1983, **22**, 3210.

15 E. Sinn and C. M. Harris, *Coord. Chem. Rev.*, 1969, **4**, 391; R. C. Rosenberg, C. A. Root, P. K. Berstein, and H. B. Gray, *J. Am. Chem. Soc.*, 1975, **97**, 2092; Yu. V. Rakitin, R. D. Kasumov, G. V. Panova, I. M. Turovets, and V. T. Kalinnikov, *Zh. Neorg. Khim.*, 1981, **26**, 659; R. C. Elder, E. A. Blubaugh, jun., W. R. Heineman, P. J. Burke, and D. R. McMillin, *Inorg. Chem.*, 1983, **22**, 2777.

16 L. Casella, M. Gullotti, and R. Viganò, *Inorg. Chim. Acta*, 1986, **124**, 121.

17 P. Baumgarten, *Chem. Ber.*, 1924, **57**, 1622.

18 J. Becher and E. G. Frandsen, *Acta Chem. Scand., Ser. B*, 1976, **30**, 863.

19 F. E. King, R. M. Acheson, and P. C. Spensley, *J. Chem. Soc.*, 1949, 1401.

20 E. S. Milner, jun., S. Snyder, and M. M. Joullié, *J. Chem. Soc.*, 1964, 4151.

21 G. A. Jameson, *J. Org. Chem.*, 1963, **28**, 2397.

22 (*a*) J. V. Dagdigian and C. A. Reed, *Inorg. Chem.*, 1979, **18**, 2623; (*b*) J. V. Dagdigian, V. McKee, and C. A. Reed, *ibid.*, 1982, **21**, 1332.

23 (*a*) M. J. Schilstra, P. J. M. W. L. Birker, G. C. Verschoor, and J. Reedijk, *Inorg. Chem.*, 1982, **21**, 2637; (*b*) F. J. Rietmeijer, P. J. M. W. L. Bircher, S. Gorter, and J. Reedijk, *J. Chem. Soc., Dalton Trans.*, 1982, 1191; (*c*) A. W. Addison, T. N. Rao, J. Reedijk, J. Van Rijn, and G. C. Verschoor, *ibid.*, 1984, 1349.

24 (*a*) B. J. Hathaway, R. J. Dudley, and P. J. Nicholls, *J. Chem. Soc. A*, 1969, 1845; (*b*) B. J. Hathaway, I. M. Procter, R. C. Slade, and A. A. G. Tomlinson, *ibid.*, p. 2219; (*c*) B. J. Hathaway and D. E. Billing, *Coord. Chem. Rev.*, 1970, **5**, 143; (*d*) J. B. Hathaway, *Struct. Bonding (Berlin)*, 1984, **57**, 55.

25 D. R. McMillin, R. S. Drago, and J. A. Nusz, *J. Am. Chem. Soc.*, 1976, **98**, 3120; B. B. Wayland and V. K. Kapur, *Inorg. Chem.*, 1974, **13**, 2517; T. Kogane, R. Hirota, K. Abe, and M. Hirota, *J. Chem. Soc., Perkin Trans. 2*, 1981, 652.

26 R. Barbucci and M. J. M. Campbell, *Inorg. Chim. Acta*, 1975, **15**, L15; R. Barbucci, A. Bencini, and D. Gatteschi, *Inorg. Chem.*, 1977, **16**, 2117; A. W. Addison, H. M. J. Hendriks, J. Reedijk, and L. K. Thompson, *ibid.*, 1981, **20**, 103; K. Takahashi, E. Ogawa, N. Oishi, Y. Nishida, and S. Kida, *Inorg. Chim. Acta*, 1982, **66**, 97.

27 A. Bencini, I. Bertini, D. Gatteschi, and A. Scozzavafa, *Inorg. Chem.*, 1978, **17**, 3194; I. Bertini and A. Scozzafava, *Met. Ions Biol. Syst.*, 1981, **12**, 31; L. Casella, M. Gullotti, C. Pessina, and A. Pintar, *Gazz. Chim. Ital.*, 1986, **116**, 41.

28 E. R. Brown and J. R. Sandifer, in 'Physical Methods of Chemistry. Electrochemical Methods,' eds. B. W. Rossiter and J. F. Hamilton, Wiley, New York, 1986, vol. 2, ch. 4.

29 W. E. Geiger, *Prog. Inorg. Chem.*, 1985, **33**, 275.

30 (*a*) G. S. Patterson and R. H. Holm, *Bioinorg. Chem.*, 1975, **4**, 257; (*b*) E. R. Dockal, T. E. Jones, W. F. Sokol, R. J. Engerer, D. B. Rorabacher, and L. A. Ochrymowycz, *J. Am. Chem. Soc.*, 1976, **98**, 4322; (*c*) U. Sakaguchi and A. W. Addison, *J. Chem. Soc., Dalton Trans.*, 1979, 600; (*d*) R. G. Brubaker, J. N. Brown, M. K. Yoo, A. R. Kinsey, T. M. Kutchan, and E. A. Mottel, *Inorg. Chem.*, 1979, **18**, 299; (*e*) K. D. Karlin, P. L. Dahlstrom, J. R. Hyde, and J. Zubieta, *J. Chem. Soc., Chem. Commun.*, 1980, 906; (*f*) A. Cinquantini, R. Cini, R. Seeber, and P. Zanello, *J. Electroanal. Chem.*, 1981, **121**, 301; (*g*) J. P. Gisselbrecht and M. Gross, *Adv. Chem. Ser.*, 1982, **201**, 109; (*h*) J. Dorfman, R. D. Bereman, and M-H. Whangbo, ref. 14*b*. p. 75; (*i*) J. Zubieta, K. D. Karlin, and J. C. Hayes, *ibid.*, p. 97; (*j*) D. B. Rorabacher, M. J. Martin, M. J. Koenigbauer, M. Malik, R. R. Schroeder, J. F. Endicott, and L. A. Ochrymowycz, *ibid.*, p. 167; (*k*) N. Aoi, G. Matsubayashi, and T. Tanaka, *J. Chem. Soc., Dalton Trans.*, 1983, 1059; (*l*) L. Siegfried and T. A. Kaden, *Helv. Chim. Acta*, 1984, **67**, 29; (*m*) K. P. Balakrishnan, T. A. Kaden, L. Siegfried, and A. D. Zuberbühler, *ibid.*, p. 1060; (*n*) N. Aoi, G. Matsubayashi, T. Tanaka, and K. Nakatsu, *Inorg. Chim. Acta*, 1984, **85**, 123; (*o*) M. F. Cabral, J. de O. Cabral, J. Van Rijn, and J. Reedijk, *ibid.*, **87**, 87; (*p*) Y. Nishida, M. Takeuchi, N. Oishi, and S. Kida, *ibid.*, 1985, **96**, 81; (*q*) T. A. Kaden, S. Kaderli, W. Sager, L. C. Siegfried-Hertli, and A. D. Zuberbühler, *Helv. Chim. Acta*, 1986, **69**, 1216.

31 L. Casella, M. Gullotti, and P. Zanello, unpublished work.

32 B. Reinhammar and B. G. Malmström, in 'Copper Proteins,' ed. T. G. Spiro, Wiley, New York, 1981, p. 109; T. Sakurai, H. Okamoto, K. Kawahara, and A. Nakahara, *FEBS Lett.*, 1982, **147**, 220; K. O. Burkey and E. Gross, *Biochemistry*, 1981, **20**, 5495; V. T. Taniguchi, B. G. Malmström, F. C. Anson, and H. B. Gray, *Proc. Natl. Acad. Sci. USA*, 1982, **79**, 3387.

Received 11*th May* 1988; *Paper* 8/01850B