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ARTICLE

Copper hydrotris(3,5-diphenylpyrazolyl)borate dithiocarbamates: mimicking green copper proteins

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Three novel copper hydrotris(3,5-diphenylpyrazolyl)borate (Tp^{Ph2}) dithiocarbamate complexes, [Tp^{Ph2}Cu(dtc)] (dtc = S_2CNEt_2 **1**, S_2CNBz_2 **2** and $S_2CN(CH_2)_4$ **3**) have been prepared in a simple one pot reaction by sequential addition of KTp^{Ph2} and Na(dtc) to $CuCl_2 \cdot 2H_2O$. IR, UV-Vis and ESR spectroscopic studies suggest a mostly κ^3 coordinated Tp^{Ph2} ligand, bidentate dithiocarbamate ligands and therefore, a five coordinate copper centre. Unusually, a κ^3 to κ^2 isomerisation of the Tp^{Ph2} ligand is found in solution in **3** and to a lesser extent in **1**. The X-ray crystal structures reveal geometries intermediate between trigonal bipyramidal and square pyramidal depending on the steric bulk of the dithiocarbamate ligand and a long Cu-N bond resulting in an asymmetrically bound Tp^{Ph2} ligand. Electrochemical studies reveal quasi-reversible one-electron oxidation and reduction to Cu(I) with the reversibility and reduction potential strongly dependent on the dithiocarbamate. DFT calculations reveal a weakly antibonding Cu-S π^* SOMO and a strongly antibonding Cu-S σ^* LUMO consistent with the significant effect of the dithiocarbamate ligand on the electrochemical behaviour of these complexes.

Introduction

Blue copper proteins are amongst the most widely studied proteins in chemistry.[1–4] They are very efficient electron transfer proteins and play a critical role in many enzymatic processes.[1–4] Two of the most common proteins belonging to this family are plastocyanin and azurin. Both proteins exhibit an intense ligand-to-metal charge transfer band at *ca*. 600 nm making the proteins blue in colour hence their name. In the case of plastocyanin, the copper centre is four coordinate with two histidine ligands, a short Cu-S cysteine bond and a long Cu-S bond to a neutral methionine residue leading to a trigonally distorted tetrahedral centre.[5] In contrast, azurin is five coordinate with an additional glycine residue weakly bound to the Cu centre through a carbonyl oxygen.[6–8] The increase in coordination number results in a distorted trigonal bipyramidal geometry with the histidines and cysteine occupying the trigonal plane and the methionine and glycine axially coordinated. The fact that both of these axial ligands are weakly bound (Cu-S(Met) ≈ 3.2 Å, Cu-O(Gly) ≈ 2.9 Å) results in a short Cu-S bond (ca. 2.1 Å) and is directly responsible for the blue colour of this protein.[6] Indeed, studies on modified azurins have shown that introduction of a better donor in the axial position results in a decrease in the S (p_π)-to-Cu^{2+} LMCT band

at *ca*. 600 nm and a concomitant increase in a new band at *ca*. 400 nm assigned to a S (p_σ)-to-Cu^{2+} LMCT band and a change in colour to form so-called green copper proteins.[9–11] This change in colour has been ascribed by Solomon and co-workers to a 'coupled distortion' model.[12] According to the model, distortion at the copper centre towards a more tetragonal structure results in more effective overlap of the d_{x2-y2} orbital with the S σ orbital and consequently a more intense band at *ca*. 400 nm.[13,14] Several green copper proteins are known with the best studied being nitrite reductase.[15]

In order to better understand blue copper proteins two families of model complexes have been prepared which closely mimic that of native copper blue enzymes.[16,17] Of particular relevance to the current work are the hydrotris(pyrazolyl)borate series investigated by amongst others Solomon and Fujisawa, [Tp^RCuSAr] (Tp^R = substituted hydrotris(pyrazolyl)borate; Ar = aryl).[18] Although they possess a N_3S donor set rather than the N_2S_2 donor set of the native enzyme one of the pyrazolyl arms is only weakly bound to the Cu centre and thus mirrors that of the methionine donor in plastocyanin.[16,17] The electronic spectral properties also closely resemble those of the enzyme and have provided significant insight into the nature of the Cu-S bond.[18]

Despite the success of Tp^R ligands in modeling plastocyanin their use in the modeling of azurin has not been reported to date. We have recently prepared a series of nickel and cobalt dithiocarbamate complexes supported by the electron poor Tp^{Ph2} ligand finding that the dithiocarbamate and in the case of cobalt the Tp^{Ph2} ligand are bound asymmetrically.[19] We hypothesized that an asymmetrically bound Tp^{Ph2} and dithiocarbamate ligand should allow us to mimic some features of the azurin active site. In this paper we report the synthesis, structural and electrochemical studies of $[Tp^{Ph2}Cu(dtc)]$ (dtc = S_2CNEt_2 **1**, S_2CNBz_2 **2** and $S_2CN(CH_2)_4$ **3**) and rationalize our results with DFT calculations.

Results and Discussion

Synthesis and basic characterization of $[Tp^{Ph2}Cu(dtc)]$

The reaction of $CuCl_2 \cdot 2H_2O$ with KTp^{Ph2} yields the intermediate $[Tp^{Ph2}CuCl]$ as a green solution. Subsequent addition of Na(dtc) results in a gradual change in colour to dark green and after work-up the compounds $[Tp^{Ph2}Cu(dtc)]$ (dtc = S_2CNEt_2 **1**, S_2CNBz_2 **2** and $S_2CN(CH_2)_4$ **3**; Scheme 1) are isolated in good yields. $[Tp^{Ph2}CuCl(MeOH)]$ was used as an intermediate as the isolated complex from this reaction is $[Tp^{Ph2}CuCl(Hpz^{Ph2})]$ formed as a result of decomposition of the Tp^{Ph2} ligand.[20] This latter complex proved to be less suitable for use as a starting material with lower yields in all cases.
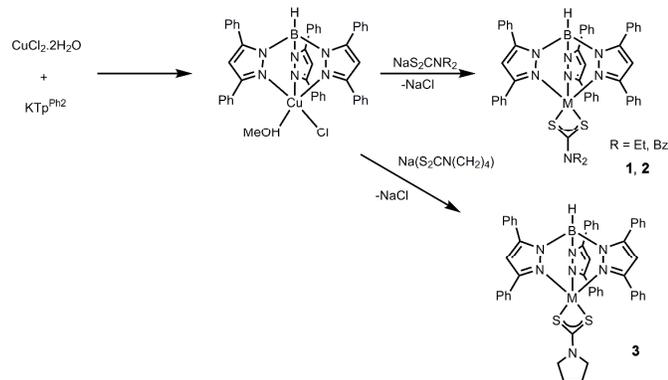
Scheme 1 Synthesis of **1-3**.

IR spectroscopic studies of **1-3** reveal B-H stretches between 2619-2586 cm^{-1} and consistent with κ^3 coordinated Tp^{Ph2} (Table 1). Similar bands have been observed for other five coordinate $[Tp^{Ph2}CuL]$ compounds.[19–22] Examining the dithiocarbamate stretches we find that the C-N stretch is observed at 1478-1503 cm^{-1} and indicative of a bidentate coordination mode.[23] This is approximately 20 cm^{-1} higher than the corresponding $[Tp^{Ph2}M(dtc)]$ (M = Co, Ni) complexes.[19] In addition, there is a concomitant decrease in the energy of the C-S stretch this time by 5-10 cm^{-1}. The changes in the C-N and C-S stretches suggest a greater prevalence of the thioureide resonance form in the case of the copper complexes.

Table 1 Spectroscopic data for $[Tp^{Ph2}Cu(dtc)]$ **1-3**.

Complex	IR $(cm^{-1})^a$			UV-Vis (nm, ε)
	vBH	vCN	vCS	
1	2619	1478	1008	417 (4,880), 664 (373)
2	2613	1503	997	428 (12,900), 580sh (780)
3	2586	1481	1009	430 (25,200), 620sh (1,650)

^{a}As KBr discs

Following ESR spectroscopic studies (*vide infra*) we undertook solution IR spectroscopic studies for **3** in CH_2Cl_2. The solution initially contains a single band at 2593 cm^{-1} but after 10 minutes a small band is observed at 2522 cm^{-1} consistent with the Tp^{Ph2} ligand being κ^2 coordinated (see Figure S1).[24] This suggests that in solution, **3** exists as a mixture of κ^3 and κ^2 species (Figure 1). The low intensity of the peak at 2522 cm^{-1} indicates that the equilibrium lies towards the five coordinate κ^3 complex, a fact confirmed by UV-Vis and ESR spectroscopic studies.

κ^3-Tp^{Ph2} κ^2-Tp^{Ph2}

v_{BH} = 2593 cm^{-1} v_{BH} = 2522 cm^{-1}
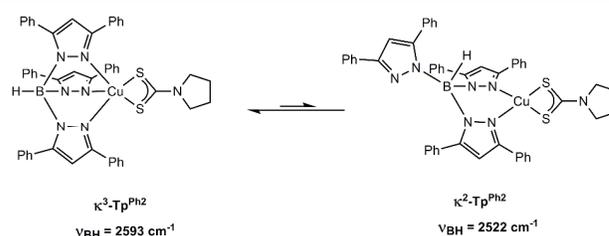
Figure 1 κ^3 to κ^2 isomerisation in $[Tp^{Ph2}Cu(S_2CN(CH_2)_4)]$ **3** (values in CH_2Cl_2).

Although, no identical system exists in Cu(II) Tp^R chemistry κ^2-κ^3 isomerisation is known in $[Tp^{Me2}RhL(CO)]$ (Tp^{Me2} = hydrotris(3,5-dimethylpyrazolyl)borate, L = phosphine) and $[Tp^{iPr2}Rh(nbd)]$ (nbd = norbornadiene) with the balance between the isomers so fine in the latter case that both isomers crystallize in the same unit cell.[24–26] Moreover, using a modified Tp ligand, $PhB(3-C_2F_2pz)_3$ ($3-C_2F_5pz$ = 3-penta-fluoroethylpyrazole) κ^2-coordinated $PhB(3-C_2F_2pz)_3$ is found in the Cu(I) complex, $[\{PhB(3-C_2F_2pz)_3\}Cu(\eta^2-H_2C=CH_2)]$.[27]

The UV-Vis spectra were recorded in CH_2Cl_2 and are shown in Figure 2. The spectra are dominated by a single intense band at *ca*. 430 nm. By comparison with other five coordinate copper compounds this is assigned to a S (p_σ)-to-Cu^{2+} LMCT band.[9,28,29] In contrast, azurin absorbs at 628 nm making the protein appear blue. The presence of a stronger band at higher energy in **1-3** in solution is due to stronger axial coordination to the Cu^{2+} centre (and thus more effective overlap of the d_{x2-y2} orbital with the S σ orbital) rather than the very weak axial bonds found in azurin (Cu-S(met) = 3.26 Å and Cu-O(gly) = 2.94 Å), which favours overlap with the S π orbital. Indeed, studies on variants of azurin with stronger donor amino acids have shown transformation of the blue copper protein into a green copper protein. However, there are weaker bands found at 580-664 nm which may assigned to a S (p_π)-to-Cu^{2+} LMCT band.[9,28,29] It is noteworthy that the position and intensity of the band is strongly dependent on the dithiocarbamate ligand increasing in the order **1** < **2** < **3**. A similar shift in the charge

transfer bands is noted in [Tp^{Ph2}Ni(dtc)], although for the nickel compounds the intensity of the transition among these compounds is essentially the same. The presence of small amounts of the κ^2 complex in the case of **3** may also influence the intensity of this band. Particularly striking is the increase in the intensity of the band at 430 nm compared with [Tp^{Ph2}Ni(dtc)] by a factor of *ca*. 10.[19] Interestingly, there is also a significant increase in intensity in the S (p$_\pi$)-to-Cu^{2+} LMCT band on moving from Ni to Cu in the [Tp^{i-Pr2}M(SC$_6$F$_5$)] series.[18] There are no obvious features in the spectra above 750 nm consistent with the results reported by Solomon *et al*. for [Tp^{iPr2}Cu(SMeIm)] (SMeIm = 1-methylimidazole-2-thiolate).[29]
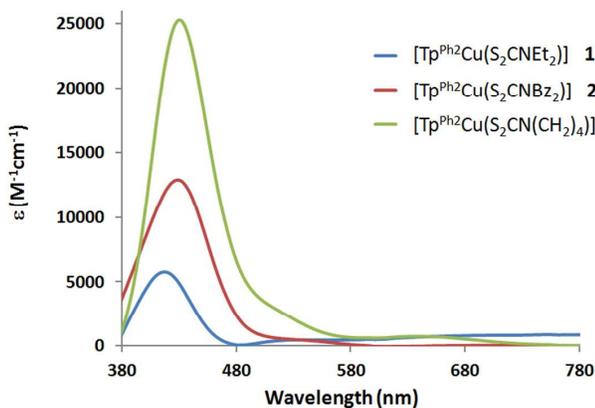
Figure 2 UV-Vis spectra of [Tp^{Ph2}Cu(dtc)] **1-3**.

Structural studies of [Tp^{Ph2}Cu(dtc)]

The compounds have been crystallized from CH$_2$Cl$_2$/hexane and their structures determined by X-ray crystallography. Crystallographic data are presented in Tables 2 and 3 while Figure 3 shows the structure of **3** as a representative example (Figures S2 and S3 for **1** and **2**, respectively are contained in the ESI). The structures are all broadly similar with a five coordinate Cu centre. The geometry around the copper centre is subtly different for the complexes with **1** and **3** slightly closer to a square pyramidal geometry while **2** is closer to a trigonal bipyramidal geometry; τ = 0.39, 0.55 and 0.39 for **1**, **2**, and **3**, respectively.[30] In these structures, S1, S2, N3 and N5 define the basel plane while N1 is in the apical position. In the case of [Tp^{Ph2}Cu(S$_2$CNBz$_2$)], N1, N5 and S2 are in the equatorial positions while N3 and S1 occupy the axial positions with this geometry preferred probably due to the greater steric bulk of the benzyl substituents. Similar distortion parameters have been reported in the related Co and Ni complexes (τ = 0.40-0.46), although none of these structures contains the dibenzyldithiocarbamate ligand.[19] Very recently, the structure of [Tp^{Me2}Cu(S$_2$CNEt$_2$)] was reported and also displays a square pyramidal geometry (τ = 0.37) which is similar to **1-3** despite the different Tp^R ligands.[31] The only other crystallographically characterized Cu(II) Tp^R complex with an N$_3$S$_2$ donor set is [Cu(Tp$^{Ph-2-SMe}$)]$^+$ (Tp$^{Ph-2-SMe}$ = hydrotris[3-2-(methylsulfanyl)-

phenylpyrazol-1-yl]borate) which also has a square pyramidal geometry (τ = 0.15).[32]

Table 2 Bond lengths and angles for [Tp^{Ph2}Cu(dtc)] **1-3** (Å, °).

	1	2	3
Cu-N1	2.236(3)	2.236(4)	2.235(3)
Cu-N3	2.047(3)	2.024(4)	2.040(3)
Cu-N5	2.038(3)	2.058(4)	2.031(3)
Cu-S1	2.331(1)	2.336(2)	2.340(1)
Cu-S2	2.327(1)	2.312(2)	2.321(1)
S1-Cu-S2	75.65(4)	75.97(5)	76.13(3)
N1-Cu-S1	97.37(8)	96.2(1)	111.88(7)
N1-Cu-S2	113.95(8)	123.3(1)	95.55(7)
N3-Cu-S1	174.89(8)	175.2(1)	152.86(8)
N3-Cu-S2	101.18(8)	99.2(1)	96.56(8)
N5-Cu-S1	95.56(8)	95.7(1)	100.76(8)
N5-Cu-S2	151.46(8)	142.0(1)	176.39(8)
N1-Cu-N3	87.6(1)	86.7(2)	94.7(1)
N1-Cu-N5	93.9(1)	94.2(2)	87.3(1)
N3-Cu-N5	85.4(1)	87.9(2)	85.4(1)

In contrast to [Tp^{Ph2}M(dtc)] (M = Co, Ni), one of the Cu-N bond lengths is *ca*. 0.2 Å longer than the other two indicating that the Tp^{Ph2} ligand is asymmetrically coordinated.[19] Similar observations have been made concerning other five coordinate [Tp^{R}Cu(L)] complexes and are consistent with complete occupation of the d$_{z2}$ orbital.[20,21,29] The Cu-S bond lengths are *ca*. 0.07 Å shorter on average than the Ni compounds and consistent with the different ionic radii of Ni(II) and Cu(II). Moreover, the Cu-S bond lengths are more typical of a type 2 Cu centre (Cu-Cys 2.29 Å).[1] Surprisingly, the dithiocarbamate ligands are essentially symmetrically bound in all complexes while in the analogous Co and Ni systems the ligands are asymmetrically bound.[19]
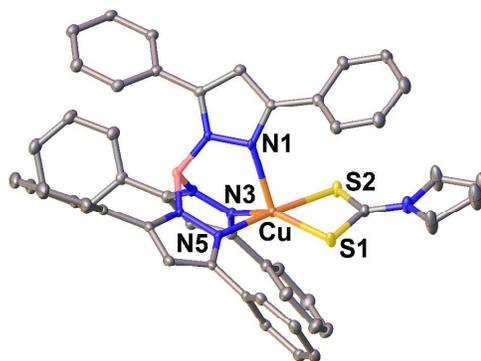
Figure 3 Structure of [Tp^{Ph2}Cu(S$_2$CN(CH$_2$)$_4$)] **3**. Hydrogen atoms are omitted and only selected atoms labelled in the interests of clarity.

In addition, the S-Cu-S bite angles are 75.7, 76.0 and 76.5° and slightly larger than those found in [Tp^{Ph2}M(dtc)] (M = Co, Ni) consistent with the shorter M-S bond lengths in the Cu(II) compounds. Overall, as planned one of the pyrazolyl donors of the Tp^{Ph2} ligand is coordinated loosely to the Cu centre mimicking the weakly coordinated glycine residue in azurin. Sadly, the dithiocarbamate ligand does not coordinate

asymmetrically and thus the coordination environment more closely resembles so-called green copper proteins than azurin.

Table 3 Crystallographic data and structure refinement parameters for **1-3**.

	1	**2**	**3**
Formula	$C_{50}H_{44}BCuN_7S_2$	$C_{60}H_{48}BCuN_7S_2$	$C_{50}H_{42}BCuN_7S_2$
Molecular weight / gmol^{-1}	881.39	1005.52	879.38
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$
a / Å	13.9619(7)	17.804(5)	13.9204(14)
b / Å	25.3276(14)	18.099(5)	25.042(3)
c / Å	12.5670(6)	17.810(5)	12.6285(13)
α / °	90	90	90
β / °	104.037(3)	119.686(6)	102.523(2)
γ / °	90	90	90
T / K	100(2)	150(2)	100(2)
Cell volume / Å^3	4311.3(4)	4986(2)	4297.4(8)
Z	4	4	4
Absorption coefficient / mm^{-1}	0.649	0.570	0.651
Reflections collected	40791	41115	25061
Independent reflections, R_{int}	9752, 0.0899	11407, 0.1298	8000, 0.0655
Max. and min. transmission	0.9808 and 0.7953	0.9452 and 0.8297	0.8809 and 0.7368
Restraints/ parameters	0/552	507/640	416/550
Final R indices [$I>2\sigma(I)$]: R_1, wR_2	0.0601, 0.1773	0.0689, 0.2489	0.0448, 0.1717

ESR spectroscopic studies of [Tp^{Ph2}Cu(dtc)]

ESR spectra of **1-3** were recorded in CH_2Cl_2 at 295 K and also in frozen CH_2Cl_2 at 150 K. The isotropic spectra are shown in Figure 4 with anisotropic spectra in the supporting information (Figure S4). ESR parameters at 295 and 150 K in solution and as a glass are given in Table 4. The spectra of **1-3** display four well resolved lines consistent with hyperfine coupling to ^{63}Cu and ^{65}Cu (I = 3/2).[20,21] There is also hyperfine coupling to the N atoms of the Tp^{Ph2} ligand on the m_I = -3/2 line. Similar observations have been made concerning a range of five coordinate [Tp^{R}CuX(Hpz^R)] (X = Cl, OAc) complexes and [Tp^{iPr2}Cu-(SMeIm)] suggesting that the structure found in the crystallographic studies is preserved in solution.[20,21,29] It should be noted that the spectrum of **3** contains an additional species at higher field consistent with the four coordinate κ^2 species observed in the IR spectroscopic studies. Moreover, integration of the spectra clearly indicate that there are only 2 species in solution in **3** and a single species for **1** and **2** (Figure S5). We have also explored the effect of time on the spectrum of **3** and find that the equilibrium is rapid being reached after 10 minutes and then remaining unchanged even after 4 hours (Figure S7). However, changing the concentration does result in a change in the spectrum further supporting the proposed κ^3 to κ^2 isomerisation (Figure S8). We hypothesize that as the concentration increases the individual molecules become closer allowing formation of favourable interactions but only if the Tp^{Ph2} ligand becomes κ^2-coordinated.

Table 4 ESR parameters for **1-3** at 295 and 150 K.

	g	A ^{63,65}Cu x 10^4 (cm^{-1})	A ^{14}N x 10^4 (cm^{-1})
1	2.085 (g_{iso})	70	7
	2.18 ($g_\parallel$)	145 ($A_\parallel$)	-
	2.03 ($g_\perp$)		
2	2.086 (g_{iso})	70	7
	2.18 ($g_\parallel$)	140 ($A_\parallel$)	-
	2.03 ($g_\perp$)		
3^a	2.085 (g_{iso})	73	7
	2.19 ($g_\parallel$)	150 ($A_\parallel$)	-
	2.03 ($g_\perp$)		

^{a} Simulated ESR spectra at 295 K may be found in the ESI (Figure S6)

While an exactly similar system is not known in Cu(II) Tp^R chemistry, [Cu(Br^{Mes}pz^{o-Py})$_2$]$_2$ (hydro[bis(4-mesityl-3-methyl-thioxotriazolyl)-3-(2-pyridyl)pyrazolyl]borate) exists as a S_2N_2 bonded dimer in the solid state with two thioxotriazolyl donors from one ligand and a pyrazolyl and pyridyl donor from an another Br^{Mes}pz^{o-Py} ligand.[33] In solution this dimer is fluxional with an equilibrium between the S_2N_2 and S_2N Cu coordinated dimers in which the pyridyl ligand in the latter dimer is now non-bonded to the Cu centre. It follows that a similar situation may occur in **3**.
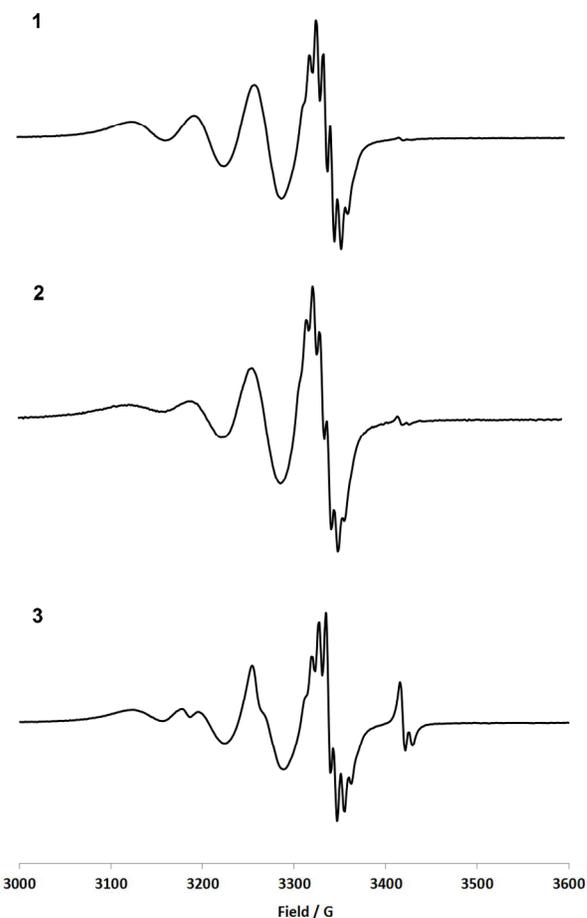
Figure 4 ESR spectra of **1**, **2** and **3** in CH_2Cl_2 at 295 K.

The spectra are similar to those previously reported for [Cu(dtc)$_2$][34] and [Cu(dtc)(S$_2$P(i-Pr)$_2$)][35] and suggest that the

SOMO is likely to be Cu and dithiocarbamate based, a fact later confirmed by DFT calculations.

The ESR spectra of the samples at 150 K in CH_2Cl_2 reveal pseudo-axial symmetry and are characteristic of a tetragonal $\{d_{x2-y2}\}^1$ electronic structure in line with the structural studies above. Although the g values for **1-3** are broadly similar to azurin (g_z = 2.262, g_y = 2.056, g_x = 2.042), the hyperfine coupling to ^{63,65}Cu in **1-3** varies from 140-150 G and is typical of 'normal' Cu(II) and very much larger than that of azurin (A_z = 59 G) consistent with the stronger Cu-S bonds found in **1-3**. It is also important to note that the spectra are now virtually identical and clearly indicate that the higher field species in the room temperature spectrum of **3** is converted to a single five coordinate species at 150 K consistent with the proposed κ^3 to κ^2 isomerisation of the Tp^{Ph2} ligand and ruling out any possible impurity in the sample.

Electrochemical studies of [Tp^{Ph2}Cu(dtc)]

The native azurin copper enzyme has a reversible well defined Cu$^{II/I}$ redox couple at ca. 0.27 V (NHE).[1] In view of this we investigated the redox properties of these model complexes in CH_2Cl_2 using cyclic voltammetry. Representative cyclic voltammograms are shown in Figure 5 with data for the compounds given in Table 5. All the compounds exhibit a reversible one-electron oxidation which is tentatively assigned to oxidation of the coordinated dithiocarbamate ligand oxidation of the coordinated dithiocarbamates based on computational studies (*vide infra*). For **1-3** the redox couple is observed between 0.76-0.80 V and is consistent with the relatively minor alterations in the dithiocarbamates in this series. Compared with [Cu(S$_2$CNEt$_2$)$_2$], **1** is found to be 0.65 V harder to oxidize consistent with the presence of the more electron poor Tp^{Ph2} ligand.[36]

Interestingly, the CVs of **1** and **3** include a small peak at *ca.* 0.50 V which based on the IR and ESR spectroscopic studies is assigned to the κ^2 coordinated isomer. The fact that this is absent in **2** clearly indicates that the κ^3 to κ^2 isomerisation is very sensitive to the electronic properties of the R groups on the dithiocarbamate as would be expected in such an isomerisation process. The presence of a significant peak at 0.50 V in the case of **1** is unexpected as ESR and UV-Vis spectroscopic studies both suggest that there is very little of the κ^2 species. This apparent inconsistency is probably due to the electrolyte used in the electrochemical studies. As Gieger and co-workers have shown electrolytes can affect the position of the redox potentials and in our system it's not unreasonable to suppose that it may affect the relative stability of the two isomers in **1**.[37]

Table 5 Electrochemical data for **1-3**.

	Oxidation (E$_{½}$, V)	Cu^{2+} / Cu^{+} (V)
1	0.77	-1.02(I)^a
2	0.80	-1.01(I)^a
3	0.76	-0.90(I)

^{a} (I) = Irreversible.

A reduction peak is observed for all compounds between 0.90-1.02 V. By comparison with [Cu(S$_2$CNEt$_2$)$_2$], where reduction occurs at -0.86 V, this peak is assigned to reduction to Cu(I). The peak is much lower than that observed for azurin and reflects the strongly electron donating character of the dithiocarbamate ligand and the five coordinate Cu centre in **1-3** compared with the more trigonal planar environment found in azurin.
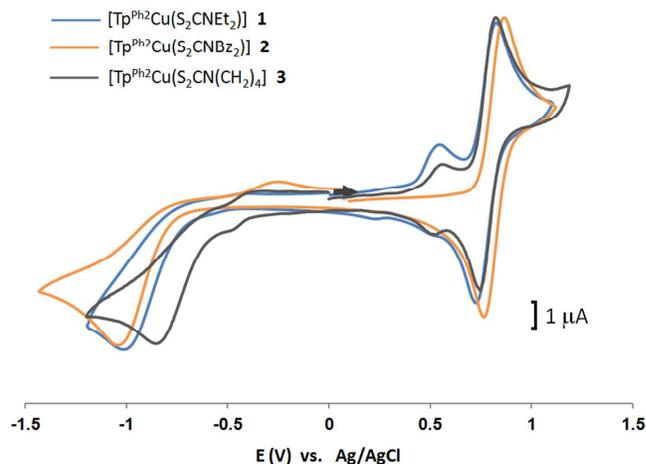
Figure 5 Cyclic voltammograms of **1-3** in CH_2Cl_2 at 100 mV/s.

DFT calculations of [Tp^{Ph2}Cu(dtc)]

DFT calculations were performed on all the complexes to try to better understand the electronic structure of **1-3**. All calculations were performed using the Gaussian 03 software package[38] with the B3LYP functional and a 6-31G** or SDD basis set. Computed bond lengths and those found in the X-ray crystal structure are shown in Table 6. Comparing the SDD and 6-31G** basis sets we find that the latter is better with a mean standard deviation of 0.066 and 0.041 Å, respectively and thus the following discussion will focus on the 6-31G** basis set. The axial Cu-N distances differs from that found experimentally by between 0.069 – 0.097 Å. Similar discrepancies have been noted in modelling the related four coordinate [Tp^{i-Pr2}Cu(SC$_6$F$_5$)] complexes and simply reflect the weakness of this Cu-N interaction and the comparatively small energy difference between structures even when the Cu-N bond length increases by 0.1 Å.[18] Interestingly, the Cu-S bond lengths are overestimated by as much as 0.08 Å but are consistent with the deviations reported in the analogous Co and Ni complexes, [Tp^{Ph2}M(dtc)].[19] Moreover, the dithiocarbamate ligands are computed to coordinate symmetrically just as is found in the crystal structures. Overall, the DFT calculations adequately model the complexes.

The SOMO for each complex is essentially identical, with **1** shown in Figure 6 as a representative example. The SOMO is found to be a weakly antibonding Cu dπ*-S interaction constructed from an asymmetric combination of the S p$_z$ orbitals and a Cu d$_{xz}$ orbital. The metal only contributes *ca.* 10

% to this orbital with electron density mostly present on the S atoms. Interestingly, a similar Cu-S π* interaction is found in azurin also with significant delocalization of electron density onto the cysteine residue.[39]

Table 6 Computed and X-ray crystallographically determined bond lengths for [Tp^{Ph2}Cu(dtc)] (Å).

	1^a	2^a	3^a
Cu-N1	2.236(3)	2.236(4)	2.235(3)
	2.139	2.159	2.166
Cu-N3	2.047(3)	2.024(4)	2.040(3)
	2.047	2.046	2.047
Cu-N5	2.038(3)	2.058(4)	2.031(3)
	2.072	2.059	2.050
Cu-S1	2.331(1)	2.336(2)	2.340(1)
	2.397	2.399	2.404
Cu-S2	2.327(1)	2.312(2)	2.321(1)
	2.399	2.394	2.400

^{a} Computed values using a B3LYP functional and a 6-31G* basis set are shown beneath the experimentally observed values.

For **1-3**, this delocalization may explain why the dithiocarbamate is found to influence the electrochemical behaviour and in particular the presence of peaks due to the κ^3 and κ^2 species in **1** and **3**. In contrast, in the related Co and Ni complexes the SOMO is a strong antibonding M-S σ* bond. However, this is consistent with the findings of Fujisawa *et al.* for [Tp^{iPr2}M(SC$_6$F$_5$)] where there is an increasing π contribution on going from Mn(II) to Cu(II).[18]
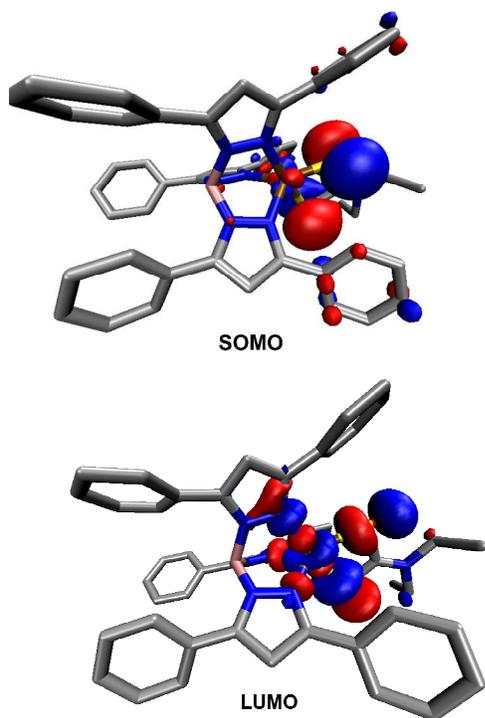
SOMO

LUMO

Figure 6 SOMO and LUMO of [Tp^{Ph2}Cu(S$_2$CNEt$_2$)].

The two orbitals below the SOMO also contain significant M-S interactions with the SOMO-1 containing a Cu-S π* interaction, this time involving a symmetric combination of the

S p$_z$ orbitals and a Cu d$_{yz}$ orbital. In contrast, the SOMO-2 is weakly antibonding and comprises a Cu-S σ* bond. Interestingly, a similar order of π- and σ bonds is found in [Tp^{iPr2}Cu(SC$_6$F$_5$)] despite this compound being four coordinate.[18] Finally, the LUMO in all the complexes is a strongly antibonding Cu-S σ* orbital being an asymmetric combination of a S p$_x$ and p$_y$ orbital and a Cu d$_{x2-y2}$ orbital (see Figure 6). This orbital is strongly Cu based (*ca.* 60%) and supports our assignment of the reduction process observed in the CV as being due to Cu(I).

Conclusions

In conclusion, we have successfully prepared a series of copper dithiocarbamate complexes. The tris(pyrazolyl)borate ligand proves to be a very suitable supporting ligand allowing isolation of mixed ligand complexes with an N$_3$S$_2$ donor set. Structural studies have revealed that as expected the Tp^{Ph2} ligand is asymmetrically coordinated with a single elongated Cu-N bond while the dithiocarbamate is symmetrically coordinated giving compounds which more closely resemble copper green proteins. Spectroscopic studies indicate that the compounds are mostly five coordinate in solution, although a κ^3 to κ^2 isomerisation of the Tp^{Ph2} ligand exists in the case of **3** and to a lesser extent in **1**. Electrochemical studies are consistent with the spectroscopic findings and reveal only minor changes in the positions of the redox potentials but emphasize the effect that even subtle changes in the R groups on the dithiocarbamate ligand can have a significant impact on the relative stability of the κ^2 and κ^3 isomers. Overall, these studies highlight the difficulties in successfully modelling a *nominally* five coordinate enzyme like azurin where one of the sulfur donors is so loosely bound. However, they do provide a new model for green copper proteins. Future work will focus on developing asymmetric S,S donor ligands which may be used with the hope of more accurately modelling the azurin active site.

Experimental Section

General Remarks

All manipulations were performed in air with HPLC grade solvents. Tris(3,5-diphenylpyrazolyl)borate (KTp^{Ph2}) was prepared by a literature procedure.[40] All other chemicals were purchased from Fluka or Aldrich Chemical Company and used as received.

Infrared spectra (as KBr discs) were recorded on a Perkin-Elmer Spectrum One infrared spectrophotometer in the range 400-4000 cm^{-1}. Electronic spectra were recorded in CH$_2$Cl$_2$ at room temperature on a Shimadzu UV-1700 UV-Visible spectrophotometer. ESR spectra were recorded at 295 K on a Bruker Biospin ELEXSYS-II E500 spectometer using a silica flat cell for CH$_2$Cl$_2$ solutions and a 3 mm diameter cylindrical silica cell for solid samples. The ESR modulation amplitude = 0.1 G, time constant = 10 ms and microwave power = 0.2 mW. Elemental analyses were carried out on a Eurovector EA3000

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analyser. ESI-MS were carried out on a Bruker Daltonics 7.0T Apex 4 FTICR Mass Spectrometer. Electrochemical studies were carried out using a palmsensPC Vs 2.11 potentiosat in conjunction with a three electrode cell. The auxiliary electrode was a platinum rod and the working electrode was a platinum disc (2.0 mm diameter). The reference electrode was a Ag-AgCl electrode. Solutions in CH_2Cl_2 dried over CaH_2, were 5×10^{-4} mol·dm^{-3} in the test compound and 0.1 mol·dm^{-3} in [NBu$^n_4$][PF$_6$] as the supporting electrolyte. Under these conditions, $E^{o'}$ for the one-electron oxidation of [Fe(η-C$_5$Me$_5$)$_2$] added to the test solutions as an internal calibrant is -0.08 V.

Synthesis of complexes

[Tp^{Ph2}Cu(S$_2$CNEt$_2$)] 1

$CuCl_2 \cdot 2H_2O$ (85 mg, 0.5 mmol) was dissolved in MeOH (10 ml) giving a green solution. KTp^{Ph2} (354 mg, 0.5 mmol) was dissolved in THF (5 ml) and added to the solution resulting in a red-brown solution which was stirred for 1 hr. NaS$_2$CNEt$_2$ (113 mg, 0.55 mmol) was then added resulting in a gradual change to dark green. The solution was stirred for 3 hrs and reduced to dryness *in vacuo*. The solid was redissolved in CH_2Cl_2 (2 ml), filtered and layered with hexanes (15 ml). After 2 days dark green crystals formed which were washed with Et$_2$O (2 x 5 ml) and air dried (303 mg, 69%). ν_{max}(KBr)/cm^{-1} 3055, 2973, 2931 (ν_{CH}), 2619 (ν_{BH}), 1478 ($\nu_{C=N}$), 1008 (ν_{CS}). UV-Vis λ_{max}(CH$_2$Cl$_2$)/nm (ϵ, dm^{3}mol^{-1}cm^{-1}) 417 (4,880), 664 (373). *m/z* (ESI) 732 [M-S$_2$CNEt$_2^-$]$^+$. *Anal*. Calc. for C$_{50}$H$_{44}$N$_7$BS$_2$Cu: C 68.49, H 5.06, N 11.18; Found: C 68.35, H 5.02, N 11.13.

Complexes **2-3** were synthesized in a similar manner to **1** using the appropriate dithiocarbamate salt and recrystallized from the solvents indicated.

[Tp^{Ph2}Cu(S$_2$CNBz$_2$)] 2

Dark green crystals (crystallised from CH$_2$Cl$_2$-hexane). 58% yield. ν_{max}(KBr)/cm^{-1} 3056, 3027, 2937 (ν_{CH}), 2613 (ν_{BH}), 1503 ($\nu_{C=N}$), 997 (ν_{CS}). UV-Vis λ_{max}(CH$_2$Cl$_2$)/nm (ϵ, dm^{3}mol^{-1}cm^{-1}) 428 (12,900), 580sh (780). *m/z* (ESI) 732 [M-S$_2$CNBz$_2^-$]$^+$. *Anal*. Calc. for C$_{60}$H$_{48}$N$_7$BS$_2$Cu: C 72.00, H 4.83, N 9.80; Found: C 71.67, H 4.84, N 9.79.

[Tp^{Ph2}Cu(S$_2$CN(CH$_2$)$_4$)] 3

Dark green crystals (crystallised from CH$_2$Cl$_2$-hexane). 55% yield. ν_{max}(KBr)/cm^{-1} 3058, 2970 (νCH), 2586 (ν_{BH}), 1481 (νC=N), 1009 (νCS). UV-Vis λ_{max}(CH$_2$Cl$_2$)/nm (ϵ, dm^{3}mol^{-1}cm^{-1}) 430 (25,200), 620sh (1,650). m/z (ESI) 732 [M-S$_2$CN(CH$_2$)$_4^-$]+. Anal. Calc. for C$_{50}$H$_{42}$N$_7$BS$_2$Cu: C 68.65, H 4.84, N 11.21; Found: C 68.84, H 5.01, N 11.19.

X-ray crystallography

Crystal data and data processing parameters for the structures of **1**, **2** and **3** are given in Tables 2 and 3. X-ray quality crystals of **1**, **2** and **3** were grown by allowing hexane to diffuse into a concentrated solution of the complex in CH$_2$Cl$_2$. Crystals were mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 100 or 150 K in a stream of cold nitrogen. All diffraction data were collected on a Bruker Smart CCD area detector with graphite monochromated Mo Kα(λ = 0.71073 Å).[41] After data collection, in each case an empirical absorption correction (SADABS)[42] was applied, and the structures were then solved by direct methods and refined on all F^2 data using the SHELX suite of programs.[43] In all cases non-hydrogen atoms were refined with anisotropic thermal parameters; hydrogen atoms were included in calculated positions and refined with isotropic thermal parameters which were *ca*. 1.2 × (aromatic CH, CH$_2$) or 1.5 × (Me) the equivalent isotropic thermal parameters of their parent carbon atoms. All pictures were drawn using OLEX2.[44]

Computational details

All calculations were performed with Gaussian 03 (Revision C.02) and used the B3LYP density functional.[38] The structural properties of the complexes obtained from X-ray crystallographic data were used as initial structures for full optimization. Calculations were performed at the DFT-B3LYP level of theory using a SDD or 6-31G** basis set. Geometry optimizations were performed in the gas phase for each given spin state. The molecular orbital analyses were then conducted at those geometries. The SOMO and LUMO three-dimensional isosurface plots were generated using Avogadro.[45]

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Notes and references

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