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ARTICLE

N,N'-substituted thioureas and their metal complexes: syntheses, structures and electronic properties

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The synthesis of a six N,N'-substituted thiourea ligands (**L**^{1a}-**L**^{3b}) was achieved in two steps. A corresponding extensive series of Cu(I), Cu(II), Ni(II) and Zn(II) complexes (**1-24**) with varying formulations were synthesised from these ligands by the reaction of a 1:1 or a 1:2 mixture of Cu(II), Ni(II) and Zn(II) perchlorate or chloride salts. Complexes **1-24** have been comprehensively characterised by mass spectrometry, elemental analysis, UV-vis., IR, and ¹H and ¹³C{¹H} NMR spectroscopies where applicable. The X-ray crystal structures were obtained for eight examples: [(**L**^{1a})₂Cu]ClO₄ (**1**), [(**L**^{1c})₂Zn](ClO₄)₂ (**4**), [(**L**^{2a})₂Cu]ClO₄ (**6**), [(**L**^{2c})₂Ni](ClO₄)₂ (**7**), [(**L**^{1b})₂Cu](ClO₄) (**15**), [(**L**^{1b})CuCl] (**16**), [(**L**⁴)₂CuCl₂] (**19**) and [(**L**^{3b})CuClO₄] (**21**). These studies reveal that **L**^{1c} and **L**^{2c} represent ligands that have undergone cleavage during reaction with the metal salt; **L**⁴ represents an intramolecular rearrangement (*via* a Hagershoff reaction) of **L**^{2b}; and in most cases Cu(II) is reduced to Cu(I) during the ligand reaction. The X-ray crystal structures also reveal that **1**, **4**, **6**, **15** and **16** are monometallic species in the solid state; that Cu(I) in **1**, **6**, **15** and **16** and Zn(II) in **4** are arranged in a distorted tetrahedral geometry; that Cu(I) in **21** adopts a trigonal planar geometry; and that in **7** and **19** the Ni(II) and Cu(II) centres, respectively, possess square planar geometry. Preliminary studies on the biological activity (using the Malaria Sybr Green I Fluorescence assay) of the thiourea containing complexes suggests that the d¹⁰ complexes, and increased ligand stoichiometries, may afford higher potency.

Introduction

The acylthiourea group is a versatile and readily synthesised functional group which has been utilised in synthesis and incorporated into various molecules, including co-ordination complexes. Such systems have attracted significant attention due to these complexes having potential applications in medicinal chemistry as pesticides,¹ bacteriocides,^{2,3} antiviral,⁴ antihelminthic,⁵ antifungal⁶ and antimalarial⁷ compounds. Additionally, specific studies have shown a variety of acyl thiourea compounds to be extremely important in a biological context as they are, for example: (i) selective inhibitors of platelet-derived growth factor (PDGF) receptor;⁸ (ii) potent inhibitors of the Hedgehog signaling pathway;⁹ (iii) a c-Met (RTK or HGFR) inhibitor, for deactivating mechanisms by which various tumours and cancer stem cells promote angiogenesis

and metastasis;¹⁰ and (iv) an HDAC8 activator in non-catalytic HDAC8 mutants for research models of cohesinopathies.¹¹

In addition to these biological applications, the structural rigidity of the acylthiourea group and its potential as a multiple hydrogen bond donor has prompted investigations into its behaviour as an anion binder,¹² including via a multi-array of hydrogen bond donors,¹³ and as a ligand for the construction of polynuclear complexes.¹⁴

In its role in co-ordination chemistry the acylthiourea group is potentially a bidentate ligand, co-ordinating to metal ions via both the hard oxygen and soft sulfur donor atoms.^{15,16} Alternatively, the ligand may form a strong intramolecular hydrogen bond between the carbonyl oxygen and a NH group in the thiourea, which induces a monodentate ligand bonding mode via the sulfur atom only, thus favouring soft metal ions.^{2,3,17-18} When an additional donor atom (e.g. pyridine) is placed on the thiourea framework, the ligand can then bind in a bidentate fashion in both cases, as shown in Figure 1, with the structures observed being dependent on the nature of the metal ion.

With widespread and important biological activity, it is clearly advantageous to be able to modify these acylthiourea derived ligands and understand their co-ordination chemistry to a variety of metal centres. Clearly a better understanding of the nature of these complexes and properties is of potential value. Herein, we present an extensive structural and spectroscopic investigation into a series of metal complexes that incorporate

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the acylthiourea moiety. Importantly, we report interesting reactivities that can result in ligand cleavage and rearrangements which will have significant implications in the design and biological application of such systems in the future.

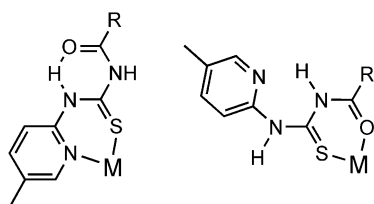
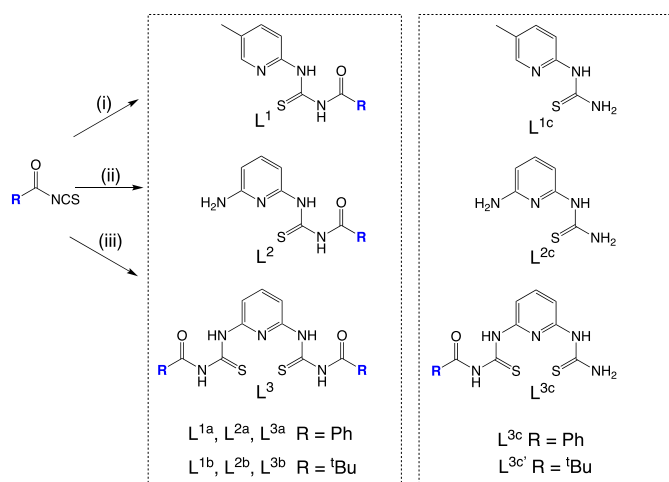


Figure 1. Common bidentate co-ordination modes of pyridyl-acylthioureas.

Results and Discussion

Ligand Synthesis

Two series of substituted thiourea derived ligands were prepared. The synthesis of **L^{1a}-L^{3a}** and **L^{1b}-L^{3b}** required the preparation of the benzoyl isothiocyanate and pivaloyl isothiocyanate precursors through the reaction of the corresponding acid chloride with potassium thiocyanate. The target ligands **L^{1a}-L^{3a}** and **L^{1b}-L^{3b}** were obtained by reaction of either 2-amino-5-methyl pyridine or 2,6-diaminopyridine with benzoyl isothiocyanate or pivaloyl isothiocyanate in acetonitrile (Scheme 1). The purification and recrystallisation approaches for these various ligands are described in the Experimental Section. All samples were gently heated under vacuum prior to elemental analyses.

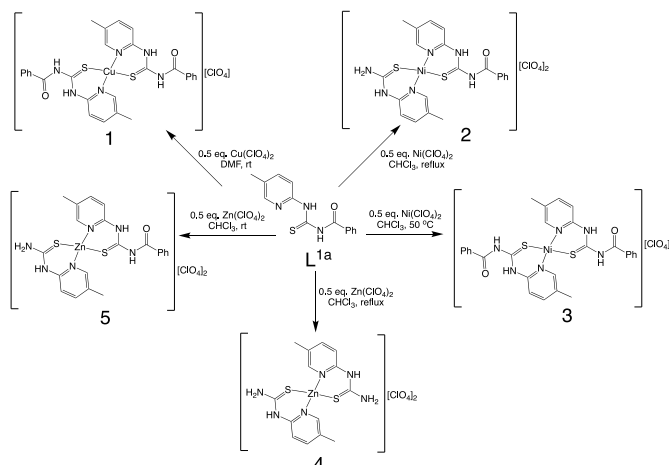


Scheme 1. Left: Synthesis of the ligands: (i) 1 equiv. 2-amino-5-methylpyridine, MeCN, reflux; (ii) 1 equiv. 2,6-diaminopyridine, MeCN, reflux; (iii) 0.5 equiv. 2,6-diaminopyridine, MeCN, reflux. Inset right: the structures of fragmented ligand variants obtained during the co-ordination chemistry.

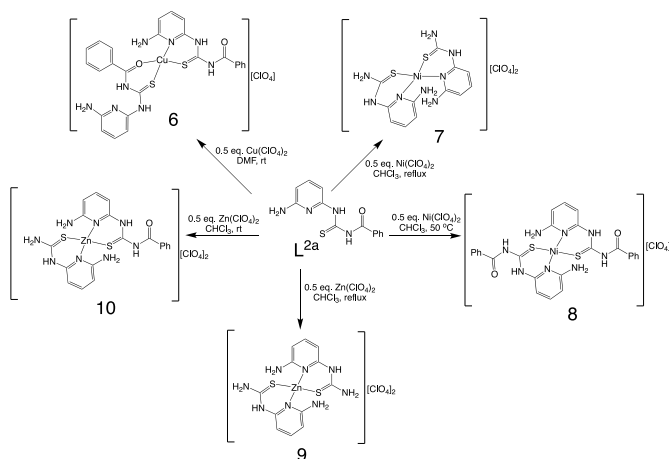
Co-ordination chemistry

The chelating properties of the new ligands were investigated using a variety of Cu(II), Ni(II), and Zn(II) sources. Schemes 2-7 provide the reaction conditions for the proposed complex

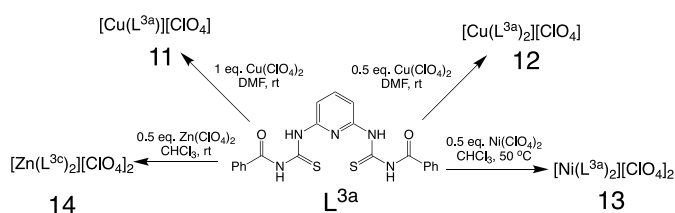
formulations. Table 1 also summarises the isolated complexes and their respective ligand formulations obtained in this study.



Scheme 2. Synthesis of complexes **1-5** from **L^{1a}**.



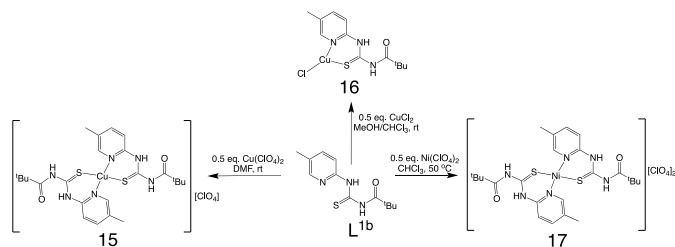
Scheme 3. Synthesis of complexes **6-10** from **L^{2a}**.



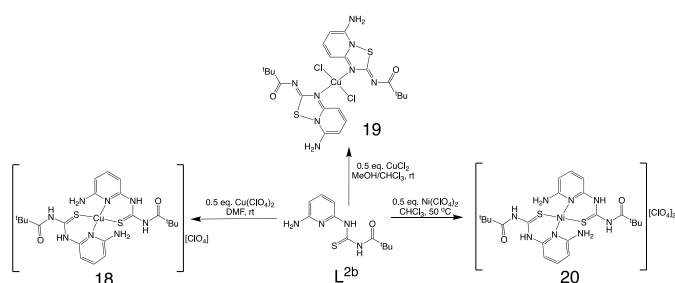
Scheme 4. Synthesis of complexes **11-14** from **L^{3a}**.

For example, reaction of the different ligands with $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in a 2:1 stoichiometry was carried out in DMF/water at room temperature, yielding Cu(I) complexes of **L^{1a}** and **L^{1b}** (**1** and **15**), **L^{2a}** and **L^{2b}** (**6** and **18**), **L^{3a}** and **L^{3b}** (**12** and **22**). In all cases, analytical, spectral and crystallographic data

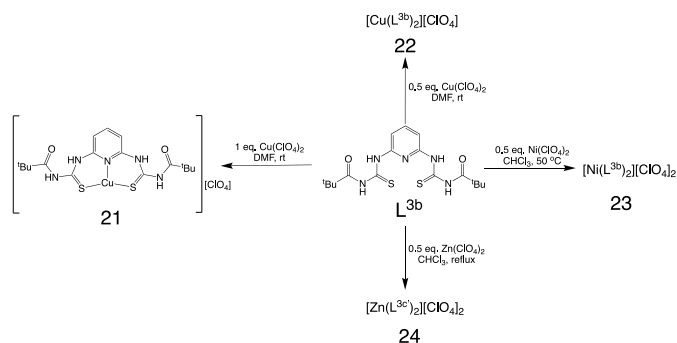
(discussed later) indicated the reduction of the source Cu(II) to form $[\text{Cu}(\text{L})_2](\text{ClO}_4)$ species. These Cu(I) complexes were isolated as red, orange or yellow solids, and were stable at room temperature. In the cases of **L^{3a}** and **L^{3b}**, when the reaction was repeated using a metal:ligand ratio of 1:1, Cu(I) complexes **11** and **21** were successfully isolated in the form of $[\text{Cu}(\text{L})](\text{ClO}_4)$.



Scheme 5. Synthesis of complexes **15-17** from **L^{1b}**.



Scheme 6. Synthesis of complexes **18-20** from **L^{2b}**.



Scheme 7. Synthesis of complexes **21-24** from **L^{3b}**.

Interestingly, using CuCl_2 instead of $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ with **L^{2b}** resulted in a Cu(II) complex, **19**, where the ligand had undergone a transformation to give **L⁴** (Scheme 6). The characterization of **19** revealed that the pyridylthiourea group of the ligand had undergone a Hegershoff reaction^{19,20}. Previously, the oxidation of pyridylthioureas by bromine has been reported to yield the related heterocyclic 1,2,4-thiadiazolo[2,3-*a*]pyridine^{21,23} and here it is assumed that CuCl_2 acts as an oxidant that promotes the rearrangement of the ligand. We postulate that formation of **L⁴**, which results in the

loss of the thiourea donor, is subsequently less suitable for supporting a Cu(I) centre. The analysis of **19**, supported by X-ray crystallographic studies (see below), suggests the Cu(II) ion is four co-ordinate with two trans arranged monodentate **L⁴** ligands and two co-ordinated chloride ions. While not in the scope of this current work, clearly future studies will address the limitations of this reaction with related ligands and varying conditions.

Reaction of the ligands with $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in a 2:1 ratio were initially undertaken at 75 °C in CHCl_3 /methanol. Characterisation of these Ni(II) complexes indicated cleavage (these coordinated ligands are thus referred to as **L^{1c}**, **L^{2c}**, **L^{3c}**) of one or two of the benzoyl or pivaloyl groups (see Scheme 1). Repeating the reaction at 50 °C prevented cleavage of these groups and gave the anticipated complexes. The Ni(II) complexes were collected as brown or green coloured solids and were stable at room temperature.

Mononuclear Zn(II) complexes were formed as colourless powders by the reaction of the ligands with $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (2:1 molar ratio) in a mixture of CHCl_3 /methanol at room temperature and 75 °C. As observed with the Ni(II) coordination chemistry, the Zn(II) complexes again formed with cleavage (giving complexes of **L^{1c}**, **L^{2c}**, **L^{3c}**) of one or both acyl moieties from the co-ordinated ligands. In contrast to the analogous Ni(II) chemistry, repeating the reactions at lower temperatures did not prevent cleavage of these groups.

Table 1. Summary of the metal complexes isolated in this work.

Complex	Metal	Ligand(s)	Complex	Metal	Ligand(s)
1	Cu(I)	L^{1a}	13	Ni(II)	L^{3a}
2	Ni(II)	L^{1a} , L^{1c}	14	Zn(II)	L^{3c}
3	Ni(II)	L^{1a}	15	Cu(I)	L^{1b}
4	Zn(II)	L^{1c}	16	Cu(I)	L^{1b} , Cl
5	Zn(II)	L^{1a} , L^{1c}	17	Ni(II)	L^{1b}
6	Cu(I)	L^{2a}	18	Cu(I)	L^{2b}
7	Ni(II)	L^{2c}	19	Cu(II)	L⁴
8	Ni(II)	L^{2a}	20	Ni(II)	L^{2b}
9	Zn(II)	L^{2c}	21	Cu(I)	L^{3b} (1:1)
10	Zn(II)	L^{2a} , L^{2c}	22	Cu(I)	L^{3b} (2:1)
11	Cu(I)	L^{3a} (1:1)	23	Ni(II)	L^{3b}
12	Cu(I)	L^{3a} (2:1)	24	Zn(II)	L^{3c}

X-ray Crystallography Studies

X-ray crystal structures of $[\text{Cu}(\text{L}^{1a})_2]\text{ClO}_4 \cdot \text{CH}_3\text{CN}$ (**1**) and $[\text{Cu}(\text{L}^{1b})_2]\text{ClO}_4 \cdot \text{H}_2\text{O}$ (**15**)

Red, monoclinic crystals of **1** and orange orthorhombic crystals of **15** were obtained by vapour diffusion of diethyl ether into an acetonitrile solution of **1**, or a chloroform solution of **15**. Selected bond distances and bond angles are given in Table 2. Figure 2 shows **1**, with the metal centre tetrahedrally coordinated by two bidentate ligands. Each ligand co-ordinates via a pyridine ring and the sulfur of the thiourea. Bond angles about the Cu(I) centre range from 98.04(6)-128.23(3) degrees, demonstrating a significant distortion from an ideal tetrahedral

geometry. The most acute of these angles (N1–Cu1–S1 and N21–Cu1–S21) are associated with the bond angles between the two donors of each bidentate ligand. The largest bond angle is observed for S21–Cu1–S1 (128.23(3)°). These observations are in line with previous work: of the four previously reported Cu(I) crystal structures of pyridyl thiourea derivatives,²² all were tetrahedral and the metal ion was coordinated by the pyridyl group and the sulfur donor. Typical for this class of ligand, intermolecular hydrogen bond interactions were also observed. More specifically, and typical of acyl thioureas, hydrogen bonding between the C=O and an N–H group results in the formation of a six-membered ring (N2–H2···O1 and N22–H22···O21). Furthermore, there are additional weaker intermolecular hydrogen bonds between the ligand and the perchlorate counter anion.

Table 2. Selected bond lengths and angles for structures **1** and **15**.

Compound 1			
Bond length (Å)			
Cu1–N1	2.074(2)	Cu1–S21	2.2191(7)
Cu1–N21	2.079(2)	Cu1–S1	2.2235(7)
Bond angles (°)			
N1–Cu1–N21	111.87(9)	N21–Cu1–S21	98.12(6)
N1–Cu1–S21	111.55(6)	N1–Cu1–S1	98.04(6)
N21–Cu1–S1	109.21(6)	S21–Cu1–S1	128.23(3)
Compound 15			
Bond length (Å)			
Cu1–N1	2.054(7)	Cu1–S21	2.213(2)
Cu1–N21	2.050(6)	Cu1–S1	2.231(2)
Bond angles (°)			
N1–Cu1–N21	110.9(3)	N1–Cu1–S1	97.41(18)
N1–Cu1–S21	116.06(18)	N21–Cu1–S1	109.83(18)
N21–Cu1–S21	98.88(18)	S21–Cu1–S1	123.97(9)

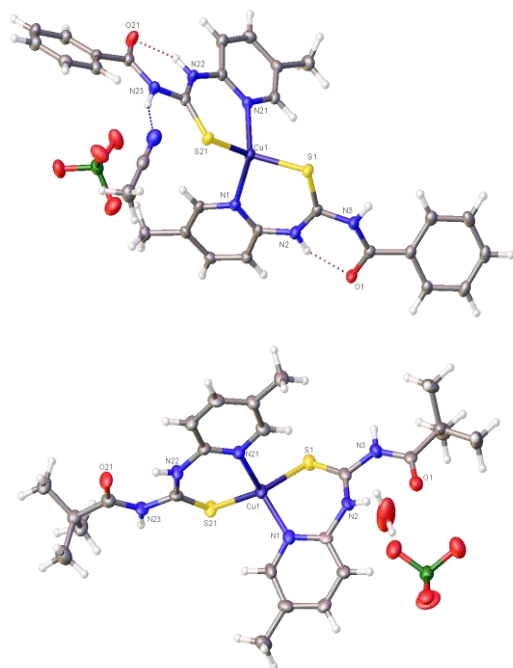


Figure 2. The asymmetric units of **1** (top) and **15** (bottom). Displacement ellipsoids are shown at 50% probability.

X-ray crystal structure of [Zn(L^{1c})₂](ClO₄)₂ (**4**)

Monoclinic colourless crystals of **4** were obtained by vapour diffusion of diethyl ether into an acetonitrile solution of **4** (Figure 3). Selected bond distances and bond angles are given in Table 3. The complex crystallises in the monoclinic space group *P*2₁. The Zn(II) ion displays a tetrahedral geometry, with bond angles about the metal centre ranging from 99.33(14)–115.51(18)°. The variation from tetrahedral geometry is less pronounced than that seen in **1** and **15**. The metal ion in **4** is coordinated by two bidentate ligands via pyridine and sulfur donor atoms. The structure clearly shows that the ligand has hydrolysed in the reaction to give L^{1c} and benzoic acid. There are extensive intermolecular hydrogen bond interactions between the complex and the perchlorate counter-ions. One interaction is between a thiourea, acting as a bidentate hydrogen bond donor, and a perchlorate (N1–H1b···O22, N2–H2···O23) and the other interaction is a perchlorate ion hydrogen bonding with two separate thioureas, each acting as a monodentate donor (N1–H1a···O31¹ and N11–H11b¹···O32) were observed between the thiourea N–H and the perchlorate oxygen atom. (Symmetry transformation to generate O31¹: x+1,y,z)

Table 3. Selected bond lengths and angles for structure **4**.

Bond length (Å)			
Zn1–N3	2.021(5)	Zn1–S11	2.2535(15)
Zn1–N13	2.025(5)	Zn1–S1	2.2596(16)
Bond angles (°)			
N3–Zn1–N13	115.51(18)	N3–Zn1–S1	99.73(14)
N3–Zn1–S11	114.13(14)	N13–Zn1–S1	113.64(14)
N13–Zn1–S11	99.33(14)	S11–Zn1–S1	115.37(5)

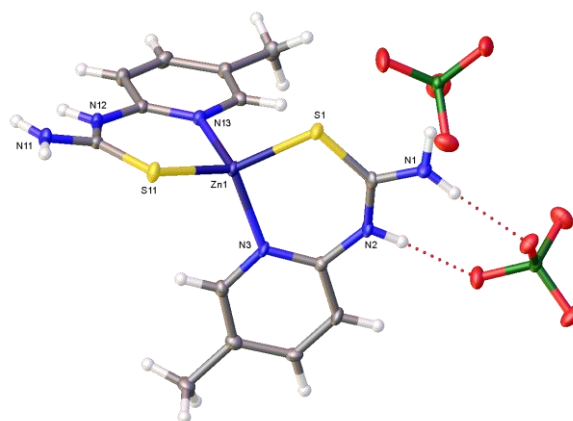


Figure 3. The asymmetric unit of **4**. Displacement ellipsoids are shown at 50% probability.

X-ray crystal structure of [Cu(L^{2a})₂](ClO₄) (**6**)

Monoclinic dark orange crystals of **6** were obtained by vapour diffusion of diethyl ether into an acetonitrile/methanol (2:1) solution of the complex. The molecular structure of the complex $[\text{Cu}(\text{L}^{2a})_2]\text{ClO}_4$ (**6**) was established by X-ray crystallography and is illustrated in Figure 4, along with key bond lengths and angles in Table 4. The Cu(I) centre is chelated by two L^{2a} ligands resulting in a distorted structure with three short Cu-S or Cu-N bonds and one longer Cu-O bond (2.3703(16) Å). Of note, L^{2a} and L^{1a} are similar except for the substitution of the pyridine ring, with L^{1a} having a methyl group in the 5-position and L^{2a} an amino group in the 6-position. These groups play no direct role in the co-ordination of the metal centre, and the amino group does not appear to be involved in any strong hydrogen bonding interactions, suggesting the differences between the two structures, **1** and **6**, appears to be due to the differing steric demands of the two ligands. More specifically, the greater steric demand of L^{2a} results in the ligand having two different co-ordination modes in **6**. One ligand co-ordinates to the metal in an identical manner to that observed in **1**, while the second ligand also co-ordinates in a bidentate manner, but through the sulfur and oxygen donors. In this co-ordination mode, the pyridine nitrogen is now forming an intramolecular hydrogen bond with the thiourea NH groups (N21-H21...N23). Presumably, the soft Cu(I) centre forms the Cu(I)-O interaction in the absence of other possible softer donors. The Cu-O bond is significantly longer than the other Cu-donor interactions and this 3+1 interaction might be considered as a trigonal planar structure or as a highly distorted tetrahedral geometry.

Table 4. Selected bond lengths and angles for structure 6.

Bond length (Å)			
Cu1-N3	2.0148(17)	Cu1-S21	2.2515(6)
Cu1-S1	2.2127(6)	Cu1-O21	2.3703(16)
Bond angles (°)			
N3-Cu1-S1	102.76(5)	N3-Cu1-O21	101.80(6)
N3-Cu1-S21	125.50(5)	S1-Cu1-O21	109.06(5)
S1-Cu1-S21	126.94(2)	S21-Cu1-O21	83.50(4)

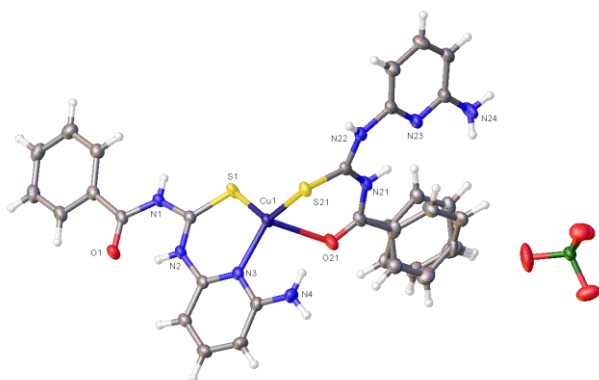


Figure 4. The asymmetric unit of **6**. Displacement ellipsoids are shown at 50% probability.

X-ray structures of $[\text{Ni}(\text{L}^{2c})_2](\text{ClO}_4)_2 \cdot \text{H}_2\text{O} \cdot \text{EtOH}$ (**7**)

Monoclinic red coloured crystals of **7** were obtained by vapour diffusion of diethyl ether into an ethyl acetate solution of **7**. The selected bond distances and bond angles are given in Table 5 and the structure of **7** is shown in Figure 5. The complex contains two bidentate ligands, each demonstrating loss of the benzoyl group. The ligands again co-ordinate through the pyridine ring and sulfur atom of the thiourea. The Ni(II) complex has a slightly distorted square planar geometry: the torsion angle between the four donors range from 13.4-14.5(5)° with bond angles about the metal centre ranging from 88.08(3)-92.55(9)° and *trans* angles of 169.95(6)° and 170.57(6)°. The observed Ni(II)-S/Ni(II)-N bond lengths are in the expected range.²

Table 5. Selected bond lengths and angles for structure 7.

Bond length (Å)			
Ni1-N3	1.923(2)	Ni1-S1	2.1647(8)
Ni1-N3'	1.922(2)	Ni1-S1'	2.1647(8)
Bond angles (°)			
N3-Ni1-N3'	92.25(14)	S1-Ni1-S1'	87.80(4)
N3'-Ni1-S1	169.76(7)	N3'-Ni1-S1'	90.84(7)
N3-Ni1-S1	90.85(7)	N3-Ni1-S1'	169.76(7)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,y,-z+1/2

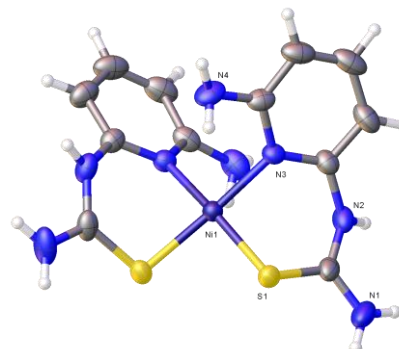


Figure 5. The asymmetric unit of **7**. Displacement ellipsoids are shown at 50% probability.

X-ray structure of $[\text{Cu}(\text{L}^{1b})\text{Cl}]$ (**16**)

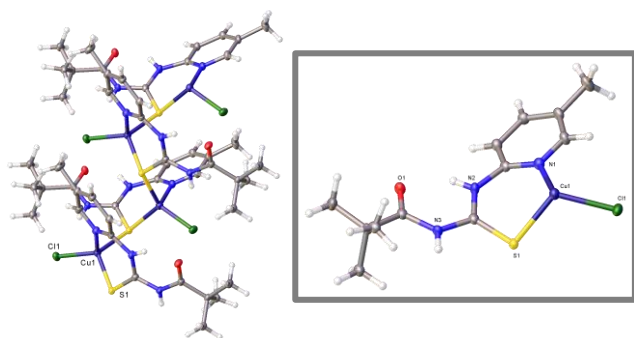
Monoclinic red crystals of **16** were obtained by vapour diffusion of diethyl ether into a CHCl_3 solution of the complex. Selected bond lengths and angles are listed in Table 6 and the structure is shown in Figure 6. Each copper atom is co-ordinated by two bidentate ligands where one ligand binds through a sulfur atom and a pyridine donor. The sulfur donor also co-ordinates to a second Cu(I) centre, and this arrangement is reciprocated by another complex unit leading to the formation of a polymeric chain. The Cu(I) co-ordination sphere is completed by a chloride atom. Bond angles about the metal centre range from 92.15(5)-116.958(13)°, and as expected, the most acute angle is that formed by the two donors within the same ligand (N1-Cu1-S1: 92.13(5)°), but it is slightly more acute than the analogous bite angles observed in **1** and **15**. An intramolecular hydrogen bond is again observed in the acyl thiourea moiety (1.83 Å) and this is similar to that observed for **1** and **15**. The structure observed for **16** is similar to the polymeric tetrahedral complex $[\text{Cu}(\text{L})\text{Br}]_n$ (L = N-(2-pyridyl)-N'-phenylthiourea) reported by Saxena.²³

Table 6. Selected bond lengths and angles for structure **16**.

Bond length (Å)			
Cu1–Cu1	2.2504(5)	Cu1–S1 ⁱ	2.2881(6)
Cu1–N1	2.0863(17)	Cu1–S1	2.3080(5)
Bond angles (°)			
N1–Cu1–Cl1	112.57(5)	N1–Cu1–S1	92.15(5)
N1–Cu1–S1 ⁱ	103.38(5)	Cl1–Cu1–S1	114.25(2)
Cl1–Cu1–S1 ⁱ	114.59(2)	S1 ⁱ –Cu1–S1	116.958(13)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1, y-1/2, -z+1/2

**Figure 6.** The polymeric nature of **16**, with the co-ordination sphere of Cu(I) shown inset.**X-ray structure of [Cu(L⁴)₂Cl₂] (**19**)**

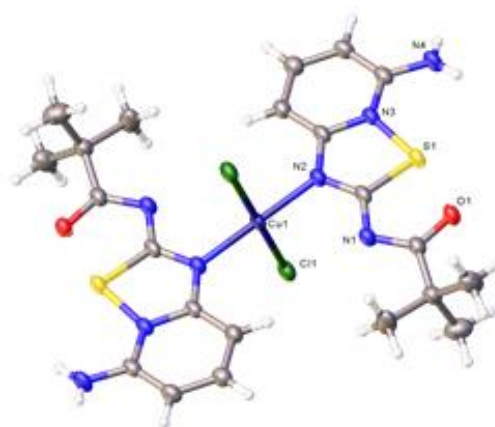
Monoclinic dark orange crystals of **19** were obtained by vapour diffusion of diethyl ether into a dichloromethane:ethanol (1:1) solution of **19**. Selected bond distances and bond angles are given in Table 7 and the structure is shown in Figure 7. The Cu(II) complex is clearly square planar with bond angles about the metal centre 89.28(6)–90.72(6) and two bond angles at 180.00 degrees, with the Cu centre lying in a special position, at the centre of symmetry about the complex. A related complex [(X)₂CuCl₂] (X = (N-(7-methyl-2H-[1,2,4]thiadiazolo[2,3-a]pyridine-2-ylidene)benzamide) reported by Adhami *et al.* exhibited the same N₂Cl₂ square planar coordination environment, with similar bond lengths (Cu–Cl1 2.2637(14), Cu–N2 1.988(2) Å).²⁴ Intramolecular hydrogen bonding (N4–H4A...S1, 2.62 Å) was also observed within the heterocycle with two weak intermolecular interactions (N4–H4A...Cl1ii and N4–H4B...Cl1iii 2.53(4) and 2.54(4)Å). (Symmetry transformations used to generate equivalent atoms: Cl1ii: x, -y+1/2, z+1/2; Cl1iii: -x+2, y-1/2, -z+1/2)

Table 7. Selected bond lengths and angles for structure **19**.

Bond length (Å)			
Cu1–Cl1	2.3047(6)	Cu1–Cl1 ⁱ	2.3047(6)
Cu1–N2 ⁱ	1.962(2)	Cu1–N2	1.962(2)
Bond angles (°)			
N2 ⁱ –Cu1–N2	180.00(3)	N2 ⁱ –Cu1–Cl1	90.75(6)
N2 ⁱ –Cu1–Cl1 ⁱ	89.25(6)	N2–Cu1–Cl1	89.25(6)
N2–Cu1–Cl1 ⁱ	90.75(6)	Cl1 ⁱ –Cu1–Cl1	180.0

Symmetry transformations used to generate equivalent atoms:

#1 -x+2, -y+1, -z+1

**Figure 7.** The asymmetric unit of **19**. Displacement ellipsoids are shown at 50% probability.**X-ray structure of [Cu(L^{3b})](ClO₄) (**21**)**

Monoclinic yellow crystals of **21** were obtained by vapour diffusion of diethyl ether into an ethanol:dichloromethane (3:1) solution of **21**. Selected bond lengths and angles are given in Table 8. The metal centre (Figure 8) is co-ordinated by a single ligand that acts as a tridentate ligand through a nitrogen pyridine ring and the sulfur atoms of the two thioureas. The Cu(I) centre is approximately trigonal planar, although the bond angles around Cu(I) (107.40(18), 107.69(18) and 144.87(7)°) highlight the distortion caused by the strain in the six-membered chelate rings. This geometry is not uncommon for Cu(I), and an analysis of monodentate homoleptic donor sets with Cu(I) has revealed a significant propensity to form trigonal planar complexes,²⁵ and examples exist for Cu(I) trigonal planar complexes with a NS₂ donor set.^{26, 27}

Table 8. Selected bond lengths and angles for structure **21**.

Bond length (Å)			
Cu1–N1	1.992(5)	Cu1–S2	2.141(2)
Cu1–S1	2.140(2)		
Bond angles (°)			
N1–Cu1–S1	107.54(18)	C1–N1–Cu1	121.4(5)
N1–Cu1–S2	107.56(18)	C6–S1–Cu1	102.1(2)
S1–Cu1–S2	144.87(7)	C8–S2–Cu1	101.3(3)
C5–N1–Cu1	120.9(5)		

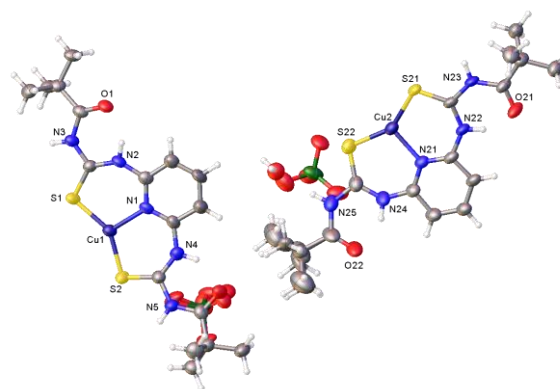


Figure 8. The asymmetric unit of **21**. Displacement ellipsoids are shown at 50% probability.

Spectroscopic Characterization of the Complexes

^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR Spectroscopy

The ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR chemical shifts for the free ligands and their respective Cu(I), Ni(II) and Zn(II) complexes are listed in the Experimental Section. For comparison, the chemical shifts for the two signature NH resonance (CONH and CSNH, the latter being hydrogen bonded) were observed around 11.53–11.85 and 12.99–13.22 ppm in $\text{L}^{1\text{a}}\text{-L}^{3\text{a}}$ and around 10.58–10.90 and 12.93–13.19 ppm in $\text{L}^{1\text{b}}\text{-L}^{3\text{b}}$. Upon co-ordination, the CSNH and CONH resonances in the Cu(I), Ni(II) and Zn(II) complexes were shifted to 14.10–11.99 and 11.74–8.94 ppm, respectively for Cu(I) complexes, 13.24–10.61 and 11.71–10.46 for Ni(II) complexes and 12.93–10.46 and 10.61–8.82 ppm for Zn(II) complexes. ^1H NMR spectra for complexes **2**, **4**, **5**, **7**, **9**, **10** and **14** showed new peaks in the range 10.00–10.47 and 8.66–9.00 ppm, which were assigned

to the -NH_2 groups that were formed from the cleavage of the benzoyl/pivaloyl groups. Consistent with this observation, the ^1H NMR spectra for these complexes also show the disappearance of the proton signals of the phenyl or *tert*-butyl groups in complexes **2**, **4**, **5**, **7**, **9**, **10** and **14**.

The $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of the ligands and complexes showed the expected number of resonances at typical chemical shifts. For $\text{L}^{1\text{a}}\text{-L}^{3\text{a}}$, signature resonances due to C=O and C=S appeared at 168.48–168.92 and 177.09–178.47 ppm, respectively; for $\text{L}^{1\text{b}}\text{-L}^{3\text{b}}$ they appear further downfield at 176.86–178.30 and 180.34–180.65 ppm, respectively. In the complexes, these resonances shift significantly indicating co-ordination of the ligands to the metal centre via the S donor of the thiourea group. $^{13}\text{C}\{^1\text{H}\}$ NMR spectra for complexes **4**, **7**, and **9** showed the loss of the C=O signals consistent with the cleavage of the benzoyl/pivaloyl groups from those ligands.

Infrared spectra

IR spectra were recorded in the solid state. The spectra of the free ligands ($\text{L}^{1\text{a}}\text{-L}^{3\text{b}}$) showed characteristic bands at 3298–3485 (for N-H), 1672–1692 (C=O), 1468–1512 (C=N) and 1325–1366 cm^{-1} (C=S). The IR spectra of thiourea complexes (**1-24**) showed these absorption bands at 3267–3485 (N-H), 1636–1692 (C=O), 1439–1504 (C=N) and 1252–1287 cm^{-1} (C=S). In particular, a weakening of the C=S bond upon co-ordination is consistent with these observations. The IR spectra of complexes of $\text{L}^{2\text{a}}$ (**6** and **8**) show considerable lowering of the C=O stretching frequency ($\sim 1660 \text{ cm}^{-1}$ *cf.* $\sim 1670 \text{ cm}^{-1}$), suggesting co-ordination with the metal centre through the carbonyl group, which is consistent with solid state the X-ray structure for **6**. Complex **20** has a C=O stretching frequency of 1664 cm^{-1} suggesting that this ligand binds in a similar manner (bidentate through O and S). For complexes **4**, **7**, and **9**, the most striking change is the loss of the C=O indicating cleavage of the benzoyl and pivaloyl groups from the complexes. The complexes **1-3**, **5**, **10-17**, **18** and **21-23** show little change in C=O stretching frequency when compared to the corresponding free ligand, implying the

carbonyl group is non-co-ordinating for these complexes. The presence of two characteristic bands at 1053–1096 and 621–627 cm^{-1} indicated that the T_d symmetry of ClO_4^- is maintained in all cationic complexes and thus implies non-co-ordinating ClO_4^- .^{28, 29}

Electronic spectra

The UV-vis. spectra of the ligands $\text{L}^{1\text{a}}\text{-L}^{3\text{b}}$ and their complexes were recorded as DMF solutions and their full data are presented in the Experimental Section. Spectra of the free ligands $\text{L}^{1\text{a}}\text{-L}^{3\text{b}}$ showed strong absorption bands at λ_{max} 214–293 nm and 299–367 nm which are attributed to the presence of allowed ligand-centred $\pi \rightarrow \pi^*$ transitions. The corresponding spectra for the d^{10} Cu(I) and Zn(II) complexes are thus dominated by the ligand-centred bands in the UV region, with minor shifts noted upon coordination. In contrast, the spectra for the square planar Ni(II) complexes **2**, **3**, **7**, **8**, **17** and **20** also display weaker additional bands between 390–421 nm (ca. $400 \text{ M}^{-1}\text{cm}^{-1}$) and around 584–612 nm ($< 100 \text{ M}^{-1}\text{cm}^{-1}$). The latter of these bands is likely to be the $d(xy) \rightarrow d(x^2-y^2)$ transitions which is in good agreement with previously reported Ni(II) complexes.^{30,31} The spectra of the six co-ordinate, pseudo octahedral Ni(II) complexes **13** and **23** also showed two very weak d-d bands in the visible and near-IR region, assigned to the $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{F})$ and $^3\text{A}_{2g} \rightarrow ^3\text{T}_{2g}$ transitions, respectively. From these ligand field spectra it was possible to deduce (assuming O_h geometry) Dq, B and β parameters, of 1068 cm^{-1} , 855 cm^{-1} and 0.82 for **13**, and 1050 cm^{-1} , 875 cm^{-1} and 0.84 for **23**.

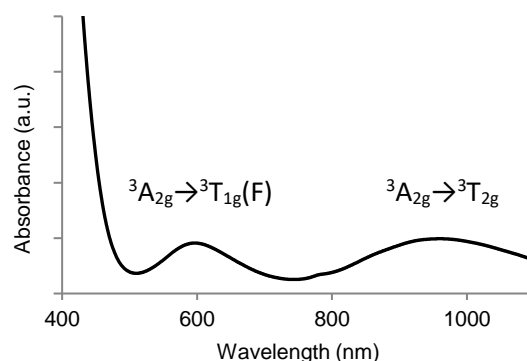


Figure 9. Electronic spectrum of the nickel complex **23** (DMF, room temperature).

Magnetic susceptibility measurements

The observed magnetic moments of Ni(II) complexes **2**, **3**, **7**, **8**, **17** and **20** were measured using the Evan's method and suggest a diamagnetic square planar structure, while the magnetic moments for complexes **13** and **23** are 2.94 and 2.98 BM and, though lower than might be expected, are more consistent with a pseudo octahedral geometry at Ni(II). The magnetic moment of complex **19** is 1.80 BM, consistent with a Cu(II) oxidation state.

Electrochemical measurements

The electrochemical data for Cu(I), Cu(II) and Ni(II) complexes were measured in acetonitrile using $[\text{Bu}_4\text{N}][\text{PF}_6]$ (0.1 M) as supporting electrolyte. The cyclic voltammograms of the Cu(I) complexes **1**, **6**, **11**, **12**, **15**, **16**, **18**, **21** and **22** are very similar, typically showing a quasi-reversible process between -0.20 to -0.45 V (*vs* Fc/Fc⁺) with large peak-to-peak separations being observed (200-350 mV). This potential is typical for a Cu(I)/Cu(II) couple and the peak to peak separations, being much greater than those observed with the ferrocene internal standard, suggest a quasi-reversible nature. This is possibly due to a structural/geometric rearrangement induced between the Cu(I) and Cu(II) oxidation states and their resultant geometric preferences. Furthermore, it was noted that the application of high negative potentials for prolonged periods caused a sharp anodic peak between -0.5 to -0.7 V suggestive of a species being deposited upon the electrode. All Cu(I) complexes except **16** showed an irreversible oxidative process in the range +0.520 to +1.08 V. Interestingly, **19** was unique among these copper complexes as the voltammogram displayed a single reversible process at +0.250 V *vs* Fc/Fc⁺; ($\Delta E = 72$ mV). To the best of our knowledge, the electrochemical properties of the heterocycle within **19** has not been reported and therefore we tentatively assign the signal at +0.250 V to this moiety.

The cyclic voltammograms of the Ni(II) complexes **2**, **3**, **7**, **8**, **13**, **17**, **20** and **23** revealed two irreversible reductions at -1.11 to -1.34 V and -1.63 to -1.99 V *vs* Fc/Fc⁺. Similar behaviour has been reported by Saad *et al.* for the Ni(II) complex of bis(6-benzoylthiourea-2-pyridylmethyl)(2-pyridyl methyl)amine which showed two similar irreversible reductions at -1.37 V and -1.78 V in acetonitrile.¹³

Preliminary Biological Antimalarial Testing

Table 8. EC₅₀ values for selected complexes.

Complex	EC ₅₀ (μM)	EC ₅₀ 95% CI	Complex	EC ₅₀ (μM)	EC ₅₀ 95% CI
1 (Cu)	23.3	10.2 to 15.1	10 (Zn)	6.1	4.2 to 8.9
3 (Ni)	62.5	52.6 to 74.2	21 (Cu)	14.6	7.6 to 22.3
5 (Zn)	12.4	20.8 to 26.1	22 (Cu)	1.2	0.6 to 2.4
6 (Cu)	20.5	18.8 to 22.3	23 (Ni)	12.2	10.7 to 14.0
8 (Ni)	95.1	85.7 to 105.6	24 (Zn)	14.9	12.5 to 17.8

Previously, the (bio)activity of thiourea ligands has been ascribed, in part, to interactions of the sulfur atom with biological substrates.¹⁻⁷ However, once coordinated to the metal centre, this group may become less accessible. Therefore we performed preliminary studies to ascertain the biological activity of some selected complexes. Affecting some 150-300 million people and causing the death of approximately 425,000 in 2015, malaria is one of the most important diseases of the developing world.³⁴ With concerns regarding the

recent treatment failure of, and now resistance to, artemisinin combination therapies, there is an urgent demand to identify novel chemotypes to target this devastating disease. Thus, a selection of complexes was tested here, using the Malaria Sybr Green I Fluorescence assay³³ including the Ni(II), Cu(I) and Zn(II) salts of L^{1a}, L^{2a} and L^{3b}. The tabulated results (Table 3) show the 50% Effective Concentration (EC₅₀) and the 95% Confidence Intervals (CI) for each selected compound. The EC₅₀ value is therefore the concentration of compound required to inhibit growth of the intraerythrocytic asexual stage of *Plasmodium falciparum* by 50%. The biological testing results should be placed in context with previous discussion on the hydrolysis of the thiourea ligand in the zinc complexes which may not, therefore, allow a direct comparison between the different coordinated metals.

From the preliminary data it is clear that the EC₅₀ values of all compounds were > 1 μM, with complex **22** demonstrating the most significant activity (EC₅₀ = 1.2 μM). Overall, the results suggest that the more labile d¹⁰ complexes of Zn(II) and Cu(I) yield more active complexes, whereas the Ni(II) variants of all ligands appear to be less potent among the series of compounds. For example, comparison of **1 vs 3** and **6 vs 8** shows that for a given ligand the Cu(I) species is much more active. Interestingly, comparison of **21** and **22** suggest that doubling the molar equivalents of the ligand (from 1:1 to 2:1) within the complex increases potency again alluding to the biological activity of the ligand. However, while we wished to compare these activities of the complexes against the free ligand, the low solubility of the ligand once diluted in aqueous media meant such a comparison would not be valid. Overall, these preliminary studies suggest that in the d¹⁰ complexes the C=S group may be more biologically accessible *via* partial or complete dissociation of the complex suggesting an avenue for further study.

Conclusions

In this study, six new N,N'-disubstituted thiourea derivatives (L^{1a}-L^{3b}) and the products resulting from their reactions with Cu(I), Cu(II), Ni(II) and Zn(II) yielded complexes (**1-24**). The synthesis and reactivity of the ligands has been explored revealing a range of metal-ligand interactions as well as varied reactivity, including controllable cleavage of ligand substituents, and heterocycle formation which can be promoted and controlled by the choice of metal ion source. X-ray crystallographic studies confirm the versatility of these ligands to form stable complexes with a range of transition metal ions. Of particular interest is the flexible binding modes of the ligand and how these are supported by commensurate H-bonding within the structure. Ease of cleavage of the acyl groups from the ligand is dependant on the metal ion coordinated: no cleavage was observed with Cu(II/I), where as Ni(II) facilitates cleavage at raised temperature and Zn(II) causes cleavage at room temperature. It is conceivable that ligands with such behaviour may, in future, be incorporated into metal ion sensing molecules or for thermally sensitive drug delivery devices.

Experimental

All reagents and solvents were of reagent grade quality and obtained from commercial suppliers, and used without further purification. Elemental analyses for carbon, hydrogen and nitrogen were performed on London Metropolitan University. Magnetic susceptibilities were determined at room temperature (20 °C) using the Evans Method.³⁴ Electronic spectra were recorded using a Shimadzu UV-1800 UV spectrophotometer with complexes were dissolved in CH₃CN unless otherwise stated. IR spectra were carried out with a Shimadzu IR AFFINITY-1S. Electrospray mass spectroscopy (ESI-MS) was measured on a Waters LCT Premier XE (oa-TOF) mass spectrometer. The ¹H and ¹³C NMR spectra were obtained on a Bruker AC 250 instrument using CDCl₃, DMSO-d₆ and acetonitrile-d₃ as solvents. Cyclic voltammetric measurements were performed using a PARSTAT potentiometer with a single compartment three-electrode cell using a platinum disk (2 mm diameter) working electrode and a platinum wire auxiliary electrode with a non aqueous Ag/AgNO₃ reference electrode. The ferrocene/ferrocenium couple was used as an internal reference at the end of each set of measurements. All experiments were carried out under an atmosphere of dry nitrogen. The concentration of electroactive species was approximately 1.5 × 10⁻³ M with tetrabutylammonium hexafluorophosphate (0.1 M) as the supporting electrolyte.

X-ray crystallography

Data collection and processing

Suitable crystals were selected and data collected following a standard method,³⁵ on a Rigaku AFC12 goniometer at 100K equipped with an enhanced sensitivity (HG) Saturn724+ detector mounted at the window of an FR-E-Superbright molybdenum anode generator with either VHF Varimax optics (70µm focus) for **1**, **15** and **21** or HF Varimax optics (100µm focus) for **4**, **6**, **7**, **16** and **19**. Cell determination and data collection were carried out using CrystalClear.³⁶ With the data reduction, cell refinement and absorption correction using either CrystalClear for **1**, **6**, **7**, **16** and **19** or CrystalisPro³⁷ for **4**, **15** and **21**. Structure solution and refinement using SHELX programs³⁸ within Olex2.³⁹

CCDC 2082368 - 2082375 contains supplementary X-ray crystallographic data for **1**, **4**, **6**, **7**, **15**, **16**, **19** and **21** respectively. This data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, Union Road, Cambridge, CB2 1EZ; fax(+44) 1223-336-033 or email: deposit@ccdc.cam.ac.uk.

Antiplasmodial activity assays

Plasmodium falciparum Dd2^{luc} were cultured using standard continuous culture conditions (RPMI1640 medium supplemented with 37.5 mM HEPES, 10 mM D-glucose, 2 mM L-glutamine, 100 µM hypoxanthine, 25µg mL⁻¹ gentamycin, 4% v/v human serum, 0.25% v/v Albumax II, 5nM WR99210 and 2.5

µg mL⁻¹ blasticidin S) at a 2% haematocrit in an atmosphere of 1% O₂, 3% CO₂, and 96% N₂. Concentration-response growth assays following exposure to tested compounds (solubilised in DMSO) were performed using the Malaria Sybr Green I Fluorescence assay as described.³³ Growth (%) normalised against an untreated control was plotted against log₁₀-transformed compound concentration and the 50% Effective Concentration (EC₅₀ and the 95% Confidence Intervals, CI) determined using a nonlinear regression (sigmoidal concentration–response/variable slope equation) in GraphPad Prism v5.0 (GraphPad Software, Inc., San Diego, CA).

Synthesis of the ligands

Synthesis of N-((5-methylpyridin-2-yl)carbamothioyl)benzamide (L^{1a})

The ligand was synthesised by a modification to a previously described method.⁴⁰ To a suspension of potassium thiocyanate (3.89 g, 40 mmol) in acetonitrile (40 cm³) was added dropwise a solution of benzoyl chloride (5.62 g, 40 mmol) in acetonitrile (10 cm³). The reaction mixture was heated to reflux for 3 hrs. After this time, the mixture was a yellow solution with a white precipitate. The mixture was filtered to remove the white KCl precipitate. The yellow solution was added to a solution of 2-amino-5-methyl pyridine (4.32 g, 40 mmol) in acetonitrile (15 cm³) and the reaction mixture was heated to reflux for a further 15 hrs. The solution was left to cool and the resultant white precipitate was collected by filtration. This product was washed with acetonitrile (30 cm³) and purified by recrystallization from chloroform:ethanol (1:1) to obtain white crystals (yield: 3.7 g, 85%). Melting point = 158-159 °C. ¹H NMR (250 MHz, DMSO-d₆): δ = 13.22 (1H, s, NHCS), 11.68 (1H, s, NHCO), 8.63 (1H, app. T, J_{HH} = 5.0 Hz), 8.26 (1H, s), 7.97 (2H, d, J_{HH} = 7.5 Hz), 7.72 (1H, d, J_{HH} = 5.0 Hz), 7.65 (1H, d, J_{HH} = 5.0 Hz), 7.54 (2H, app. T, J_{HH} = 7.5 Hz), 2.29 (3H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): δ = 177.39 (C=S), 168.48 (C=O), 148.75, 148.31, 137.95, 133.01, 131.91, 130.69, 128.58, 128.31, 115.02, 17.42 (CH₃) ppm. ESMS (m/z): 272.10 [M + H]⁺; HRMS found m/z 272.0845, calc. 272.0858. IR (selected, cm⁻¹): 3298 (N-H), 1672 (C=O), 1333 (C=S). UV-vis. λ_{max} (ε / M⁻¹cm⁻¹): 245 (11150), 269 (15200), 316 (9200) nm.

Synthesis of N-((6-aminopyridin-2-yl)carbamothioyl)benzamide (L^{2a})

Using the same procedure as described for L^{1a}, but using potassium thiocyanate (3.89 g, 40 mmol), benzoyl chloride (5.62 g, 40 mmol) and 2,6-diamino pyridine (4.36 g, 40 mmol). The product was obtained as yellow crystals (yield: 3.5 g 80%). Melting point = 180-182 °C. ¹H NMR (250 MHz, DMSO-d₆): δ = 12.99 (1H, s, NHCS), 11.53 (1H, s, NHCO), 7.96 (3H, m), 7.66 (1H, app. T, J_{HH} = 7.5 Hz), 7.53 (2H, d, J_{HH} = 7.5 Hz), 7.46 (1H, d, J_{HH} = 10.0 Hz), 6.31 (1H, d, J_{HH} = 7.5 Hz), 6.14 (2H, s, NH₂) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): δ = 177.09 (C=S), 168.68 (C=O), 159.03, 149.54, 138.75, 133.24, 132.18, 128.77, 128.54, 106.07, 102.82 ppm. ESI-MS (m/z): 272.07 [M]⁺; HRMS found m/z 272.0617, calc. 272.0630. IR (selected, cm⁻¹): 3485 (N-H), 3364 (N-H), 1672 (C=O), 1341 (C=S). UV-vis. λ_{max} (ε / M⁻¹cm⁻¹): 248 (14900), 278 (8050), 301 (6600), 337 (5900) nm.

Synthesis of N,N'-((pyridine-2,6-diylbis(azanediyl))bis(carbonothioyl))dibenzamide (L^{3a})

Using the same procedure as described for L^{1a}, but using potassium thiocyanate (3.89 g, 40 mmol), benzoyl chloride (5.62 g, 40 mmol) and 2,6-diamino pyridine (2.18 g, 20 mmol). The product was obtained as white crystals (yield: 2.00 g, 91%). Melting point = 197-198 °C. ¹H NMR (250 MHz, DMSO-d⁶): δ = 13.15 (2H, s, NHCS), 11.85 (2H, s, NHCO), 8.53 (2H, d, J_{HH} = 5.0 Hz), 8.01 (1H, app. T, J_{HH} = 10.0 Hz), 7.98 (4H, d, J_{HH} = 7.5 Hz), 7.65 (2H, app. T, J_{HH} = 7.5 Hz), 7.53 (4H, app. T, J_{HH} = 7.5 Hz) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d⁶): δ = 178.47 (C=S), 168.92 (C=O), 150.18, 140.38, 133.59, 132.40, 129.13, 128.78, 113.41 ppm. ESI-MS (*m/z*): 436.09 [M + H]⁺; HRMS found *m/z* 436.0915, calc. 436.0902. IR (selected, cm⁻¹): 3321 (N-H), 1667 (C=O), 1325 (C=S). UV-vis. λ_{max} (ε / M⁻¹cm⁻¹): 278 (19400), 331 (12200) nm.

Synthesis of N-((5-methylpyridin-2-yl)carbamoithioyl)pival amide (L^{1b})

To a suspension of potassium thiocyanate (0.81 g, 8.3 mmol) in acetonitrile (15 cm³) was added dropwise the solution of trimethyl acetyl chloride (1 g, 8.3 mmol) in acetonitrile (10 cm³). The reaction mixture was heated to reflux for 3 hrs. The mixture was filtered to remove the white KCl precipitate. The yellow solution was then added to a solution of 2-amino-5-methyl pyridine (0.9 g, 8.3 mmol) in acetonitrile (5 cm³) and the reaction mixture was heated to reflux for 21 hrs. The solution was concentrated to half of its original volume and the white precipitate of product was collected by filtration. The product was washed with cold acetonitrile (5 cm³) and purified by recrystallization from ethanol (yield: 0.78 g, 87%). Melting point = 86-88 °C. ¹H NMR (250 MHz, DMSO-d⁶): δ = 13.16 (1H, s, NHCS), 10.75 (1H, s, NHCO), 8.57 (1H, d, J_{HH} = 10.0 Hz), 8.25 (1H, s), 7.72 (1H, d, J_{HH} = 2.5 Hz), 2.29 (3H, s, CH₃), 1.25 (9H, s, CH₃) ppm. ¹³C{¹H} NMR (100 MHz, DMSO-d⁶): δ = 180.65 (C=S), 177.84 (C=O), 148.86, 148.44, 138.10, 131.00, 115.32, 40.11, 26.13 (CH₃), 17.39 (CH₃) ppm. ESI-MS(*m/z*): 252.08 [M + H]⁺; HRMS found *m/z* 252.1169, calc. 252.1171. IR (selected, cm⁻¹): 3341 (N-H), 1676 (C=O), 1331 (C=S). UV-vis. λ_{max} (ε / M⁻¹ cm⁻¹): 254 (11700), 306 (10850) nm.

Synthesis of N-((6-aminopyridin-2-yl)carbamoithioyl)pival amide (L^{2b})

Using the same procedure as described for L^{1b}, but using potassium thiocyanate (0.81 g, 8.3 mmol), trimethyl acetyl chloride (1 g, 8.3 mmol) and 2,6-diaminopyridine (0.9 g, 8.3 mmol). The product was obtained as white crystals (yield: 0.71 g, 79%). Melting point = 164-165 °C. ¹H NMR (250 MHz, DMSO-d⁶): δ = 12.93 (1H, s, NHCS), 10.58 (1H, s, NHCO), 7.91 (1H, d, J_{HH} = 7.5 Hz), 7.44 (1H, app. T, J_{HH} = 7.5 Hz), 6.30 (1H, d, J_{HH} = 7.5 Hz), 6.12 (2H, s, NH₂), 1.25 (9H, s, CH₃) ppm. ¹³C{¹H} NMR (100 MHz, DMSO-d⁶): δ = 180.34 (C=S), 176.86 (C=O), 158.83, 149.38, 138.62, 105.97, 102.51, 40.02, 26.17 (CH₃) ppm. ESI-MS (*m/z*): 252.08 [M]⁺; HRMS found *m/z* 252.1044, calc. 252.1045. IR (selected, cm⁻¹): 3401 (N-H), 3302 (N-H), 1685 (C=O), 1356 (C=S). UV-vis. λ_{max} (ε / M⁻¹cm⁻¹): 232 (31900), 267 (17750), 292 (12850), 328 (14850) nm.

Synthesis of N,N'-((pyridine-2,6-diylbis(azanediyl))bis(carbonothioyl))bis(2,2-dimethylpropanamide) (L^{3b})

Using the same procedure as described for L^{1b}: potassium thiocyanate (1.94 g, 20 mmol), trimethyl acetyl chloride (2.4 g, 20 mmol) and 2,6-diamino pyridine (1.09 g, 10 mmol). The product was obtained as white crystals (yield: 2.00 g, 86 %). Melting point = 176-177 °C. ¹H NMR (250 MHz, DMSO-d⁶): δ = 13.19 (2H, s, NHCS), 10.90 (2H, s, NHCO), 8.53 (2H, d, J_{HH} = 7.5 Hz), 7.97 (1H, app. T, J_{HH} = 10.0 Hz), 1.26 (18H, s, CH₃) ppm. ¹³C{¹H} NMR (100 MHz, DMSO-d⁶): δ = 180.64 (C=S), 178.30 (C=O), 149.78, 139.99, 113.27, 40.19, 26.12 (CH₃) ppm. ESI-MS (*m/z*): 396.14 [M + H]⁺; HRMS found *m/z* 396.1522, calc. 396.1528. IR (selected, cm⁻¹): 3445 (N-H), 3414 (N-H), 1692 (C=O), 1673 (C=O), 1366 (C=S). UV-vis. λ_{max} (ε / M⁻¹ cm⁻¹): 267 (42000), 322 (47200) nm.

Synthesis of the complexes 1 – 24

CAUTION: Perchlorate compounds of metal ions are potentially explosive especially in presence of organic ligands. Only a small amount of material should be prepared and handled with care. All yields are calculated with respect to the moles of metal ions isolated from the reaction mixture.

Synthesis of [Cu(L^{1a})₂]ClO₄ (1)

A solution of Cu(ClO₄)₂·6H₂O (0.185 g, 0.5 mmol) in H₂O (3 cm³) was added to a solution of L^{1a} (0.272 g, 1.0 mmol) in DMF (4 cm³). The mixture was stirred at room temperature for 3 hrs. The colourless solution turned orange and formed a precipitate. The resultant orange precipitate was filtered, washed with CHCl₃ (20 cm³) to remove unreacted ligand and dried under vacuum. Red crystals of 1 were grown at room temperature by the diffusion of diethyl ether vapour into an acetonitrile solution (yield: 0.25 g, 70 %). ¹H NMR (250 MHz, acetone-d⁶): δ = 14.10 (2H, s, NHCS), 11.14 (2H, s, NHCO), 8.28 (2H, s), 8.06 (4H, d, J_{HH} = 7.5 Hz), 7.91 (2H, d, J_{HH} = 7.5 Hz), 7.72 (2H, app. T, J_{HH} = 7.5 Hz), 7.59 (4H, app. T, J_{HH} = 7.5 Hz), 7.35 (2H, app. T, J_{HH} = 10 Hz), 2.25 (6H, s, CH₃) ppm. ¹³C NMR (62.5 MHz, acetone-d⁶): δ = 170.47 (C=S), 149.49 (C=O), 148.99, 142.04, 135.03, 133.81, 132.68, 129.93, 129.65, 119.06, 111.87, 17.86 ppm. ESI-MS (*m/z*): 605.09 [M-ClO₄]⁺; HRMS found *m/z* = 605.0854, calc. 605.0855. IR (selected, cm⁻¹): 3267 (N-H), 1672 (C=O), 1281 (C=S), 1091, 625 (Cl-O). UV-vis. λ_{max} (ε / M⁻¹ cm⁻¹): 248 (24250), 268 (30600), 315 (17550) nm. Anal. Calc. For C₂₈H₂₆ClCuN₆O₆S₂ (%): C, 47.66; H, 3.71; N, 11.91; found (%): C, 47.58; H, 3.68; N, 11.97.

Synthesis of [Ni(L^{1a})(L^{1c})](ClO₄)₂ (2)

[Ni(L^{1a})(L^{1c})](ClO₄)₂ was obtained by adding a solution of Ni(ClO₄)₂·6H₂O (0.236 g, 0.65 mmol) in methanol (5 cm³) to a solution of L^{1a} (0.35 g, 1.3 mmol) in CHCl₃ (10 cm³). The mixture was heated to reflux for 5 hrs. The colourless solution turned green and then a brown precipitate formed and was filtered off, washed with CHCl₃ (20 cm³) to remove the unreacted ligand, and dried under vacuum to give a brown powder (yield: 0.28 g, 70%). ¹H NMR (250 MHz, DMSO-d⁶): δ = 13.24 (1H, s, NHCS),

11.70 (1H, s, NHCS), 10.46 (2H, s, NH₂), 8.81 (1H, s, NHCO), 8.64 (1H, d, $J_{\text{HH}} = 5.0$ Hz), 8.27 (1H, s), 8.05 (1H, s), 7.96 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 7.73 (1H, d, $J_{\text{HH}} = 5.0$ Hz), 7.66 (1H, d, $J_{\text{HH}} = 7.5$ Hz), 7.58 (3H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.05 (1H, d, $J_{\text{HH}} = 7.5$ Hz), 2.29 (3H, s, CH₃), 2.20 (3H, s, CH₃) ppm. ¹³C NMR (62.5 MHz, DMSO-d₆): $\delta = 177.38(\text{C}=\text{S}), 168.51(\text{C}=\text{O}), 151.44, 145.31, 139.48, 133.17, 132.41, 128.68, 128.44, 127.01, 112.32, 17.37$ (CH₃) ppm. ESI-MS (m/z): 495.04 [M-2ClO₄]⁺; HRMS found m/z 495.0575, calc. 495.0572. IR (selected, cm⁻¹): 3314 (N-H), 1672 (C=O), 1283 (C=S); 1090, 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 242 (15100), 272 (21500), 303 (14100), 411 (390), 584 (56) nm. Anal. Calc. For C₂₁H₂₂Cl₂N₆NiO₉S₂ (%): C, 36.23; H, 3.19; N, 12.07; found (%): C, 36.31; H, 3.12; N, 12.06.

Synthesis of [Ni(L^{1a})₂](ClO₄)₂ (3)

[Ni(L^{1a})₂](ClO₄)₂ was obtained by stirring a mixture of Ni(ClO₄)₂·6H₂O (0.337 g, 0.92 mmol) in methanol (5 cm³) and a solution of L^{1a} (0.5 g, 1.9 mmol) in CHCl₃ (10 cm³) at 50 °C for 5 hrs. The colourless solution turned green and then a brown precipitate formed and was filtered off, washed with CHCl₃ (20 cm³) to remove the unreacted ligand and dried under vacuum to give a brown powder (yield: 0.38 g, 52%). ¹H NMR (250 MHz, DMSO-d₆): $\delta = 13.24$ (2H, s, NHCS), 11.71 (2H, s, NHCO), 8.66 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 8.27 (2H, s), 7.96 (4H, d, $J_{\text{HH}} = 7.5$ Hz), 7.73 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 7.65 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 7.55 (4H, app. t, $J_{\text{HH}} = 5.0$ Hz), 2.29 (6H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): $\delta = 176.08(\text{C}=\text{S}), 167.22(\text{C}=\text{O}), 157.59, 147.11, 136.76, 131.99, 127.53, 127.44, 116.26, 110.61, 16.21$ (CH₃) ppm. ESI-MS (m/z): 599.01 [M-2ClO₄]⁺; HRMS found m/z 599.0829, calc. 599.0834. IR (selected, cm⁻¹): 3404 (N-H), 1668 (C=O), 1283 (C=S), 1087, 624 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 245 (16600), 269 (24400), 314 (12500), 394 (377), 598 (11) nm. Anal. Calc. For C₂₈H₂₆Cl₂N₆NiO₁₀S₂ (%): C, 42.02; H, 3.27; N, 10.50. Found (%): C, 41.95; H, 3.34; N, 10.39.

Synthesis of [Zn(L^{1c})₂](ClO₄)₂ (4)

A methanolic solution (5 cm³) of Zn(ClO₄)₂·6H₂O (0.28 g, 0.75 mmol) was added drop wise to a solution of L^{1a} (0.408 g, 1.5 mmol) in CHCl₃ (10 cm³). The mixture was heated to reflux for 8 hrs. The white precipitate formed was filtered, washed with CHCl₃ (20 cm³) to remove the unreacted ligand and dried under vacuum. Colourless crystals of 4 were grown at room temperature by the diffusion of diethyl ether vapour into an acetonitrile solution (yield: 0.34 g, 76%). ¹H NMR (250 MHz, DMSO-d₆): $\delta = 10.52$ (2H, s, NHCS), 10.47 (2H, s, NH₂), 8.83 (2H, s, NH₂), 8.06 (2H, s), 7.60 (2H, d, $J_{\text{HH}} = 10.0$ Hz), 7.06 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 2.21 (6H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): $\delta = 180.44$ (C=S), 151.78, 145.47, 139.84, 126.59, 112.84, 17.37 (CH₃) ppm. ESI-MS (m/z): 397.05 [M-2ClO₄]⁺; HRMS found m/z 397.0230, calc. 397.0248. IR (selected, cm⁻¹): 3381 (N-H), 1279 (C=S), 1080, 626 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 240 (14900), 273 (28450), 299 (25600) nm. Anal. Calc. For C₁₄H₁₈Cl₂N₆O₈S₂Zn (%): C, 28.09; H, 3.03; N, 14.04; found (%): C, 28.16; H, 3.01; N, 14.12.

This product was also obtained via the same procedure as described for 4 but using Zn(ClO₄)₂·6H₂O (0.22 g, 0.6 mmol) and

L^{1b} (0.3 g, 1.2 mmol). The product was isolated as a white powder (yield: 0.2 g, 69%).

Synthesis of [Zn(L^{1a})(L^{1c})](ClO₄)₂ (5)

A methanolic solution (5 cm³) of Zn(ClO₄)₂·6H₂O (0.34 g, 0.92 mmol) was added drop wise to a solution of L^{1a} (0.5 g, 1.84 mmol) in CHCl₃ (10 cm³). The mixture was stirred at room temperature for 8 hrs. The white precipitate formed was filtered, washed with CHCl₃ (20 cm³) to remove the unreacted ligand and dried under vacuum (yield: 0.36 g, 56%). ¹H NMR (250 MHz, DMSO-d₆): $\delta = 10.52$ (1H, s, NHCS), 10.46 (1H, s, NHCS), 8.82 (1H, s, NHCO), 8.05 (2H, s), 7.95 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 7.65 (1H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.60 (1H, d, $J_{\text{HH}} = 2.5$ Hz), 7.57 (1H, d, $J_{\text{HH}} = 2.5$ Hz), 7.52 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.05 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 4.01 (2H, s, NH₂), 2.20 (6H, s, CH₃) ppm. ¹³C NMR (62.5 MHz, DMSO-d₆): $\delta = 180.35$ (C=S), 166.30(C=O), 151.65, 145.53, 139.77, 133.47, 129.71, 129.25, 128.92, 127.14, 112.43, 17.33 ppm. ESI-MS (m/z): 501.00 [M-H-2ClO₄]⁺; HRMS found $m/z = 501.0331$, calc. 501.0339. IR (selected, cm⁻¹): 3377 (N-H), 1670 (C=O), 1278 (C=S), 1084, 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 235 (24300), 273 (33950), 299 (29800) nm. Anal. Calc. For C₂₁H₂₂Cl₂N₆O₉S₂Zn (%): C, 35.89; H, 3.16; N, 11.96; found (%): C, 35.72; H, 2.88; N, 11.82.

Synthesis of [Cu(L^{2a})₂](ClO₄)₂ (6)

Using the same procedure as described for 1, but using Cu(ClO₄)₂·6H₂O (0.4 g, 1.1 mmol), L^{2a} (0.589 g, 2.2 mmol). Dark orange crystals of 6 were grown at room temperature by the diffusion of diethyl ether vapour into an acetonitrile:methanol (2:1) solution of it (yield: 0.51 g, 66%). ¹H NMR (250 MHz, CD₃CN): $\delta = 13.23$ (2H, s, NHCS), 9.68 (2H, s, NHCO), 7.91 (4H, d, $J_{\text{HH}} = 7.5$ Hz), 7.69 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.55 (6H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.34 (2H, d, $J_{\text{HH}} = 10.0$ Hz), 6.49 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 5.29 (4H, s, NH₂) ppm. ¹³C{¹H} NMR (62.5 MHz, CD₃CN): $\delta = 174.72$ (C=S), 168.88 (C=O), 158.06, 149.87, 140.22, 133.52, 132.61, 128.68, 128.59, 103.07, 100.66 ppm. ESI-MS (m/z): 607.08 [M-ClO₄]⁺; HRMS found $m/z = 607.0754$, calc. 607.0760. IR (selected, cm⁻¹): 3323 (N-H), 1661 (C=O), 1258 (C=S), 1080, 624 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 247 (33650), 279 (18200), 302 (14700), 344 (12850) nm. Anal. Calc. For C₂₆H₂₄ClCuN₈O₆S₂ (%): C, 44.13; H, 3.42; N, 15.84; found (%): C, 44.04; H, 3.47; N, 15.72.

Synthesis of [Ni(L^{2c})₂](ClO₄)₂ (7)

[Ni(L^{2c})₂](ClO₄)₂ was obtained by using the same procedure as described for 2, using [Ni(ClO₄)₂].6H₂O (0.2 g, 0.55 mmol) and L^{2a} (0.3 g, 1.1 mmol). Red crystals of 7 were grown at room temperature by the diffusion of diethyl ether vapour into an ethyl acetate solution (yield: 0.21 g, 64%). ¹H NMR (250 MHz, DMSO-d₆): $\delta = 10.61$ (2H, s, NHCS), 10.05 (2H, s, NH₂), 8.66 (2H, s, NH₂), 7.28 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 6.20 (6H, m), 6.00 (2H, d, $J_{\text{HH}} = 7.5$ Hz) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): $\delta = 179.99$ (C=S), 157.50, 139.08, 129.08, 128.78, 100.98, 98.88 ppm. ESI-MS (m/z): 393.02 [M-H-2ClO₄]⁺; HRMS found $m/z = 393.0206$, calc. 393.0215. IR (selected, cm⁻¹): 3343 (N-H), 1271 (C=S), 1071, 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1} \text{cm}^{-1}$): 215 (16900), 251 (20050),

272 (18950), 319 (22950), 401 (205), 603 (17) nm. Anal. Calc. For $C_{12}H_{16}Cl_2N_8NiO_8S_2$ (%): C, 24.26; H, 2.72; N, 18.86; found (%): C, 24.20; H, 2.83; N, 18.79.

This product was also obtained via the same procedure described for **2**, but with $[Ni(ClO_4)_2] \cdot 6H_2O$ (0.25 g, 0.69 mmol) and **L^{2b}** (0.35 g, 1.4 mmol). The product was isolated as a brown powder (yield: 0.24 g, 69%).

Synthesis of $[Ni(L^{2a})_2](ClO_4)_2$ (**8**)

$[Ni(L^{2a})_2](ClO_4)_2$ was obtained as a brown powder by using the same procedure as described for **3**, but using $Ni(ClO_4)_2 \cdot 6H_2O$ (0.336 g, 0.92 mmol) and **L^{2a}** (0.5 g, 1.84 mmol). The product was isolated as a brown powder (yield: 0.34 g, 46%). 1H NMR (250 MHz, DMSO- d_6): δ = 13.00 (2H, s, NHCS), 11.55 (2H, s, NHCO), 7.95 (4H, d, J_{HH} = 5.0 Hz), 7.64 (4H, d, J_{HH} = 5.0 Hz), 7.52 (4H, app. t, J_{HH} = 7.5 Hz), 7.28 (2H, app. t, J_{HH} = 7.0 Hz), 6.21 (4H, s, NH_2), 6.18 (2H, app. t, J_{HH} = 10.0 Hz) ppm. $^{13}C\{^1H\}$ NMR (62.5 MHz, DMSO- d_6): δ = 176.09 (C=S), 165.60 (C=O), 158.36, 156.75, 138.90, 132.87, 132.77, 128.33, 128.04, 109.43, 105.80 ppm. ESI-MS (m/z): 601.08 $[M-H-2ClO_4]^+$; HRMS found m/z = 601.0742, calc. 601.0739. IR (selected, cm^{-1}): 3331 (N-H), 1660 (C=O), 1275 (C=S), 1071, 626 (Cl-O). UV-vis. λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 235 (16550), 250 (19300), 273 (13550), 324 (11500), 421 (423), 612 (5) nm. Anal. Calc. For $C_{26}H_{24}Cl_2N_8NiO_{10}S_2$ (%): C, 38.93; H, 3.02; N, 13.97; found (%): C, 38.87; H, 3.13; N, 13.92.

Synthesis of $[Zn(L^{2c})_2](ClO_4)_2$ (**9**)

Using the same procedure as described for **4**, using $Zn(ClO_4)_2 \cdot 6H_2O$ (0.24 g, 0.64 mmol) and **L^{2a}** (0.35 g, 1.3 mmol). The product was isolated as a white powder (yield: 0.28 g, 73%). 1H NMR (400 MHz, DMSO- d_6): δ = 10.63 (2H, s, NHCS), 10.06 (2H, s, NH_2), 8.68 (2H, s, NH_2), 7.29 (2H, app. t, J_{HH} = 2.5 Hz), 6.22 (6H, m), 6.02 (2H, d, J_{HH} = 5.0 Hz) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, DMSO- d_6): δ = 180.05 (C=S), 157.74, 152.40, 139.39, 101.00, 98.79 ppm. ESI-MS (m/z): 399.00 $[M-H-2ClO_4]^+$; HRMS found m/z 399.0000, calc. 399.0000. IR (selected, cm^{-1}): 3375 (N-H), 1267 (C=S), 1067 (Cl-O), 626 (Cl-O). UV-vis. λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 214 (28200), 251 (34100), 272 (31750), 320 (38250) nm. Anal. Calc. For $C_{12}H_{16}Cl_2N_8O_8S_2Zn$ (%): C, 23.99; H, 2.68; N, 18.65; found (%): C, 24.13; H, 2.73; N, 18.48.

This product was also obtained as described for **4** but using $Zn(ClO_4)_2 \cdot 6H_2O$ (0.25 g, 0.67 mmol) and **L^{2b}** (0.34 g, 1.3 mmol). The product was isolated as a white powder (yield: 0.27 g, 81%).

Synthesis of $[Zn(L^{2a})(L^{2c})](ClO_4)_2$ (**10**)

Using the same procedure as described for **5** but using $Zn(ClO_4)_2 \cdot 6H_2O$ (0.17 g, 0.46 mmol) was added drop wise to a solution of **L^{2a}** (0.25 g, 0.92 mmol). The product was isolated as a white powder (yield: 0.18 g, 57%). 1H NMR (250 MHz, DMSO- d_6): δ = 10.62 (2H, s, NHCS), 10.06 (1H, s, NHCO), 8.67 (2H, s, NH_2), 7.95 (2H, d, J_{HH} = 7.5 Hz), 7.66 (1H, app. t, J_{HH} = 7.5 Hz), 7.52 (2H, app. t, J_{HH} = 7.5 Hz), 7.29 (2H, app. t, J_{HH} = 7.5 Hz), 6.19 (2H, d, J_{HH} = 7.5 Hz), 6.02 (2H, d, J_{HH} = 7.5 Hz), 3.85 (4H, s, NH_2) ppm. $^{13}C\{^1H\}$ NMR (62.5 MHz, DMSO- d_6): δ = 180.35 (C=S), 166.26 (C=O), 157.86, 152.35, 139.55, 133.48, 129.65, 129.25, 128.93, 101.20, 98.79 ppm. ESI-MS (m/z): 504.05 $[M-H-2ClO_4]^+$; HRMS found m/z 504.0663, calc. 504.0674. IR (selected, cm^{-1}):

3366 (N-H), 1668 (C=O), 1277 (C=S), 1070 (Cl-O), 626 (Cl-O). UV-vis. λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 222 (21100), 275 (14000), 326 (8150), 367 (10300) nm. Anal. Calc. For $C_{19}H_{20}Cl_2N_8O_9S_2Zn$ (%): C, 32.38; H, 2.86; N, 15.90; found (%): C, 32.40; H, 3.14; N, 15.84.

Synthesis of $[Cu(L^{3a})]ClO_4$ (**11**)

Using the same procedure as described for **1**, but using $Cu(ClO_4)_2 \cdot 6H_2O$ (0.21 g, 0.57 mmol) and **L^{3a}** (0.25 g, 0.57 mmol). The product was isolated as a brown powder (yield: 0.16 g, 47%). 1H NMR (250 MHz, DMSO- d_6): δ = 12.14 (2H, s, NHCS), 11.74 (2H, s, NHCO), 8.25 (2H, d, J_{HH} = 7.5 Hz), 8.11 (2H, d, J_{HH} = 7.5 Hz), 7.93 (1H, d, J_{HH} = 7.5 Hz), 7.69 (1H, app. t, J_{HH} = 7.5 Hz), 7.59 (7H, m) ppm. $^{13}C\{^1H\}$ NMR (62.5 MHz, DMSO- d_6): δ = 176.50 (C=S), 169.51 (C=O), 150.24, 140.39, 133.53, 132.77, 132.27, 131.50, 128.66, 128.59, 113.19, 107.09 ppm. ESI-MS (m/z): 498.02 $[M-ClO_4]^+$; HRMS found m/z 498.0110, calc. 498.0120. IR (selected, cm^{-1}): 3387 (N-H), 1665 (C=O), 1260 (C=S), 1096 (Cl-O), 621 (Cl-O). UV-visible λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 263 (23200), 316 (18400), 359 (19400) nm. Anal. Calc. For $C_{21}H_{17}ClCuN_5O_6S_2$ (%): C, 42.14; H, 2.86; N, 11.70; found (%): C, 42.30; H, 3.00; N, 11.69.

Synthesis of $[Cu(L^{3a})_2]ClO_4$ (**12**)

Using the same procedure as described for **1** but using $Cu(ClO_4)_2 \cdot 6H_2O$ (0.106 g, 0.29 mmol) and **L^{3a}** (0.25 g, 0.57 mmol). The product was isolated as an orange powder (yield: 0.17 g, 57%). 1H NMR (250 MHz, DMSO- d_6): δ = 12.15 (4H, s, NHCS), 11.73 (4H, s, NHCO), 8.23 (8H, d, J_{HH} = 2.5 Hz), 8.14 (2H, app. t, J_{HH} = 5.0 Hz), 8.02 (4H, d, J_{HH} = 5.0 Hz), 7.64 (4H, app. t, J_{HH} = 5.0 Hz), 7.56 (8H, J_{HH} = 5.0 Hz) ppm. $^{13}C\{^1H\}$ NMR (62.5 MHz, DMSO- d_6): δ = 176.42 (C=S), 168.78 (C=O), 162.32, 141.10, 133.58, 132.20, 129.05, 128.67, 114.61 ppm. ESI-MS (m/z): 933.09 $[M-H-ClO_4]^+$; HRMS found m/z 933.1029, calc. 933.1045. IR (selected, cm^{-1}): 3340 (N-H), 1667 (C=O), 1252 (C=S), 1096 (Cl-O), 621 (Cl-O). UV-visible λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 268 (40950), 336 (24600) nm. Anal. Calc. For $C_{42}H_{34}ClCuN_{10}O_8S_4$ (%): C, 48.79; H, 3.31; N, 13.55; found (%): C, 48.46; H, 2.92; N, 13.47.

Synthesis of $[Ni(L^{3a})_2](ClO_4)_2$ (**13**)

Obtained using the same procedure as described for **3**, but with $Ni(ClO_4)_2 \cdot 6H_2O$ (0.11 g, 0.29 mmol) and **L^{3a}** (0.25 g, 0.57 mmol). The product was isolated as a green powder (yield: 0.17 g, 50%). ESI-MS (m/z): 928.10 $[M-2ClO_4]^+$; HRMS found m/z 928.2207, calc. 928.2233. IR (selected, cm^{-1}): 3469 (N-H), 1663 (C=O), 1277 (C=S), 1064 (Cl-O), 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / M^{-1} cm^{-1}$): 281 (24300), 331 (14200), 413 (212), 583 (21), 936 (12) nm. Anal. Calc. For $C_{42}H_{34}Cl_2N_{10}NiO_{12}S_4$ (%): C, 44.70; H, 3.04; N, 12.41; found (%): C, 44.67; H, 2.68; N, 12.39.

Synthesis of $[Zn(L^{3a})_2](ClO_4)_2$ (**14**)

Using the same procedure as described for **5** but using $[Zn(ClO_4)_2] \cdot 6H_2O$ (0.214 g, 0.57 mmol) and **L^{3a}** (0.5 g, 1.1 mmol). The product was isolated as a white powder (yield: 0.32 g, 49%). 1H NMR (250 MHz, DMSO- d_6): δ = 12.86 (2H, s, NHCS), 11.67 (2H, s, NHCO), 10.61 (2H, s, NH_2), 9.00 (2H, s, NH_2), 7.94-7.99 (4H, m), 7.84 (4H, d, J_{HH} = 7.5 Hz), 7.66 (4H, app. t, J_{HH} = 7.5 Hz), 7.44 (2H, d, J_{HH} = 7.5 Hz), 7.02 (2H, d, J_{HH} = 10.0

Hz) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (62.5 MHz, DMSO- d_6): δ = 180.23 (C=S), 178.09 (C=S), 168.13 (C=O), 152.04, 148.35, 140.66, 133.51, 132.27, 128.94, 128.65, 109.97, 109.76 ppm. IR (selected, cm^{-1}): 3318 (N-H), 1664 (C=O), 1273 (C=S), 1095 (Cl-O), 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 281 (29900), 326 (20800) nm. Anal. Calc. For $\text{C}_{28}\text{H}_{26}\text{Cl}_2\text{N}_{10}\text{O}_{10}\text{S}_4\text{Zn}$ (%): C, 36.28; H, 2.83; N, 15.11; found (%): C, 35.90; H, 2.66; N, 14.95.

Synthesis of $[\text{Cu}(\text{L}^{1b})_2](\text{ClO}_4)$ (**15**)

As described for **1** but using $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.22 g, 0.59 mmol) and L^{1b} (0.298 g, 1.2 mmol). Orange crystals of **15** were grown at room temperature by the diffusion of diethyl ether vapour into a CHCl_3 solution (yield: 0.20 g, 51 %). ^1H NMR (400 MHz, CD_3CN): δ = 13.60 (2H, s, NHCS), 9.09 (2H, s, NHCO), 8.15 (2H, s), 7.75 (2H, d, $J_{\text{HH}} = 5.0$ Hz), 7.45 (2H, d, $J_{\text{HH}} = 5.0$ Hz), 2.29 (6H, s, CH_3), 1.29 (18H, s, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_3CN): δ = 182.39 (C=S), 176.90 (C=O), 149.41, 148.51, 141.72, 133.93, 118.97, 41.21, 26.36 (CH_3), 18.19 (CH_3) ppm. ESI-MS (m/z): 565.15 $[\text{M}-\text{ClO}_4]^+$; HRMS found m/z 565.1470, calc. 565.1481. IR (selected, cm^{-1}): 3358 (N-H), 1676 (C=O), 1283 (C=S), 1096 (Cl-O), 621 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 254 (23900), 307 (22000) nm. Anal. Calc. For $\text{C}_{24}\text{H}_{34}\text{ClCuN}_6\text{O}_6\text{S}_2$ (%): C, 43.30; H, 5.15; N, 12.62; found (%): C, 43.34; H, 5.06; N, 12.57.

Synthesis of $[\text{Cu}(\text{L}^{1b})\text{Cl}](\text{16})$

A solution of L^{1b} (0.30 g, 1.2 mmol) in CHCl_3 (4 cm^3) was added to a solution of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.10 g, 0.6 mmol) in methanol (4 cm^3). The mixture was stirred for 4 hrs at room temperature. The colourless solution turned orange with a precipitate. The orange precipitate formed was filtered, washed with CHCl_3 (20 cm^3) to remove unreacted ligand, and dried under vacuum. Red crystals of **16** were grown at room temperature by the diffusion of diethyl ether vapour into a chloroform solution (yield: 0.26 g, 78%). ^1H NMR (400 MHz, CDCl_3): δ = 13.73 (1H, s, NHCS), 9.67 (1H, s, NHCO), 8.50 (1H, s), 7.67 (1H, d, $J_{\text{HH}} = 5.0$ Hz), 7.17 (1H, d, $J_{\text{HH}} = 5.0$ Hz), 2.38 (3H, s, CH_3), 1.43 (9H, s, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ = 181.94 (C=S), 174.69 (C=O), 149.19, 146.70, 140.06, 132.60, 117.88, 40.96, 26.65, 17.95 ppm. ESI-MS (m/z): 371.13 $[\text{M} + \text{Na}]^+$. IR (selected, cm^{-1}): 3450 (N-H), 1673 (C=O), 1275 (C=S). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 293 (9500), 318 (7600) nm. Anal. Calc. For $\text{C}_{12}\text{H}_{17}\text{ClCuN}_3\text{OS}$ (%): C, 41.14; H, 4.89; N, 11.99; found (%): C, 40.94; H, 4.65; N, 12.04.

Synthesis of $[\text{Ni}(\text{L}^{1b})_2](\text{ClO}_4)_2$ (**17**)

Obtained using the same procedure as described for **3**, but with $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.255 g, 0.7 mmol) and L^{1b} (0.35 g, 1.4 mmol). The product was isolated as a brown powder (yield: 0.27 g, 51%). ^1H NMR (250 MHz, DMSO- d_6): δ = 13.15 (2H, s, NHCS), 10.74 (2H, s, NHCO), 8.56 (2H, d, $J_{\text{HH}} = 5.0$ Hz), 8.23 (2H, s), 7.69 (2H, d, $J_{\text{HH}} = 10.0$ Hz), 2.27 (6H, s, CH_3), 1.24 (18H, s, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (62.5 MHz, DMSO- d_6): δ = 177.23 (C=S), 174.83 (C=O), 161.21, 147.56, 137.53, 125.84, 114.22, 40.00, 25.52 (CH_3), 17.02 (CH_3) ppm. ESI-MS (m/z): 559.15 $[\text{M}-\text{H}-2\text{ClO}_4]^+$; HRMS found m/z 559.1451, calc. 559.1460. IR (selected, cm^{-1}): 3321 (N-H), 1675 (C=O), 1287 (C=S), 1092 (Cl-O), 626 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 257 (9100), 304 (9250), 390 (329), 597

(11) nm. Anal. Calc. For $\text{C}_{24}\text{H}_{34}\text{Cl}_2\text{N}_6\text{NiO}_{10}\text{S}_2$ (%): C, 37.92; H, 4.51; N, 11.05; found (%): C, 37.80; H, 4.58; N, 10.97.

Synthesis of $[\text{Cu}(\text{L}^{2b})_2](\text{ClO}_4)$ (**18**)

The same procedure as described for **1** but using $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.26 g, 0.69 mmol) and L^{2b} (0.35 g, 1.4 mmol). The product was isolated as a brown powder (yield: 0.29 g, 63%). ^1H NMR (250 MHz, CD_3CN): δ = 13.25 (2H, s, NHCS), 8.94 (2H, s, NHCO), 7.54 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 7.01 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 6.50 (2H, d, $J_{\text{HH}} = 10.0$ Hz), 5.37 (4H, s, NH_2), 1.26 (18H, s, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (62.5 MHz, CD_3CN): δ = 182.51 (C=S), 176.62 (C=O), 159.48, 149.07, 141.61, 41.38, 27.18 (CH_3) ppm. ESI-MS (m/z): 567.20 $[\text{M}-\text{ClO}_4]^+$; HRMS found m/z 567.1367, calc. 567.1386. IR (selected, cm^{-1}): 3343 (N-H), 1671 (C=O), 1267 (C=S), 1079 (Cl-O), 625 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 230 (12000), 268 (6400), 296 (4300), 332 (5650) nm. Anal. Calc. For $\text{C}_{22}\text{H}_{32}\text{ClCuN}_8\text{O}_6\text{S}_2$ (%): C, 39.58; H, 4.83; N, 16.78; found (%): C, 39.37; H, 4.70; N, 16.46.

Synthesis of $[\text{Cu}(\text{L}^4)_2\text{Cl}_2]$ (**19**)

A solution of $\text{CuCl}_2 \cdot 6\text{H}_2\text{O}$ (0.1 g, 0.59 mmol) in methanol (4 cm^3) was added to a solution of L^{2b} (0.3 g, 1.2 mmol) in CHCl_3 (8 cm^3). The mixture was stirred for 3 hrs at room temperature. The colourless solution turned orange with a precipitate. The orange precipitate was collected by filtration, washed with CHCl_3 (20 cm^3) to remove unreacted ligand, and dried under vacuum. Dark orange crystals of **19** were grown at room temperature by the diffusion of diethyl ether vapour into a DCM:ethanol (1:1) solution of the product (yield: 0.18 g, 48%). ESI-MS (m/z): 667.04 $[\text{M} + \text{MeOH}]^+$. IR (selected, cm^{-1}): 3320 (N-H), 1683 (C=O), 1273 (C=S). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 264 (26900), 282 (22800), 326 (22100), 470 (139) nm. Anal. Calc. For $\text{C}_{22}\text{H}_{28}\text{Cl}_2\text{CuN}_8\text{O}_2\text{S}_2$ (%): C, 41.61; H, 4.44; N, 17.64; found (%): C, 41.28; H, 4.43; N, 17.25.

Synthesis of $[\text{Ni}(\text{L}^{2b})_2](\text{ClO}_4)_2$ (**20**)

Obtained using the same procedure described for **3**, but with $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.36 g, 1 mmol) and L^{2b} (0.5 g, 2 mmol). The product was isolated as a brown powder (yield: 0.38 g, 51%). ^1H NMR (250 MHz, DMSO- d_6): δ = 12.91 (2H, s, NHCS), 10.56 (2H, s, NHCO), 7.88 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 7.42 (2H, app. t, $J_{\text{HH}} = 7.5$ Hz), 6.28 (2H, d, $J_{\text{HH}} = 7.5$ Hz), 6.10 (4H, s, NH_2), 1.22 (18H, s, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (62.5 MHz, DMSO- d_6): δ = 179.81 (C=S), 176.03 (C=O), 158.53, 148.85, 138.08, 105.48, 102.15, 30.37, 25.81 (CH_3) ppm. ESI-MS (m/z): 561.09 $[\text{M}-2\text{ClO}_4]^+$; HRMS found m/z 561.1377, calc. 561.1365. IR (selected, cm^{-1}): 3377 (N-H), 1664 (C=O), 1277 (C=S), 1071 (Cl-O), 627 (Cl-O). UV-vis. λ_{max} ($\epsilon / \text{M}^{-1}\text{cm}^{-1}$): 232 (41600), 268 (24100), 294 (15500), 328 (21550), 410 (340), 606 (7) nm. Anal. Calc. For $\text{C}_{22}\text{H}_{32}\text{Cl}_2\text{N}_8\text{NiO}_{10}\text{S}_2$ (%): C, 34.67; H, 4.23; N, 14.70; found (%): C, 34.58; H, 4.29; N, 14.72.

Synthesis of $[\text{Cu}(\text{L}^{3b})\text{ClO}_4]$ (**21**)

Using the same procedure as described for **1** but using $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (0.328 g, 0.89 mmol) and L^{3b} (0.35 g, 0.89 mmol). Yellow crystals of **21** were grown at room temperature by the diffusion of diethyl ether vapour into an ethanol:DCM (3:1) solution of the product (yield: 0.28 g, 56%). ^1H NMR (250 MHz,

DMSO-d₆): δ = 11.99 (2H, s, NHCS), 11.00 (2H, s, NHCO), 8.17 (1H, app. t, J_{HH} = 7.5 Hz), 7.94 (1H, d, J_{HH} = 7.5 Hz), 7.64 (1H, d, J_{HH} = 7.5 Hz), 1.29 (18H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, DMSO-d₆): δ = 187.38 (C=S), 181.39 (C=O), 149.85, 140.40, 139.85, 112.84, 107.67, 26.23 (CH₃), 25.84, 25.32 (CH₃), 24.96 ppm. ESI-MS (m/z): 458.06 [M-ClO₄]⁺; HRMS found m/z 458.0869, calc. 458.0871. IR (selected, cm⁻¹): 3400 (N-H), 1688 (C=O), 1277 (C=S), 1090 (Cl-O), 625 (Cl-O). UV-vis. λ_{max} (ϵ / M⁻¹cm⁻¹): 298 (6650), 350 (6500) nm. Anal. Calc. For C₁₇H₂₅ClCuN₅O₆S₂ (%): C, 36.56; H, 4.51; N, 12.54; found (%): C, 36.31; H, 4.41; N, 12.68.

Synthesis of [Cu(L^{3b})₂](ClO₄) (22)

Using the same procedure as described for **1** but using Cu(ClO₄)₂·6H₂O (0.164 g, 0.44 mmol) and L^{3b} (0.35 g, 0.89 mmol). The product was isolated as a brown powder (yield: 0.23 g, 55%). ¹H NMR (250 MHz, CD₃CN): δ = 13.64 (4H, s, NHCS), 9.18 (4H, s, NHCO), 7.99 (2H, app. t, J_{HH} = 7.5 Hz), 7.73 (4H, d, J_{HH} = 10.0 Hz), 1.29 (36H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, CD₃CN): δ = 182.79 (C=S), 178.32 (C=O), 149.38, 143.13, 117.19, 41.85, 26.96 (CH₃) ppm. ESI-MS (m/z): 853.22 [M-ClO₄]⁺; HRMS found m/z 853.2182, calc. 853.2195. IR (selected, cm⁻¹): 3397 (N-H), 1690 (C=O), 1277 (C=S), 1077 (Cl-O), 624 (Cl-O). UV-vis. λ_{max} (ϵ / M⁻¹cm⁻¹): 278 (20700), 290 (20750), 326 (14800) nm. Anal. Calc. For C₃₄H₅₀ClCuN₁₀O₈S₄ (%): C, 42.80; H, 5.28; N, 14.68; found (%): C, 42.46; H, 4.93; N, 14.63.

Synthesis of [Ni(L^{3b})₂](ClO₄)₂ (23)

Obtained using the same procedure described for **3**, but using Ni(ClO₄)₂·6H₂O (0.14 g, 0.38 mmol) and L^{3b} (0.3 g, 0.76 mmol). The product was isolated as a green powder (yield: 0.20 g, 50%). ESI-MS (m/z): 847.25 [M-2ClO₄]⁺; HRMS found m/z 847.2164; calc. 847.2175. IR (selected, cm⁻¹): 3312 (N-H), 1687 (C=O), 1262 (C=S), 1090 (Cl-O), 626 (Cl-O). UV-vis. λ_{max} (ϵ / M⁻¹cm⁻¹): 267 (38800), 323 (39050), 421 (242), 591 (5), 952 (3) nm. Anal. Calc. For C₃₄H₅₀Cl₂N₁₀NiO₁₂S₄ (%): C, 38.94; H, 4.81; N, 13.36; found (%): C, 39.10; H, 4.72; N, 13.46.

Synthesis of [Zn(L^{3c})₂](ClO₄)₂ (24)

Using the same procedure described for **4**, but using Zn(ClO₄)₂·6H₂O (0.165 g, 0.44 mmol) and L^{3b} (0.35 g, 0.89 mmol). The product was isolated as a white powder (yield: 0.26 g, 67%). ¹H NMR (250 MHz, CD₃CN): δ = 12.93 (2H, s, NHCS), 10.77 (2H, s, NHCS), 10.60 (2H, s, NHCS), 10.00 (2H, s, NHCS), 8.99 (2H, s, NHCO), 7.91 (2H, d, J_{HH} = 7.5 Hz), 7.82 (2H, t, J_{HH} = 10.0 Hz), 7.01 (2H, d, J_{HH} = 10.0 Hz), 1.25 (18H, s, CH₃) ppm. ¹³C{¹H} NMR (62.5 MHz, CD₃CN): δ = 180.39, 180.23 (C=S), 178.28 (C=O), 151.88, 150.30, 148.22, 140.66, 110.09, 40.27, 26.30 (CH₃) ppm. ESI-MS (m/z): 685.09 [M-2ClO₄]⁺; HRMS found m/z 685.0972; calc. 685.0962. IR (selected, cm⁻¹): 3317 (N-H), 1689 (C=O), 1258 (C=S), 1075 (Cl-O), 626 (Cl-O). UV-vis. λ_{max} (ϵ / M⁻¹cm⁻¹): 282 (27500), 326 (21200) nm. Anal. Calc. For C₂₄H₃₄Cl₂N₁₀O₁₀S₄Zn (%): C, 32.49; H, 3.86; N, 15.79; found (%): C, 32.28; H, 3.54; N, 15.54.

Author Contributions

We strongly encourage authors to include author contributions and recommend using [CRediT](#) for standardised contribution descriptions. Please refer to our general [author guidelines](#) for more information about authorship.

Conflicts of interest

There are no conflicts to declare.

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‡ Footnotes relating to the main text should appear here. These might include comments relevant not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.