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Synthesis and Anti-HIV Activity of New 2-Thiolumazine and 2-Thiouracil Metal Complexes

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ABSTRACT: *A series of new Cu(II), Pt(II), VO(II), Fe(II), and Co(II) complexes (***1–5***) with 3-methyl-6,7-diphenyllumazine are described. Similarly, complexes from 2-thiouracil with Cu(II) (***6,7***) and Pt(II) (***8***) have been prepared and characterized by spectroscopic methods. All the complexes were assayed for their anti-HIV-1 and HIV-2 activity by examination of their inhibition of HIV-induced cytopathogenicity in MT-4 cells. Compound* **3** *was found to be the most active inhibitor against HIV-2 in cell culture (EC_{50} = >18.95 μg/mL, selectivity index (SI) = 3), which provided a good lead for further optimization. Compounds* **6** *and* **7** *exhibited some activity (EC_{50} = >7.12 μg/mL and >2.23 μg/mL) against HIV-1 and HIV-2, but no selectivity was observed (SI <1).* © 2010 Wiley Periodicals, Inc. Heteroatom Chem 22:44–50, 2011; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20654

INTRODUCTION

A considerable interest has been emerging on the metal complexes of pteridines such as molybdopterin or tetrahydropterin due to their biological importance. Pfleiderer et al. [1–5] had focused on the synthesis and biological activity of lumazine, pteridine, pterine, and tetrahydropterin derivatives for many years. Several pteridine derivatives have been studied from a variety of perspectives by many different research groups [6–9]. Recently, Schmidt et al. [10–13] have synthesized various tertrahydropterin analogues with remarkable inhibition of the nitric oxide synthase, the enzyme responsible for the mental disorder. It is known that pteridine and pterin act by inhibiting the xanthin oxidase, as a key enzyme in the biosynthesis of DNA precursors and a generator of free radicals [14,15]. The capability of pteridines and pterines for simulating the reactivity of metal sites in several enzymes [16–19] encouraged many laboratories to synthesize the metal complexes of these molecules [20,21].

A considerable interest has been emerging on the great importance of certain synthetic substituted uracils in many metabolic processes [22]. 4-Amino-2-thiouracil, for example, a thiopyrimidine derivative, exhibited antiviral and chemotherapeutic activity [23]. Therefore, several laboratories have focused their interest on the synthesis of 2-thiouracil–metal complexes [24–27].

Singh et al. [28] prepared metal complexes of 5-carboxy-2-thiouracil with their activity against Sarcoma-180 (S-180) tumor cells; meanwhile, Masoud et al. [22] published a series of papers to throw light on the chemistry of the biologically active pyrimidines.

We report here the synthesis, structural studies, and anti-HIV activity of some new complexes of

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metal ions of 3-methyl-6,7-diphenyl-2-thiolumazine and 2-thiouracil.

RESULTS AND DISCUSSION

Chemistry

Recently, Moreno-Carretero et al. [29] have reported the synthesis of some metal complexes of 1-methyl- and 1,6,7-trimethyllumazines with their improvement in coordination of the metal with the lumazine backbone as bidentate bonding through the N-5 and O-4 atoms. In our present work, 3-methyl-2-thiolumazine (MDPhTL) has been selected for the coordination with various metals. MDPhTL was prepared from condensation of 5,6-diamino-3-methyl-2-thiouracil with benzil in refluxing EtOH, whereas its metal complexes **1–5** were prepared from salts of Cu(II), Pt(II), VO(II), Co(II), and Fe(II) (see Fig. 1). Characterization of **1–5** was carried out by elemental analysis, IR, and mass spectra. The 2-thiolumazine ligand behaves as a flexidentate ligand and commonly coordinated through the sulfur atom (C^2-S) of the 2-thiopyrimidine ring and the nitrogen atom (N-1) of the azomethine group.

The IR spectra complexes **1–5** showed a similar pattern of spectra, especially for the lumazine backbone. The complexes **1,2**, and **5** exhibited a broad band at 3405 cm^{-1} assigned to the lattice water, whereas the absence of such broad bands in VO and Fe complexes is a convenient with the analytical data, where water molecules do not exist [30]. In the 3210–2800 cm^{-1} region, the IR spectra showed the ν(N—H) and g ν(C—H) bands. The absorption band located at 1633 cm^{-1} in the IR spectrum of the free thiolumazine was attributed to ν(C=O). Furthermore, the IR spectra of the ligand exhibited a band at 1556 cm^{-1} assigned to ν(C=N) of azomethine. This band shifts to a lower wave number by about 25–30 cm^{-1} on the chelation of the ligand with a metal. MDPhTL exhibited thione-thiol tautomerism adopted the thione form in the solid and was readily deprotonated to the corresponding thionate anion in solution [31]. Deprotonation of the ligand was accompanied by a substantial

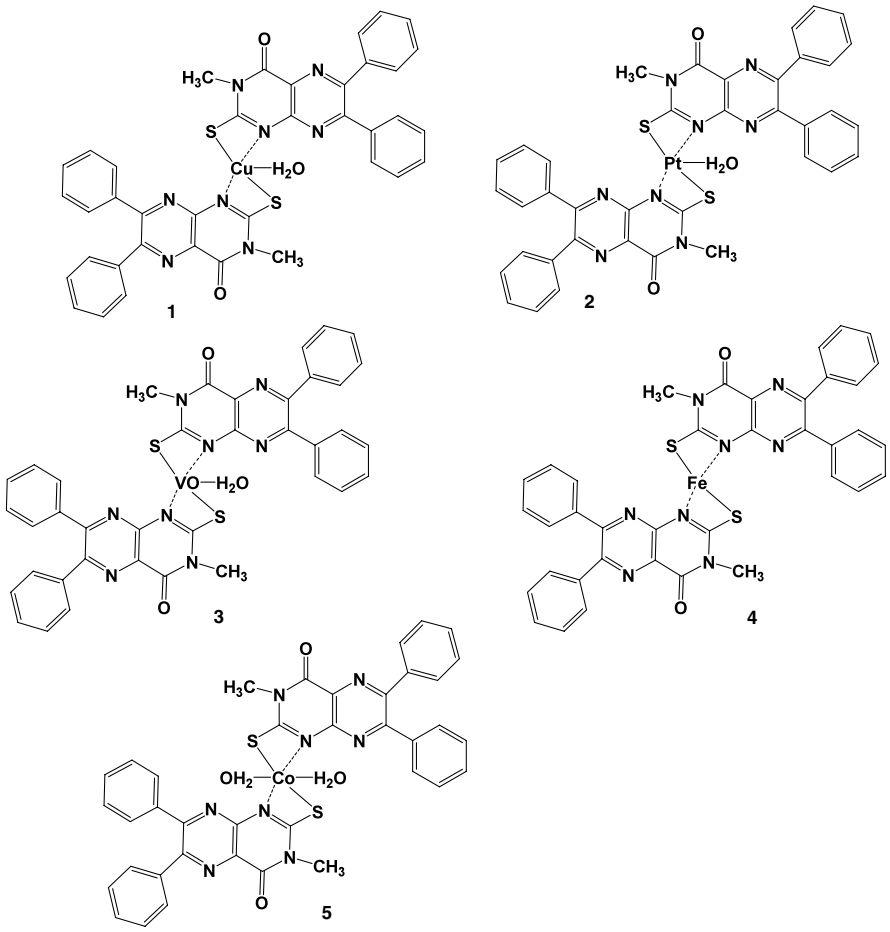


FIGURE 1 Complexes of Cu(II), Pt(II), VO(II), Fe(II), and Co(II) with 3-methyl-6,7-diphenyl-2-thiolumazine.

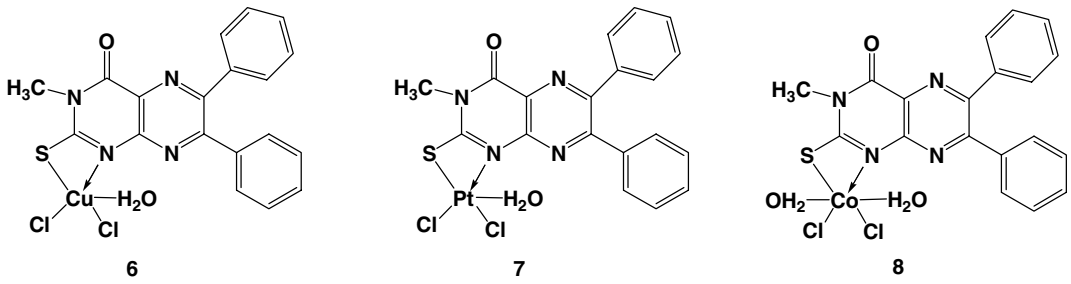


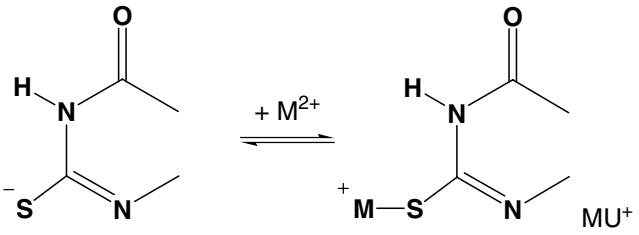
FIGURE 2 Complexes of Cu(II), Pt(II), and Co(II) with 3-methyl-6,7-diphenyl-2-thiolumazine.

modification of its IR spectra with a significant perturbation of the two thioamide bands, and such a vibrational activity is indicative of S,N-coordination of the ligand in a monoanionic form [30]. These bands were shifted in the corresponding complexes, indicating the involvement of the N-1 atom and C—S in coordination to the metal ion. In conclusion, the position of the (C=S) band in the complexes around 1209 cm^{-1} changed insignificantly and indicated the coordination of the ligand through S.

The structures of **1–5** were depicted by the ^{1}H- and ^{13}C NMR and the mass spectra and showed a similar pattern. The ^{1}H NMR spectrum of the ligand MDPhTL was in agreement with the authentic sample prepared previously [2c], whereas the ^{13}C NMR spectrum showing a resonance at δ 177.6 ppm was assigned to C=S carbon atom. On comparing main peaks of MDPhTL with its complexes, it is observed that all the signals of the free ligand are present in the ^{1}H and ^{13}C NMR spectra of the complexes. In the ^{13}C NMR spectra of **1–5**, the resonances for C-8 (δ 158.7–157.3 ppm), C=O (δ 156.4–156.0 ppm), C-6 (δ 148.9–148.0 ppm), and C-8a together with C-7 (145.8–145.1 ppm) were practically unchanged since they lie far from the binding site of the ligand. However, a C^2=S carbon atom of MDPhTL (177.6 ppm) shifted downfield by about 11 ppm compared to the complexes (166.9–161.1 ppm), indicative of MDPhTL in its monoanionic form acts as a chelate coordinating through its S and N-1 donor atoms.

Elemental analyses confirmed the ML_2 composition of the complexes **1–5**, in which M is Cu(II), Pt(II), VO(II), Fe(II), Co(II), and L is 2-thiolumazine, using M:L (1:2) molar ratio. The molecular ion peaks at *m/z* 777 $[(M\text{-}H_2O) + Na]^+$, 908 $[(M\text{-}H_2O) + Na]^+$, 758 $[M + H]^+$, 769 $[M + Na]^+$, and 772 $[(M\text{-}2H_2O) + Na]^+$ are additional structural assignments of **1–5**, respectively.

The mechanism of complexation is based on hydrogen ion liberation and formation of a covalent bond between the divalent metal ion and the negatively charged sulfur as follows:



Furthermore, Cu(II), Pt(II), and Co(II) complexes **6–8**, with monodentate 2-thiolumazine, were isolated by using M:L (1:1) molar ratio (Fig. 2). Karl–Fischer titration indicated the presence of water molecule. In the far-infrared region, one ν(M—Cl) band was observed in the spectra of the $CuCl_2(MDPhTL)H_2O$ (**6**) (306 cm^{-1}) and $Co—Cl_2(MDPhTL)H_2O$ (**8**) (247 cm^{-1}), suggesting a trans arrangement of the chlorine atoms [32], whereas in the $PtCl_2(MDPhTL)H_2O$ (**7**) (352, 322 cm^{-1}) complexes were assigned to the chlorine atoms in a cis arrangement. Furthermore, these complexes exhibited a broad band around 3410–3520 cm^{-1} and are assigned to water molecules, ν(OH), associated with the complexes. Additional support of the proposed structures is obtained from mass spectral data, which showed the correct molecular ions, as suggested by their molecular formulas.

Next, our work was extended to 2-thiouracil complexes, aiming to evaluate their anti-HIV activity. Thus, copper(II) and platin(II) complexes of 2-thiouracil **9–11** were prepared (see Fig. 3). The elemental analysis suggests a range of 1**:**1 and 2**:**1 stoichiometries. The structures of the complexes were assigned from their ^{1}H and ^{13}C NMR, IR, and mass spectra. The IR spectra of the complexes **9–11** showed broad bands in the 3392–3387 cm^{-1} region that could be considered as an indication of lattice water. The spectra (in solution) revealed the presence of characteristic bands for —SH at 2550 cm^{-1} and 1623 cm^{-1} for C=N overlapped with a weak band of C=O. The bands at 3210–3200 cm^{-1} assignable to NH_2 were remarkably affected by complexation, indicating that both NH_2 at C-5 and C-6 are the

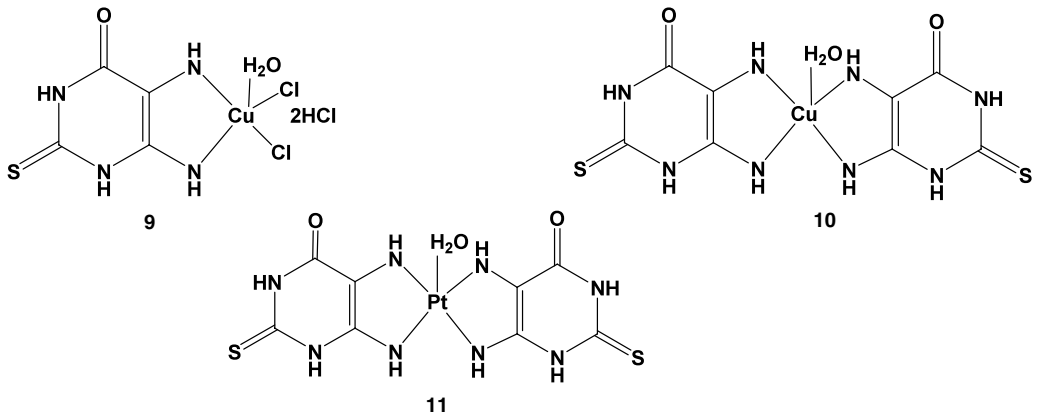


FIGURE 3 Complexes of Cu(II) and Pt(II) with 5,6-diamino-2-thiouracil.

binding sites of complexation with the metals. In the far-infrared region of **9**, one ν(Cu—Cl) band was observed in the spectrum (309 cm^{-1}), suggesting a trans arrangement of the chlorine atoms [32].

The ^1H NMR spectra of the complexes exhibited signals at the region δ 8.03–6.89 ppm, exchangeable with D_2O, corresponding to NH protons (a tautomer of the SH). The ^{13}C NMR spectra of **9–11** contained similar resonance signals of the 2-thiouracil ring carbons. The chemical shifts at δ 176.7, 176.8, and 176.6 ppm were assigned to the C^2=S group, respectively The higher field signals at δ 158.3, 158.0, and 158.7 ppm were attributed to C^4=O, respectively. The resonance at δ 142.7, 142.5, and 143.4 ppm was assigned to C-6, whereas the resonance at δ 100.0, 104.8, and 101.2 ppm was attributed to C-5, respectively.

In Vitro Anti-HIV Assay

Compounds **1–11** were evaluated for their in vitro anti-HIV activity by using the III_B strain for HIV-1 and the ROD strain for HIV-2 in human T-lymphocyte (MT-4) cells, and the results are summarized in Table 1, in which the data for Nevirapine (BOE/BIRG587) [33] and azidothymidine [34] were included for comparison purposes.

Compound **3** was found to be the only compound from the series inhibiting HIV-2 replication in cell culture. Compounds **6** and **7** exhibited some activity (EC_{50} = >7.12 μg/mL and >2.23 μg/mL) against HIV-1 and HIV-2, but no selectivity was observed (selectivity index (SI) <1).

Based on the chemical structure and the fact that compound **3** inhibit HIV-2, but not HIV-1 replication, this molecule can be proposed to act as non-nucleoside reverse transcriptase inhibitor (NNRTI). This hypothesis was further confirmed by assaying the compounds against a typical NNRTI-resistant HIV-1 strain (double mutation in RT: K103N and Y181C). Compounds **3** completely lost its inhibitory activity against this resistant strain.

TABLE 1 In Vitro Anti-HIV-1[a] and HIV-2[b] of Some New Metal Complexes

Compound	*Virus Strain*	*EC_{50} (μg/mL)[c]*	*CC_{50} (μg/mL)[d]*	*SI[e]*
1	III_B	>14.51	14.51	<1
	ROD	>14.51	14.51	<1
2	III_B	>77.30	77.30	<1
	ROD	>77.30	77.30	<1
3	III_B	>61.43	61.43	<1
	ROD	18.95	61.43	3
4	III_B	>49.40	49.40	<1
	ROD	>49.40	49.40	<1
5	III_B	>47.35	47.35	<1
	ROD	>47.35	47.35	<1
6	III_B	>7.12	7.12	<1
	ROD	>7.12	7.12	<1
7	III_B	>2.23	2.23	<1
	ROD	>2.23	2.23	<1
8	III_B	>15.2	15.2	<1
	ROD	>15.2	15.2	<1
9	III_B	>11.76	11.76	<1
	ROD	>11.76	11.76	<1
10	III_B	>9.40	9,40	<1
	ROD	>9.40	9,40	<1
11	III_B	>79.38	79.38	<1
	ROD	>79.38	79.38	<1
Nevirapine	III_B	0.050	>4.00	>80
	ROD	>4.00	>4.00	<1
Azidothymidine	III_B	0.00094	>25.00	>11587
	ROD	0.00094	>25.00	>26731

[a]Anti-HIV-1 activity measured with strain III_B.
[b]Anti-HIV-2 activity measured with strain ROD.
[c]Compound concentration required to achieve 50% protection of MT-4 cells from the HIV-1- and 2-induced cytopathogenic effect.
[d]Compound concentration that reduces the viability of mock-infected MT-4 cells by 50%.
[e]SI: Selectivity index (CC_{50}/EC_{50}).

Compound **3** was subjected to the quantum structure–activity relationship study using comparative molecular field analysis [35]. The study suggested the importance of a VO(II) atom by manifesting an HIV-2 activity with a therapeutic index (SI = 3), other than that of the corresponding analogues having Cu(II), Pt(II), Fe(II), and Co(II) metals. Such a result would lead us to modify our new target molecules by the introduction of more potential molecules with VO(II).

Although the SI values of **6–9** is <1, but the existence of a dichloro group on the metal has optimized the inhibitory activity. Such an encouraging result prompts us to select various potentially substituted 2-thiolumazine and 2-thiouracil derivatives.

CONCLUSION

In summary, the results showed that compounds **3** was an active inhibitor against HIV-2 replication in the cell culture (EC_{50} = >18.95 μg/mL, SI = 3), as well as **6** and **7** EC_{50} = >7.12 μg/mL and >2.23 μg/mL, SI <1, respectively) against HIV-1 and HIV-2, which provide a good lead for designing and discovery of new high potent HIV NNRTIs by a structure-based molecular modification.

EXPERIMENTAL

General

Melting points were measured on a Büchi melting point apparatus B-545 (Büchi Labortechnik AG, Switzerland) and are uncorrected. Microanalytical data were obtained with a Vario elemental apparatus (Shimadzu, Japan). IR spectra were measured on a 1330 Perkin–Elmer spectrophotometer, using Nujol mull. NMR spectra were recorded on 400 MHz (^{1}H) and 150.91 MHz (^{13}C) spectrometers (Bruker, Karlsruhe, Germany) with TMS as an internal standard and on a δ scale in ppm. Mass spectra were recorded on 70 eV EI and FAB MAT 8200 spectrometers (Finnigan MAT, San Jose, MA), using nitrobenzyl alcohol (NBOH) or glycerol as matrixes.

Synthesis of the Complexes

The solid complexes were prepared by adding aqueous solutions of the metal salts $CuCl_2 \cdot 2H_2O$, K_2PtCl_4, $VOSO_4 \cdot H_2O$, $FeSO_4 \cdot 3H_2O$, and $CoCl_2 \cdot 6H_2O$ to the ethanolic solution of the thiolumazine ligand (MDPhTL) in a 1:2 molar ratio. The pH of the mixture was adjusted between 3.5 and 4.0 by addition of KOH with continuous stirring. The mixture was heated at 50°C for 4 h. The solid complexes were separated on cooling, filtered, washed with water and alcohol, and followed by drying under vacuum. The purity of the solid complexes $Cu(MDPhTL)_2 \times H_2O$ (**1**) $VO(MDPhTL)_2$ (**3**) $Fe(MDPhTL)_2 \times H_2O$ (**4**), and $Co(MDPhTL)_2 \times 2H_2O$ (**5**) was checked by elemental analysis, melting points, and IR spectra.

The synthesis of $Pt(MDPhTL)_2 \times H_2O$ (**2**) was prepared as follows: a mixture of K_2PtCl_4 (1.0 mmol) and the 2-thiolumazine ligand (MDPhTL) (2.0 mmol) was stirred in water (5 mL) for 16 h at 25°C.

Similarly, the complexes $CuCl_2(MDPhTL) \times H_2O$ (**6**), $PtCl_2(MDPhTL) \times H_2O$ (**7**) and $CoCl_2$ (MDPhTL) $\times 2H_2O$ (**8**) were prepared from the corresponding metal chloride (1.0 mmol) and the ligand (MDPhTL) (0.35 g, 1.0 mmol) in a 1:1 molar ratio.

$Cu(MDPhTL)_2 \times H_2O$(**1**). Yield: 1.05 g, (68%); light brown. ^{1}H NMR (DMSO-d_6): δ 7.42–7.35 (m, 20H, Ar-H); 3.67 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): 166.5(C—S); 158.7 (C-8); 156.1 (C=O); 148.1 (C-6); 145.3 (C-8a); 131.6, 129.7, 129.5, 128.1, 127.2, 124.6 (Ar-C + C-4a); 33.2 (N-Me). Anal. calcd for $C_{38}H_{28}CuN8O_3S_2$ (772.36): C, 59.09; H, 3.65; N, 14.51. Found: C, 58.79; H, 3.55; N, 14.31. *m/z*(FAB) 777 $[(M\text{-}H_2O) + Na]^+$.

$[Pt(MDPhTL)_2 \cdot H_2O]$ (**2**). Yield: 1.44 g (80%); deep gray. ^{1}H NMR (DMSO-d_6): δ 7.47–7.33 (m, 20H, Ar-H); 3.68 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 166.4. (C=S); 157.5 (C-8); 156.0 (C=O); 148.8 (C-6); 145.7 (C-8a + C-7); 131.3, 130.0, 129.4, 128.3, 127.5, 125.1 (Ar-C + C-4a); 33.7 (N-Me). Anal. calcd for $C_{38}H_{28}N_8O_3PtS_2$ (903.89): C, 50.49; H, 3.12; N, 12.40. Found: C, 50.19; H, 3.02; N, 12.19. *m/z*(FAB) 908 $[(M\text{-}H_2O) + Na]^+$.

$[VO(MDPhTL)_2]$ (**3**). Yield: 1.13 g (75%); light green. ^{1}H NMR (DMSO-d_6): δ 7.44–7.34 (m, 20H, Ar-H); 3.70 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 166.1 (C—S); 157.3 (C-8); 156.4 (C=O); 148.9 (C-6); 145.8 (C-8a + C-7); 129.6, 129.4, 128.7, 128.2, 128.0 (Ar-C + C-4a); 33.9 (N-Me). Anal. calcd for $C_{38}H_{26}N_8O_3S_2V$ (757.74): C, 60.23; H, 3.46; N, 14.79. Found: C, 59.95; H, 3.36; N, 14.68. *m/z*(FAB) 758 $[M + H]^+$.

$[Fe(MDPhTL)_2]$ (**4**). Yield: 0.97 g (65%); green. ^{1}H NMR (DMSO-d_6): δ 7.47–7.33 (m, 20H, Ar-H); 3.70 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 166.9 (C-S); 157.8 (C-8); 156.3 (C=O); 148.5 (C-6); 145.4 (C-8a + C-7); 129.4, 128.1, 127.7, 126.7, 125.0 (Ar-C + C-4a); 33.4 (N-Me). Anal. calcd for $C_{38}H_{26}FeN_8O_2S_2$ (746.64): C, 61.13; H, 3.51; N, 15.01. Found: C, 60.89; H, 3.40; N, 14.81. *m/z*(FAB) 769 $[M + Na]^+$.

$[Co(MDPhTL)_2 \cdot 2H_2O]$ (**5**). Yield: 1.10 g (70%); yellow. ^{1}H NMR (DMSO-d_6): δ 7.497–7.25 (m, 20H, Ar-H); 3.76 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 166.1 (C-S); 157.9 (C-8); 156.1 (C=O); 146.7 (C-6); 145.8 (C-8a + C-7); 129.9, 128.7, 127.9, 126.6, 125.2 (Ar-C + C-4a); 33.5 (N-Me). Anal. calcd for

$C_{38}H_{30}CoN_8O_4S_2$ (785.76): C, 58.08; H, 3.85; N, 14.26. Found: C, 57.88; H, 3.79; N, 13.98. *m/z*(FAB) 772 $[(M\text{-}2H_2O) + Na]^+$.

[$CuCl_2$(MDPhTL)·H_2O] (**6**). Yield: 0.34 g (69%); green. ^{1}H NMR (DMSO-d_6): δ 7.46–7.29 (m, 10H, Ar-H); 3.64 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 165.9 (C-S); 158.4 (C-8); 156.3 (C=O); 148.2 (C-6); 145.3 (C-8a + C-7); 131.3, 129.1, 128.9, 128.0, 126.7, 124.5 (Ar-C + C-4a); 33.1 (N-Me). Anal. calcd for $C_{19}H_{15}Cl_2CuN_4O_2S$ (497.87): C, 45.84; H, 3.04; N, 11.25. Found: C, 45.62; H, 2.93; N, 11.25. *m/z*(FAB) 501.503 $[(M\text{-}H_2O) + Na]^+$.

[$PtCl_2$(MDPhTL)·H_2O] (**7**). Yield: 0.46 g (73%); light brown. ^{1}H NMR (DMSO-d_6): δ 7.44–7.27 (m, 10H, Ar-H); 3.61 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 166.0 (C-S); 158.3 (C-8); 156.1 (C=O); 148.0 (C-6); 145.1 (C-8a + C-7); 131.0, 129.0, 129.2, 128.2, 126.5, 124.0 (Ar-C + C-4a); 33.3 (N-Me). Anal. calcd for $C_{19}H_{15}Cl_2N_2O_2PtS$ (629.4): C, 36.26; H, 2.40; N, 8.90. Found: C, 36.01; H, 2.30; N, 8.70. *m/z*(FAB) 633/635 $[(M\text{-}H_2O) + Na]^+$.

[$CoCl_2$(MDPhTL)·$2H_2O$] (**8**). Yield: 0.42 g (82%); light yellow. ^{1}H NMR (DMSO-d_6): δ 7.49–7.31 (m, 10H, Ar-H); 3.60 (s, 6H, 2×Me). ^{13}C NMR (DMSO-d_6): δ 165.9 (C-S); 158.6 (C-8); 156.4 (C=O); 148.8 (C-6); 145.8 (C-8a + C-7); 130.5, 129.0, 128.5, 128.4, 126.5, 124.2 (Ar-C + C-4a); 33.0 (N-Me). Anal. calcd for $C_{19}H_{15}Cl_2CoN_4O_3S$ (511.27): C, 44.63; H, 3.35; N, 10.96. Found: C, 44.41; H, 3.24; N, 10.71. *m/z*(FAB) 515/517 $[M + Na]^+$.

[Cu(DAMTU)Cl_2·H_2O.2HCl] (**9**). Yield: 0.29 g (78%); ^{1}H NMR (DMSO-d_6): 7.99 (s, 1H, NH); 7.58 (s, 1H, NH); 7.21–6.97 (br s, 2H, 2×NH). ^{13}C NMR (DMSO-d_6): 176.7 (C=S); 158.3 (C=O); 142.7 (C-6); 100.0 (C-5). Anal. calcd for $C_4H_8Cl_4CuN_4O_2S$ (381.55): C, 12.59; H, 2.11; N, 14.68. Found: C, 12.32; H, 2.02; N, 14.42.

[Cu(DAMTU)$_2$(H_2O)] (**10**). Yield: 0.33 g (84%); ^{1}H NMR (DMSO-d_6): 8.01 (s, 1H, NH); 7.52 (s, 1H, NH); 7.26–6.89 (br s., 2H, 2×NH). ^{13}C NMR (DMSO-d_6): δ 176.8 (C=S); 158.0 (C=O); 142.5 (C-6); 104.8 (C-5). Anal. calcd for $C_8H_{10}CuN_8O_3S_2$ (393.89): C, 24.39; H, 2.56; N, 28.45. Found: C, 24.03; H, 2.47; N, 28.16.

[Pt(DAMTU)$_2$(H_2O)] (**11**). Yield: 0.41 g (78%); ^{1}H NMR (DMSO-d_6): 8.03 (s, 1H, NH); 7.55 (s, 1H, NH); 7.40–6.90 (br s, 2H, NH). ^{13}C NMR (DMSO-d_6): δ 176.6 (C=S); 158.7 (C=O); 143.4 (C-6); 101.2 (C-5). Anal. calcd for $C_8H_{10}N_8O_3PtS_2$ (525.42): C, 18.29; H, 1.92; N, 21.33. Found: C, 17.98; H, 1.79; N, 21.03.

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