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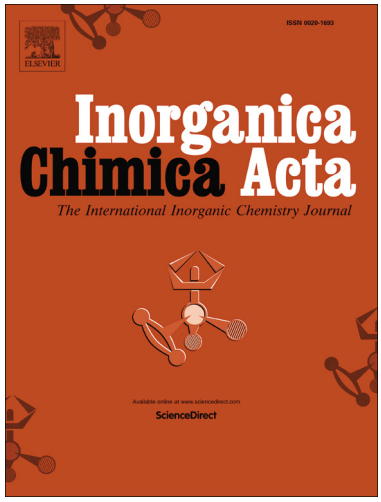

Research paper

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Pyrrole thioamide complexes of the d^8 metals platinum(II), palladium(II) and gold(III)

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ABSTRACT

Reactions of the cycloaurated gold(III) complexes [$AuCl_2$(2-benzylpyridyl)] and [$AuCl_2(C_6H_4CH_2NMe_2)$] with a set of pyrrole-2-thioamide ligands, containing various substituents on the pyrrole ring, gave a series of new gold(III) pyrrole thioamide complexes. X-ray crystal structures on two complexes indicate that the pyrrole thioamide ligand is coordinated through the deprotonated pyrrole nitrogen, as well as the sulfur atom of the deprotonated thioamide group, forming five-membered chelate ring complexes. In both complexes, the two highest *trans*-influence donor atoms (C and S) are mutually *cis*. Related sets of platinum(II) and palladium(II) pyrrole thioamide complexes were similarly prepared by reactions of *cis*-[$PtCl_2(PPh_3)_2$] and [$PdCl_2$(dppe)] (dppe = $Ph_2PCH_2CH_2PPh_2$)] respectively. The complexes were characterised by NMR and IR spectroscopies, and ESI mass spectrometry. A preliminary investigation of the activity of a selection of compounds towards A549 (adenocarcinomic human alveolar basal epithelial) cells was also carried out.

Keywords: Pyrrole; Thioamide; X-ray structures; Platinum; Palladium; Gold

1. Introduction

Sulfur-nitrogen donor ligands are a highly attractive ligand class, because of the combination of hard and soft donor atoms, potentially allowing coordination – in a diverse range of binding modes – to a wide range of metal centres. For example, the coordination chemistry of N-heterocyclic thionate ligands has been summarised in two reviews by Raper.[1,2] Pyridine-derived thioamide ligands have attracted attention, because of the built-in ancillary ligand properties of the pyridine group. A wide range of synthesised and characterised pyridyl thioamide complexes include those of ruthenium and osmium,[3,4,5,6,7,8,9] gold,[10,11] palladium,[12,13,14] copper and nickel.[15] While a common theme in many of the recent studies concerns biological activity, especially of ruthenium and osmium arene derivatives,[6-9] pyridine thioamide complexes of palladium [16] and ruthenium(II) [17,18,19] have also been studied for their catalytic potential.

We subsequently wished to investigate thioamide ligands derived from other nitrogen-containing heterocycles, and were interested in the possibility of utilising the pyrrole group, where the heterocyclic NH could potentially be deprotonated, furnishing a dianionic ligand. To the best of our knowledge, there are no reports on gold and platinum group complexes containing pyrrole-derived thioamide ligands, though deprotonated pyrrole complexes of gold,[20] palladium [21,22,23,24] and platinum [24,25] are all well established. In this contribution, we report the synthesis and characterisation of a series of complexes of this type, together with a preliminary study on their biological activity.

2. Results and discussion

2.1. Synthesis and characterisation of pyrrole thioamide ligands

Using the methodology by Bullock and Abraham (Scheme 1),[26] three compounds (**1a**, **1b** and **1c**) were prepared by refluxing (solvent-free) the respective pyrrole with an excess of phenyl isothiocyanate. After work-up and isolation, compounds **1b** and **1c** were obtained by recrystallisation from ether/heptane, which is in line with the literature procedure. However, compound **1a** was isolated in a much lower yield, because of the much longer reaction time required, and the larger number of steps involved in the workup.

The analogous 4-nitrophenyl compounds **1d-1f** were synthesised in an analogous manner to **1a-1c**, using an excess of 4-nitrophenyl isothiocyanate and the pyrrole. The reaction was stirred until TLC analysis (ethyl acetate: dichloromethane: hexane = 1:20:20) indicated the complete consumption of the starting pyrrole. Compound **1d** was purified by crystallisation from heptane, but compounds **1e** and **1f** were both purified by chromatography (silica gel; eluting with ethyl acetate: dichloromethane: petroleum ether = 1:3:5).

The identity of **1f** was unambiguously confirmed by the determination of its single-crystal X-ray structure. The ORTEP diagram and atom numbering scheme are shown in Figure 1, and selected bond lengths and angles are summarised in Table 1. The pyrrole N-C distances N(1)-C(4) and N(1)-C(1) are different, 1.380(2) Å and 1.355(2) Å respectively, as a result of different substituents (electron-withdrawing or electron-donating) on the pyrrole ring. The C=S bond length of **1f** is 1.6775(17) Å, which is longer than the pyrrole thioamide *N,N'*-diphenyl-1H-pyrrole-2,5-dithiocarboxamide [1.664(3) Å].[27] The three bond angles around C(9) are 121.89(13)° for S(1)-C(9)-C(4), 124.10(13)° for S(1)-C(9)-N(2) and 114.01(14)° for C(4)-C(9)-N(2). Interestingly, except for the ethyl group, all the atoms are almost coplanar. The molecule forms a dimer in the solid state, Figure 2, *via* interactions of the thiocarbonyl group and the pyrrole NH and CH_3 substituent hydrogens.

All of the pyrrole thioamide ligands show a multiplet in their ^{1}H NMR spectra in the range δ 7.24–8.66 ppm for the phenyl protons, and triplets around δ 1.07 ppm and quartets δ

2.40 ppm for the ethyl protons in the compounds **1c** and **1f**. In addition, ligands **1a-1f** show two singlet peaks in the region 9.42–9.78 and 8.53–8.76 ppm in their ^{1}H NMR spectra, which are assigned to the pyrrole NH and CSNH protons respectively. This was confirmed by a COSY NMR spectrum of **1a**, which displays couplings between the pyrrole NH proton and pyrrole CH protons. In comparison to **1a**, for compound **1b**, the pyrrole NH and CSNH resonances are shifted upfield at 9.50 and 8.54 ppm, presumably due to the electron-donating effect of the methyl groups on the pyrrole ring.

All compounds were characterised by ESI mass spectrometry in CH_3OH and gave intense $[M+H]^+$ ions at a low capillary exit voltage (80 V) at *m/z* values that agreed well with predicted values. The exception was ligand **1d**, which gave only a weak $[M+Na]^+$ ion. Furthermore, the compounds were also investigated in negative ion mode. The expected $[M-H]^-$ ion of compounds **1a-1c** and **1e-1f** was observed at a low capillary exit voltage.

In the IR spectra of the ligands **1a-1f**, absorption bands at 703–796 and 3285–3383 cm^{-1} are assigned to thioamide group $\nu_{C=S}$ vibrations and the pyrrole group ν_{N-H}, respectively. Additionally, in the cases of compounds **1d-1f**, absorption bands due to the asymmetric ν_{NO_2} and symmetric ν_{NO_2} are observed at 1505-1512 and 1333-1339 cm^{-1} respectively.[28]

2.2. Synthesis of platinum(II) and gold(III) pyrrole thioamide complexes

Reactions of the cycloaurated gold(III) complex $[AuCl_2$(2-benzylpyridyl)] with equimolar amounts of the pyrrole-derived thioamide ligands **1a-1f** in the presence of trimethylamine in refluxing methanol gave, after cooling and filtration, the complexes **2a-2f** in moderate to good yields (57-88%), Scheme 2. These complexes were found to show good solubility in chloroform and dichloromethane, but were poorly soluble in methanol. In a similar fashion, the reaction of $[AuCl_2(C_6H_4CH_2NMe_2)]$ with pyrrole-derived thioamide ligands **1a** and **1d-1f** in a 1:1 molar ratio in the presence of trimethylamine yielded

complexes **3a** and **3d-3f** (Scheme 2). Complexes **3d** to **3f** were obtained in significantly higher yield than compound **3a**. In addition, **3a** has good solubility in methanol, chloroform and dichloromethane, but complexes **3d-3f** are only soluble in chloroform and dichloromethane.

A series of complexes containing the $Pt(PPh_3)_2$ or Pd(dppe) (dppe = $Ph_2PCH_2CH_2PPh_2$) moieties were also synthesised by analogous procedures, starting from *cis*-$[PtCl_2(PPh_3)_2]$ or $[PdCl_2(dppe)]$ respectively.

2.3. X-ray crystal structure determinations of pyrrole thioamide complexes

To confirm the binding mode of the pyrrole thioamide ligand to the metal centre in these d^8 complexes, X-ray crystal structure determinations were carried out on the gold complexes **2b** and **3d**. The molecular structures of **2b** and **3d** are shown in Figures 3 and 4 respectively, and selected bond lengths and angles are given in Tables 2 and 3.

In both complexes the gold atom is in an approximately square-planar coordination environment, with τ^4 parameters of 0.118 (**2b**) and 0.097 (**3d**). The τ^4 parameter can be used to provide a coordination geometry metric for four-coordinate transition metal complexes [29] compared to theoretical values of 0 for a perfect square plane to 1 for a perfect tetrahedron. The gold atom is coordinated with the nitrogen of the deprotonated pyrrole group, the sulfur atom of the thioamide, and the σ-C and N of the cycloaurated ligand, with the pyrrole-derived thioamide ligand forming a five-membered chelate ring. In both structures **2b** and **3d**, the S and C donor atoms show antisymbiosis,[30] with the two highest *trans*-influence donor atoms (C and S) mutually *cis*. This is similar to other closely related cycloaurated gold(III) complexes [31] containing *S,N* [32,33,34,35] or *S,O* [36] donor ligands.

The C-S bond lengths of the complexes are relatively long [**2b** 1.803(6); **3d** 1.789(5) Å], which represent a C-S single bond [37,38,39,40,41] and contrasts the C=S bond distance of **1f** [1.6775(17) Å]. Additionally, the exocyclic C(9)-N(2) distances [**2b** 1.284(8); **3d** 1.280(6) Å] are as expected for a C-N double bond (1.27-1.29 Å) [42,43] and are significantly shorter than the corresponding C-N bond distance in **1f** [1.362(2) Å]. Together, these bond length data indicate that the pyrrole thioamide ligand is coordinated in the deprotonated thiol(ate) tautomeric form. In both structures, the exocyclic imine phenyl substituent is approximately perpendicular to the metallacyclic ring, presumably to minimise steric interaction between the *ortho* phenyl hydrogen and the sulfur atom.

In **2b**, the interplanar angle between the N(1)-Au(1)-S(1) and C(4)-C(9)-S(1) planes is 13.69°, indicating that the five-membered Au(1)-N(1)-C(4)-C(9)-S(1) ring is slightly puckered. The corresponding angle in **3d** is smaller (10.40°).

The benzylpyridyl ligand of complex **2b** has the typical boat conformation, as observed in other structural determinations of complexes containing this moiety. An example of this is the starting complex [$AuCl_2$(2-benzylpyridyl)].[44] In **2b**, this puckering also minimises steric interaction of the benzylpyridyl ligand with the methyl substituent adjacent to the pyrrole nitrogen, and such steric interaction may also be responsible for the slightly greater deviation from square planarity of complex **2b**. Complex **2b** also crystallises with dichloromethane in the lattice, which participates in a weak C-H…S intermolecular interaction.

2.4. Spectroscopic characterisation of pyrrole thioamide complexes

In their ^{1}H NMR spectra the singlet peaks corresponding to –NH protons of the free ligands disappear upon complex formation. Interestingly, compared to the pyrrole-derived thioamide ligands, the ^{1}H NMR spectra of the gold complexes **2** and **3** show the signals of the

pyrrole CH protons shifted downfield, whereas the same signals were shifted upfield in the platinum complexes **4** and palladium complexes **5**. This effect is most likely due to the high electronegativity of gold [45,46], compared to the lower electronegativity of platinum and palladium, which are coordinated by electron-donating phosphine ligands which provide a shielding effect on neighbouring protons.

As expected, the $^{31}P\{^{1}H\}$ NMR spectrum of the triphenylphosphine platinum complex **4a** shows an AB pattern for two inequivalent PPh_3 ligands, with two resonances at δ 19.5 and 13.5. The $^{1}J(PtP)$ coupling constants are 2843 and 3178 Hz, respectively, while the $^{2}J(PP)$ coupling is 24 Hz. In comparison, the analogous compound **4d** has similar $^{1}J(PtP)$ coupling constants of 2893 and 3167 Hz. The difference in coupling constants is consistent with strong thiolate and weaker pyrrole nitrogen donors. In contrast, the coupling constants of **4e** (3081 and 3094 Hz) and **4f** (3084 and 3092 Hz) are fairly similar to each other, but significantly different to **4a** and **4d**. The more balanced coupling constants in **4e** and **4f** may be due to the presence of alkyl substituents on the pyrolle ligands in these complexes, increasing their π-donor strength. The palladium complexes **5** also showed two signals in their $^{31}P\{^{1}H\}$ NMR spectra with coupling between the two phosphorus atoms. The dppe palladium complexes show the expected substantial downfield shift of the phosphorus atoms, which is well-known to be an indicator of phosphine chelation in dppe complexes.[47]

In the IR spectra, the free ligand $\nu_{C=S}$ and pyrrole ν_{N-H} absorption bands are lost upon coordination to the metal centre. The ν_{C-S} band of the suite of complexes **2**, **3**, **4** and **5** generally shifts to medium energy in the region 1279–1393 cm^{-1}. The symmetric and asymmetric νNO_2 modes are observed at 1298-1396 ($\nu^{s}NO_2$) cm^{-1} and 1464-1586 ($\nu^{as}NO_2$) cm^{-1} in those complexes containing the 4-nitrophenyl substituent.

The electrospray ionisation (ESI) mass spectra of the palladium complexes **5** and the gold complexes **2** and **3** all give the expected intense $[M+H]^+$ ions at a relatively high

capillary exit voltage (160 V), without any observed fragmentation. This is consistent with the presence of two metallacyclic rings that are relatively resilient towards fragmentation. In contrast, the mass spectra of platinum complexes **4** give, in addition to an intense $[M+H]^+$ ion at the expected *m/z* values, the additional fragment ion of $[M-PPh_3+H]^+$, at a capillary exit voltage of 160 V.

2.5. Biological activity

The toxicities of compounds **2c-f**, **3a, 3d, 3e**, **4a, 4d-f**, **5d** and **5f** were evaluated toward A549 cells (adenocarcinomic human alveolar basal epithelial cells) by MTT assay. Due to their poor solubility in water, **2a**, **2b**, **3f**, **5a** and **5e** were not tested. Compared to a control, where the cells were allowed to grow without any treatment, it was found that compounds **2d**, **3d** and **4a** caused a significant reduction in A549 cell viability at 100 μM concentration. Therefore, compounds **2d**, **3d** and **4a** were selected for further investigation, and evaluated at a range of concentrations (3-100 μM). Inspection of the data given in Figure 4 reveals that treatment with **4a** at 25 μM seems to have moderate toxicity on A549 cells, while the complexes **2d** and **3b** show moderate toxicity at concentrations >50 μM. The antiproliferative activities of the ligands **1a-f** were also studied against the same cell line, but they showed no obvious cytotoxicity.

3. Conclusions

In this work, a range of novel gold, platinum and palladium complexes have been synthesised using pyrrole-thioamide ligands, and were characterised by NMR, MS and FTIR. X-ray structure determinations of two gold complexes confirms that the gold atom is bound to the ligand *via* the nitrogen of the deprotonated pyrrole group and the sulfur of the

deprotonated thioamide. We are currently investigating other precious metal complexes of these ligands and results will be reported in due course.

4. Experimental

4.1. Materials and instrumentation

The following materials were used as supplied from Sigma Aldrich: pyrrole, phenyl isothiocyanate, 4-nitrophenyl isothiocyanate. 2,4-Dimethylpyrrole and 3-ethyl-2,4-dimethylpyrrole were used as supplied from Tokyo Chemical Industries (TCI). Aqueous trimethylamine solution (BDH) was used as supplied. All solvents were AR grade, and petroleum spirits refers to the fraction of boiling range 30-60 °C. The complexes $[AuCl_2(2\text{-benzylpyridyl})]$ [48] and $[AuCl_2(C_6H_4CH_2NMe_2)]$ [49] were prepared by the literature procedures. The complexes *cis*-$[PtCl_2(PPh_3)_2]$ and $[PdCl_2(dppe)]$ were prepared by ligand substitution of the $[MCl_2(cod)]$ complex (M = Pd [50], or M = Pt [51], cod =1,5-cyclo-octadiene) with the molar amount of phosphine in CH_2Cl_2, and the product precipitated with petroleum spirits.

All reactions were carried out without any attempts to exclude air or moisture. Elemental microanalyses were carried out by the Campbell Microanalytical Laboratory, University of Otago, Dunedin, New Zealand. ESI mass spectra were recorded in methanol solution on a Bruker MicrOTOF instrument that was calibrated using a solution of sodium formate; a capillary exit voltage in the range 60-180 V was used; *m/z* values were calculated using ChemBioDraw Ultra 12.0. NMR spectra were recorded in $CDCl_3$ on a Bruker AVIII 400 instrument using Topspin 3.0 software; signals were referenced relative to residual non-deuterated solvent peaks or external H_3PO_4 (for ^{31}P NMR spectra). Coupling constants (J) are reported in Hz. Infrared spectra were recorded as KBr disks on a PerkinElmer Spectrum 100

FT-IR spectrophotometer. Melting points were determined on a Reichert-Jung hot-stage apparatus and are uncorrected.

*4.2. Synthesis of N-phenyl-1H-pyrrole-2-carbothioamide **1a***

This compound has been synthesised previously,[26] using a slightly different procedure, and characterised by melting point and elemental analysis. A mixture of pyrrole (5 g, 0.075 mol) and phenyl isothiocyanate (11 g, 0.082 mol) was heated to reflux for 19 h. When the reaction mixture became very viscous, cold heptane (20 mL) was added; the product solidified when scratched with a glass rod. The black solid was dissolved in diethyl ether (100 mL) and the insoluble solid was removed by filtration. Heptane (100 mL) was added to the diethyl ether extract, resulting in precipitation of a black oil. Decanting the solution from the oil, and filtering through filter paper gave an orange solution. Additional heptane (100 mL) was added to the residue. A yellow solid (720 mg, 5%) was precipitated, filtered and washed with heptane. ^{1}H NMR: δ (ppm) 9.89 (s, 1H), 8.78 (s, 1H), 7.73 (d, J 7.6 Hz, 2H), 7.46 (m, 2H), 7.31 (m, 1H), 7.08 (m, 1H), 6.67 (s, 1H), 6.36 (m, 1H). ESI MS: positive-ion $[M+H]^+$, *m/z* 203.071, calculated *m/z* 203.056; $[M+Na]^+$, *m/z* 225.054, calculated *m/z* 225.056; negative-ion $[M-H]^-$, *m/z* 201.084, calculated *m/z* 201.056. IR: 703 ($\nu_{C=S}$), 3341 (ν_{N-H}) cm^{-1}.

*4.3. Synthesis of **1b** and **1c***

Compounds **1b** and **1c** were prepared in the same manner as **1a**; these have been synthesised and characterised by melting point and elemental analysis previously.[26]

*3,5-Dimethyl-N-phenyl-1H-pyrrole-2-carbothioamide **1b***

Yield 35%. ^{1}H NMR: δ (ppm) 9.95 (s, 1H), 8.56 (s, 1H), 7.71 (d, J 8.4, 2H), 7.44 (m, 2H), 7.30 (m, 1H), 5.59 (d, J 2.8, 1H), 2.48 (s, 3H), 2.30 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 231.088, calculated *m/z* 231.088; negative-ion $[M-H]^-$, *m/z* 229.014, calculated *m/z* 229.088. IR: 749 ($\nu_{C=S}$), 3349 (ν_{N-H}) cm^{-1}.

4-Ethyl-3,5-dimethyl-N-phenyl-1H-pyrrole-2-carbothioamide ***1c***

Yield 38%. ^{1}H NMR: δ (ppm) 9.94 (s, 1H), 8.53 (s, 1H), 7.68 (d, J 8.0, 2H), 7.41 (m, 2H), 7.23 (m, 1H), 2.39 (q, 5H), 2.24 (s, 3H), 1.07 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 259.156, calculated *m/z* 259.119; negative-ion $[M-H]^-$, *m/z* 257.045, calculated *m/z* 257.119. IR: 750 ($\nu_{C=S}$), 3285 (ν_{N-H}) cm^{-1}.

4.4. Synthesis of N-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide ***1d***

A mixture of 4-nitrophenyl isothiocyanate (400 mg, 2.22 mmol) and pyrrole (950 mg, 14.16 mmol) was refluxed with stirring for 5 h until TLC analysis (eluting with ethyl acetate/dichloromethane/n-hexane 1:20:20) indicated the complete consumption of 4-nitrophenyl isothiocyanate. A dark yellow suspension formed during the course of addition of cold heptane (5 mL). The precipitate (385 mg, 70%) was filtered and washed with heptane (3 mL). M.p. 130-136 °C. Found: C, 53.71; H, 3.67; N, 17.08%. $C_{11}H_9N_3O_2S$ requires C, 53.43; H, 3.67; N, 16.99%. ^{1}H NMR: δ (ppm) 9.75 (s, 1H), 8.87 (s, 1H), 8.30 (d, J 9.2, 2H), 8.05 (d, J 9.2, 2H), 7.13 (m, 1H), 6.76 (m, 1H), 6.38 (m, 1H). ESI MS: positive-ion $[M+Na]^+$, *m/z* 270.036, calculated *m/z* 270.042; negative-ion $[M-H]^-$, *m/z* 245.982, calculated *m/z* 246.042. IR: 760 ($\nu_{C=S}$), 3383 (ν_{N-H}), 1505 ($\nu^{as}_{NO_2}$), 1339 ($\nu^{s}_{NO_2}$) cm^{-1}.

4.5. Synthesis of 3,5-dimethyl-N-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide ***1e***

A mixture of 4-nitrophenyl isothiocyanate (250 mg, 1.39 mmol) and 2,4-dimethyl-1H-pyrrole (792 mg, 8.33 mmol) was refluxed with stirring for 5 h until TLC analysis (eluting with ethyl acetate/dichloromethane/n-hexane 1:20:20) indicated the complete consumption of 4-nitrophenyl isothiocyanate. The mixture was evaporated to afford the crude product which was chromatographed on silica gel (ethyl acetate/dichloromethane/petroleum ether 1:3:5) to give **1e** (212 mg, 56%) as a brown solid. M.p. 170-176 °C. Found: C, 57.00; H, 4.84; N, 15.10%. $C_{13}H_{13}N_3O_2S$ requires C, 56.71; H, 4.76; N, 15.26%. ^{1}H NMR ($CDCl_3$): δ (ppm) 9.50 (s, 1H), 8.70 (s, 1H), 8.30 (d, J 9.2, 2H), 8.04 (d, J 9.2, 2H), 5.96 (d, J 2.8, 1H), 2.51 (s, 3H), 2.32 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 276.088, calculated *m/z* 276.073; negative-ion $[M-H]^-$, *m/z* 274.010, calculated *m/z* 274.073. IR: 796 ($\nu_{C=S}$), 3321 (ν_{N-H}), 1512 ($\nu^{as}NO_2$), 1333 ($\nu^{s}NO_2$) cm^{-1}.

*4.6. Synthesis of 4-ethyl-3,5-dimethyl-N-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1f***

A mixture of 4-nitrophenyl isothiocyanate (200 mg, 1.11 mmol) and 3-ethyl-2,4-dimethyl-1H-pyrrole (547 mg, 4.44 mmol) was refluxed with stirring for 2 h until TLC analysis (eluting with ethyl acetate/dichloromethane/n-hexane 1:20:20) indicated the complete consumption of 4-nitrophenyl isothiocyanate. Pentane (5 mL) was added, resulting in precipitation of a dark brown solid. The crude product was filtered and washed with pentane (3 mL). The solid was chromatographed on silica gel (ethyl acetate/dichloromethane/petroleum sprits 1:3:5) to give **1f** (150 mg, 45%) as a black crystalline solid. M.p. 188-190 °C. Found: C, 59.36; H, 5.73; N, 13.71%. $C_{15}H_{17}N_3O_2S$ requires C, 59.38; H, 5.65; N, 13.85%. ^{1}H NMR: δ (ppm) 9.42 (s, 1H), 8.66 (s, 1H), 8.27 (d, J 9.2, 2H), 8.00 (d, J 9.2, 2H), 2.42 (q, 5H), 2.26 (s, 3H), 1.07 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 304.272, calculated *m/z* 304.104; negative-ion $[M-H]^-$, *m/z* 302.035, calculated *m/z* 302.104. IR: 747 ($\nu_{C=S}$), 3325 (ν_{N-H}), 1510 ($\nu^{as}NO_2$), 1333 ($\nu^{s}NO_2$) cm^{-1}.

*4.7. Synthesis of **2a***

A suspension of [$AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) in methanol (10 mL) was added in one portion to a stirred solution of *N*-phenyl-1H-pyrrole-2-carbothioamide **1a** (26 mg, 0.126 mmol) in methanol (10 mL), and the mixture was heated to 50 °C. Aqueous trimethylamine (5 drops, excess) was added and the reaction mixture was refluxed for 2 h. A light green solid precipitated out after 10 min. reaction. The product was filtered, washed with methanol (3 mL) and water (3 mL) and dried under vacuum. Yield 57 mg, 88%. M.p. 190-196 °C. Found: C, 48.70; H, 3.18; N, 7.34%. $C_{23}H_{18}AuN_3S$ requires C, 48.86; H, 3.21; N, 7.43%. ^{1}H NMR: δ (ppm) 9.03 (dd, J 5.6, 1H), 8.09 (t, 1H), 7.80 (d, J 7.6, 1H), 7.62 (t, 1H), 7.50 (dd, J 7.6, 1H), 7.33 (m, 2H), 7.10 (m, 7H), 6.66 (m, 1H), 6.44 (m, 1H), 4.50 (d, J 14.8, 1H), 4.05 (d, J 14.8, 1H). ESI MS: positive-ion $[M+H]^+$, *m/z* 566.109, calculated *m/z* 566.089. IR: 1588 ($\nu_{C=N}$), 1393 (ν_{C-S}) cm^{-1}.

The following complexes were prepared by the same method as for **2a**.

*4.8. Synthesis of **2b***

[$AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) with 3,5-dimethyl-*N*-phenyl-1H-pyrrole-2-carbothioamide **1b** (44 mg, 0.140 mmol) and trimethylamine (5 drops, excess) in methanol (20 mL) gave an orange powder (46 mg, 73%). M.p. 186-190 °C. Found: C, 49.72; H, 3.73; N, 6.91%. $C_{25}H_{22}AuN_3S$ requires C, 50.59; H, 3.74; N, 7.08%. ^{1}H NMR: δ (ppm) 8.93 (dd, J 5.6, 1H), 8.01 (t, 1H), 7.77 (d, J 7.6, 1H), 7.58 (d, J 7.6, 1H), 7.49 (m, 1H), 7.34 (m, 2H), 7.10 (m, 6H), 5.99 (s, 1H), 4.58 (d, J 14.8, 1H), 4.06 (d, J 14.8, 1H), 2.45 (s, 3H), 1.70 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 594.131, calculated *m/z* 594.120. IR: 1563 ($\nu_{C=N}$), 1308 (ν_{C-S}) cm^{-1}.

*4.9. Synthesis of **2c***

[$AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) with 4-ethyl-3,5-dimethyl-*N*-phenyl-1H-pyrrole-2-carbothioamide **1c** (33 mg, 0.126 mmol) and trimethylamine (5 drops, excess) in methanol (25 mL) gave a yellow ochre powder (60 mg, 84%). M.p. 192-196 °C. Found: C, 52.27; H, 4.27; N, 6.65%. $C_{27}H_{26}AuN_3S$ requires C, 52.17; H, 4.22; N, 6.76%. ^{1}H NMR: δ (ppm) 8.89 (dd, J 5.6, 1H), 8.00 (t, 1H), 7.75 (d, J 7.6, 1H), 7.46 (m, 1H), 7.31 (m, 2H), 7.07 (m, 6H), 4.55 (d, J 14.4, 1H), 4.04 (d, J 14.4, 1H), 2.41 (m, 5H), 1.61 (s, 3H), 1.06 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 622.177, calculated *m/z* 622.151. IR: 1574 ($\nu_{C=N}$), 1325 (ν_{C-S}) cm^{-1}.

*4.10. Synthesis of **2d***

[$AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) with *N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1d** (31mg, 0.126 mmol) and trimethylamine (5 drops, excess) in methanol (25 mL) gave a yellow powder (46 mg, 66%). M.p. 196-200 °C. Found: C, 45.09; H, 2.88; N, 9.16%. $C_{23}H_{17}AuN_4O_2S$ requires C, 45.25; H, 2.81; N, 9.18%. ^{1}H NMR: δ (ppm) 9.02 (d, J 5.6, 1H), 8.20 (m, 2H), 8.13 (t, 1H), 7.83 (d, J 8.0, 1H), 7.65 (t, 1H), 7.47 (dd, J 7.6, 1H), 7.16 (m, 6H), 6.68 (m, 1H), 6.45 (m, 1H), 4.52 (d, J 14.8, 1H), 4.09 (d, J 14.8, 1H). ESI MS: positive-ion $[M+H]^+$, *m/z* 611.080, calculated *m/z* 611.074. IR: 1558 ($\nu_{C=N}$), 1333 (ν_{C-S}), 1504 ($\nu^{as}_{NO_2}$), 1390 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.11. Synthesis of **2e***

[$AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) with 3,5-dimethyl-*N*-phenyl-1H-pyrrole-2-carbothioamide **1e** (35 mg, 0.126 mmol) and trimethylamine (5 drops, excess) in methanol (25 mL) gave an orange powder (42 mg, 57%). M.p. 194-196 °C. Found: C, 47.02;

H, 3.35; N, 8.76%. $C_{25}H_{21}AuN_4O_2S$ requires C, 47.03; H, 3.32; N, 8.77%. ^{1}H NMR: δ (ppm) 8.91 (dd, J 5.6, 1H), 8.21 (m, 1H), 8.06 (t, 1H), 7.78 (d, J 7.2, 1H), 7.50 (m, 2H), 7.13 (m, 4H), 7.00 (m, 1H), 5.99 (s, 1H), 4.56 (d, J 14.8, 1H), 4.07 (d, J 14.8, 1H), 2.40 (s, 3H), 1.69 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 639.104, calculated *m/z* 639.105. IR: 1572 ($\nu_{C=N}$), 1333 (ν_{C-S}), 1503 ($\nu^{as}NO_2$), 1311 ($\nu^{s}NO_2$) cm^{-1}.

4.12. Synthesis of ***2f***

$[AuCl_2$(2-benzylpyridyl)] (50 mg, 0.115 mmol) with 4-ethyl-3,5-dimethyl-*N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1f** (38 mg, 0.126 mmol) and trimethylamine (5 drops, excess) in methanol gave an orange powder (65 mg, 57%). M.p. 202-204 °C. Found: C, 48.62; H, 3.82; N, 8.38%. $C_{27}H_{25}AuN_4O_2S$ requires C, 48.65; H, 3.78; N, 8.41%. ^{1}H NMR: δ (ppm) 8.92 (dd, J 5.6, 1H), 8.22 (m, 2H), 8.06 (t, 1H), 7.80 (d, J 8.0, 1H), 7.52 (m, 2H), 7.17 (m, 4H), 7.02 (m, 1H), 4.59 (d, J 14.4, 1H), 4.09 (d, J 14.4, 1H), 2.41 (m, 5H), 1.67 (s, 3H), 1.09 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 667.090, calculated *m/z* 667.136. IR: 1563 ($\nu_{C=N}$), 1328 (ν_{C-S}), 1499 ($\nu^{as}NO_2$), 1309 ($\nu^{s}NO_2$) cm^{-1}.

4.13. Synthesis of ***3a***

A solution of $[AuCl_2(C_6H_4CH_2NMe_2)]$ (50 mg, 0.124 mmol) in methanol (10 mL) was added in one portion to a stirred solution of *N*-phenyl-1H-pyrrole-2-carbothioamide **1a** (28 mg, 0.137 mmol) in methanol (10 mL), and the mixture was heated to 50 °C. After aqueous trimethylamine (5 drops, excess) was added, the reaction mixture was heated to reflux for 2 h. After cooling to room temperature, water (2 mL) was added, resulting in precipitation of a yellow solid. The product was filtered and washed with petroleum spirits (3 mL), yield 38 mg, 58%. M.p. 158-160 °C. Found: C, 44.51; H, 4.02; N, 7.63%. $C_{20}H_{20}AuN_3S$ requires C, 45.20; H, 3.79; N, 7.91%. ^{1}H NMR: δ (ppm) 7.38 (m, 3H), 7.21 (m, 2H), 7.11 (m,

6H), 6.54 (q, 1H), 4.35 (s, 2H), 3.38 (s, 6H). ESI MS: positive-ion $[M+H]^+$, *m/z* 532.120, calculated *m/z* 532.104. IR: 1566 ($\nu_{C=N}$), 1390 (ν_{C-S}) cm^{-1}.

*4.14. Synthesis of **3d***

$[AuCl_2(C_6H_4CH_2NMe_2)]$ (50 mg, 0.124 mmol) with *N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1d** (34 mg, 0.137 mmol) and trimethylamine (5 drops, excess) in methanol gave a brownish yellow powder (53 mg, 74%). M.p. 198-202 °C. Found: C, 41.37; H, 3.18; N, 9.64%. $C_{20}H_{19}AuN_4O_2S$ requires C, 41.67; H, 3.32; N, 9.72%. ^{1}H NMR: δ (ppm) 8.22 (m, 2H), 7.30 (d, J 7.76, 1H), 7.22 (m, 2H), 7.15 (m, 2H), 7.10 (m, 2H), 6.97 (br, 1H), 6.53 (q, 1H), 4.32 (s, 2H), 3.39 (s, 6H). ESI MS: positive-ion $[M+H]^+$, *m/z* 577.183, calculated *m/z* 577.089. IR: 1578 ($\nu_{C=N}$), 1331 (ν_{C-S}), 1504 ($\nu^{as}NO_2$), 1391 ($\nu^{s}NO_2$) cm^{-1}.

*4.15. Synthesis of **3e***

$[AuCl_2(C_6H_4CH_2NMe_2)]$ (50 mg, 0.124 mmol) with 3,5-dimethyl-*N*-phenyl-1H-pyrrole-2-carbothioamide **1e** (38 mg, 0.137 mmol) and trimethylamine (5 drops, excess) in methanol gave a brown powder (57 mg, 73%). M.p. 172-178 °C. Found: C, 43.36; H, 3.75; N, 9.06%. $C_{22}H_{23}AuN_4O_2S$ requires C, 43.71; H, 3.84; N, 9.27%. ^{1}H NMR: δ (ppm) 8.15 (m, 2H), 7.21 (m, 1H), 7.19 (m, 2H), 7.08 (m, 3H), 6.10 (s, 1H), 4.26 (s, 2H), 3.30 (s, 6H), 2.49 (s, 3H), 2.40 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 605.242, calculated *m/z* 605.121. IR: 1569 ($\nu_{C=N}$), 1331 (ν_{C-S}), 1502 ($\nu^{as}NO_2$), 1306 ($\nu^{s}NO_2$) cm^{-1}.

*4.16. Synthesis of **3f***

$[AuCl_2(C_6H_4CH_2NMe_2)]$ (40 mg, 0.099 mmol) with 4-ethyl-3,5-dimethyl-*N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1f** (33 mg, 0.109 mmol) and trimethylamine (5 drops, excess) in methanol gave a brown powder (38 mg, 60%). M.p. 164-170 °C. Found: C,

45.50; H, 4.22; N, 8.76%. $C_{24}H_{27}AuN_4O_2S$ requires C, 45.57; H, 4.30; N, 8.86%. ^{1}H NMR: δ (ppm) 8.16 (m, 2H), 7.22 (m, 3H), 7.12 (m, 3H), 4.27 (s, 1H), 3.31 (s, 6H), 2.47 (m, 5H), 2.40 (d, J 3.2, 3H), 1.12 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 633.290, calculated *m/z* 633.152. IR: 1561 ($\nu_{C=N}$), 1332 (ν_{C-S}), 1503 ($\nu^{as}_{NO_2}$), 1390 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.17. Synthesis of **4a***

A mixture of *cis*-$[PtCl_2(PPh_3)_2]$ (100 mg, 0.126 mmol) with *N*-phenyl-1H-pyrrole-2-carbothioamide **1a** (28 mg, 0.139 mmol) and trimethylamine (5 drops, excess) in methanol gave **4a** as a light yellow powder (67 mg, 58%). M.p. 290-292 °C. Found: C, 61.22; H, 4.10; N, 3.18%. $C_{47}H_{38}N_2P_2PtS$ requires C, 61.36; H, 4.16; N, 3.05%. ^{31}P{^{1}H} NMR, δ (ppm) 19.4 [d, ^{1}J(PtP) 2849, ^{2}J(PP) 24], δ 13.4 [d, ^{1}J(PtP) 3177, ^{2}J(PP) 24]. ^{1}H NMR: δ (ppm) 7.40 (m, 6H), 7.37 (m, 6H), 7.30 (m, 5H), 7.15 (m, 15H), 6.97 (m, 2H), 6.85 (m, 1H), 6.69 (m, 1H), 6.00 (s, 1H), 5.70 (m, 1H). ESI MS: positive-ion $[M+H]^+$, *m/z* 920.217, calculated *m/z* 920.188. IR: 1557 ($\nu_{C=N}$), 1281 (ν_{C-S}) cm^{-1}.

*4.18. Synthesis of **4d***

A mixture of *cis*-$[PtCl_2(PPh_3)_2]$ (100 mg, 0.126 mmol) with *N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1d** (34 mg, 0.139 mmol) and trimethylamine (5 drops, excess) in methanol gave **4d** as a light orange powder (72 mg, 59%). M.p. decomp. > *ca*. 282 °C turns black. Found: C, 58.37; H, 3.77; N, 4.33%. $C_{47}H_{37}N_3O_2P_2PtS$ requires C, 58.50; H, 3.86; N, 4.35%. ^{31}P{^{1}H} NMR, δ (ppm) 19.2 [d, ^{1}J(PtP) 2900, ^{2}J(PP) 24], δ 12.6 [d, ^{1}J(PtP) 3163, ^{2}J(PP) 24]. ^{1}H NMR: δ (ppm) 7.99 (m, 2H), 7.45 (m, 6H), 7.41 (m, 6H), 7.33 (m, 6H), 7.17 (m, 12H), 7.03 (m, 2H), 6.64 (s, 1H), 6.02 (m, 1H), 5.72 (m, 1H). ESI MS: positive-ion

$[M+H]^+$, *m/z* 965.204, calculated *m/z* 965.173. IR: 1531 ($\nu_{C=N}$), 1329 (ν_{C-S}), 1504 ($\nu^{as}_{NO_2}$), 1396 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.19. Synthesis of **4e***

A mixture of *cis*-$[PtCl_2(PPh_3)_2]$ (100 mg, 0.126 mmol) with 3,5-dimethyl-*N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1e** (38 mg, 0.139 mmol) and trimethylamine (5 drops, excess) in methanol (25 mL) gave **4e** as an orange powder (63 mg, 50%). M.p. 220-224 °C. Found: C, 59.03; H, 4.11; N, 4.36%. $C_{49}H_{41}N_3O_2P_2PtS$ requires C, 59.27; H, 4.16; N, 4.23%. $^{31}P\{^1H\}$ NMR, δ (ppm) 15.8 [d, ^1J(PtP) 3088, ^2J(PP) 24], δ 7.1 [d, ^1J(PtP) 3100, ^2J(PP) 24]. ^1H NMR: δ (ppm) 7.91 (m, 2H), 7.52 (m, 6H), 7.34 (m, 6H), 7.20 (m, 12H), 7.12 (m, 6H), 6.90 (m, 2H), 5.43 (dd, J 3.6, 1H), 2.42 (s, 3H), 1.46 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 993.519, calculated *m/z* 993.204. IR: 1527 ($\nu_{C=N}$), 1333 (ν_{C-S}), 1498 ($\nu^{as}_{NO_2}$), 1298 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.20. Synthesis of **4f***

A mixture of *cis*-$[PtCl_2(PPh_3)_2]$ (80 mg, 0.101 mmol) with 4-ethyl-3,5-dimethyl-*N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1f** (34 mg, 0.111 mmol) and trimethylamine (5 drops, excess) in methanol gave **4f** as a dark orange powder (75 mg, 73%). M.p. 222-224 °C. Found: C, 59.98; H, 4.46; N, 4.23%. $C_{51}H_{45}N_3O_2P_2PtS$ requires C, 59.99; H, 4.44; N, 4.12%. $^{31}P\{^1H\}$ NMR, δ (ppm) 16.1 [d, ^1J(PtP) 3090, ^2J(PP) 23], δ 7.2 [d, ^1J(PtP) 3084, ^2J(PP) 23]. ^1H NMR: δ (ppm) 7.90 (m, 2H), 7.52 (m, 6H), 7.33 (m, 6H), 7.24 (m, 12H), 7.12 (m, 6H), 6.89 (m, 2H), 2.40 (s, 3H), 1.98 (q, 2H), 1.42 (s, 3H), 1.98 (t, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 1021.157, calculated *m/z* 1021.236. IR: 1520 ($\nu_{C=N}$), 1323 (ν_{C-S}), 1542 ($\nu^{as}_{NO_2}$), 1299 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.21. Synthesis of **5a***

A mixture of [$PdCl_2$(dppe)] (50 mg, 0.087 mmol) with *N*-phenyl-1H-pyrrole-2-carbothioamide **1a** (19 mg, 0.096 mmol) and trimethylamine (5 drops, excess) in methanol gave an orange powder (35 mg, 56%). M.p. 172-176 °C. Found: C, 62.17; H, 4.63; N, 4.11%. $C_{37}H_{32}N_2P_2PdS$ requires C, 63.03; H, 4.57; N, 3.97%. $^{31}P\{^1H\}$ NMR, δ (ppm) 56.9 [d, ^2J(PP) 29], δ 50.4 [d, ^2J(PP) 29]. ^1H NMR: δ (ppm) 7.71 (m, 8H), 7.40 (m, 12H), 7.15 (m, 2H), 7.03 (m, 2H), 6.82 (m, 2H), 6.18 (s, 1H), 5.94 (s, 1H), 2.33 (m, 4H). ESI MS: positive-ion $[M+H]^+$, *m/z* 705.133, calculated *m/z* 705.080. IR: 1551 ($\nu_{C=N}$), 1279 (ν_{C-S}) cm^{-1}.

*4.22. Synthesis of **5d***

[$PdCl_2$(dppe)] (50 mg, 0.087 mmol) with *N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1d** (24 mg, 0.096 mmol) and trimethylamine (5 drops, excess) in methanol gave a red powder (53 mg, 81%). M.p. 270-276 °C. Found: C, 59.05; H, 4.07; N, 5.72%. $C_{37}H_{31}N_3O_2P_2PdS$ requires C, 59.25; H, 4.17; N, 5.60%. $^{31}P\{^1H\}$ NMR, δ (ppm) 58.0 [d, ^2J(PP) 29], δ 51.5 [d, ^2J(PP) 28]. ^1H NMR: δ (ppm) 8.05 (m, 2H), 7.77 (m, 4H), 7.67 (m, 4H), 7.41 (m, 12H), 7.06 (m, 2H), 6.74 (s, 1H), 6.18 (m, 1H), 5.94 (m, 1H), 2.37 (m, 4H). ESI MS: positive-ion $[M+H]^+$, *m/z* 750.073, calculated *m/z* 750.065. IR: 1544 ($\nu_{C=N}$), 1324 (ν_{C-S}), 1586 ($\nu^{as}_{NO_2}$), 1386 ($\nu^{s}_{NO_2}$) cm^{-1}.

*4.23. Synthesis of **5e***

[$PdCl_2$(dppe)] (50 mg, 0.087 mmol) with 3,5-dimethyl-*N*-phenyl-1H-pyrrole-2-carbothioamide **1e** (26 mg, 0.096 mmol) and trimethylamine (5 drops, excess) in methanol gave a dark red powder (56 mg, 83%). M.p. 190-196 °C. Found: C, 59.34; H, 4.51; N, 5.75%. $C_{39}H_{35}N_3O_2P_2PdS$ requires C, 60.20; H, 4.53; N, 5.40%. $^{31}P\{^1H\}$ NMR, δ (ppm) 61.8 [d, ^2J(PP) 32], δ 47.3 [d, ^2J(PP) 34]. ^1H NMR: δ (ppm) 7.89 (m, 6H), 7.64 (m, 4H), 7.49 (m, 8H),

7.40 (m, 4H), 6.94 (m, 2H), 5.69 (d, J 3.4, 1H), 2.37 (s, 3H), 2.21 (m, 4H), 1.48 (s, 3H). ESI MS: positive-ion $[M+H]^+$, *m/z* 778.112, calculated *m/z* 778.096. IR: 1511 ($\nu_{C=N}$), 1279 (ν_{C-S}), 1464 ($\nu^{as}NO_2$), 1327 ($\nu^{s}NO_2$) cm^{-1}.

*4.24. Synthesis of **5f***

$[PdCl_2(dppe)]$ (50 mg, 0.087 mmol) with 4-ethyl-3,5-dimethyl-*N*-(4-nitrophenyl)-1H-pyrrole-2-carbothioamide **1f** (29 mg, 0.096 mmol) and trimethylamine (5 drops, excess) in methanol gave a dark red powder (55 mg, 79%). M.p. 220-226 °C. Found: C, 60.37; H, 4.95; N, 5.53%. $C_{41}H_{39}N_3O_2P_2PdS$ requires C, 61.08; H, 4.88; N, 5.21%. $^{31}P\{^1H\}$ NMR, δ (ppm) 61.6 [d, ^2J(PP) 34], δ 47.3 [d, ^2J(PP) 34]. ^1H NMR: δ (ppm) 7.88 (m, 3H), 7.67 (m, 4H), 7.46 (m, 8H), 7.36 (m, 4H), 7.06 (t, 2H), 6.89 (d, J 8.2, 2H), 6.79 (t, 1H), 2.40 (s, 3H), 2.22 (m, 6H), 1.45 (s, 3H), 0.87 (t, 4H). ESI MS: positive-ion $[M+H]^+$, *m/z* 806.143, calculated *m/z* 806.127. IR: 1544 ($\nu_{C=N}$), 1308 (ν_{C-S}), 1494 ($\nu^{as}NO_2$), 1326 ($\nu^{s}NO_2$) cm^{-1}.

*4.25. X-ray structure determinations of **1f**, **2b**•0.75CH_2Cl_2 and **3d***

Black crystals of **1f** were obtained by rotary evaporation of an ethyl acetate/dichloromethane/hexane 1:3:5 solution. Orange crystals of **2b**•0.75CH_2Cl_2 and yellow crystals of **3d** were obtained by slow diffusion of diethyl ether into a dichloromethane solution of the compounds at room temperature.

Intensity data were obtained on an Agilent SuperNova, Single source at offset, Atlas diffractometer with graphite-monochromated Cu—Kα radiation and corrected for absorption using a multi-scan procedure.[52] Using Olex2,[53] the structures were solved with the Olex2.solve [54] structure solution program using Charge Flipping and refined with the

Olex2.refine [54] refinement package using Gauss–Newton minimisation. The peak electron densities of **2b** and **3b** lie close to Au(1) (within 1.1 Å).

Crystallographic details are presented in Table 4.

4.26. Biological assays

The MTT assay was used to examine the cytotoxic effect of the compounds toward human A549 cells, which are used as models for the study of lung cancer. Cells were seeded in a complete growth medium in 96-well plates (Costar Corning, NY), at a density of 1×10^4 cells/well, and grown for 24 h before treatment. The growth medium was then substituted with fresh medium containing the compounds to be tested at appropriate concentrations. After incubation for 24 h, cells were washed with PBS three times and 100 μL of fresh culture medium containing MTT (5 mg/mL) was added to each well. Cells were continually incubated for another 4 h before the media with MTT were removed. Furthermore, 150 μL of DMSO was added to each well and incubated at 37 °C for 10 min. The absorbance of each sample at 490 nm was measured using a microplate reader (Perkin-Elmer, Victor X4).

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Disclosure statement

No potential conflict of interest

Supplementary material

CCDC 1948345 - 1948347 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. Supplementary data to this article can be found online at http://.....

Table 1 Selected bond lengths (Å) and angles (°) for 1f, with esds in parentheses.

Atoms	Lengths (Å)	Atoms	Angles (°)
N(1)-C(4)	1.380(2)	N(1)-C(4)-C(9)	119.95(15)
C(4)-C(9)	1.437(2)	C(4)-C(9)-S(1)	121.89(13)
C(9)-S(1)	1.6775(17)	S(1)-C(9)-N(2)	124.10(13)
C(9)-N(2)	1.362(2)	C(9)-N(2)-C(11)	134.31(15)
N(2)-C(11)	1.404(2)	C(4)-C(9)-N(2)	114.01(14)
N(1)-C(1)	1.355(2)		

Table 2 Selected bond lengths (Å) and angles (°) for the complex **2b**•CH_2Cl_2, with esds in parentheses

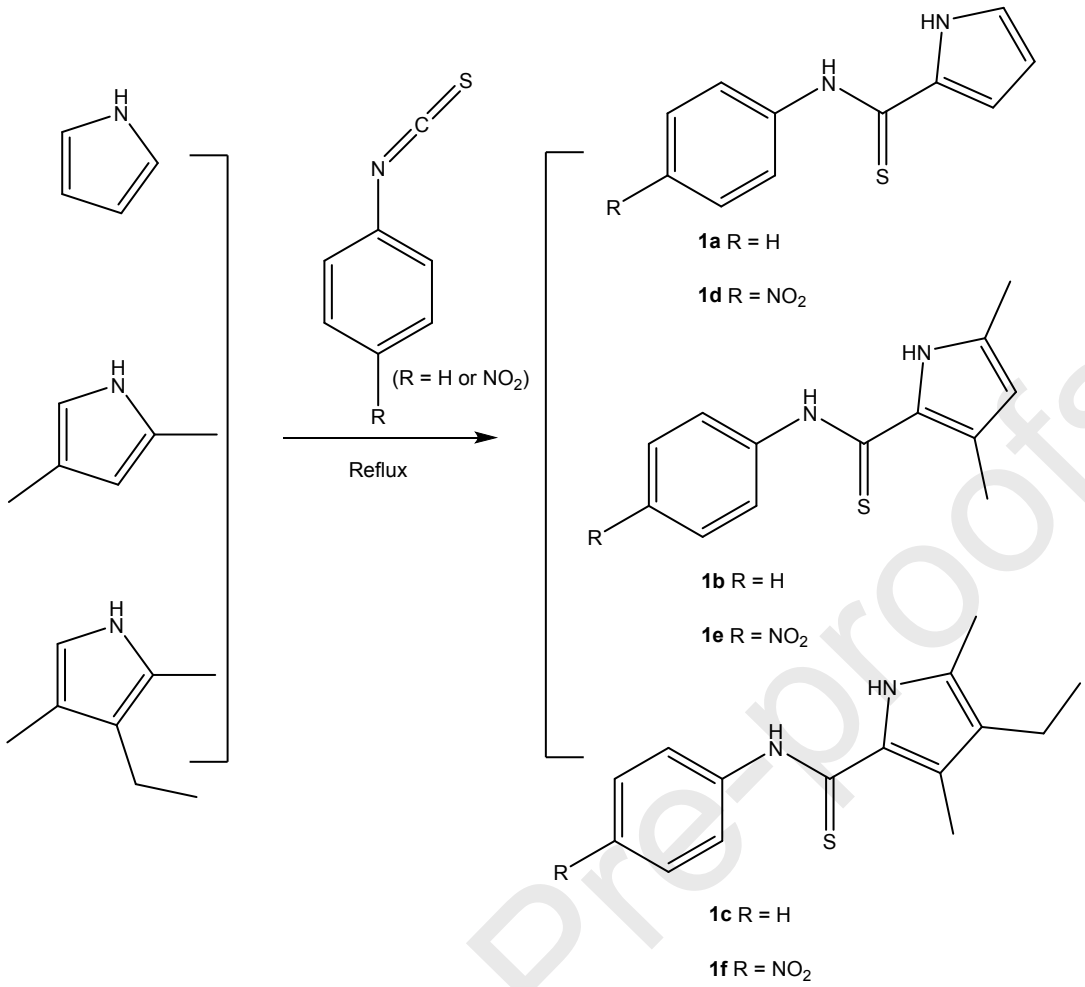
Atoms	Lengths (Å)	Atoms	Angles (°)
Au(1)-N(1)	2.062(6)	N(4)-Au(1)-C(31)	87.1(2)
Au(1)-N(4)	2.090(5)	C(31)-Au(1)-S(1)	90.71(19)
Au(1)-C(31)	2.043(7)	S(1)-Au(1)-N(1)	85.07(15)
Au(1)-S(1)	2.2630(15)	N(1)-Au(1)-N(4)	98.0(2)
S(1)-C(9)	1.803(6)	S(1)-Au(1)-N(4)	170.68(16)
N(2)-C(9)	1.284(8)	N(1)-Au(1)-C(31)	172.6(3)
		Au(1)-N(1)-C(4)	117.9(4)
		Au(1)-S(1)-C(9)	99.4(2)

Table 3 Selected bond lengths (Å) and angles (°) for the complex **3d**, with esds in parentheses

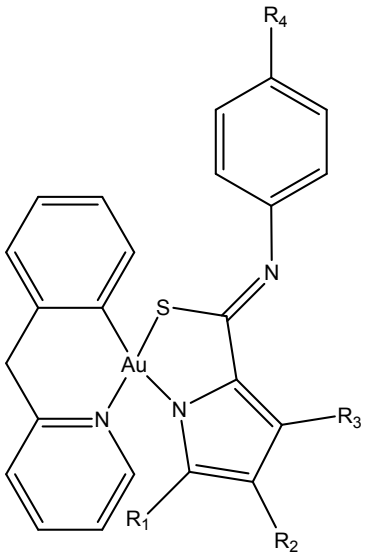
Atoms	Lengths (Å)	Atoms	Angles (°)
Au(1)-N(1)	2.080(4)	N(4)-Au(1)-C(21)	81.17(18)
Au(1)-N(4)	2.144(4)	C(21)-Au(1)-S(1)	90.84(14)
Au(1)-C(21)	2.028(5)	S(1)-Au(1)-N(1)	85.61(12)
Au(1)-S(1)	2.2797(11)	N(1)-Au(1)-N(4)	102.57(16)
S(1)-C(9)	1.789(5)	S(1)-Au(1)-N(4)	170.73(11)
N(2)-C(9)	1.280(6)	N(1)-Au(1)-C(21)	175.62(19)
		Au(1)-N(1)-C(4)	117.2(3)
		Au(1)-S(1)-C(9)	99.64(17)

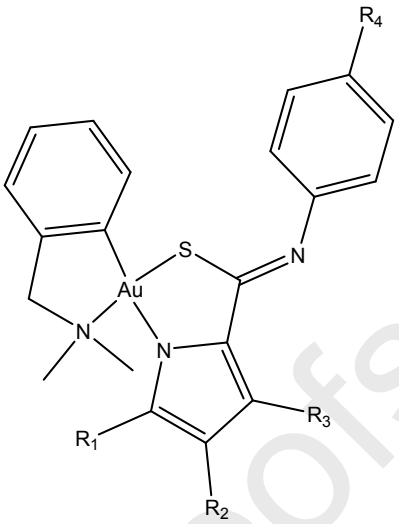
Table 4 Crystal and refinement data for the compounds **1f**, **2b**•0.75CH_2Cl_2 and **3d**

Complex	**1f**	**2b**•0.75CH_2Cl_2	**3d**
Formula	$C_{15}H_{17}N_3O_2S$	$C_{25.75}H_{23.5}AuC_{l1.5}N_3S$	$C_{20}H_{19}AuN_4O_2S$
Molecular Weight	303.39	657.21	576.43
T/K	100.05(16)	111(15)	99.95(13)
Crystal system	Triclinic	Triclinic	Monoclinic
Space group	*P*-1	*P*-1	$P2_1/n$
a (Å)	6.9323(4)	10.3271(5)	15.0999(2)
b (Å)	8.5240(6)	12.0211(6)	8.23711(15)
c (Å)	12.5071(8)	12.2148(5)	15.1811(2)
α (°)	89.096(5)	118.107(5)	90
β (°)	79.418(6)	98.606(4)	92.8016(14)
γ (°)	82.735(5)	105.272(4)	90
V (Å^3)	720.64(8)	1221.73(13)	1885.96(5)
Z	2	2	4
D_{calc} (g cm^{-3})	1.398	1.786	2.030
Residual electron density (max, min e Å^{-3})	0.360, -0.401	4.437, -2.216	1.698, -1.597
$T_{max,min}$	1.000, 0.672	0.793, 0.622	0.816, 0.454
No. of unique reflections	2798	4783	3659
No. of observed reflections [I>2σ(I)]	2347	4433	3233
R [I>2σ(I)]	0.0371	0.0456	0.0263
wR_2 (all data)	0.0946	0.1240	0.0739
Goodness of Fit	1.032	1.037	1.068



Scheme 1 Syntheses of pyrrole-derived thioamide ligands 1a-1f

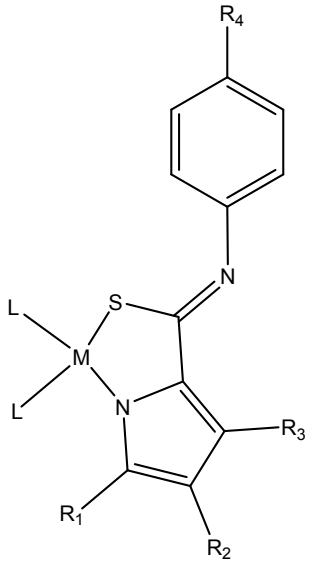




	R_1	R_2	R_3	R_4
2a	H	H	H	H
2b	Me	H	Me	H
2c	Me	Et	Me	H
2d	H	H	H	NO_2
2e	Me	H	Me	NO_2
2f	Me	Et	Me	NO_2

	R_1	R_2	R_3	R_4
3a	H	H	H	H
3d	H	H	H	NO_2
3e	Me	H	Me	NO_2
3f	Me	Et	Me	NO_2

Scheme 2 Gold(III) complexes containing pyrrole thioamide ligands



	M	L	R_1	R_2	R_3	R_4
4a	Pt	PPh_3	H	H	H	H
4d	Pt	PPh_3	H	H	H	NO_2
4e	Pt	PPh_3	Me	H	Me	NO_2
4f	Pt	PPh_3	Me	Et	Me	NO_2
5a	Pd	dppe	H	H	H	H
5d	Pd	dppe	H	H	H	NO_2
5e	Pd	dppe	Me	H	Me	NO_2
5f	Pd	dppe	Me	Et	Me	NO_2

Scheme 3 Platinum(II) and palladium(II) complexes containing pyrrole thioamide ligands

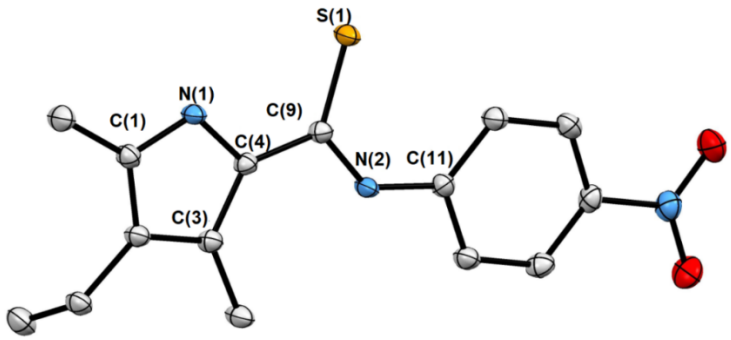


Figure 1 Molecular structure of the pyrrole thioamide **1f** (thermal ellipsoids at 50% probability). Hydrogen atoms have been omitted for clarity**.**

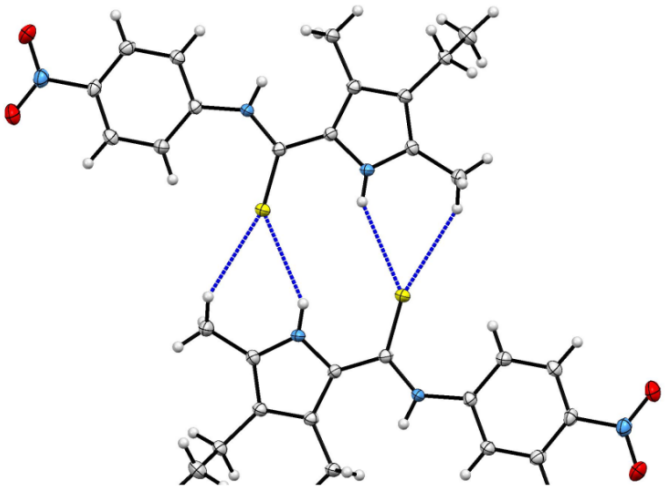


Figure 2 View of the structure of **1f** showing the formation of a dimer through hydrogen bonding interactions

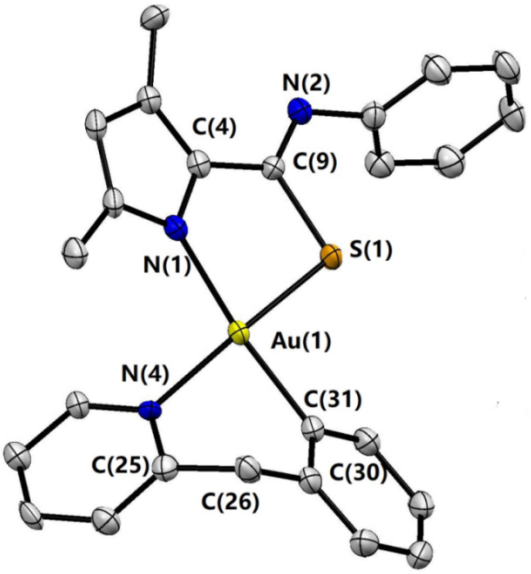


Figure 3 Molecular structure of **2b**•0.75CH_2Cl_2 (thermal ellipsoids at 50% probability). Hydrogen atoms and the CH_2Cl_2 of crystallisation have been omitted for clarity

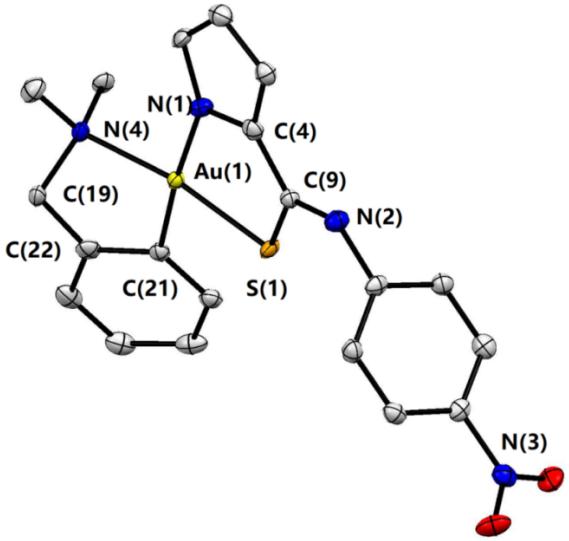


Figure 3 Molecular structure of **3d** (thermal ellipsoids at 50% probability). Hydrogen atoms have been omitted for clarity

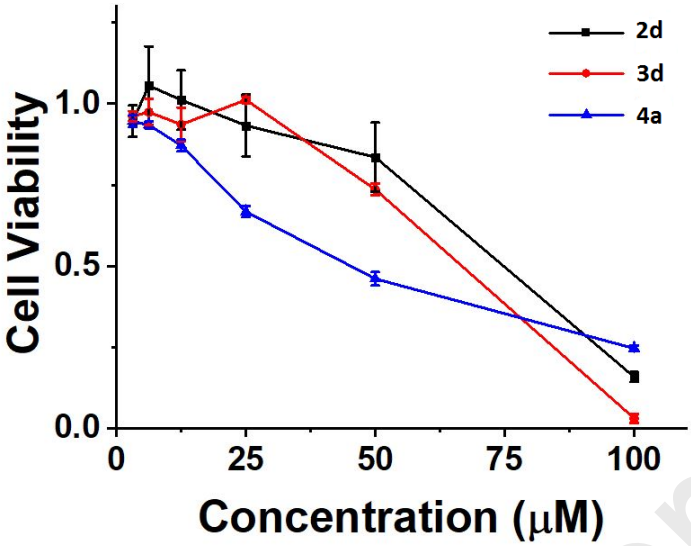
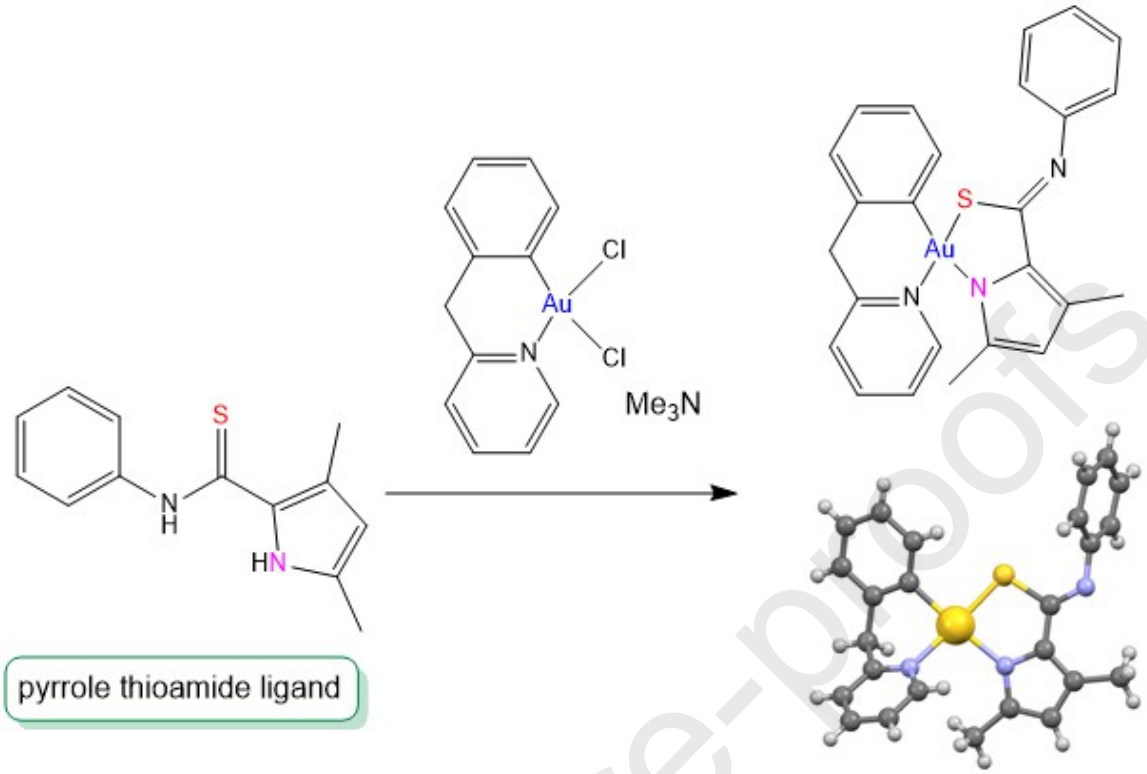


Figure 4 Viability of adenocarcinomic human alveolar basal epithelial (A549) cells, after 24 h of treatment with **2d**, **3d** and **4a** at a range of concentrations in the range 3-100 μM

References



Highlights

- Series of Pt(II), Pd(II) and Au(III) complexes of pyrrole thioamide ligands synthesised
- Ligand coordinates through thiolate sulfur and deprotonated pyrrole
- X-ray structures of three derivatives are reported
- Complexes screened against adenocarcinomic human alveolar basal epithelial cells

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

None

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