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A Convenient Mode to Stabilize M^I Metal Ions by Using Thiosemicarbazones

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We investigated the coordinative behaviour of the phosphanylthiosemicarbazone ligand 2-[2-(diphenylphosphanyl)-benzylidene]-*N*-phenylthiosemicarbazone (HLPPh) towards coinage M^I metal ions (M = Cu, Ag, Au). The complexes obtained, with formulae $[Cu(HLPPh)_2]Br$ (**1**), $[Cu(HLPPh)_2]I\cdot H_2O$ (**2**), $[Ag(HLPPh)(NO_3)]\cdot 3H_2O$ (**3**) and $[Au_2(HLPPh)_2]\cdot 3CH_3OH$ (**4**), were satisfactorily characterized by elemental analysis, IR and $^1H/^{31}P$ NMR spectroscopy as well as ESI mass spectrometry. In addition, we obtained the crystal structure of the complex $[Au_2(\mu\text{-}S,P\text{-}HLPPh)_2]Cl_2$ (**5**), which is the first example of a homoleptic thiosemicarbazone Au^I complex, because the Au^I ion has been stabilized by exclusively using a phosphanylthiosemicarbazone ligand. We also performed preliminary luminescence studies for these complexes, as well as the screening of its biological activity against human cervical carcinoma (HeLa) cells.

Introduction

Thiosemicarbazone ligands are versatile molecules, not only because of their pharmacological activity, they also give rise to an enormous variety of structures for their metal complexes.[1–6] This versatility arises from the possibility to act as N,S-donor systems, forming stable four and five-membered metallacycles. In addition, the coordination capacity of thiosemicarbazones can be increased by using aldehydes or ketones that contain additional donor functional groups in suitable positions for chelation or by using appropriate co-ligands (e.g. phosphanes) for their preparation.

On the other hand, the coordination behaviour of thiosemicarbazone ligands towards M^I metal ions remains still quite unexplored. The great majority of the cases reported are heteroleptic copper(I) compounds, which contain the M^I ion coordinated to the thiosemicarbazone ligand and phosphanes as coligands. Phosphanes have been widely employed as a coordinative strategy to synthesize M^I complexes with thiosemicarbazones and therefore generating M^I heteroleptic complexes. On the contrary there are very limited studies on M^I homoleptic thiosemicarbazone complexes, which can be defined as metal(I) compounds exclusively derived from thiosemicarbazone ligands. The reported cases are mainly Cu^I and Ag^I dinuclear bishelical or tetranuclear cluster compounds formed by spontaneous self assembly processes.[3–7] In contrast, the chemistry of homoleptic Au^I complexes with thiosemicarbazones remains totally unexplored.

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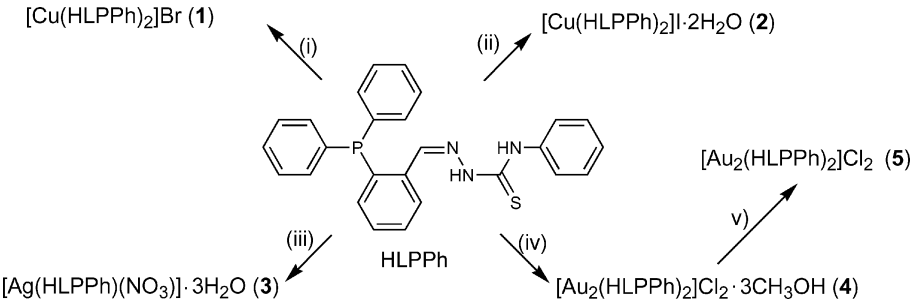
Keeping in view the above observations, we think that the use of phosphanylthiosemicarbazone ligands could be a convenient method to obtain homoleptic M^I thiosemicarbazone complexes. Surprisingly, the coordinative studies with this ligand type are very limited since they were previously employed only to prepare platinum(II) and gold(III) monomer species.[7] For that reason, we have decided to use a phosphanylthiosemicarbazone ligand as suitable approach to stabilize homoleptic Cu^I, Ag^I and Au^I complexes.

Results and Discussion

Chemistry

The phosphanylthiosemicarbazone ligand 2-[2-(diphenylphosphanyl)benzylidene]-*N*-phenylthiosemicarbazone (HLPPh, Scheme 1) was prepared as reported before.[8] Reaction of HLPPh with copper(I) bromide and copper(I) iodide resulted in the formation of the copper(I) complexes, $[Cu(HLPPh)_2]Br$ (**1**) and $[Cu(HLPPh)_2]I\cdot 2H_2O$ (**2**), both containing the corresponding halide atom as counterion. It must be pointed out here that the formation of complexes **1** and **2** occurs instantaneously in the presence of air, with the colour of the solution changing from yellow to orange after the halide salt was added. This fact rules out the Cu^I oxidation during the synthesis of these two systems. Nevertheless, the copper(I) complexes easily experienced oxidation in dmso (bromide and iodide complexes **1** and **2**) and in dmf (iodide complex **2**). When silver(I) nitrate was treated with the ligand HLPPh, we obtained the yellow solid **3**, showing a $[Ag(HLPPh)(NO_3)]\cdot 3H_2O$ stoichiometry, while complex $[Au_2(HLPPh)_2]Cl_2\cdot 3MeOH$ (**4**) was isolated when we employed an aqueous $H[AuCl_4]$ solution, previously reduced with 2,2′-thiodiethanol. The four com-

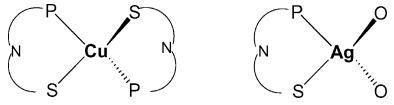


Scheme 1. (i) CuBr, MeOH; (ii) CuI, MeOH; (iii) $AgNO_3$, MeOH; (iv) $H[AuCl_4]$ in H_2O, 2,2′-thiodiethanol, MeOH; (v) MeOH, room temp., 10 d.

plexes were readily characterized by the usual techniques. The low molar conductivity value measured for the silver complex **3** is indicative of the non-electrolytic nature of this compound. On the contrary, the conductivity values obtained for the copper(I) complex **1** and the gold(I) complex **4** confirmed their 1:1 and 1:2 electrolytic character, respectively. We identified peaks corresponding to fragments $[M(HLPPh) + H]^+$ in the ESI(+) mass spectra of all the complexes, except for the copper(I) compounds **1** and **2**, for which the fragment $[M(HLPPh)_2+H]^+$ was identified. Furthermore, the presence of the positive ion $[Au_2(HLPPh)_2+H]^+$ in the ESI mass spectrum of gold complex **4** supports the dinuclear nature proposed for this complex. Despite the lack of conductivity studies for the copper iodide complex **2**, the absence of the $[Cu(HLPPh)_2I]$ fragment in the ESI mass spectrum together with the probed affinity of Cu^I by soft phosphorus and sulfur atoms, lead us to propose that iodide acts as counterion in this complex. The IR spectra of all the complexes show the presence of ν(NH) bands in the range 3400–3200 cm^{-1}, which suggest that the thiosemicarbazone ligand is coordinated to the M^I centres in its neutral form. We also observed that the ν(C=N) and ν(C–N) bands remain unaffected for the silver and gold complexes. This precludes the possibility of coordination through the imine nitrogen atom for these metal compounds. In the case of silver, the appearance of the strong ν(N–O) bands at 1510 and 1275 cm^{-1} indicates that the nitrate group is covalently bound to the silver centre in a bidentate mode.

The ^1H NMR spectra for the silver and gold complexes show the characteristic NH signals attributable to the thiosemicarbazone shifted upfield with respect to those for the free ligand, which points towards the single protonation of the ligand in these complexes. The imine signal does not modify its position which seems to indicate that this atom does not participate in the coordination to these metal centres. The ^{31}P NMR spectra of the silver(I) and gold(I) complexes exhibit single peaks at δ = 9.9 and 40.7 ppm, respectively. The appearance of a single signal for the gold(I) complex suggests that the two phosphane units coordinated to the gold ions are magnetically equivalent.

All the experimental data allow us to propose mononuclear tetracoordinate $[P_2S_2]$ and $[PSO_2]$ environments for the copper(I) and silver(I) complexes, respectively (Scheme 2), whereas the experimental evidences point to a [PS] kernel for the gold complex.[9]



Scheme 2.

Slow concentration of the mother liquor of complex **4** afforded colourless needle-like crystals. The molecular structure, depicted in Figure 1, shows that the compound is a cationic dinuclear gold(I) complex. Every gold(I) atom possesses a distorted linear geometry, coordinated to the phosphorus atom of a ligand molecule and the thiocarbonyl sulfur atom of a second ligand unit [P(1)–Au(1)–S(2) 173.39(5), P(2)–Au(2)–S(1) 175.79(6)°]. The thiosemicarbazone ligands are both neutral and the cationic charge of the complex is compensated by two chloride ions acting as counterions.

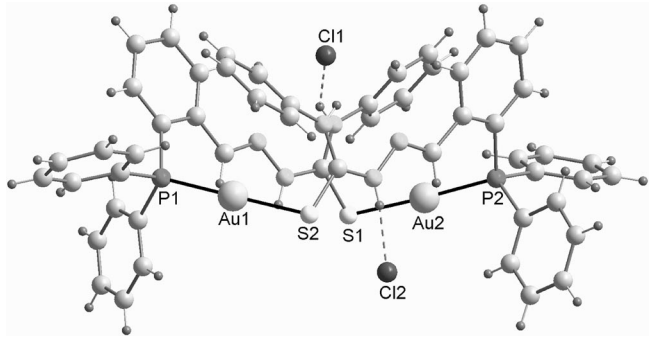


Figure 1. Molecular structure of the complex $[Au_2(\mu\text{-}S,P\text{-}HLPPh)_2]Cl_2$ (**5**). Broken lines indicate N–H···Cl hydrogen bonds.

The angles Au–P–S (Table 1) are consistent with a linear geometry around the gold atoms (Figure 1), but slightly more distorted for Au(1). Both ligands do not cross and the two thiosemicarbazone moieties adopt a pseudo *anti* conformation, probably to avoid unfavourable steric crowding. This situation is not the normal, most of the phosphanylthiolate complexes adopt a *cis*-conformation. As consequence of this arrangement, the separation between the gold(I) centres is notably large [Au(1)–Au(2), 7.719(8) Å] to consider the existence of aurophilic interactions. Neverthe-

less, this conformation permits the formation of an 18 membered metallomacrocycle that is approximately 7.72 Å long and 4.65 Å wide. This macrocycle could be considered as a receptor-type complex, because it binds one chloride guest atom in the proximities of the cavity through hydrogen bond interactions. This behaviour resembles that found for related amide or thiocarbamate complexes, which are considered effective containers capable to bound, store, transport or even react upon multiple substrate molecules.[10]

Table 1. Main bond lengths [Å] and angles [°] for **5**.

$[Au_2(\mu\text{-}S,P\text{-}HLPPh)_2]Cl_2$ (**5**)			
Au(1)–S(2)	2.332(1)	Au(1)–P(1)	2.257(1)
Au(2)–S(1)	2.329(2)	Au(2)–P(2)	2.262(2)
P(1)–Au(1)–S(2)	173.39(5)	P(2)–Au(2)–S(1)	175.79(6)

Bond lengths Au–S and Au–P are typical for Au^I phosphanylthiolate complexes and do not merit further analysis.[11]

The molecular structure of **5** exhibits the typical intramolecular hydrogen bond interactions for neutral thiosemicarbazones (Table 2) established by the terminal thioamide nitrogen atoms as donors and the imine nitrogen atoms as acceptors [N(14)–H(14A)···N(12), 2.626(8) Å and N(24)–H(24A)···N(22), 2.624(8) Å]. In addition, the acceptor chloride ions are involved in the formation of intramolecular hydrogen bonds with a hydrazide nitrogen atom [N23–H23A···Cl(2) 3.078(5) Å], and intermolecular hydrogen bonds with thioamide nitrogen atoms [N(14)–H(14A)···$Cl(1)^I$, 3.218(6) Å/146.3°, and N(24)–H(24A)···$Cl(1)^I$, 3.272(5) Å/143.9°, (symmetry code: *x + 1/2, –y + 1/2, z + 1/2*)]. These selective intermolecular hydrogen bonds established between one of the chloride ions and the cavity rim of the host metallomacrocycle gives rise to a pair of 13 membered macrobicycles, reinforced by an extra C–H···Cl contact [C(212)–H(212)···Cl(2), 3.603(9) Å/176.7°]. The crystal packing in complex **5** is additionally stabilized by multiple C–H···π interactions: intramolecular between the phosphane rings of one of the ligands and the terminal phenyl thioamide ring corresponding to the second ligand strand in the dimer, and intermolecular between the aromatic rings of the bulky phosphane belonging to different dimer molecules. The existence of these weak contacts leads to the formation of an infinite zigzag 2D network in the plane (010) (Figure 2).

Table 2. Hydrogen bond interactions [Å] for **5**.

N(14)–H(14A)···N(12)	2.626(8)	N(24)–H(24A)···N(22)	2.624(8)
N(23)–H(23A)···Cl(2)	3.078(5)	C(212)–H(212)···Cl(2)	3.603(9)
[a]N(14)–H(14A)···$Cl(1)^I$	3.218(6)	[a]N(24)–H(24A)···$Cl(1)^I$	3.272(5)

[a] Symmetry code: *x* + 1/2, *–y* + 1/2, *z* + 1/2.

After careful literature search concerning gold complexes derived from thiosemicarbazone ligands, we have found several examples of Au^{III} complexes with this ligand type.[12] Nevertheless, the number of complexes containing Au^I is still scarce. Only recently, Casas et al. published a gold(I) compound derived from a vitamin K_3-thiosemicarbazone ligand using triphenylphosphane as coligand.[13] Having this fact into account, we must stress the novelty of the gold(I) compound **5** reported in this article, because it is the first example of a homoleptic Au^I thiosemicarbazone complex.

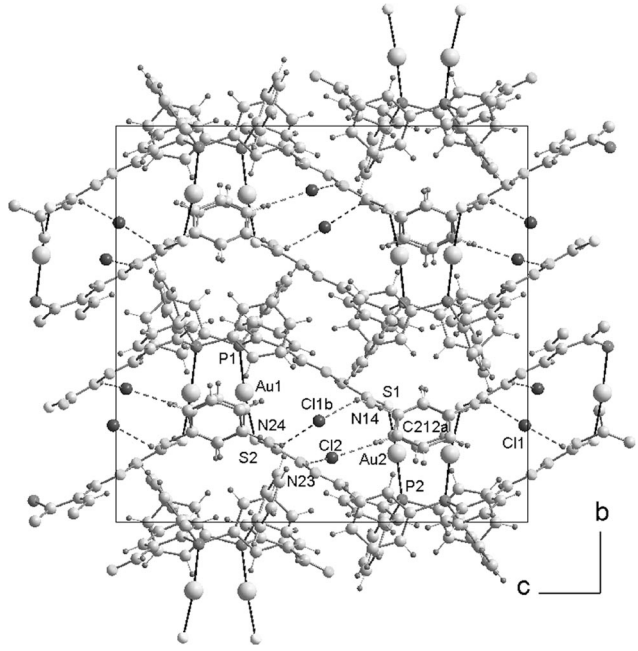


Figure 2. Molecular packing scheme in complex **5** along the *a* axis, illustrating the assembly of a 2D zigzag network.

Luminescence Studies

Numeral M^I-triphenylphosphane complexes with organic molecules have been extensively investigated for their interesting emission properties, which could be potentially exploitable in organic light-emitting devices, in the past years.[14] It is well known that the existence of luminescence properties in d^{10} metal compounds arises from diverse factors like the ligands nature, the geometry of the metal centre or the presence of intermetallic interactions. Moreover, until now, only a few of these M^I complexes have been reported to emit light at room temperature,[15] since most of them only exhibit emission at low temperature.[16]

The emission spectra of the ligand HLPPh and its Cu^I, Ag^I and Au^I complexes **1**, **3** and **4** were recorded at room temperature in methanol (Figure 3). We must note that the copper complex (**1**) did not show any emission band. On the contrary, the ligand HLPPh and its silver(I) and gold(I) complexes **3** and **4** are emissive species. The emission spectra of the ligand HLPPh and the complexes **3** and **4** exhibit intense bands, with maximums at ca. 478, 483 and 470 nm, respectively (when they are excited at 330 nm). The fact that the ligand and its Ag^I and Au^I complexes exhibit bands at close energy values suggests that these emissions are probably originated from the same electronic states that could be assignable to intraligand (IL) transitions and/or metal-to-ligand charge-transfer transitions (MLCT), but not modi-

fied by any kind intermetallic interactions [the Au···Au distance in the gold(I) complex is ca. 7.72 Å, which put in clear that the existence of gold–gold interactions is not a necessary condition for luminescence].[17] Moreover, the emission in both complexes is notably enhanced relative to the emission in the ligand, especially for the gold(I) compound. This enhancement can be ascribed to different factors like the increase of the conformational rigidity and the conjugation of charge in the ligand after coordination.[18] Another factor involved could be the existence of strong M^I-anion interactions in these complexes.[19] This fact is clearly shown by the crystal structure of the gold complex $[Au_2(\mu\text{-}S,P\text{-HLPPh})_2]Cl_2$ (**5**) where the crystal packing is specially conditioned by the presence of two chloride anions in the structure (see above).

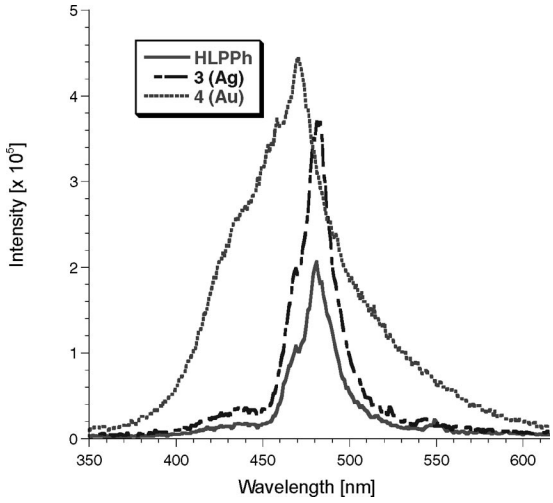


Figure 3. Emission spectra of the ligand HLPPh and the complexes **3** (Ag) and **4** (Au) in methanol (1×10^{-5} M).

For the time being, the number of luminescence studies for M^I thiosemicarbazone complexes is scarce,[8,20] which makes it difficult to determine the exact origin of the emission displayed. For that reason, more work is still necessary in this area.

Biological Activity

Preliminary experiments to evaluate the in vitro activity of the ligand HLPPh and its Ag^I and Au^I complexes **3** and **4** against the human cervical carcinoma cell line HeLa 229 showed that the compounds screened have very little effect on the cancer cells as it is indicated by the low IC_{50} values. We are currently exploring if the introduction of new structural features in the phosphanylthiosemicarbazone ligands has some effect on the biological properties of the ligands and their derived complexes.

Conclusions

Applying a known approach based in the use of P,S ligands we have demonstrated that a phosphanylthiosemicarbazone ligand provides a suitable mode to easily stabilize monovalent Cu^I, Ag^I and Au^I complexes. This fact is especially relevant in the case of gold(I), because the gold(I) complex herein reported is the unique case of a gold(I) complex exclusively derived from a thiosemicarbazone ligand.

Experimental Section

Materials: All solvents, 4-*N*-phenylthiosemicarbazide, copper(I) bromide, copper(I) iodide and silver(I) nitrate are commercially available and were used without further purification. $H[AuCl_4]$ was reduced with 2,2′-thiodiethanol.

Methods: Elemental analyses of C, H, N and S were performed with a FISONS EA 1108 analyzer. ^1H, ^{13}C and ^{31}P NMR spectroscopic studies (H_3PO_4 was used as internal reference) were carried out with a VARIAN MERCURY 300 spectrometer. Infrared spectra were measured from KBr pellets with a BRUKER IFS-66V spectrophotometer in the ranges 4000–100 or 500–100 cm^{-1}. Electrospray ionization mass spectra (ESI) were recorded with an API4000 Applied Biosystems mass spectrometer with a Triple Quadrupole analyzer. Conductivity measurements were performed at 25 °C from 10^{-3} M solutions in dmf on a Crison micro CM 2200 conductivimeter. Luminescence spectra were recorded with a Jovin Yvon-Spex Fluoromax-2 spectrophotometer.

Ligand Synthesis: The synthesis method and the experimental data for the ligand 2-[2-(diphenylphosphanyl)benzylidene]-*N*-phenylthiosemicarbazone (HLPPh) have been previously reported by us.[8]

Synthesis of Complexes: The M^I complexes (M = Cu^I, Ag^I, Au^I) were synthesized by reaction of the ligand HLPPh with CuBr, CuI, $AgNO_3$ and $H[AuCl_4]$, respectively. The experimental procedures and characterization data are summarized below.

$[Cu(HLPPh)_2]Br$ (1): Copper(I) bromide (13.32 mg, 0.091 mmol) was added to the ligand HLPPh (80 mg, 0.182 mmol), previously dissolved in methanol (50 mL). The deep orange suspension formed was refluxed for 2 h and then left stirring overnight. Afterwards, the solution was concentrated to a small volume (20 mL) and the orange solid suspended was filtered off, washed with diethyl ether, and finally dried under vacuo. Yield 78 mg (84%). M.p. 223 °C. $C_{52}H_{44}BrCuN_6P_2S_2$ (1022.5): calcd. C 61.1, H 4.3, N 8.2, S 6.3; found C 61.0, H 4.3, N 8.3, S 6.3. ESI-MS: *m*/*z* = 502.0 $[Cu(HLPPh) +H]^+$; 957.2 $[Cu(HLPPh)_2O+H]^+$. IR (KBr): = ν(OH) + ν(NH) 3419, 3314, ν(C=N) + ν(C–N) 1597, ν(N–N) 1091, ν(C=S) 748 cm^{-1}. UV/Vis (nm): λ = 380. Λ_M = 56.3 μS cm^{-1}.

$[Cu(HLPPh)_2]I\cdot 2H_2O$ (2): Copper(I) iodide (17.70 mg, 0.091 mmol) was added to the ligand HLPPh (80 mg, 0.182 mmol), previously dissolved in methanol (50 mL). The light orange suspension formed was refluxed for 2 h and then left stirring overnight. Afterwards, the solution was concentrated to a small volume (20 mL) and the orange solid suspended was filtered off, washed with diethyl ether, and finally dried under vacuo. Yield 87 mg (87%). M.p. 225 °C. $C_{52}H_{48}CuIN_6O_2P_2S_2$ (1105.5): calcd. C 56.5, H 4.4, N 7.6, S 5.8; found C 56.4, H 4.5, N 7.4, S 5.7. ESI-MS: *m*/*z* = 502.1 $[Cu(HLPPh)+H]^+$; 518.0 $[Cu(HLPPhO)+H]^+$; 957.2 $[Cu(HLPPh)_2O+H]^+$. IR (KBr): = ν(OH) + ν(NH) 3420, 3294, ν(C=N) + ν(C–N) 1597, ν(N–N) 1093, ν(C=S) 749 cm^{-1}.

$[Ag(HLPPh)(NO_3)]\cdot 3H_2O$ (3): Silver(I) nitrate (7.72 mg, 0.091 mmol) was dissolved in water (2 mL) and the resulting solution was added to the ligand HLPPh (40 mg, 0.091 mmol), previously dissolved in methanol (50 mL). The yellow solution formed

was refluxed for 2 h and then left stirring overnight in light absence. Afterwards, the solution was concentrated to a small volume (10 mL) and the yellow solid suspended was filtered off, washed with diethyl ether, and finally dried under vacuo. Yield 59 mg (98%). M.p. > 223 °C. $C_{26}H_{28}AgN_4O_6PS$ (663.4): calcd. C 47.1, H 4.2, N 8.4, S 4.8; found C 47.1, H 4.1, N 8.4, S 4.7. ESI-MS: *m/z* = 547.4 $[Ag(HLPPh)]^+$, 610.4 $[Ag(HLPPh)(NO_3)+H]^+$. ^{1}H NMR ([D$_6$]dmso): δ = 6.75–7.61 (m, 18 H), 8.17 (s, 1 H), 10.15 (br. s, 1 H), 11.73 (s, 1 H) ppm. ^{31}P NMR ([D$_6$]dmso): δ = 9.9 ppm. IR (KBr): ν(OH) + ν(NH) 3443, 3314, ν(C=N) + ν(C–N) 1594, ν(N–O) 1510, 1275, ν(N–N) 1094, ν(C=S) 747 cm^{-1}. UV/Vis (MeOH): λ_{max} = 330 nm. Λ_M = 4.7 μS cm^{-1}.

$[Au_2(HLPPh)_2]Cl_2$·3MeOH (4): 2,2′-Thiodiethanol (35.84 mg, 0.273 mmol) was added to H[AuCl$_4$] (35.84 mg, 0.091 mmol), previously dissolved in water (ca. 1 mL). The transparent solution formed was mixed with the ligand HLPPh (40 mg, 0.091 mmol), dissolved in methanol (30 mL). The orange solution was refluxed for 2 h and then left stirring overnight. Afterwards, the solution was concentrated to a small volume (10 mL) and the orange solid suspended was filtered off, washed with diethyl ether, and finally dried under vacuo. Yield 77 mg (64%). M.p. > 215 °C. $C_{55}H_{47}Au_2Cl_2N_3O_3PS$ (1325.8): calcd. C 45.8, H 3.9, N 5.8, S 4.4; found C 45.8, H 3.8, N 5.7, S 4.6. ESI-MS: *m/z* = 636.1 [*AuL*+H]$^+$; 1075.2 $[Au(HLPPh)_2+H]^+$; 1221.2, $[Au_2(HLPPh)_2+H]^+$. ^{1}H NMR ([D$_6$]dmso): δ = 6.70–8.21 (m, 18 H), 8.79 (s, 1 H), 10.36 (br. s, 1 H), 12.33 (s, 1 H) ppm. ^{31}P NMR ([D$_6$]dmso): δ = 40.7 ppm. IR (KBr): ν(OH) + ν(NH) 3423, 3292, ν(C=N) + ν(C–N) 1592, ν(N–N) 1082, ν(C=S) 761 cm^{-1}. UV/Vis (MeOH): λ_{max} = 320 nm. Λ_M = 90.2 μS cm^{-1}. The crystalline compound $[Au_2(\mu\text{-}S,P\text{-}HLPPh)_2]Cl_2$ (**5**) was obtained by recrystallization of solid **4** in methanol at room temperature.

Crystal Structure Determinations: A colourless needle-shaped crystal of $[Au_2(HLPPh)_2]Cl_2$ was mounted on a glass fibre and used for data collection. Crystal data were collected at 100(2) K, by using a Bruker X8 Kappa APEXII diffractometer with graphite monochromated Mo-K_α radiation (λ = 0.71073 Å). The data were processed with APEX2[21] and corrected for absorption with SADABS (transmissions factors: 1.000–0.657).[22] The structure was solved by direct methods by using the program SHELXS-97 (SHELXS-86)[23] and refined by full-matrix least-squares techniques against F^2 with SHELXL-97 (SHELXL-93).[24] Positional and anisotropic atomic displacement parameters were refined for all heteroatoms. The carbon atoms were refined isotropically. Therefore, the contribution of the density of the disordered solvent molecules was subtracted from the measured structure factors by using the SQUEEZE option.[25] Subsequent refinement then converged with R factors and parameter errors significantly better than for all attempts to model the solvent disorder. Hydrogen atoms were included in geometrically idealized positions employing appropriate models with isotropic displacement parameters constrained to ca. 1.2 U (eq) of their carrier atoms. N–H hydrogen atoms were initially positioned at sites determined from difference maps. Criteria of a satisfactory complete analysis were the ratios of "*rms*" shift to standard deviation less than 0.001 and no significant features in the final difference maps. Atomic scattering factors were taken from "International Tables for Crystallography".[26] Molecular graphics from PLATON[25] and SCHAKAL.[27]

CCDC-695067 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via ww.ccdc.cam.ac.uk/data_request.cif.

Data for $[Au_2(\mu\text{-}S,P\text{-}HLPPh)_2]Cl_2$ (5): ($C_{52}H_{44}Au_2Cl_2N_6P_2S_2$), *Mw* = 1343.83; crystal dimensions: 0.24 × 0.02 × 0.02 mm^3, monoclinic, $P2_1/n$, a = 14.922(1) Å, b = 18.615(2) Å, c = 19.345(2) Å, β = 91.331(4)°, V = 5371.9(9) Å^3, Z = 4, $\rho_{calcd.}$ = 1.662 Mg/m^3, F(000) = 2608. Radiation λ(Mo–K_α) = 0.71073 Å, T = 100(2) K, reflections collected/unique 53810/12279 (R_{int} = 0.0647). R = 0.0214, *wR* = 0.0694, GOF = 0.842, max/min residual density 1.244/–1.530 e Å^{-3}.

Cell Line and Culture Conditions: The cells were seeded into 96-well plates (Becton-Dickinson, Spain) at 4000 cells/well in 100 μL of medium After attachment to the culture surface the cells were incubated for 24 h and then treated with a solution of the complexes in MeOH/water (0.1% v/v). Concentration-response curves were performed between concentrations of 10^{-9} and 10^{-4} M to determine the IC_{50} values. The IC_{50} value corresponds to the compound concentration that inhibited cell proliferation by 50%. After incubation, the cells were fixed and the inhibition of cell growth was measured by a previously described method.[28] For comparison, the cytotoxicity of cisplatin was evaluated under the same experimental conditions. All these in vitro studies were performed at the Screening Unit of the Institute for Industrial Pharmacy, University of Santiago de Compostela.

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