Synthesis, Structural Characteristics and Biological Activities of Complexes of Zn^{II}, Cd^{II}, Hg^{II}, Pd^{II}, and Pt^{II} with 2-Acetylpyridine 4-Methylthiosemicarbazone

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Reaction of 2-acetylpyridine 4-methylthiosemicarbazone (H4ML) with halides of zinc(II), cadmium(II), and mercury(II) afforded complexes of the form $[M(H4ML)X_2]$ [M = Zn^{II} (**1**–**3**), Cd^{II} (**4**–**6**) or Hg^{II} (**7**–**9**); X = Cl, Br, or I]. Reaction of H4ML with K_2PdCl_4 and K_2PtCl_4 gave compounds of the form [M(4ML)Cl] [M = Pd^{II} (**10**) or Pt^{II} (**11**)]. In all the new compounds, which were characterized by elemental analyses, conductance measurements, and electronic, IR and ^{1}H- and ^{13}C-NMR spectroscopy, and by ^{113}Cd-, ^{195}Pt-, or ^{199}Hg-NMR spectroscopy when relevant, the ligand is N,N,S-tridentate, coordinating to the metal centre through its pyridine and azomethine nitrogen atoms and its thiocarbonyl sulfur atom, as was confirmed by X-ray diffraction studies in the cases of **4** · 2 DMSO, **5** · 2 DMSO, **6** · 2 DMSO, **7** · 2 DMSO, **10**, and **11**. In in-vitro assays, only $[Zn(H4ML)Cl_2]$ and $[Zn(H4ML)Br_2]$ showed some sign of antifungal activity against *Aspergillus niger* or *Paecilomyces variotii*.

Introduction

It has been known for some time that thiosemicarbazones have a wide range of actual or potential medical applications as antiviral,[1] antitumoral,[2] antimalarial,[3] antifungal,[4] and antibacterial[5] agents. Their mechanism of action is still controversial in many respects, but it is known that heterocyclic thiosemicarbazones act by inhibiting ribonucleotide reductase, a key enzyme in the biosynthesis of DNA precursors.[6] This effect is probably due to the thiosemicarbazone's binding to the metallic centre of the enzyme as an N,N,S-tridentate ligand, and interest in the coordination chemistry of these compounds has grown accordingly. Most work in this area has concerned coordination to transition metals;[7−13] nontransition metals have received relatively little attention.[14−16] In this article we describe the synthesis, structural characteristics and antifungal activity of complexes of zinc(II), cadmium(II), mercury(II), palladium(II), and platinum(II) with a heterocyclic thiosemicarbazone derived from 2-acetylpyridine 4-methylthiosemicarbazone (H4ML).

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Results and Discussion

The condensation of 2-acetylpyridine with 4-methylthiosemicarbazide affords 2-acetylpyridine 4-methylthiosemicarbazone (H4ML). H4ML is a powerful ligand able to form coordination compounds of the types $[M(H4ML)X_2]$ (M = Zn^{II}, Cd^{II}, or Hg^{II} and X = Cl, Br, or I) and [M(4ML)X] (M = Pd^{II} or Pt^{II}, X = Cl). The ligand and its complexes are stable in air. The complexes are pale yellow or orange solids that are moderately soluble in common organic solvents. Their molar conductance values of 6.27−13.97 ohm^{-1} cm^2 mol^{-1} in DMF solution indicate nonelectrolytic behaviour. Their melting points and analytical data are listed in Table 1.

Molecular Structures

Figure 1 shows that in the solid state H4ML adopts an (*E*) conformation (for the nomenclature of the conformations of thiosemicarbazones derived from 2-formyl- and 2-acetylpyridine, see refs.[17][18]). This places the C(5)−N bond of the pyridine ring *trans* to the azomethine bond. Selected bond lengths and bond angles of H4ML are listed in Table 2. The N−N distance, 1.381(4) Å, is similar to those found in related thiosemicarbazones.[19] In particular, it is shorter than the accepted length of single N−N bonds (1.44 Å) which is compatible with the notion that charge delocalization extends throughout the molecule, affecting the thiosemicarbazone chain as well as the ring. Likewise, as in other thiosemicarbazones,[20] the partial double-bond nature of the C−S bond is shown by a length [1.675(4) Å] between those of single and double bonds (1.82 and 1.56 Å, respectively)[21] and partial double bonding is similarly

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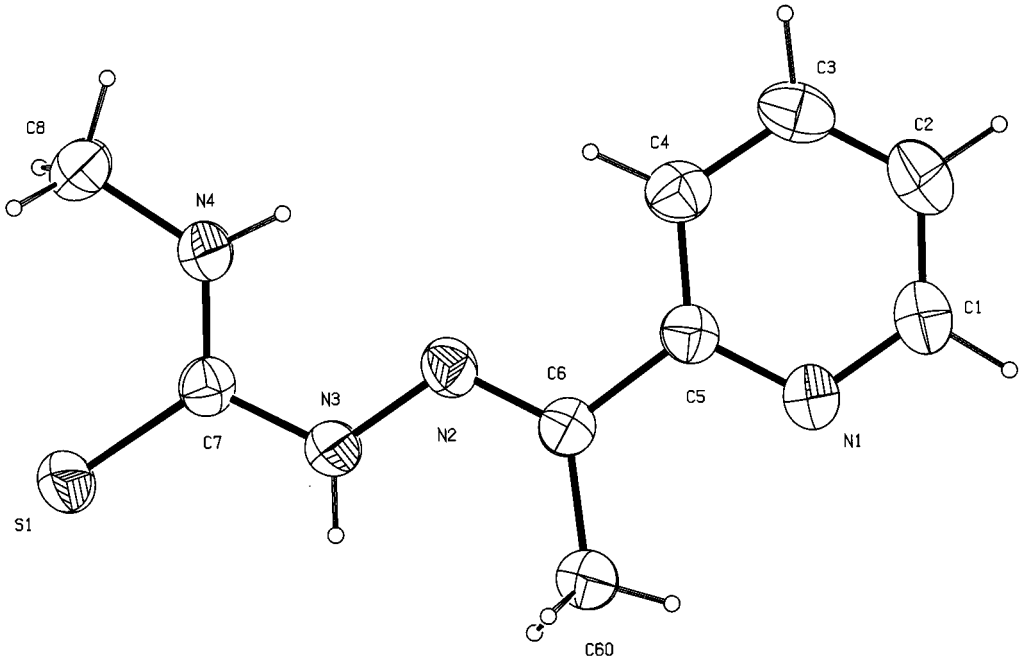

Figure 1. Molecular structure of H4ML and numbering scheme

shown by the lengths of C(7)−N(3), C(7)−N(4) and, in particular, the azomethine bond [length 1.284(4) Å]. There is an intramolecular hydrogen bond between the terminal thioamide hydrogen atom and the azomethine nitrogen atom [N(4)−H(40)−N(2): 1.02(5), 2.17(4), 2.68(3) Å, 105(3)°].

The $[M(H4ML)X_2]$ complexes for which crystals suitable for X-ray diffraction were obtained are **4** · 2 DMSO, **5** · 2 DMSO, **6** · 2 DMSO, and **7** · 2 DMSO; selected bond lengths and bond angles of the ligand in these complexes are listed in Table 2 and those involving the metal atom in Table 3. Figures 2−5 show the molecular structures. The crystals of all these compounds include two molecules of DMSO per molecule of complex, and **5** · 2 DMSO, **6** · 2 DMSO, and **7** · 2 DMSO are mutually isotypic.[22] In all these complexes H4ML is a neutral N,N,S-tridentate ligand, coordinating through its pyridine and azomethine nitrogen atoms and its thiocarbonyl sulfur atom to a metal atom whose coordination number is made up to five by bonds with the two halogen atoms. The values of 0.05−0.11 obtained for τ[23](Table 4) show that, in spite of the large deviations of both α and β from 180°, the coordination

Table 1. Analytical[a] data and some properties of the H4ML complexes

Compound	Complex	Colour	Yield (%)	Analysis (%) C	H	N	M.p. [°C]
1	$[Zn(H4ML)Cl_2]$	yellow	60	31.5 (31.4)	4.3 (3.5)	16.1 (16.3)	> 300
2	$[Zn(H4ML)Br_2]$	yellow	63	25.0 (24.9)	2.7 (2.8)	13.0 (12.9)	280[b]
3	$[Zn(H4ML)I_2]$	yellow	73	20.8 (20.5)	2.3 (2.8)	10.6 (10.6)	287
4	$[Cd(H4ML)Cl_2]$	yellow	67	27.1 (27.6)	2.7 (3.0)	13.8 (14.3)	296
5	$[Cd(H4ML)Br_2]$	yellow	77	22.8 (22.5)	2.5 (2.5)	11.4 (11.7)	291
6	$[Cd(H4ML)I_2]$	yellow	71	18.8 (18.8)	1.9 (2.1)	9.5 (9.8)	270[b]
7	$[Hg(H4ML)Cl_2]$	yellow	80	23.1 (22.5)	2.5 (2.5)	11.7 (11.7)	165
8	$[Hg(H4ML)Br_2]$	yellow	67	18.4) (19.0)	1.3 (2.1)	9.8) (9.9)	> 300
9	$[Hg(H4ML)I_2]$	orange	68	15.9 (16.3)	1.1 (1.8)	8.5 (8.5)	206[b]
10	[Pd(4ML)Cl]	yellow	78	29.6 (30.9)	2.9 (3.4)	15.0 (16.0)	> 300
11	[Pt(4ML)Cl]	orange	74	24.5 (24.6)	2.4 (2.7)	12.1 (12.8)	> 300

[a] Calculated values are given in parentheses. − [b] Temperature of decomposition.

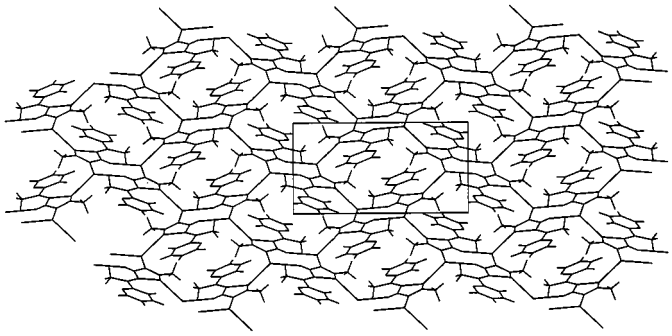

Figure 2. Crystal packing of H4ML viewed perpendicularly to the *a* axis; intermolecular hydrogen bonding parameters: N(3)−H(30)−S(1^{i}), 0.84(3), 2.80(3), 3.594(2) A, 158(3)° ($i = 1 - x$, $1 - y$, $-z$); N(4)−H(40)−S(1^{ii}), 0.84(3), 2.86(3), 3.510(2) A, 136(2)° ($ii = 1 - x$, $1/2 + y$, $1/2 - z$)

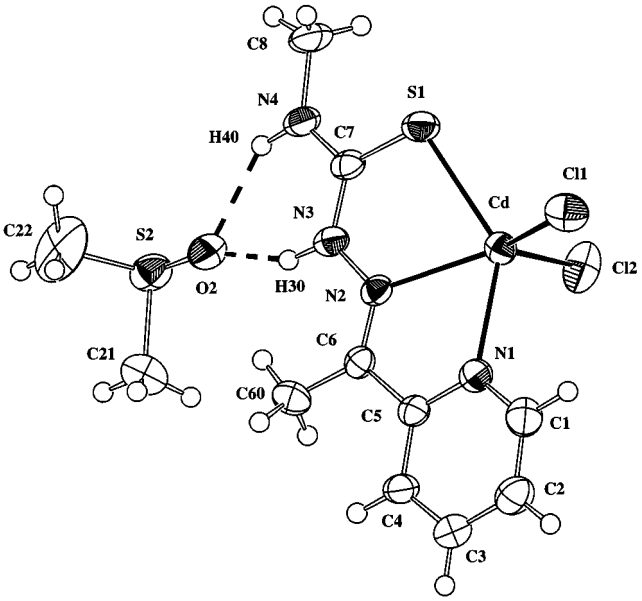

Figure 3. Molecular structure of the cadmium complex **4** · 2 DMSO, showing the hydrogen bonding

polyhedron around the metal atom is in all cases more nearly a tetragonal pyramid with halogen X(2) at its apex than a trigonal bipyramid; distorsion towards a trigonal bipyramid with N(2) and X(1) at its poles increases with the size of the halogen and with the size of the metal. The Cd−S distances (Table 3) are within the usual range for cadmium coordinated to thiocarbonyl[16][24] or thiolato[25] sulfur atoms. The distances between the cadmium atom and the pyridine and azomethine nitrogen atoms are also unexceptional,[16][24] but it may be noted that the Cd−N(azomethine) bond is in all three cases the weaker, whereas the reverse is the case in **10** and **11** (see below) and in $[Cd(HL')Cl_2] \cdot H_2O$ (HL′ = pyridine-2-carbaldehyde thiosemicarbazone).[16] In **7** · 2 DMSO the Hg−S, Hg−N(pyridine), and Hg−Cl distances are all similar to those found in other complexes of mercury(II) halides with ligands coordinating through carbonyl sulfur and pyridine nitrogen atoms,[26][27] but the Hg−N(azomethine) bond, longer than Hg−S, is very weak.

In the isotypic compounds **10** and **11** (Figures 6 and 7), in which the ligand is deprotonated, the metal centre again coordinates to the pyridine and azomethine nitrogen atoms and the thiolato sulfur atom, but has just one halogen ligand. The four donor atoms are almost coplanar, and the metal atom itself lies just 0.01 Å from the least-squares plane through the four, but distorsion of the plane tetragon appears in the S−M−N(1) and N(2)−M−Cl angles [165.7(2)° and 178.4(2)° respectively in **10**, 166.0(5)° and 177.4(5)° in **11**]. Comparison of the M−N(1) and M−N(2) distances [2.051(4) versus 1.950(3) Å in the Pd complex, 2.029(14) versus 1.969(16) Å in the Pt complex] shows that the bond with the azomethine nitrogen atom is the stronger, doubtless due to the greater basicity of this nitrogen atom and, possibly, the *trans* effect. The M−S and M−Cl distances are similar to those found in other complexes in which Pd and Pt coordinate to S[13][28] or Cl.[29] The delocalization of the charge originated by deprotonation at N(3) is apparent upon comparison of the thiosemicarbazone bond lengths in the complexes and the free ligand (Table 2): In the complexes N(3)−C(7) is shorter and C(7)−S is longer than in free H4ML, showing that, as in similar complexes,[18] bond order is increased in the former

Table 2. Selected bond lengths [Å] and angles [°] of H4ML and the complexes[a]

	H4ML	**4** · 2 DMSO	**5** · 2 DMSO	**6** · 2 DMSO	**7** · 2 DMSO	**10**	**11**
C(6)−N(2)	1.286(3)	1.295(6)	1.25(1)	1.28(2)	1.27(1)	1.297(4)	1.273(13)
N(2)−N(3)	1.372(3)	1.357(5)	1.346(9)	1.38(2)	1.37(1)	1.373(3)	1.365(13)
N(3)−C(7)	1.366(3)	1.370(6)	1.38(1)	1.36(1)	1.34(1)	1.320(4)	1.328(15)
C(7)−S(1)	1.680(2)	1.695(5)	1.69(1)	1.696(8)	1.691(9)	1.755(3)	1.755(13)
C(7)−N4)	1.326(3)	1.320(6)	1.36(1)	1.33(1)	1.35(1)	1.336(4)	1.306(14)
N(1)−C(5)−C(4)	122.2(2)	122.0(4)	121(2)	122.6(8)	122.9(9)	120.5(3)	120.0(12)
C(4)−C(5)−C(6)	122.5(2)	121.2(4)	123.0(9)	120.4(7)	122.1(8)	123.9(3)	124.5(12)
N(1)−C(5)−C(6)	115.3(2)	116.9(4)	115.5(9)	117.1(7)	116.7(9)	115.5(3)	115.4(12)
C(5)−C(6)−N(2)	115.8(2)	115.1(4)	116.1(9)	114.0(6)	113.0(8)	114.2(3)	114.6(12)
C(6)−N(2)−N(3)	118.3(2)	120.0(4)	119.4(8)	119.8(6)	120.3(7)	118.9(3)	120.2(11)
N(2)−N(3)−C(7)	119.0(2)	119.2(4)	116.9(7)	118.9(6)	118.2(7)	112.0(3)	113.7(10)
N(3)−C(7)−S(1)	119.8(2)	123.3(4)	125.8(9)	124.0(7)	126.5(8)	125.5(2)	124.1(10)
N(3)−C(7)−N(4)	116.3(2)	114.9(5)	113.9(8)	113.5(7)	114.2(8)	117.6(3)	118.6(12)
S(1)−C(7)−N(4)	124.0(2)	121.7(3)	120.2(8)	122.5(7)	119.2(7)	116.9(3)	117.2(10)

[a] Estimated standard deviations in units of the least significant figures given in each case are quoted in parentheses.

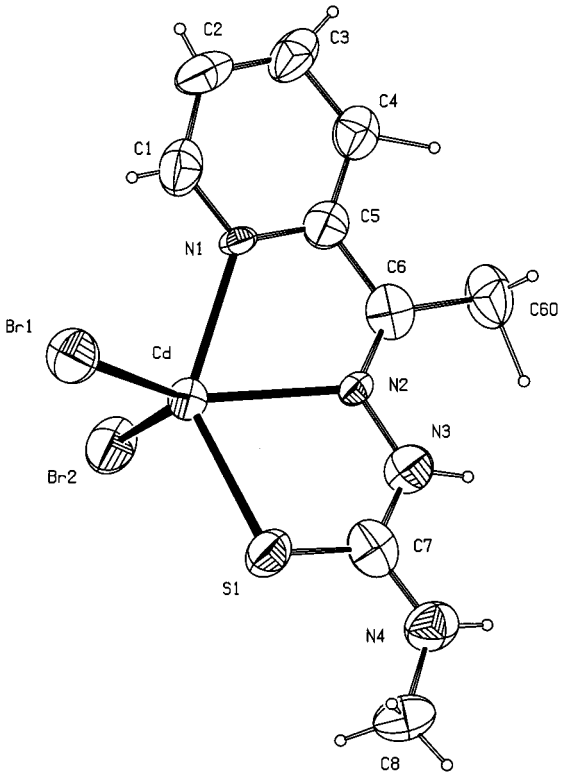

Figure 4. Molecular structure of the cadmium complex **5**

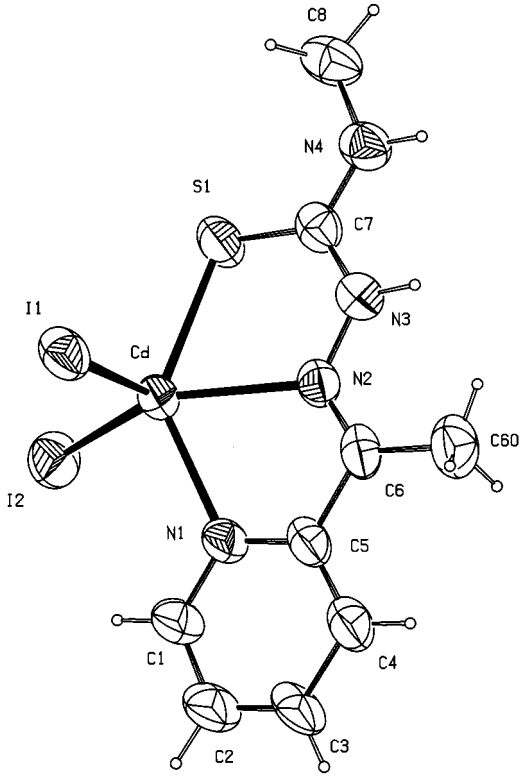

Figure 5. Molecular structure of the cadmium complex **6**

case and decreased in the latter. The stability of the complex is no doubt increased by the rigidity of the planar tricyclic system formed by the pyridine ring and the two five-membered chelation rings.

Electronic Spectra

The electronic spectra of the palladium(II) and platinum(II) complexes were recorded in DMF/MeCN solutions. The positions of the absorption bands were not significantly different from those observed in the solid-state diffuse-reflectance spectra indicating that these complexes underwent no electronic or geometric changes upon dissolution.

The absorption bands of the Pd^{II} complex, with maxima at $\tilde{\nu}$ = 21,692, 24,096, and 27,100 cm^{-1}, may be assigned to spin-allowed *d-d* transitions corresponding to the one-electron transitions $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow {}^1E_g$. Similarly, the Pt^{II} complex displayed an absorption spectrum with maxima at $\tilde{\nu}$ = 22,124, 25,126−25,707, and 26,882 cm^{-1} attributed to these same transitions. These wavenumbers are comparable to those observed previously

Table 3. Coordinating bond lengths [Å] and angles [°] of the complexes[a]

	4 · 2 DMSO	**5** · 2 DMSO	**6** · 2 DMSO	**7** · 2 DMSO	**10**	**11**
M−X(1)	2.450(1)	2.574(1)	2.761(1)	2.460(3)	2.310(1)	2.304(3)
M−X(2)	2.432(2)	2.575(1)	2.758(1)	2.476(5)	−	−
M−S(1)	2.596(1)	2.581(4)	2.588(3)	2.561(4)	2.256(1)	2.256(3)
M−N(1)	2.345(4)	2.348(9)	2.351(7)	2.423(8)	2.056(3)	2.023(9)
M−N(2)	2.405(4)	2.408(8)	2.414(6)	2.532(7)	1.955(2)	1.961(10)
N(1)−M−X(1)	96.7(2)	95.4(2)	97.6(9)	93.3(2)	98.05(8)	97.2(3)
N(1)−M−X(2)	102.2(2)	101.8(2)	100.3(8)	96.0(3)	−	−
N(1)−M−N(2)	67.8(1)	67.3(4)	66.8(2)	63.2(3)	80.57(11)	80.6(4)
N(2)−M−X(1)	139.8(1)	139.9(2)	139.9(2)	138.7(2)	178.34(8)	177.7(3)
N(2)−M−X(2)	103.8(1)	102.0(2)	101.5(6)	100.1(2)	−	−
X(1)−M−X(2)	115.69(5)	117.30(5)	117.94(2)	116.6(1)	−	−
S(1)−M−X(1)	101.92(5)	102.01(8)	100.38(6)	108.9(1)	96.23(4)	96.85(12)
S(1)−M−X(2)	106.01(5)	105.82(7)	106.44(5)	109.6(1)	−	−
S(1)−M−N(1)	136.7(1)	135.3(3)	135.2(4)	132.4(2)	165.72(8)	165.9(3)
S(1)−M−N(2)	72.8(1)	73.0(2)	72.9(5)	72.9(2)	85.16(8)	85.4(3)

[a] Estimated standard deviations in units of the least significant figures given in each case are quoted in parentheses.

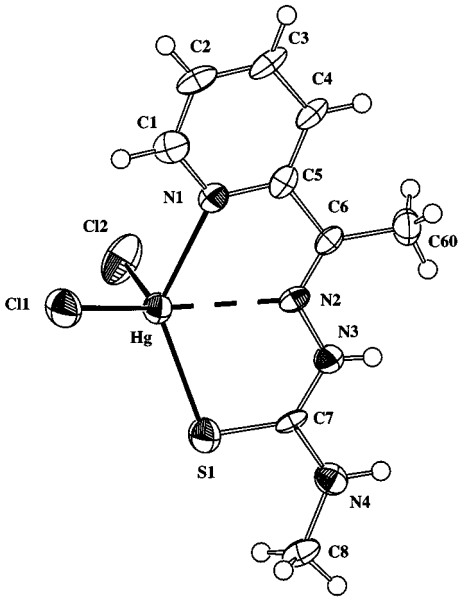

Figure 6. Molecular structure of the mercury complex **7** [the weaker Hg−N(azomethine) interaction is shown by the dashed line]

Table 4. Deviation from tetragonal-pyramidal coordination in the compounds **4**− **7**

Compound	β(N−M−X)	α(S−M−N)	β − α	τ = (β − α)/60
4 · 2 DMSO	139.8	136.7	3.1	0.05
5 · 2 DMSO	139.9	135.3	4.6	0.08
6 · 2 DMSO	140.1	135.2	4.9	0.08
7 · 2 DMSO	138.7	132.4	6.3	0.11
bpt[a]	120.0	180.0	60.0	1.00
t-p[b]	180.0	180.0	0.0	0.00

[a] Trigonal bipyramid. − [b] Tetragonal pyramid.

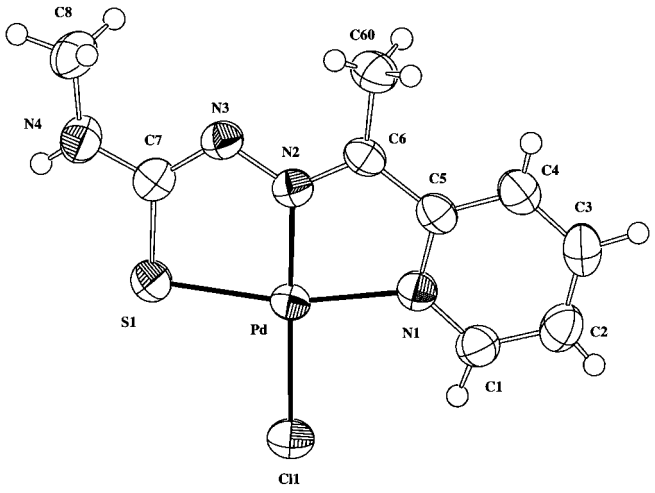

Figure 7. Molecular structure of the palladium complex **10**

for square-planar palladium and platinum complexes involving similar donor atoms. In the UV region, the strong absorptions above 28,000 cm^{-1} may be charge-transfer bands[30] or intraligand bands.

Infrared Spectra

The chief IR bands of free H4ML[31] and the complexes are listed and assigned in the Supporting Information. Most of the ligand bands shift to higher frequencies upon complexation. In particular, the shifts in ν(C=N) and ν(N−N) are evidence of coordination through the azomethine nitrogen atom[32][33], while coordination through the pyridine nitrogen atom is shown by the shift to higher frequencies of the ν(CN) + ν(CC) (1539 cm^{-1}), α(CCC) (626 cm^{-1}), and φ(CC) (403 cm^{-1}) ring vibrations.[34] The shifts to lower frequencies of ν(CS) at 833 cm^{-1} in the free ligand[31] and, in the Zn, Cd, and Hg complexes, ν(NH), are the result of coordination through the thiocarbonyl sulfur atom[35] and the nitrogen atom bound to N(3).[36] The spectra of the Pd and Pt complexes, in which the ligand is deprotonated, show only one strong band instead of two in the ν(NH) region. Deprotonation results in the frequency of this remaining band increasing (rather than decreasing, as it does in the Zn, Cd, and Hg complexes), and enhances the shifts of other bands affected by complexation. In particular, the shift of about 160 cm^{-1} in ν(CS), as against about 120 cm^{-1} in the Zn, Cd, and Hg compounds, shows the ligand to be closer to a thiolato form in the Pd and Pt compounds than in the others.

In the 500−100 cm^{-1} region, the one or two strong bands whose frequencies increase in the order I complex < Br complex < Cl complex for a given metal and in the order Hg complex < Cd complex < Zn complex for a given halogen (Table 5) are attributed to metal-halogen stretching vibrations, in keeping with which the resulting values of ν(M−Br)/ν(M−Cl) (av. 0.70) and ν(M−I)/ν(M−Cl) (av. 0.63) (see Supporting Information) are similar to previously reported values.[26,27,37] The less intense band observed in the range 300−280 cm^{-1} in the Zn, Cd, and Hg compounds and around 360 cm^{-1} in the Pd and Pt compounds is attributable to ν(M−S), and those appearing in the ranges 350−330 and 330−310 cm^{-1} or at 500 and 490 cm^{-1} to ν(M−N) vibrations.[38] In the Pd and Pt compounds this latter pair are very close together; in the others it is probably the higher frequency band that corresponds to the pyridine nitrogen atom, the M−N(1) distances being slightly shorter than the M−N(2) distances in the crystals of **7** · 2 DMSO and all the Cd complexes.

^{1}H-NMR Spectra

The ^{1}H-NMR signals of H4ML and the complexes are listed in the Supporting Information. The nonappearance of the N(3)H signal (at δ = 10.34 in the free ligand), in the spectra of **10** and **11** shows that in these complexes the ligand remains deprotonated in DMSO solution. The deshielding of N(4)H in these compounds is probably due to withdrawal of charge from N(4) as the result of an increase in charge delocalization upon complexation through the thiocarbonyl sulfur atom; the shielding of the N(4) methyl protons is attributable to the same mechanism. The H(1) signal shifts upfield in the Pd complex because coordination

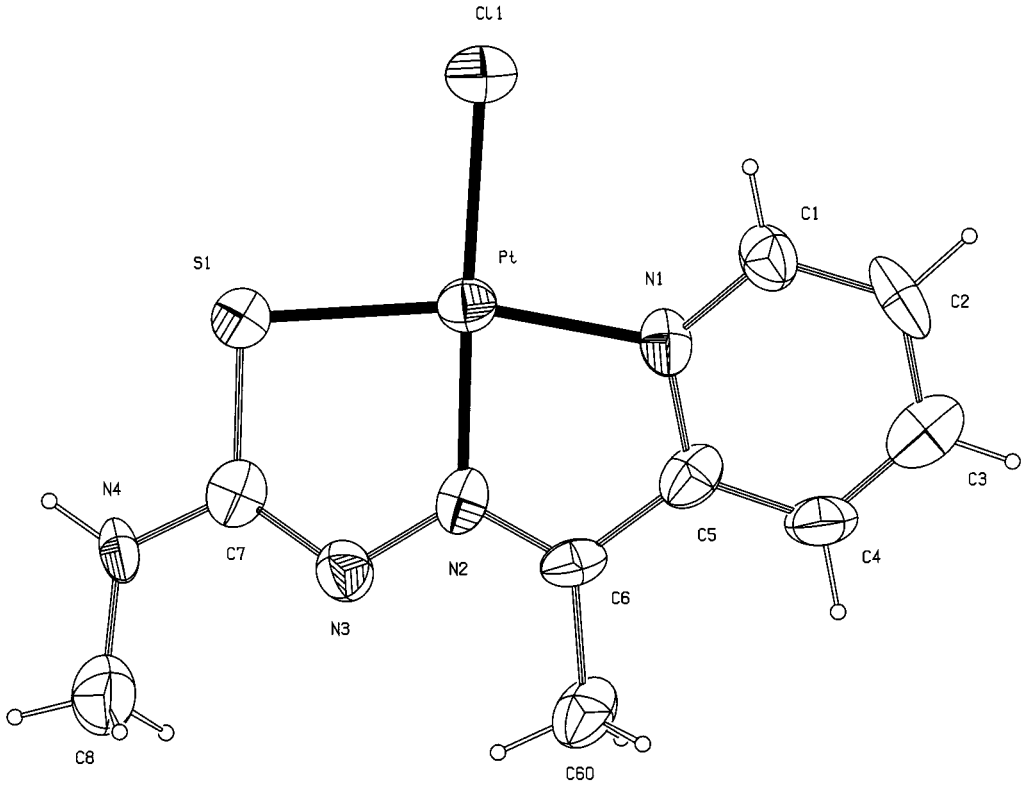

Figure 8. Molecular structure of the platinum complex **11**

through the pyridine nitrogen atom prevents H(1) from being deshielded, as it is in the free ligand, as the result of the anisotropy of the C(6)=N(2) bond and the proximity of the nitrogen atom with sp^2 hybridization.[39] In the Pt complex, on the other hand, the H(1) signal shifts downfield (as in the complex of Pt^{II} with 1-phenyl-2-formylpyridine thiosemicarbazone[40]), possibly due to the replacement of the chloride ion *trans* to the azomethine nitrogen atom by a DMSO molecule. In the $[M(H4ML)X_2]$ complexes the persistence of the N(3)H signal shows that this proton is retained in DMSO solution. The downfield shifts of the N(3)H and N(4)H signals, which increase in the order Cd < Zn < Hg, are attributable to coordination through the azomethine nitrogen atom and thiocarbonyl sulfur atom, respectively, and/or to the formation of hydrogen bonds between N(3)H [and to a much lesser extent N(4)H] and DMSO.

^{13}C-NMR Spectra

The ^{13}C-NMR signals of H4ML and all the complexes except **4**, for which we were unable to obtain a spectrum of adequate quality, are listed in the Supporting Information. The deshielding of C(7) and C(8) in the [M(4ML)Cl] complexes is attributable to a combination of the inductive effect of the metal and the move towards the thiol form induced by complexation. The simultaneous shift of the C(6) signal to higher field and that of C(60) to lower field is in consonance with coordination through the azomethine nitrogen atom in these compounds, whereas coordination through the pyridine nitrogen atom is pointed to by the behaviour of the pyridine carbon signals [shielding of the *ortho*-carbon atoms C(1) and C(5), deshielding of the others], which is qualitatively similar to their behaviour in the pyridinium ion[41] and in the protonated form of other thiosemicarbazones derived from 2-acetylpyridine.[40] In the $[M(H4ML)X_2]$ complexes C(8) (δ = 31.27) is deshielded (except in **1** and **2**) but C(7) (δ = 179.24) is shielded (although **1** is again an exception); the greatest shielding is shown in the complexes of the "*soft*" metal Hg. The other carbon signals exhibit more or less the same pattern in $[M(H4ML)X_2]$ as in [M(4ML)Cl], although the pyridine carbon shifts are generally less marked.

^{113}Cd-, ^{195}Pt and ^{199}Hg-NMR Spectra

The ^{113}Cd-NMR spectra of the Cd compounds show a single signal at δ = 363.7, 345.7, or 279.8 for the Cl, Br, and I derivatives, respectively. The nuclide is thus less shielded than in the corresponding halide CdX_2 in DMSO,[42] especially in the case of the Cl derivative. The progressive increase in shielding upon replacement of Cl by Br and of Br by I is in keeping with the decreasing electronegativity of the halogen, and the observed chemical shifts are within what may be expected for pentacoordinate halide complexes.[43]

Of the mercury compounds, only **7** was sufficiently soluble for ^{199}Hg-NMR spectroscopy. The spectrum obtained exhibits a single signal at δ = −1092.4, which is compatible with pentacoordination to the extent that it shows the nu-

Table 5. Diameters [mm] of growth inhibition zones in in-vitro antifungal activity assays (6.0 indicates no inhibition)

Concentration [μg mL^{-1}]	200	400	600	1000	1600
Aspergillus niger					
H4ML	6.0	9.8	12.2	16.2	17.5
1	6.0	6.0	15.5	–	–
NYSTATIN	9.0	10.7	12.8	17.3	19.2
Paecilomyces variotii					
H4ML	6.0	8.3	10.0	14.4	17.7
1	6.0	6.0	6.0	10.6	–
2	6.0	6.0	6.0	10.2	–
NYSTATIN	12.8	14.5	16.5	25.2	26.0

clide to be more shielded than is usual in tetrahedral complexes of the form HgL_2Cl_2.[44]

The Pt^{II} complex give rise to single, relatively sharp ^{195}Pt resonance at $\delta = -3092$. This supports the idea that the coordination mode of of the platinum(II) complex in solution is similar to that observed in the solid state; there is probably no exchange of the Cl^- ion for another donor.[40]

Biological Results

H4ML and the complexes were assayed in vitro for antifungal activity against the pathogens *Aspergillus niger* and *Paecilomyces variotii* (for previous data for H4ML see ref.[45]). Table 5 lists the results obtained with the compounds that at some concentration inhibited fungal growth, together with those obtained with the currently prescribed drug nystatin. Only the zinc complexes displayed some activity: At a concentration of 600 μg·mL^{-1} **1** inhibited *A. niger* rather more than either H4ML or nystatin, and at a concentration of 1000 μg·mL^{-1} both **1** and **2** inhibited *P. variotii*, though considerably less than nystatin did.

Experimental Section

General: All commercial reagents were Aldrich, Merck, or Ventron reagent-grade products. – Elemental analysis was performed with a Carlo Erba 1108 analyser. – Melting points were determined with a Büchi apparatus. – Infrared spectra were recorded with a Mattson Instruments Cygnus 100 FTIR spectrometer using KBr discs for spectra run from 4000 to 400 cm^{-1} and polyethylene-sandwiched Nujol mulls for the range 500–100 cm^{-1}. – UV/Vis spectra and reflectance spectra were recorded with a Shimadzu UV-3101PC spectrophotometer. – ^{1}H- and ^{13}C-NMR spectra were run with a Bruker WM-300 using DMSO as internal reference; chemical shifts are referred to TMS. ^{113}Cd-, ^{195}Pt-, and ^{199}Hg-NMR spectra were run with a Bruker WM-250 using DMSO solutions of about 10^{-2} M, and are referred to 0.1 M $Cd(ClO_4)_2$, H_2PtCl_6, and $HgMe_2$, respectively.

2-Acetylpyridine 4-Methylthiosemicarbazone (H4ML): H4ML was synthesized using the general procedure by Klayman et al.[3][46] for condensation of amines with aldehydes or ketones. To an aqueous solution of 4-methylthiosemicarbazide heated to 60 °C was slowly added a solution of an equimolecular amount of 2-acetylpyridine in ethanol. The reaction mixture was refluxed for 2 h, and upon cooling afforded a whitish crystalline solid which was filtered off and recrystallized from warm ethanol. After storage at low temperature, the remaining recrystallization solution afforded crystals suitable for study by X-ray diffraction. Yield 98%, m.p. 176 °C. – $C_9H_{12}N_4S$ (208): calcd. C 51.8, , H 5.8, N 27.0; found C 51.8, H 6.2, N 26.7.

Preparation of the Complexes: Complexes of the form $[M(H4ML)X_2]$ (M = Zn^{II}, Cd^{II}, Hg^{II}; X = Cl, Br, I) (**1**–**9**) were obtained by treating H4ML with the corresponding metal salts in a 1:1 molar ratio in ethanol. After prolonged stirring (about 1 week) at room temperature, the reaction mixture afforded solids (generally microcrystalline) that were filtered off, washed with ethanol, and vacuum-dried. In the cases of the cadmium complexes and $[Hg(H4ML)Cl_2]$ it was possible to obtain single crystals by redissolving the solids in DMSO and slowly evaporating the sol-

Table 6. Crystal and structure refinement data for H4ML and the complexes **4**–**7**, **10**, and **11**

Compound	H4ML	**4** · 2 DMSO	**5** · 2 DMSO	**6** · 2 DMSO	**7** · 2 DMSO	**10**	**11**
Empirical formula	$C_9H_{12}N_4S$	$C_{13}H_{24}CdCl_2N_4O_2S_3$	$C_{13}H_{24}Br_2CdN_4O_2S_3$	$C_{13}H_{24}CdI_2N_4O_2S_3$	$C_{13}H_{24}Cl_2HgN_4O_2S_3$	$C_9H_{11}ClN_4PdS$	$C_9H_{11}ClN_4PtS$
Formula weight	208.29	547.88	636.78	730.78	636.06	349.13	437.82
Crystal size [mm]	0.30×0.25×0.15	0.75×0.10×0.10	0.50×0.40×0.30	0.50×0.40×0.30	0.30×0.15×0.10	0.35×0.10×0.05	0.30×0.20×0.15
Crystal shape	prism	prism	prism	prism	prism	plate	prism
Crystal system	monoclinic	monoclinic	triclinic	triclinic	triclinic	monoclinic	monoclinic
Space group	$P2_1/c$ (No 14)	$P2_1/c$ (No 14)	$P-1$ (No. 2)	$P-1$ (No 2)	$P-1$ (No 2)	$P2_1/n$ (No 14)	$P2_1/n$ (No 14)
a [Å]	8.813(2)	9.535(1)	8.939(4)	9.428(3)	8.605(1)	7.764(2)	7.695(3)
b [Å]	7.720(1)	10.217(1)	10.156(5)	10.484(5)	10.109(1)	16.660(2)	16.778(3)
c [Å]	15.580(3)	22.893(2)	13.597(5)	13.699(4)	13.375(1)	9.302(3)	9.340(4)
α [°]	90	90	96.21(3)	93.72(2)	97.07(1)	90	90
β [°]	106.11(1)	90.23(2)	107.74(2)	109.51(3)	104.16(1)	93.87(2)	94.17(1)
γ [°]	90	90	102.18(3)	104.70(3)	100.61(1)	90	90
V [Å^3]	1018.4(3)	2230.1(4)	1129.3(9)	1217.8(9)	1091.5(2)	1200.5(5)	1202.7(7)
Z	4	4	2	2	2	4	4
$D_{calcd.}$ [Mg/m^3]	1.358	1.632	1.872	1.994	1.935	1.932	2.418
F(000)	440	1104	624	696	616	688	816
θ range	3.09–28.93	3.00–33.00	2.00–27.00	3.00–31.00	3.00–33.00	3.29–28.92	3.27–28.89
Temperature [K]	293(2)	223(2)	213(2)	223	223(2)	293(2)	293(2)
h_{min}/h_{max}	0/11	−14/14	−1/11	−13/13	0/13	0/10	0/10
k_{min}/k_{max}	0/10	0/15	−12/12	−2/15	−15/15	0/22	0/22
l_{min}/l_{max}	−21/21	0/35	−17/17	−19/19	−20/20	−12/12	−12/12
μ [mm^{-1}]	0.283	1.51	2..40	1.85	7.85	1.919	12.040
Max./min. transmissions	0.9587/0.9198	1.003/0.553	1.206/0.717	1.319/0.698	1.197/0.744	0.830/0.474	0.804/0.418
Refl. collected/unique	2838/2676 [R_{int} = 0.038]	9763/7973 [R_{int} = 0.024]	5885/3959 [R_{int} = 0.026]	9540/5784 [R_{int} = 0.017]	4453/3531 [R_{int} = 0.032]	3369/3157 [R_{int} = 0.019]	3372/3157 [R_{int} = 0.070]
Data/parameters	2676/175	4702/238	2503/230	4946/227	3234/227	3157/189	3157/147
Final R	0.051	0.044	0.048	0.048	0.041	0.031	0.057
Final $wR2$	0.108	0.047	0.053	0.052	0.050	0.057	0.081
GOOF	1.013	1.042	0.987	1.012	2.493	1.027	0.986
Max. Δρ [eÅ^{-3}]	0.244	0.927	1.05	1.842	2.402	0.384	1.210

vent. − For [Pd(4ML)Cl] and [Pt(4ML)Cl] (**10** and **11**) the metal salts were dissolved in water and the reaction mixture was refluxed for 1 h. Evaporation of the solvent from the filtered reaction mixture at room temperature gave monocrystals suitable for study by X-ray diffraction.

X-ray Crystallography: Crystals of H4ML, **4**−**7**, **10**, and **11** suitable for X-ray diffraction were mounted on glass fibres and transferred to an Enraf Nonius CAD4 diffractometer. Accurate unit-cell parameters and an orientation matrix were determined by least-squares refinement of the setting angles of a set of well-centred reflections (SET4)[47] in the θ range 6.1−11.7 (H4ML), 9.0−13.0 (**4**), 4.6−12.0 (**5**), 5.7−13.2 (**6**), 7.3−14.9 (**7**), 6.1−13.3 (**10**), and 4.9−13.0° (**11**). Reduced cell calculations did not indicate higher lattice symmetry.[48] Crystal data and details of the data collection and refinement are given in Table 6. Data were corrected for Lp effects and for observed linear decay of the reference reflections. An empirical absorption correction (DIFABS)[49] was applied for all compounds. The structures were solved by automated Patterson or direct methods and subsequent difference Fourier techniques (SHELX86)[50] and refined on F (SDP/VAX)[51] or F^2 (SHELXL97).[52] Hydrogen atoms were included in the refinement in calculated positions riding on their carrier atoms. In two structures, a DMSO molecule proved to be disordered and a disorder model consisting of two (**4**) or three (**5**) alternative sites was included in the refinement; the occupation factors for **4** were 0.75 [S(31)] and 0.25 [S(32)] and for **5** were 0.40, [S(31)], 0.40, [S(32)], and 0.20 [S(33)]. Neutral atom scattering factors and anomalous dispersion corrections were taken from the International Tables for X-ray Crystallography.[53] Geometrical calculations and illustrations were performed or generated with the SHELXL97,[52] ZORTEP,[54] and PLATON98[55] packages. Crystallographic data for the structures reported in this paper (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-106651 and -106653 to -106658. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk).

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