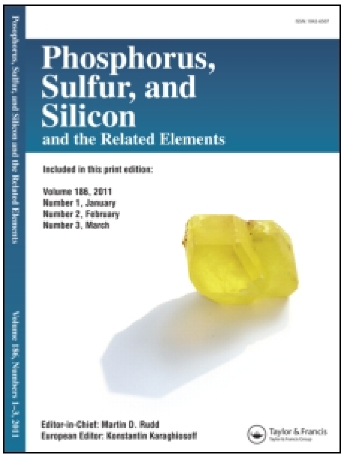

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Fahmi, Nighat , Gupta, I. J. and Singh, R. V.(1998) 'SULFUR BONDED PALLADIUM(II) AND PLATINUM(II) COMPLEXES OF BIOLOGICALLY POTENT THIOAMIDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 132: 1, 1 — 8

To link to this Article: DOI: 10.1080/10426509808036968

URL: http://dx.doi.org/10.1080/10426509808036968

Phosphorus Sulphur and Silicon, Vol. 132 pp. 1–8
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SULFUR BONDED PALLADIUM(II) AND PLATINUM(II) COMPLEXES OF BIOLOGICALLY POTENT THIOAMIDES

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(Received 24 July 1997; Revised 14 December 1997 In final form 14 December 1997)

Sulfur bonded square planar complexes of the type, $[M(NSH)_2]Cl_2$ and $[M(NS)_2]$, where, M=Pd^{II} and Pt^{II} and NSH = 2-[1-furanyl)-ethyledene]hydrazinecarbothioamide, 2-[1-(2-thienyl)-ethyledene]hydrazinecarbothioamide, 2[1-(2-naphthenyl)ethyledene]-hydrazinecarbothioamide with sulfur donor ligands have been synthesised and characterised. Chemical analysis, IR, UV-visible, ^1H NMR, magnetic measurements, conductance measurements and molecular weight determinations have been utilised for establishing the geometries of the free ligands and their metal complexes. The spectral data are consistent with a square planar geometry around Pd^{II} and Pt^{II} in which the ligand acts as a neutral bidentate and monoanionic bidentate ligand coordinating through nitrogen and sulfur atoms. To discuss bioinorganic aspects of the complexes, representative free ligands and their metal complexes were tested **in vitro** against a number of microorganisms and **in vivo** on male albino rats. Findings are positive.

INTRODUCTION

Thiosemicarbazones constitute an interesting class of N/S donor ligands which possess enormous pharmacological activities which in several cases are known to have been enhanced by the presence of transition metals. [1-3] Transition metal complexes of these ligands are gaining enormous importance on account of their inherent biological potential. They are known to function as antimicrobial, [4] antifertility, [5] antimalarial [6] and antileukemic agents. [7] In an efforts to gain more insight into the coordination pattern, stereochemistry and biological

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properties present in this class of compounds, palladium(II) and platinum(II) complexes of hydrazinecarbothioamides derived from heterocyclic and cyclic ketones have been synthesised and studied. The fungicidal and bactericidal activities of the ligands along with their metal complexes have also been undertaken using conventional fungicide, **Bavistin** and **Streptomycin** as the standards for the respective activities. Sterlizing ability of a representative ligand along with its substitution product has also been tested on male albino rats.

EXPERIMENTAL

Preparation of Ligands

2-[1-(2-Furanyl)ethyledene]hydrazinecarbothioamide, yellow, m.p. 165°C, (L_1H), 2-[1-(2-thienyl)ethyledene]hydrazinecarbothioamide, light yellow, m.p. 155°C (L_2H), 2-[1-(2-pyridinyl)-ethyledene]hydrazinecarbothioamide, yellow, m.p. 142°C (L_3H) and 2-[1-(2-naphthenyl)ethyledene]hydrazinecarbothioamide, white, m.p. 144°C (L_4H), were prepared by the condensation of [1-(2-furanyl)ethanone], [1-(2-thienyl)ethanone], [1-(2-pyridinyl)ethanone] and [1-(2-napthenyl)ethanone], respectively, with thiosemicarbazide in 1:1 molar ratio in the medium of ethanol. These were recrystallised from the same solvent and dried in vacuo.

Synthesis of $[Pd(NSH)_2]Cl_2$ Complexes

The solution of $PdCl_2$ in ethanol was mixed with the ethanolic solution of ligand in 1:2 molar ratio. Few drops of HCl were added and the reaction mixture was stirred for 24h at room temperature. The precipitate obtained was filtered, washed with ethanol and dried in vacuo.

Synthesis of $[Pt(NSH)_2]Cl_2$ Complexes

$K_2[PtCl_4]$ was dissolved in a 1:1 mixture of water and ethanol. To this solution an ethanolic solution of ligand in (1:2) molar ratio was added and it was then refluxed for about an hour in the presence of few drops of concentrated HCl. On cooling, the complexes separated out which were filtered and washed several times with a mixture of water and ethanol and dried in vacuo.

Synthesis of $[Pd(NS)_2]$ Complexes

The reactions of $PdCl_2$ with thioligands were carried out in alcohol in bimolar ratios (Metal:Ligand). Aqueous NH_4OH was added to the reaction mixture dropwise *until* the solution was weakly alkaline and was refluxed for 1h. The solid derivative so obtained was filtered off, washed with ethanol and dried in vacuo.

Synthesis of [Pt(NS)$_2$] Complexes

The 1:1 water ethanol solution of $K_2[PtCl_4]$ was mixed with an ethanolic solution of ligands in 1:2 molar ratio. The above mixture was boiled under reflux for about two hours after adding aqueous ammonia dropwise till the solution was weakly alkaline. The solid compound so obtained was filtered out and washed with a mixture of water and ethanol and finally dried in vacuo. The physical properties and analyses of palladium and platinum complexes are recorded in Table I.

ANALYTICAL METHODS AND PHYSICAL MEASUREMENTS

The analytical methods and procedures of physical measurements are the same as reported elsewhere. [8] Palladium and platinum were estimated gravimetrically. [9] The antifungal activity was evaluated against **Fusarium oxysporum, Alternaria alternata** and **Sclerotium rolfsi** using standard food poisoning technique and a procedure recommended for testing new chemicals. [10] The growth inhibition was calculated after angular transforming the data and the efficacy was statistically analysed using completely randomised design and compared using critical difference (CD 5% or $P = 0.05$). [10] Antibacterial activity was tested against **Escherichia coli, Staphylococcus aureus** and **Xanthomonas compestris**. The method for screening antimicrobial activity was reported earlier. [11] The antifertility activity of one representative ligand (L_2H) and its palladium complex $[Pd(L_2)_2]$ was studied.

RESULTS AND DISCUSSION

The metals interact with the thioligands having NS donor set in 1:2 molar ratio in presence of few drops of concentrated HCl to form products of the type $[M(NSH)_2]Cl_2$. (M = Pd or Pt). However, complexes of the type $[M(NS)_2]$ are obtained when the reaction was carried out in presence of aqueous ammonium hydroxide. The refluxing medium used for preparing palladium complexes was ethanol while 1:1 water ethanol solution was used in case of platinum complexes.

TABLE I Physical properties and analytical data of Pd(II) and Pt(II) complexes

S.No.	Compound	Colour and state	M.P. (°C)	% Analysis (Found/Calcd.)		Mol.wt. Found (Calcd.)	
				Pd/ Pt	N	S	
1.	$[Pd(L_1H)_2]Cl_2$	Yellow solid	220d	19.66 (19.56)	15.54 (15.44)	11.70 (11.79)	521 (544)
2.	$[Pd(L_1)_2]$	Orangish brown solid	80	22.12 (22.59)	17.25 (17.84)	13.32 (13.61)	450 (471)
3.	$[Pd(L_2H)_2]Cl_2$	Yellow solid	245d	18.38 (18.47)	14.50 (14.58)	22.35 (22.86)	551 (571)
4.	$[Pd(L_2)_2]$	Dark brown solid	180d	21.19 (21.15)	16.52 (16.70)	25.31 (25.49)	485 (503)
5.	$[Pd(L_3H)_2]Cl_2$	Yellow solid	250d	18.72 (18.80)	19.52 (19.79)	11.30 (11.33)	534 (566)
6.	$[Pd(L_3)_2]$	Deep orange	210d	21.35 (21.58)	22.61 (22.72)	12.85 (13.00)	465 (493)
7.	$[Pd(L_4H)_2]Cl_2$	Orangish yellow solid	220d	15.82 (16.02)	12.41 (12.65)	9.47 (9.65)	640 (664)
8.	$[Pd(L_4)_2]$	Dim green solid	150d	17.95 (18.00)	14.25 (14.21)	10.71 (10.84)	580 (591)
9.	$[Pt(L_1H)_2]Cl_2$	Light brown solid	300d	30.24 (30.84)	13.12 (13.28)	10.01 (10.14)	602 (632)
10.	$[Pt(L_1)_2]$	Yellowish brown solid	180	34.11 (34.86)	14.45 (15.01)	11.57 (11.46)	520 (559)
11.	$[Pt(L_2H)_2]Cl_2$	Cream solid	>300	28.53 (29.35)	12.30 (12.63)	18.72 (19.29)	627 (664)
12.	$[Pt(L_2)_2]$	Light brown solid	241d	32.01 (32.97)	14.27 (14.19)	22.18 (21.67)	570 (591)
13.	$[Pt(L_3H)_2]Cl_2$	Reddish brown solid	200d	28.22 (29.80)	16.87 (17.11)	9.83 (9.79)	618 (654)
14.	$[Pt(L_3)_2]$	Chocholate solid	220d	32.89 (33.54)	18.78 (19.25)	11.13 (11.02)	558 (581)
15.	$[Pt(L_4H)_2]Cl_2$	Dim green solid	230d	25.83 (25.92)	11.35 (11.16)	8.68 (8.52)	717 (752)
16.	$[Pt(L_4)_2]$	Yellowsh brown solid	>250	28.30 (28.70)	12.09 (12.35)	9.37 (9.43)	643 (680)

TABLE II Electronic spectral data of Pd(II) and Pt(II) complexes

S.No. cm^{-1}	Complexes	Spectralbandscm^{-1}	Transitions	Δ_1	Δ_2	Δ_3	ν_2/ν_1
1.	$[Pd(L_4H)_2]Cl_2$	21000	$^1A_{1g} \rightarrow {}^1A_{2g}$	23100	2670	2730	1.07
		22470	$^1A_{1g} \rightarrow {}^1B_{1g}$				
		25500	$^1A_{1g} \rightarrow {}^1E_g$				
2.	$[Pd(L_4)_2]$	20800	$^1A_{1g} \rightarrow {}^1A_{2g}$	22900	2600	3200	1.06
		22200	$^1A_{1g} \rightarrow {}^1B_{1g}$				
		25700	$^1A_{1g} \rightarrow {}^1E_g$				
3.	$[Pt(L_2H)_2]Cl_2$	19230	$^1A_{1g} \rightarrow {}^1A_{2g}$	21330	6360	3881	1.26
				24390	$^1A_{1g} \rightarrow {}^1B_{1g}$		
				28571	$^1A_{1g} \rightarrow {}^1E_g$		
4.	$[Pt(L_2)_2]$	19305	$^1A_{1g} \rightarrow {}^1A_{2g}$	21405	6404	3762	1.26
		24509	$^1A_{1g} \rightarrow {}^1B_{1g}$				
		28571	$^1A_{1g} \rightarrow {}^1E_g$				

All the derivatives are coloured solids with high melting/decomposition temperature and are insoluble in common organic solvents. The molar conductance of 10^{-3}M solutions of $[M(NSH)_2]Cl_2$ in DMF lie in the range of 210-230 ohm^{-1} mol^{-1} cm^2, indicating that they behave as 1:2 electrolytes. However, the $[M(NS)_2]$ complexes are non-electrolytes (molar conductance values 10-15 ohm^{-1} mol^{-1} cm^2) in dry DMF at 28 ± 1°C. All the derivatives are monomers as unveil by their molecular weight determinations. These derivatives are diamagnetic as expected for square planar d [8] complexes. Their magnetic susceptibilities lie in the range $(0.3\text{-}0.8 \times 10^{-6})$ c.g.s. units.

SPECTRAL STUDIES

The newly synthesized compounds were characterised by different spectral techniques. In the electronic spectra of metal complexes three spin allowed d-d transitions from three lower lying d orbitals to the empty $d_{x^2-y^2}$ orbital corresponding to transitions $1_{A_{1g}} \rightarrow 1_{A_{2g}}$, $1_{A_{1g}} \rightarrow 1_{B_{1g}}$ and $1_{A_{1g}} \rightarrow 1_{E_g}$ are observed. The three orbital parameters Δ_1, Δ_2 and Δ_3 were calculated using a value of $F_2 = 10F_4 = 6090$ cm^{-1} for Slater Condon interelectronic repulsion. [12] The ν_2/ν_1 were also calculated (Table-II) and are in close agreement with data reported earlier for square planar complexes. [12-14]

Two bands around (25000 cm^{-1}) and (19000 cm^{-1}) are observed. These two bands indicate a trans- planar configuration and are attributed to $1_{A_g} \rightarrow 1_{B_g}$ and $1_{A_g} \rightarrow 1_{A_{2g}}$ transition respectively on the basis of above information and other

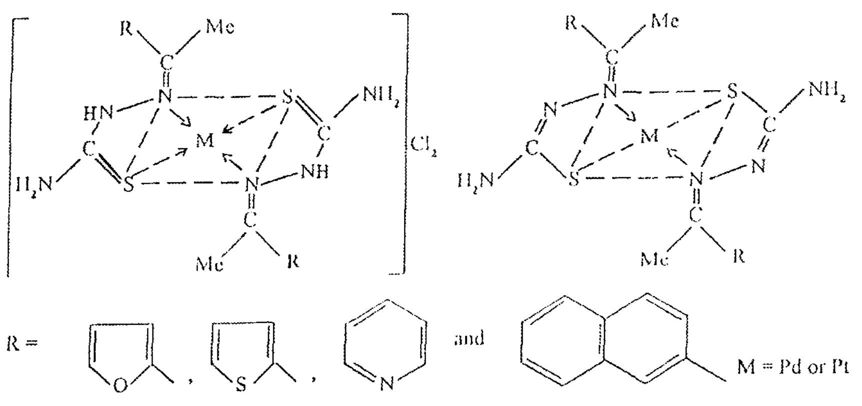
TABLE III ^{1}HNMR spectral data (δ, ppm) of ligands and their Pd(II) and Pt(II) complexes

S.No.	Compound	-NH	-NH$_2$	-CH$_3$	Aromatic
1.	L_1H	9.90	2.83	1.80	6.60-7.80
2.	$[Pd(L_1H)_2]Cl_2$	10.08	2.84	2.02	6.94-8.12
3.	$[Pd(L_1)_2]$	—	2.88	2.12	7.08-8.18
4.	$[Pt(L_1H)_2]Cl_2$	10.14	2.84	2.04	7.02-8.08
5.	$[Pt(L_1)_2]$	—	2.92	2.16	7.12-8.24
6.	L_2H	10.68	2.81	1.68	7.16-8.68
7.	$[Pd(L_2H)_2]Cl_2$	10.86	2.82	1.80	7.56-8.82
8.	$[Pd(L_2)_2]$	—	2.86	1.84	7.48-8.94
9.	$[Pt(L_2H)_2]Cl_2$	10.84	2.80	1.72	7.46-8.84
10.	$[Pt(L_2)_2]$	—	2.84	1.80	7.52-8.92
11.	L_3H	10.64	2.84	1.86	7.48-8.92
12.	$[Pt(L_3H)_2]Cl_2$	10.80	2.88	2.12	7.68-9.14
13.	$[Pt(L_3)_2]$	—	2.86	2.18	7.78-9.20
14.	L_4H	10.65	2.90	1.91	7.55-8.92
15.	$[Pd(L_4)_2]Cl_2$	10.84	2.92	2.12	7.64-9.04
16.	$[Pd(L_4)_2]$	—	2.96	2.20	7.62-9.10

published results, a trans square-planar geometry is assigned to these metal complexes. [13]

The thio-ligands exist in tautomeric forms as evidenced from the infrared spectral data. Broad and strong bands at ca. 3280 cm^{-1} and ca. 820 cm^{-1} assigned to νNH and νC=S vibrations, respectively, disappeared in the solution spectra of ligands and a new band at ca. 2570 cm^{-1} due to ν(SH) was observed indicating tautomerisation of the ligands. On complexation, these bands disappear in the corresponding $[M(NS)_2]$ type of complexes. The band at ca. 1610 cm^{-1} in the free ligands, due to ν(C=N), is shifted to a higher wave number ($\Delta\nu$ = 10-20 cm^{-1}) in the metal complexes, suggesting coordination through the azomethine nitrogen.

The presence of non-ligand bands in the far IR spectra of metal complexes in the regions ca. 360 cm^{-1}, ca. 440 cm^{-1} and ca. 310 cm^{-1} are assigned to ν(Pd-N), ν(Pt-N) and ν(M-S), respectively. [14-15] However, no ν(M-Cl) band is observed in the spectra of $[M(NSH)_2]Cl_2$ type of complexes suggesting the ionic nature of chloride ion. [15] It is known that the cis form of such type of complexes give rise to two νM-N bands whereas the trans complexes give rise to only one IR active νM-N band. The presence of only one ν(M-N) band in the present case, suggests that the complexes exist in the trans form. [16] The coordination of ligands to central metal atom is further substantiated by ^{1}H NMR spectral data of ligands and their respective metal complexes. Chemical shift values are given in Table III. Thus on the basis of preceding discussion, the following structures have been proposed for the metal complexes.



ANTIMICROBIAL SCREENING

To assess the biological potential of the newly synthesized compounds, the parent thioimines and their respective metal complexes were tested against selected pathogenic fungi and bacteria. The antimicrobial data were transformed using 0 transformation for statistical analysis and the superiority of the complexes have been determined by above mentioned data. The enhanced activities of the metal complexes compared to free ligands may be ascribed to increased lipophilic nature of these complexes arising due to chelation. [17]

STERILIZING ACTIVITIES

The present study suggests that exposure of the ligand (L_2H) and its palladium complex hampers the fertility in male rats. Reduction in the testicular weight corresponds to suppression of the spermatogenesis and reduction in motility may be due to the defective maturation of spermatozoa at the epididymis. [18] It is known that the maintenance of the structure and functions of accessory reproductive organs, including the epididymis is dependent on circulating levels of androgens. [19] Since a number of androgen sensitive parameters (sialic acid, protein, fructose, total cholesterol) in target organs were found to be altered by these compounds, it is possible that the structure and functions of the epididymis and other sex organs are changed. The data of biological activity and antifertility activity may be obtained from the authors on request.

Acknowledgements

The authors are thankful to C.S.I.R., New Delhi, India for financial assistance through grant No. 09/149(201)95-EMR-I in the form of RA to N. Fahmi.

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