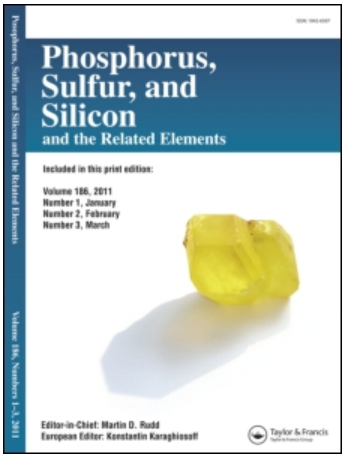

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SULFUR BONDED PALLADIUM(II) COMPLEXES: SYNTHETIC, BIOLOGICAL AND SPECTRAL ASPECTS

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SULFUR BONDED PALLADIUM(II) COMPLEXES: SYNTHETIC, BIOLOGICAL AND SPECTRAL ASPECTS

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Synthesis, characterization, and antimicrobial activities of some palladium(II) complexes of sulfur containing benzothiazolines having NS donor set are described. The resulting biologically active $[Pd(NSH)_2]Cl_2$ and $[Pd(NS)_2]$ type of complexes have been characterized by elemental analyses, molecular weight determinations and conductivity measurements. Based on infrared and ^1H n.m.r. spectral studies a square planar structure has been established for all the derivatives. The benzothiazolines and their respective metal complexes have been screened for their antimicrobial activities.

Key words: Palladium(II) complexes, benzothiazolines, heterocyclic ketones, spectral studies, antimicrobial activity.

INTRODUCTION

Azomethines bonding through nitrogen and sulfur atoms to the metal ion forms an important class of biologically active ligands and provide models for metal ligand binding sites in several enzymes.[1] Considerable importance has been given to transition metal complexes of these ligands on account of their biological properties.[2] They are known to function as antimicrobial,[3] antifertility,[4] antimalarial[5] and antileukemic agents.[6] It has been observed that metal chelation apparently plays a definite role in the cause and treatment of malignancy.[7] The palladium chelates of N and S donor ligands were found to display cytostatic activity in the 9KB test—a human epidermoid carcinoma of the nasopharynx.[7] Systematic study of the antitumour activity of transition metal chelates of thio-ligands derived from S-methyldithiocarbazate was carried out.[8] The results indicated that the incidence of activity among the palladium chelates was maximum.

The mechanism of sulfur toxicity has intrigued the scientifically curious ever since sulfur was found to have "Pest-averting" qualities. Many types of organic sulfur compounds and those organic compounds that contain a sulfur bridge were investigated to study mechanisms of fungicidal action. The inherent biological potential of sulfur donor ligands prompted us to undertake systematic studies with transition metals and particularly with palladium. We report herein the preparation, characterization and antimicrobial properties of Pd(II) complexes with biologically active, monofunctional bidentate benzothiazolines Bzt_1H, Bzt_2H, Bzt_3H and Bzt_4H derived by the condensation of 2-aminobenzenethiol with heterocyclic ketones, e.g. [1-(2-furanyl)ethanone], [1-(2-thienyl)ethanone], [1-(2-pyridinyl)ethanone] and [1-(2-naphthenyl)ethanone], respectively.

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EXPERIMENTAL

All the reagents used were of analytical grade. Palladium(II) chloride was used as such. The benzothiazolines were prepared by the condensation of [1-(2-furanyl)ethanone], [1-(2-thienyl)-ethanone], [1-(2-pyridinyl)ethanone] or [1-(2-naphthenyl)ethanone] with 2-aminobenzenethiol in 1:1 molar ratio in EtOH. The reaction mixture was stirred for *ca.* 3–4 h and the solid which separated out was filtered off, recrystallized from EtOH and dried in vacuo. All of the products were yellow solids, m.p. Bzt_1H: 73°C, Bzt_2H: 88°C, Bzt_3H: 84°C and Bzt_4H: 78°C.

Synthesis of Palladium Complexes

$[Pd(NSH)_2]Cl_2$type of Complexes: Solution of $PdCl_2$ and the ligand in MeOH containing a few drops of concentrated HCl were mixed in 1:2 molar ratio and stirred for 2 h. The precipitate obtained was filtered, washed with MeOH and dried in vacuo.

$Pd(NS)_2$ Type of Complexes: $PdCl_2$ and ligand were dissolved in MeOH separately and the solutions were mixed together in 1:2 molar ratio. Aqueous NH_4OH was added dropwise to the above mixture until the solution was weakly alkaline. The mixture was refluxed for 1 h, the precipitate was filtered and washed with MeOH and dried in vacuo. Their physical properties and analytical data are reported in Table I. In both type of complexes the resulting products have been washed by MeOH in which both of the starting materials are soluble but the complexes are insoluble. Therefore, any unreacted materials will washout and the compounds so obtained were completely pure. Their purity was further checked by T.L.C. using silica gel-G.

Analytical Methods and Physical Measurements

Palladium was estimated gravimetrically.[8] The analytical methods and procedures of physical measurements are the same as reported earlier.[9]

Antimicrobial Screening

Antifungal and antibacterial activities were evaluated by the methods reported elsewhere.[2]

RESULTS AND DISCUSSION

Spectral studies and conductance measurements indicate the formation of $[Pd(NSH)_2]Cl_2$ and $[Pd(NS)_2]$ type of products, where (NSH) is the ligand molecule and NS^{-1} its conjugate base. The products were obtained by reaction of $PdCl_2$ with benzothiazolines in 1:2 molar ratio in MeOH as indicated below:

$$PdCl_2 + 2NSH \rightarrow [Pd(NSH)_2]Cl_2$$

However, in presence of aqueous NH_4OH the two chlorines could also be replaced as depicted below:

$$PdCl_2 + 2NSH + 2NH_4OH \rightarrow [Pd(NS)_2] + 2NH_4Cl + 2H_2O$$

All the new derivatives are coloured solids and the molar conductances of 10^{-3} M solutions of $[Pd(NSH)_2]Cl_2$ 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 $[Pd(NS)_2]$ type of complexes are non-electrolytes. The monomeric nature of these complexes is confirmed by the molecular weight determinations. All the complexes are soluble in DMF and DMSO but insoluble in common organic solvents.

TABLE I

Analysis and physical properties of Pd(II) complexes of benzothiazolines

Compound	Colour and M.P.(°C)	% Analysis Found/(Calc.) Pd	N	S	Molecular weight Found (Calc.)
$[Pd(Bzt_1H)_2]Cl_2$	Brown	17.10	4.43	10.32	570
	240d	(17.39)	(4.57)	(10.48)	(611)
$[Pd(Bzt_1)_2]$	Dark green	19.69	5.09	11.93	501
	>320	(19.74)	(5.19)	(11.89)	(539)
$[Pd(Bzt_2H)_2]Cl_2$	Yellowish brown	16.61	4.28	19.82	620
	245d	(16.52)	(4.34)	(19.91)	(644)
$[Pd(Bzt_2)_2]$	Black	18.71	4.65	22.30	540
	150	(18.63)	(4.90)	(22.45)	(571)
$[Pd(Bzt_3H)_2]Cl_2$	Reddish brown	16.81	8.75	10.03	613
	>320	(16.78)	(8.83)	(10.11)	(633)
$[Pd(Bzt_3)_2]$	Dark green	18.89	9.82	11.32	550
	>320	(18.96)	(9.98)	(11.43)	(561)
$[Pd(Bzt_4H)_2]Cl_2$	Yellowish brown	14.62	3.89	8.98	700
	310d	(14.53)	(3.82)	(8.75)	(732)
$[Pd(Bzt_4)_2]$	Greyish black	16.01	4.23	9.68	617
	>320	(16.14)	(4.24)	(9.72)	(659)

d = decomposed

TABLE II

Electronic spectral data of Pd(II) complexes

Complex	Spectral bands cm^{-1}	Transitions	Δ_1 cm^{-1}	Δ_2 cm^{-1}	Δ_3 cm^{-1}	ν_2/ν_1
$[Pd(Bzt_1H)_2]Cl_2$	15432	$^1A_{1g} \rightarrow {}^1A_{2g}$	17532	4635	5223	1.22
	18867	$^1A_{1g} \rightarrow {}^1B_{1g}$				
	24390	$^1A_{1g} \rightarrow {}^1E_{1g}$				
$[Pd(Bzt_1)_2]$	15503	$^1A_{1g} \rightarrow {}^1A_{2g}$	17603	4744	5162	1.23
	19047	$^1A_{1g} \rightarrow {}^1B_{1g}$				
	24509	$^1A_{1g} \rightarrow {}^1E_{1g}$				
$[Pd(Bzt_2H)_2Cl_2$	15503	$^1A_{1g} \rightarrow {}^1A_{2g}$	17603	4927	5161	1.24
	19230	$^1A_{1g} \rightarrow {}^1B_{1g}$				
	24691	$^1A_{1g} \rightarrow {}^1E_{1g}$				
$[Pd(Bzt_2)_2]$	15527	$^1A_{1g} \rightarrow {}^1A_{2g}$	17627	4903	5345	1.24
	19230	$^1A_{1g} \rightarrow {}^1B_{1g}$				
	24875	$^1A_{1g} \rightarrow {}^1E_{1g}$				

TABLE III

^{1}H n.m.r. data (δ, ppm) of Pd(II) complexes of benzothiazolines

Compound	-NH	H_3C-C=N	-SH	Aromatic protons
Bzt_1H	5.44	3.40	-	6.40-7.24
$[Pd(Bzt_1H)_2]Cl_2$	-	3.48	5.62	6.48-7.56
$[Pd(Bzt_1)_2]$	-	3.52	-	6.66-7.80
Bzt_2H	4.32	-	-	6.44-7.36
$[Pd(Bzt_2H)_2]Cl_2$	-	3.38	5.48	6.64-7.52
$[Pd(Bzt_2)_2]$	-	3.40	-	6.68-7.48
Bzt_4H	5.52	3.42	-	6.40-7.32
$[Pd(Bzt_4H)_2]Cl_2$	-	3.48	5.64	6.58-7.60
$[Pd(Bzt)_2]$	-	3.54	-	6.62-7.64

Electronic Spectra

In the electronic spectra of palladium(II) 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 $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} - {}^1E_g$ are observed. The three orbital parameters, Δ_1, Δ_2, and Δ_3, were calculated using a value of $F_2 = 10F_4 = 600$ cm^{-1} for a Slater Condon interelectronic repulsion. The ν_2/ν_1 were also calculated and are in close agreement with data reported earlier for square planar complexes[10] (Table II).

I.r. Spectra

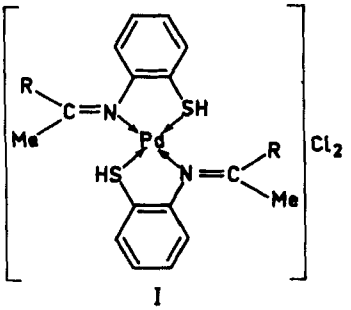
In the spectra of free ligands the absence of ν(SH) at 2500–2600 cm^{-1} and appearance of ν(NH) at *ca.* 1670 cm^{-1} is strong evidence for a ring structure.[10] Further, in metal complexes ν(NH) disappears, suggesting deprotonation of the ligand on complexation. A strong and sharp band at *ca.* 1590 ± 10 cm^{-1} ascribed to ν(C=N), is observed in palladium chelates confirming that the ligands adopt the Schiff base form in complexes. In case of addition products band due to ν(SH) at *ca.* 2520 cm^{-1} is observed. The coordination of the ligands through azomethine nitrogen and thiolato sulfur further gets support by the appearance of new bands of medium to weak intensity in the regions 305–310 cm^{-1} and 355–360 cm^{-1} attributable to ν(Pd—S) and ν(Pd ← N) vibrations, respectively.[10]

^{1}H n.m.r. Spectra

The ^{1}H n.m.r. spectra of free Bzt_1H, Bzt_2H, Bzt_4H and their derivatives were recorded in DMSO-d_6. Chemical shifts values are summarized in Table III. Signals at δ5.44, 4.32 and 5.52, respectively are assigned to the NH protons. However, these disappear from the spectra of the substitution products, indicating deprotonation of this functional group on complexation, whilst in addition products the signals appearing at δ5.48–5.64 are due to the SH proton and this is not observed in $[Pd(NS)_2]$ type of complexes.

The free ligands show a complex multiplet at δ6.40–7.36 for the aromatic protons and this remains more or less at the same position in the spectra of the complexes, whilst the methyl proton signals were slightly shifted downfield in the metal complexes.

On the basis of the foregoing results, I and II structures can be proposed for the complexes.



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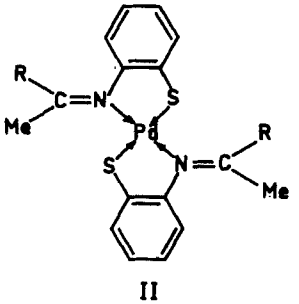

II

TABLE IV

Fungicidal screening data of ligands and their complexes. Inhibition % after 96 h (conc. in ppm)

Compound	F. oxysporum		P. species		S. rolfsi		A. alternata	
	100	200	100	200	100	200	100	200
Bzt_2H	35	41	72	78	77	83	*	*
$[Pd(Bzt_2H)_2]Cl_2$	39	52	79	83	81	90	*	*
$[Pd(Bzt_2)_2]$	38	53	81	88	80	94	*	*
Bzt_4H	52	64	74	79	76	85	*	*
$[Pd(Bzt_4H)_2]Cl_2$	54	66	83	86	87	94	*	*
$[Pd(Bzt_4)_2]$	57	70	79	84	92	*	*	*
Standard	*	*	92	*	*	*	*	*

* = no growth

TABLE V

Bactericidal screening data of the ligands and their complexes. Inhibition (mm) after 24 h (conc. in ppm)

Compound	K. aerogenous		E. coli		X. compestris	
	500	1000	500	1000	500	1000
Bzt_2H	4	5	4	8	3	4
$[Pd(Bzt_2H)_2]Cl_2$	5	7	6	9	4	5
$[Pd(Bzt_2)_2]$	6	7	7	9	5	6
Bzt_4H	4	7	5	8	3	5
$[Pd(Bzt_4H)_2]Cl_2$	6	9	5	9	4	6
$[Pd(Bzt_4)_2]$	5	8	7	10	4	5
Standard	+++++	+++++	+++++	+++++	+++	++++

Antimicrobial Activity

The thioligands and their corresponding palladium(II) complexes were screened for their antifungal activity against Fusarium oxysporum, Alternaria alternata, Sclerotium rolfsi and Penicillium species. Their antibacterial property was also evaluated by testing them against E. coli, and S. aureus. The experimental results showed that all the complexes are much more active than the original thioligands. Standard fungicide (Mancozeb) and bactericide (Streptomycin) were used for comparing the results. Solubility and concentration of the compounds play vital roles in ascertaining the extent of inhibition. The biological potency of these compounds may be attributed to their ability to inactivate various cellular enzymes which play vital roles in different metabolic pathways of these microorganisms. It has been proposed that the ultimate action of these compounds is the denaturation of one or more proteins of the cell as a result of which normal cellular processes are impaired.[11] It may also be postulated that these complexes might act as uncoupling agents of oxidative phosphorylation. These agents allow electron transport to continue but prevent the phosphorylation of ADP to ATP.[12] These agents are less effective for bacteria. Organic compounds that contain a sulfur bridge were extensively employed to study the mecanisms of fungicidal action. The results indicate that the sulfur-bridged compounds are generally fungitoxic. Very few compounds were found to be non-toxic and the factor responsible for the negative results was poor permeation. The ability of the compounds to permeate through the semipermeable defenses of the cell is the major factor in determining their toxicity.[13]

The antifungal activity of these compounds may well be explained in the light of modern electronic theory, as resonating rings also exert effects on fungitoxicity. Resonating structures, such as benzene rings, thiophene rings, and other conjugated systems may serve as power houses to activate potentially reactive groupings. If fungitoxicity is dependent on one or more chemical reactions, as it must undoubtedly be in most cases, then any property of the fungitoxic molecule which would increase the rate of chemical reactions must, perforce, enhance fungitoxicity.[13] The enhanced activities of the metal complexes compared to free ligands can be ascribed to increased lipophilic nature of these complexes arising due to chelation.[14] It is natural to hypothesize that more lipophilic compounds are more active simply because they enter the lipoid layers of cell membranes more rapidly. Furthermore, these compounds show greater potency towards particular fungi in inhibiting their growth than the others, while in some cases they completely inhibit the growth of microorganisms.

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