



Synthesis and Characterization of New Pd(II) Complexes of Some 2,4-Disubstituted Thiazole Ligands and Their Antimicrobial Activities

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Abstract

Mononuclear complexes with a metal-ligand ratio of 1:2 of some 2,4-disubstituted thiazole ligands have been prepared with chloride salt of Pd(II). The structures of the complexes have been established by elemental analysis, IR, UV-vis, ¹³C- and ¹H NMR. spectra, and magnetic susceptibility measurements. The complexes are mononuclear and diamagnetic. Thermal properties of the complexes have been studied by TGA and DSC techniques. Antimicrobial activities of the ligands and the complexes have been tested against eight different microorganisms. It has been observed that both ligands and their complexes were found to be inactive against microorganisms studied.

Keywords: Cyclobutane, Pd(II) complexes, thiazole

Bazı 2,4-Disüstitüe Tiyazol Ligandlarının Yeni Pd(II) Komplekslerinin Sentezi, Karakterizasyonu ve Biyolojik Aktiviteleri

Özet

Bu çalışmada, Schiff bazı ve hidrazon grupları içeren, 2,4-disüstitüe tiyazol ligandlarının metal:ligand oranı 1:2 olan mononükleer Pd(II) kompleksleri hazırlanmıştır. Komplekslerin yapıları elementel analiz, IR, ¹³C- ve ¹H NMR spektrumları ve magnetik süseptibilite ölçümleri yardımı ile aydınlatıldı. Komplekslerin mononükleer ve diamagnetik oldukları gözlemlendi. Ligand ve komplekslerin termal özellikleri TGA ve DSC teknikleri ile incelendi. Ligandlar ve komplekslerin çalışılan mikroorganizmalar üzerinde kayda değer bir aktivitelerinin olmadığı gözlemlendi.

Anahtar kelimeler: Siklobütan, Pt(II) kompleksleri, tiyazol.

1. Introduction

The palladium complexes were found to be effective catalyst for promoting specific carbon-carbon, carbon-oxygen, carbon-nitrogen and nitrogen-hydrogen bond formation under mild conditions [1]. In particularly, Pd(II) salicylaldiminates are important catalyst for the hydrogenation of unsaturated organic compounds, therefore, the mechanisms of the reactions have become the subject of much interesting work [2]. Thiosemicarbazones, cyclobutanes, thiazoles and Schiff bases are of great importance for the preparation of various pharmaceuticals and are used in many other areas of chemistry as starting materials. Schiff bases derived from the salicylaldehydes are well known polydentate ligands [3,4]. It has been shown that Schiff base complexes derived from 4-hydroxysalicylaldehyde and amines have strong anticancer activity *e.g.* Ehrlich ascites carcinoma (EAC) [5]. Some thiazole derivatives containing tetralin moiety have been synthesized and used in biological activity studies [6]. Recently, there has been considerable interest in the chemistry of Schiff base compounds containing thiosemicarbazones and their metal complexes due to their biological activities [7] and non-linear optical properties [8]. Research has concentrated on the chemistry of 3-substituted cyclobutane carboxylic acid derivatives having antiinflammatory and antidepressant activities [9], liquid crystal properties [10], and various thiazole derivatives having herbicidal [11],

antiinflammatory [12], antimicrobial [13] or anthelmintic resistance and Parasitic nematode properties [14].

2-Aminothiazoles are known mainly as biologically active compounds with a broad range of activity and as intermediates in the synthesis of antibiotics and dyes. Substituted α -haloketones, like those used in the production of our ligands, are used for different purposes, especially in the synthesis of heterocyclic substances [15].

The ligands used in this work have three different and important functionalities of cyclobutane, thiazole and Schiff base character. The extensive synthetic possibilities of these heterocycles, due to the presence of several reaction sites, hold promise for the preparation of new thiazole derivatives.

Since the complexation of these ligands (Scheme 1a,b) with palladium were not reported in the literature, our paper deals with in preparation, characterization and biological activity of the complexes with palladium(II).

2. Experimental

PdCl₂, NaCl, chloroform, thiosemicarbazide, salicylaldehyde, 2-hydroxy-5-bromo benzaldehyde, 2-hydroxy-1-naphthalaldehyde, 2,4-dihydroxybenzaldehyde and 2-hydroxy-3-methoxy benzaldehyde were purchased from Merck (pure) and were used without further purification. 1-Methyl-1-mesityl-3-(2-chloro-1-oxoethyl) cyclobutane and 1-methyl-1-phenyl-3-(2-chloro-1-oxoethyl) cyclobutane were prepared according to a known procedure [16] and were purified by column chromatography prior to use. Solvents were analytical grade and purified by standard methods. Elemental analyses were determined on a LECO CHNSO-932 auto elemental analysis apparatus. IR spectra were recorded on a Mattson 1000 FT-IR Spectrometer as KBr pellets. ¹³C and ¹H NMR spectra were recorded on a Bruker GmbH Dpx-400 MHz High Performance Digital FT-NMR or JEOL FX-90Q Spectrometer. Electronic spectra were obtained on a CECIL CE 5502 UV-Vis. spectrophotometer. Magnetic susceptibilities were determined on a Sherwood Scientific magnetic susceptibility balance (Model MK1) at room temperature (20° C) using Hg[Co(SCN)₂] as calibrant; diamagnetic corrections were calculated from Pascal's constants. Melting points were determined on a Gallenkamp apparatus. Thermal analysis curves were recorded on a Shimadzu TG-50 thermobalance.

2.1. Preparation of the Ligands

The 2,4-disubstituted thiazole derivative ligands, which containing cyclobutane and azomethine functional groups are used in complexation with Pd(II). The complexes were synthesized according to the procedure reported previously [16,17]. The formula of the ligands is given in Scheme 1a and 1b.

2.2. Preparation of the Complexes

A solution of Pd(II), prepared by refluxing PdCl₂ (0.0512 g, 2.89 mmol) and NaCl (0.034 g, 5.78 mmol) in absolute EtOH (10 mL), was added to a warmed solution of 5.78 mmol of the appropriate quantity of the Schiff base ligand [0.2469 g of L¹H, 0.2303 g of L²H, 0.2546 g of L³H, 0.2436 g of L⁴H, 0.2517 g of L⁵H and 0.210 g of L⁶H] in absolute EtOH (30 mL). The complexes of ligands L⁴H, L⁵H and L⁶H formed immediately while the solutions were warm, but the complexes of ligands L¹H, L²H and L³H formed in 2 hours stirring period. The mixtures were stirred for 2 h at 30-40 °C under an argon atmosphere and stirring was continued

overnight at room temperature. The resulting precipitates were filtered off, washed with EtOH and water several times, and dried at 110 °C to the constant weight.

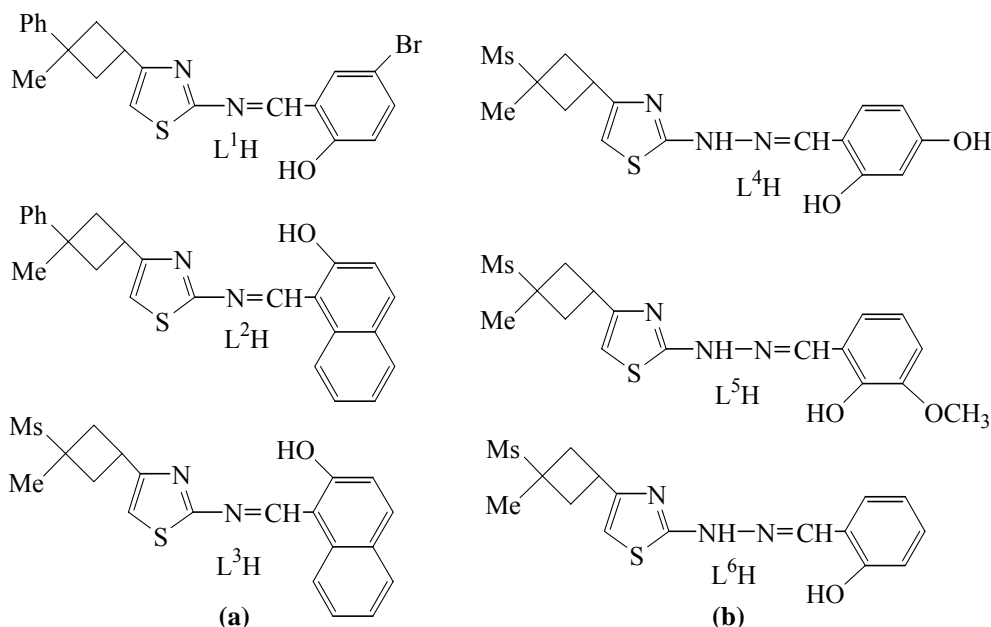
2.3. Preparation of microbial cultures

Microorganisms were provided from the culture collection of the Microbiology Laboratory of the Biological Sciences of Faculty of Science and Arts, Firat University, Turkey. In this work, *Bacillus megaterium* DSM 32 (B.m.), *Candida albicans* FMC 17 (C.a.), *Enterobacter aeruginosa* CCM 2531 (E.a.), *Eschericia coli* ATCC 25922 (E.c.), *Listeria monocytogenes* SCOTTA (L.m.), *Pseudomonas aeruginosa* DSM 50071 (P.a.), *Saccharomyces cerevisiae* FMC 16 (S.c.) and *Staphilococcus aureus* COWAN I (S.a.) were used to investigate the bacteriological and antifungal activities of ligands and their Pd(II) complexes.

The bacteria and yeast strains were nourished in nutrient broth (Difco) and in malt extract broth (Difco), and incubated for 24 and 48 h, respectively. In the Disc Diffusion method, the sterile Mueller Hinton Agar (Oxoid) for bacteria and Sabourou Dextrose Agar for yeast were separately inoculated with the test microorganisms. The compounds, dissolved in CHCl₃ as 50 µg/disc solutions, were placed in wells (6 mm diameter) placed in the agar media, and the plates were incubated at 32° C for bacteria (18-24 h) and at 25° C for yeast (72 h). The resulting inhibition zones on the plates were measured in mm after 48 h (Table 5). The control samples were only absorbed in CHCl₃. The data reported in Table 5 are the average of three experiments.

3. Results and Discussion

In this study, mainly two types of compounds were used; the first group (Scheme 1a) is azomethine dyes; the second group is also azomethine dyes (Scheme 1b) but contains (-NH-) group attached to azomethine side of the ligands.



Scheme 1

Table 1 lists the analytical data for the ligands L¹H-L⁶H, and their Pd(II) complexes. 1-Phenyl-1-methyl-3-(2-chloro-1-oxoethyl) cyclobutane and 1-Mesityl-1-methyl-3-(2-chloro-1-oxoethyl) cyclobutane were prepared according to the literature procedure published previously [18]. The compounds are very soluble in polar organic solvents, such as diethyl ether (Et₂O), CHCl₃, methanol (MeOH), and in non-polar organic solvents, such as Et₂O and benzene. They are not stable for long under ordinary laboratory conditions, and are highly affected by direct sunlight, decomposing over 2 months. Hence, it was used, as prepared, without delay. Substituted benzaldehyde derivatives of thiosemicarbazide were freshly prepared in excellent yields according to the well-known Schiff base preparation methods. The ligands L¹H, L²H and L³H, were obtained in good yields, *ca.* 75-85%, and are very soluble in Me₂CO, DMF, DMSO, THF and CHCl₃, sparingly soluble in EtOH and MeOH. The ligands L⁴H, L⁵H and L⁶H, were obtained in moderate yields, *ca.* 62-65%, and are very soluble in common organic solvents, such as Me₂CO, DMF, DMSO and CHCl₃, and partially soluble in apolar organic solvents such as EtOH and MeOH. Furthermore, hot alcoholic solutions of the ligands were used during complexation. In general, reactions of the ligands with metal salts were rapid and gave good yields of mononuclear complexes corresponding to the general formula M(L)₂; they are stable at room temperature and soluble in Me₂CO, DMF, DMSO and CHCl₃, but sparingly soluble in MeOH and EtOH solvents. Attempts to crystallize the complexes of the ligands in different solvents failed.

Table 1. Analytical and physical data of the compounds.

Comp.	F.W. (g·mol ⁻¹)	Color	M.p. (°C)	Yield (%)	Found (Calcd.) (%)			
					C	H	N	S
L ¹ H	427.37	yellow	180	85	58.0 (59.0)	4.1 (4.5)	6.2 (6.6)	8.4 (7.5)
L ² H	398.53	light brown	154	75	75.1 (75.4)	5.5 (5.6)	7.2 (7.0)	8.3 (8.1)
L ³ H	440.61	yellow	199	76	75.9 (76.3)	6.3 (6.4)	6.1 (6.4)	7.4 (7.3)
L ⁴ H	421.57	light brown	160	65	68.5 (68.4)	6.5 (6.5)	9.7 (10.0)	7.1 (7.6)
L ⁵ H	435.60	yellow	121	62	70.5 (70.0)	6.7 (6.7)	9.4 (9.7)	7.3 (7.4)
L ⁶ H	363.49	pale yellow	194	64	69.8 (69.4)	5.9 (5.8)	11.3 (11.6)	9.1 (8.8)
(L ¹)Pd	959.12	dark brown	230	51	52.3 (52.6)	3.4 (3.8)	5.9 (5.8)	6.5 (6.7)
(L ²) ₂ Pd	901.45	dark brown	175	59	66.7 (66.6)	4.4 (4.7)	6.7 (6.2)	7.1 (7.1)
(L ³) ₂ Pd	985.61	brown	241	63	67.3 (68.3)	5.8 (5.5)	5.7 (5.7)	6.7 (6.5)
(L ⁴) ₂ Pd	947.52	light brown	189	78	60.2 (60.9)	5.7 (5.5)	8.3 (8.9)	6.8 (6.8)
(L ⁵) ₂ Pd	975.57	light brown	166	73	61.7 (61.6)	5.3 (5.8)	8.1 (8.6)	6.3 (6.6)
(L ⁶) ₂ Pd	831.36	brown	254	64	60.8 (60.7)	4.7 (4.9)	9.4 (10.1)	7.1 (7.7)

The IR spectral data of the ligands and their metal complexes are listed in Table 2. Since there are no C=O, C-Cl and -NH₂ absorptions in the IR spectra of all the ligands L¹H-L⁶H, absence of these peaks indicate the formation of the expected compounds. The strong bands observed at 3126, 3121 and 3131 cm⁻¹ for the ligands L⁴H, L⁵H and L⁶H can be attributed to the -NH- group vibrations. In the complexes, these bands are not shifted and it may therefore be that the nitrogen atom of this group is not coordinated to the metal ion. The ligands exhibit broad medium intensity bands in the 2700-2560 cm⁻¹ range which are assigned to the intermolecular H-bonding vibrations (O-H...N). This situation is common for aromatic azomethine compounds containing *o*-OH groups [19]. In the complexes, these bands disappear completely. The azomethine group vibrations of the free ligands occur at 1625 cm⁻¹ for the ligands L¹H, L²H, L³H and L⁶H, 1631 cm⁻¹ for L⁴H ligand and 1612 cm⁻¹ for L⁵H, respectively. In the IR spectra of the complexes, these bands were not observed at the same frequencies and the same intensities. They shift to lower frequencies and, at the same time, their intensities are lowered. These results indicate that the azomethine groups were highly affected by complexation. In the free ligands, the bands at 1124, 1295, 1176, 1118, 1253 and 1285 cm⁻¹ for the ligands, respectively, can be attributed to the phenolic (C-O) group vibration [19]. In the metal complexes of L¹H-L⁶H ligands, these bands are shifted to higher frequencies, indicating coordination of oxygen to the metal atoms. Despite their presence in the ligand and the possibility of complexation by the C=N group and sulphur atoms in the thiazole rings, the unchanged band positions for these groups in the IR spectra of the complexes indicate that the thiazole ring does not involve to the complexation. In the complexes, the bands in the 660-475 and 455-405 cm⁻¹ range can be attributed to the ν (M-N) and ν (M-O) modes.

Table 2. IR spectral data (cm⁻¹) of the ligands and their complexes.

Compound	ν (O-H)*	ν (C-O)	ν (C=N) thiazole	ν (C=N) azomethine	ν (-NH-)	ν (C-S-C) thiazole
L ¹ H	3464	1124	1600	1625	-	685
L ² H	3464	1295	1576	1625	-	657
L ³ H	3454	1176	1606	1625	-	657
L ⁴ H	3416	1118	1612	1631	3126	637
L ⁵ H	3256	1253	1580	1612	3121	650
L ⁶ H	3182	1285	1600	1625	3131	657
Pd(L ¹) ₂	-	1132	1600	1581	-	685
Pd(L ²) ₂	-	1315	1573	1619	-	657
Pd(L ³) ₂	-	1220	1606	1585	-	657
Pd(L ⁴) ₂	-	1129	1612	1620	3126	637
Pd(L ⁵) ₂	-	1276	1580	1600	3121	650
Pd(L ⁶) ₂	-	1305	1600	1619	3131	657

* the (-OH) group at the *ortho* position

Electronic absorption spectral data of $L^X H$ and $(L^X)_2 Pd$ in $CHCl_3$ are given in Table 3. The spectra of $L^2 H$ and $L^4 H$ are similar to each other and show three group bands at about the 245-275, 340-355 and 414-480 nm regions as maximum or a shoulder bands. The bands at the first region are attributed to intraligand $\pi \rightarrow \pi^*$ transitions. The bands at 340-355 nm are attributed to $n \rightarrow \pi^*$ transitions in the azomethine group. The bands observed as a maximum or a shoulder in the 410-480 nm region and band at 600 nm (for $L^6 H$) are attributed to dipolar ketoamine tautomer forms of its zwitterionic dipolar structure which is characteristic for salicylaldimines [20-22]. Surprisingly, although the formula of $L^5 H$ and $L^6 H$ ligands are very similar, their electronic spectra are different. In the electronic spectra of $(L^X)_2 Pd$ compounds in $CHCl_3$ solution bands at 410-420 and 455-525 nm, attributable to the transitions $^1 A_{1g} \rightarrow ^1 B_{1g}$ and $^1 A_{1g} \rightarrow ^1 A_{2g}$, respectively, were observed [23]. Note that in these regions, the appearance of the bands attributable to the metal-to-ligand charge-transfer transition probably arising from the metal- t_{2g} -to-ligand π^* which are considered to be sensitive to changes in molecular geometry also can not be ruled out [23]. In the complexes, the low intensity bands in the 650-500 nm range are consistent with $d \rightarrow d$ transitions of the metal ions and intraligand $n \rightarrow \pi^*$ [24] transitions. The more intense 475-310 nm bands in the complexes may be due to the coincidence of charge transfer, $d \rightarrow \pi^*$ and $L \rightarrow M$ transitions [25].

Table 3. Electronic spectra of the Schiff base ligands and their complexes

Compound	Solvent	$\lambda_{max}/(nm)$
$L^1 H$	$CHCl_3$	246, 277, 335 ^a , 350 ^a
$L^2 H$	$CHCl_3$	246, 265 ^a , 275 ^a , 340, 355, 414, 450 ^a , 480 ^a
$L^3 H$	$CHCl_3$	245, 265 ^a , 275 ^a , 340, 355, 417, 450 ^a , 480 ^a
$L^4 H$	$CHCl_3$	246, 270 ^a , 352, 490
$L^5 H$	$CHCl_3$	244, 260 ^a , 337, 370
$L^6 H$	$CHCl_3$	244, 340 ^a , 357, 450 ^a , 600
$(L^1)_2 Pd$	$CHCl_3$	246, 265 ^a , 315 ^a , 330, 350, 387, 415 ^a , 475 ^a , 660
$(L^2)_2 Pd$	$CHCl_3$	248, 320 ^a , 340, 355, 420, 455 ^a , 480 ^a
$(L^3)_2 Pd$	$CHCl_3$	246, 325 ^a , 340 ^a , 355, 410 ^a , 420, 455 ^a , 475 ^a , 525 ^a
$(L^4)_2 Pd$	$CHCl_3$	245, 270 ^a , 310 ^a , 405 ^a , 475 ^a , 525 ^a , 600 ^a
$(L^5)_2 Pd$	$CHCl_3$	244, 260 ^a , 345, 415 ^a , 510 ^a
$(L^6)_2 Pd$	$CHCl_3$	250, 315 ^a , 346, 405, 475 ^a , 520 ^a , 600 ^a

^a Shoulder

The magnetic moments of the complexes were measured at room temperature and all the complexes were found to be diamagnetic as expected from the d^8 system.

The $^1 H$ and $^{13} C$ NMR spectra of the ligands were recorded in $CDCl_3$. The $^1 H$ NMR assignments are detailed in Table 4 and the $^{13} C$ NMR assignments are given in the Experimental section. Very similar spectra were obtained for the ligands. It is important to emphasize that the $^1 H$ resonance of the O-H group at 12.20, 13.6, 13.7, 13.6, 11.7, 11.9 and 10.7 ppm for the ligands $L^1 H$ - $L^6 H$, respectively, as singlet, is due to the presence of intramolecular

hydrogen bonding [26]. These signals do not exist in the complexes of the mentioned ligands. The ^1H NMR signal observed for the protons of C-OH and -NH- disappeared with the addition of D_2O to the solution. The single proton resonances in the ^1H NMR spectra of these ligands occur at 9.0, 7.88, 8.02, 8.09, 8.21 and 8.12 ppm for $\text{L}^1\text{H}-\text{L}^6\text{H}$, respectively, and have been attributed to the azomethine group proton. The proton resonances of the azomethine group of the ligands in the ^1H NMR spectra of the complexes exhibit very little shifts which are indicating the azomethine group of the ligands involve in complexation. The aromatic ring resonances are observed at 7.24-7.54, 7.16-7.55, 7.16-7.55, 6.34-7.35, 6.73-7.20 and 6.86-7.34 ppm as multiplets for $\text{L}^1\text{H}-\text{L}^6\text{H}$, respectively. The detailed ^1H NMR spectral data of the ligands are given in Table 4, and a more detailed spectral investigation of a similar cyclobutane compound, synthesized and published by the same authors, can be found in the literature [27].

In the ^{13}C NMR spectra, azomethine carbon signals are observed at 137.28, 131.31, 167.11, 144.00, 135.49 and 153.20 ppm, respectively, for $\text{L}^1\text{H}-\text{L}^6\text{H}$. The ^{13}C NMR spectral data of the ligands confirm the ^1H spectral results. These signals were observed at 133.36, 127.56, 163.03, 143.33, 128.87 and 147.78 ppm, respectively, for the $(\text{L}^1)_2\text{Pd}-(\text{L}^6)_2\text{Pd}$ complexes. These results indicate that the azomethine groups of the ligands take part in complexation. On the basis of the spectral and magnetic data, all the Pd(II) complexes of the ligands have tetrahedral geometry [28]. The suggested structure for the complexes is shown in Figs. 1 and 2

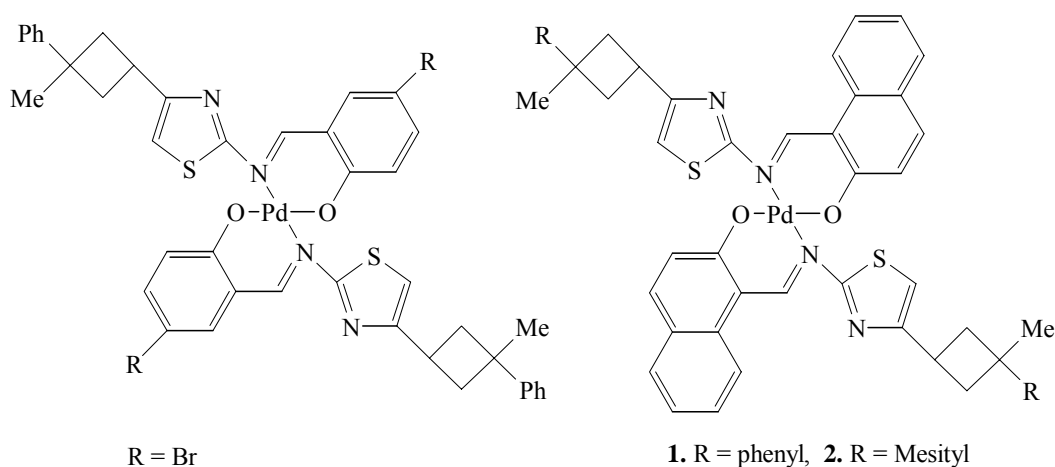


Fig. 1. Suggested structure of the Pd(II) complexes of L^1H , L^2H and L^3H ligands.

The thermogravimetric, TGA, curves for the ligands and the complexes were obtained at a heating rate of $10\text{ }^\circ\text{C}/\text{min}$ in a nitrogen atmosphere over a temperature range of $20\text{-}900\text{ }^\circ\text{C}$. Approximately 10 mg of samples of the ligands and complexes were used in each case. All the thermogravimetric curves have been obtained in $30\text{ mL}/\text{min}$ flowing nitrogen atmosphere.

**Table 4.** The ^1H -n.m.r spectral data of the Schiff base ligands

Functional Group	Chemical Shift (δ , p.p.m.)		L^3H	L^4H	L^5H	L^6H
	L^1H	L^2H				
HC=N	9.00 (s, 1H)	7.88 (s, 1H)	8.02 (s, 1H)	8.09 (s, 1H)	8.21 (s, 1H)	8.12 (s, 1H)
>C-H	3.67 (q, 1H)	3.94 (q, 1H)	3.94 (q, 1H)	3.32 (q, 1H)	3.33 (q, 1H)	3.65 (q, 1H)
CH ₃	1.57 (s, 3H)	1.53 (s, 3H)	1.53 (s, 1H)	1.53 (s, 3H)	1.51 (s, 3H)	1.47 s, 3H)
OCH ₃	-	-	-	-	3.80 (s, 3H)	-
Ms-CH ₃ , <i>ortho</i>	-	-	2.13 (s, 6H)	2.16 (s, 6H)	2.17 (s, 6H)	-
Ms-CH ₃ , <i>para</i>	-	-	2.43 (s, 3H)	2.45 (s, 3H)	2.47 (s, 3H)	-
CH ₂	2.57 (d, 4H)	2.60 (d, 4H)	2.60 (d, 4H)	2.61 (d, 4H)	2.65 (d, 4H)	2.49 (d, 4H)
C-H (thiazole)	6.83 (s, 1H)	6.82 (s, 1H)	5.95 (s, 1H)	6.31 (s, 1H)	6.44 (s, 1H)	6.06 (s, 1H)
-NH-	-	-	-	9.85 (s, 1H)	9.51 (s, 1H)	10.01 (s, 1H)
-OH*	12.2 (s, 1H)	13.64 (s, 1H)	13.63 (s, 1H)	11.65 (s, 1H)	11.93 (s, 1H)	10.63 (s, 1H)
Aromatics	7.24-7.54 (m, 8H)	7.16-7.55 (m, 11H)	7.16-7.55 (m, 6H)	6.34-7.35 (m, 5H)	6.73-7.20 (m, 5H)	6.86-7.34 (m, 9H)

- the (-OH) group at the *ortho* position

Table 5. Antimicrobial effects of the ligands and their complexes*

Compound	E. c.	S. a.	K. p.	B. m.	P. v.	L. m.	S. c.	C. a.
	ATCC 25022	COWAN I	FMC 5	DSM 32	FMC 1	SCOTTA	FMC 16	FMC 17
L ¹ H	-	-	-	-	-	-	-	-
L ² H	-	-	-	-	-	-	-	-
L ³ H	-	-	-	-	-	-	-	-
L ⁴ H	-	-	-	-	-	-	-	-
L ⁵ H	-	-	-	-	-	-	-	-
L ⁶ H	-	-	-	-	-	-	-	8.00±0.00
(L ¹) ₂ Pd	-	-	-	-	-	-	-	-
(L ²) ₂ Pd	-	-	-	-	-	-	-	-
(L ³) ₂ Pd	-	-	-	-	-	-	-	-
(L ⁴) ₂ Pd	-	-	-	-	-	-	-	-
(L ⁵) ₂ Pd	-	9.00±0.001	-	-	10.00±0.00	-	-	-
(L ⁶) ₂ Pd	-	-	-	-	-	-	-	-
A.10	10.00±0.01	16.00±0.04	17.00±0.02	14.00±0.01	14.00±0.01	12.00±0.04	-	-
B.10	-	-	-	-	-	-	14.00±0.03	17.00±0.09

* Compound concentration = 50 µg/disc. Including disc diameter (6 mm). A.10: Ampicillin 10 µg/disc, B.10: Nystatin 10 µg/disc, The symbol (-) reveals that the compound has any activity against the microorganisms studied.
 E. c. ATCC 25922: Eschericia coli, S. a. COWAN 1: Staphlococcus aureus, K. p. FMC 5: Klebsiella Pneumoniae, B. m. DSM 32: Bacillus megaterium, P. v. FMC 1: Proteus vulgaris, L. m. SCOTTA: Listeria monocytogenes, S. c. FMC 16: Saccharomyces cerevisiae, C. a. FMC 17: Candida albicans.

The TGA curves studied in the 20-900° C temperature range showed that the thermal decomposition of the complexes takes place in several steps. It is possible that the different groups in the ligands lead to a decrease in the stability of all the complexes. Furthermore, it is known that the electronegativity and the atomic radius of the central metal atom also affect the thermal stability [29,30]. The temperature range for the dehydration process shows a strong relationship with the binding mode of water molecules of the respective metal complexes. Since no elimination of water occurs in TGA curves implies that not any one of the ligands and complexes contains hydration or coordinated water. Essentially, the ligands and complexes have been dried to the constant weight, is an expected result. The weight losses are approximately the same as the percentages estimated stoichiometrically from their chemical formulas given in Table 1. The observed weight losses for all complexes are in good agreement with the calculated values. All the complexes completely decompose to the corresponding metal oxides, Co₃O₄, CuO, NiO or ZnO.

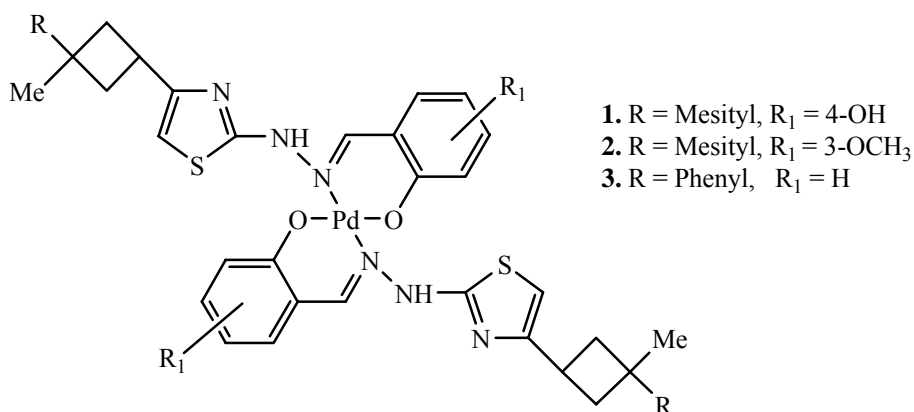


Fig. 2. Suggested structure of the Pd(II) complexes of L⁴H, L⁵H and L⁶H ligands.

The fungicidal and bacteriological activities of the Schiff base ligands and their metal complexes were determined against eight different bacteria and yeasts, mentioned above and in Table 5.

It has been suggested that the ligands with the N and O donor system might have inhibited the enzyme production, since enzymes which require a free hydroxy group for their activity appear to be especially susceptible to deactivation by the ions of the complexes. Chelation reduces the polarity of the central ion mainly because of the partial sharing of its positive charge with the donor groups and possible π -electron delocalization within the whole chelate ring [29]. This chelation increases the lipophilic nature of the central atom which favors its permeation through the lipid layer of the membrane. It has been shown that some substances exhibited extensive biological activities, containing thiazole and azomethine, thiazole and carbazone, azomethine and hydroxylamine, and azomethine and indolinylidene hydrazine groups mentioned in the introduction. Since the compounds studied have similar functional groups with those mentioned above, it is expected to exhibit biological activities. The results show that, unexpectedly, all the ligands and much of the complexes derived from the ligands exhibit no inhibition towards all the microorganisms under the test conditions. One of the ligands, L⁶H, showed weak activity against *Candida albicans*, and one of the complexes,

(L⁵)₂Pd, exhibited very weak activity against *Staphylococcus aureus* and *Proteus vulgaris*. The detailed biological activity data are given in Table 5.

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