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Synthesis, crystal structures and antimicrobial activity of palladium metal complexes of sulfonyl hydrazone ligands

Samina Karimkha Tadavi [1], Ratnamala Subhash Bendre [2], Satish Vittal Patil [3], Shubha Gaguna [4] and Jamatsing Darbarsing Rajput [5,*]

[1] *Department of Chemistry, Jashbhai Muljibhai Patel Arts, Commerce and Science College, Bhandara, Maharashtra, 441904, India*
saminatadavi30@gmail.com (S.K.T.)
[2] *School of Chemical Sciences, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon, Maharashtra, 425001, India*
bendrers@rediffmail.com (R.S.B.)
[3] *School of Life Sciences, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon, Maharashtra, 425001, India*
satish.patil7@gmail.com (S.V.P.)
[4] *Solid State and Structural Chemistry Unit, Indian Institute of Science, Bangalore, 560012, India*
shu.sg13@gmail.com (S.G.)
[5] *Department of Chemistry, Faculty of BP Arts, SMA Science and KKC Commerce College Chalisgaon, Maharashtra, 424101, India*
jamatsingh50@gmail.com (J.D.R.)

* *Corresponding author at: Department of Chemistry, Faculty of BP Arts, SMA Science and KKC Commerce College Chalisgaon, Maharashtra, 424101, India.*
e-mail: jamatsingh50@gmail.com (J.D. Rajput).

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ABSTRACT

Palladium complexes of sulfonyl hydrazone based ligands have been prepared by refluxing with the corresponding ligands and Pd(II) salt in 2:1 ratio. The compounds have been characterized by FT-IR and UV-Vis spectroscopic methods. The crystal structure of the prepared palladium complexes has been determined by single-crystal X-ray crystallographic technique. Crystal data for $C_{40}H_{50}N_4O_6PdS_2$ (PMHT-Pd(II) complex): triclinic, space group *P*-1 (no. 2), a = 7.1561(6) Å, b = 12.1300(11) Å, c = 12.6117(17) Å, α = 63.498(11)°, β = 86.694(9)°, γ = 81.451(7)° and Z = 1. The final R_1 was 0.0699 (I > 2σ(I)) and wR_2 was 0.1834 (all data). Crystal data for $C_{36}H_{42}N_4O_6PdS_2$ (PTHC-Pd(II) complex): monoclinic, space group $P2_1/n$ (no. 14), a = 8.6726(2) Å, b = 20.8824(4) Å, c = 10.3351(2) Å, β = 104.429(2)° and Z = 2. The final R_1 was 0.0344 (I > 2σ(I)) and wR_2 was 0.0840 (all data). Crystal data for $C_{36}H_{42}N_4O_6PdS_2$ (PTHT-Pd(II) complex): monoclinic, space group $P2_1/n$ (no. 14), a = 9.7658(2) Å, b = 10.0488(3) Å, c = 18.7714(4) Å, β = 99.602(2)° and Z = 2. The final R_1 was 0.0334 (I > 2σ(I)) and wR_2 was 0.0832 (all data). Crystal data for $C_{40}H_{50}N_4O_6PdS_2$ (PMHC-Pd(II) complex): triclinic, space group *P*-1 (no. 2), a = 10.2070(9) Å, b = 12.1841(13) Å, c = 16.8879(19) Å, α = 109.005(6)°, β = 90.061(5)°, γ = 99.032(5)° and Z = 2. The final R_1 was 0.0822 (I > 2σ(I)) and wR_2 was 0.2293 (all data). The single-crystal structure data showed a good agreement with the experimental results. The synthesized complexes were screened for their *in vitro* antibacterial activity against one Gram-negative (*Escherichia coli*) and two Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) bacterial strains and for *in vitro* antifungal activity against *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus fumigatus*. The PTHC-Pd(II) complex possesses the nearby significant antifungal activity analogous to the standard drug fluconazole against selected fungal strains *Aspergillus niger*, *Aspergillus Flavus* and *Aspergillus fumigatus* as well as the same complex showed the antibacterial activity for *Staphylococcus aureus* as comparable to standard ofloxacin drug.

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1. Introduction

Sulfonamides and sulfonyl hydrazones have been shown to be active in several pharmacological tests, demonstrating antibacterial, antitumor, diuretic, antiviral, and antinociceptive activities; and specific enzyme inhibition such as carbonic anhydrase, c-secretase HIV protease, metalloproteinase, and hormone regulation among others [1,2]. Although a large number of antimicrobial drugs are existing commercially, the requirement for more effective ones continues to exist, because the most common bacteria are resistant to available drugs [3]. Due to their significant pharmacology applications and widespread use in medicine, these compounds have gained importance in bioinorganic and metal-based drug chemistry [4,5]. To find better compounds, some metal sulphonamides have attracted much attention due to the fact that the complexes showed more activity than both free ligands and the corresponding metallic salts [6]. Some metal sulfonamide complexes have attracted much attention due to the fact that shows greater biological activity than the sulfonamide ligands or metallic salts [7,8].

In our previous studies, we reported a series of novel hydrazone and sulfonyl hydrazine linkages containing carvacrol, thymol, and eugenol derivatives, thereafter anticancer and

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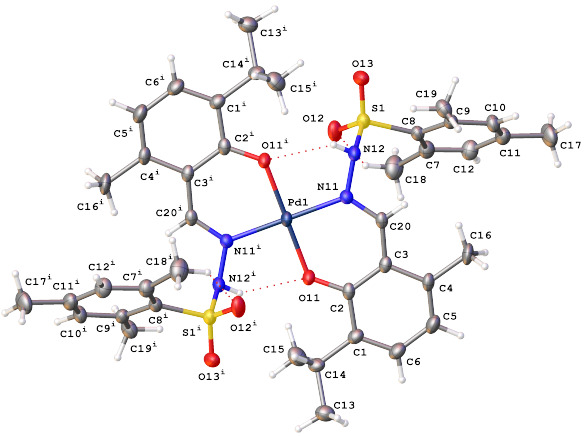


Figure 1. The molecular structure of PMHT-Pd(II) complex with atom numbering scheme.

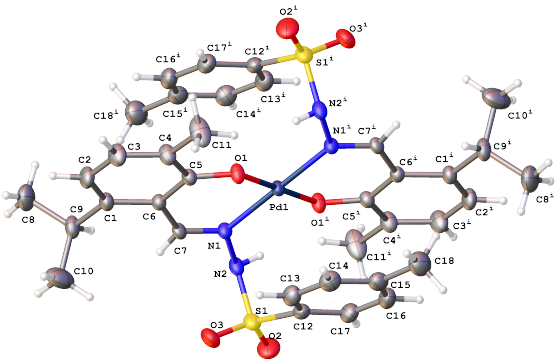


Figure 2. The molecular structure of PTHC-Pd(II) complex with atom numbering scheme.

antioxidant activities were tested using sulforhodamine B (SRB) assay and 2,2-diphenyl-1-picrylhydrazyl free radical scavenging assay (DPPH), respectively. Molecular docking studies of all derivatives against the active site of human Heme oxygenase-1 indicated that interaction with the number of amino acid residues of human Heme oxygenase-1 was crucial for antioxidant activity. In the present study, reporting four palladium(II) complexes of sulfonyl hydrazine derivatives of carvacrol, thymol based nitrogen, and oxygen-containing donor ligands. The sulfonyl hydrazides have explored to synthesize new Schiff bases, as it involves two chemical parts as well as biological key moieties viz. sulfonyl groups and hydrazines and have a connection with some other important chemical classes; sulfonamides (O2S-N) and azomethines (C=N) [9]. The structures of all synthesized palladium(II) complexes have been examined using FT-IR and UV-Vis spectrophotometric methods and finalized by single-crystal X-ray crystallographic technique. The synthesized complexes were screened for their *in vitro* antibacterial activity against one Gram-negative (*Escherichia coli*) and two Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) bacterial strains and for *in vitro* antifungal activity against *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus fumigatus*.

2. Experimental

2.1. Materials and methods

All solvents and palladium metal salt were purchased from Aldrich and used without further purification. FT-IR spectra were recorded as KBr pellets on a Shimadzu FT-IR-8400 spectrometer. The electronic spectra were recorded as DMF solution on the Shimadzu UV-2400 series spectrophotometer.

2.2. Single-crystal X-ray diffraction data collection

The crystals of PMHC-Pd(II) complex were grown by slow evaporation of chloroform solvent by dissolving 0.5 g of the compound at 7-10 °C. The X-ray single crystal diffraction data were recorded on a Bruker APEX II κ-CCD diffractometer. A suitable crystal was selected and mounted on a Bruker APEX-II CCD diffractometer. The data were collected with MoKα (λ = 0.71073 Å) radiation for PMHC-Pd(II) complex. The cell refinement and data reduction were performed using APEX2/SAINT [10] and SAINT/XPREP [11], respectively. The structure has solved by using SHELXS [12] and refined by SHELXL [13]. The suitable crystals of PMHT-Pd(II), PTHC-Pd(II), and PTHT-Pd(II) for X-ray crystallography analysis were obtained by slow evaporation of chloroform at room temperature. The X-ray single crystal diffraction data were recorded on an Oxford Xcalibur Eos (Nova) CCD diffractometer using MoKα radiation (λ = 0.71073 Å). A suitable crystal was selected and mounted on the diffractometer. The structures are solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELXT software package [14]. All geometrical data were calculated using PLATON [15]. Molecular structure and packing diagrams were generated using OLEX2 and MERCURY, respectively [16,17]. The molecular structure of the complexes with the atomic numbering scheme is shown in Figures 1-4. The crystallographic parameters, data collection, and refinement data for the complexes are given in Table 1. The bond lengths, bond angles, and hydrogen bonds for all complexes are given in Tables 2-4, respectively.

Table 1. Crystal data and structure refinement for palladium complexes.

Compound	PMHT-Pd(II) complex	PTHC-Pd(II) complex	PTHT-Pd(II) complex	PMHC-Pd(II) complex
CCDC	1887978	1887979	1887980	1888204
Empirical formula	$C_{40}H_{50}N_4O_6PdS_2$	$C_{36}H_{42}N_4O_6PdS_2$	$C_{36}H_{42}N_4O_6PdS_2$	$C_{40}H_{50}N_4O_6PdS_2$
Formula weight	853.36	797.25	797.25	853.36
Temperature (K)	298.15	293(2)	293(2)	293(2)
Crystal system	Triclinic	Monoclinic	Monoclinic	Triclinic
Space group	P-1	$P2_1/n$	$P2_1/n$	P-1
a (Å)	7.1561(6)	8.6726(2)	9.7658(2)	10.2070(9)
b (Å)	12.1300(11)	20.8824(4)	10.0488(3)	12.1841(13)
c (Å)	12.6117(17)	10.3351(2)	18.7714(4)	16.8879(19)
α (°)	63.498(11)	90	90	109.005(6)
β (°)	86.694(9)	104.429(2)	99.602(2)	90.061(5)
γ (°)	81.451(7)	90	90	99.032(5)
Volume (Å^3)	968.8(2)	1812.70(7)	1816.32(8)	1958.1(4)
Z	1	2	2	2
ρ_{calc} (g/cm^3)	1.463	1.461	1.458	1.447
μ (mm^{-1})	0.639	0.677	0.676	0.632
F(000)	444.0	824.0	824.0	888.0
Crystal size (mm^3)	0.25 × 0.2 × 0.2	0.25 × 0.2 × 0.2	0.25 × 0.2 × 0.2	0.25 × 0.2 × 0.2
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection (°)	6.798 to 52.734	6.744 to 52.724	6.894 to 52.744	4.046 to 49.998
Index ranges	$-8 \le h \le 8$	$-10 \le h \le 10$	$-12 \le h \le 12$	$-12 \le h \le 12$
	$-14 \le k \le 15$	$-26 \le k \le 26$	$-12 \le k \le 12$	$-14 \le k \le 14$
	$-15 \le l \le 15$	$-12 \le l \le 12$	$-23 \le l \le 23$	$-20 \le l \le 20$
Reflections collected	11772	30464	22204	27355
Independent reflections	3939 [R_{sigma} = 0.0913]	3695 [R_{sigma} = 0.0246]	3714 [R_{sigma} = 0.0312]	27355 [R_{sigma} = 0.1141]
Data/restraints/parameters	3939/0/249	3695/0/231	3714/0/235	27355/57/527
Goodness-of-fit on F^2	1.057	1.093	1.055	1.046
Final R indexes [I≥2σ (I)]	R_1 = 0.0699	R_1 = 0.0344	R_1 = 0.0334	R_1 = 0.0822
	wR_2 = 0.1623	wR_2 = 0.0809	wR_2 = 0.0788	wR_2 = 0.1942
Final R indexes [all data]	R_1 = 0.1022	R_1 = 0.0394	R_1 = 0.0409	R_1 = 0.1278
	wR_2 = 0.1834	wR_2 = 0.0840	wR_2 = 0.0832	wR_2 = 0.2293
Largest diff. peak/hole (e Å^{-3})	1.45/-1.13	0.41/-0.26	0.42/-0.27	1.72/-2.30

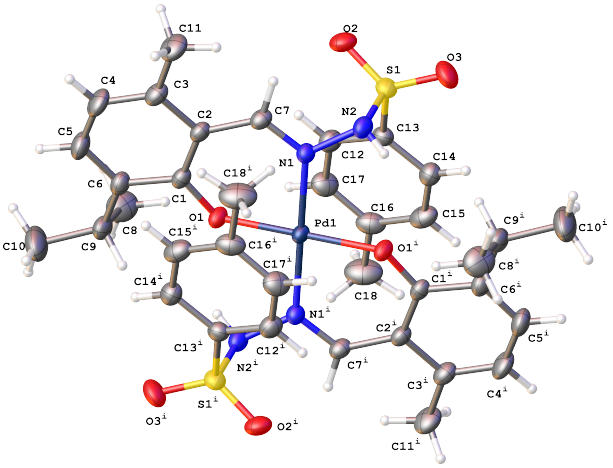


Figure 3. The molecular structure of PTHT-Pd(II) complex with atom numbering scheme.

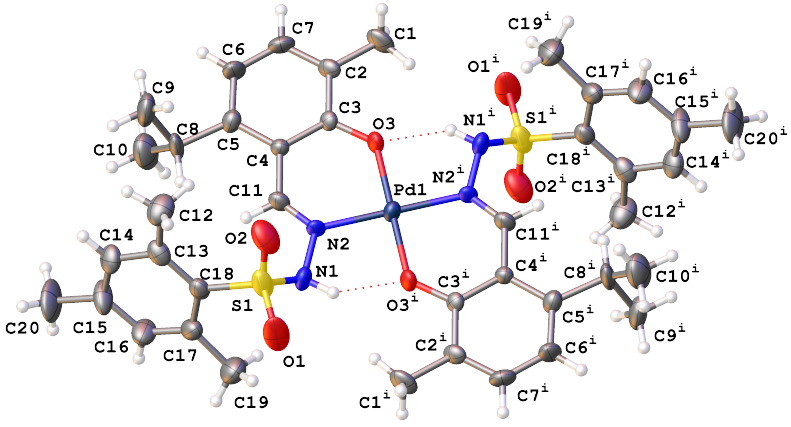


Figure 4. The molecular structure of PMHC-Pd(II) complex with atom numbering scheme.

Table 2. Bond lengths for palladium complexes.

Atom	Atom	Length (Å)	Atom	Atom	Length (Å)	Atom	Atom	Length (Å)	Atom	Atom	Length (Å)
PMHT-Pd(II) complex											
Pd1	O11[1]	1.988(4)	O11	C2	1.310(6)	C3	C2	1.433(8)	C14	C15	1.517(9)
Pd1	O11	1.988(4)	N11	C20	1.312(7)	C4	C5	1.362(8)	C5	C6	1.394(9)
Pd1	N11[1]	2.001(4)	N11	N12	1.416(7)	C4	C16	1.515(8)	C8	C7	1.415(8)
Pd1	N11	2.001(4)	C20	C3	1.425(8)	C2	C1	1.440(8)	C10	C11	1.379(9)
S1	N12	1.690(5)	C9	C8	1.403(8)	C1	C14	1.521(8)	C7	C12	1.393(8)
S1	O13	1.442(5)	C9	C10	1.390(8)	C1	C6	1.368(8)	C7	C18	1.516(9)
S1	O12	1.423(5)	C9	C19	1.518(8)	C14	C13	1.525(8)	C12	C11	1.374(9)
S1	C8	1.783(6)	C3	C4	1.443(8)						
PTHC-Pd(II) complex											
Pd1	O1	1.9811(16)	O1	C5	1.319(3)	C1	C9	1.519(4)	C15	C16	1.375(5)
Pd1	O1[2]	1.9810(16)	N1	C7	1.299(3)	C1	C2	1.368(4)	C15	C18	1.505(5)
Pd1	N1[2]	1.9809(19)	N1	N2	1.427(3)	C9	C8	1.521(4)	C15	C14	1.385(4)
Pd1	N1	1.9809(19)	C6	C7	1.431(3)	C9	C10	1.498(5)	C12	C13	1.382(4)
S1	N2	1.684(3)	C6	C5	1.418(3)	C4	C3	1.368(4)	C12	C17	1.387(4)
S1	O3	1.427(2)	C6	C1	1.431(3)	C4	C11	1.506(4)	C13	C14	1.376(4)
S1	O2	1.427(2)	C5	C4	1.415(4)	C2	C3	1.401(4)	C16	C17	1.386(4)
S1	C12	1.757(3)									
PTHT-Pd(II) complex											
S1	O3	1.423(2)	O1	C1	1.320(3)	C1	C2	1.425(4)	C12	C17	1.376(4)
S1	O2	1.423(2)	N1	N2	1.421(3)	C6	C5	1.379(4)	C5	C4	1.392(4)
S1	C13	1.745(3)	N1	C7	1.298(3)	C6	C9	1.511(4)	C15	C16	1.388(4)
S1	N2	1.689(3)	C13	C14	1.384(4)	C2	C7	1.419(4)	C17	C16	1.380(4)
Pd1	O1	1.9745(17)	C13	C12	1.383(4)	C2	C3	1.434(4)	C9	C8	1.523(5)
Pd1	O1[3]	1.9745(17)	C14	C15	1.370(4)	C3	C4	1.353(4)	C9	C10	1.524(4)
Pd1	N1	1.980(2)	C1	C6	1.419(3)	C3	C11	1.503(4)	C16	C18	1.501(4)
Pd1	N1[3]	1.980(2)									
PMHC-Pd(II) complex											
C1	C2	1.490(14)	C12	C13	1.477(15)	N1	S1	1.661(10)	Pd1	N2[4]	1.976(8)
C2	C3	1.415(13)	C13	C14	1.404(14)	N2	Pd1	1.976(8)	Pd1	O3[4]	1.964(7)
C2	C7	1.376(14)	C13	C18	1.402(15)	N3	S2	1.666(9)	Pd2	N4[5]	1.969(8)
C3	C4	1.425(13)	C14	C15	1.368(16)	N4	Pd2	1.969(8)	Pd2	O6[5]	1.958(7)
C3	O3	1.323(11)	C15	C16	1.381(16)	O3	Pd1	1.964(7)	C8	C9	1.62(3)
C4	C5	1.423(13)	C15	C20	1.522(15)	O4	S2	1.446(9)	C8	C10	1.46(2)
C4	C11	1.464(13)	C16	C17	1.367(15)	O5	S2	1.401(8)	C8	C9'	1.47(2)
C5	C6	1.376(14)	C17	C18	1.406(15)	N1	N2	1.408(12)	C8	C10'	1.57(3)
C5	C8	1.536(14)	C17	C19	1.515(15)	C11	N2	1.233(11)	S1	O2	1.423(9)
C6	C7	1.376(15)	C18	S1	1.781(11)	O6	Pd2	1.958(7)	S1	O1	1.442(8)

[1] -*x*, 1-*y*, -*z*, [2] 1-*x*, -*y*, -*z*, [3] -*x*, 1-*y*, -*z*, [4] 2-*x*, -*y*, -*z*; [5] 1-*x*, -*y*, 1-*z*.

2.3. Synthesis of ligands

The synthesis of sulfonyl hydrazone based ligands was prepared by multistep process reaction. In the first step, the synthesis of ortho formyl phenolic monoterpenoids (ortho formyl thymol (2-hydroxy-3-isopropyl-6-methylbenzaldehyde) or ortho formyl carvacrol (2-hydroxy-6-isopropyl-3-methyl-benzaldehyde)) was carried out using a previously reported method [18-20]. In the second step, synthesis of substituted sulfonyl hydrazides (2,4,6-trimethylbenzenesulfonohydrazide and 4-methylbenzenesulfonohydrazide) [19] was carried out in which hydrazine hydrate (0.25 mol, 2.5 equiv.) was added dropwise to a solution of 4-methylbenzene-1-sulfonylchloride or 2,4,6-trimethyl benzene sulfonyl chloride (0.1 mol, 1 equiv..) in THF (100 mL) at 0 °C under inert atmosphere. After stirring for 0 to 5 °C for 30 min, ice-cold ethyl acetate (200 mL) was added to the cooled reaction mixture and the mixture was washed repeatedly with ice-cold 10% aqueous sodium chloride (5 × 150 mL). The organic layer was dried over sodium sulphate at 0 °C, and was then added slowly to a stirring solution of hexane (1.2 L) during 5 min. Substituted benzene sulfonyl hydrazide precipitated as a white solid and was collected by vacuum filtration. The filter cake was washed with hexane (2 × 50 mL) and then dried in vacuo, yielding the substituted sulfonyl hydrazides compound as a white solid. In the third step, the synthesis of phenolic monoterpenoid-based sulfonyl hydrazones [21] was carried out, in which the hydrazone derivatives (*N*'-(2-hydroxy-6-isopropyl-3-methylbenzylidene)-4-methylbenzenesulfonohydrazide (PTHC), *N*'-(2-hydroxy-3-isopropyl-6-methylbenzylidene)-4-methylbenzenesulfonohyd razide (PTHT), *N*'-(2-hydroxy-6-isopropyl-3-methylbenzylide ne)-2, 4, 6-trimethylbenzenesulfonohydrazide (PMHC), *N*'-(2-hydroxy-3-isopropyl-6-methylbenzylidene)-2, 4, 6-trimethyl benzenesulfonohydrazide (PMHT)) were prepared by the reaction of equimolar quantities of substituted benzene sulfonyl hydrazide and ortho formyl thymol or ortho formyl carvacrol. Each reactant was dissolved in a minimum amount of ethanol, and then they were mixed, adding 2-3 drops of acetic acid. The reaction mixture was refluxed for 2 h, then cooled to room temperature and poured into ice-cold water. The solid product obtained was collected by filtration and then dried in a drying oven at 70 °C. The product was crystallized from ethanol and dried to obtain the pure product [21].

2.4. Common procedure for the synthesis of sulfonyl hydrazone based on palladium metal complexes

The complexes were prepared by a general procedure, palladium(II) chloride solution in 0.1 M (1 mmol) taken and treated with an equal volume of water. The hot methanolic solution of ligand (2 mmol) was added drop by drop to the hot palladium(II) chloride solution. The reaction mixture was stirred at room temperature for 30 min and then continued with constant reflux for 5 h. The green-coloured precipitated products were collected, washed for several times with water and cold methanol to remove impurities, and dried at room temperature (Scheme 1] [22].

2.5. Antimicrobial activity

The agar well diffusion method was used for the determination of antimicrobial activity of the synthesized compounds against three fungal and three bacterial strains. The fungal strains *Aspergillus niger* (ATCC 6275), *Aspergillus flavus* (ATCC 6202), *Aspergillus fumigates* (ATCC 36606), and bacterial strains *Escherichia coli* (ATCC 35218), *Staphylococcus aureus* (ATCC 25923), *Bacillus subtilis* (ATCC 23857) were obtained from the National Chemical Laboratory, Pune, India.

Table 3. Bond angles for palladium complexes.

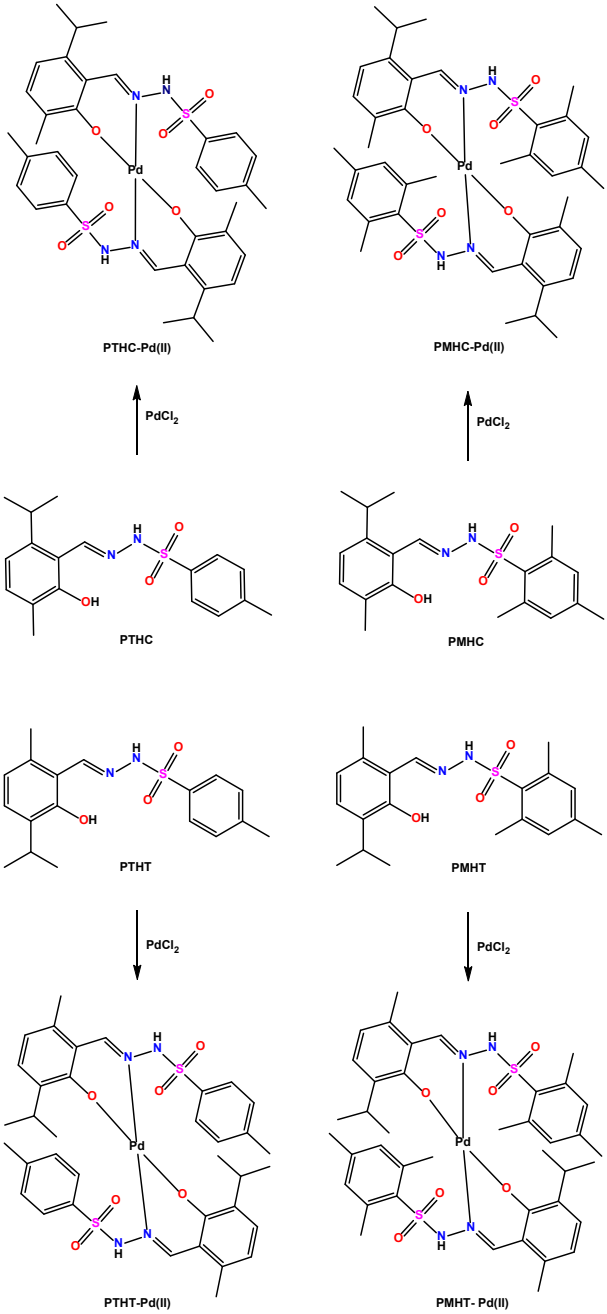
Atom	Atom	Atom	Angle (°)	Atom	Atom	Atom	Angle (°)	Atom	Atom	Atom	Angle (°)
PMHT-Pd(II) complex											
O11[1]	Pd1	O11	180.0(3)	C5	C4	C3	118.1(5)	C1	C14	C13	114.3(5)
O11[1]	Pd1	N11	88.72(16)	C5	C4	C16	120.5(5)	C15	C14	C1	110.9(5)
O11[1]	Pd1	N11[1]	91.28(16)	O11	C2	C3	123.9(5)	C15	C14	C13	110.7(5)
O11	Pd1	N11[1]	88.72(16)	O11	C2	C1	117.2(5)	C4	C5	C6	121.7(6)
O11	Pd1	N11	91.28(16)	C3	C2	C1	118.8(5)	C9	C8	S1	118.3(4)
N11	Pd1	N11[1]	180.0	C2	C1	C14	118.6(5)	C9	C8	C7	121.4(5)
N12	S1	C8	103.4(3)	C6	C1	C2	118.0(6)	C7	C8	S1	119.8(5)
O13	S1	N12	102.9(3)	C6	C1	C14	123.4(6)	C11	C10	C9	121.7(6)
O13	S1	C8	110.1(3)	N11	C20	C3	127.6(5)	C1	C6	C5	123.0(6)
O12	S1	N12	110.9(3)	N11	N12	S1	113.5(4)	C8	C7	C18	126.3(6)
O12	S1	O13	118.1(3)	C8	C9	C19	124.3(5)	C12	C7	C8	116.7(6)
O12	S1	C8	110.2(3)	C10	C9	C8	118.1(5)	C12	C7	C18	117.0(6)
C2	O11	Pd1	128.7(4)	C10	C9	C19	117.5(5)	C11	C12	C7	122.9(6)
C20	N11	Pd1	125.2(4)	C20	C3	C4	116.6(5)	C10	C11	C17	121.0(6)
C20	N11	N12	113.5(5)	C20	C3	C2	123.2(5)	C12	C11	C10	118.9(6)
N12	N11	Pd1	121.3(3)	C2	C3	C4	120.2(5)	C12	C11	C17	120.2(6)
C3	C4	C16	121.4(6)								
PTHC-Pd(II) complex											
O1[1]	Pd1	O1	180.0	C4	C5	C6	119.4(2)	C10	C9	C8	111.2(3)
N1	Pd1	O1	90.24(8)	C6	C1	C9	121.9(2)	C5	C4	C11	119.0(2)
N1[1]	Pd1	O1[2]	90.24(8)	C2	C1	C6	118.7(2)	C3	C4	C5	119.2(3)
N1	Pd1	O1[2]	89.76(8)	C2	C1	C9	119.3(2)	C3	C4	C11	121.8(3)
N1[1]	Pd1	O1	89.76(8)	C1	C9	C8	113.6(3)	C1	C2	C3	121.1(3)
N1[1]	Pd1	N1	180.0	C10	C9	C1	110.9(3)	C16	C15	C18	120.7(3)
N2	S1	C12	106.31(12)	C7	C6	C1	118.3(2)	C16	C15	C14	118.5(3)
O3	S1	N2	105.46(13)	C5	C6	C7	121.8(2)	C14	C15	C18	120.8(3)
O3	S1	C12	108.96(15)	C5	C6	C1	119.8(2)	C13	C12	S1	119.4(2)
O2	S1	N2	103.41(15)	N1	C7	C6	126.2(2)	C13	C12	C17	120.3(3)
O2	S1	O3	121.18(15)	N1	N2	S1	113.82(17)	C17	C12	S1	119.8(2)
O2	S1	C12	110.31(15)	O1	C5	C6	125.0(2)	C4	C3	C2	121.6(3)
C5	O1	Pd1	125.76(15)	O1	C5	C4	115.6(2)	C14	C13	C12	119.9(3)
C7	N1	Pd1	126.01(17)	N2	N1	Pd1	119.16(15)	C15	C16	C17	121.9(3)
C7	N1	N2	114.8(2)	C13	C14	C15	120.9(3)	C16	C17	C12	118.6(3)
PTHT-Pd(II) complex											
O3	S1	C13	110.00(13)	N1	N2	S1	112.72(17)	C7	C2	C3	117.6(2)
O3	S1	N2	103.53(13)	C1	C6	C9	119.0(2)	N1	C7	C2	125.6(3)
O2	S1	O3	121.67(13)	C5	C6	C1	117.5(3)	C2	C3	C11	121.6(3)
O2	S1	C13	108.95(13)	C5	C6	C9	123.4(2)	C4	C3	C2	118.5(3)
O2	S1	N2	105.22(13)	C1	C2	C3	119.5(2)	C4	C3	C11	119.9(3)
N2	S1	C13	106.23(12)	C7	C2	C1	122.8(2)	C17	C12	C13	119.8(3)
O1	Pd1	O1[3]	180.0	C14	C13	S1	120.2(2)	C6	C5	C4	122.5(3)
O1	Pd1	N1	89.90(8)	C12	C13	S1	119.4(2)	C14	C15	C16	121.6(3)
O1[1]	Pd1	N1[3]	89.90(8)	C12	C13	C14	120.0(3)	C12	C17	C16	121.0(3)
O1[1]	Pd1	N1	90.10(8)	C15	C14	C13	119.3(3)	C6	C9	C8	110.4(3)
O1	Pd1	N1[3]	90.10(8)	O1	C1	C6	116.2(2)	C6	C9	C10	114.0(3)
N1	Pd1	N1[3]	180.0	O1	C1	C2	123.8(2)	C8	C9	C10	111.3(3)
C1	O1	Pd1	126.22(16)	C6	C1	C2	120.0(2)	C3	C4	C5	121.7(3)
N2	N1	Pd1	118.84(15)	C7	N1	N2	114.9(2)	C15	C16	C18	121.0(3)
C7	N1	Pd1	126.16(19)	C17	C16	C18	120.7(3)	C17	C16	C15	118.3(3)
PMHC-Pd(II) complex											
C3	C2	C1	120.2(9)	C18	C13	C14	116.4(10)	N2[1]	Pd1	N2	180.0
C7	C2	C1	121.7(10)	C15	C14	C13	122.6(11)	O3	Pd1	N2	91.2(3)
C7	C2	C3	118.0(10)	C14	C15	C16	118.4(11)	O3	Pd1	N2[4]	88.8(3)
C2	C3	C4	120.5(9)	C14	C15	C20	120.8(12)	O3[1]	Pd1	N2[4]	91.2(3)
O3	C3	C2	116.0(9)	C16	C15	C20	120.7(12)	O3[1]	Pd1	N2	88.8(3)
O3	C3	C4	123.5(9)	C17	C16	C15	122.8(11)	O3	Pd1	O3[4]	180.0
C3	C4	C5	119.3(9)	C16	C17	C18	117.6(10)	C5	C8	C9	104.8(15)
C3	C4	C11	120.5(9)	C18	C17	C19	124.7(11)	C5	C8	C10'	108.0(16)
C5	C4	C11	120.2(9)	C13	C18	C17	122.1(10)	C10	C8	C5	115.9(16)
C4	C5	C8	124.7(9)	C13	C18	S1	120.1(9)	C10	C8	C9	111.9(18)
C6	C5	C4	118.0(10)	C17	C18	S1	117.8(9)	C9'	C8	C5	120.6(17)
C6	C5	C8	117.2(9)	N2	N1	S1	119.8(7)	C9'	C8	C10'	113(2)
C5	C6	C7	122.3(10)	C11	N2	N1	117.4(9)	N1	S1	C18	102.8(5)
C2	C7	C6	121.8(10)	C11	N2	Pd1	125.5(7)	O2	S1	C18	110.7(5)
N2	C11	C4	129.7(10)	N1	N2	Pd1	116.6(6)	O2	S1	N1	110.1(5)
C14	C13	C12	115.9(10)	O1	S1	N1	103.4(5)	O2	S1	O1	119.3(6)
C18	C13	C12	127.7(10)	C3	O3	Pd1	128.8(6)	O1	S1	C18	109.2(5)

[1] *-x, 1-y, -z,* [2] 1-*x, -y, -z,* [3] *-x,* 1-*y, -z,* [4] 2-*x, -y, -z.*

Standard solutions of antifungal (Fluconazole, 25 mg/mL) and antibacterial (Ofloxacin, 25 mg/mL) agents were taken as positive control and the negative control used as DMSO. All synthesized complexes were dissolved to prepare stock solutions of 25 mg/mL in DMSO. The bacterial strain culture and fungal spore suspension were adjusted to give a final concentration of 10^7 cfu/mL. About 25 mL of media (Potato Dextrose Agar) was poured into Petri plates and inoculated with the respective test organisms. Wells 6 mm in diameter were made with a borer in solid agar and loaded with 40 µL of the test compounds. All fungal and bacterial strains were incubated at 28 °C. The average diameter of the inhibition zone surrounding the wells was measured in mm (Tables 5 and 6) [19,23].

Table 4. Hydrogen bonding for palladium complexes.

D-H...A	d(D-H)	d(H...A)	d(D...A)	∠(DHA)	Symmetry
PMHT-Pd(II) complex					
N(12)-H(12)...O(11)	0.74(8)	2.24(7)	2.803(7)	134(7)	-*x*, 1-*y*, -*z*
C(15)-H(15C)...O(11)	0.96	2.57	3.126(8)	117	
C(18)-H(18A)...O(12)	0.96	1.92	2.722(10)	139	
C(19)-H(19A)...O(13)	0.96	2.40	3.026(9)	122	
PTHC-Pd(II) complex					
N(2)-H(2)...O(1)	0.79(3)	2.20(3)	2.818(3)	136(3)	1-*x*, -*y*, -*z*
C(11)-H(11A)...O(1)	0.96	2.24	2.718(4)	109	
PTHT-Pd(II) complex					
N(2)-H(2)...O(1)	0.76(3)	2.24(3)	2.833(3)	136(3)	-*x*, 1-*y*, -*z*
C(8)-H(8B)...O(1)	0.96	2.58	3.121(4)	116	
C(12)-H(12)...O(2)	0.93	2.59	2.941(4)	103	
PMHC-Pd(II) complex					
C(39)-H(39A)...O(4)	0.96	1.90	2.724(15)	142.8	
N(1)-H(1)...O(3)	0.85(4)	1.93(8)	2.660(11)	142(10)	2-*x*, -*y*, -*z*
N(3)-H(3)...O(6)	0.84(4)	1.90(6)	2.675(10)	152(10)	1-*x*, -*y*, 1-*z*



Scheme 1. Reaction scheme for the synthesis of palladium(II) complexes.

Table 5. Comparison of zone of inhibition values (in mm) of palladium(II) complexes and standard drug against different antibacterial strains *.

Compound	*E. coli*	*S. aureus*	*B. subtilis*
PMHC-Pd(II)	10	6	10
PMHT-Pd(II)	8	12	8
PTHC-Pd(II)	10	16	12
PTHT-Pd(II)	6	4	4
Ofloxacin	30	30	32

* Concentration in 25 mg/mL.

Table 6. Comparison of the zone of inhibition values (in mm) of palladium(II) complexes and standard drug against different fungal strains *.

Compound	*A. niger*	*A. flavus*	*A. fumigatus*
PMHC-Pd(II)	12	16	10
PMHT-Pd(II)	10	14	12
PTHC-Pd(II)	32	30	32
PTHT-Pd(II)	26	24	26
Fluconazole	36	38	36

* Concentration in 25 mg/mL.

3. Results and discussion

3.1. Synthesis and characterization

The palladium(II) complexes synthesized by the reaction of $PdCl_2$ salt and ligand in a 1:2 molar ratio. The complexes are less soluble in common organic solvents, like alcohols, acetonitrile, hexane, acetone, and soluble in DMF and chloroform. In the UV-visible spectra, the Pd(II) complexes showed a broad *d-d* transition band near 450-438 nm assignable to $^1A1g \rightarrow {}^1B1g$ transition for square planar. A relatively strong charge transfer band has been observed in the spectra of all Pd(II) complexes in the region 309-280 nm [24]. The IR spectra of the complexes are related with those of the free ligands to define the coordination sites that may get involved in chelation. The absence of ν(OH) in the IR spectrum of the complex confirms that the ligands are coordinated in its deprotonated form. The very strong C=N stretch for free ligands around 1615-1630 cm^{-1}, shifted to lower frequency upon coordination of azomethine, in good agreement with data described previously for the related Pd(II) complexes. Another two strong bands at 1585 and 1445 cm^{-1} compared to the theoretical bands of 1595 and 1500 cm^{-1}, are because of ν(C=C) and a mixture of ν(C=C) and ν(C=N), respectively. The $Pd(N_2O_2)$ exhibits a band at 3080 cm^{-1} due to CH stretch of aromatic rings and the calculated values are 3017-3093 cm^{-1}. The ligands coordinate through nitrogen's of C=N group and the oxygen's of C–O is further supported by the appearance of a lower-intensity band in 530-503 cm^{-1} [25-28].

3.2. X-ray crystallographic analysis

The single-crystal X-ray crystallographic studies of all complexes are agreed well with the proposed structure of the complexes. The presented structures illustrate that the complexes are formed by the deprotonation of tetradentate sulfonyl hydrazone based ligands (Figures 1-4). The crystal structures indicate that two nitrogen and two oxygen atoms are coordinated to the central palladium ion after elimination of two hydrogens from the ligands and all palladium ions lie on an inversion center and adopt a slightly distorted square planar geometry while the bond lengths and bond angles have to fall within the expected range comparable to reported values [29]. All the structures of complexes adopt the *trans* configuration with two attached ligands with palladium(II) ion.

Pd-O [1.988(4), 1.9811(16), 1.9745(17), 1.964(7) Å] and Pd-N [2.001(4), 1.9809(19), 1.980(2), 1.976(8) Å] bond lengths for all complexes are in the expected ranges [26]. The C-O bond lengths are C(2)-O(11) 1.310(6), C(5)-O(1) 1.319(3), C(1)-O(1) 1.320(3), C(3)-O(3) 1.323(11) Å for PMHT-Pd(II), PTHC-Pd(II), PTHT-Pd(II) and PMHC-Pd(II) complexes, respectively, are longer than the C=O bond distance (1.221 Å) and slightly shorter than the C-O bond distance (1.362 Å) [30]. This indicates the existence of electron delocalization over the six-member chelate rings (Pd-O-C-C-C-N) due to the coordination of the oxygen and nitrogen atoms with the palladium(II) ion.

In the case of PTHC-Pd(II) and PTHT-Pd(II) complexes, the Pd-N distances for both complexes are 1.9809(19) and 1.980(2) Å which are next to the sum of the covalent radii in ranges of palladium and nitrogen and these confirm signifying strong coordination through the azomethine nitrogen [31]. The values for C=N 1.299(1) Å, C-O 1.319(1) Å, N-N 1.427(6) Å, and S-O 1.427(2) Å for both complexes are near about same. The O-Pd-O and N-Pd-N angles for both complex (PTHC-Pd(II): O(1)-Pd(1)-O(1)^i (^{i} 1-*x*, -*y*, -*z*), N(1)-Pd(1)-N(1)^i (^{i} 1-*x*, -*y*, -*z*) and PTHT-Pd(II): O(1)-Pd(1)-O(1)^{ii} (^{ii} -*x*, 1-*y*, -*z*), N(1)-Pd(1)-N(1)^{ii} (^{i} -*x*, 1-*y*, -*z*)) are 180°. The torsion angles for both complexes are near close in the series. Both the complexes show the N-H···O and C-H···O type intramolecular hydrogen bonding.

In PMHC-Pd(II) and PMHT-Pd(II) complexes, the Pd-N distances are Pd(1)-(N2) 1.976(8) Å and Pd(1)-N(11) 2.001(4) Å, respectively, and the Pd-O bond distances are Pd(1)-O(3) 1.964(7) Å and Pd(1)-O(11) 1.988(4) Å, respectively. Similarly, the C=N double bond distance of C(11)-N(2) and N(11)-C(20) are 1.233(11) and 1.312(7) Å for PMHT-Pd(II) and PMHC-Pd(II) complexes, respectively. The phenolic single bond C-O distances are C(2)-O(11) 1.310(6) Å, and C(3)-O(3) 1.323(11) Å for PMHC-Pd(II) and PMHT-Pd(II) complexes, respectively. The N-N bond length values are N(11)-N(12) 1.416(7) Å and N(1)-N(2) 1.408(12) Å for PMHC-Pd(II) and PMHT-Pd(II) complexes, respectively. The S-O bond lengths for both complexes are near about 1.42(2) Å. The bite angles for both complex O(11)-Pd(1)-N(11) and O(3)-Pd(1)-N(2) are 91.28(16)° and 91.2(3)° for PMHT-Pd(II) and PMHC-Pd(II) complexes, respectively, so the bite angles of the complex deviate slightly from the ideal angle 90°. The PMHC-Pd(II) and PMHT-Pd(II) complexes show the N-H···O and C-H···O type molecular hydrogen bonding [22,32].

3.3. Antimicrobial activity

The PTHC-Pd(II) and PTHT-Pd(II) complexes showed the highest antifungal activity than PMHC-Pd(II) and PMHT-Pd(II) complexes (Table 5). The PTHC-Pd(II) complex possesses the very close significant activity comparable to the standard drug fluconazole against the fungal strains *Aspergillus niger*, *Aspergillus flavus*, and *Aspergillus fumigatus*. Such enhanced activity of metal chelates can be described based on the overtone concept and chelation theory. The chelation considerably decreases the polarity of the metal ion because of the partial sharing of its positive charge with donor groups and possible π-electron delocalization over the whole chelate ring. Such chelation could enhance the lipophilic character of the central metal atom, which subsequently favours its permeation through the lipid layer of the cell membrane. The antibacterial activity of all complexes was investigated by screening them against the Gram-negative *Escherichia coli* and Gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis* by agar well

diffusion technique (Table 4). The results showed that all complexes possess lesser antibacterial activity. The PTHC-Pd(II) complex showed antibacterial activity for Gram-positive *Staphylococcus aureus* as comparable to ofloxacin as a standard drug. The low activity of the compound is attributed to its low cell permeability, the suitability of the particle size of the metal ion, and the bulkier organic moieties [26,33,34].

4. Conclusions

The present work has shown the successful synthesis and spectroscopic characterization of the Pd(II) complex of sulfonyl hydrazone-based ligands which acts as a bidentate ligand. Single-crystal X-ray diffraction technique has shown the possibilities of hydrogen bonding and intermolecular interaction and it proves the good agreement with experimental synthesis and coordination sites. Antifungal activity results show that PTHC-Pd(II) complex possesses better activity comparable to the standard drug fluconazole against all selected fungal strains and makes it a good drug.

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Supporting information

CCDC-1888204, 1887978, 1887979 and 1887980 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or by e-mailing data request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Disclosure statement

Conflict of interest: The authors declare that they have no conflict of interest.
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ORCID

Samina Karimkha Tadavi
http://orcid.org/0000-0002-2772-0329
Ratnamala Subhash Bendre
http://orcid.org/0000-0002-2699-4096
Satish Vittal Patil
http://orcid.org/0000-0001-6167-2511
Shubha Gaguna
http://orcid.org/0000-0001-7112-958X
Jamatsing Darbarsing Rajput
http://orcid.org/0000-0002-4588-1345

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