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Ruthenium(II) carbonyl complexes of dehydroacetic acid thiosemicarbazone: Synthesis, structure, light emission and biological activity

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ABSTRACT

The reaction of $[RuHCl(CO)(B)(EPh_3)_2]$ (where E = As, B = $AsPh_3$; E = P, B = PPh_3, py, pip, or mor) and dehydroacetic acid thiosemicarbazone (abbreviated as H_2dhatsc where H_2 stands for the two dissociable protons) in benzene under reflux afford a series of new ruthenium(II) carbonyl complexes containing dehydroacetic acid thiosemicarbazone of general formula $[Ru(dhatsc)(CO)(B)(EPh_3)]$ (where E = As, B = $AsPh_3$; E = P, B = PPh_3, py, pip or mor; dhatsc = dibasic tridentate dehydroacetic acid thiosemicarbazone). All the complexes have been characterized by elemental analyses, FT-IR, UV–Vis, and ^{1}H NMR spectral methods. The thiosemicarbazone of dehydroacetic acid behaves as dianionic tridentate O, N, S donor and coordinates to ruthenium via phenolic oxygen of dehydroacetic acid, the imine nitrogen of thiosemicarbazone and thiol sulfur. In chloroform solution, all the complexes exhibit metal-to-ligand charge transfer transitions (MLCT). The crystal structure of one of the complexes $[Ru(dhatsc)(CO)(PPh_3)_2]$ (**1**) has been determined by single crystal X-ray diffraction which reveals the presence of a distorted octahedral geometry in the complexes. All the complexes exhibit an irreversible oxidation (Ru^{III}/Ru^{II}) in the range 0.76–0.89 V and an irreversible reduction (Ru^{II}/Ru^{I}) in the range −0.87 to −0.97 V. Further, the free ligand and its ruthenium complexes have been screened for their antibacterial and antifungal activities. The complexes show better activity in inhibiting the growth of bacteria *Staphylococcus aureus* and *Escherichia coli* and fungus *Candida albicans* and *Aspergillus niger*. These results made it desirable to delineate a comparison between free ligand and its ruthenium complexes.

1. Introduction

Derivatives of semicarbazones and thiosemicarbazones are amongst the most widely studied nitrogen and oxygen/sulphur donor ligands [1–4]. Particularly, thiosemicarbazones have emerged as an important class of sulphur donor ligands for transition metal ions because of their mixed hard–soft donor character and versatile coordination behaviour. In particular, transition metal complexes of thiosemicarbazones have been receiving considerable interest largely because of their pharmacological property.

Complexation of the thiosemicarbazone usually occurs via dissociation of the acidic proton, resulting in the formation of a five-membered chelate ring. Such studies received a new impetus with the discovery of significant antibacterial, antiviral, antimalarial, antileprotic, and even anticancer activities of such ligands and some of their metal complexes, both in vitro and in vivo [5–11]. When an additional donor site D is incorporated in such ligands, linked to the carbonylic carbon via one or two intervening atoms, D, N, S coordination usually takes place. Such donor systems are able to generate novel stereochemical, electrochemical and electronic properties [12,13]. Moreover, the –N=CH– (imine group) imparts in elucidating the mechanism of transaminations and rasemisation reactions [14,15].

Carbon monoxide is an important building block for the synthesis for many compounds [16]. The interaction of small molecules such as "CO" and "O_2" with transition metal complexes particularly those containing a ruthenium metal centre coordinated to nitrogen and oxygen donor ligands have attracted a great deal in recent years. Kenny et al. have recently reported the in vitro anticancer activity of some *N-ortho*-ferrocenyl benzoyl dipeptide esters [17]. Organometallic technetium and rhenium complexes of a 5′-carboxamide 5-ethyl-2′-deoxyuridine derivative are able to selectively inhibit Herpes simplex virus thymidine kinase type 1 (HSV1-TK) [18]. The use of organometallic compounds in the treatment of cancer has also been an active field of research [19].

Chelation causes drastic changes in the biological properties of a ligand and also the metal moiety. Several metal chelates have also been shown to inhibit tumour growth [20] and their interactions with DNA have been reported [21]. The chemistry of ruthenium is currently receiving a lot of attention, primarily because

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of the fascinating electron transfer and energy transfer properties displayed by the complexes of this metal [22]. Ruthenium complexes have appeared to be promising candidates after *cis*-platin in several areas of chemistry from synthetic molecular electronic devices to their interactions with biomolecules [23–25]. A direct correlation between cytotoxicity and DNA binding property of ruthenium complex has been reported by Clarke et al. [26].

Over the past few years, our group has been working on the coordination chemistry of ruthenium with different ligand systems and on their characterization [27–30]. In the present work, we report the results of our study on ruthenium(II) carbonyl complexes of dehydroacetic acid thiosemicarbazone incorporating PPh_3/$AsPh_3$ and nitrogen heterocycles. The complexes have been characterized by physiochemical methods. The structure of one of the complexes has been probed with the help of single crystal X-ray diffraction analysis. Further, the electrochemical behaviour has been examined by cyclic voltammetry along with the antimicorbial activity of these complexes in terms of their growth-inhibition capacity against Gram +ve and Gram −ve bacteria *Staphylococcus aureus* (209 P) and *E. coli* (2231), respectively and fungus *Candida albicans* and *Aspergillus niger*.

2. Experimental

2.1. Reagents and materials

Commercially available $RuCl_3 \cdot 3H_2O$ was used as supplied from Loba Chemie. All the reagents used were chemically pure and analytical grade. The solvents were freshly distilled using the standard procedures [31]. Dehydroacetic acid (DHA) and thiosemicarbazide were purchased from SRL. The supporting electrolyte tetrabutyl ammonium perchlorate (TBAP) was dried in vacuum prior to use.

2.2. Physical measurements

The analysis of carbon, hydrogen, nitrogen and sulphur were performed at Sophisticated Test and Instrumentation Centre (STIC) Cochin University, Kochi. Infrared spectra of complexes were recorded in KBr pellets with a Perkin-Elmer 597 spectrophotometer in the range 4000–400 cm^{-1}. Electronic spectra of the complexes were recorded in $CHCl_3$ solution with a Cary 300 Bio UV–Vis Varian spectrophotometer in the range 800–200 nm. Emission intensity measurements were carried out by using a Jasco FP-6500 spectrofluorimeter with 5 nm exit slit. The ^1H NMR spectra were recorded in $CDCl_3$ and DMSO with Bruker 400 MHz instrument using TMS as internal reference. Melting Points were recorded in the Boetius micro heating table and are uncorrected. Electrochemical measurements were made using a Princeton EG and G-Parc model potentiostat using a glassy carbon-working electrode and [(n-C_4H_9)$_4$N](ClO_4) (TBAP) as supporting electrolyte. All the potentials were referenced to Ag/AgCl electrode and the solutions were purged with N_2 before each set of experiments. The bacterial and fungal species were obtained from National Chemical Laboratory (NCL), Pune, India. The precursor complexes [$RuHCl(CO)(PPh_3)_3$] [32], [$RuHCl(CO)(B)(PPh_3)_2$] [33] (where B = py, pip (or) mor) and [$RuHCl(CO)(AsPh_3)_3$] [34] and the ligands [35] were prepared by reported literature methods.

2.3. Preparation of H_2dhatsc

To the hot solution of thiosemicarbazide (0.182 g; 0.002 mol), hot ethanolic solution of dehydroacetic acid (0.336 g; 0.002 mol) was added and refluxed for 3 h. On reducing the solvent followed by subsequent cooling, the solid product was separated out and was recrystallized from ethanol.

2.4. Synthesis of ruthenium(II) carbonyl complexes of DHATSC

To a solution of 0.1 mmol of [$RuHCl(CO)(B)(EPh_3)_2$] (where E = As, B = $AsPh_3$; E = P, B = PPh_3, py, pip (or) mor) in benzene (20 ml) was added 0.1 mmol ligand H_2dhatsc (mole ratio of ruthenium complex and ligand is 1:1) and the mixture was refluxed for 10 h. The solution was concentrated to about 3 ml and petroleum ether was added where by the ruthenium(II) thiosemicarbazones were separated. The resulting complexes were recrystallized from CH_2Cl_2/petroleum ether and dried under vacuo. The purity of the complexes was checked by TLC. Yield: ~68%.

2.5. X-ray crystallography

Single crystals of [$Ru(dhatsc)(CO)(PPh_3)_2$] (**1**) are grown by slow evaporation of chloroform solution at room temperature. A single crystal of suitable size was covered with Paratone oil, mounted on the top of a glass fiber, and transferred to a Stoe IPDS diffractometer using monochromated Mo Kα radiation (kI = 0.71073). Data were collected at 183 K. Corrections were made for Lorentz and polarization effects as well as for absorption (numerical). The structure was solved with direct method using SIR-97 [36,37] and was refined by full matrix least-squares method [38] on F^2 with SHELXL-97. Non-hydrogen atoms were refined with anisotropy thermal parameters. All hydrogen atoms were geometrically fixed and allowed to refine using a riding model.

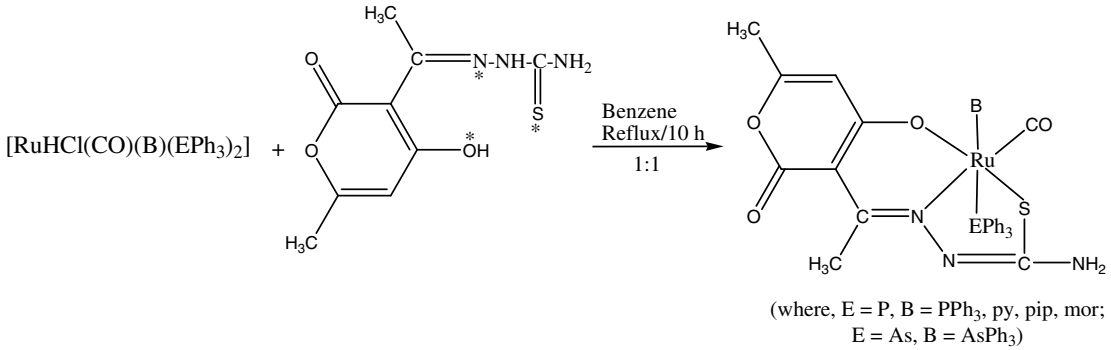
2.6. Microbial assay

The in vitro antimicrobial screenings of the free ligand and its ruthenium(II) complexes containing dhatsc were tested for their effect on certain human pathogenic bacteria and fungus by disc diffusion method. The ligand and their ruthenium(II) complexes were stored dry at room temperature and dissolved in 10% dimethyl sulphoxide in methanol. Both the Gram +ve (*S. aureus*) and Gram −ve (*E. coli*) bacteria were grown in nutrient agar medium and incubated at 37 °C for 48 h followed by frequent subculture to fresh medium and were used as test bacteria. *C. albicans* and *A. niger* grown as Sabourard Dextrose Agar medium were incubated at 27 °C for 72 h followed by periodic sub culturing to fresh medium and were used as test fungus. Then the petriplates were inoculated with a loop full of bacterial and fungal culture and spread throughout the petriplates uniformly with a sterile glass spreader. To each disc the test samples and reference antibiotic (ciproflaxin 5 μg/clotrimazole 10 μg) were added with a sterile micropipette. The plates were then incubated at 35 ± 2 °C for 24–48 h and at 27 ± 1 °C for bacteria and fungus, respectively. Plates with disc containing respective solvents served as control. Inhibition was recorded by measuring the diameter of the inhibitory zone after the period of incubation. The experiment was repeated thrice and the average values are presented.

3. Results and discussion

The new ruthenium(II) carbonyl complexes of dehydroacetic acid thiosemicarbazone of the type [$Ru(dhatsc)(CO)(B)(EPh_3)$] (Scheme 1) have been obtained from the reaction of [$RuHCl(CO)(B)(EPh_3)_2$] (where E = P, B = PPh_3, py, pip (or) mor; E = As, B = $AsPh_3$) with tridentate Schiff base H_2dhatsc in dry benzene in 1:1 molar ratio.

All the new tridentate ruthenium(II) carbonyl complexes are colored, stable to air and light and soluble in chloroform, dichloromethane, benzene, DMF, DMSO. They are found to be diamagnetic, characteristic of the low spin d^6 ruthenium(II) acceptor center. The analytical data are given in Table 1 and are in good agreement with



Scheme 1. Structure of ruthenium(II) carbonyl complexes of dhatsc.

Table 1
Analytical data of ruthenium(II) carbonyl complexes of DHATSC

S. no.	Complexes	Calculated(Found) (%)			
		C	H	N	S
1	[Ru(dhatsc)(CO)(PPh_3)$_2$]	61.80(61.40)	4.42(4.20)	4.75(4.38)	3.56(3.75)
2	[Ru(dhatsc)(CO)(py)(PPh_3)]	55.75(55.45)	4.22(3.98)	7.88(7.48)	4.55(4.10)
3	[Ru(dhatsc)(CO)(pip)(PPh_3)]	60.29(60.71)	4.85(4.93)	7.84(7.45)	4.45(4.22)
4	[Ru(dhatsc)(CO)(mor)(PPh_3)]	53.63(53.29)	4.47(4.13)	7.82(7.44)	4.47(4.17)
5	[Ru(dhatsc)(CO)($AsPh_3$)$_2$]	56.24(55.88)	4.07(3.78)	4.27(3.96)	3.26(2.98)

the general molecular formula proposed. In all the reactions, the ligand behaves as dibasic tridentate ligand replacing one hydride, one chloride and one triphenylphosphine or triphenylarsine molecule from the precursors.

3.1. Characterization

In principle, the ligand H_2dhatsc exhibit thione–thiol tautomerism, since it contains a thioamide –NH–C=S functional group [39]. The free ligand displays $\nu_{(C=S)}$ and $\nu_{(N-H)}$ absorptions at 788 cm^{-1} and 3181 cm^{-1} respectively and were disappeared upon complexation. These observations may be attributed to the enolization of –NH–C=S and subsequent coordination through the deprotonated sulfur [40]. The ligand showed a strong band at 1627 cm^{-1} which is characteristic of the azomethine group (C=N). Co-ordination of the Schiff base to the ruthenium ion through azomethine nitrogen atom is expected to reduce the electron density in the azomethine link and thus lowers the $\nu_{C=N}$ absorption frequency in the region 1587–1609 cm^{-1} (Table 2) after complexation indicating the co-ordination of azomethine nitrogen [41] to ruthenium ion. The strong band observed at 1247 cm^{-1} in the ligand has been assigned to phenolic ν_{C-O} stretching. On co-ordination, this band shifts to higher frequency in the range 1258–1262 cm^{-1} showing that the other co-ordination is through the phenolic oxygen atom [42]. This fact is further supported by the disappearance of broad band ν_{OH} around 3350–3450 cm^{-1} in all the complexes indicating deprotonation of the phenolic proton prior to coordination. For all complexes, a strong band in the region 1952–1954 cm^{-1} is due to the terminally coordinated carbonyl group and is observed at higher frequency than in the precursor complexes. The spectra of the free dhatsc ligand show strong bands at 3380 cm^{-1} due to the NH_2 group [43] and at 1682 cm^{-1} for ($\nu_{C=O}$) lactone carbonyl groups. These absorption remains same even after the coordination indicates that the groups are not involved in coordination. In addition, other characteristic bands due to triphenylphosphine/triphenylarsine are also present around 1434 cm^{-1} in the spectra of all the complexes. A medium intensity band is observed in the 1092 cm^{-1} region characteristic of the co-ordinated pyridine and piperidine [44]. Bands in the region 410–400 cm^{-1} due to M–O, M–N [42,44] and M–S [44], respectively.

The electronic spectra of the complexes in $CHCl_3$ showed two bands in the region 366–261 nm (Table 2). The ground state of ruthenium(II) is ^1A_1g, arising from the $t^6{}_{2g}$ configuration in an octahedral environment. Excited state corresponding to the $t^5{}_{2g}e^1{}_g$ configuration are $^3T_{1g}$, $^3T_{2g}$, $^1T_{1g}$, $^1T_{2g}$. Hence, four bands corresponding to the transitions $^1A_{1g} \rightarrow {}^3T_{1g}$, $^1A_{1g} \rightarrow {}^3T_{2g}$, $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ are possible, in order of increasing energy. The bands in the 366–311 nm region present in all the complexes may be assigned to the Ru(4dπ) $\rightarrow \pi^*$ (imine) (MLCT) transition [45–47]. The charge transfer bands are prominent in the low energy region, which obscures d–d bands in these complexes due to the presence of the unsaturated amine ligands for which a very large body of CT exists [48]. The other lower wavelength bands below 275 nm are due to intra ligand transitions occurring within ligand orbitals. The

Table 2
IR and electronic spectral data of ruthenium(II) carbonyl complexes of DHATSC

Complexes	$\nu_{(C\equiv O)}$ (cm^{-1})	$\nu_{(C=O)}$ (cm^{-1})	$\nu_{(C=N)}$ (cm^{-1})	$\nu_{(C-O)} + \nu_{(C-S)}$ (cm^{-1})	λ_{max} (nm) ε (dm^3/mol/cm)	Fluorescence data λ_{max} (nm)
1	1953	1682	1609	1258	366(24612)[a], 267(84709)[b]	530
2	1952	1685	1594	1262	365(21967)[a], 272(55258)[b]	495
3	1952	1684	1587	1258	312(18677)[a], 269(49225)[b]	500
4	1954	1680	1604	1260	330(20486)[a], 264(40256)[b]	485
5	1952	1682	1601	1262	311(34709)[a], 261(74612)[b]	450

[a] MLCT.
[b] Intra-ligand charge transfer.

pattern of the electronic spectra of all the complexes indicate the presence of an octahedral geometry around ruthenium(II) ion [49].

The light emitting property of all the complexes was investigated in DMSO at ambient temperature (298 K). The excitation was made at the charge transfer band for all the complexes. The emission maxima of all the complexes have experienced a positive shift of the order of 130–188 nm and are listed in Table 2. The emission maximum fall in the range 450–530 nm and a representative spectrum is shown in Fig. 1. The observed CT luminescence in these complexes may be due to the presence of imine functional group. It is likely that the emission originates from the lowest energy metal to ligand charge transfer (MLCT) state, probably derived from the excitation involving $d\pi(Ru) \rightarrow \pi^*$ (imine) MLCT transitions and similar MLCT observed in ruthenium(II) bipyridyl complexes [50]. The present result shows that the Ru(II) carbonyl Schiff base complexes have decreased emission intensity when compared to ruthenium bipyridyl complexes [51]. Among triphenylphosphine and triphenylarsine complexes, the emission maxima is reduced in the arsine complex where the heavier atom As induces the spin forbidden transition [30].

The bonding arrangement is further confirmed by ^{1}H NMR spectra (Table 3). In the spectra of all the complexes, a multiplet observed around 7.0–7.9 ppm is assigned to aromatic protons of the phenyl group of triphenylphosphine/arsine and pyridine. The methine proton appeared as a singlet around 5.2–5.3 ppm and for NH_2 protons a singlet occurs in the 3.0–3.3 ppm region. The CH_3 protons of azomethine group appeared as a singlet at 2.1 ppm and the ring CH_3 proton as singlet at 1.8–1.9 ppm. The signal for methylene proton appeared at 1.4 ppm in **3** and a representative spectrum of **5** is shown in Fig. 2. The signal at δ 3.8 ppm is due to methylene proton nearer to oxygen and at δ 2.8 ppm is due to methylene proton nearer to nitrogen in **4**. The spectra of **3** and **4** showed a singlet at δ 9.3 ppm and at δ 9.6 ppm which have been assigned to the NH protons of piperidine and morpholine. The absence of resonance for OH/SH protons in the complexes indicate deprotonation of the phenolic/thiophenolic group of the Schiff base on complexation and coordination to ruthenium through phenolic oxygen and thiophenolic sulphur atom.

3.2. X-ray structure

The molecular structure of one of the complexes [Ru(dhatsc)-(CO)$(PPh_3)_2$] (**1**) has been determined by single crystal X-ray diffraction to find out the coordination mode of the dehydroacetic acid thiosemicarbazone in the complexes and stereochemistry of the complexes. The ORTEP view is shown in Fig. 3. The summary of the data collection and refinement parameters are shown in Table 4 and selected bond lengths and bond angles are given in Table 5. The thiosemicarbazone ligand coordinates in a tridentate manner to ruthenium ion via the phenolic oxygen, azomethine nitrogen and thiolate sulfur in addition to two PPh_3 and one carbonyl groups. Ruthenium is therefore sitting in a $CNSOP_2$ coordination environment, which is distorted octahedral in nature as reflected in all the bond parameters around ruthenium. The bite angles around Ru(II) are N(1)–Ru(1)–O(2) = 87.29(19)°; N(1)–Ru(1)–S(1) = 81.18(15)°; O(2)–Ru(1)–C(28) = 99.2(2)° and S(1)–Ru(1)–C(28) = 92.3(2)°, summing up the in-plane angle to be exactly 360°. This shows the high planarity of the CO and O, N, S donor atoms of dehydroacetic acid thiosemicarbazone. Thus the coordinated thiosemicarbazone ligand (dhatsc) and carbonyl constitute one equatorial plane with the metal at the center and the CO group is trans to the azomethine (–C=N–) nitrogen. The thiosemicarbazone ligand binds the metal center at O, N and S forming one five membered and one six membered chelate ring with bite angles of $87.29(19)^0$ O(2)–Ru(1)–N(1) and $81.18(15)^0$ N(1)–Ru(1)–S(1) and bond lengths of 2.096(5) Å Ru(1)–O(2), 2.114(5) Å Ru(1)–N(1) and 2.3613(17) Å Ru(1)–S(1). The two PPh_3 ligands are mutually trans to each other. Usually the PPh_3 ligands prefer to occupy mutually *cis* positions for better π-interaction [52]. However, in these complexes the presence of CO, which is stronger π-acidic ligand, has probably forced the bulky PPh_3 to take up mutually trans position for steric reasons. The Ru–C bond length 1.867(7) Å in Ru(1)–C(28) fragment is quite normal like that in the structurally characterized carbonyl complexes of ruthenium [53]. Coordination causes C(41)–O(2), 1.283(8) Å to be substantially longer than C(45)–O(4), 1.214(8) Å, which is formally a dou-

Table 3
^{1}H NMR spectral data of Ru(II) carbonyl complexes of DHATSC

Complexes	^{1}H NMR data (ppm)						
	Ar–H (m)	NH_2 (s)	=CH (s)	$CNCH_3$ (s)	CH_3 (ring) (s)	NH (s)	CH_2 (s)
1	7.2–7.9	3.4	5.2	2.0	1.8		
2	7.1–7.9	3.3	5.3	2.1	1.8		
3	7.0–7.9	3.2	5.2	2.1	1.9	9.3	1.4
4	7.0–7.8	3.1	5.1	2.0	1.8	9.6	3.8 2.8
5	7.2–7.9	3.1	5.4	2.1	1.8		

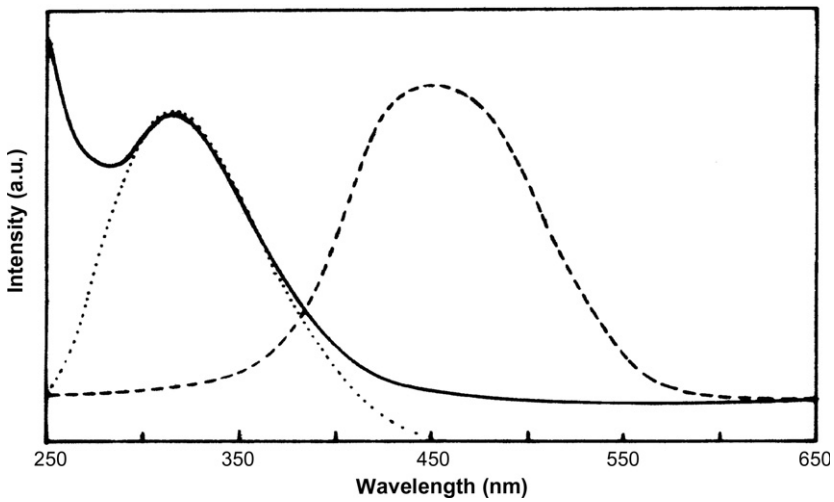


Fig. 1. Absorption (–), fluorescence (----) and excitation (.....) spectra of complex [Ru(dhatsc)(CO)$(AsPh_3)_2$] (**5**).

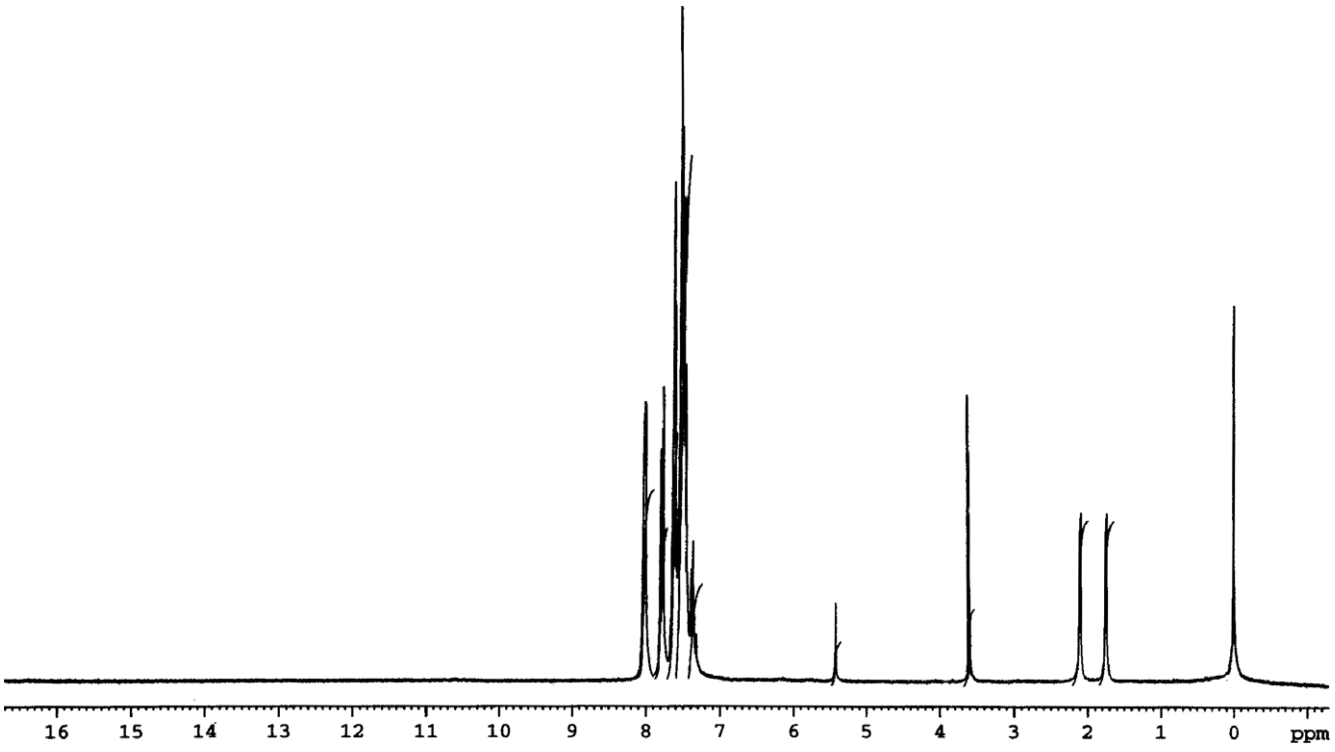


Fig. 2. ^{1}H NMR spectrum of complex [Ru(dhatsc)(CO)($AsPh_3$)$_2$] (**5**).

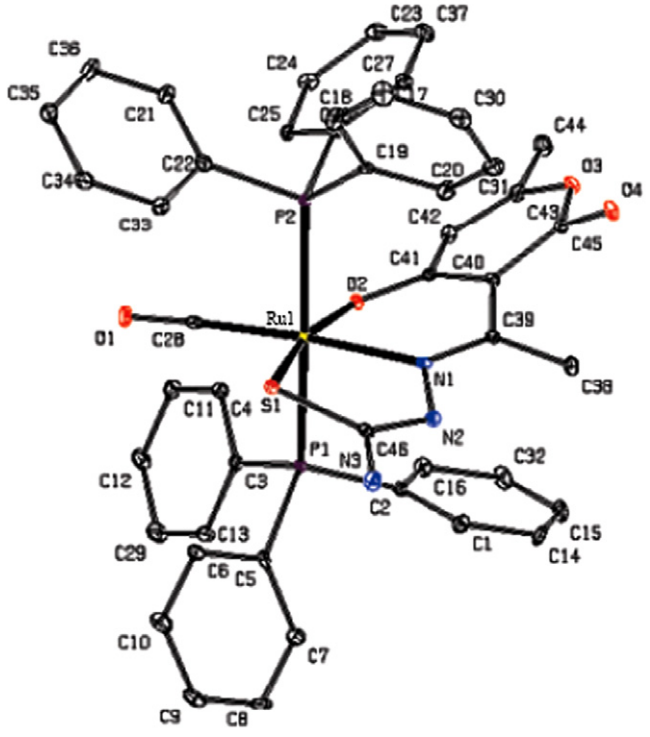


Fig. 3. The ORTEP diagram of the complex [Ru(dhatsc)(CO)(PPh_3)$_2$] (**1**). For reasons of clarity, hydrogen atoms have been omitted.

Table 4
Crystal data and structure refinement for complex **1**

Empirical formula	$C_{46}H_{39}N_3O_4P_2RuS$
Formula weight	892.87
Temperature (K)	183(2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	*P*2(1)/*n*
Unit cell dimensions	
a (Å)	14.663(3)
b (Å)	18.079(4)
c (Å)	15.616(3)
α (°)	90
β (°)	103.88(3)
γ (°)	90
Volume (Å^3)	4019.0(14)
Z	4
D_{calc} (Mg/m^3)	1.476
Absorption coefficient (mm^{-1})	0.571
F(000)	1832
Crystal size (mm^3)	0.18 × 0.15 × 0.11
θ Range for data collection (°)	1.75–23.20
Index ranges	$-16 \leqslant h \leqslant 16$, $-20 \leqslant k \leqslant 19$, $-12 \leqslant l \leqslant 17$
Reflections collected	22 162
Independent reflections [R_{int}]	5724 [0.1592]
Completeness to θ = 23.20°	99.8%
Absorption correction	Numerical
Maximum and minimum transmission	0.6076 and 0.4332
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5724/0/516
Goodness-of-fit on F^2	1.094
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0650, wR_2 = 0.1641
R indices (all data)	R_1 = 0.0798, wR_2 = 0.1775
Largest difference in peak and hole (e Å^{-3})	2.560 and −1.598

ble bond, but considerably shorter than the formal single bonds C(43)–O(3), C(45)–O(3) which are 1.378(8) Å and 1.407(8) Å, respectively. This suggests considerable back π-bonding to the ring system by the ruthenium(II) center.

3.3. Electrochemical study

As the ligand used in this work are not reversibly reduced or oxidized within the potential limits employed, we believe that

Table 5
Selected bond lengths (Å) and angles (°) for complex **1**

Bond lengths (Å)		Bond angles (°)	
Ru1–S1	2.3613 (18)	S1–Ru1–P1	96.92 (6)
Ru1–P1	2.4035 (17)	S1–Ru1–P2	92.33 (6)
Ru1–P2	2.4073 (17)	S1–Ru1–O2	168.27 (13)
Ru1–O2	2.096 (4)	S1–Ru1–N1	81.17 (15)
Ru1–N1	2.114 (5)	S1–Ru1–C28	92.3 (2)
Ru1–C28	1.867 (7)	P1–Ru1–P2	170.19 (7)
S1–C46	1.739 (7)	P1–Ru1–O2	80.79 (13)
P1–C2	1.813 (6)	P1–Ru1–N1	89.95 (15)
P1–C3	1.843 (6)	P1–Ru1–C28	88.8 (2)
P1–C5	1.844 (6)	P2–Ru1–O2	90.79 (13)
P2–C19	1.831 (6)	P2–Ru1–N1	94.70 (15)
P2–C22	1.827 (8)	P2–Ru1–C28	87.5 (2)
P2–C26	1.829 (6)	O2–Ru1–N1	87.31 (19)
O1–C28	1.158 (9)	O2–Ru1–C28	99.2 (3)
O2–C41	1.283 (8)	N1–Ru1–C28	173.1 (3)
O3–C43	1.378 (9)	Ru1–S1–C46	95.4 (2)
O3–C45	1.407 (9)	C43–O3–C45	121.6 (6)
O4–C45	1.214 (9)	Ru1–N1–N2	118.2 (4)
N1–N2	1.407 (8)	Ru1–N1–C39	127.3 (4)
N2–C46	1.312 (9)	N2–N1–C39	114.2 (5)
N3–C46	1.366 (9)	N1–N2–C46	114.4 (5)
		Ru1–C28–O1	175.9 (6)
		N1–C39–C38	119.3 (5)
		N1–C39–C40	120.1 (5)
		S1–C46–N2	126.0 (5)
		S1–C46–N3	116.7 (5)
		N2–C46–N3	117.3 (6)

ESD in parentheses.

the redox processes observed for the complexes are metal centered only. Electrochemical study was carried out for all the Ru(II) carbonyl complexes in acetonitrile solution at a glassy carbon working electrode. The supporting electrolyte used was 0.05 M $[Bu_4N]ClO_4$ and the concentration of the complex is 10^{-3} M. A representative voltammogram is shown in Fig. 4.

The cyclic voltammograms of all the complexes exhibit an irreversible oxidation and an irreversible reduction at the scan rate of 100 mV s^{-1}. The redox potential of the complexes is characterized by well defined waves in the range 0.76–0.89 V (oxidation) and −0.87 V to −0.97 V (reduction). The irreversible redox process observed for these complexes may be due to short-lived oxidized/reduced state of the metal ion. It has also been observed that there is not much variation in the redox potential due to the replacement of triphenylphosphine/triphenylarsine by pyridine, piperidine or morpholine.

3.4. Antimicrobial studies

The free ligand and its ruthenium(II) carbonyl complexes were screened in vitro for their microbial activity against certain pathogenic bacterial and fungal species at two different concentration

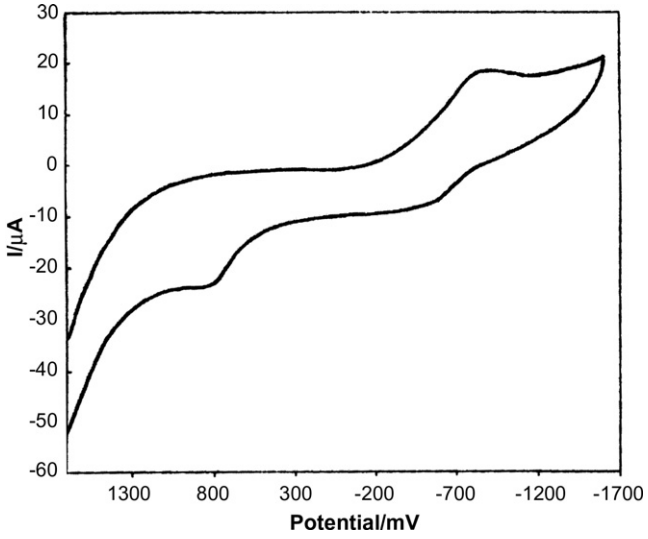


Fig. 4. Cyclic voltammogram of complex [Ru(dhatsc)(CO)(py)(PPh_3)] (**2**).

using disc diffusion method. These compounds were found to exhibit considerable activity against Gram +ve (*S. aureus* NCIM 2079), Gram −ve (*E. coli* NCIM 2065) bacteria and the fungus *C. albicans* and *A. niger*. The test solutions were prepared in dimethyl sulphoxide and the results of the antimicrobial activities are summarized in Table 6. In classifying the antibacterial activity as Gram +ve or Gram −ve, it would generally be expected that a much greater number would be active against Gram-positive than Gram-negative bacteria [54]. The effectiveness of an antimicrobial agent in sensitivity testing is based on the size of the zones of inhibition. The diameter of the zone is measured to the nearest millimeter. In all our biological experiments, $RuCl_3 \cdot 3H_2O$ and Ru(II) carbonyl precursors are taken as blank along with Schiff base ligand and its complexes in identical experimental conditions. From the results it was found that $RuCl_3 \cdot 3H_2O$ and Ru(II) carbonyl precursors does not show any activity. It has been observed that ruthenium chelates possess high antimicrobial activity than that of the respective free ligand against the same microorganism. Higher antifungal activity has been displayed for *A. niger* than the *C. albicans*. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane [55,56] and can be explained by Tweedy's chelation theory [57].

Chelation considerably reduces the polarity of the metal ion because of partial sharing of its positive charge with donor groups and possible π-electron delocalization over the whole chelate ring. Such a chelation could enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layers of cell membrane and blocking the metal binding sites on enzymes of microorganism. The other possible mode of ac-

Table 6
Antimicrobial activity of ruthenium(II) carbonyl complexes of DHATSC

Complex	Antibacterial				Antifungal			
	Staphylococcus aureus (ppm)		*Escherichia coli* (ppm)		*Candida albicans* (ppm)		*Aspergillus niger* (ppm)	
	50	100	50	100	50	100	50	100
DHATSC	[a]	9	[a]	10	[a]	[a]	[a]	[a]
1	10	12	8	10	11	11	10	11
2	10	12	8	10	10	15	8	9
3	9	12	11	10	8	10	10	10
4	8	10	10	11	8	9	9	10
5	9	11	7	8	8	8	11	11

[a] No inhibition; Standard; Solvent: DMSO (No inhibitory against the microorganisms).

tion may also be explained by Overtone's concept [58]. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favours the passage of only the lipid-soluble materials due to which liposolubility is an important factor, which controls the antimicrobial activity. It has been observed that different compounds exhibit microbial activity of little variation against bacterial and fungal species. This difference in activity depends either on the impermeability of the cells of the microbes which, in case of Gram +ve is single layered and in the case of Gram −ve is multilayered structure [59] or differences in ribosomes of microbial cells [60]. It can possibly be concluded that the chelation increased the activity of these complexes. The present results show that the ruthenium(II) carbonyl Schiff base complexes possess better cytotoxicity than the other metal complexes against the same microbes [61–63]. Although the complexes are active, they did not reach the effectiveness of the conventional bacteriocide ciprofloxacin and fungicide clotrimazole.

4. Conclusion

Five new ruthenium(II) carbonyl complexes containing dehydroacetic acid thiosemicarbazone of the general formula [Ru(dhatsc)(CO)(B)(EPh_3)] (where, E = P, B = PPh_3, py, pip or mor; E = As, B = $AsPh_3$) have been synthesized from the reactions of [RuHCl(CO)(B)(EPh_3)$_2$] (where, E = P, B = PPh_3, py, pip or mor; E = As, B = $AsPh_3$) with tridentate dhatsc ligand (H_2dhatsc). The characterization of the complexes were accomplished by analytical and spectral (IR, UV–Vis, ^{1}H NMR) methods which suggests the co-ordination of the ligand to the metal through O, N, S donors. X-ray diffraction study reveals the presence of an distorted octahedral geometry around Ru(II). All the complexes undergo one electron transfer process and are irreversible in nature. Further, the possible mode of action of these complexes against *S. aureus* (209 P), *E. coli* (2231), *C. albicans* and *A. niger* are described.

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Appendix A. Supplementary material

CCDC 639241 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.03.023.

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