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Synthesis and characterization of some biologically active ruthenium(II) complexes of thiosemicarbazones of pyridine 2-aldehyde and thiophene 2-aldehyde involving some ring substituted 4-phenylthiosemicarbazides and 4-cyclohexylthiosemicarbazide. Crystal structure of *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2\cdot 2H_2O$ [L^6H = 4-(cyclohexyl) thiosemicarbazone of pyridine 2-aldehyde]

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Abstract

A series of ruthenium(II) complexes of potentially NNS tridentate but functionally NS bidentate chelating ligands in the form of 4-substituted 4-phenyl and 4-cyclohexyl thiosemicarbazones of pyridine 2-aldehyde and thiophene 2-aldehyde (LH) have been synthesized using $Ru(PPh_3)_3Cl_2$ as the starting material. The complexes are of the general formula $[Ru(PPh_3)_2(LH)_2]X_2$, [L^1H, L^2H, L^3H, L^4H, L^5H and L^6H are 4-(*p*-fluorophenyl), 4-(*p*-chlorophenyl) 4-(*p*-iodophenyl), 4-(*p*-hydroxyphenyl), 4-(*p*-methylphenyl) and 4-(*p*-cyclohexyl) thiosemicarbazones of pyridine 2-aldehyde and L^7H is the 4-cyclohexyl thiosemicarbazone of thiophene 2-aldehyde (Figure 1) and X = ClO_4, PF_6]. A complex $[Ru(bipy)(L^6H)_2](ClO_4)_2$, has also been synthesized. All the complexes were characterized by elemental analyses, measurement of conductance in solution, magnetic susceptibility at room temperature and by spectroscopic techniques. Electrochemical behavior of the complexes has been examined by cyclic voltammetry. Structure of one of the complexes *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2\cdot 2H_2O$, has been solved by single crystal X-ray diffraction technique. All the ligands are found to be chelated to the ruthenium(II) center in its thione form through its imine nitrogen and the thione sulfur. The pyridine ring nitrogen remained uncoordinated. The two PPh_3 molecules are situated *cis* to each other. All the complexes are found to exhibit biological activity in terms of *Escherichia coli* growth-inhibition capacity and two of them hold the possibility of displaying antitumor activity.

Keywords: Ruthenium(II) complexes; NS-donors; Thiosemicarbazones; X-ray crystal structures; Biological activity

1. Introduction

Coordination chemistry of the thiosemicarbazides and thisemicarbazones in general, and that of the α-N heteroaromatic thiosemicarbazides and their thiosemicarbazones in particular, has been studied in the past because of their mixed hard–soft donor character and versatile coordination behavior [1–5]. 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 [6–23]. It is also known that in their metal complexes such donor systems are able to generate novel stereochemical, electrochemical and electronic properties [24–34].

Over the past few years our group has been working on the coordination chemistry of ruthenium and has reported synthesis, characterization, chemical and electrochemical properties of an array of ruthenium(II) and

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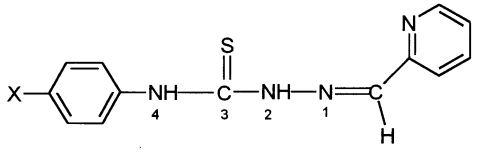
ruthenium(III) complexes [2–11,35,36] along with the exploration of the biological activity of some of them [6–11]. In the present work we report the results of our study on ruthenium(II) complexes of a number of thiosemicarbazones of pyridine 2-aldehyde and thiophene 2-aldehyde involving various ring substituted 4-phenylthiosemicarbazides and 4-cyclohexylthiosemicarbazide (Fig. 1). The ligands are potentially tridentate NNS ligands which can also function as N–N/N–S bidentate donors. In the present study the ligands are found to act as neutral bidentate N–S donors. A number of ruthenium(II) complexes of these thiosemicarbazones (LH) of the general formula $[Ru(PPh_3)_2(LH)_2]X_2$, ($X = ClO_4$, PF_6) have been isolated in the solid state and characterized by several physicochemical techniques. Their electrochemical behavior has been examined by cyclic voltammetry. Biological activity of these complexes in terms of their *Escherichia coli* growth-inhibition capacity has also been examined. Structure of one of the reported complexes *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2 \cdot 2H_2O$, which may be considered as a representative of all the reported complexes, has been solved by single crystal X-ray diffraction technique. We also report here a ruthenium(III) species electrogenerated from the above *cis*-ruthenium(II) complex in solution and characterized by EPR spectroscopy.

2. Experimental

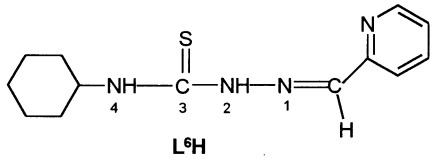
2.1. Materials

Commercial ruthenium trichloride, $RuCl_3 \cdot xH_2O$, purchased from Arora Matthey (Calcutta, India), was processed by repeated evaporation to dryness with concentrated HCl. $Ru(PPh_3)_3Cl_2$ was prepared from $RuCl_3$ using a previously published procedure [37]. Pyridine 2-aldehyde and thiophene 2-aldehyde were purchased from Aldrich. All other chemicals were of reagent grade and were used without further purification. Tetraethylammonium perchlorate (TEAP) used for electrochemical work was prepared as reported in the literature [38].

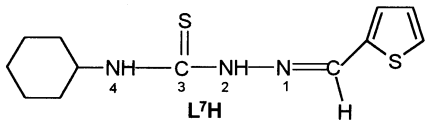
Caution! Perchlorate salts of metal complexes are generally explosive. Care should be taken while handling such complexes.



X = -F (**L^1H**); -Cl (**L^2H**); -I (**L^3H**); -OH (**L^4H**); -CH_3 (**L^5H**)



L^6H



L^7H

Fig. 1. Keto (thione) form of the ligands.

2.2. Physical measurements

Elemental analyses were performed with a Perkin–Elmer 240 CHNS/O analyzer. IR and electronic spectra were recorded on a Perkin–Elmer 783 spectrophotometer (as KBr pellets) and on Shimadzu UV–Vis 2100 recording spectrophotometer, respectively. Solution conductance was measured on a Systronics direct reading conductivity meter (Model 304) and magnetic susceptibility was measured at 298 K with a (PAR Model 155) vibrating sample magnetometer using $Hg[Co(SCN)_4]$ as the calibrant. Electrochemical data were collected with a BAS CV-27 electrochemical analyzer and a BAS Model X-Y recorder at 298 K. Cyclic voltammetry experiments were carried out with a platinum working electrode, a platinum auxiliary electrode and a Ag–AgCl reference electrode. Coulometric oxidation was done in nitrogen atmosphere using a PC-controlled EG&G/PAR-273A potentiostat. EPR spectra at X-band frequencies were recorded with a Varian E-109C spectrometer equipped with a gas-flow temperature controller for variable-temperature studies. Spectra at 77 K were recorded using a quartz dewar. The calibrant was DPPH ($g = 2.0037$). The ^1H NMR spectra were recorded with a Bruker 300-MHz NMR spectrometer relative to $SiMe_4$ using $(CD_3)_2SO$ as solvent.

2.3. Synthesis of the ligands and the complexes

The ligands, 4-(*p*-fluorophenyl)thiosemicarbazone (L^1H), 4-(*p*-chlorophenyl)thiosemicarbazone (L^2H), 4-(*p*-iodophenyl)thiosemicarbazone (L^3H), 4-(*p*-hydroxyphenyl)thiosemicarbazone (L^4H), 4-(*p*-methylphenyl)thiosemicarbazone (L^5H), 4-(cyclohexyl)thiosemicarbazone (L^6H) of pyridine 2-aldehyde and 4-(cyclohexyl)thiosemicarbazone of thiophene 2-aldehyde (L^7H) were prepared by standard procedures [6,7].

All the complexes $[Ru(PPh_3)_2(L^1H)_2](ClO_4)_2$ (**1**), $[Ru(PPh_3)_2(L^2H)_2](ClO_4)_2$ (**2**), $[Ru(PPh_3)_2(L^3H)_2](ClO_4)_2$ (**3**), $[Ru(PPh_3)_2(L^4H)_2](ClO_4)_2$ (**4**), $[Ru(PPh_3)_2(L^5H)_2](ClO_4)_2$ (**5**), $[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2$ (**6**), $[Ru(bipy)(L^6H)_2](ClO4)_2$ (**7**), $[Ru(PPh_3)_2(L^7H)_2](PF_6)_2$ (**8**)

and $[Ru(PPh_3)_2(L^7H)_2](ClO_4)_2$ (**9**) were synthesized following a general procedure described below.

Ligand (0.5 mmol) was dissolved in 30 ml methanol by refluxing and solid $Ru(PPh_3)_3Cl_2$ (240 mg, 0.25 mmol) was added to it. The mixture was refluxed for 4 h. The clear solution was then concentrated in a rotary evaporator to about 10 ml. The perchlorate compound was isolated by adding saturated aqueous $NaClO_4$ solution and the hexafluorophosphate compound by adding aqueous NH_4PF_6 solution to the concentrated solution. The precipitated compound was filtered, washed thoroughly with distilled water and dried over fused $CaCl_2$. It was finally recrystallized from dichloromethane. Yield: 60–80%.

2.4. X-ray crystallography

The reddish brown crystals of compound **6** were grown by slow diffusion of *n*-hexane into dichloromethane solution for several days. A crystal of size $0.56 \times 0.32 \times 0.22$ mm was chosen for X-ray diffraction study. The complex *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2 \cdot 2H_2O$ (**6**) crystallized in the triclinic space group $P\bar{1}$. Crystal data are summarized in Table 2. Intensity data were collected at 293(2) K on a Siemens P4 four-circle-diffractometer using graphite monochromatized Mo Kα radiation ($\lambda = 0.71073$ Å). A total of 9739 reflections were collected of which 8377 were independent reflections ($R_{int} = 0.0328$), covering indices $-1 \leq h \leq 13$, $-15 \leq k \leq 15$, $-19 \leq l \leq 19$. The intensities were corrected for Lorentz and polarization effects. Absorption corrections were made by using the ABSCOR program [39]. The structure was solved by the direct method. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares on F^2 with a riding model for the hydrogen atoms using the SHELXTL PLUS-PC version [40].

3. Results and discussion

The thiosemicarbazone ligands were prepared by condensing the appropriate thiosemicarbazide with pyridine 2-aldehyde and thiophene 2-aldehyde respectively by the standard procedure [6,7] and the complexes (**1**–**9**) were obtained as described in the Section 2. All the complexes are of different shades of brown and yellow and are air and heat stable. They are found to be diamagnetic which is characteristic of the low spin d^6 ruthenium(II) acceptor center present in all of them. Conductivity data for all the complexes in CH_3CN lie in the 220–250 Ω^{-1} cm^2 mol^{-1} and point to their 1:2 electrolytic nature. The complexes have been satisfactorily characterized by elemental analysis (Table 1), IR and electronic spectral data. Cyclic voltammograms of all the complexes were recorded in CH_3CN (Table 1). Biological activity data are presented in Table 1. A ruthenium(III) species was generated in solution by constant potential electro-oxidation (at +1.0 V) of the corresponding ruthenium(II) complex **6**. Attempt to isolate the oxidized species in the form of a pure salt has been unsuccessful.

3.1. Description of crystal structure

Inspite of repeated effort we succeeded in isolating good single crystals of only the compound **6**. Perspective view of the complex **6** is given in Fig. 2. The coordination environment around the ruthenium(II) center in this complex consists of a distorted octahedral arrangement of $N_2P_2S_2$ donor points. The triphenylphosphine moieties are situated *cis* to each other. The two sulfur atoms are *trans* to each other with the two nitrogen atoms in mutually *cis* positions. Phosphorous and nitrogen atoms lie *trans* to each other and the asymmetric unit contains two water molecules. The crystal data and refinement parameters are summarized in Table 2 and selected bond lengths and bond angles are presented in Table 3. Bite angles S(2)–Ru(1)–N(4) and S(1)–Ru(1)–N(1) of the two thiosemicarbazone molecules acting as bidentate chelating N–S donors and forming five membered chelate rings at ruthenium(II) are practically same [81.4(2)° and 81.9(2)°] indicating identical binding of the two ligands. These bite angles are practically same as the corresponding N–S bite angles (81.5°) of the thiosemicarbazone moiety observed in another previously reported ruthenium(II) complex [3]. Ru–N bonds in **6** [2.141(8) and 2.150(8) Å] are a bit longer than the values found in most other thiosemicarbazone complexes. This comparative lengthening of the Ru–N bond is the effect of the two coordinated triphenylphosphines present *trans* to the two N-atoms. Lengths of the two Ru–P bonds are unexceptional. The large deviation of the P(1)–Ru–P(2) angle [101.74(9)°] from 90° may be ascribed to the steric repulsion between the two adjacent bulky PPh_3 molecules which makes this part of the molecule reactive and render them susceptible to substitution, specially towards bidentate chelating ligands. This expectation is substantiated by the preparation of $[Ru(bipy)(L^6H)_2](ClO_4)_2$ by reacting **6** with 2,2′-bipyridine in refluxing ethanol.

3.2. Infrared spectra

IR spectra of the complexes were found to differ in certain respects from the ruthenium(II) complexes of analogous thiosemicarbazone ligands [3]. Coordination of the ligands in their thione form is indicated by the presence of ν(C=S) band in the 850–750 cm^{-1} region. Shift of the ν(C=S) band of the ligand to the 750–850 cm^{-1} region along with the shift of the ν(C=N)+ν(C=

Table 1
Elemental analyses, cyclic voltammetric and biological activity data of the Ru(II) complexes

Complexes	Found (Calc.) (%)			Cyclic voltammetric data [a] $E_{1/2}$ (V); (ΔE_p (mV)) [b]	MIC (μg ml^{-1})	MIC (μM ml^{-1})
	C	H	N			
$[Ru(PPh_3)_2(L^1H)_2](ClO_4)_2$ (**1**)	53.9 (54.2)	3.54 (3.78)	8.07 (8.15)	+0.51(60)	150	0.109
$[Ru(PPh_3)_2(L^2H)_2](ClO_4)_2$ (**2**)	52.7 (52.9)	3.49 (3.69)	7.7 (7.9)	+0.52(50)	200	0.142
$[Ru(PPh_3)_2(L^3H)_2](ClO_4)_2$ (**3**)	46.5 (46.8)	3.12 (3.27)	6.8 (7.0)	+0.56(80)	120	0.075
$[Ru(PPh_3)_2(L^4H)_2](ClO_4)_2$ (**4**)	53.9 (54.3)	3.72 (3.94)	8.17 (8.1)	+0.55(60)	100	0.073
$[Ru(PPh_3)_2(L^5H)_2](ClO_4)_2$ (**5**)	55.8 (56.2)	4.18 (4.25)	8.02 (8.2)	+0.50(80)	150	0.109
$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2 \cdot 2H_2O$ (**6**)	53.04 (53.7)	5.12 (5.05)	8.12 (8.08)	+0.65(80)	100	0.072
$[Ru(bipy)(L^6H)_2](ClO4)_2$ (**7**)	44.08 (44.1)	4.44 (4.48)	14.1 (14.3)	+0.67(60), −1.57(60)	15	0.015
$[Ru(PPh_3)_2(L^7H)_2](PF_6)_2$ (**8**)	49.3 (49.6)	4.2 (4.41)	7.7 (7.76)	+0.71(70)	50	0.034
$[Ru(PPh_3)_2(L^7H)_2](ClO_4)_2$ (**9**)	52.7 (52.9)	4.66 (4.7)	6.2 (6.17)	+0.75(60)	100	0.073

[a] Conditions: Solvent, CH_3CN; supporting electrolyte, TEAP (0.1 M); working electrode, platinum; reference electrode, Ag|AgCl; solute concentration, 10^{-3} M; scan rate, 0.2 V s^{-1}; and temperature, 298 K.

C) band at ~1590–1560 cm^{-1} by 5–20 cm^{-1} in the complexes indicate that the ligand is attached to the metal ion through the thiocarbonyl sulfur and the azomethine nitrogen atom of the thiosemicarbazone moiety. In addition, the IR spectra of the complexes **1**–**7** and **9** exhibit characteristic bands of the uncoordinated perchlorate ion in the 1090–1130 cm^{-1} region [7], while complexes **8** displays $\nu(PF_6)$ vibrations of the ionic PF_6 around 840 cm^{-1}. Characteristics band of PPh_3 is present in the complexes except the complex **7**.

3.3. NMR spectra

Fig. 1 shows the numbering used for assignments of ^1H protons in the ligands. Presence of all the ligand–proton signals in the ^1H NMR spectra of the complexes substantiates that the ligands coordinate in their thione form in all the complexes. The NMR spectrum of the ligand L^1H exhibits δ 9.52 ppm (1H, s), δ 8.12 ppm (1H, s) and δ 7.85 ppm (1H, s) which are assigned to the aldimine proton ($-^2NH-$), CH= and Ph–NH proton

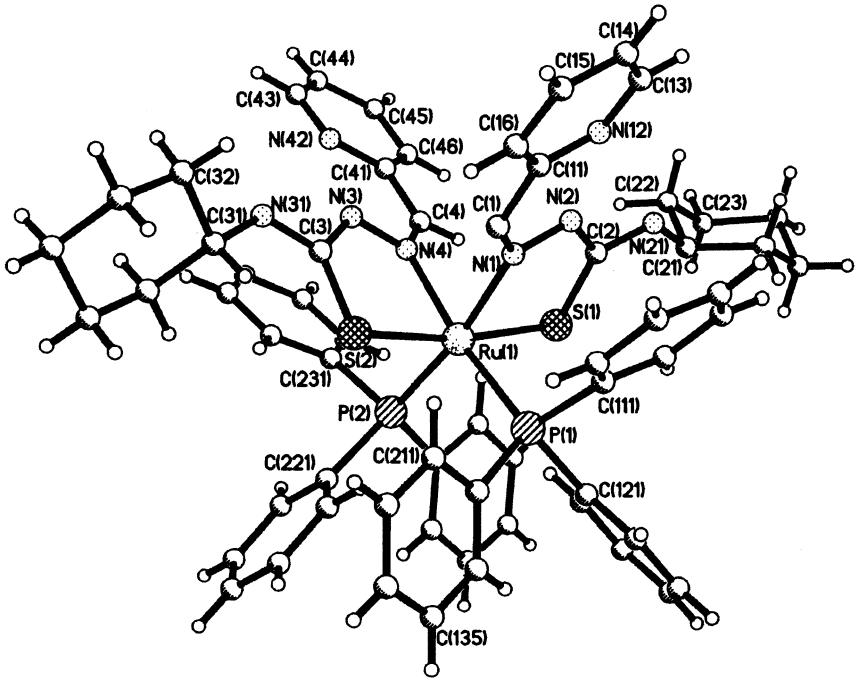


Fig. 2. Perspective view of the cation $[Ru(PPh_3)_2(L^6H)_2]^{2+}$ in the complex *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2 \cdot 2H_2O$ (**6**).

Table 2
Crystal data and structure refinement for *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2\cdot 2H_2O$ (**6**)

Empirical formula	$C_{62}H_{66}Cl_2N_8O_{10}P_2RuS_2$
Formula weight	1381.26
Temperature	293(2) K
Crystal system	triclinic
Space group	$P\bar{1}$
Unit cell dimensions	
a (Å)	12.932(4)
b (Å)	14.633(4)
c (Å)	17.807(4)
α (°)	103.729(10)
β (°)	95.90(2)
γ (°)	91.38(3)
Volume (Å^3)	3252.1(15)
Z	2
Absorption coefficient (mm^{-1})	0.499
$F(000)$	1428
θ range for data collection (°)	1.87–37.25
Reflections collected	9739
Independent reflections	8377 ($R_{int} = 0.0328$)
Goodness-of-fit on F^2	1.009
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0793$, $wR_2 = 0.1864$
R indices (all data)	$R_1 = 0.1240$, $wR_2 = 0.2177$

Table 3
Selected bond lengths (Å) and bond angles (°) for *cis*-$[Ru(PPh_3)_2(L^6H)_2](ClO_4)_2\cdot 2H_2O$ (**6**)

Bond lengths			
Ru(1)–N(1)	2.141(8)	Ru(1)–N(4)	2.150(8)
Ru(1)–S(2)	2.367(3)	Ru(1)–S(1)	2.370(3)
Ru(1)–P(2)	2.379(3)	Ru(1)–P(1)	2.386(3)
P(1)–C(121)	1.846(5)	P(2)–C(211)	1.838(5)
P(1)–C(131)	1.850(5)	P(2)–C(221)	1.844(5)
P(1)–C(111)	1.862(5)	P(2)–C(231)	1.858(6)
S(1)–C(2)	1.717(10)	S(2)–C(3)	1.701(10)
N(1)–C(1)	1.303(11)	N(1)–N(2)	1.386(10)
C(11)–N(12)	1.327(13)	N(12)–C(13)	1.331(14)
N(2)–C(2)	1.365(12)	N(3)–C(3)	1.371(13)
Cl(1)–O(21)	1.438(7)	Cl(1)–O(4)	1.441(7)
Bond angles			
N(1)–Ru(1)–N(4)	81.4(3)	N(1)–Ru(1)–S(2)	90.9(2)
N(4)–Ru(1)–S(2)	81.4(2)	N(1)–Ru(1)–S(1)	81.9(2)
N(4)–Ru(1)–S(1)	91.8(2)	S(2)–Ru(1)–S(1)	170.81(9)
N(1)–Ru(1)–P(2)	169.9(2)	N(4)–Ru(1)–P(2)	88.5(2)
S(2)–Ru(1)–P(2)	88.19(10)	S(1)–Ru(1)–P(2)	97.84(9)
N(1)–Ru(1)–P(1)	88.4(2)	N(4)–Ru(1)–P(1)	169.7(2)
S(2)–Ru(1)–P(1)	97.57(9)	S(1)–Ru(1)–P(1)	88.02(9)
P(2)–Ru(1)–P(1)	101.74(9)	N(2)–N(1)–Ru(1)	117.0(6)
O(51)–Cl(2)–O(81)	109.2(8)	O(71)–Cl(2)–O(81)	108.4(7)

(–^{4}NH), respectively. The low field position of –^{4}NH– could be attributed to the deshielding caused by the phenyl ring. NMR spectra of all the other ligands exhibit closely similar characteristics. In complex **4** the –OH proton appears at δ 10.72 ppm (1H, s) and complex **5** exhibits –CH_3 protons at δ 2.38 ppm (3H, s).

3.4. Electronic spectra

Electronic spectra of low-spin d^6 complexes of ruthenium(II) are generally dominated by high intensity metal-to-ligand charge transfer bands in the visible region [25,41,42]. Because of the unsymmetrical donor environment around ruthenium(II) in the complexes reported in this work, all the occupied d-orbital are non-degenerate and at least three MLCT transitions are expected. However, possibly due to the small difference in energy between these d-orbital and consequent lack of resolution, only two such MLCT bands could be located. One of them (Band-I) is located around 480–460 nm while the other (Band-II) is observed in the 390–330 nm region. All other bands found in the UV region are assigned to intra-ligand transitions. The band in the 480–460 nm region may be assigned to $Ru(4d\pi) \rightarrow \pi^*$ (imine). In the complex **7**, $[Ru(bipy)(L^6H)_2](ClO_4)_2$ this transition overlaps with $Ru(4d\pi) \rightarrow \pi^*$ (bipy) transition increasing the intensity of the resultant band.

3.5. Electrochemical properties

Electron transfer behavior of the complexes was examined in acetonitrile solution and the results are presented in Table 1. Cyclic voltammograms of all the complexes of the pyridine 2-aldehyde thiosemicarbazones involving ring-substituted 4-phenyl thiosemicarbazides in CH_3CN exhibit a distinct ruthenium(III)/ruthenium(II) reversible to quasi-reversible couple at approximately $\sim$0.5–0.7 V. ΔE_P values vary between 60 and 90 mV. Some ΔE_P values, though a little larger than the ideal Nernstian value of 59 mV, are commonly observed for this type of complexes [3,43,44]. It also opens up the possibility of synthesizing the corresponding ruthenium(III) complexes by electrolytic oxidation of the ruthenium(II) complexes. In fact the compound **6** was electrochemically oxidized at +1.0 V versus SCE. Electrolysis was complete when 1.98 C had passed. The calculated one-electron coulomb count is 1.93. Frozen glass epr spectra (77 K, dichloromethane–toluene glass) of the oxidized solution exhibits rhombic signals at $g_1 = 1.98$, $g_2 = 2.14$, and $g_3 = 2.32$, characteristic of ruthenium(III) complexes in distorted octahedral environment. This clearly suggests that the redox couple at $\sim$0.5–0.7 V for these complexes is due to metal-based oxidation. The magnitudes of ruthenium(III)/ruthenium(II) couples in complexes **1**–**5** containing ring-substituted 4-phenyl thiosemicarbazone ligands are little influenced by the nature of the substituents present in the benzene ring. Bipyridine containing complex **7** exhibits an additional reversible reductive couple of the bipyridine moiety above −1.5 V.

3.6. Study of biological activity

Following the line of our earlier works [6–11] we have determined the minimum inhibitory concentration (MIC) values (Table 1) of all the complexes reported here against *E. coli 10536*. A culture of *E. coli 10536* was grown for 18 h in nutrient broth (Difco) at 37 °C. Standard solutions of the compound were prepared in 1:1 DMSO–ethanol mixture. Ten ml of the sterilized medium was taken in each of several 20 ml sterilized test tubes and 0.2 ml cell suspension (5×10^5 cfu ml^{-1}) was added to each test tube. Different volumes of the standard solution of the compound being studied were then added to these test tubes which were incubated at 37 °C for 24 h. The result of bacterial growth-inhibition study in terms of MIC is reported in Table 1.

Our previous experience on antibacterial ruthenium complexes of some selected thiosemicarbazone ligands [6,7,9] indicate that complexes **7** and **8** possessing MIC values of 15 and 50 μg ml^{-1} hold the possibility of exhibiting antitumor activity. We intend to pursue further studies on compound **7** and **8** to explore their antitumor activity against properly selected tumor models, both in vitro and in vivo. The most active complex **7** is obtained by the replacement of two *cis* PPh_3 groups by a bipyridine ligand. So, it is quite possible that substitution of the two *cis* PPh_3 groups by bipyridine in all the complexes will generate heterochelate complexes with greater activity.

One of our previous works [9] indicated that antitumor activity could be related to the number of sulfur donor points present around the ruthenium acceptor center. Complexes **4**, **6**, **7**, **8** and **9** have structural features which can be utilized for introducing more sulfur donor points in them leading to enhancement of antitumor activity of these complexes. Thus, structure determination of one of these complexes could lead to a strategy of design and synthesis of new potential antitumor active ruthenium complexes.

4. Concluding remarks

A number of ternary complexes of ruthenium(II) containing the potentially NNS-tridentate but functionally N–S bidentate ligands in the form of 4-substituted thiosemicarbazones of pyridine 2- and thiophene 2-aldehydes have been isolated and fully characterized. Structure of one representative member has been solved. Structural features of one of the complexes suggest a synthetic route for preparing heterochelate complexes of different types. Some of the complexes exhibit biological activity in term of growth inhibition of *E. coli* 10536 and at least one of them possess the potential of exhibiting antitumor activity. A possible way of increasing biological activity of the ruthenium(II) complexes is also indicated.

5. Supplementary data

Crystallographic data have been deposited with the Cambridge Crystallographic Data Center, and are available on request to The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk) quoting the deposition number 173283 for the complex **6**.

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