Transition Met Chem (2013) 38:291–298
DOI 10.1007/s11243-013-9690-z

Synthesis, DNA binding, antioxidant and cytotoxic activities of ruthenium(II) complexes of a Schiff base ligand

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Received: 31 October 2012 / Accepted: 3 January 2013 / Published online: 24 January 2013
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Abstract Three ruthenium(II) complexes, [Ru(CO)Cl(PPh_3)L], [Ru(CO)Cl($AsPh_3$)L] and [Ru(CO)Cl(Py)L], were synthesized from the reactions of 2-(benzothiazol-2-yliminomethyl)-phenol (HL) with [RuHCl(CO)B(EPh_3)$_2$], where B = PPh_3, $AsPh_3$ or pyridine, and E = P or As. All the complexes have been characterized by physicochemical and spectroscopic methods. The structure of the free ligand HL was determined by single crystal X-ray diffraction. The binding of the free ligand and its complexes with CT-DNA was studied using electronic absorption spectroscopy. In addition, the free ligand and its complexes were subjected to antioxidant activity tests, which showed that they all possess significant scavenging effects against DPPH and OH radicals. The in vitro cytotoxicities of the compounds were assessed using tumor (HeLa and MCF-7) cell lines.

Introduction

In recent years, researchers have focused their curiosity on metal containing drugs and their interactions with DNA [1]. An understanding of the interaction between metal complexes and DNA at the molecular level is important for the design of new drugs and probes that can recognize specific DNA sequences and structural motifs [2]. Moreover, certain metal complexes have been shown to be capable of cleaving DNA strands. In the case of cancer genes, cleavage of the DNA double strands can destroy their replication ability. Ruthenium complexes are presently the objective of a great deal of attention in the field of medicinal chemistry, as potential antitumor agents with selective antimetastatic properties and low systemic toxicity [3]. Ruthenium complexes appear to penetrate reasonably well into tumor cells and bind effectively to DNA [4].

Over recent years, a number of bisbenzimidazoles [5], arybenzothiazoles [6] and 2-aminobenzothiazoles have been found to possess bioorganic and medicinal applications in drug discovery, including potent antitumour activity. From modeling studies, they appear to act as minor groove binding agents, spanning a number of base pairs which allows sequence specificity to be included in the ligand design.

Based on the above facts, we herein report on the synthesis and characterization of ruthenium(II) Schiff base complexes containing 2-(benzothiazol-2-yliminomethyl)-phenol (HL) as ligand. The single crystal X-ray structure of the free ligand has been determined. DNA-binding abilities of the free ligand and its ruthenium(II) complexes were investigated with calf-thymus DNA (CT-DNA). We have also investigated the relationship between co-ligand structure and the cytotoxicities of these complexes for two cancer cell (HeLa and MCF-7) lines. Furthermore, their antioxidant effects were evaluated in vitro by their abilities to scavenge DPPH and hydroxyl radicals.

Experimental

Materials and instrumentation

Reagent grade chemicals were used without further purification in all the synthetic work. Solvents were purified by

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standard methods [7]. Salicylaldehyde and 2-aminobenzothiazole were purchased from Sigma-Aldrich. $RuCl_3 \cdot 3H_2O$, PPh_3 and $AsPh_3$ were purchased from Himedia. CT-DNA was purchased from Bangalore Genei, Bangalore, India.

Infrared spectra were recorded on an FTIR Perkin Elmer spectrophotometer RXI model as KBr pellets in the range of 4,000–400 cm^{-1}. Elemental analyses were obtained with a model Vario ELIII CHNS at the Sophisticated Test and Instrumentation Centre (STIC), Cochin University, Kerala. Electronic spectra were recorded in DMSO solution in a Systronics 2202 double beam spectrophotometer in the range of 800–200 nm. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker WM DCX 500 MHz instrument using TMS and orthophosphoric acid as internal standards at SAIF, Indian Institute of Technology, Chennai. Antioxidant and anticancer studies were carried out at the Kovai Medical Centre and Hospital Pharmacy College, Coimbatore, Tamil Nadu. The metal precursors [RuHCl(CO)$(PPh_3)_3$] [8], [RuHCl(CO)$(AsPh_3)_3$] [9] and [RuHCl(CO)$(PPh_3)_2$(py)] [10] were prepared according to the reported literature procedures.

Crystal structure determination

Single crystals of HL were grown by slow evaporation of a solution of the ligand in chloroform. Selected crystal data are given in Tables 1 and 2, and Fig. 1. The X-ray diffraction data were collected on a Bruker Kappa APEXII CCD diffraction instrument using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) by ϕ and ω scans. X-ray data reduction, structure solution and refinement were performed using the SHELXS-97 and SHELXL-97 packages [11]. The structure was solved by direct methods.

Synthesis of 3-(benzothiazol-2-yliminomethyl)-phenol (HL)

A solution of salicylaldehyde (1.1 ml, 10 mmol) in ethanol (15 ml) was added to a stirred solution of 2-amino benzothiazole (1.5 g, 10 mmol) in ethanol (20 ml). The mixture was stirred for 30 min and then refluxed for 6 h. After cooling the reaction mixture to room temperature, the solid product formed was filtered off, washed with ethanol and dried under vacuum. This solid was recrystallized from chloroform, yielding needle-shaped yellow crystals that were suitable for X-ray diffraction analysis.

Synthesis of the complexes

The complexes were prepared by the following general procedure (Scheme 1). A solution of [RuHCl(CO)$B(EPh_3)_2$] (0.1510–0.1904 g, 0.2 mmol) in benzene (20 ml) (B = PPh_3, $AsPh_3$ or pyridine (py), E = P or As) was added to a

Table 1 Crystal and structure refinement data for Schiff base ligand (HL)

Empirical formula	C_{14} H_{10} N_2 O S
Formula weight	254.30
Temperature	273(2) K
Wavelength	0.71073 A
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	
a (Å)	12.1518(5)
b (Å)	8.9528(5)
c (Å)	22.0200
α (°)	90
β (°)	90
γ (°)	90
Volume	2,395.6(2) $Å^3$
Z	8
Density (calculated)	8.1.410 mg/m^3
Crystal size	0.30 × 0.20 × 0.20 mm
Theta range for data collection	2.50°–25.00°
Limiting indices	$-14 \leq h \leq 14$
Reflections collected	$-10 \leq k \leq 7$
Data/restraints/parameters	$-25 \leq l \leq 26$
Goodness-of-fit on F^2	1.066
Final *R* indices [$I > 2$ sigma(I)]	$R1 = 0.0317$, $wR2 = 0.0832$
R indices (all data)	$R1 = 0.0479$, $wR2 = 0.0945$

Table 2 Selected bond lengths (Å) and angles (°) for Schiff base ligand (HL)

Bond lengths	Bond angles
S C(1)–O(1) 1.343(2)	N(1)–C(7)–C(6) 122.23(14)
C(1)–C(2) 1.380(3)	N(1)–C(7)–H(7) 118.9
C(1)–C(6) 1.413(2)	C(6)–C(7)–H(7) 118.9
C(2)–C(3) 1.376(3)	N(2)–C(8)–N(1) 121.11(15)
C(2)–H(2) 0.9300	N(2)–C(8)–S(1) 115.65(13)
C(3)–C(4) 1.377(3)	N(1)–C(8)–S(1) 123.24(13)
C(3)–H(3) 0.9300	C(8)–N(2)–C(10) 110.80(14)
C(4)–C(5) 1.364(3)	N(2)–C(10)–C(11) 125.30(16)
C(4)–H(4) 0.9300	N(2)–C(10)–C(15) 115.36(16)
C(5)–C(6) 1.396(2)	C(11)–C(10)–C(15) 119.34(17)
C(5)–H(5) 0.9300	C(12)–C(11)–C(10) 119.66(18)
C(6)–C(7) 1.430(2)	C(12)–C(11)–H(11) 120.2
C(7)–N(1) 1.285(2)	C(10)–C(11)–H(11) 120.2
C(7)–H(7) 0.9300	C(11)–C(12)–C(13) 120.7(2)
C(8)–N(2) 1.290(2)	C(11)–C(12)–H(12) 119.6
C(8)–N(1) 1.380(2)	C(13)–C(12)–H(12) 119.6
C(8)–S(1) 1.7688(17)	C(14)–C(13)–C(12) 121.0(2)
N(2)–C(10) 1.380(2)	C(14)–C(13)–H(13) 119.5

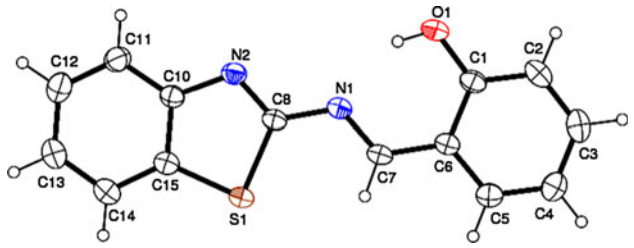
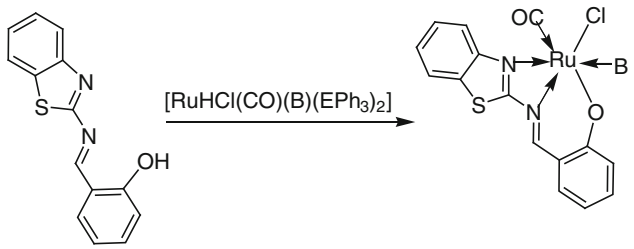


Fig. 1 Labeled ORTEP diagram of HL with thermal ellipsoid at 50 % probability

stirred solution of HL (0.05086 g, 0.2 mmol) in chloroform (15 ml). The mixture was refluxed for 8 h. The solvent was then evaporated under reduced pressure, and the solid mass was filtered out and washed with petroleum ether. The purity of the complexes was checked by thin layer chromatography, and they were further purified by column chromatography using 1:10 acetonitrile–benzene as an eluent and silica gel (60–120 mesh) as stationary phase, then recrystallized from CH_2Cl_2/*n*–hexane mixture. Extensive efforts to obtain single crystals of the complexes were unsuccessful.

DNA interaction experiments

Experiments involving the interaction of HL and its ruthenium(II) complexes with CT-DNA were carried out in double distilled water with tris(hydroxymethyl)-aminomethane (Tris, 5 mM) and sodium chloride (50 mM) and adjusted to pH 7.2 with hydrochloric acid. A solution of CT-DNA in the buffer gave a ratio of UV absorbance of about 1.9 at 260 and 280 nm, indicating that the DNA was sufficiently free of protein. The DNA concentration per nucleotide was determined by absorption spectroscopy using the molar extinction coefficient value of 6,600 $dm^3\ mol^{-1}\ cm^{-1}$ at 260 nm. Electronic absorption titration experiments were performed by maintaining the concentration of test compound as constant (25 μM) but with variable nucleotide concentration from 0 to 25 μM. While measuring the absorption spectra, equal amounts of DNA were added to both the compound and reference solutions to eliminate the absorbance of DNA itself. The



Scheme 1 Formation of ruthenium(II) Schiff base complexes. B = PPh_3, $AsPh_3$ or py

data were then processed with the following equation, and the intrinsic binding constant K_b was calculated in each case [12].

$$[\mathrm{DNA}]/(\varepsilon_a - \varepsilon_f) = [\mathrm{DNA}]/(\varepsilon_b - \varepsilon_f) + 1/K_b(\varepsilon_b - \varepsilon_f)$$

where [DNA] is the concentration of DNA in the base pairs, and the apparent absorption coefficients ε_a, ε_f and ε_b correspond to A_{obsd}/[complex], the extinction coefficient of the free compound and the extinction coefficient of the compound when fully bound to DNA, respectively. In plots of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA], K_b is given by the ratio of slope to the intercept.

Antioxidant studies

The free radical scavenging abilities of the compounds were determined against both DPPH and hydroxyl radicals. The DPPH radical scavenging activity of the compounds was investigated using the method described by Elizabeth [13], while the hydroxyl radical scavenging activity of the compounds was evaluated by the modified method of Yu [14]. For each of the assays, the tests were run in triplicate at varying concentrations. The percentage activity was calculated using the following formula: % activity = $[(A_o - A_c)/A_o] \times 100$, where A_o and A_c represent the absorbance in the absence and presence of the test compounds, respectively. The 50 % activity (IC_{50}) was calculated from the % activities.

Cytotoxicity studies

Cytotoxicity studies of the compounds were carried out on human cervical cancer (HeLa) and human breast cancer (MCF-7) cell lines, which were obtained from the National Centre for Cell Science, Pune, India. Cell viability was assayed using the MTT assay method. The HeLa and MCF-7 cells were grown in Eagles minimum essential medium containing 10 % fetal bovine serum (FBS). For the screening experiments, the cells were seeded into 96-well plates in 100 μL of the medium containing 10 % FBS, at a plating density of 10,000 cells/well, and incubated at 37 °C, under conditions of 5 % CO_2, 95 % air and 100 % relative humidity for 24 h prior to the addition of the test compounds. The test compounds were dissolved in DMSO and diluted in the medium containing 1 % FBS. After 24 h, the medium was replaced with the medium with 1 % FBS containing the compounds at various concentrations and incubated at 37 °C under conditions of 5 % CO_2, 95 % air and 100 % relative humidity for 48 h. Experiments were carried out in triplicate, and the medium not containing the compounds served as the control. After 48 h, 10 μL of MTT (5 mg/mL) in phosphate-buffered saline (PBS) was added to each well and incubated at 37 °C for 4 h. The

medium with MTT was then flicked off, and the formazan crystals were dissolved in 100 μL of DMSO. The absorbance was then measured at 570 nm using a micro-plate reader. The % cell inhibition was determined using the following formula:

$$\%\,\text{Growth inhibition} = 100 - \text{Abs (sample)}/\text{Abs (control)} \times 100.$$

Nonlinear regression graphs were plotted between % cell inhibition and Log_{10} concentration and used to obtain IC_{50} values [15].

Results and discussion

The molecular structure of HL, along with the atom numbering scheme, is given in Fig. 1. The crystal data and structural refinement parameters are given in Table 1 and selected bond lengths and angles are given in Table 2. The compound crystallized into an orthorhombic lattice with space group Pbca. The azomethine bond, C7–N1 1.285(2) Å, is in conformity with a formal C=N double bond, and the C1–O1 bond distance of 1.343(2) Å is slightly shorter than the normal C–O single bond distance. The bond distances for C8–N2, at 1.290(2) Å, and C8–S1, for thiazole group at 1.7688(17) Å, are closer to C=N double and C–S single bonds, respectively. The single crystal X-ray diffraction study unambiguously shows that this compound exits in the imine-ol form.

Three air stable, mononuclear octahedral ruthenium(II) Schiff base complexes of the type [RuCl(CO)B(L)] (where B = PPh_3, $AsPh_3$ or py; L = monobasic tridentate Schiff base) have been prepared by the reaction of [RuHCl(CO)B(EPh_3)$_2$] (E = P or As) with the Schiff base in 1:1 molar ratio in chloroform–benzene mixture. The analytical data (Table 3) for the complexes agree well with the proposed molecular formulae (Scheme 1).

The IR spectrum of the ligand was compared with those of the ruthenium(II) complexes in order to confirm the binding mode of the Schiff base ligand (Table 4). For the free Schiff base, the most characteristic bands were observed at 3,426 cm^{-1} ν(OH), 1,654 cm^{-1} ν(C=N azomethine), 1,605 cm^{-1} ν(C=N thiazole ring), 1,251 cm^{-1} ν(CO) and 750 cm^{-1} ν(C–S–C). The ν(C=N) band at 1654 cm^{-1} was shifted to lower frequency (1,618–1,614 cm^{-1}) for the complexes, indicating bonding of the azomethine nitrogen to the metal [16]. The phenolic ν(C–O) band at 1,251 cm^{-1} for the Schiff base [16] was shifted toward higher frequencies (1,261–1,260 cm^{-1}) in the complexes, confirming coordination of the phenolic oxygen. A low frequency band at 430–470 cm^{-1} is attributed to (M–O) and one at 560–580 cm^{-1} to (M–N) [17]. The thiazole C=N band of the free ligand at 1,605 cm^{-1} is shifted to lower frequency at about 1,588–1,582 cm^{-1} for the complexes, whereas the ν(C–S–C) band at 750 cm^{-1} for the free ligand is not much shifted for the complexes, suggesting coordination of the thiazole through N rather than S. A strong band in the region 1,950–1,944 cm^{-1} is assigned to the terminally coordinated carbonyl. For the complex [RuCl(CO)(py)L)], the IR spectrum showed a medium intensity band at 1,125 cm^{-1}, which is characteristic of the coordinated nitrogen base. For the other complexes, characteristic bands for triphenylphosphine and arsine are also present in the expected regions [18].

The electronic spectra of the free Schiff base and its complexes were recorded in DMSO (Table 4). The electronic spectrum of the free ligand showed four bands at 261, 296, 366 and 412 nm, assigned to the π–π^* and n–π^* transitions in the aromatic ring and C=N chromophore [19]. In electronic spectra of all three complexes, five to six bands were observed at 262–502 nm. Those at 262–366 nm may be due to intra-ligand transitions. The charge transfer bands observed for all three complexes due to M → L transitions are observed in the range of 471–502 nm [20, 21]. The electronic spectra of these complexes indicate of an octahedral coordination geometry, similar to other octahedral ruthenium(II) complexes [20].

The ^{1}H NMR spectra of the free ligand and its complexes were recorded in DMSO-d_6. The spectra of HL and [Ru(CO)Cl(PPh_3)L] are shown in Figs. 2 and 3, and the assignments are given in Table 5. The aromatic protons for free HL appear as a multiplet at 7.04–8.10 ppm. On complexation, these signals show only slight variations [22] and cannot be distinguished from the aromatic signals of PPh_3 or $AsPh_3$, due to their extensive overlap at

Table 3 Analytical data of ligand and ruthenium(II) complexes

Ligand/complexes	Color	Yield (%)	Melting point (°C)	Elemental analysis calculated (found)			
				C (%)	H (%)	N (%)	S (%)
HL	Yellow	74	152	66.12 (66.24)	3.96 (3.75)	11.02 (11.18)	12.61 (12.48)
[Ru(CO)Cl(PPh_3)L]	Pink	67	178	58.29 (58.37)	3.55 (3.69)	4.11 (3.95)	4.71 (4.89)
[Ru(CO)Cl($AsPh_3$)L]	Pink	68	192	54.75 (54.89)	3.33 (3.61)	3.86 (3.89)	4.42 (4.19)
[Ru(CO)Cl(Py)L]	Pink	61	186	48.33 (48.04)	2.83 (2.96)	8.45 (8.17)	6.43 (6.65)

Table 4 IR and electronic spectroscopic data of ligand and ruthenium(II) complexes

Ligand/complexes	FT-IR cm^{-1}				UV–Vis
	ν(C=N)	ν(Ph–CO)	ν(C≡O)	ν(C=N) thiazole	λ_{max} (nm)
HL	1,654	1,251	–	1,605	261, 296, 366, 412
[Ru(CO)Cl(PPh_3)L]	1,618	1,260	1,944	1,585	262, 293, 365, 404, 471
[Ru(CO)Cl($AsPh_3$)L]	1,614	1,261	1,945	1,582	262, 294, 351, 397, 502
[Ru(CO)Cl(Py)L]	1,617	1,260	1,950	1,588	262, 294, 366, 428, 466, 488

6.63–7.80 ppm [23]. The hydroxyl proton gives a singlet at 10.21 for the free Schiff base. The equivalent signal is absent from the spectra of the complexes, consistent with coordination of the hydroxyl oxygen to the metal [24]. The signal due to the azomethine proton is considerably deshielded at 9.06–9.24 ppm relative to the free Schiff base ligand at 8.62 ppm, as a consequence of electron donation to the metal center.

The ^{13}C NMR data were recorded in DMSO-d_6 and the assignments are given in Table 5. The spectrum of the free Schiff base displayed a single azomethine resonance at 153 ppm [25], indicating only one tautomer. A signal at 167 ppm is assigned to the thiazole C=N carbon [25]. The downfield shifts of these two signals in the complexes, at 162–163 and 171–173 ppm, respectively, clearly indicate that both the C=N carbons are affected by coordination [26]. The aromatic carbons of both the free ligand and its complexes show signals in the region of 107–135 ppm. For all the complexes, the terminal carbonyl group appeared in the range of 191–194 ppm [27].

The ^{31}P NMR spectrum of the complex [Ru(CO)Cl(PPh_3)L] in DMSO-d_6 showed a sharp singlet at 26.2 ppm, confirming the presence of only one phosphine group. The coordination of PPh_3 to the metal changes its chemical shift by about 32 ppm [28].

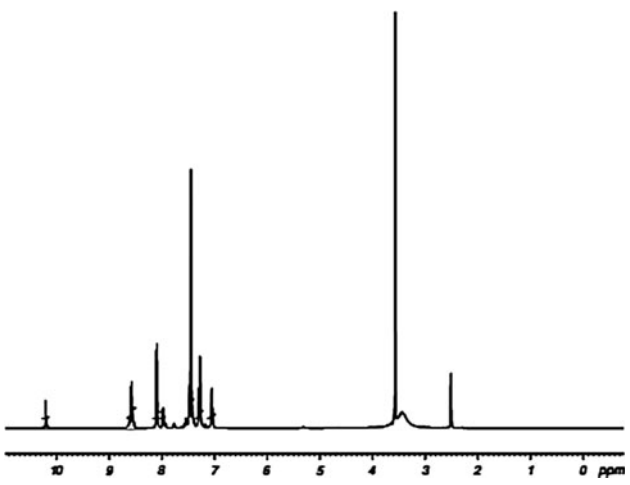


Fig. 2 ^1H NMR spectrum of HL

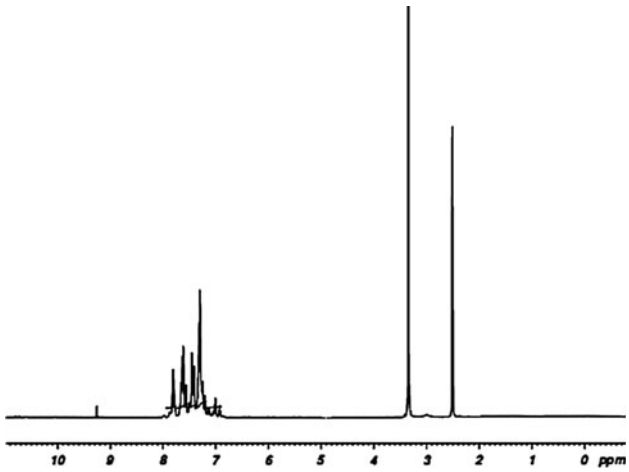


Fig. 3 ^1H NMR spectrum of complex [Ru(CO)Cl(PPh_3)L]

DNA-binding experiments

The DNA-binding properties of both the ligand and its complexes were investigated by UV–Vis spectral titration. The electronic spectra of HL and the complexes upon the addition of DNA are shown in Fig. 4. The titration results showed that with increasing concentrations of DNA, significant hyperchromism with a red shift was observed in all cases. This can be attributed to a strong interaction between DNA and the complexes. However, there were no appreciable wavelength shifts in the charge transfer band. From these results, we infer a nonintercalative mode of binding with DNA. In general, the observation of hypochromism is indicative of intercalative binding, along with stabilization of the DNA double helix structure [29]. On the other hand, the observation of hyperchromism is indicative of disruption of the secondary structure of DNA [30]. Hence, the observation of hyperchromism and a red shift in the present case suggests that these compounds disrupt the double helix structure of DNA.

The intrinsic binding constants K_b for these compounds are given in Table 6 and Fig. 5. The constants were determined by monitoring the changes in the absorbance of the IL (intraligand) band at the corresponding λ_{max} with

Table 5 ^{1}H and ^{13}C NMR data of ligand and ruthenium(II) complexes

Ligand/complexes	^{1}H NMR data (ppm)			^{13}C NMR data (ppm)			
	Ph–OH (s)	HC=N (s)	Aromatic (m)	Aromatic carbon	C=N imine	C≡O	C=N thiazole
HL	10.21	8.62	7.40–8.10	117–134	153	–	167
[Ru(CO)Cl(PPh_3)L]	–	9.24	6.90–7.80	109–135	163	191	173
[Ru(CO)Cl($AsPh_3$)L]	–	9.06	6.63–7.80	107–134	162	191	171
[Ru(CO)Cl(Py)L]	–	9.12	6.94–7.78	118–134	163	194	171

increasing concentrations of DNA, as given by the ratio of the slope to the Y intercept in plots of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA]. From the binding constant values, it is inferred that [RuCl(CO)PPh_3(L)] shows the strongest binding to DNA. The values of K_b for these complexes are comparable to those of some polypyridyl ruthenium(II) complexes, at 1.0–4.8 × 10^4 M^{-1} [31].

Antioxidant properties

The antioxidant activities of the free Schiff base and its complexes were evaluated in a series of in vitro assays involving 2-2′-diphenyl-1-picrylhydrazyl (DPPH) and hydroxyl radicals along with ascorbic acid as a standard and the determination of 50 % activity (IC_{50}) values. The IC_{50} values of HL for DPPH and OH radicals are 136 and 117 μM, respectively, whereas the complexes [Ru(CO)Cl(PPh_3)L], [Ru(CO)Cl($AsPh_3$)L] and [Ru(CO)Cl(Py)L] gave IC_{50} values of 20.4, 85.4 and 65.6 μM, respectively, for DPPH radical and 13.5, 57.3 and 29.5 μM, respectively, for OH radical. Hence, the ruthenium(II) complexes possess higher radical scavenging activities than the free ligand. These results are generally better than those

Table 6 Binding constant value for interaction of the compounds with CT-DNA

Compounds	$K_b \times 10^4$ M^{-1}
HL	3.56
[Ru(CO)Cl(PPh_3)L]	9.49
[Ru(CO)Cl($AsPh_3$)L]	3.65
[Ru(CO)Cl(Py)L]	5.15

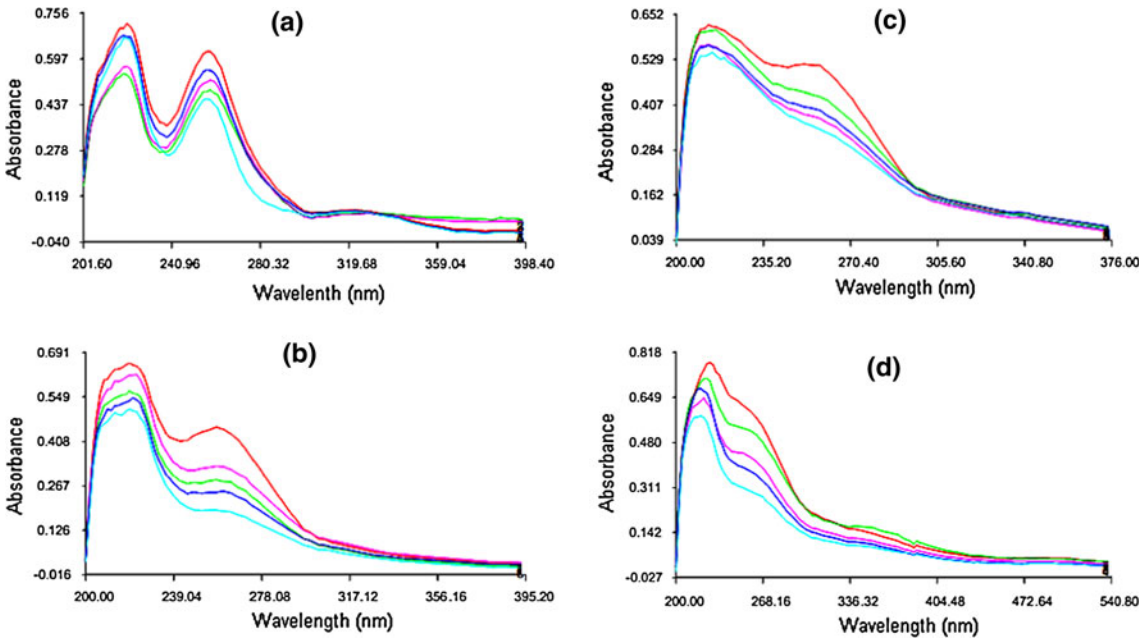


Fig. 4 Absorption spectral traces of the ligand HL (**a**) and the complexes [Ru(CO)Cl(PPh_3)L] (**b**), [Ru(CO)Cl($AsPh_3$)L] (**c**) and [Ru(CO)Cl(py)L] (**d**) with increasing concentration of CT-DNA in a Tris HCl–NaCl buffer (pH 7.1)

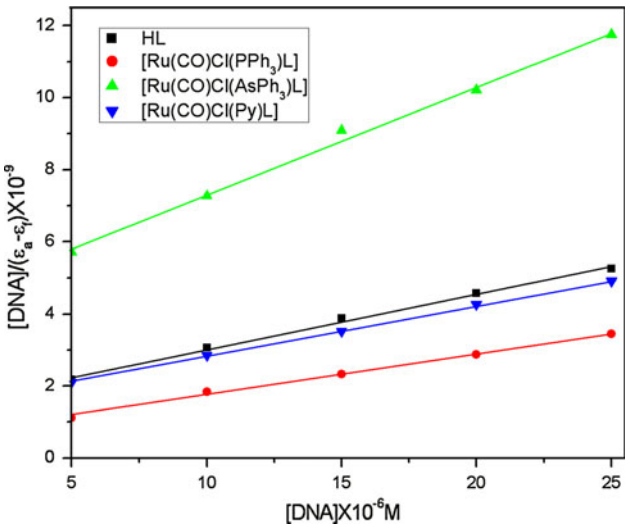


Fig. 5 Plots of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA] for the titration of compounds with CT-DNA

Table 7 The cytotoxic activity of the compounds

Compounds	IC_{50} values (μM)	
	HeLa	MCF-7
HL	178.21	184.15
[Ru(CO)Cl(PPh_3)L]	27.12	32.54
[Ru(CO)Cl($AsPh_3$)L]	54.69	58.53
[Ru(CO)Cl(Py)L]	44.38	46.12

observed for ascorbic acid, which gave IC_{50} values of 46.8 μM for DPPH and 34.3 μM for OH radicals.

Cytotoxic activities

Cytotoxicity is a common limitation in terms of the introduction of new compounds into the pharmaceutical industry. In order to determine the in vitro cytotoxicities of these compounds, experiments were carried out using a human cervical cancer (HeLa) and human breast cancer (MCF-7) cell lines, assayed with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). The results were analyzed by means of cell viability curves and expressed as IC_{50} values in the studied concentration range from 1 to 500 μM. The complexes exhibit greater activities than the free ligand against both HeLa and MCF-7 cells, and [Ru(CO)Cl(PPh_3)L] demonstrated a much higher inhibitory effect than the other two complexes (Table 7). Hence, these complexes are active against the tumor cell lines under in vitro conditions, and the results are comparable to those obtained for other ruthenium complexes [32].

Conclusion

Three new mononuclear ruthenium(II) complexes containing 3-(benzothiazol-2-yliminomethyl)-phenol Schiff base ligand have been prepared and characterized by spectroscopic techniques. The complexes show groove binding modes with CT-DNA, with the strongest DNA binding observed for [Ru(CO)Cl(PPh_3)L]. In addition, [Ru(CO)Cl(PPh_3)L] shows significant antioxidant properties. The complexes [Ru(CO)Cl(PPh_3)L] and [Ru(CO)Cl(Py)L] show considerable cytotoxic activities against HeLa and MCF-7 cancer cell lines, with higher inhibition of HeLa cells compared to MCF-7 cells. From the above results, we conclude that the complex containing triphenylphosphine as co-ligand shows higher biological activity than the other two complexes and the free ligand.

Supplementary data

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC 866090. Copy of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CB21 EZ, UK (fax: +44-1223-336033: e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk/deposi).

Acknowledgments We sincerely thank University Grants Commission (UGC), New Delhi, for financial support [MRP Scheme. No. 38-222/2009 (SR)].

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