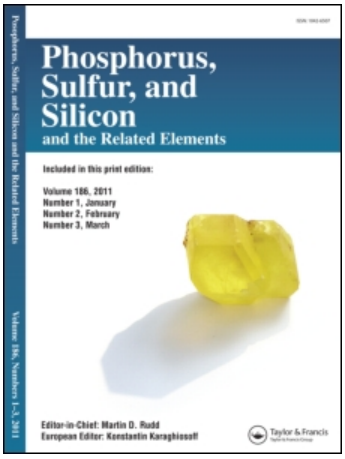

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Synthesis, Characterization, and Antitumor Activity of Some Metal Complexes with Schiff Bases Derived from 9-Fluorenone as a Polycyclic Aromatic Compound

Nabil S. Youssef,[1] Eman A. El Zahany,[1] Manal M. Anwar,[2] and Sohair A. Hassan[2]
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New bidendate Schiff base ligands HL^1 [(9H-fluorene-9-ylidene)-thiosemicarbazide], HL^2 [(9H-fluorene-9-ylidene)semicarbazide] and L^3 [N^1,N^2-di(9H-fluorene-9-ylidene)ethan-1,2-diamine] derived from the condensation of thiosemicarbazide, semicarbazide, and ethylenediamine with 9-fluorenone as polycyclic aromatic compound (PAC). Ag(I), Cu(II), VO(IV), La(III), and Zn(II) of the ligands HL^1, HL^2, and L^3 have been prepared and characterized by conductance and magnetic measurements, and electronic, infrared, and ^1H NMR spectral data. Tetrahedral structures are suggested for Ag (I) with HL^1, HL^2, and L^3, whereas Cu(II)-HL^1 and VO(IV)-HL^2 have octahedral and square-planar structures, respectively. The Erlich antitumor activity in vivo (E. A. A.) have been studied and showed that the free ligands L^3, HL^2, and its VO(IV)-HL^2 complex are the most active in the inhibition of cell viability, whereas the ligands HL^1, La(III) -L^3, and Cu(II)-HL^1 are the least active ones.

Keywords Antitumor activity; 9-fluorenone; polycyclic aromatic compound; semicarbazide; thiosemicarbazide

INTRODUCTION

Thiosemicarbazones and their metal complexes have been the subject of extensive investigations, not only because of their potential pharmacological properties,[1–5] but also their wide variation in their multifunctional coordination modes of bonding and stereochemistry. However, semicarbazones are also reported to possess versatile structural features,[2] and antifungal and antibacterial properties.[6,7] The biological

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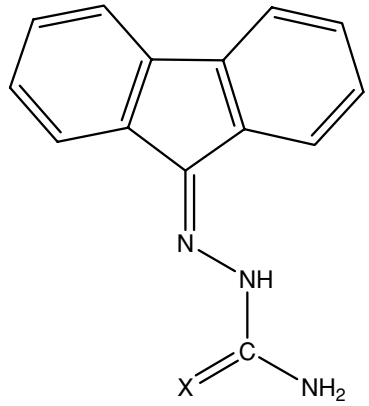


FIGURE 1 Structure of ligands of HL^1(X=S), HL^2(X=O).

activity of these compounds may come from their interaction with potential donors of biological heterocyclic in vivo.[8–10] Recently, the interest in the studies of semicarbazones is due to their unusual coordination modes when bound to metals, high pharmacological potentiality, and good chelating property.

The use of PACS and their derivatives as anticancer agents has been explored.[11,12] These studies mainly focused on the synthesis of the polycyclic ring systems and the examination of their metabolic activation within target cells. In addition, the structure–activity relationship of PACs as anticancer agents were studied, because the anticancer agents revealed two common structural features: They have a planar ring system and a basic-side chain group.[13]

The coordination chemistry of transition metals, particularly that of vanadium, has received considerable attention. Vanadium biological importance includes potent cytotoxic activity against human cancer cells.[14]

In the present study, we describe the synthesis and characterization of HL^1, HL^2, and L^3 ligands (Figures 1 and 2) and their metal complexes with Ag(I), Cu(II), VO(IV), La (III), and Zn(II) ions, together with the examination of their antitumor activity.

EXPERIMENTAL

Chemicals

All chemicals used were of highest available purity. They included 9-fluorenone, semicarbazide hydrogen chloride, thiosemicarbazide,

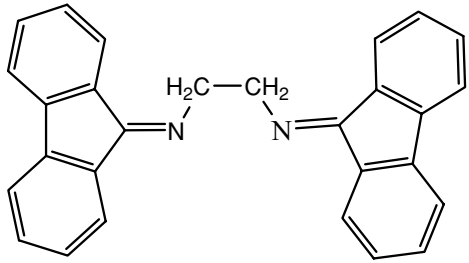


FIGURE 2 Structure of ligand L^3.

lanthanum chloride $LaCl_3.7H_2O$, zinc chloride $ZnCl_2$ and silver nitrate $AgNO_3$ (Merck), copper acetate $Cu(Ac)_2$ (Aldrich), vanadyl sulphate $VOSO_4.H_2O$ (BDH), and ethylenediamine (Rasayan). Organic solvents used, including absolute ethyl alcohol, methyl alcohol, diethyl ether, and dimethyl sulfoxide (DMSO), were purchased from Merck or Sigma.

Measurements

All melting points were determined on electrothermal melting point apparatus and were uncorrected. All the analytical and spectral data were carried out at the Microanalytical Center, Cairo University. The infrared spectra were carried out using BRUKER VECTOR2 (Germany). The ^1H NMR spectra were measured with Gemini 200 MHz and Varian mercury VX-300 MHz spectrometers in DMSO-d_6, and chemical shifts were recorded in δ ppm relative to TMS. The mass spectra were run at 70 ev with HP Model MS. 5988A and/or GCMS. Cap 1000 EX SHIMADZU spectrometer using Electron Impaction Technique. The electronic spectra of the ligands and their complexes were obtained in Nujol mulls and in saturated DMF or DMSO solutions using a Shimadzu UV-240 UV-visible recording spectrophotometer. Molar conductivities in DMF at 25°C were measured using a model CM-1K-TOA company (Japan) conductivity meter. Magnetic moments at 25°C were determined using the Gouy method with $Hg[Co(SCN)_4]$ as calibrant. Antitumor activity was performed in the pharmacology unit, National Cancer Institute of Cairo University.

Preparation of ligand HL[1]

To a warm solution containing 9-fluorenone (1.8 g, 0.01 mol), a warm solution of thiosemicarbazide (0.91 g, 0.01 mol) was added in 30 mL ethyl alcohol, then 5 drops of glacial acetic acid. The resulting solution was refluxed at 50–60°C for 15 h, where a yellowish white precipitate

was formed. The precipitate was then filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum. The ligand HL^1 was previously prepared[15] by a different method using fluorenone to replace diazafluorenone in 4,5 diazafluorenone thiosemicarbazone. Structure of ligand HL^1 is shown in Figure 1.

Preparation of HL^1 complexes

Ag-HL^1. A complex Ag-HL^1 was synthesized by the direct reaction of silver nitrate with the ligand HL^1. A solution of silver nitrate (0.16 g, 0.001 mol) in 5 mL water was added dropwise to a hot solution of ligand HL^1 (0.253 g, 0.001 mol) in 20 mL ethyl alcohol/chloroform mixture (1:1). The resulting solution was refluxed for 24 h at 50°C, and the solution turned dirty green. The solution was then allowed to evaporate slowly. The formed precipitate was filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Cu(II)-HL^1. This complex was obtained when a hot solution of copper acetate (0.182 g, 0.001 mol) was added to a hot solution of HL^1 (0.253 g, 0.001 mol) in 20 mL of ethyl alcohol/chloroform mixture (1:1) with stirring. A deep brown precipitate was immediately formed. The stirring was continued for 2 h at 50°C, after which the precipitate was filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Preparation of ligand HL^2

To an aqueous solution containing 9-fluorenone (1.44 g, 0.008 mol) in 30 mL ethyl alcohol solution (50%) containing anhydrous sodium acetate (1.31 g, 0.016 mol) at 35–40°C, the semicarbazide hydrochloride (0.89 g, 0.008 mol) in 10 mL ethyl alcohol (50%) was added. The resulting solution was then refluxed for 6 h, and a yellow precipitate was formed. The precipitate was filtered, washed, with ethyl alcohol and diethyl ether, and finally dried in vacuum. The synthesis of the hydrochloride salt of HL^2 was reported,[16] but the condition of the reaction is not similar. Structure of ligand HL^2 is shown in Figure 1.

Preparation of HL^2 complexes

Ag(I)-ligand HL^2. This complex was prepared when a hot solution of silver nitrate (0.16 g, 0.001 mol) was added to a hot solution of ligand HL^2 (0.237 g, 0.001 mol) in 20 mL ethyl alcohol/chloroform (1:1) mixture with continuous stirring, which resulted in a brown precipitate immediately. The stirring was continued with reflux for 1 h at 40°C. A dark green precipitate was formed after slow evaporation of the

resulting solution. The produced precipitate was filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

2) VO-ligand HL^2. This complex was prepared by adding solution of $VOSO_4 . H_2O$ (0.181 g, 0.001 mol) in 5 mL water to a hot solution of ligand HL^2 (0.237 g, 0.001 mol) in 20 mL ethyl alcohol-chloroform mixture (1:1 by volume). The stirring was continued for 1 h, and a green precipitate was formed. The resulting precipitate was filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Preparation of ligand L^3

To an aqueous solution containing 9-F (3.6 g, 0.02 mol) in 15 mL ethyl alcohol) at 35°C, ethylendiamine (0.6 g, 0.01 mol) was added followed by 5 drops of glacial acetic acid. The resulting solution was refluxed at 50°C for 15 h, and a yellowish white precipitate was formed. The precipitate was washed, with ethyl alcohol and diethyl ether, and dried in vacuum. Structure of ligand L^3 is shown in Figure 2.

Preparation of L^3 complexes

La(III)-ligand L^3. To a warm suspension ($\sim$ 40°C) of the Schiff base ligand L^3 (0.384 g, 0.001 mol) in 50 mL methyl alcohol, a hot solution of $LaCl_3.7H_2O$ (0.371 g, 0.001 mol) in 20 mL ethyl alcohol was added. The resulting mixture was refluxed at 40°C for 6 h, and the produced solution was allowed to evaporate slowly at 60°C when yellow crystals were obtained. The crystals formed were filtered, washed, with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Zn (II)-L^3. This complex was formed when a warm solution of $ZnCl_2$ (0.136 g, 0.001 mol) in 10 mL ethyl alcohol was added to a hot suspension of the Schiff base ligand L^3 (0.38 g, 0.001 mol). The resulting solution was refluxed at 60°C for 10 h. Upon allowing this solution to evaporate slowly at 60°C, yellow crystals were formed. The crystals were filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Ag(I)-L^3. Upon adding a warm solution of $AgNO_3$ (0.169 g, 0.001 mol) in 5 mL H_2O to a hot suspension of the Schiff base ligand L^3 (0.38 g, 0.001 mol) with stirring at 50°C, a yellowish green precipitate was formed immediately. The precipitate was then filtered, washed with ethyl alcohol and diethyl ether, and finally dried in vacuum.

Antitumor activity of the (E. A. A.)

A set of sterile test tubes was used, where 2.5×10^5 tumor cells per mL were suspended in phosphate buffer saline. Then, 25, 50, and

100 μg/mL from each of the ligands HL^1, HL^2 and L^3, Cu(II)-HL^1, La(III)-L^3, and VO(IV)-HL^2 complexes were added to the suspension and kept at 37°C for 2 h. Trypan blue dye exclusion test was then carried out to calculate the percentage of nonviable cells.[17]

RESULTS AND DISCUSSION

The elemental analyses of the ligands HL^1, HL^2, and L^3 and their complexes were listed in Table I.

Mass Spectra

The mass spectra of the ligands used, HL^1, HL^2, L^3, exhibit the molecular ion peaks at m/e 253, 237, and 384, respectively (Figure 3), which confirms the proposed formulas. Their proposed pathway fragmentation patterns are described in Schemes 1–3.

IR Spectra

The significant IR bands of the ligands and their metal complexes are given in Table II. Both ligands HL^1 and HL^2 can exhibit tautomerism, since they contain NH—C=S and NH—C=O functional groups, respectively. However, the absence of the ν(S-H) band at 2570 cm^{-1} in the case of ligand HL^1 and a band at higher than 3500 cm^{-1} from the spectrum of ligand HL^2 (representative of hydroxyl form of the enolic structure) indicates the thionic and ketonic nature of these ligands, respectively, in the solid state.[18,19] Moreover, the bands around 1597 cm^{-1}, 1057 cm^{-1}, and 850 cm^{-1} in the ligand HL^1 spectra are assigned, respectively, to ν C=N, ν N—N and ν C=S groups. These bands are shifted or weakened upon complexation with silver and copper ions, indicating the participation of both of S and imine N in complexation. Also, the new band appeared around 1708 cm^{-1} due to a new C=N group in the case of Cu-ligand. HL^1 complex shows the coordination via the S atom with the displacement of one hydrogen atom upon thioenolization. In addition, the band observed at 1296 cm^{-1} in case of Ag-HL^1 complex may be due to a coordinated nitrate group.[20]

The infrared spectra of ligand HL^2 exhibit two bands around 1708, 1575 cm^{-1} are assigned respectively, to νC=O and νC=N of the semicarbazone ligand. These bands are shifted and weakened upon complexation in the case of vanadyl and silver complexes. This indicates that coordination takes place through the nitrogen and oxygen of the C=N and C=O groups, respectively. The coordination of the azomethine

TABLE I Analytical and Physical Data of the Ligands HL^1, HL^2, L^3 and Their Metal Complexes

Ligand and complexes	Yield %	F.W	color	M.P (D.P) °C	%C Calc. (Found)	%H Calc. (Found)	%N Calc. (Found)	%S Calc. (Found)	Molar conductance Λ_m (Ω^{-1} cm^2 mol^{-1})	M:L
HL^1	89	253	Yellow	186	66.40	4.35	16.60	12.65		
$C_{14}H_{11}N_3S$					(66.44)	(4.29)	(16.24)	(12.51)		
HL^2	70	237.2	Pale yellow	210	70.89	4.64	17.68			
$C_{14}H_{11}N_3O$					(70.51)	(4.50)	(17.59)			
L^3	78	384	Yellowish	195	87.50	5.21	7.29			
$C_{28}H_{20}N_2$			white		(87.11)	(5.36)	(7.31)			
$[Ag(HL^1)(H_2O)NO_3]$	62	441.0	Dirty green	290	38.09	2.95	12.69	7.25	13.5	1:1
$C_{14}H_{13}N_4SO_4Ag$					(38.01)	(2.83)	(12.72)	(7.18)		
$[Cu(L^1)_2(H_2O)_2].2H_2O$	66	639.5	Deep brown	>300	52.54	4.38	13.13	10.00	20.4	1:2
$C_{28}H_{28}N_6S_2O_4Cu$					(51.97)	(4.69)	(13.25)	(9.88)		
$[Ag(HL^2)(H_2O)NO_3].H_2O$	59	443	Dirty green	285	37.92	3.39	12.64		9.10	1:1
$C_{14}H_{15}N_4O_6Ag$					(38.07)	(3.50)	(12.45)			
$[VO(HL^2)(H_2O)SO_4].2H_2O$	56	438	Green	250	38.35	3.89	9.59	7.30	11.5	1:1
$C_{14}H_{17}N_3SO_8V$					(37.83)	(3.88)	(9.47)	(7.19)		
$[La(L^3)_2(H_2O)Cl_3]$	63	1031.5	Yellow	>300	65.15	4.07	5.43		7.7	1:2
$C_{56}H_{42}ON_4Cl_3La$					(65.62)	(4.18)	(5.36)			
$[Zn(L^3)_2Cl_2].4H_2O$	69	976.4	Yellow	275	68.82	4.92	5.74		23	1:2
$C_{56}H_{48}N_4O_4Cl_2Zn$					(68.95)	(4.92)	(5.52)			
$[Ag(L^3)_2]NO_35H_2O$	71	1028	Green	260	65.37	4.86	6.81		85.24	1:2
$C_{56}H_{50}N_5O_8Ag$					(65.79)	(4.66)	(6.62)			

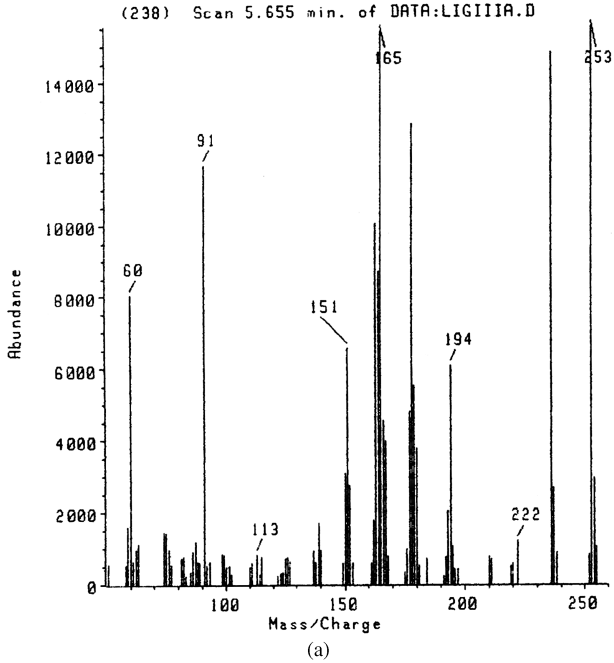
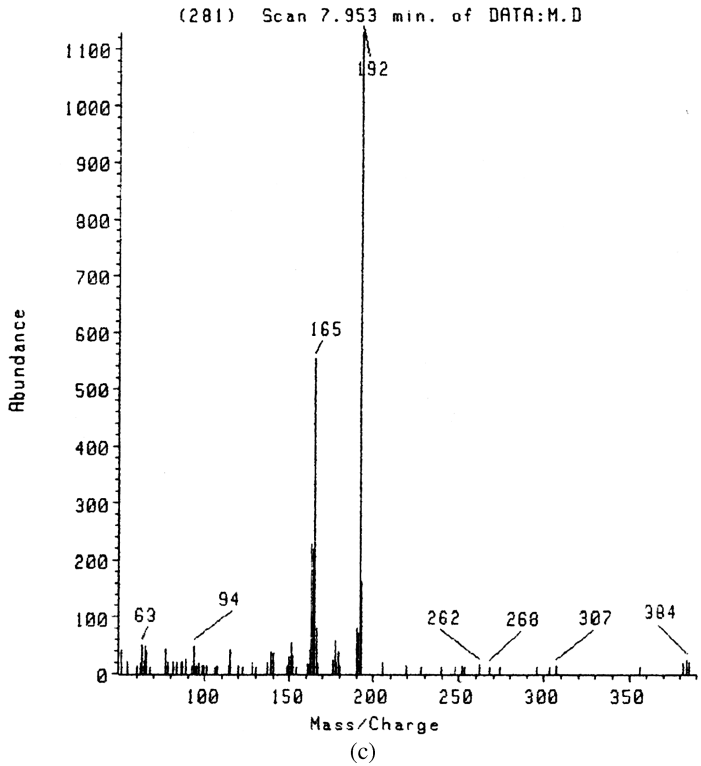


FIGURE 3 (Continued on next page)



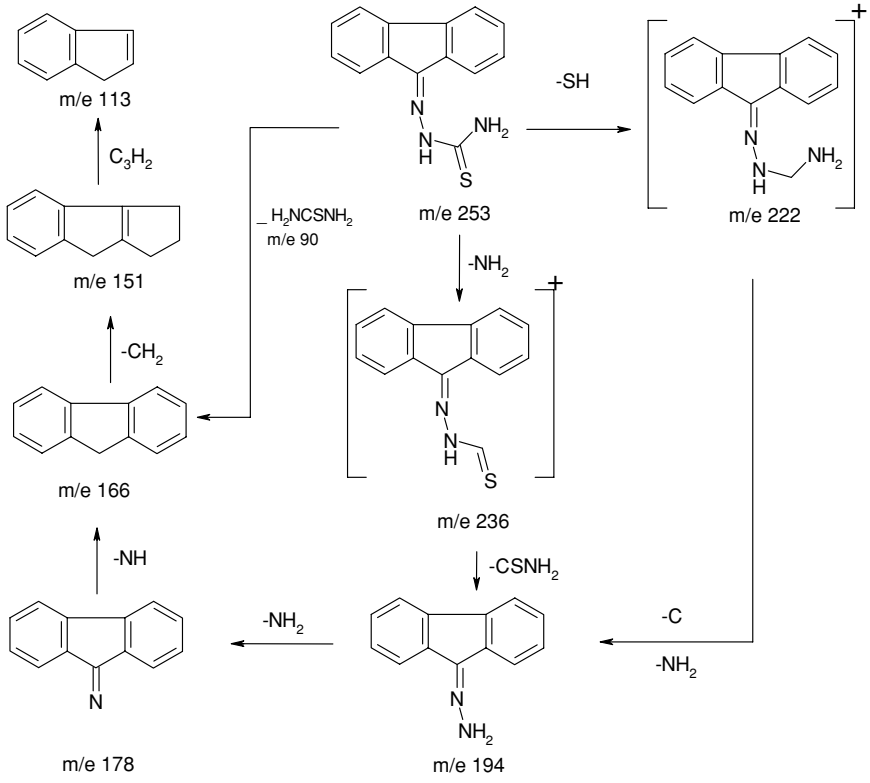
(c)

FIGURE 3 Mass spectra of HL^1 (a), HL^2 (b), L^3 (c).

nitrogen atom is also supported by the shift of the band assigned to the N-N stretching from 1068 cm^{-1} to 1129 cm^{-1} in Ag(I)-HL^2 and 1172 cm^{-1} in the case of the VO-HL^2 complex.[21]

The two bands that appeared at 1381 and 812 cm^{-1} show that the nitrate group acts as a monodonate coordinating agent in Ag(I)-HL^2 complex.[18] Also, the appearance of the two new bands at 1119 and 615 cm^{-1} indicates unidentate behavior of the sulphate group,[22] whereas the new band shown around 998 is due to ν V=O stretching in case of HL^2-VO complex.[23]

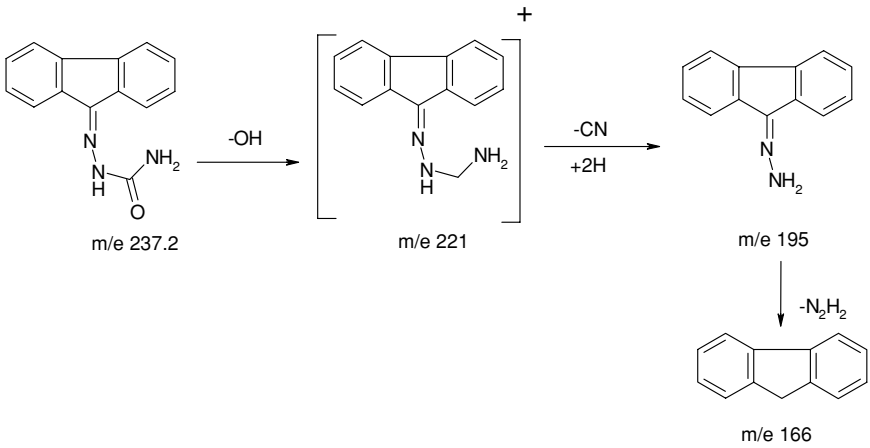
The infrared spectra of ligand L^3 shows two bands at 1642 and 1601 cm^{-1}. These bands can be attributed to the two azomethine groups, R−C=N indicating the formation of the Schiff base products.[18] The band at 1641 cm^{-1} is shifted to higher wavenumber (1713 cm^{-1}) in both the La and Zn complexes, while the other band is observed at nearly the same position in the IR spectra of the ligand, indicating



Fragmentation of HL[1]

SCHEME 1

involvement of only one azomethine nitrogen in chelation. However, these bands are shifted towards lower frequency in the spectra of the Ag complex (1630 and 1594 cm^{-1}), which suggests the coordination through both azomethine groups. Also, the appearance of two characteristic bands at 827 and 1341 cm^{-1} indicates the participation of the nitrate group in the complex formation as ionic fashion.[24] The presence of new broad band in the 3376–3463 cm^{-1} region may be due to ν OH of water in the ligands HL^1, HL^2, and L^3 complexes.



Fragmentation of HL[2]

SCHEME 2

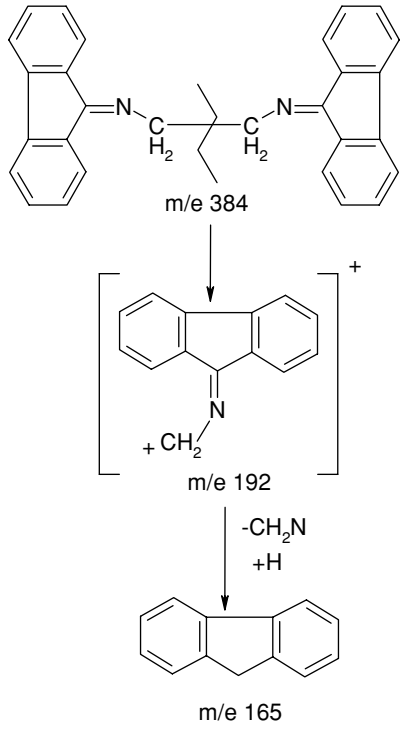
^{1}H NMR spectra

The ^{1}H NMR spectra of the ligands HL^1 and HL^2 and their diamagnetic complexes in DMSO solutions with assignments are collected in Table III, and shown in Figures 4–6.

The ^{1}H NMR spectra of the free ligands shows beside the aromatic proton signals appearing at 7.33–8.08 and 7.32–8.31 ppm exchangeable signals at 10.85 and 10.08 ppm assigned to the imino proton and 8.45–8.75 and 6.97 ppm assigned to amino protons in case of the ligands HL^1 and HL^2, respectively. These later signals disappeared in presence of D_2O. The high frequency singlets at 10.85 ppm and at 10.08 ppm in case of HL^1 and HL^2 ligands are assigned to hydrazinic (N(2)-H) protons, indicating that in solution the ligands HL^1 and HL^2 exist in thionic and ketonic forms, respectively.[25]

Unfortunately, the ligand L^3 is insufficiently soluble in DMSO to acquire a ^{1}H NMR spectrum.

The signals due to the hydrazinic protons are either shielded or deshielded in the case of HL^1-Ag and HL^2-Ag complexes, confirming non-deprotonation and S-coordination or O-coordination in these complexes, respectively.[26]



Fragmentation of L^3

SCHEME 3

Electronic Spectra

The significant electronic absorption bands of the ligands and their metal complexes are listed in Table IV. The free semicarbazone, thiosemicarbazone, and ethylenediamine ligands have bands in the range 240–285 nm, 260–295 nm, and 265–290 nm in case of the ligands HL^1, HL^2, and L^3, respectively. These bands are assigned to $\pi \rightarrow \pi^*$ transition, while the bands around 355, 320, and 300 nm in case of the ligands HL^1, HL^2, and L^3 are assigned to $n \rightarrow \pi^*$, respectively.[27–29] These bands were shifted on complexation, and the new bands around 430 nm in the case of Ag-HL^1 and 425 nm in the case of Cu(II)-HL^1, and 330 nm in Ag-HL^1 and VO-(IV) may be considered as M-L charge transfer bands.[30] In addition the two bands appearing at 460 nm and 590 nm in the case of the Cu(II)-HL^1 complex

TABLE II IR Spectra (4000-400 cm^{-1}) of the Ligands HL^1, HL^2, L^3 and Their Metal Complexes

Compound	$\upsilon NH_2/OH_{(H_2O)}$	υNH	$\upsilon C{=}S$	$\upsilon C{=}N$	$\upsilon N\text{-}N$	$\upsilon C{=}O$	υNO_3	υSO_4	$\upsilon V{=}O$
HL^1	3410 S 3262 S	3153 S	850 S	1597 S	1057 S				
$[Ag(HL^1)(H_2O)NO_3]$	3402 m 3260 m	3153 m	837 m	1612 S	1104 m		1296		
$[Cu(L^1)_2(H_2O)_2]2H_2O$	3449 Vw 3346 Vw		874 w	1708 S 1589 S	1175 m				
HL^2	3463 m 3367 m	3207 m		1575m	1068	1707 VS			
$[Ag(HL^2)(H_2O)NO_3]H_2O$	3419 m 3331 m	3177 S		1526m	1129 S	1679 w 1674 S	1381 S 812 S		
$[VO(HL^2)(H_2O)SO_4]2H_2O$	2460 m 3367 w	3205 w		1574w	1172 S	1705 m		1119 VS, 615 m	998 m
L^3				1641 S 1601 S					
$[La(L^3)_2(H_2O)Cl_3]$	3393 Vb			1713 S 1599 S					
$[Zn(L^3)_2Cl_2].4H_2O$	3401 b			1713 S 1602 S					
$[Ag(L^3)_2]NO_3.5H_2O$	3376 b			1603 S 1594 S					

TABLE III ^{1}H NMR Spectral Data of the Ligand (HL^1), (HL^2) and Their Diamagnetic Ag (I) Complexes Recorded in DMSO-d_6 Solution

Ligands and their Complexes	Ar-H	CS-NH_2	CS-NH	CO-NH_2	CO-NH
Ligand HL^1	7.33–8.08	8.75, 8.45	10.85		
HL^1- Ag(I)	7.39–7.91	9.00, 9.39	11.60		
Ligand HL^2	7.32–8.31			6.97	10.08
HL^2- Ag(I)	7.32–8.30			6.94	10.50

may be assigned to d-d transition, suggesting the six-coordinated Oh geometry of the copper(II) complex.[31] The expected d-d transition in the case of VO-(IV) can not be detected even with concentrated solutions. It may be lost in the low energy tail of the charge transfer transition.[32–35]

Molar Conductance Data

The metal complexes discussed herein were dissolved in DMF, and the molar conductivities of 10^{-3} M of their solutions at room temperature were measured to establish the charge of the metal complexes. The conductance data in Table II indicate that all the metal complexes except Ag-L_3 have conductivity values in the range characteristic for the non-electrolytic nature, suggesting that these complexes are neutral.[36] Ag-L_3 complex has molar conductance value of 85 Ω^{-1}, which indicates that the nitrate group is uncoordinated, and which may also be supported by the presence of two bands observed at 827 and 1341 cm^{-1}, indicating the participation of the ionic nitrate group in complex formation.

Magnetic Susceptibility Measurements

The μ eff values of Cu-HL^1 and VO-HL^2 are 1.87 and 1.66 BM, respectively. These results of the magnetic susceptibility measurements at room temperature showed that these complexes were paramagnetic and copper (II) and oxovanadium (IV) have single electron in the d-orbital, suggesting octahedral and square pyramidal geometries for the Cu(II) and VO(IV) complexes, respectively.[37]

The complexes: Ag-HL^1, Ag-HL^2, La-L^3, Ag-L^3, and Zn-L^3 are diamagnetic, and according to the elemental analyses data of these complexes, we suggest the tetrahedral geometry for the silver and zinc complexes, whereas La-L^3 has an octahedral geometry.

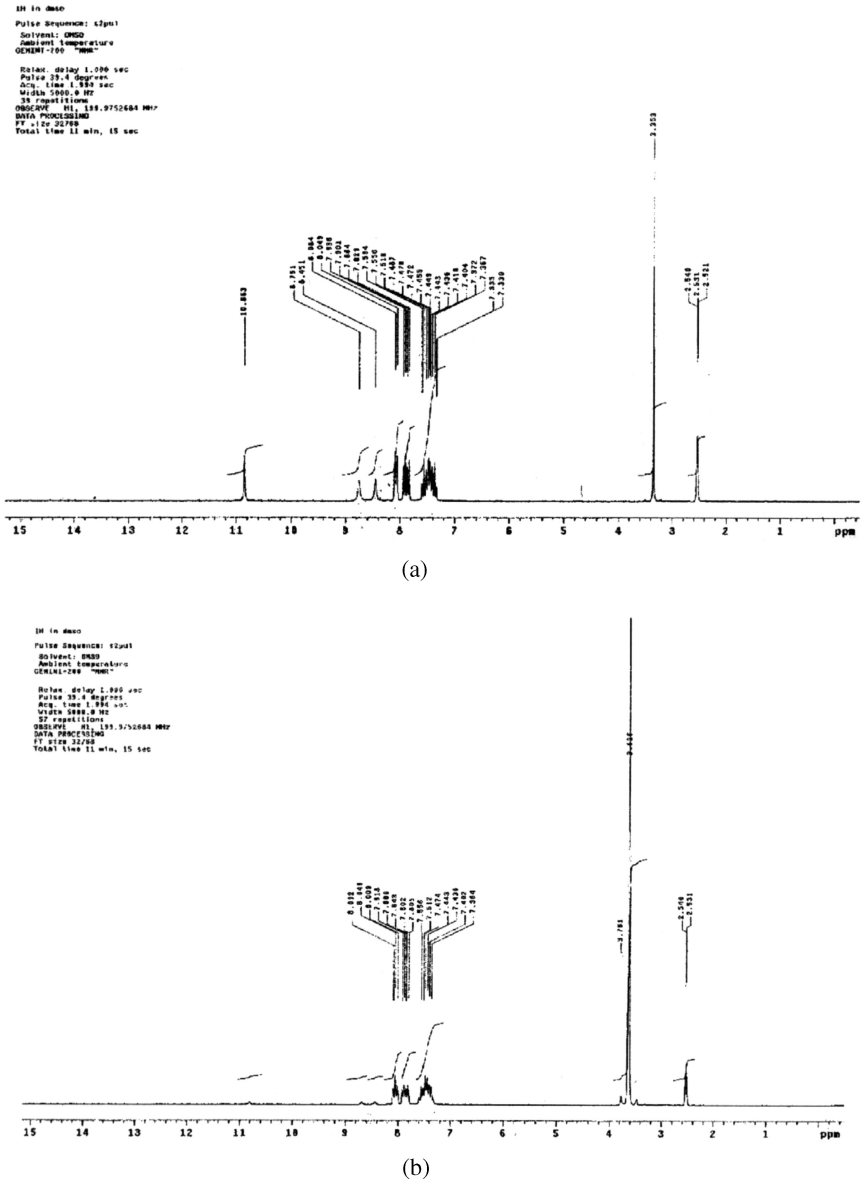


FIGURE 4 ^{1}HNMR spectra of HL^{1} ligand in DMSO (a) and in D_2O (b).

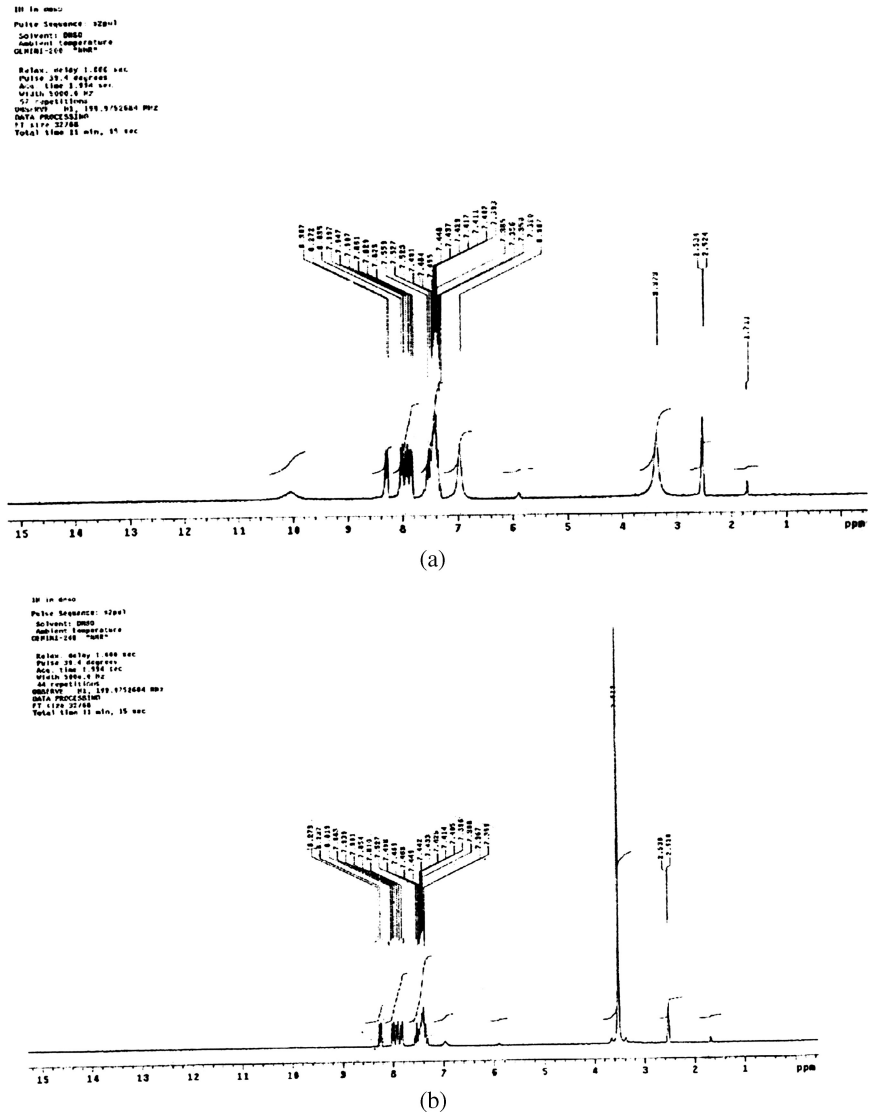
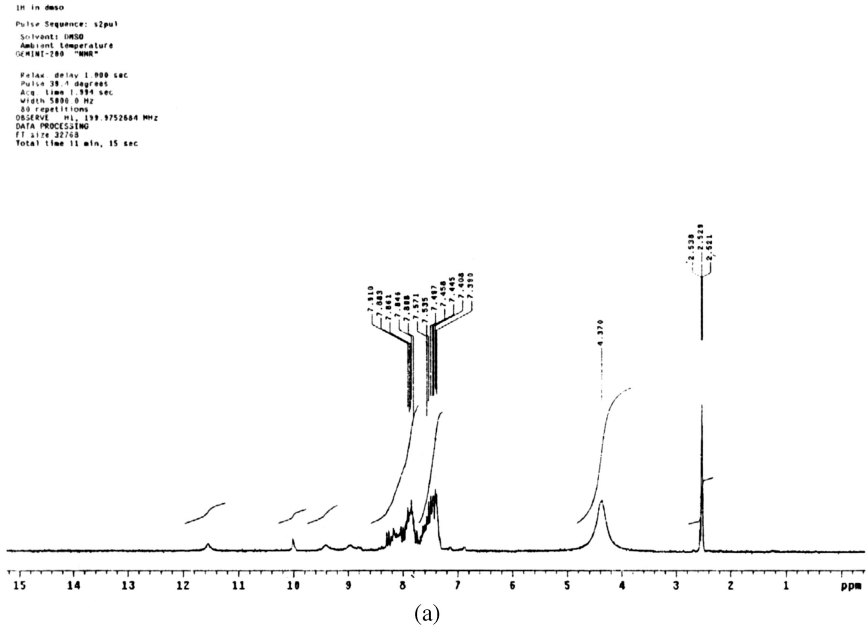


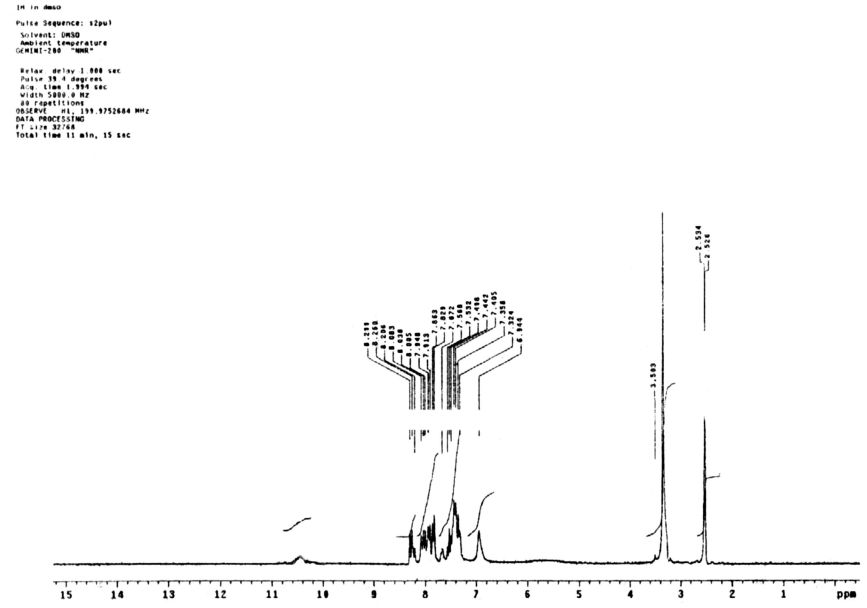
FIGURE 5 ^{1}HNMR spectra of HL^{2} ligand in DMSO (a) and in D_2O (b).

Suggested Structural Formulas of the Complexes

From the spectral data and the elemental analyses, the structural of the prepared complexes may be formulated as shown in the Figures 7–9.



(a)



(b)

FIGURE 6 ^{1}HNMR Spectra of Ag-HL^{1} (a) and Ag-HL^{2} (b) complexes.

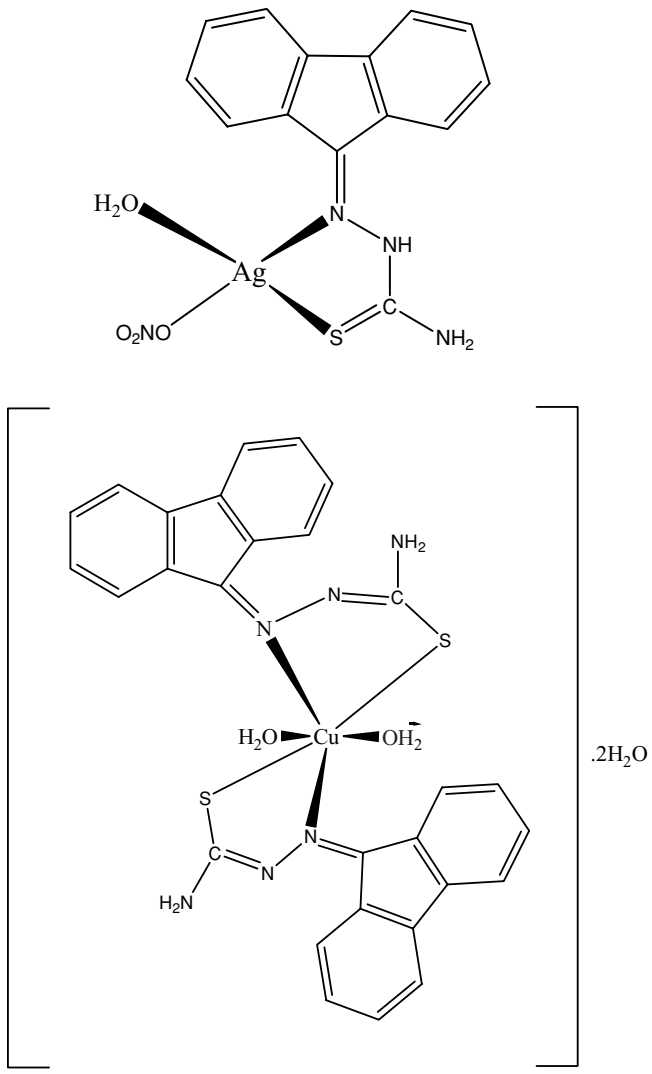


FIGURE 7 Suggested structures of HL^1 complexes M L=1:2 and1:1.

Biological Evaluation

Antitumor activity of ligands HL^1, HL^2, L^3 and Cu (II)-HL^1, VO(IV)-HL^2, La(III)-L^3 complexes are listed in Table V.

The synthesis of polycyclic aromatic systems by various methodologies has been published extensively, and the carcinogenic properties

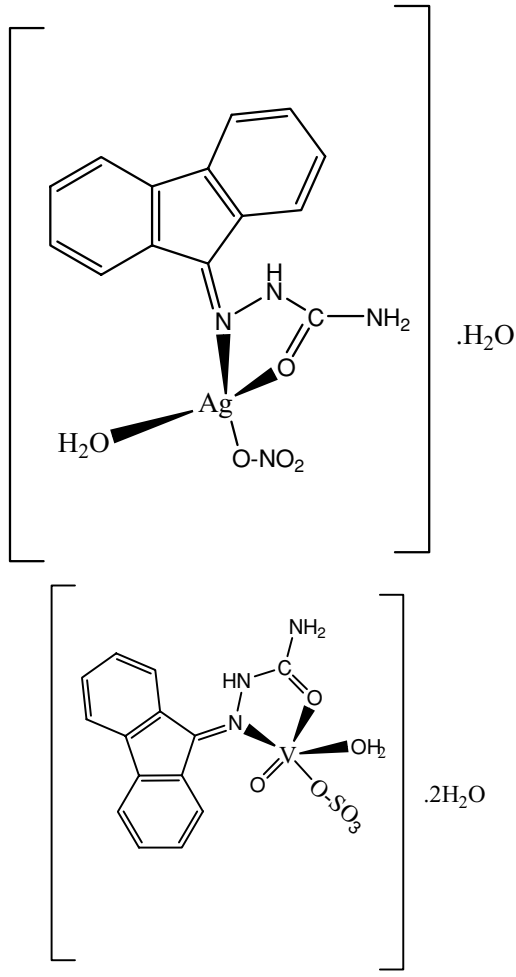


FIGURE 8 Suggested structures of HL^2 complexes M;L=1;1.

of such compounds have been explained by advancing a number of different mechanisms.[12] The antitumor activity of such compounds is suggested to depend on intercalation with or covalent binding to DNA, whereas many other sites of interaction such as the cell membrane have also been identified.

The results of antitumor activity using (E. A. A.) for ligands and their complexes showed no antitumor activity of ligand HL^1, La (III)- L^3, and Cu(II)-HL^1 complexes for all concentrations, whereas ligand L^3 shows more activity than ligand HL^2 at 25 and 50 μg/mL concentrations. This

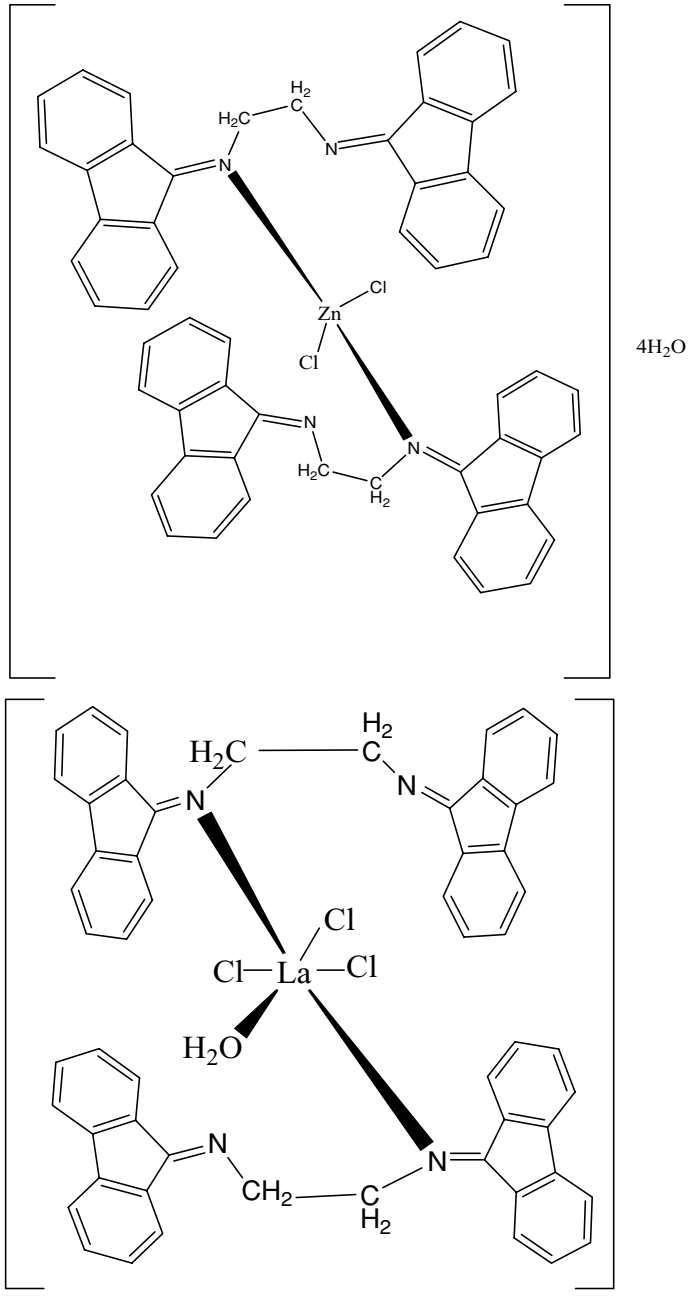


FIGURE 9 (Continued on next page)

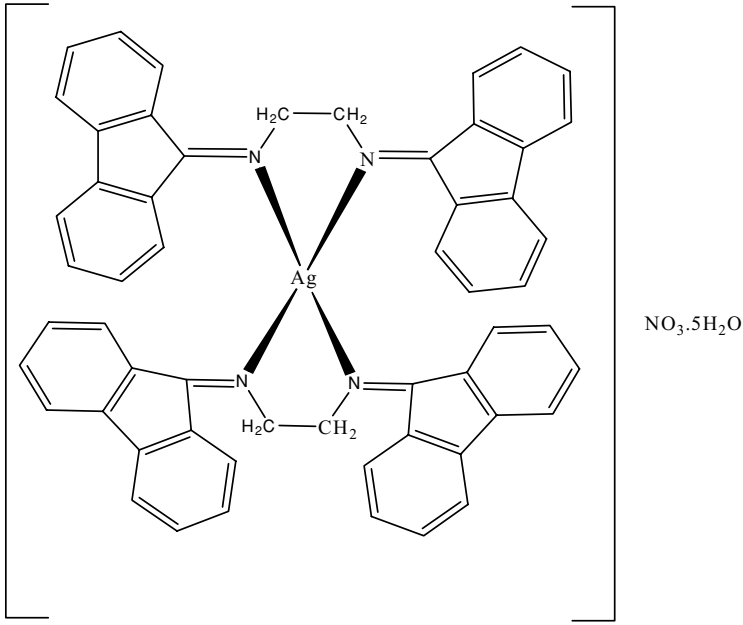


FIGURE 9 Suggested structures of the L^3 complexes M L=1:2.

TABLE IV Electronic Absorption Spectral Bands of the Ligands and Their Complexes

Ligand and their complexes	Electronic absorption bands ($\lambda_{max\ nm}$)		
	Intra ligand and CT bands	d-d bands	μeff (B.M)
HL^1	240, 285, 355		
$[Ag(HL^1)(H_2O)NO_3]$	260, 290, 330, 430		diamagnetic
$[Cu(L^1)_2(H_2O)_2]2H_2O$	260, 295, 370, 425	460, 590	1.87
HL^2	230, 250, 260, 295, 320		
$[Ag(HL^2)(H_2O)NO_3]H_2O$	240, 255, 300, 330		diamagnetic
$[VO(HL^2)(H_2O)SO_4]2H_2O$	235, 245, 260, 300, 330		1.66
L^3	265, 290, 300		
$[La(L^3)_2(H_2O)Cl_3]$	270, 285, 295, 310, 325, 390		Diamagnetic
$[Zn(L^3)_2Cl_2].4H_2O$	265, 285, 295, 310, 330, 390		Diamagnetic
$Ag(L^3)_2NO_3.5H_2O$	255, 275, 295		diamagnetic

may be attributed to the aromatic ring stacking between nucleobases, which is considered to be a major driving force that leads to binding to DNA, and the extent of binding is expected to depend on the size and electron density of the interacting aromatic rings, as well as on

TABLE V Antitumor Activity of Ligands HL^1, HL^2, and L^3 and Their Metal Complexes Cu(II), VO(IV), and La(III) Using (E. A. A.)

	% Inhibition of cell viability μg/mL		
Compound	25	50	100
HL^1	0%	0%	0%
Cu (II)-HL^1	0%	0%	0%
HL^2	30%	50%	90%
VO (IV)-HL^2	50%	70%	90%
L^3	40%	60%	90%
La (III)-L^3	0%	0%	0%

the combined effect of hydrophobic and hydrophilic interactions.[38] On the other hand, VO(IV)-HL^2 complex exhibited the maximum antitumor activity at all concentrations. It should be noted that the chelation could facilitate the ability of a complex to cross a cell membrane and can be explained by Tweedy's chelation theory. Chelation considerably reduces the polarity of the metal ion, mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole chelate ring. Such chelation could also enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane.[39]

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