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Template Synthesis and Physicochemical Studies of 14-Membered Functionalized Pendant Arm Schiff-Base Macrocyclic Complexes of Co(II), Ni(II), Cu(II), and Zn(II): DNA Binding Studies on a Cu(II) Complex

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Template Synthesis and Physicochemical Studies of 14-Membered Functionalized Pendant Arm Schiff-Base Macrocyclic Complexes of Co(II), Ni(II), Cu(II), and Zn(II): DNA Binding Studies on a Cu(II) Complex

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A series of functional pendant armed 14-membered Schiff-base macrocyclic complexes [ML(NO_3)$_2$], where M = Co(II), Ni(II), Cu(II), and Zn(II), has been synthesized by template condensation of 3,3′-diaminobenzidene and acetylacetone. The complexes have been characterized by elemental analyses, molar conductance measurements, magnetic susceptibility measurements, and electrospray ionization (ESI) mass, ^{1}H-nuclear magnetic resonance (NMR), infrared (IR), electronic, and electron paramagnetic resonance (EPR) spectral studies. The results of elemental analyses, ESI mass spectroscopy, and conductivity measurements confirmed the stoichiometry of the complexes, while the characteristic absorption bands and resonance peaks in IR and NMR spectra confirmed the formation of frameworks of complexes. The molar conductance measurements of the complexes in dimethyl sulfoxide (DMSO) correspond to being non-electrolyte in nature. However, the overall geometry of the complexes has been assigned on the positions of bands in electronic spectra and magnetic moment data. The distortion in Cu(II) complexes has been deduced on the basis of EPR data. Absorption and fluorescence studies on the Cu(II) complex show a significant binding to CT DNA.

Keywords DNA binding studies, functional pendant arm, Schiff base macrocyclic complexes, spectral studies, template synthesis

INTRODUCTION

The design and study of well-arranged metal-containing macrocycles have gained an accelerated research interest in recent years and have been the subject of numerous reports because of the compounds' unique coordination chemistry.[1,2] Such compounds usually behave as model ligands for metal enzymes, as metal ion-selective ligands, and as metal-chelating agents for medical purposes and are also significant for the development of new methodologies.[3] Schiff bases have been of great importance in the macrocyclic area of chemistry due to their selective chelation to certain metal ions depending on the number, type, and position of their donor atoms, the ionic radius of the metal center, coordinating properties of counterions, and rational synthetic routes involving metal ion as template, which orient the reacting groups of linear substrates in the desired conformation prior to ring closure.[4,5] Much effort has now been focused on pendant arm macrocyclic complexes due to the fact that the ligating group attached to the macrocyclic skeleton can offer additional donor groups to maintain the coordination sphere of metals in the macrocycles.[6] These molecules play an important role in the processes of molecular recognition of organic compounds.[7,8] Complexes of modified aza-crowns are useful as agents for the selective binding of actinides.[9] Pendant arms can enhance the selectivity of the ligand for a given ion and may allow for fine-tuning of the properties of the complexes.[10] These ligands have the ability to stabilize complexes with unusual oxidation states and mixed valence states. Their complexes exhibit antitumor or anti-HIV activity, act as probes and model molecules for biochemical processes, and also have the ability to cleave DNA.[11–13] Further, bimetallic complexes have a possibility of magnetic interactions between two metal ions, leading to the design of molecular magnetic materials.[14] Functionalized pendant arm macrocyclic complexes have been designed and prepared to mimic the structure and properties of certain metalloenzymes and metalloproteins.[15] Currently, the chemistry of tetraaza macrocyclic ligands bearing a functionalized pendant arm continues to develop intensively, because of their applications in various areas such as medical, environmental sciences, biomimetic chemistry, catalysis, and molecular electronics.[10,16–20] Such ligands show enhanced thermodynamic and kinetic stabilities due to their modified complexation properties relative to the corresponding simple macrocycle precursor.[21]

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These properties stimulate researchers to further exploit their derivatives.[22]

Keeping these facts in mind, we have synthesized and characterized 14-membered functionalized pendant arm Schiff base macrocyclic complexes by the template condensation reaction of 3,3′-diaminobenzidene and acetylacetone.

EXPERIMENTAL

Materials and Methods

Metal salts (all from Merck) were commercially available pure samples. The chemicals 3,3′-diaminobenzidene (Acros) and acetylacetone (Fluka) were used as received. All the solvents used were of standard analytical grade. Highly polymerized calf-thymus DNA sodium salt (7% Na content) was purchased from Sigma Chemical Co. Other chemicals were of reagent grade and used without further purification.

Preparation of Stock Solutions

Calf thymus DNA was dissolved to 0.5% w/w, (12.5 mM DNA/phosphate) in 0.1 *M* sodium phosphate buffer (pH 7.40) at 310 K for 24 h with occasional stirring to ensure formation of homogeneous solution. The purity of the DNA solution was checked from the absorbance ratio A_{260}/A_{280}. Since the absorption ratio lies in the range $1.8 < A_{260}/A_{280} < 1.9$, no further deproteinization of DNA was needed. A stock solution of [CuL$(NO_3)_2$] complex at 5 mg/mL concentration was also prepared.

Synthesis of the Complexes

Dinitrato[2,3:9,10-biphenyldiamine-5,7,12,14-tetramethyl-1,4,8,11-tetraazacycloteradecane-4,7,11,14-tetraene] Metal(II), [MLNO$_3$] [M = Co(II), Ni(II), Cu(II), and Zn(II)

To a solution of 3,3′-diaminobenzidine (0.002 mol, 0.428 g) in 20 mL of acetonitrile and distilled water (1:1 ratio) placed in a round-bottom flask was slowly added a solution of acetylacetone (0.002 mol, 0.20 mL) taken in 20 mL acetonitrile and the mixture was stirred for about 2–3 h. This was followed by addition of metal nitrate (0.001 mL) solution in 20 mL acetonitrile. The reaction mixture was stirred for 12 h, leading to the isolation of a solid product. The solid product thus formed was filtered, washed with methanol, and dried in vacuum.

Physical Measurements

The elemental analyses were obtained from the microanalytical laboratory of the Central Drug Research Institute (CDRI), Lucknow, India. The infrared (IR) spectra (4000–200 cm^{-1}) were recorded as KBr/CsI discs on the Perkin-Elmer 2400 spectrometer. Metals were determined volumetrically.[23] ^{1}H-Nuclear magnetic resonance (NMR) spectra were recorded in DMSO-d_6 using a Bruker Avance II 400 NMR spectrometer with Me$_4$Si as an internal standard from SAIF, Punjab University, Chandigarh, India. Electrospray mass spectra of the complexes were recorded on a Micromass Quattro II triple-quadruple mass spectrometer. Electron paramagnetic resonance (EPR) spectra were recorded at room temperature on a Varian E-4 X-band spectrometer using TCNE as the g-marker. The ultraviolet (UV)–visible spectrophotometric studies of the freshly prepared 10^{-3} *M* dimethyl sulfoxide (DMSO) solutions of the complexes in the range 200–1100 nm were conducted using a Cintra 5 GBC Scientific Spectrophotometer at room temperature. Magnetic susceptibility measurements were carried out using a Faraday balance at 25°C. The electrical conductivities (10^{-3} *M* solution in DMSO) were obtained on a Systronic type 302 conductivity bridge thermostated at 25.00 ± 0.05°C. Fluorescence measurements were performed on a spectrofluorimeter model RF-5301PC (Shimadzu, Japan) equipped with a 150-W xenon lamp and a slit width of 5 nm. A 1.00-cm quartz cell was

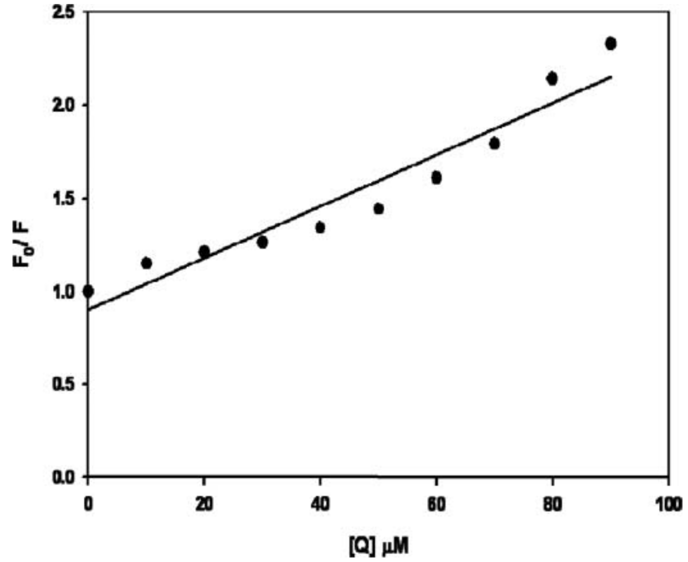


FIG. 1. Stern–Volmer plot for binding of Cu(II) complex with DNA at 298 K.

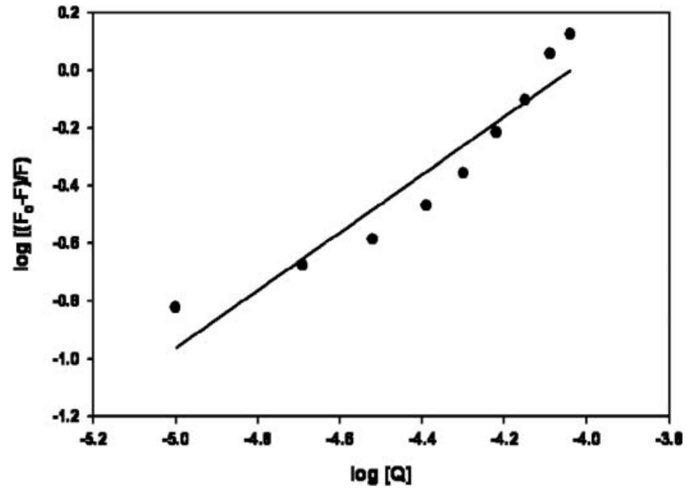


FIG. 2. Plot of log(F$_0$ – F)/F versus log[Q] for determining the binding constant and number of binding sides of Cu(II) complex on DNA.

used for measurements. For the determination of binding parameters, 30 μM of complex solution was placed in a quartz cell and increasing amounts of ctDNA solution were titrated. Fluorescence spectra were recorded at temperature 310 K in the range of 300–400 nm upon excitation at 365 nm (λ_{ex} was 365 nm). The UV measurements of calf thymus DNA were recorded on a Shimadzu double-beam spectrophotometer model UV1700 using a cuvette of 1 cm path length. Absorbance value of DNA in the absence and presence of the complex was made in the range of 220–300 nm. DNA concentration was fixed at 0.1 μM, while the complex concentration was varied from 5 to 20 μM.

Binding Equilibrium

To further elaborate the fluorescence quenching mechanism the Stern–Volmer equation (Eq. 1) was used for data analysis[24]:

$$F_0/F = 1 + K_{SV}[Q] \quad [1]$$

where F_0 and F are the steady-state fluorescence intensities in the absence and presence of quencher, respectively. K_{SV} is the Stern–Volmer quenching constant and [Q] is the concentration of quencher (DNA). The Ksv for the $[CuL(NO_3)_2]$ complex was found to be of the order of 10^4 (1.39×10^4 $Lmol^{-1}$). The linearity of the F_0/F versus [Q] (Stern–Volmer) plots for the DNA-$[CuL(NO_3)_2]$ complex (Figure 1) depicts that the quenching may be static or dynamic, since the characteristic Stern–Volmer plot of combined quenching (both static and dynamic) has an upward curvature. When ligand molecules bind independently to a set of equivalent sites on a macromolecule, the equilibrium between free and bound molecules is given by Eq. 2[25]:

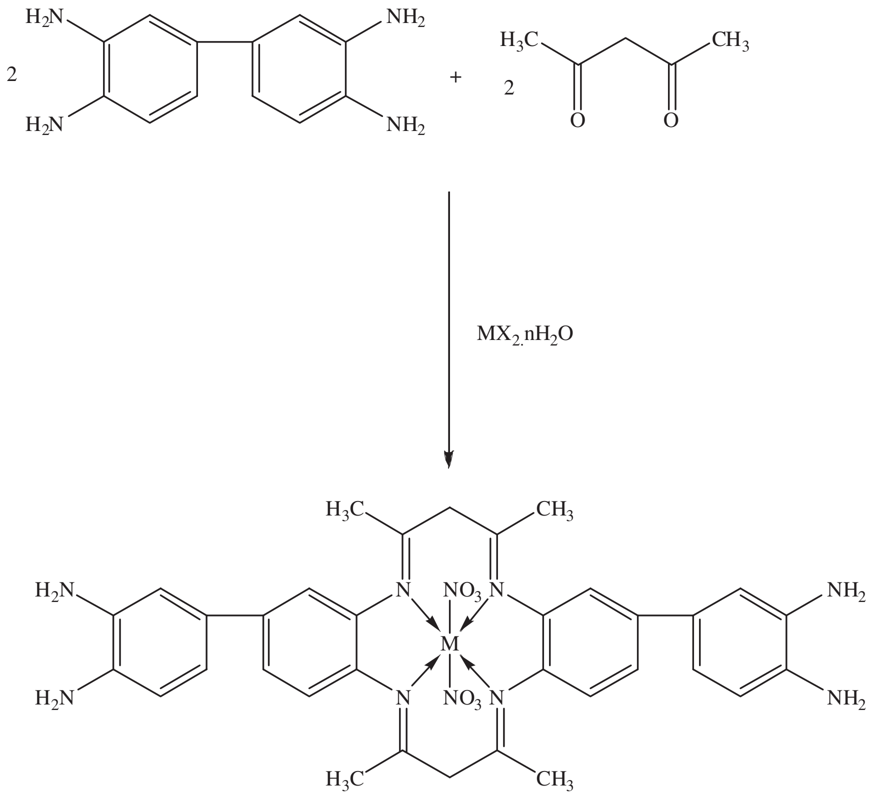
$$\log[(F_0 - F)/F] = \log K + n \log[Q] \quad [2]$$

where K and n are the binding constant and the number of binding sites, respectively. Thus, a plot of $\log(F_0 - F)/F$ versus log[Q] can be used to determine K as well as n (Figure 2). The values of K and n were found to be $(1.11 \pm 1.13) \times 10^4$ M^{-1} and 1.01, respectively.

RESULTS AND DISCUSSION

The template condensation reaction between 3,3′-diaminobenzidene and acetylacetone (1:2:2 molar ratio) resulted in the formation of a novel series of Schiff-base pendant armed macrocyclic complexes, $[ML(NO_3)_2]$ [M = Co(II), Ni(II), Cu(II), and Zn(II)] (Scheme 1). The progress of the reaction was monitored by running thin-layer chromatography (TLC) on silica gel-coated plates. The complexes formed are solids at room temperature and soluble in DMSO.

The formation of complexes was ascertained on the basis of results of elemental analyses, electrospray ionization (ESI) mass



SCH. 1. Suggested structure of Schiff base macrocyclic complexes. M = Co(II), Ni(II), Cu(II), and Zn(II).

TABLE 1
Elemental analyses, *m/z* values, colors, yields, molar conductance, and melting points of complexes

Complexes	*m/z* Found (calc.)	Color	Yield (%)	Found (calc.)%				Molar conductivity (ohm^{-1} cm^2 mol^{-1})/ m.p. (°C)
				M	C	H	N	
[CoL$(NO_3)_2$]	738.79	Black	55	7.56	55.83	4.42	18.53	22/282
$C_{34}H_{36}N_{10}CoO_6$	(739.65)			(7.96)	(55.21)	(4.91)	(18.94)	
[NiL$(NO_3)_2$]	738.32	Brown	58	7.40	55.65	4.15	18.25	21/272
$C_{34}H_{36}N_{10}NiO_6$	(739.41)			(7.94)	(55.23)	(4.91)	(18.94)	
[CuL$(NO_3)_2$]	743.15	Black	62	8.33	54.45	4.35	18.70	23/265
$C_{34}H_{36}N_{10}CuO_6$	(744.27)			(8.54)	(54.87)	(4.87)	(18.82)	
[ZnL$(NO_3)_2$]	738.32	Gray	56	8.15	54.94	4.58	18.33	24/263
$C_{34}H_{36}N_{10}ZnO_6$	(746.10)			(8.76)	(54.73)	(4.86)	(18.77)	

spectra (Table 1), Fourier-transform infrared (FT-IR) (Table 2), and ^{1}H-NMR spectra. The overall geometry of the complexes was inferred from the observed values of magnetic moments and electronic spectra (Table 3). The molar conductance measurements of all the complexes in DMSO suggest their non electrolytic nature.[26]

IR Spectra

Preliminary identification of the synthesized pendant-armed Schiff-base macrocyclic complexes has been obtained from IR spectra (Table 2). The absence of bands characteristic of the carbonyl group of acetyl acetone and the appearance of the υ(C=N) bands in the 1590–1620 cm^{-1} region strongly suggests that the macrocyclic framework has been formed.[27] This is further supported by the appearance of a new band in the region 480–500 cm^{-1} assignable to υ(M−N) vibration.[28] However, the appearance of a doublet in the region 3380–3350 cm^{-1} in all macrocyclic complexes may be due to the N–H stretching frequency of the primary amino groups of the benzidine moiety. A weak absorption band in the region 2920–2925 cm^{-1} may be assigned to the CH_3 stretching vibration.[29] All the complexes show sharp bands corresponding to υ(C−H), δ(C−H), and phenyl ring vibrations, which appear at their expected positions (Table 2). The coordination of nitrato groups has been ascertained by appearance of bands in the 230–240 cm^{-1} regions, which may reasonably be assigned to υ(M−O) of the O–NO_2 group in [M(L)$(NO_3)_2$] complexes.[29] The IR spectra of these complexes show additional bands in the 1230–1270, 1040–1070, and 860–890 cm^{-1} region, which are consistent with monodentate coordination of the nitrato group.[29]

^{1}H-NMR Spectra

The ^{1}H-NMR spectra of the Zn(II) complex show a sharp signal at 2.47 ppm corresponding to imine methyl ($CH_3C{=}N$; 12H) protons, while a singlet at 2.13 ppm may be assigned to central methylene (C-CH_2-C; 4H) protons of the 2,4-pentanedione.[30] However, a singlet at 4.29 ppm may be attributed to the primary amino protons (C_6H_3-NH_2, 8H) of benzidine. A broad multiplet observed in the 6.95–7.21 ppm region may be assigned to the aromatic ring protons.[31]

EPR Spectra

The EPR spectrum of the powdered solid copper(II) complex was recorded on X-band at frequency 9.1 GHz under a magnetic field strength of 3000 G and scan rate 2000, recorded at room temperature. The $g_{\parallel\parallel}$ and $g_{\perp}$ values were computed from the spectrum using TCNE free radical as g marker, which gives $g_{\parallel} = 2.13$ and $g_{\perp} = 2.05$. The observed $g_{\parallel}$ value is less than 2.3, which is in agreement with the covalent character of the metal–ligand bond. The observed trend $g_{\parallel} > g_{\perp} > 2.0023$ suggests that the unpaired electron is localized in the d_{X^2}-d_{y^2} orbital of the Cu(II) ion.

TABLE 2
IR spectral data of the complexes (cm^{-1})

Complexes	υ(C=N)	υ(C–H)	δ(C–H)	υ(M–N)	υ(M–O)	Ring vibrations
[CoL$(NO_3)_2$]	1590 s	2925 s	1450 s	480 s	240 m	1460 s, 1070 s, 785 s
[NiL$(NO_3)_2$]	1605 s	2895 s	1442 s	500 s	237 m	1455s, 1095 s, 775 s
[CuL$(NO_3)_2$]	1620 s	2882 s	1450 s	485 s	235 m	1480 s, 1080 s, 770 s
[ZnL$(NO_3)_2$]	1600 s	2905 s	1468 s	490 s	230 m	1470 s, 1090 s, 790 s

TABLE 3
Magnetic moments and electronic spectral bands with their assignments of the complexes

Complexes	$\mu_{\text{eff.}}$ (BM)	Band position (cm^{-1})	Assignments
$[CoL(NO_3)_2]$	4.59	9185	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$
		16,850	$^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$
		21,200	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
$[NiL(NO_3)_2]$	2.92	10,030	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$,
		15,650	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$
		24,360	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$
$[CuL(NO_3)_2]$	1.86	11,425	$^2B_{1g} \rightarrow {}^2A_{1g}$
		18,750	$^2B_{1g} \rightarrow {}^2B_{2g}$
		27,355	$^2B_{1g} \rightarrow {}^2E_g$

$G = (g_{\parallel} - 2)/(g_{\perp} - 2)$, which measures the exchange interaction between the metal centers in polycrystalline solid, was calculated and it has been found to be less than 4, suggesting considerable exchange interaction in the solid complexes.[32]

Electronic Spectra and Magnetic Moments

The electronic spectrum of the $[CoL(NO_3)_2]$ complex showed three absorption bands at 9185, 16,850, and 21,200 cm^{-1} assignable to the $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$, and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions, respectively, corresponding to the octahedral geometry around the cobalt(II) ion. The observed magnetic moment value of 4.59 B.M. corresponding to a high-spin state further supports the octahedral geometry around the Co(II) ion.[33,34]

The proposed octahedral geometry around the Ni(II) ion in $[NiL(NO_3)_2]$ has been inferred from the observed band positions at 10,030, 15,650, and 24,360 cm^{-1} attributed to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$, and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ transitions, respectively, similar to those reported earlier.[35] The observed magnetic moment of 2.92 B.M. further corroborates an octahedral environment around the Ni(II) ion in the high-spin configuration.[36]

The absorption spectrum of the six-coordinate Cu(II) complex shows three bands at 11,425, 18,750, and 27,355 cm^{-1}, corresponding to the transitions $^2B_{1g} \rightarrow {}^2A_{1g}$, $^2B_{1g} \rightarrow {}^2B_2$, and $^2B_{1g} \rightarrow {}^2E_g$, respectively. Therefore, it may be concluded that the complex possesses tetragonally distorted octahedral geometry. It has been further confirmed by the magnetic moment value of 1.82 B.M. for this complex.[37]

Fluorescence Measurements: Binding Property of the $[CuL(NO_3)_2]$ Complex with DNA

The fluorescence spectroscopy provides insight into the changes taking place in the microenvironment of the DNA–$[CuL(NO_3)_2]$ complex. The interaction of $[CuL(NO_3)_2]$ complex with calf thymus DNA was studied by monitoring the changes in the intrinsic fluorescence of $[CuL(NO_3)_2]$ complex at varying DNA concentration. Figure 3 shows the representative fluorescence emission spectra of the synthesized compound upon excitation at 280 nm. The addition of DNA

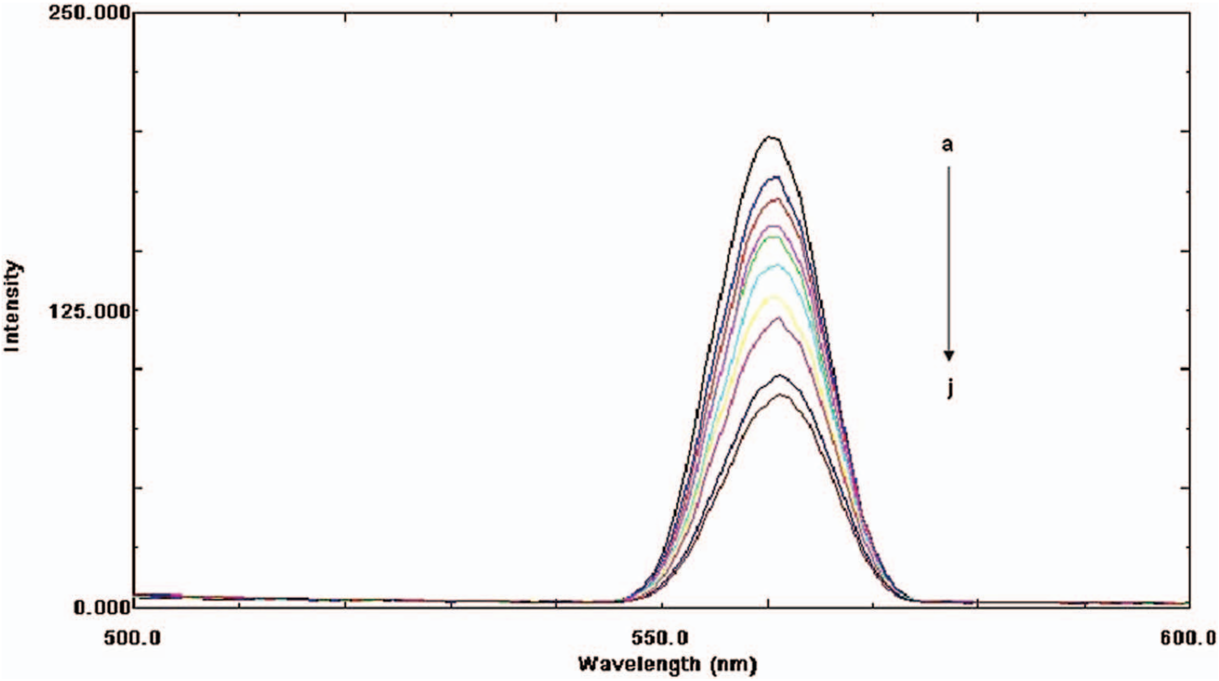


FIG. 3. Fluorescence emission spectra of Cu(II) complex in the absence and presence of increasing amount of DNA from (a) to (j); pH 7.4; T = 298 K (color figure available online).

caused a gradual decrease in the fluorescence emission intensity of the complex with a conspicuous change in the emission spectra. It can be seen that a higher excess of DNA led to more effective quenching of the fluorophore molecule fluorescence. The quenching of the compound fluorescence clearly indicated that the binding of the DNA to the[$CuL(NO_3)_2$] complex has changed the microenvironment of the fluorophore residue. The reduction in the intrinsic fluorescence of the synthesized molecule upon interaction with DNA could be due to masking or burial of [$CuL(NO_3)_2$] complex fluorophore upon interaction between the stacked bases within the helix and/or surface binding at the reactive nucleophilic sites on the heterocyclic nitrogenous bases of DNA molecule.

Absorption Spectroscopy

UV-Vis absorption studies were performed to further ascertain the DNA–[$CuL(NO_3)_2$] complex interaction. The UV absorbance showed an increase with the increase in drug concentration (Figure 4). Since [$CuL(NO_3)_2$] complex does not show any peak in this region (Figure 4), the rise in the DNA absorbance is indicative of the complex formation between DNA and [$CuL(NO_3)_2$]. The [$CuL(NO_3)_2$] complex at 260 nm exhibited hyperchromism of 30% at 1:1 molar ratio. Hypochromism and hyperchromism are both spectral features of DNA concerning its double-helix structure. Hypochromism means the DNA binding mode of the complex is electrostatic effect or intercalation, which can stabilize the DNA duplex, and hyperchromism means the breakage of the secondary structure of DNA.[38,39] So we primarily speculate that complex is interacting with the secondary structure with calf thymus DNA, resulting in its breakage and perturbation. After interaction with the base pairs of DNA, the π–π^* orbital of the bound ligand can couple with the π orbital of the base pairs, due to decreased π–π^* transition energy, which results in bathochromic shift. The prominent shift in the spectra also suggests the tight complexation of synthesized molecule with DNA, which resulted in the change in the absorption maxima of the DNA. The changes just described are indicative of the conformational alteration of DNA on Cu(II) complex binding.

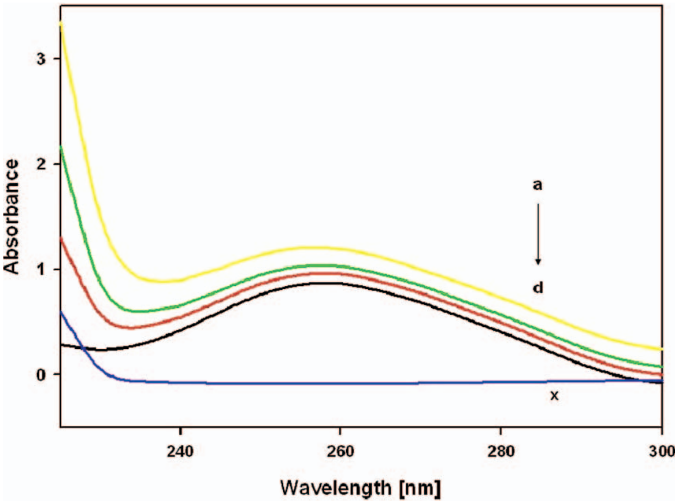


FIG. 4. Absorption spectra of DNA in the absence and presence of different concentration of Cu(II) complex. DNA concentration was 0.10 mM (a). Cu(II) complex concentration for DNA-compound system was at 12.5 μM (b), 25 μM (c), and 50 μM (d), and x represents Cu(II) complex alone (color figure available online).

REFERENCES

1. (a) Lindoy, L.F. Heavy metal ion chemistry of linked macrocyclic systems incorporating oxygen and/or sulfur in their donor sets. *Coord. Chem. Rev.* **1998**, *174*, 327–342. (b) Lindoy, L.F. The transition metal ion chemistry of linked macrocyclic ligands. *Adv. Inorg. Chem*. **1998**, *45*, 75–125. (c) Kaden, T.A. Dinuclear metal complexes of bis-macrocycles. *Coord. Chem. Rev*. **1999**, *190*, 371. (d) Chartres, J.D.; Lindoy, L.F.; Meehan, G.V. Transition and post-transition metal systems incorporating linked synthetic macrocycles as structural elements. *Coord. Chem. Rev*. **2001**, *216*, 249–286.
2. Chandra, S.; Gupta, K. Chromium(III), manganese(II), iron(III), cobalt(II), nickel(II) and copper(II) complexes with a pentadentate, 15-membered new macrocyclic ligand. *Transition Met. Chem.*, **2002**, *27*, 196–199.
3. Bayri, A.; Bahadir, A.R.; Avcu, F.M.; Aytekin, O. Surprising magnetic behavior of cobalt(II) ion in recently prepared macrocycle complexes. Distortion versus intermolecular antiferromagnetic exchange interactions. *Transition. Metal Chem.* **2005**, *30*, 987–991.
4. Radecka-Paryzck, W.; Patroniak, V.; Lisowski, J. Metal complexes of polyaza and polyoxaaza Schiff base macrocycles. *Coord. Chem. Rev.*, **2005**, *249*, 2156–2175.
5. Keypour, H.; Goudarziafshar, H.; Brisdon, A.K.; Pritchard, R.G.; Rezaeivala, M. New macrocyclic Schiff-base complexes incorporating a phenanthroline unit. Part 2: Template synthesis of some manganese(II) complexes and crystal structure studies *Inorg. Chim. Acta* **2008**, *361*, 1415–1420.
6. Adams, H.; Bailey, H.A.; Fenton, D.E.; Hursthouse, M.B.; Kanda, W.; Kanesato, M.; Malik, K.M.A.; Sadler, E.J. Dinuclear copper-(I) and -(II) complexes derived from a diprotonated Schiff-base cryptand. *J. Chem. Soc. Dalton Trans.* **1997**, 921–926.
7. Kruppa, M.; König, B. Reversible coordinative bonds in molecular recognition. *Chem. Rev.* **2006**, *106*, 3520–3560.
8. Wainwright, K.P. Applications for polyaza macrocycles with nitrogen-attached pendant arms. *Adv. Inorg. Chem.*, **2001**, *52*, 293–334.
9. Gorden, A.E.V.; Xu, J.; Raymond, K.N.; Durbin, P. Rational design of sequestering agents for plutonium and other actinides. *Chem. Rev.* **2003**, *103*, 4207–4282.
10. Maimon, E.; Zilbermann, I.; Golub, G.; Ellern, A.; Shames, A.I.; Cohen, H.;Meyerstein, D. Comproportionation and redox catalyzed isomerization of Cu(II) (1*R*,4*S*,8*R*,11*S*-1,4,8,11 tetramethyl-1,4,8,11-tetraazacyclotetradecane)$^{2+}$ in aqueous solutions, *Inorg. Chim. Acta* **2001**, *324*, 65–72.
11. Kimura, E.; Kitamura, H.; Koike, T.; Shiro, M. Facile and selective electrostatic stabilization of uracil N(1)$^-$ anion by a proximate protonated amine: A chemical implication for why uracil N(1) is chosen for glycosylation site. *J. Am. Chem. Soc.* **1997**, *119*, 10909–10919.
12. Demeunynck, M.; Baily, C.; Wilson, W. D. (Eds.). *Small Molecule DNA and RNA Binders: From Synthesis to Nucleic Acid Complexes*; Wiley VCH: Weinheim, 2002, p. 754.
13. Sigman, D.S. Nuclease activity of 1,10-phenanthroline-copper ion. *Acc. Chem. Res.* **1986**, *19*, 180–186.
14. Rodriguez, M.; Liobet, A.; Corbella, M.; Muller, P.; Uson, M.A.; Martell, A.E.; Reibenspies, J. Solvent controlled nuclearity in Cu(II) complexes

linked by the $CO_3{}^{2-}$ ligand: synthesis, structure and magnetic properties. *J. Chem. Soc. Dalton Trans.* **2002**, 2900–2906.

15. Christensen, A.; Jensen, H.S.; McKee, V.; McKenzie, C.J.; Munch, M. Tsalen-and Tsalpn-based nickel complexes with two aldehyde functionalities as potential synthons for thiophenolate-containing di- and polynucleating acyclic and macrocyclic ligands. *Inorg. Chem.*, **1997**, *36*, 6080–6085.
16. Adam, K.R.; Atkinson, I.M.; Lindoy, L.F. Local density functional theory analysis of the structures and energies of the isomers of low-spin $[Ni(cyclam)]^{2+}$. *Inorg. Chem.* **1997**, *36*, 480–481.
17. Parker, D. Tumour targeting with radiolabelled macrocycle-antibody conjugates. *Chem. Soc. Rev.*, **1990**, *19*, 271–291.
18. Wuerthner, F; Rebek, J., Jr. Light-switchable catalysis in synthetic receptors. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 446–448.
19. Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M.T.; Venturi, M. Artificial molecular-level machines: Which energy to make them work? *Acc. Chem. Res.* **2001**, *34*, 445–455.
20. Feringa, B.L. *Molecular Switches*; Wiley-VCH: Weinheim, 2001.
21. Wainwright, K.P. Synthetic and structural aspects of the chemistry of saturated polyaza macrocyclic ligands bearing pendant coordinating groups attached to nitrogen. *Coord. Chem. Rev.* **1997**, *166*, 35–90.
22. Kimura, E.; Aoki, S.; Koike, T.; Shiro, M. A tris (Zn^{II}−1,4,7,10-tetraazacyclododecane) Complex as a New Receptor for Phosphate Dianions in Aqueous Solution. *J. Am. Chem. Soc.* **1997**, *119*, 3068–3076.
23. Reilley, C.N., Schmid, R.W., and Sadek, F.S. Chelon approach to analysis(II) illustrative experiments. *J. Chem. Ed.* **1959**, *36*, 619–626.
24. Pyle, A.M.; Rehmann, J.P.; Meshoyrer, R.; Kumar, C.V.; Turro, N.J.; Barton, J. K. Mixed-ligand complexes of ruthenium (II): Factors governing binding to DNA. *J. Am. Chem. Soc.* **1989**, *111*, 3051–3058.
25. Feng, X.-Z.; Lin, Z.; Yang, L.-J.; Wang, C.; Bai, C.-L., Investigation of the interaction between acridine orange and bovine serum albumin. *Talanta* **1998**, *47*, 1223–1229.
26. Geary, W.J. The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. *Coord. Chem. Rev.* **1971**, *7*, 81–122.
27. Singh, A.K.; Singh, R.; Saxena, P. Macrocyclic metal complexes: Synthesis and characterization of 14- and 16- membered tetraaza macrocyclic complexes of transition metals. *Transition. Metal Chem*. **2004**, *29*, 867–869.
28. Rosokha, S.V.; Lampeka, Y.D.; Matoshtan, I.M. Synthesis and properties of a new series of bis(macrocyclic) dicopper(II,II), dinickel(II,II) and dinickel(III,III) complexes based on the 14-membered pentaaza unit. *J. Chem. Soc. Dalton Trans.* **1993**, 631–636.
29. Shakir, M.; Azim, Y.; Chishti, H.T.N.; Begum, N.; Chingsubam, P.; Siddiqi, M.Y. Synthesis physico-chemical and antimicrobial screening studies on 14- and 16-membered hexaazamacrocyclic complexes bearing pendant amine groups. *J. Braz. Chem. Soc.* **2006**, *17*, 272–278.
30. Khan, T.A.; Ghani, S.S.; Shakir, M.; Tabassum, S. metal ion directed synthesis of 12 and 14-membered tetraaza macrocyclic complexes and their physico-chemical studies. *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.* **2005**, *35*, 509–513.
31. Shakir, M.; Mohamed, A.K.; Varkey, S.P.; Nasman, O.S.M.; Siddiqi, Z.A. Preparation and structural characterization of 14–16-membered pendent arm macrocyclic complexes of transition metal ion. *Polyhedron* **1995**, *14*, 1277–1282.
32. Hathaway, B.J.; Billing, D.E. The electronic properties and stereochemistry of mono-nuclear complexes of the copper(II) ion. *Coord. Chem. Rev.* **1970**, *5*, 143–207.
33. Rana, V.B.; Singh, P.; Singh, D.P.; Teotia, M.P. Divalent nickel, cobalt and copper complexes of tetradentate macrocycle, dibenzo (f, n) 2,4,10,12-tetramethyl-1,5,9,13-tetrazacyclohexadeca[16] 1,3,9,11-tetraene. *Polyhedron* **1982**, *1*, 377–381.
34. Liver, A.B.P. *Inorganic Electronic Spectroscopy*, 2nd ed.; Elsevier: Amsterdam, 1984, p. 9.
35. Chandra, S.; Gupta, L.K. Modern spectroscopic techniques in the characterization of Schiff base macrocyclic ligand and its complexes with transition metals. *Spectrochim. Acta A* **2005**, *62*, 307–312.
36. Chandra, S.; Gupta, L.K. EPR, IR and electronic spectral studies on Mn(II), Co(II), Ni(II) and Cu(II) complexes with a new 22-membered azamacrocyclic $[N_4]$ ligand. *Spectrochim. Acta A* **2004**, *60*, 1751–1761.
37. Chandra, S.; Gupta, L.K.; Jain, D. Spectroscopic studies on Mn(II), Co(II), Ni(II), and Cu(II) complexes with N-donor tetradentate (N_4) macrocyclic ligand derived from ethylcinnamate moiety. *Spectrochim. Acta A* **2004**, *60*, 2411–2417.
38. He, X.F.; Chen, H.; Xu, L.; Ji, L.N. Synthesis, characterization and dna binding study of Co(III) polypyridyl mixed-ligand complexes. *Polyhedron* **1998**, *17*, 3161–3166.
39. Long, E.C.; Barton, J.K. On demonstrating DNA intercalation. *Acc. Chem. Res.* **1990**, *23*, 271–273.