TEMPLATE SYNTHESIS OF NOVEL 14-MEMBERED TETRAAZAMACROCYCLIC TRANSITION METAL COMPLEXES: DNA CLEAVAGE AND ANTIMICROBIAL STUDIES

N. RAMAN,* J. DHAVEETHU RAJA AND A. SAKTHIVEL

Research Department of Chemistry, VHNSN College, Virudhunagar 626 001, India

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ABSTRACT

A new series of 14 membered tetraazamacrocyclic complexes of type $[ML]X_2$, where $M = Ni(II), Co(II), Cu(II), Zn(II), Hg(II), VO(IV), Cd(II)$ and $Mn(II)$; $X_2 = 2Cl^-; SO_4^{2-}$, have been synthesized by incorporating an N_4 donor site *via* the template condensation of *o*-phenylenediamine, formaldehyde, *p*-anisidine and metal salt. The structural features of the complexes have been confirmed by spectral and analytical data. From the data, a square-planar geometry around the central metal ion has been suggested except $VO(IV)$ complex which has square-pyramidal geometry. The antimicrobial screening data show good results. From the nuclease activity of the above metal complexes, it is inferred that only the copper and nickel complexes cleave DNA through redox chemistry.

Key words: *o*-phenylenediamine, *p*-anisidine, CT DNA, antimicrobial activity, nuclease activity

INTRODUCTION

Tetraaza metal complexes are considered to be models for metalloporphyrins and metallocorrins due to their intrinsic structural properties. The uses of macrocyclic metal complexes as bioinorganic models have been portrayed in many reviews such as that of Vogt *et al.*¹, McLendon *et al.*², Collman³, Jones *et al.*⁴, Niederhoffer *et al.*⁵, Alexander⁶ and Busch *et al.*⁷.

There has been considerable interest in the synthesis of new macrocyclic transition metal complexes which stabilize the unusual oxidation states of transition metals relative to that of open chain ligand complexes. The significant chemical behaviour of transition metal complexes very often depends on their facile redox properties. This is true to a good degree for the neutral and synthetic complexes involving macrocyclic ligands. During electrochemical reaction many tetradentate macrocyclic amines stabilize the unusual oxidation states of the transition metals^{8,9}. The stabilization of the unusual oxidation states of metal ions usually depends on the nature of donor site. Olson and Vasilevskis¹⁰ have shown that the tetraaza macrocyclic complexes stabilize the unusual oxidation states of the metal species.

Synthetic tetraaza macrocycle (N_4) molecules are considered typically good models for oxygen carrier due to the presence of four nitrogen donor sites confined to a single four-fold or a slightly four fold plane in a ringed structure, appropriate for metal ligand binding. A survey of the tetraaza macrocyclic ligand systems reported so far by earlier workers indicates that the ring size of 12–16 is most common for molecular model studies^{11,12}, although the quadridentate macrocycles of smaller ring sizes could also be accommodated by the metal ion by coordination in a folded form. Much work has been done on the electrochemical stabilization of the unusual oxidation states of the copper by macrocyclic ligand of a variety of types.

Transition metal complexes that are suitable for binding and cleaving double-stranded DNA are of considerable current interest due to their various applications in nucleic acid chemistry like foot-printing and sequence-specific binding agents, for modeling the restriction enzymes in genomic research, and as structural probes for therapeutic applications in cancer treatment^{13–16}. Cleavage of DNA can be achieved by targeting its basic constituents like base and/or sugar by an oxidative pathway or by hydrolysis of phosphoester linkages. Transition metal complexes are known to be useful for oxidative cleavage of DNA involving nucleobase oxidation and/or degradation of sugar by abstraction of deoxyribose hydrogen atom(s), while complexes containing strong Lewis acids like copper(II) are suitable for hydrolytic cleavage of DNA. Sigman and coworkers have reported bis(phen)copper(I) complex as the first copper-based “chemical nuclease” that cleaves DNA in the presence of H_2O_2 and a thiol^{13,17}. The study of synthetic macrocyclic compounds is a very important area of chemistry in view of their presence in many biologically significant naturally occurring metal complexes, such as the metalloproteins, vitamin B₁₂, chlorophyll *etc.* Tetraaza molecules, especially when coordinated to metal centers, are considerable to be model metalloporphyrins and metallocorrins due to the presence of four nitrogen donor sites in a ringed structure^{18–20}. A literature search reveals that a large number of tetraazamacrocyclic transition metal complexes have been prepared and characterized but no work has been done on DNA and antibacterial activity of transition metal complexes containing tetradentate N_4 donor type 14-membered tetraaza macrocyclic complexes using the template method. Hence, in this work, a new series of 14-membered tetraazamacrocyclic complexes has been synthesized by the template condensation of formaldehyde, *o*-phenylenediamine, *p*-anisidine and

metal salts in ethanol medium. Their DNA cleavage study using calf thymus DNA (CT DNA) by gel electrophoresis technique has been carried out to understand the selectivity and efficiency of DNA and thus to develop new effective cleaving agents or useful DNA probes.

EXPERIMENTAL

Materials and Methods

All reagents and solvents were purchased commercially and used without further purification unless otherwise noted. Microanalytical data of the compounds were recorded at the Sophisticated Analytical Instrument Facility, Central Drug Research Institute (SAIF, CDRI), Lucknow. The mass spectra were done at the Sophisticated Analytical Instrument Facility (SAIF), Indian Institute of Technology, Mumbai. The IR spectra of the samples were recorded on a Perkin-Elmer 783 spectrophotometer in 4000–400 cm^{-1} range using KBr pellet. The UV-Vis. spectra were recorded on a Shimadzu UV-1601 spectrophotometer using DMF as solvent. The X-band ESR spectra of the complex was recorded at 300 K and 77 K at IIT, Mumbai using TCNE (tetracyanoethylene) as the g-marker. Magnetic susceptibility measurements of the complexes were carried out by Guoy balance using copper sulphate as the calibrant. Electrochemical studies were carried out using EG&G Princeton Applied Research Potentiostat / Galvanostat Model 273A, controlled by M270 software. CV measurements were performed using a glassy carbon working electrode, platinum wire auxiliary electrode and an Ag/AgCl reference electrode. All solutions were purged with N_2 for 30 min prior to each set of experiments. The molar conductance of the complexes was measured using a Systronic conductivity bridge. Solutions of CT DNA (calf thymus DNA) in 50 mM NaCl / 50 mM tris-HCl (pH=7.2) gave a ratio of UV absorbance at 260 and 280 nm, A_{260}/A_{280} of ca. 1.8–1.9, indicating that the DNA was sufficiently free of protein contamination. The DNA concentration was determined by the UV absorbance at 260 nm after 1:100 dilutions. The molar absorption coefficient was taken as 6600 $M^{-1}cm^{-1}$. Stock solutions were kept at 4°C and used after not more than 4 days. Doubly distilled H_2O was used to prepare the buffer. The antimicrobial activities of the ligands and their complexes were carried out by well-diffusion method²¹.

General Procedure for the Syntheses of complexes

To a stirred ethanol solution of metal salts (0.01 M) slowly added *o*-phenylenediamine (0.02 M), formaldehyde (0.04 M) and *p*-anisidine (0.02 M). The mixture was heated under reflux for ca. 24 h. The solution was filtered under hot condition and the filtrate was allowed to stand at room temperature. The precipitate formed was filtered off, washed with ethanol and further dried *in vacuo*.

Copper complex synthesis

Yield: 58 %; Anal. calcd. for $CuC_{30}H_{34}N_6O_2Cl_2$: Cu, 9.9; C, 55.9; H, 5.2; N, 13.0; Found: Cu, 9.8; C, 55.6; H, 5.0; N, 12.8.

Nickel complex

Yield: 62 %; Anal. calcd. for $NiC_{30}H_{34}N_6O_2Cl_2$: Ni, 9.2; C, 56.3; H, 5.3; N, 13.1; Found: Ni, 9.1; C, 56.1; H, 5.0; N, 12.9.

Cobalt complex

Yield: 54 %; Anal. calcd. for $CoC_{30}H_{34}N_6O_2Cl_2$: Co, 9.2; C, 56.3; H, 5.3; N, 13.1; Found: Co, 8.9; C, 56.1; H, 5.2; N, 12.8.

Manganese complex

Yield: 63 %; Anal. calcd. for $MnC_{30}H_{34}N_6O_2Cl_2$: Mn, 8.6; C, 56.6; H, 5.3;

N, 13.2; Found: Mn, 8.4; C, 56.3; H, 5.0; N, 12.9.

Zinc complex

Yield: 61 %; Anal. calcd. for $\text{ZnC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$: Zn, 10.2; C, 55.7; H, 5.3; N, 13.0; Found: Zn, 9.9; C, 55.2; H, 4.9; N, 12.7.

Vanadium complex

Yield: 64 %; Anal. calcd. for $\text{VC}_{30}\text{H}_{34}\text{N}_6\text{O}_7\text{S}$: V, 7.6; C, 53.5; H, 5.1; N, 12.5; Found: V, 7.3; C, 54.9; H, 4.9; N, 12.1.

Cadmium complex

Yield: 58 %; Anal. calcd. for $\text{CdC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$: Cd, 16.2; C, 51.9; H, 4.9; N, 12.1; Found: Cd, 15.8; C, 51.4; H, 4.6; N, 11.8.

Mercury complex

Yield: 56 %; Anal. calcd. for $\text{HgC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$: Hg, 25.6; C, 46.1; H, 4.3; N, 10.7; Found: Hg, 25.2; C, 45.7; H, 4.1; N, 10.4.

Antimicrobial activity

The *in vitro* biological screening effects of the investigated compounds were tested against the bacteria: *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis* by the well diffusion method, using agar nutrient as the medium. The antifungal activities of the compounds were evaluated by the well diffusion method against the fungi viz., *Aspergillus niger*, *Aspergillus flavus* and *Rhizoctonia bataticola* cultured on potato dextrose agar as medium. Streptomycin and nystatin were used as reference drugs for bacteria and fungi respectively. The stock solution (10^{-2} M) was prepared by dissolving the compounds in DMSO and the solutions were serially diluted in order to find the MIC values. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated for 24 h in the case of bacteria and 72 h for fungi at 35 °C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The inhibition zone developed, at which the concentration was noted.

Gel electrophoresis

The gel electrophoresis experiments were performed by incubation at 35°C for 2 h as follows: CT DNA 30 μM , 50 μM each complex and 50 μM H_2O_2 in 50 mM tris-HCl buffer (pH=7.2) were electrophoresed for 2 h at 50 V on 1% agarose gel using tris-acetic acid-EDTA buffer, pH = 8.3. After electrophoresis, the gel was stained using 1 $\mu\text{g}/\text{cm}^3$ EB (Ethidiumbromide) and photographed under UV light.

RESULTS AND DISCUSSION

The synthesized complexes are found to be air stable and insoluble in water, but soluble in DMSO and DMF. The analytical data of the complexes together with some physical properties are summarized in Table 1. The mass, microanalytical data of the complexes correspond well with the general formula $[\text{ML}]\text{X}_2$ [where M = Cu(II), Ni(II), Co(II), Zn(II), Hg(II), VO(IV), Cd(II) and Mn(II); $\text{X}_2 = 2\text{Cl}^-$, SO_4^{2-} ; L = $\text{C}_{30}\text{H}_{34}\text{N}_6\text{O}_2$]. The higher conductance values of the chelates support their electrolytic nature of the metal complexes.

Table 1. Physical characterization, analytical, molar conductance, and magnetic susceptibility data of the complexes

Compound	Molecular formula	Colour	Molar Conductance (Λ_m) $\times 10^{-3}$ ($\text{ohm}^{-1}\text{cm}^2 \text{mol}^{-1}$)	μ_{eff} (BM)
[CuL]Cl ₂	$\text{CuC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Black	98	1.78
[NiL]Cl ₂	$\text{NiC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Brown	110	----
[CoL]Cl ₂	$\text{CoC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Brown	97	3.57
[MnL]Cl ₂	$\text{MnC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Brown	95	5.42
[ZnL]Cl ₂	$\text{ZnC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Light yellow	112	----
[VOL]SO ₄	$\text{VC}_{30}\text{H}_{34}\text{N}_6\text{O}_7\text{S}$	Green	98	1.67
[CdL]Cl ₂	$\text{CdC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Yellow	113	----
[HgL]Cl ₂	$\text{HgC}_{30}\text{H}_{34}\text{N}_6\text{O}_2\text{Cl}_2$	Yellow	97	----

Mass spectra

The FAB mass spectrum of the copper complex shows a molecular ion peak at m/z 644 which confirms the stoichiometry of metal chelates as $[\text{ML}]\text{X}_2$ type. It is also supported by the “Nitrogen Rule”, since the compound possesses six nitrogen atoms. The mass spectra of the other complexes support the above stoichiometry. This stoichiometry is further supported by the microanalytical data of the complexes.

Infrared spectra

The preliminary identification of the macrocyclic complexes was done from their IR spectra. The complexes give no bands assignable to carbonyl group stretching modes. The sharp band observed around 3215 cm^{-1} may be assigned to ν_{NH} of the coordinated secondary amines. A medium intensity band appearing in the 2835-2970 cm^{-1} region corresponds to ν_{CH} . The bands observed at 1400-1440, 1060-1080 and 710-730 cm^{-1} region can be assigned to phenyl ring vibrations²². In all of the metal complexes, a band seen in the 450-500 cm^{-1} region is probably due to the formation of M-N bonds^{23,24}. In addition to the other bands, the vanadyl complex shows an additional band at 960 cm^{-1} attributed to the V=O frequency²⁵.

Electronic absorption spectra

The electronic absorption spectra of Cu(II), Ni(II), Co(II) and VO(IV) complexes were recorded at 300 K. The absorption region assigned and the proposed geometry of the complexes are given in Table 2. The electronic spectrum of Cu(II) complex shows a band at 17310 cm^{-1} which is assigned to ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$ transition, characteristic for square-planar geometry. The absence of band below 10000 cm^{-1} excludes the possibility of tetrahedral geometry. In the Co(II) complex, the band appearing at 19710 cm^{-1} is attributed to ${}^1\text{A}_{1g} \rightarrow {}^1\text{B}_{1g}$ which suggests a square-planar geometry. For Ni(II) complex, the two d-d bands appearing at 21611 and 18917 cm^{-1} are assigned to ${}^1\text{A}_{1g} \rightarrow {}^1\text{A}_{2g}$ and ${}^1\text{A}_{1g} \rightarrow {}^1\text{B}_{1g}$ transitions respectively, confirming the square-planar geometry for this complex. The observed zero magnetic moment confirms the square-planar environment for the Ni(II) complex in conformity with the fact that all known square-planar complexes of Ni(II) are diamagnetic. For VO(IV) complex, the two bands observed at 12545 and 18610 cm^{-1} are assigned to ${}^2\text{B}_2 \rightarrow {}^2\text{E}$ and ${}^2\text{B}_2 \rightarrow {}^2\text{A}_1$ transitions respectively which are consistent with that of five coordinated square-pyramidal geometry. No transitions were observed in the visible region for Zn(II), Hg(II), Cd(II) complexes consistent with the d^{10} configuration of the Zn(II), Hg(II), Cd(II) ions. These complexes are also found to be diamagnetic as expected for d^{10} configuration. For Mn(II) complex, there is no allowed d-d transitions. These data are comparable with that of the other reported complexes²⁶⁻²⁹. Furthermore, the magnetic susceptibility values (Table 1) reinforce the conclusion drawn from the electronic spectral data of the complexes.

Table 2. Electronic absorption spectral data of the compounds

Compound	Solvent	Absorption (cm^{-1})	Band Assignment	Geometry
[CuL]Cl ₂	DMF	37340 28420 17310	INCT INCT ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$	Square-planar
[NiL]Cl ₂	DMF	38325 28320 21611 18917	INCT INCT ${}^1\text{A}_{1g} \rightarrow {}^1\text{A}_{2g}$ ${}^1\text{A}_{1g} \rightarrow {}^1\text{B}_{1g}$	Square-planar
[CoL]Cl ₂	DMF	38624 27972 19710	INCT INCT ${}^1\text{A}_{1g} \rightarrow {}^1\text{B}_{1g}$	Square-planar
[VOL]SO ₄	DMF	33534 26746 18610 12545	INCT INCT ${}^2\text{B}_2 \rightarrow {}^2\text{A}_1$ ${}^2\text{B}_2 \rightarrow {}^2\text{E}$	Square-pyramidal

INCT-Intra-ligand Charge transfer transition

ESR spectra

The ESR spectrum of copper complex, recorded in DMSO at 77 K (LNT) and 300 K (RT), provides useful information which is important in studying the metal ion environment. The RT spectrum shows one intense absorption band in the high field region and it is isotropic, due to the tumbling motion of the molecule. But LNT spectrum shows four well resolved peaks with low field region and one intense peak in the high field region. The magnetic moment of the copper complex is 1.78 B.M which corresponds to one unpaired electron, indicating that the complex is mononuclear. This fact was also evident from the absence of half field signal at 1600 G due to the $m_s = \pm 2$ transitions, ruling out any Cu-Cu interaction. The complex exhibits the g_{11} value of 2.34 and $g_{\perp}$ value of 2.06. The g-tensor values of the copper complex can be used to derive the ground state. In square-planar complexes, the unpaired electron lies in the $d_{x^2-y^2}$ orbital giving $^2B_{1g}$ as the ground state with $g_{11} > g_{\perp} > 2$, while the unpaired electron lies in the d_z^2 orbital giving $^2A_{1g}$ as the ground state with $g_{\perp} > g_{11} > 2$. From the observed values, it is clear that $A_{11} = 145 > A_{\perp} = 36$; $g_{11} = 2.34 > g_{\perp} = 2.06 > 2$ and coincide well with related systems which suggest that the complex has square-planar geometry and system is axially symmetric³⁰⁻³². This is also supported by the fact that the unpaired electron lies predominantly in the $d_{x^2-y^2}$ orbital. In the axial spectra, the g-values are related with exchange interaction coupling constant (G) by the expression,

According to Hathaway³³, if the G value is larger than four, the exchange interaction is negligible because the local tetragonal axes are aligned parallel or are slightly misaligned. If the value of G is less than four, the exchange interaction is considerable and the local tetragonal axes are misaligned. For the present copper complex, the G value is 5.8 which suggest that the local tetragonal axes are aligned parallel or are slightly misaligned and consistent with $d_{x^2-y^2}$ ground state.

The ESR spectrum of the vanadyl complex, recorded in DMSO solution at 300 and 77 K shows a typical eight line and sixteen line patterns respectively. The isotropic ESR parameters $g_{iso} = 1.96$ and $A_{iso} = 108$ can be calculated from the position spacing of the resonance lines from the room temperature solution spectrum of the complex. The spectrum is like a typical eight line pattern which shows that a single vanadium is present in the molecule *i.e.*, it is a monomer. In the frozen solid state, the spectrum shows two types of resonance components, one set due to the parallel features and the other set due to the perpendicular features, which indicate axially symmetric anisotropy with well resolved sixteen line hyperfine splitting, characteristic of an interaction between the electron and vanadium nuclear spin. From the anisotropic spectrum, the anisotropic parameters were calculated. The observed order ($A_{11} = 174 > A_{\perp} = 73$; $g_{\perp} = 2.02 > g_{11} = 1.97$) indicates that the unpaired electron is present in the d_{xy} orbital with square-pyramidal geometry around the VO(IV) ion^{34,35}.

Based on the above spectral and analytical data, the proposed structure of the metal complexes is given in Figure 1.

Figure 1. The proposed structure of the complexes

Redox studies

The cyclic voltammograms of copper and vanadyl complexes were recorded in DMSO solution. A noteworthy feature has been observed in the cyclic voltammograms of copper and vanadyl complexes which are shown in Figure 2 and Figure 3.

Figure 2. Cyclic voltammogram of copper complex in DMSO solution at 300 K (0.1M TBAP). Scan rate 100 mVs⁻¹.

Figure 3. Cyclic voltammogram of vanadyl complex in DMSO solution at 300 K (0.1M TBAP). Scan rate 100 mVs⁻¹.

The cyclic voltammogram of copper complex (0.1 M) shows a quasi reversible peak for the couple³⁶: $\text{Cu}^{(II)} - \text{Cu}^{(III)}$ at $E_p = 0.40$ V with the direct cathodic peak for $\text{Cu}^{(III)} - \text{Cu}^{(II)}$ at $E_p = 0.34$ V. Further, it shows two irreversible peaks characteristic for $\text{Cu}^{(II)} - \text{Cu}^{(I)}$ at $E_p = -0.69$ V and $\text{Cu}^{(I)} - \text{Cu}^{(0)}$ at $E_p = -1.06$ V reduction. In the anodic side the peak occurs due to the direct oxidation of $\text{Cu}^{(0)} - \text{Cu}^{(I)}$ at $E_p = -0.24$ V.

The cyclic voltammogram for the vanadyl complex, recorded in DMSO solution shows two well defined one-electron transfer redox peaks, corresponding to the formation of the VO(IV)/VO(V) couple at $E_p = 0.46$ V, $E_p = 0.34$ V and VO(IV)/VO(III) couple³⁷ at $E_p = -1.03$ V and $E_p = -0.21$ V. The peak current functions of both waves in complex are different which indicate the involvement of two different electroactive species in solution corresponding to VO(V) and VO(III).

Antimicrobial activity

For *in vitro* antimicrobial activity, the investigated compounds were tested against the bacteria *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis* and fungi *Aspergillus niger*, *Aspergillus flavus* and *Rhizoctonia bataicola*. The minimum inhibitory concentration (MIC) values of the investigated compounds with the standard drugs are summarized in Table 3. Antimicrobial activity of the metal chelates can be explained on the basis of chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelate ring and enhances the

penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organisms³⁸.

Table 3. Antimicrobial studies of investigated compounds (minimum inhibitory concentration $\times 10^{-2}$ M)

compound	<i>S. typhi</i>	<i>S. aureus</i>	<i>E. Coli</i>	<i>B. subtilis</i>	<i>A. niger</i>	<i>A. flavus</i>	<i>R. bataticola</i>
[CuL]Cl ₂	3.3	3.8	4.1	3.9	4.8	4.7	4.9
[NiL]Cl ₂	3.8	3.7	4.2	3.8	5.2	5.1	5.0
[CoL]Cl ₂	3.9	4.1	4.3	4.4	5.3	5.4	5.5
[MnL]Cl ₂	4.1	4.3	4.2	4.3	5.4	5.6	5.7
[ZnL]Cl ₂	4.2	4.5	4.3	4.4	5.5	5.3	5.4
[VOL]SO ₄	4.0	4.2	4.1	4.2	5.3	5.5	5.2
[CdL]Cl ₂	4.1	4.3	4.4	4.5	5.4	5.3	5.5
[HgL]Cl ₂	4.3	4.5	4.6	4.5	5.6	5.4	5.3
Streptomycin	2.8	1.6	3.0	2.2	---	---	---
Nystatin	---	---	---	---	1.2	2.4	1.8

DNA studies

In the present study, the CT-DNA gel electrophoresis experiment was conducted at 35°C using our synthesized complexes in the presence of H₂O₂ as an oxidant. As can be seen from the results (Figure 4), at very low concentration, few complexes exhibit nuclease activity in the presence of H₂O₂. Control experiments using DNA alone do not show any significant cleavage of CT-DNA even on longer exposure time. From the observed results, it is observed that in presence of H₂O₂ the copper (lane 2) and nickel complexes (lane 3) cleave DNA more efficiently than the other complexes (lanes 4-9) and the control DNA. Further, the presence of a smear in the gel diagram indicates the presence of radical cleavage³⁹.

Figure 4. Changes in the agarose gel electrophoretic pattern of calf-thymus DNA induced by H₂O₂ and metal complexes.

CONCLUSIONS

In this work, few novel 14 membered tetraazamacrocyclic transition metal complexes have been synthesized and characterized on the basis of analytical and spectral data. All the complexes exhibit square-planar geometry around the central metal ion except VO(IV) complex which has square-pyramidal geometry. The antimicrobial screening data show good results. The interaction of these complexes with CT-DNA was investigated by gel electrophoresis. From the observation, it is found that the copper and nickel complexes cleave DNA more efficiently than the other complexes and the control DNA.

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