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Feature article

Stimulated DNA binding by metalloinsertors having the 4-formyl-N, N-dimethylaniline Schiff base: Synthesis and characterization

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ABSTRACT

Four new Cu(II), Ni(II), Co(II) and Zn(II) metalloinsertors have been synthesized by using a Schiff base, formed by the condensation reaction of 4-formyl-N,N-dimethylaniline with *o*-phenylenediamine. They have been structurally characterized by IR, NMR, UV–vis, EPR, elemental analyses, magnetic susceptibility and molar conductivity studies. The molar conductance data of the complexes indicate that they are non-electrolytes. The spectral and analytical data reveal that the complexes adopt square planar geometry. They have been examined for their antibacterial and antifungal activities against few pathogens. The data reveal that the complexes exhibit better biocidal activities against bacteria and fungi than the free Schiff base ligand. The interaction studies of these complexes with calf thymus deoxyribonucleic acid (CT DNA) have also been performed by using spectral, cyclic voltammetry and viscometry techniques which collectively give evidences for intercalative binding of DNA with metal complexes. The gel electrophoresis experiment reveals that the complexes are good chemical nucleases.

Contents

DNA binding of metal complexes has been extensively investigated because they can be used as potential anticancer drugs, DNA structural probes, DNA dependent electron transfer probes, DNA foot printing agents, sequence-specific cleaving agents and so on [1–3]. DNA is the primary target molecule for most anticancer and antiviral therapies according to cell biologists. Investigations on the interaction of DNA with small molecules are important in the design of new types of pharmaceutical molecules [4]. Since the chemical nuclease activity of transition metal complexes was discovered in the year 1980, studying the interaction model and the mechanism of transition metal complexes with DNA, and exploring the application of metal complexes in antineoplastic medication, molecular biology and bioengineering have become hotspots in recent years. Some kind of metal complexes when interacted with DNA could induce the breakage of DNA strands by appropriate methods [5–8].

Schiff bases form an important division of organic compounds in chemistry due to their constructive physical and chemical properties and large number of reactions that they undergo. Schiff bases, derived from substituted aliphatic amines and aromatic aldehydes, have a wide variety of applications in many fields, *e.g.* biological, inorganic and analytical chemistry [9,10]. Schiff bases and their coordination compounds have gained importance recently because of their application as models in biological, biochemical, antimicrobial, anticancer, antibacterial and antifungal activities. Studies of new kinds of chemotherapeutic Schiff bases now fascinated the attention of biochemists [11–14]. Metal complexes of Schiff bases are extensively studied due to their synthetic flexibility and sensitivity toward a variety of metal atoms. They are found useful in catalysis, in medicine as antibiotics and anti-inflammatory agents and in the industry as corrosion inhibitors. It has been found that few of the complexes are antimicrobially active and

Abbreviations: DNA, deoxyribonucleic acid; CT DNA, calf thymus deoxyribonucleic acid; pUC19 DNA, plasmid University of California 19 deoxyribonucleic acid; Tris–HCl, tris(hydroxymethyl)aminomethane hydrochloride; L, ligand; M, metal; OC, open circular; SC, supercoiled; DMF, dimethylformamide; DMSO, dimethylsulfoxide; $CHCl_3$, chloroform; SAIF, Sophisticated Analytical Instrument Facility; IIT, Indian Institute of Technology; CDRI, Central Drug Research Institute.

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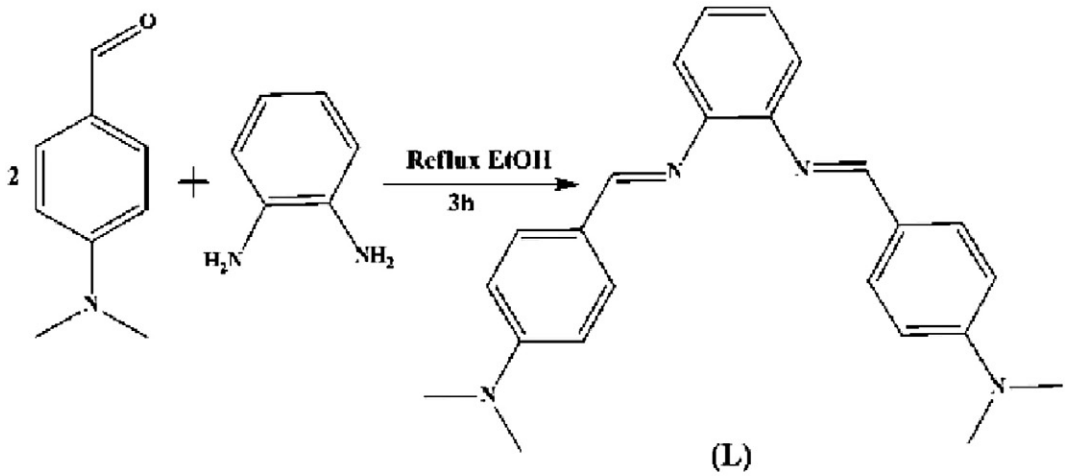
show higher activity than the free ligand. Metal chelation affects significantly the antimicrobial/bioactive behavior of organic ligands [15]. 4-Formyl-N,N-dimethylaniline is used to determine urobilinogen clinically. Very few works have been reported on 4-formyl-N,N-dimethylaniline as a ligand [16]. In literature, several reports correlate the significance of the biological activity of metal complexes with the metal ions rather than the ligands. To our knowledge, no work has been reported on the condensed reaction of the 4-formyl-N,N-dimethylaniline ligand with *o*-phenylenediamine (benzene-1,2-diamine) and its transition metal complexes as chemical nucleases. In continuation of our journey toward the exploration of efficient intercalators, we herein report the synthesis, characterization and DNA interaction of 4-formyl-N,N-dimethylaniline Schiff base transition metal(II) complexes.

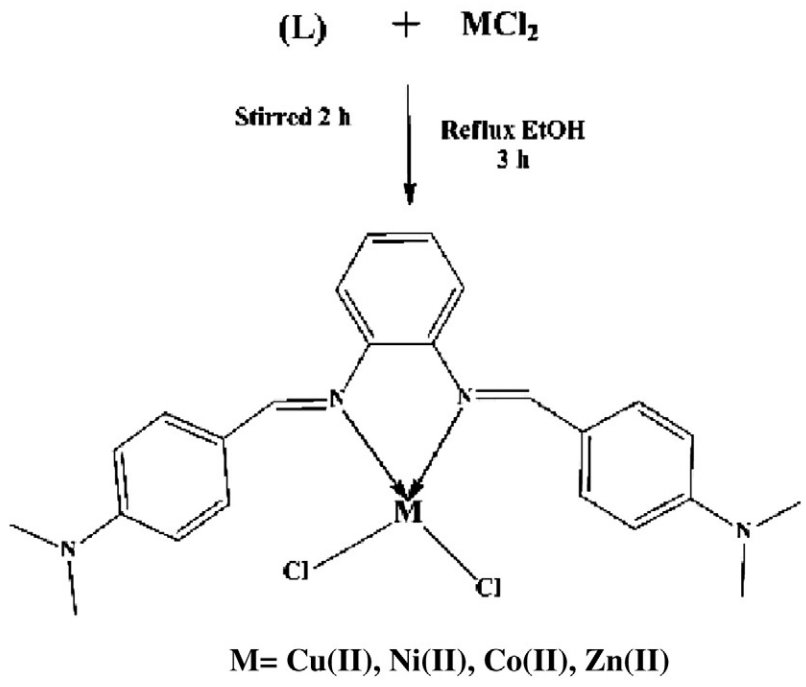
The materials and methods for the prepared Schiff base complexes and their structural elucidation were depicted as S1 and S2 (Supplementary file).

An ethanolic solution of (40 mL) 4-formyl-N,N-dimethylaniline (0.01 mol) was added to an ethanolic solution of benzene-1,2-diamine (0.01 mol). The resultant mixture was refluxed for ca. 3 h. It was poured in crushed ice, wherein orange colored precipitate was obtained. It was suction filtered, washed with water and cold ethanol and finally dried in an oven at 60 °C. The resulting Schiff base, **L** (L = N^1E,N^2E)-N^1,N^2-bis(4-(dimethylamino)benzylidene)benzene-1,2-diamine, was recrystallized from distilled ethanol (yield: 71%).

Anal. Calc. for **L** ($C_{24}H_{26}N_4$): C 77.80; H 7.07; N 15.23%. Found: C 77.35; H 6.98; N 14.97%. FT-IR (KBr) cm^{-1}: υ(C═N): 1610. ^1H NMR (DMSO-d_6, 300 MHz, δ, ppm): 6.7–7.7 (m, aromatic), λ_{max} in (DMSO) cm^{-1}: 240 nm and 334 nm.

An ethanolic solution of metal(II) chloride (1 mmol) was stirred with an ethanolic solution of the Schiff base (1 mmol) and the resultant mixture was refluxed for ca. 3 h. Then the solution was reduced to one-third on a water bath. The precipitated metal complexes were isolated and washed with distilled water. They were dried in a vacuum at





Scheme 1. Schematic route for synthesis of Schiff base ligand and its metal complexes.