

4,4'-(DIPHENYLMETHANE-4,4'-DIYLDINITRILLO)DIPENTAN-2-ONE AND 4,4'-(DIPHENYLETHER-4,4'-DIYLDINITRILLO)DIPENTAN-2-ONE LIGANDS AND THEIR Ni(II), Cu(II) COMPLEXES: SYNTHESIS, CHARACTERIZATION, DNA CLEAVAGE STUDIES

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ABSTRACT

The synthesis of two new ligands 4,4'-(diphenylmethane-4,4'-diyldinitrilo)dipentan-2-one (H_2L^1) and 4,4'-(diphenylether-4,4'-diyldinitrilo)dipentan-2-one (H_2L^2) is reported. The ligands have two acetylacetonate subunits separated by diphenylmethane or diphenylether group. The ligands form stable dinuclear complexes with Ni(II) and Cu(II) ions. Ligands and their complexes were characterized by elemental analysis, m.p., IR, molar conductivity and magnetic moment measurements. The interaction between these compounds with DNA has also been investigated by agarose gel electrophoresis, we found that the nickel(II) and copper(II) complexes can cleave supercoiled pBR322 DNA to nicked and linear forms. The copper(II) complexes with H_2O_2 as a cooxidant exhibited the strongest cleaving activity. The free ligands were also characterized by ¹H NMR spectra. The IR of the free ligands and their complexes are compared and discussed. The extraction ability of the ligands have been examined by the liquid-liquid extraction of selected transition metal [Mn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} and Pb^{2+}] cations. The ligands show strong binding ability toward mercury(II) ion.

Keywords: Schiff base; copper(II); nickel(II); DNA cleavage, extraction

INTRODUCTION

Dinuclear transition metal complexes and ligands capable of yielding them have received increasing attention in the field of synthetic and biological chemistry due to their key roles they play in many applications [1-6]. They are used as model systems for the active centers of many metalloenzymes [7,8], catalysts [9-11]. The chemical properties of these kind of compounds depend on the ligational properties of the chelating sites. For this reason, the synthesis of ligands able to form dinuclear complexes is of great interest.

Schiff base ligands are considered as privileged ligands and attractive not only due to their novel structural features but also in view of their vast biological properties. New kind of chemotherapeutic Schiff bases are now attracting the attention of biochemists [12]. Furthermore, Schiff bases allow selective complexation and extraction of metallic cations and anions of biochemical and environmental importance [13-15]. The chemistry of transition metals containing the Schiff base ligands is an area of increasing interest. They can yield mono- or polynuclear complexes and these complexes have numerous applications, such as, in the treatment of cancer, as antiviral agents, as fungicide agents and for other biological properties [16-21]. Earlier work reported that some drugs showed increased activity when administered as metal complexes rather than as organic compounds [22]. Many dinuclear complexes of Cu(II) with Schiff base ligands have been investigated [6,10,23,24] some of which are biologically relevant; for example, some copper complexes can serve as models for enzymes such as galactose oxidase and may be used as effective oxidant and redox catalysts [25-27]. In spite of the diversity in the coordination environment and the structure of these complexes, which depend on the type of Schiff base and the anion. In this study, we have synthesized and characterized a series of dinuclear nickel(II) and copper(II) complexes with a new tetradentate ligands [4,4'-(diphenylmethane-4,4'-diyldinitrilo)dipentan-2-one] (H_2L^1) and 4,4'-(diphenylether-4,4'-diyldinitrilo)dipentan-2-one] (H_2L^2) (Scheme 1). Furthermore, the interaction with plasmid DNA (pBR322 DNA) employing gel electrophoresis of the compounds is also investigated.

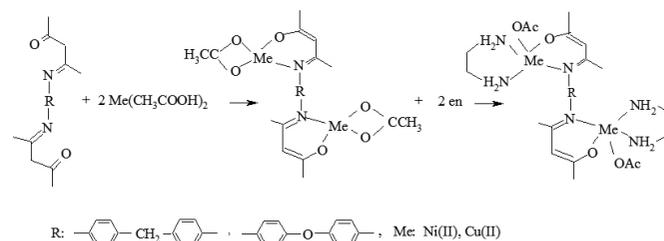
Solvent extraction is one of the most versatile procedures used for the removal, separation and concentration of metallic species. Its applications in the recycling of resources in the field of metallurgy and waste water treatment as demand increases for the development of new approaches to resolve the various problems presented [6, 28-30]. We have also investigated the effectiveness of the ligands in transferring the metals from the aqueous solutions into the organic solvents.

EXPERIMENTAL

All reagents were used as supplied by Aldrich, Merck and Fluka without further purification.

¹H NMR spectra were recorded on a Bruker AVANCE instrument, operating at 300 MHz. Proton chemical shifts are reported in part per million (ppm) relative to an internal standard of Me_4Si . Elemental analyses and metal contents were performed by using a LECO 932 CHNS analyser and a Perkin Elmer Optima 5300 DV ICP-OES Spectrometer. IR spectra were recorded as KBr pellets on a Shimadzu IRPrestige-21 FT-IR Spectrophotometer. Melting points were determined using an Electrothermal model IA 9100. The molar conductance was determined with an Optic Ivymen System conductivity meter. Magnetic susceptibility measurements were made on a powered sample at 298 K using a Sherwood Scientific Magnetic Susceptibility Balance (Model MX1).

Synthesis of Schiff Base Ligands [4,4'-(diphenylmethane-4,4'-diyldinitrilo)dipentan-2-one (H_2L^1)] (1) and 4,4'-(diphenylether-4,4'-diyldinitrilo)dipentan-2-one (H_2L^2)] (2): The synthesis of the ligands were obtained following the procedures reported in Scheme 1. To a solution of starting compounds (0.01 mol); 1.98 g 4,4'-diaminodiphenylmethane, 1.84 g 4,4'-diaminodiphenylether) in ethanol (30 mL), acetylacetonate (0.02 mol) was added. Over a period of 3 h, the reaction mixture was heated under reflux and then allowed to stand at room temperature overnight. Subsequently, the solid formed was filtered and recrystallized from EtOH and the purity was checked by TLC.



Scheme 1. The Schiff base ligands and their complexes

4,4'-(Diphenylmethane-4,4'-diyldinitrilo)dipentan-2-one (H_2L^1) (1): Dark yellow powder; yield: 94 %; m.p.: 105°C. Anal. Calc. for $C_{23}H_{26}N_2O_2$: C, 76.22; H, 7.22; N, 7.73. Found: C, 76.35; H, 7.21; N, 7.79; ¹H NMR ($CDCl_3$, ppm): 2.17 (s, 2H, CH), 3.87 (s, 2H, CH_2), 1.15 (s, 6H, $CNCH_3$), 5.10 (s, 6H, $COCH_3$) 6.63-7.18 (m, 8H, Ar). FT-IR (KBr, cm^{-1}): 1613 s (C=O), 1566 s (C=N), 1314 m (C-N).

4,4'-(Diphenylether-4,4'-diyldinitrilo)dipentan-2-one (H_2L^2) (2): Dark yellow powder; yield: 91 %; m.p.: 78°C. Anal. Calc. for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.63; N, 7.69. Found: C, 72.04; H, 6.29; N, 7.41; ¹H NMR ($CDCl_3$, ppm): 2.17 (s, 2H, CH), 1.18 (s, 6H, CH_3), 5.12 (s, 6H, CH_3) 6.80-7.02 (m, 8H, Ar). FT-IR (KBr, cm^{-1}): 1608 s (C=O), 1560 s (C=N), 1307 m (C-N).

Synthesis of the metal complexes: [Cu₂L'(OAc)₂] (3) and [Cu₂L²(OAc)₂]. The complexes were synthesized using a procedure developed previously [23]. The ligand (0.01 mol; 3.62 g **1** or 3.64 g **2**) was dissolved in 30 mL of ethanol to which a solution of Cu(OAc)₂·H₂O (4.00 g, 0.022 mol) was then added under stirring. The reaction mixture was heated under reflux for 4 h, then cooled and the solid product filtered, washed several times with EtOH, Et₂O and dried over P₂O₅.

[Cu₂L'(OAc)₂] (3) Green complex; yield: 64 %; d.p.: 247°C. Anal. Calc. for C₂₇H₃₀N₂O₆Cu₂: C, 53.55; H, 4.99; N, 4.63; Cu, 20.99. Found: C, 53.64; H, 5.12; N, 4.70; Cu, 21.10 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 10.9; μ_{eff} = 0.54 B.M.; FT-IR (KBr, cm⁻¹): 1572 s (C=N), 1402 m (C-N), 1271 m (C-O), 1518 m, 1456 w (OAc), 445 w (Cu-N), 510 w (Cu-O).

[Cu₂L²(OAc)₂] (4) Brown complex; yield: 68 %; d.p.: 230°C. Anal. Calc. for C₂₆H₂₈N₂O₆Cu₂: C, 51.40; H, 4.64; N, 4.61; Cu, 20.92. Found: C, 50.97; H, 4.63; N, 4.75; Cu, 20.59 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 10.5; μ_{eff} = 1.58 B.M.; FT-IR (KBr, cm⁻¹): 1568 s (C=N), 1404 m (C-N), 1273 m (C-O), 1516 m, 1456 w (OAc), 451 w (Cu-N), 512 w (Cu-O).

[Cu₂L'(en)₂(OAc)₂] (5) and [Cu₂L²(en)₂(OAc)₂] (6): The first complexes (3 and 4) (1 mmol; 0.606 g **3** or 0.608 g **4**) and ethylenediamine (0.240 g, 4 mmol) were suspended in EtOH (20 mL). The resulting suspension was heated under reflux for 6 h, during which the complex was dissolved with changing color. The reaction mixture was upon cooling to room temperature, the green or brown colored solid was filtered off, washed EtOH, Et₂O and dried over P₂O₅.

[Cu₂L'(en)₂(OAc)₂] (5) Brown complex; yield: 72 %; d.p.: 208°C. Anal. Calc. for C₃₁H₄₆N₆O₆Cu₂: C, 51.30; H, 6.38; N, 11.58; Cu, 17.51. Found: C, 51.57; H, 6.62; N, 11.64; Cu, 17.28 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 7.8; μ_{eff} = 1.07 B.M.; FT-IR (KBr, cm⁻¹): 3271 b (N-H), 1572 s (C=N), 1402 m (C-N), 1273 m (C-O), 1541 m, 1348 w (OAc), 444 w (Cu-N), 513 w (Cu-O).

[Cu₂L²(en)₂(OAc)₂] (6) Green complex; yield: 70 %; d.p.: 248°C. Anal. Calc. for C₃₀H₄₄N₆O₆Cu₂: C, 50.62; H, 6.23; N, 11.81; Cu, 17.86. Found: C, 50.59; H, 6.33; N, 11.84; Cu, 17.65 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 10.8; μ_{eff} = 0.56 B.M.; FT-IR (KBr, cm⁻¹): 3332 b (N-H), 1576 s (C=N), 1402 m (C-N), 1277 m (C-O), 1552 m, 1356 w (OAc), 444 w (Cu-N), 510 w (Cu-O).

[Ni₂L'(OAc)₂] (7) and [Ni₂L²(OAc)₂]. The ligand (0.01 mol; 3.62 g **1** or 3.64 g **2**) was dissolved in 30 mL of ethanol to which a solution of Ni(OAc)₂·4H₂O (5.47 g, 0.022 mol) was then added under stirring. The reaction mixture was heated under reflux for 4 h, then cooled and the solid product filtered, washed several times with EtOH, Et₂O and dried over P₂O₅.

[Ni₂L'(OAc)₂] (7) Green complex; yield: 58 %; d.p.: 350°C. Anal. Calc. for C₂₇H₃₀N₂O₆Ni₂: C, 54.42; H, 5.07; N, 4.70; Ni, 19.70. Found: C, 54.11; H, 5.12; N, 4.83; Ni, 20.02 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 12.1; μ_{eff} = 3.48 B.M.; FT-IR (KBr, cm⁻¹): 1564 s (C=N), 1387 m (C-N), 1272 m (C-O), 1528 m, 1437 w (OAc), 465 w (Ni-N), 517 w (Ni-O).

[Ni₂L²(OAc)₂] (8) Dark green complex; yield: 61 %; d.p.: 186°C. Anal. Calc. for C₂₆H₂₈N₂O₆Ni₂: C, 52.23; H, 4.72; N, 4.69; Ni, 19.63. Found: C, 51.89; H, 4.96; N, 4.80; Ni, 19.69 %; Λ_M (DMF solution, ohm⁻¹ cm² mol⁻¹): 9.0; μ_{eff} = 2.32 B.M.; FT-IR (KBr, cm⁻¹): 1564 s (C=N), 1352 m (C-N), 1278 m (C-O), 1520 m, 1437 w (OAc), 478 w (Ni-N), 520 w (Ni-O).

Cleavage of pBR322 DNA: For the agarose gel electrophoresis experiments, 0.5 μg/μL supercoiled pBR322 DNA (0.5 μL) was treated with 2 μL of 1 mM the tested ligands and their complexes in DMF and 2 μL of 0.1M Tris-HCl (pH 8.0) buffer in the absence and presence of 2 μL of 5.0 mM hydrogen peroxide as a co-oxidant reagent. After incubation at 37°C for 2 h, 1 μL of loading buffer (0.25% bromophenol blue, 0.25% xylene cyanol, 30% glycerol in H₂O) was added to each tube and the mixed solution was loaded on 1% agarose gel. The electrophoresis was carried out for 1.5 h at 100 V in TBE buffer (89 mM Tris-borate, pH 8.3, 2.5 mmol L⁻¹ EDTA). Gels were stained with ethidium bromide (1 mg mL⁻¹) for 10 min prior to being photographed under UV light. The efficiency of the DNA cleavage was measured by determining the ability of the complex to form linked circular (LC) or nicked circular (NC) DNA from its supercoiled (SC) form by quantitatively estimating the intensities of the bands using the Biolab UVItect Gel Documentation System. The fraction of each form of DNA was calculated by dividing the intensity of each band by the total intensities of all the bands in the lane.

Solvent extraction: The extraction properties of the Schiff base ligands (**1,2**) were investigated under liquid-liquid phase and neutral conditions using transition metal picrates (Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺, Hg²⁺ and Pb²⁺) as substrates and measuring by UV-vis measurements the amounts of metal picrate in the aqueous phase before and after treatment with the compounds. About 10 mL of 2x10⁻³ M aqueous picrate solution and 10 mL of 1x10⁻³ M solution of ligand in CHCl₃ were vigorously agitated in a stoppered plastic tube with a mechanical shaker for 2 min, then magnetically stirred in a thermostated

water bath at 25°C for 1 h, and finally left standing for an additional 30 min. The concentration of the picrate ion remaining in the aqueous phase was then determined spectrophotometrically. Blank experiments showed that no picrate extraction occurred in the absence of ligand. Transition metal picrates were prepared by successive addition of a 1x10⁻² M metal nitrate solution to 2x10⁻⁵ M aqueous picric acid solution and shaken at 25°C for 1 h. This metal picrates (Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺, Hg²⁺ and Pb²⁺) were measured by UV-vis using maximum wavelength 352 nm. For each combination of host and metal picrate, the picrate extraction was conducted on three different samples and the average value of percent picrate extracted was calculated. In the absence of host, a blank experiment, no metal ion picrate extraction was detected. The extractability was calculated by using the equation below:

$$\text{Extractability}(\%) = \left(\frac{A_0 - A}{A_0} \right) \times 100$$

where A₀ is the absorbance in the absence of ligand. A denotes the absorbance in the aqueous phase after extraction.

RESULTS AND DISCUSSION

Synthesis: The ligands were prepared by the condensation of 4,4'-diaminodiphenylmethane and 4,4'-diaminodiphenylether with ethylenediamine. The products, as dark yellow powder materials, were characterized by IR, ¹H NMR spectroscopy and elemental analyses. The prepared complexes are stable when kept on light in air at room temperature. Attempts to isolate crystals of the complexes suitable for X-ray diffraction were unsuccessful. Therefore, elemental analysis, spectroscopic techniques, conductivity and magnetic susceptibility techniques were employed in order to determine the structural characteristics of the complexes. The analytical data of the complexes indicate 2:1 metal-ligand stoichiometry. The experimental and calculated C, H, N and metal values are in good agreement with the proposed structures. The molar conductance of the complexes was an aid for proposing their formulas. The values of the molar conductance in DMF in 10⁻³ M solutions are in the range 7.8-12.1 ohm⁻¹ cm² mol⁻¹, suggesting a non-electrolytic nature for these complexes [23,31,32].

IR spectra: The IR spectra of the free ligands and their complexes exhibit various bands in the 400–4000 cm⁻¹ region. The free ligands exhibit the characteristic C=O band in 1613–1608 cm⁻¹ region. The C=N stretching frequencies are in the 1566–1560 cm⁻¹ region as reported for similar ligands [33,34]. The low energy position of the C=N band could be attributed to its involvement in conjugation with the aromatic system. These data indicate that the free ligands exist mainly in the ketonic form in the solid state. The appearances of only one band for each of the C=O and C=N groups indicate the symmetrical nature of the free ligands [23].

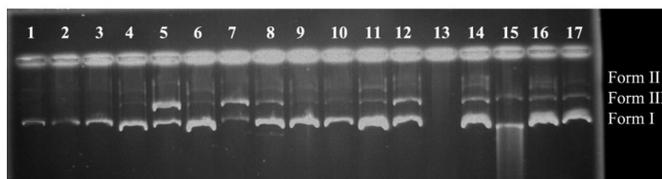
The IR spectra of all complexes did not show the band due to νC=O and instead a new medium-strong band at 1278–1271 cm⁻¹ assignable to νC–O. The spectra of the complexes exhibit upward shift of the νC=N and appeared at 1576–1564 cm⁻¹ instead of 1566–1560 cm⁻¹ region in the free ligands. The C–N stretching frequency for the free ligands occur in the 1314–1307 cm⁻¹ region and for the complexes, 1404–1352 cm⁻¹ region [34–36]. The C=N and C–N stretching frequencies are generally shifted to higher frequencies, indicating the formation of bond nitrogen of azomethine group with the metal ion. Accordingly, the ligands act as a dibasic tetradentate coordinating to the metal(II) ions via the carbonyl oxygen and azomethine-nitrogen atoms. The IR spectra of [LMe₂(OAc)₂] display bands at 1528-1518 and 1456-1437 cm⁻¹ due to the asymmetric and symmetric acetate group with about Δν = 100 cm⁻¹ characteristic of bidentate acetate group. The spectra of ethylenediamine containing complexes **5** and **6** display additional splitted broad band at 3332–3271 cm⁻¹ characteristic of coordinated NH₂ to the copper(II) ion. In these complexes, the acetate groups display the asymmetric and symmetric vibrations at 1552-1541 and 1356-1348 cm⁻¹ with about Δν = 200 cm⁻¹ characteristic of their monodentate nature [23,37]. A new weak bands at 451-444 cm⁻¹ due to νCu–N and 478-465 cm⁻¹ due to νNi–N are observed indicating the presence of metal-ligand bonding.

Nuclear magnetic resonance spectra: The ¹H NMR spectra of the free ligands were recorded in CDCl₃. The chemical shifts, expressed in ppm downfield from tetramethylsilane, are given in the experimental section. In the region of 7.18–6.63 ppm were assigned chemical shifts for hydrogen of the aromatic ring. The alkyl protons –CN–CH–CO– were observed 2.17 ppm in the two ligands. The alkyl protons of –Ar–CH₂–Ar– group were observed 3.87 ppm in the ligand L¹. The singlets for the –COCH₃ group were observed at 5.10

and 5.12 ppm and the singlets for the $-\text{CNCH}_3$ group were observed 1.15 and 1.18 ppm. These data are in agreement with previously reported for similar compounds and confirmed the suggested formulation of the ligands [23,34].

Magnetic studies: The room temperature magnetic moments of the complexes showed that all of the complexes are paramagnetic. The magnetic moments of the copper(II) complexes (3-6) are 0.54-1.58 B.M. These values are well below the spin-only value of 1.73 B.M. per one d^9 copper ion, indicating spin-exchange interaction between copper(II) ions [3,38,39]. The measured magnetic moments of the nickel(II) complexes are 3.48 and 2.32 B.M. for (7) and (8), respectively. Magnetic susceptibility measurements showed that these complexes are two electron paramagnetics, which corresponds to the +2 oxidation state of nickel (high-spin d^8 , $S = 1$) [40]. But magnetic moments of these dinuclear Ni(II) complexes are below the two spin value of 2.83 B.M. Reported some dinuclear Ni(II) complexes, exhibit moderate to weak antiferromagnetic interactions [39,41,42].

DNA cleavage activity: The cleavage of supercoiled form of pBR322 DNA with the ligands (1 and 2), their copper(II) (3-6) nickel(II) (7,8) complexes was studied in the absence or presence of H_2O_2 as a cooxidant. DNA cleavage was analyzed by monitoring the conversion of supercoiled DNA (Form I) to nicked circular DNA (Form II) and linear DNA (Form III) in aerobic condition. When circular plasmid DNA is subjected to electrophoresis, relatively fast migration will be observed for the intact supercoil form (form I). If scission occurs on one strand (nicking), the supercoil will relax to generate a slower moving open circular form (form II). If both strands are cleaved, a linear form (form III) that migrates between form I and form II will be generated [43,44]. The results of the gel electrophoresis separations of plasmid pBR322 DNA by the ligands (1,2) and their complexes (3-8) in the absence or presence of H_2O_2 are depicted in the Fig. 1. The control experiment was applied using only DNA. As shown in Fig. 1, incubation of the pBR322 DNA at 37°C for 2 h with 2 μg of the compounds cause the conversion of Form I to Form II and Form III. The supercoiled (form I) DNA was cleaved to form II and form III in the absence of H_2O_2 of the complexes (3-8). The cleavage efficiency after incubation for 2 h in the absence of H_2O_2 , follows the order: $6 > 4 > 5 > 3 > 8 > 7 > 2 > 1$. The cleavage percentages are listed in Table 1. These results indicate that the examined complexes induces very similar conformational changes on supercoiled DNA as conversion of supercoiled form to nicked form than linear form in a sequential manner. But (3) and (5) are less effective than complexes (4) and (6). On the other hand, the pBR322 DNA treated with the ligands



(1,2) and the nickel(II) complexes (7,8) showed less changes in the form levels compared with the copper(II) complexes. The different DNA cleavage efficiency of the ligands and the complexes may be due to the different binding affinity of the complexes to DNA [44,45].

Fig. 1. Gel electrophoresis diagram showing the cleavage data of pBR322 plasmid DNA (0.5 μg) by the Schiff base ligands and their complexes in DMF-Tris buffer medium (pH 8.0) in air after incubation at 37°C for 2 h. Lane 1, untreated pBR322 plasmid DNA; lanes 2-9, pBR322 plasmid DNA + the compounds; lanes 10-17, pBR322 plasmid DNA + the compounds + H_2O_2 (the compounds = 1, 2, 3, 4, 5, 6, 7, 8 respectively).

The degradation of pBR322 DNA is also dependent on cooxidant used. The cleavage mechanism of pBR322 DNA induced by the compounds (1-8) were investigated (Fig. 1) and clarified in the presence of H_2O_2 as a cooxidant (Lanes 10-17). In the ligands, the intensity of the circular supercoiled DNA (Form I) band was found decrease, while that of linear (Form III) band increase apparently (Lane 9 and 10) in the presence of H_2O_2 . The copper(II) complex (4), the cleavage is found to be much more efficient, it degraded the supercoiled pBR322 DNA completely (Lane 13). The copper complex (6) cleaved the supercoiled pBR322 DNA into form III and the nicked circular DNA (Form II) band was disappeared completely (Lane 15). But the activities of the nickel(II) complexes (7,8) was weaker than the copper(II) complexes. These observations suggest that the complexes mediated cleavage reaction proceed via oxidative pathway mechanism and imply that the singlet oxygen playing a role in the cleavage chemistry. In the presence of H_2O_2 all the complexes

(3-8) are remarkably degrading the pBR322 DNA by oxidative (O_2 -dependent pathway) cleavage mechanism using the singlet oxygen as the reactive species [44,46]. These results are similar to that observed for some Cu(II) and Ni(II) complexes as chemical nuclease [47-52].

Table 1. DNA cleavage data of pBR322 plasmid DNA by 1-8.

Lane no	Reaction conditions ^a	Form I %SC ^b	Form II %NC ^b	Form III %LC ^b
1	DNA	80.90	19.10	ND ^b
2	DNA + 1	76.67	23.33	ND
3	DNA + 2	73.19	26.81	ND
4	DNA + 3	67.92	16.60	15.48
5	DNA + 4	33.66	19.63	46.72
6	DNA + 5	61.09	20.30	18.60
7	DNA + 6	29.27	13.97	56.76
8	DNA + 7	61.30	15.52	23.18
9	DNA + 8	61.07	17.59	21.34
10	DNA + 1 + H_2O_2	56.77	15.98	27.24
11	DNA + 2 + H_2O_2	65.10	15.80	19.10
12	DNA + 3 + H_2O_2	53.31	36.56	10.13
13	DNA + 4 + H_2O_2	ND	ND	ND
14	DNA + 5 + H_2O_2	59.13	17.13	23.74
15	DNA + 6 + H_2O_2	65.16	ND	34.84
16	DNA + 7 + H_2O_2	57.47	20.68	21.85
17	DNA + 8 + H_2O_2	57.41	18.75	23.84

(a) Incubation time, 2 hours

(b) SC, NC, LC are supercoiled, nicked circular and linked circular forms of DNA, respectively. ND: not detected.

Extraction ability of the ligands: The extraction efficiencies of ligands toward some metal ions (Mn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} and Pb^{2+}) were determined by the picrate extraction method developed by Pedersen [53]. Solvent extraction of aqueous metal cation into water saturated organic hosts' solutions, were performed at 25°C. An aqueous solution containing metal picrate was extracted with the host solution (chloroform), and the data are expressed as percentages of the cation extracted (%E) by the ligands, as given in Table 2 and represented in Fig. 2.

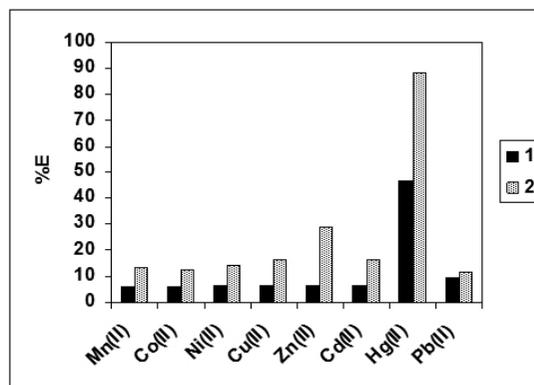


Fig. 2. Extraction percentages of the metal picrates with ligands (ligands: 1= H_2L^1 , 2= H_2L^2) $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2 = 10/10$ v/v; [picric acid] = 2×10^{-5} M, [ligand] = 1×10^{-3} M, [metal nitrate] = 1×10^{-2} M, 298K, 1 h contact time.

The extraction ability of H_2L^2 varies as $\text{Hg}^{2+} > \text{Zn}^{2+} > \text{Cu}^{2+} \geq \text{Cd}^{2+} > \text{Ni}^{2+} \geq \text{Mn}^{2+} \geq \text{Co}^{2+} \geq \text{Pb}^{2+}$. On the other hand it is clear from the Table 2 that the complexation ability of H_2L^2 toward Hg^{2+} is much higher and the ligand is excellent extractant for Hg^{2+} ion. The presence in the ligand of soft donor nitrogen groups and π bonds, which show high affinity to transition metals, causes the increase in the extraction ability of this ligand. The effectiveness in transferring transition metals by the synthesized compound indicates that a cation- π electron interaction is operative since the metal is bounded by the opposite N, N or N, O sites of this compound [54].

Table 2. Transition metal picrate extractions from aqueous solutions into chloroform by using (1) and (2)

Compounds	Percent of metal picrate extracted (%)							
	Mn(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	Cd(II)	Hg(II)	Pb(II)
(1)	6.13	6.11	6.49	6.45	6.71	6.53	46.92	9.51
(2)	13.87	12.53	14.15	16.80	29.09	16.68	88.16	12.09

$^a\text{H}_2\text{O}/\text{CHCl}_3 = 10/10$ (v/v): [picric acid] = $2 \cdot 10^{-5}$ M, [ligand] = $1 \cdot 10^{-3}$ M, [metal nitrate] = $1 \cdot 10^{-2}$ M, 298 K, 1 h contact time

CONCLUSIONS

A series of symmetrical tetradentate Schiff bases containing the N2O2 donor set and their corresponding nickel(II) and copper(II) complexes have been synthesized and characterized by elemental, ICP-OES, magnetic susceptibility, conductivity measurements and FT-IR. The magnetic, conductivity measurements and infrared data provided evidence for the structures of the isolated complexes. In addition we have tested the DNA cleavage activity of the ligands and their complexes. The DNA cleavage results showed that the copper and nickel complexes can effectively cleave supercoiled DNA to form nicked or linear DNA by performing single strand and double strand scissions under aerobic conditions. In the copper(II) complex (4), the cleavage is found to be much more efficient, it degraded the supercoiled pBR322 DNA completely. Furthermore liquid-liquid extraction of some metal ions (Mn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} and Pb^{2+}) with the ligands have been examined. H_2L^2 ligand is good extractant for mercury(II).

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