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Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry

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Synthesis and characterization of a new di-functional ligand and its metal complexes: An experimental, theoretical, cyclic voltammetric and antimicrobial study

Haci Baykara^a, Salih Ilhan^a, Abdussamet Oztomsuk^a, M.Salih Seyitoglu^a, Abdulkadir Levent^b, Veysi Okumus^c & Abdurrahman Dündar^d

^a Faculty of Art and Science, Chemistry Department, Siirt University, Siirt, Turkey

^b Batman University, Health Services Vocational College, 72100 Batman, Turkey

^c Faculty of Art and Science, Biology Department, Siirt University, Siirt, Turkey

^d Mardin Artuklu University, Vocational Higher School of Health Services, Medical Promotion and Marketing Program, 47000, Mardin/Turkey

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Synthesis and characterization of a new di-functional ligand and its metal complexes: An experimental, theoretical, cyclic voltammetric and antimicrobial study

Haci Baykara^{1*}, Salih Ilhan^{1*}, Abdussamet Oztomsuk¹, M.Salih Seyitoglu¹, Abdulkadir Levent², Veysi Okumus³, Abdurrahman Dündar⁴

¹Faculty of Art and Science, Chemistry Department, Siirt University, Siirt, Turkey
 ²Batman University, Health Services Vocational College, 72100 Batman, Turkey
 ³Faculty of Art and Science, Biology Department, Siirt University, Siirt, Turkey
 ⁴Mardin Artuklu University, Vocational Higher School of Health Services, Medical Promotion and Marketing Program, 47000, Mardin/Turkey

^{*}Corresponding Author. Email: salihsiirt@gmail.com, hacibaykara@gmail.com

A new di-functional Schiff base ligand and its some metal complexes were synthesized. The compounds were characterized by elemental analysis, ¹H-NMR, ¹³C-NMR, FT-IR, UV-VIS, magnetic susceptibility measurements, molar conductivity measurements, thermal gravimetric analysis techniques. Additionally, DPPH scavenging, metal chelating and antibacterial activity of compounds were examined via in vitro methods. The lowest DPPH scavenging activity observed by Co(II) as 36.28% and highest was Ligand as 52.00%. A cyclic voltammetric study was also carried out to determine redox potentials of the compounds. Some theoretical studies such as ¹H-NMR, HOMO-LUMO and mapped electron density of the ligand were also carried out successfully.

Keywords: Schiff base complexes, Cyclic voltammetry, antimicrobial, antioxidant, Gaussian 09, electron density.

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INTRODUCTION

Metal complexes of Schiff bases are playing an important role in the development of coordination chemistry, which is evident in number of publications, including electrochemical studies, antioxidant and antimicrobial activities ^[1-8]. A large number of reports are available on chemical properties, the biological activities and theoretical properties of Schiff base ligands and their corresponding transition metal complexes containing O,N and S,N donor atoms ^[9-11]. Some Schiff base metal complexes are used as growth inhibiting agents for most bacteria and fungi and they are useful for human health ^[12-14]. Transition metal complexes with tetradentate Schiff-base ligands have been extensively investigated as catalysts for a number of organic redox reactions and electrochemical reduction processes ^[15-17]. Theoretical calculations of electronic transitions, ¹H and ¹³C NMR, molecular parameters such as total energy, heat of bonding energy, isolated energy, electronic energy, heat of formation, dipole moment, HOMO and LUMO of the ligand and complexes have been studied recently ^[18-22].

In this study, we have synthesized a new Schiff base by reaction of 5-salicylaldehyde and 1,6bis(4-aminophenoxy)hexane. Some Schiff base metal complexes were synthesized by the reaction of some metal salts and the new Schiff base. Spectral analyses, cyclic voltammetry, antimicrobial studies, magnetic properties of the new compounds were studied in details and, theoretical calculations such as ¹H-NMR and HOMO-LUMO properties of the new ligand have been carried out successfully.

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EXPERIMENTAL

Materials and Methods

The 1,6-bis(4-aminophenoxy) hexane used in the synthesis were prepared from p-nitro phenol, 1,6-dibromohexane and K_2CO_3 as shown in scheme 1 ^[23, 24]. All the chemicals and solvents were of analytical grade and used as received. Elemental analysis was carried out on a LECO CHNS model 932 elemental analyzer. IR spectra were recorded on a PERKIN ELMER SPECTRUM 100 FTIR spectrometer on a universal ATR arm, with a wavenumber range of 4000-650 cm⁻¹. Electronic spectral studies were conducted on a PERKIN ELMER LAMBDA 750 model UV Visible spectrophotometer in the wavelength 200-900 nm. Molar conductivities were measured with a WTW LF model 330 conductivity meter using prepared solution of the complexes in N,N-dimethylformamide (DMF). Electrochemical experiments were performed with an Autolab PGSTAT 128N potentiostat, (The Netherlands) using a three electrode system, glassy carbon working electrode (Φ : 3 mm, BAS), platinum wire as auxiliary electrode and Ag/AgCl (NaCl 3M, Model RE-1, BAS, USA) as reference electrode. The reference electrode was separated from the bulk solution by a fritted-glass bridge filled with the solvent/supporting electrolyte mixture. Before starting each experiment, the glassy carbon electrode was polished manually with alumina (Φ : 0.01 µm). Cyclic voltammetric (CV) experiments were recorded at room temperature in extra pure dimethyl formamide (DMF), and ionic strength was maintained at 0.1M with electrochemical grade tetrabutylammonium perchlorate (TBAP) as the supporting electrolyte. Solutions were deoxygenated by a stream of high purity nitrogen for 15 min prior to the experiments, and during the experiments nitrogen flow was maintained over the solution.

¹H and ¹³C NMR spectra were recorded using a BRUKER AVANCE DPX-400 NMR spectrometer. Magnetic Susceptibilities were determined on a Sherwood Scientific Magnetic Susceptibility Balance (Model MK1) at room temperature $(20^{\circ}C)$ using Hg[Co(SCN)₄] as a calibrant; diamagnetic corrections were calculated from Pascal's constants^[25]. Thermal gravimetric analyses were determined on an EXSTAR S II TG/DTA 6300 Model. Gaussian computations were carried out using a standard personal computer (PC) having 4096 MB ram. Licensed Gaussian 09 and GaussView 5^[26, 27] software were used to carry out theoretical calculations such as ¹H-NMR and HOMO-LUMO computations and viewing entire input and out files respectively. 1,1-Diphenyl-2-picryl-hydrazyl (DPPH), ferrous chloride, α- tocopherol, 3-(2pyridyl)-5,6-bis (4-phenyl-sulfonic acid)-1.2.4-triazine (Ferrozine), ascorbic acid. ethylenediaminetetraacetic acid (EDTA), Trolox and dimethylformamide (DMF) were purchased from Sigma (Sigma-Aldrich GmbH, Sternheim, Germany). Methanol was purchased from E. Merck. Blank and standard antimicrobial susceptibility test discs were purchased from Oxoid. All other chemicals were analytical grade and purchased from either Sigma- Aldrich or Merck.

Synthesis of Schiff Base

Salicylaldehyde (40 mmol) in ethanol (40 mL) was added drop wise to a stirred solution of 1,6bis(aminophenoxy)hexane (20 mmol) in ethanol (60 mL). After the addition was completed, the stirring was continued for 2h, and then precipitate was filtered and washed with ethanol and dried in a vacuum oven for 24 h (Scheme 2).

Synthesis of Schiff Base Complexes

A solution of a metal salt such as Zn(II), Ni(II), Co(II), Ti(III) and V(III) in DMF (40 mL) was mixed with the Schiff base ligand (2 mmol) in DMF (60 mL) 1:1 molar ratio. The contents were

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refluxed on an oil-bath for two hours. The product was isolated by filtration, washed with ethanol and dried in vacuum oven at 30 °C for 24 h (Scheme 3). All the complexes are almost insoluble in common organic solvents such as ethanol, methanol, benzene, acetone, nitrobenzene, dichloromethane and chloroform. However, they are slightly soluble in polar organic solvents such as dimethyl sulfoxide and dimethyl formamide.

Characterization of Schiff Base (L)

Molecular Weight: 504. m.p: 122-123 ⁰C. Color: Yellow. Yield: 9.17 g (91 %). Anal Calcd. for $C_{32}H_{28}N_2O_4$: C, 76.19, H, 5.55, N, 5.55. Found: C, 76.80, H, 5.89, N, 5.62. IR (cm⁻¹): 3063 v(Ar-CH), 2944-2860 v(Alf.-CH), 1617 v(C=N), 1491-1473 v(Ar-C=C), 1294-1245 v(Ar-O), 1187-1151 v(R-O). UV-vis: $\lambda_1 = 273$ nm(ϵ =3000), $\lambda_2 = 326$ (ϵ =5000) nm λ_3 =345 nm(ϵ =5800). ¹³C NMR (ppm, in DMSO-d₆): OCH₂CH₂CH₂: 62.16, OCH₂CH₂CH₂: 25.23, OCH₂CH₂CH₂CH₂: 20.11, OH-C: 161.04, HC=N: 159.54, (Ar-C): 115.31, 115.53, 119.36, 121.57, 122.97, 126.251, 129.35, 131.15, 134.09. ¹H-NMR (ppm, in DMSO-d₆): OCH₂CH₂CH₂CH₂: 4.07 (s), OCH₂CH₂CH₂: 1.78 (s), OCH₂CH₂CH₂: 1.51(s), Ar-H: 6.97-7.63: (m), HC=N: 8.95 (s), OH: 13.33 (s).

Characterization of [NiL]

Molecular Weight: 560. m.p: 173 ^oC decompose. Color: light brown. Yield: 0.86 g (77%). Anal Calcd. for NiC₃₂H₂₈N₂O₄: C, 68.57, H, 5.00, N, 5.00. Found: C, 68.32, H, 5.27, N, 5.73. Selected IR data (KBr, v cm⁻¹): 3059 v(Ar-CH), 2943-2857 v(Alf.-CH), 1609, v(C=N), 1491-1472 v(Ar-C=C), 1294-1254 v(Ar-O), 1187-1149 v(R-O). UV-vis (λ max, nm) in DMF: $\lambda_1 = 270$ nm(ϵ =3300), $\lambda_2 = 331$ nm(ϵ =5200), $\lambda_3 = 352$ nm(ϵ =6200). $\mu_{eff} = 2.89$ Bohr Magneton (B.M.).

Characterization of [CoL]

Molecular Weight: 561. m.p: 137 ^oC decompose. Color: Brown. Yield: 0.83 g (74%). Anal Calcd. for $CoC_{32}H_{28}N_2O_4$: C, 68.45, H, 4.99, N, 4.99. Found: C, 68.92, H, 5.81, N, 5.26. Selected IR data (KBr, v cm⁻¹): 3066 v(Ar-CH), 2942, 2867 v(Alf.-CH), 1608, v(C=N), 1503, 1460 v(Ar-C=C), 1294, 1243 v(Ar-O), 1179, 1148 v(R-O). UV-vis (λ max, nm) in DMF: $\lambda_1 = 269$ nm(ϵ =9450), $\lambda_2 = 325$ nm(ϵ =10800), $\lambda_3 = 332$ nm(ϵ =10600). $\mu_{eff} = 3.83$ B.M.

Characterization of [ZnL]

Molecular Weight: 567. m.p: 172 ⁰C decompose. Color: Orange. Yield: 0.85 g (75%). Anal Calcd. for ZnC₃₂H₂₈N₂O₄: C, 67.72 , H, 4.94 , N, 4.94 . Found: C, 68.07, H, 5.15, N, 4.52. Selected IR data (KBr, v cm⁻¹): 3062 v(Ar-CH), 2942-2863 v(Alf.-CH), 1607, v(C=N), 1503-1463 v(Ar-C=C), 1297-1243 v(Ar-O), 1179-1148 v(R-O). ¹H-NMR (ppm, in DMSO-d₆): OC<u>H₂CH₂CH₂: 4.145-4.024 (t), OCH₂CH₂CH₂: 1.77 (s,), OCH₂CH₂CH₂:1.51 (s), Ar-H: 6.91-7.66 (m), HC=N: 8.56 (s). UV-vis (λ max, nm) in DMF: $\lambda_1 = 274$ nm (ϵ =3700), $\lambda_2 = 351$ nm (ϵ =7100). μ_{eff} = Diamagnetic.</u>

Characterization of [TiLCl]

Molecular Weight: 585. m.p: 167 ⁰C decompose. Color: Grey white. Yield: 0.75 g (64%). Anal Calcd. for TiC₃₂H₂₈N₂O₄: C, 65.64, H, 4.79 , N, 4.79 . Found: C, 66.23, H, 5.28, N, 5.12. Selected IR data (KBr, v cm⁻¹): 3059 v(Ar-CH), 2943-2863 v(Alf.-CH), 1607, v(C=N), 1504-1463 v(Ar-C=C), 1278-1249, v(Ar-O), 1147-1109 v(R-O). UV-vis (λ max, nm) in DMF: $\lambda_1 = 273$ nm (ϵ =7550), $\lambda_2 = 352$ nm(ϵ =10800). $\mu_{eff} = 1.72$ B.M.

Characterization of [VLCl]

Molecular Weight: 589. m.p: 151 ^oC decompose. Color: Dark Brown. Yield: 0.79 g (67%). Anal Calcd. for VC₃₂H₂₈N₂O₄: C, 65.20 , H, 4.75 , N, 4.75 . Found: C, 65.74, H, 5.21, N, 5.11. Selected IR data (KBr, v cm⁻¹): 3059 v(Ar-CH), 2943-2867 v(Alf.-CH), 1607, v(C=N), 1504-1458 v(Ar-C=C), 1280-1243 v(Ar-O), 1186-1149 v(R-O). UV-vis (λ max, nm) in DMF: $\lambda_1 = 273$ nm(ϵ =10000), $\lambda_2 = 346$ nm(ϵ =16000). $\mu_{eff} = 3.55$ B.M.

Antioxidant analyses of the ligand and its complexes

DPPH scavenging activity

The DPPH scavenging abilities of DMF solutions of six compounds were tested by Blois method (1958). This method is a spectrophotometric method based on the reduction of DPPH in methanol solution. Each compound (5, 10, 25, 50 and 100 mg/L) in DMF (1 ml) was mixed with 4 ml of DPPH's methanol solution. The mixture was shaken vigorously and left to stand for 30 min in the dark and then absorbance was measured at 517 nm against a blank which consist only 5.0 mL methanol by a spectrophotometer. Free radical inhibition percent (I%) of DPPH was calculated according to formula:

 $I\% = (A_{control} - A_{sample})/A_{control} \times 100;$

Where $A_{control}$ is the absorbance of the control reaction (containing all reagents except the test compound), and A_{sample} is the absorbance of the test compound. Tests were carried out in triplicate. Trolox and ascorbic acid were used as positive control ^[28].

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Metal chelating ability

The chelating abilities of methanol solutions of the compounds were determined according to the method of Dinis et al. (1994). Each solution (5, 10, 25, 50 and 100 mg/L) in DMF (1 mL) was added to 3.7 mL of methanol and mixed with 0.05 mL of 2 mmol/L ferrous chloride. 0.1 mL of 5 mmol/L ferrozine was added to the solution for starting the reaction. The mixture was left for standing 10 min at room temperature then the absorbance was measured at 562 nm against blank. The results were expressed as inhibition percent of the ferrozine–Fe²⁺ complex formation. EDTA was used as a positive control. The inhibition percent of the ferrozine–Fe²⁺ complex formation was calculated using the formula given below:

Chelating ability (%) = $(A_{control} - A_{sample})/A_{control} \times 100;$

Where $A_{control}$ is the absorbance of the control reaction (containing only FeCl₂ and ferrozine), and A_{sample} is the absorbance of the compounds/reference. EDTA was used as a positive control ^[29].

Antimicrobial analyses of the ligand and its complexes

Test Microorganisms

In vitro antibacterial studies were done to determine the antimicrobial potentials of compounds used in this study. *Escherichia coli* (ATCC 10536), *Staphylococcus aureus* (ATCC 6538), *Bacillus subtilis* (6051) *Legionella pneumophila* subsp. *pneumophila* (ATCC 33152), *Enterococcus hirae* (ATCC 10541), *Micrococcus luteus* (ATCC 9341), and *Pseudomonas aeruginosa* (ATCC 9027) were used as test bacteria.

Disc diffusion method

Antimicrobial activities of DMF solutions of the compounds were determined by disc diffusion method (Kalemba and Kunicka, 2003). Bacterial cultures were incubated at 37 °C for 24 h in Nutrient Broth. 25 mL of Nutrient Agar poured into petri plates. Bacteria cultures (100 μ L) were inoculated to petri plates. The blank discs (6.0 mm, Oxoid Ltd, Wade Road, Basingstoke, Hants, RG24 8PW, UK.) were impregnated with 15 μ L compound solution same volume (15 μ L) of DMF was used as a control. The inoculated plates were incubated at 37°C for 24 h. Inhibition zones were measured basically from the edge of the inhibition zone to the edge of the discs ^[30].

RESULTS AND DISCUSSION

Schiff base and complexes

The ligand and metal complexes were characterized by elemental analysis, IR, UV-vis, TGA-DTA, ¹H-NMR and ¹³C NMR, conductivity measurements, cyclic voltammetry and magnetic susceptibility techniques. In addition to experimental characterization techniques, a theoretical optimization, NMR and HOMO-LUMO studies were also done as a supportive characterization technique of new di-functional ligand. Furthermore, a linear regression analysis was also carried out to investigate the compatibility between experimental and theoretical ¹H-NMR shifts. Since the complexes were not soluble in common organic solvents, we could not crystallize the complexes. Due to that problem, single crystal X-Ray structural determination of the complexes could not be carried out.

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FTIR Spectra

Important IR peaks of the Schiff base ligand and complexes are given in table 1. Even though O-H stretching peak or band should be observed around 3300 cm⁻¹ but it was not observed in the IR spectra of the ligand. This is because of strong intramolecular hydrogen bonding. Similar situations were observed at the same frequency in the IR spectra of salicylideneanilines ^[31, 32]. This band disappeared in the IR spectra of the complexes. The band at 1285 cm⁻¹ in the IR spectrum of the ligand is ascribed to the phenolic C-O stretching vibration. This band is found in the region 1275-1285 cm⁻¹ in the spectra of the complexes. These changes suggest that the o-OH group of this Schiff base moiety has taken part in complex formation. IR spectra of the ligand showed the absence of bands at 1735 and 3420 cm^{-1} due to v(C=O) and $v(NH_2)$ stretching vibrations and instead, a new band appeared at ~1620 cm⁻¹ assigned to azomethine v(HC=N). This suggested that amino and aldehyde moieties of the starting reagents have been converted into the corresponding Schiff bases. The strong band within the range at $ca.1620 \text{ cm}^{-1}$ in the spectra of all the complexes can be attributed to stretching vibrations of imine $v(-C=N)^{[33-35]}$. The IR spectra of the complexes compared with those of the ligand indicate that the C=N band ca.1620 cm⁻¹ is shifted to lower values for complexes; these IR values are indicating coordination of the azomethine nitrogen to metal ^[36]. In the spectra of all the complexes are dominated by bands at 2965-2855 cm⁻¹ due to v(Alph.-CH) groups ^[37].

Electronic Spectra

Electronic absorption spectral data of the compounds in dimethylformamide (DMF) at room temperature are presented in experimental section. The electronic spectra of the complexes in DMF show few bands in the ultraviolet-visible region. The absorption bands below at *ca*.300

nm are practically identical and can be attributed to $\pi \rightarrow \pi^*$ transitions in the benzene ring and azomethine (-C=N) groups. The absorption bands observed within the *ca*. 300-400 nm are due to the $n \rightarrow \pi^*$ transitions in imine groups ^[38]. The general character of these spectra is very similar to the phenoxy groups of corresponding complexes. The results we have obtained are consistent with the literature ^[38, 39].

Magnetic measurements and Molar Conductivity

The magnetic moment measurements of compounds were carried out at 25 °C. Magnetic susceptibility measurements provide sufficient data to characterize the structures of the complexes. The magnetic moments of the complexes were given in the characterization section. The complexes are non-electrolytes as shown by their molar conductivities (Λ_M) in DMF (dimethyl formamide) at 10⁻³ M, which are in the range 5-10 Ω^{-1} cm²mol⁻¹. The molar conductivities of the compounds in DMF are in the range reported for non-electrolytes ^[34-36].

¹H-NMR and ¹³C NMR (ppm)

The ¹H-NMR (ppm) and ¹³C NMR (ppm) spectra of free ligand and its diamagnetic complexes were recorded in DMSO-d₆ and reported along with possible assignments in the experimental section. Comparison of chemical shifts of the ligand with those of the complexes shows that the signal due to phenolic proton of the ligand were absent in the complexes, suggesting coordination after deprotonation. The azomethine proton (-CH=N-) undergoes a significant shift, indicating coordination of the azomethine nitrogen. More detailed information about the structure of the ligand was provided by ¹³C NMR spectra. All the carbon atoms due to heteroatomic and aromatic groups were found in their expected region ^[40]. In the spectra of diamagnetic complexes, these signals shifted downfield due to the increased conjugation and

coordination to the metal ions. The number of protons and carbons calculated from the integration curves agreed with those obtained from the values of the CHN analysis^[41].

TGA Studies

The thermal stability of the complexes was investigated using TGA. The termogravimetric analysis (TGA) and curves were obtained at a heating rate of 10°C/min in a nitrogen atmosphere over a temperature range of 50-900 °C.

The ligand was stable up to 280 °C and its decomposition started at this temperature. The ligand underwent decomposition in one stage (280-550 0 C). The decomposition (280-550 0 C) corresponds to loss of C₁₄H₁₂O₂N₂ (two C₇H₆NO group).

The [NiL] was stable up to 320 °C and its decomposition started at this temperature. The complexes underwent decomposition in one step (320-900 0 C). The decomposition corresponds to loss of many organic groups and residue of NiO.

The [CoL] was stable up to 310 °C and its decomposition started at this temperature. The complexes underwent decomposition in one step (310-900 0 C). The decomposition corresponds to loss of many organic groups and residue of CoO.

The [ZnL] was stable up to 290 °C and its decomposition started at this temperature. The complexes underwent decomposition in one step (290-900 0 C). The decomposition with DTG peak at 421,3 0 C corresponds to loss of many organic groups and residue of ZnO.

The [TiLCl] was stable up to 200 °C and its decomposition started at this temperature. The complexes underwent decomposition in one step (200-900 0 C). The decomposition corresponds to loss of many organic groups and residue of Ti₂O₃.

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The [VLCl] was stable up to 320 °C and its decomposition started at this temperature. The complexes underwent decomposition in three stages (320-900 0 C). The decomposition corresponds to loss of many organic groups and of residue V₂O₃) ^{[38,39].}

We couldn't isolate single crystals of the complexes from any solvents, thus no definitive structure could be described. However, the analytical, spectroscopic and magnetic data enable us to propose the possible structures for ligand and its complexes.

3.6. Theoretical Studies

Structure optimization ^[42-60] was carried out by B3LYP level of Density Functional Theory (DFT)^[43-60] at the 6-311G basis set. Optimized 3D structure with an electron density (Isovalue= 0.0004; mapped with Electrostatic Potential computed from Total Self-Consistent Field (SCF) Density)^[44] of the ligand is represented in Figure 2. NMR calculations ^[45] carried out by applying DFT and Hatree-Fock (HF)^[46] theories with different levels of the theories and basis sets (Figure 3-4). The Gauge-Independent Atomic Orbital (GIAO) method was carried out to calculate theoretical ¹H-NMR shifts of the ligand ^[56-60]. Theoretical calculations were carried out in gas phase ^[47-51].

The energy values of Highest Occupied Molecular Orbital (HOMO), Lowest Unoccupied Molecular Orbital (LUMO)) and HOMO-LUMO transition energy (energy gap, eV) values are shown in Figure 1. The energies of frontier molecular orbitals were computed at B3LYP/6-311G level of the DFT method, the same method and level of the method with the optimization part of the study^[42,52-60]. The energy values for HOMO and LUMO structures were found -5.5538 eV and -1.9341 eV respectively. The excitation energy value for the HOMO-LUMO transition was found as 3.6197 eV and, this energy value is assigned to the $\pi \rightarrow \pi^*$ transitions in phenyl groups

and C=N groups (Figure 1). Formation of π bonds in phenyl and C=N groups can be clearly seen in Figure 1 by the interaction of p orbitals, in the HOMO view (see figure 1). On the other hand, electron dense sides of the optimized di-functional Schiff base was also visualized and, as seen in Figure 2, electron density increases around electronegative oxygen atoms in the ligand structure as it was expected. This Figure gives the information about reactive sides of the molecule and its reactivity. By this information potential reactions and reaction pathways for the molecule can be estimated. The information and results about electron density of the ligand are consistent with the previously reported articles ^[53-55].

A linear regression analysis also was done to control the compatibility between experimental and theoretical ¹H-NMR shifts of the ligand, as a supportive characterization technique. Comparison of experimental and theoretical ¹H-NMR shifts can be seen in figure 3 (HF/6-31G(d)) and figure 4 (B3LYP/6-311G(2d,p)). According to the both figures experimental and theoretical ¹H-NMR shifts show good conformity. The regression analyses equations in comparison of experimental ¹H-NMR to theoretical ((HF/6-31G (d))) ¹H-NMR and experimental ¹H-NMR to theoretical (B3LYP/6-311G(2d,p)) ¹H-NMR are y= 0.7499x + 0.8494 (R²=0.7544), y= 0.7499x + 0.1339 (R²= 0.7544) respectively. These results were obtained with outlier. Although outlier, being the most extreme observations, can have many anomalous causes, its exclusion makes the model methodologically sounds and accurate. The correlation coefficient square values (R²) 0.7544 for each comparison with outlier, indicate a slight deviation between the variables According to the regression analysis, there is a good conformity between experimental and theoretical ¹H-NMR shifts (see figure 3-4) but only experimental ¹H-NMR shift of one phenolic proton (13.3272 ppm) is very different than theoretical (HF= 4.1481 ppm)

and B3LYP= 3.4326 ppm) ¹H-NMR shifts. This deviation between theoretical and experimental NMR shifts is be assigned to acidic character of phenolic protons and executing theoretical calculations in the gas phase ^[56-58].

On the other hand, according to the regression analyses results it can be said thatB3LYP/6-311G (2d,p) is a better method for the theoretical ¹H-NMR calculations of the ligand studied ^[62-64]. Because, this method showed a lower linear regression analysis constant (0.1339, closer to zero) than the HF/6-31G (d) method's linear regression analysis constant (0.8494).

Cyclic Voltammetry of the complexes

The electrochemical properties of the present compounds were investigated by CV on a glassy carbon electrode in DMF containing 0.1 M TBAP, in the concentration of 1 mM vs. Ag/AgCl. The electrochemical data upon the peak potentials have been reported in table 2. The oxidation potentials and HOMO-LUMO values can be measured by cyclic voltammetry ^[59]. The corresponding HOMO and LUMO levels were calculated using IIc and IIa waves for the L ligand. The estimations were done with the empirical relation E_{LUMO} = [(E_{Ve^-} $E_{1/2}$ (ferrocene)) +4.8] eV or E_{HOMO} = [(E_{IIIa^-} $E_{1/2}$ (ferrocene)) +4.8] eV. Ferrocene was used as external standard. It shows two peaks at 0.37 and 0.41 V hence the $E_{1/2}$ (ferrocence) is equal to 0.39 V which can be used in equation to calculate the E_{HOMO} and E_{LUMO} . Based on cyclic voltammetry results, L shows E_{HOMO} = 4.72 eV, Egap= 2.50 eV and E_{LUMO} = 2.22.

In the cathodic direction from +1.0 V to -2.3 V at scan rate of 100 mVs⁻¹, the CV of L is characterized by four cathodic waves (Ic, IIc, IIIc and IVc at about +0.11, -0.85, -1.68 and -2.19 V, respectively) and three anodic waves were observed (Ia, IIa and IIIa at about -1.55, -0.10, and

+0.31 V, respectively) as depicted by cyclic voltammograms given in Figure 5A. The effect of scan rates on **L** compound was investigated between 50-1000 mV/s (Figure 5A). At high scan rate (200 mV/s>), the new reduction wave was observed at -0.65 V, but IIa wave wasn't observed.

The voltammograms of [**NiL**], [**CoL**] and [**ZnL**] complex were investigated in the same experimental conditions (from +1.0 V to -2.3 V at 100 mVs⁻¹ in Figure 5B-5C-5D), four cathodic waves (Ic, IIc, IIIc and IVc at about potentials close to each other) and three anodic waves observed (Ia, IIa, and IIIa at about potentials close to each other).

From the CVs (Figure 6), it was found that the initial oxidation peak current of **L**, [NiL], [CoL] and [ZnL] gradually increased and a negative shift in the peak potential existed with increasing scan rate. From the results obtained between 50 and 1000 mVs⁻¹, a plot of logarithm of peak current significantly correlated with the logarithm of scan rate for all **L**, [NiL], [CoL] and [ZnL] with slopes between 0.47, 0,48, 0.45 and 0.47, respectively (correlation coefficient between 0.989, 0.995, 0.986 and 0.979). These findings showed that the redox processes were predominantly diffusion controlled in the whole scan rate range studied ^[59].

Antimicrobial Studies

DPPH Scavenging Activity

The antioxidant activity of the newly synthesized ligands have attracted increasing interests and been substantially investigated ^[60, 61]. In this study DPPH scavenging, metal chelating and antibacterial activity of compounds were examined via in vitro methods.

Free radicals may oxidize nucleic acids, proteins, lipids or DNA and can initiate degenerative disease. DPPH is a stable free radical and it is very popular for the study of natural and synthetic

compounds which have antioxidant capacity. This is a rapid, simple and inexpensive method ^[62, 63]. The reduction capability of DPPH radicals was determined by the decrease in its absorbance at 517 nm induced by compounds and standards. The decrease in absorbance of DPPH radical was caused by antioxidant compounds because of the reaction between antioxidants and the radicals, thus resulting the scavenging of the radical by hydrogen donation. A discoloration from purple to yellow is visually noticeable. The percentage scavenging capacities of compounds increased from 27.54% to 52.00%, from 17.84% to 50.59%, from 24.94% to 36.28%, from 26.71% to 48.93%, from 26.47% to 49.40% and from 25.76% to 46.80% at 5 to 100 mg/L for Ligand, Ni(II), Co(II), Zn(II), Ti(III) and V(III) respectively (Figure 7). Ascorbic acid and trolox were used as standards and exhibited higher DPPH scavenging activity than the compounds at all the concentrations. These results are revealed that DMF solutions of compounds were moderate when compared to standards. The DPPH scavenging activity findings of this study are approximately similar with Taha et al. and lower than Bukhari et al. study findings ^[64-68].

Metal Chelating Activity

The chelating activity of the extracts against Fe^{2+} was determined according to method of Dinis et al. ^[29]. Transition metals are triggered both initiation and propagation of lipid peroxidation ^[64]. It is clear that, the compounds interfering with the catalytic activity of metal ions could affect the peroxidative process. Among the various species of metal ions Fe^{2+} ions are the most powerful specie as prooxidant ^[65]. In this study the chelating effect of the compounds and EDTA on ferrous ions increased with increasing of concentration (Figure 8). V(III) showed the most active chelating activity among the compounds and its value was 48.45% at 100 mg/L concentration at the same concentration this is followed by Ti(III) 45.15%, Ligand 43.71%,

Ni(II) 34.22%, Co(II) 28.45% and Zn(II) 25.36%. EDTA showed excellent activity (91.37-100%) at all the concentrations studied.

Antibacterial activity of the compounds

The antimicrobial effect of DMF solutions of the compounds was tested against four species of Gram-positive bacteria and three species of Gram-negative bacteria. In the range of 7– 11 mm inhibition zones were obtained (Table 3). V(III) showed the highest inhibitory activity against M. luteus (11 mm). All of the compounds showed inhibitory effect against M. luteus and B. subtilis microorganisms. On the other hand none of the compounds exhibited antibacterial activity against S. aureus. Illian et al. have reported that Schiff base derived from 5bromosalicylaldehyde with 1,2-bis(4-chloro-2 aminophenoxy) ethane and its all metal complexes showed weak antibacterial activities against E. coli, but did not exhibit antibacterial activities against P. aeruginosa^[70]. The results of the study mentioned^[70] for E. coli. is in an agreement with our study, but our findings showed that ligand (L), Co(II), Zn(II) and Ti(III) complexes showed weak antibacterial activities against P. aeruginosa. Keypour et al. studied dimeric Ni(II) complex solutions against S. aureus, E. coli and B. cereus for antibacterial activity and they found out that $[NiL_5]_2(ClO_4)_2$ showed 20 and 27 mm inhibition zones against to E. coli and B. cereus respectively. Keypour et al.'s [71] compounds showed better anti-bacterial activities than the compounds we have studied. In our study, the results showed that when comparing the antimicrobial activity of compounds to standards, it can be referred that the compounds showed moderate activities against bacteria.

CONCLUSION

The Ni(II), Co(II) and Zn(II) complexes probably show tetrahedral geometry, Ti(III) and V(III) complexes probably have square pyramid geometries ^[70-75]. According to the obtained data it is obvious that the antimicrobial activity results show that the synthesized compounds possessed intermediate antibacterial activity when compared with amikacin and tetracyclin. It is obvious that the antimicrobial activity of studied compounds can be improved by some modifications. Many antimicrobial medicines have low water solubility. Due to that, their antimicrobial activity is also limited ^[76]. Antimicrobial activity depends on the solvent and chelating ability of the Schiff base or complexes and, complex formation abilities of the compounds with bacterial strain. These interactions may involve hydrogen bonding too. So, it can be concluded that the better hydrogen bonding ability means more active compound ^[77].

The antioxidant activity of the compounds on DPPH scavenging and metal chelating activity were concentration dependent and the levels of activities are moderate according to standard antioxidants. Metal chelating activities were concentration dependent and the levels of activities are moderate according to standard antioxidants.

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SCH.1. Synthesis of the 1,6-bis(4-aminophenoxy)hexane



SCH.2. Synthesis of the Ligand (L)



SCH.3. Synthesis metal complexes of the ligand (L)



FIG.1. Mesh view of the frontier orbitals (HOMO-LUMO) of the ligand and the energy

levels (optimized with B3LYP/6-311G).

G1.M1V1 - Dectron density from Alph



FIG.2. Electron density in the ligand (From total SCF Density).



FIG.3. Regression analysis result between experimental and theoretical (HF/6-31G(d)) ¹H-NMR shifts.



FIG.4. Regression analysis result between experimental and theoretical (B3LYP/6-311G(2d,p)) ¹H-NMR shifts.



FIG.5. Cyclic voltammograms of compounds solutions in DMF at glassy carbon electrode; A:L,
B:NiL, C:CoL, D:ZnL scan rate, v: 100 mV s⁻¹.



FIG.6. Cyclic voltammograms of 1×10^{-3} mol L⁻¹ compound solutions at different scan rates; A:L, B:NiL, C:CoL, D:ZnL



FIG.7. DPPH scavenging activity of different concentrations of Schiff base and its metal



FIG.8. Metal chelating activity of different concentrations of Schiff base and its metal complexes

complexes

TABLE 1

Physical properties, elemental analysis, magnetic susceptibility values and spectral data of the

compounds.

Compound	Yield	Color	m.p.	Molecular	Elemental Analysis (Calculated)/Found				
	g/%		(°C)	weight (g/mol)			υ (-HC=N-)	μ(B.M.)	
					С %	Н%	N %		
Ligand (L)	9.24	Yellow	122-123	508	(76.19)	(5.55)	(5.55)	1617 m	-
	(91)				76.80	5.89	5.62		
[NiL]	0.87	Light	173	564	(68.08)	(5.31)	(4.96)	1609m	2.89
	(77)	Brown	Decom.		68.32	5.17	5.73		
[CoL]	0.83	Brown	137	565	(67.96)	(5.31)	(4.95)	1608 m	3.83
	(74)		Decom.		68.92	5.81	5.26		
[ZnL]	0.86	Orange	172	571	(67.25)	(5.25)	(4.90)	1607m	-
	(75)		Decom.		68.07	5.15	4.52		
[TiLCl]	0.75	Grey	167	589	(65.41)	(4.77)	(4.77)	1607 m	1.72
	(64)	white	Decom.		66.23	5.28	5.12		
[VLCl]	0.79	Dark	151	592	(65.08)	(4.74)	(4.74)	1607 m	3.55
	(67)	Brown	Decom		65.74	5.21	5.11		

m: medium

TABLE 2

Voltammetric results at scan rate of 100 mVs⁻¹ vs. Ag/AgCl. Ec: cathodic potential, Ea: anodic

potential.

Compound	Ec (V)	Ea (V)
L	Ic:+0.11, IIc:-0.85, IIIc:-1.68, IVc:-2.19	Ia:-1.55, IIa:-0.10, IIIa:+0.31
NiL	Ic:+0.12, IIc:-0.82, IIIc:-1.67, IVc:-2.20	Ia:-1.52, IIa:-0. 09, IIIa:+0.33
CoL	Ic:+0.09, IIc:-0.95, IIIc:-1.71, IVc:-2.11	Ia:-1.98, IIa:-1.60, IIIa:-0.28 IVa:+0.05
ZnL	Ic:+0.13, IIc:-0.80, IIIc:-1.66, IVc:-2.18	Ia:-1.51, IIa:-0.08, IIIa:+0.32

TABLE 3

Antimicrobial activity of compounds and standard antibiotics.

	Compounds and Antibiotic discs ^a								
Bacteria	Ligand	Ni(II)	Co(II)	Zn(II)	Ti(III)	V(III)	AK	ТЕ	
P. aeruginosa	8	0	9	7	9	0	20	25	
S. aureus	0	0	0	0	0	0	24	33	
L. pneumophila subsp pneumophila	7	7	8	7	0	8	16	19	
B. subtilis	8	9	8	7	10	8	20	24	
M. luteus	7	10	9	8	7	11	18	24	
E. hirae	0	8	7	10	0	0	22	18	
E. coli	8	0	8	8	0	0	25	22	

^a Inhibition diameter in millimeters. AK= Amikacin (30 μ g), TE=Tetracycline (30 μ g)