



Biologically active Schiff bases containing thiophene/furan ring and their copper(II) complexes: Synthesis, spectral, nonlinear optical and density functional studies



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ABSTRACT

Schiff bases; 1,8-bis(thiophene-2-carboxaldimine)-p-menthane (L^1) and 1,8-bis(furan-2-carboxaldimine)-p-menthane (L^2) have been synthesized and characterized by elemental analysis, ^1H – ^{13}C NMR, UV–vis, FT-IR and LC-MS methods. ^1H and ^{13}C shielding tensors for L^1 and L^2 were calculated with GIAO/DFT/B3LYP/6-311++G(d,p) methods in CDCl_3 . The vibrational band assignments, nonlinear optical (NLO) activities, frontier molecular orbitals (FMOs) and absorption spectrum have been investigated by the same basis set. Schiff base-copper(II) complexes have been synthesized and structurally characterized with spectroscopic methods, magnetic and conductivity measurements. The spectroscopic data suggest that Schiff base ligands coordinate through azomethine-N and thiophene-S/furan-O donors (as SNNS and ONNO chelating systems) to give a tetragonal geometry around the copper(II) ions. Schiff bases and Cu(II) complexes have been screened for their biological activities on different species of pathogenic bacteria, those are, Gram positive bacteria: *Bacillus subtilis*, *Yersinia enterocolitica*, *Bacillus cereus*, *Listeria monocytogenes*, *Micrococcus luteus* and Gram negative bacteria: *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella dysenteriae*, *Salmonella typhi*, *Klebsiella pseudomonas* by using microdilution technique (MIC values in mM). Biological activity results show that Cu(II) complexes have higher activities than parent ligands and metal chelation may affect significantly the antibacterial behavior of the organic ligands.

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1. Introduction

Schiff base ligands have been widely used in many fields e.g., biological, inorganic, analytical and drug synthesis in coordination chemistry. Schiff bases obtained by the reaction of aldehydes with amines are the compounds containing azomethine group ($-\text{HC}=\text{N}-$) [1,2] known as imine which is important for elucidating the mechanism of transamination and racemization reactions in biological systems [3,4]. Schiff bases are also known to have biological activities such as antibacterial [5,6], antifungal [7], antitumor [8] and herbicidal [9]. Schiff bases are especially studied due to their synthetic flexibility, selectivity and sensitivity towards the metallic ions [3,10–12]. Schiff base metal complexes have a variety of

biological applications in clinical and pharmacological areas [13,14] and several derivatives have been used as drugs and their effectiveness have been proved as bacteriocides, pesticides, fungicides and insecticides [2,15]. Some of them which having structural similarities with natural biological substances have been used as models in biological macro systems, radiopharmaceuticals for cancer targeting, dioxygen carriers, medical substrates and catalyst [1,16].

It has been known that metal ions are involved in biological processes of life through coordinating to the heterocyclic residues of biological molecules as proteins, enzymes and nucleic acids [17]. Various transition metal (cobalt, nickel, iron and copper etc.) complexes were reported to have antimicrobial activities against microorganisms [18–21]. In which, copper complexes are great of interest since they exhibit numerous biological activities such as antitumor, antifungal, antimicrobial activities [22,23].

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As continuation of our studies we report synthesis and spectral properties (^1H NMR, ^{13}C NMR, UV–vis, FT-IR, LC-MS) [3,24,25] of Schiff bases with potential antibacterial activities. ^1H and ^{13}C shielding tensors for \mathbf{L}^1 – \mathbf{L}^2 were calculated with GIAO/DFT/B3LYP/6-311++G(d,p) methods in CDCl_3 . The vibrational band assignments were also performed at B3LYP/6-311++G(d,p) theory level combined with scaled quantum mechanics force field (SQMFF) methodology. Furthermore, we have reported nonlinear optical properties (NLO), frontier molecular orbitals (FMOs) analysis and absorption spectra with same method.

Ligands give tetragonally monomeric Cu(II) complexes in SNNS and ONNO donor systems. The structures of the complexes were determined by using FT-IR, LC-MS, magnetic moments and molar conductivities. The antibacterial activities of Schiff bases and their Cu(II) complexes were tested against Gram positive bacteria: *Bacillus subtilis*, *Yersinia enterocolitica*, *Bacillus cereus*, *Listeria monocytogenes*, *Micrococcus luteus* and Gram negative bacteria: *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella dysenteriae*, *Salmonella typhi*, *Klebsiella pseudomonas* by using microdilution method (as MIC values in mM). The activity results show that Cu(II) complexes are more potent antibacterial agents than free ligands.

2. Experimental

2.1. Reagents and physical measurements

Thiophene-2-carboxaldehyde, furan-2-carboxaldehyde and 1,8-diamino-*p*-menthane were purchased from Sigma and used without further purification. All other reagents and solvents were purchased from commercial sources and were analytical grade.

^1H NMR and ^{13}C -NMR spectra were recorded on a Bruker-Spectrospin Avance DPX-400 Ultra-Shield. TMS was used as internal standard and deuterated DMSO as solvent. LC-MS(ES) spectra were recorded on Acilent 1100 LC-MSD using argon gas (55–70 eV). FT-IR spectra were recorded on KBr discs on a Bruker Vector 22 spectrophotometer, assisted by a computer, between KBr windows in the 4000–400 cm^{-1} region. The UV–vis spectra were recorded with a UNICAM-UV 2-100 spectrophotometer. The UV–vis absorption spectra of the title compounds were recorded in the CHCl_3 solutions. Elemental analyses were obtained by using a LECO–CHSNO-9320 analysis instrument. Magnetic susceptibilities were performed on Sherwood Scientific MKI Evans balance. Molar conductivities of Schiff base ligands and their metal complexes in 1×10^{-3} M MeOH or DMF/HAc solution were determined at room temperature using an Orion 5 star multimeter.

2.2. Synthesis of Schiff bases

1,8-bis(thiophene-2-carboxaldimine)-*p*-menthane (\mathbf{L}^1) was synthesized as recorded by us [3]. 1,8-diamino-*p*-menthane (25.00 mmol) was dissolved in 30 cm^3 of methanol by heating on magnetic stirrer. A solution of thiophene-2-carboxaldehyde (50.00 mmol) in 20 mL methanol was added dropwise with stirring at 40 °C for 2 h. Then reaction mixture was left on the magnetic stirrer at room temperature for a day. The pale brown crystals were recrystallized from MeOH/isopropyl ether mixture and then dried at 50 °C in the oven. 1,8-bis(furan-2-carboxaldimine)-*p*-menthane (\mathbf{L}^2) was synthesized with similar methods.

\mathbf{L}^1 : m.p.:76–77 °C, yield:78%. $\text{C}_{20}\text{H}_{26}\text{N}_2\text{S}_2$ (MW:358 g/mol) calc: C%, 67.04; H%, 7.26; N%, 7.82; S%, 17.88; found: C%, 67.04; H%, 7.26; N%, 7.62; S%, 17.35. λ_{max} : 262–280 nm; Λ_{M} : 5.47 (MeOH). \mathbf{L}^2 : m.p.:65–66 °C, yield:75%. $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2$ (MW:326 g/mol) calc: C%, 73.62; H%, 7.98; N%, 8.59; found: C%,71.84; H%,7.83; N%,8.33. λ_{max} : 269 nm; Λ_{M} : 15.68 $\mu\text{S}/\text{cm}$ (MeOH).

2.3. Synthesis of Schiff base-Cu(II) complexes

The present complexes were synthesized following the general procedure: To a MeOH solution (10 mL) of metal chloride, a solution of Schiff base was added and the reaction mixture was stirred for 5 h at 40 °C. The precipitate was separated by filtration and dissolved in MeOH for recrystallization. After a week, colorful crystals were obtained by slowly evaporation of the reaction mixture and then washed with a little amount of diethyl ether, successively [3,22]. These were dried in glass oven (with vacuo) at 170 °C to leave crystal and coordinated water molecules.

Cu(II)-L^1 : m.p.>250 °C, yield:68%; $\text{C}_{20}\text{H}_{26}\text{N}_2\text{S}_2\text{CuCl}_2$ (FW:492.5 g/mol). μ_{eff} : 2.15 BM; λ_{max} :266 nm; IR(KBr): $\nu_{(\text{C}=\text{N})}$ 1600 cm^{-1} , $\delta_{(\text{C}-\text{S}-\text{C})}$: 724 cm^{-1} ; Λ_{M} : 139.34 $\mu\text{S}/\text{cm}$ (MeOH).

Cu(II)-L^2 : m.p.>240 °C, yield:65%; $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2\text{CuCl}_2$ (FW:460.5 g/mol). μ_{eff} : 2.24 BM; λ_{max} :272 nm; IR(KBr): $\nu_{(\text{C}=\text{N})}$ 1600 cm^{-1} , $\nu_{(\text{C}-\text{O}-\text{C})}$ 1112 cm^{-1} ; Λ_{M} : 129.53 $\mu\text{S}/\text{cm}$ (DMF/HAc).

2.4. Antimicrobial activity

The antibacterial activities of Schiff bases and their Cu(II) complexes were tested against Gram positive bacteria: *B. subtilis*, *Y. enterocolitica*, *B. cereus*, *L. monocytogenes*, *M. luteus* and Gram negative bacteria: *E. coli*, *Pseudomonas aeruginosa*, *S. dysenteriae*, *S. typhi*, *K. pseudomonas* in Nutrient Broth medium by using microdilution method (as MIC values in mM) according to the National Committee for Clinical Laboratory Standards [26,27]. Minimum inhibitory concentration (MIC as mM) was considered to be the lowest concentration of the test substance exhibiting no visible growth of bacteria on the tube.

Ligands and their Cu(II) complexes were dissolved in %10 DMSO by ultrasonic bath. The Nutrient Broth, which contained logarithmic serially diluted amount of test compound and controls, was inoculated with approximately 5×10^5 c.f.u. Aqueous DMSO (10%) was used as negative control (containing compounds but no inoculum). The micro plates were incubated at 37 °C and read visually after 24 h [28–31]. The observed inhibition of the growth was exhibited as MIC values in mM.

2.5. Theoretical calculations

The molecular geometry optimizations, frontier molecular orbital (HOMO and LUMO) energies, nonlinear optical (NLO) activities and vibration frequency calculations were performed with the Gaussian 03W software package [32] by using DFT approaches. The split valence 6-311++G (d, p) basis set was used for the expansion of the molecular orbital [33]. The geometries were fully optimized without any constraint with the help of an analytical gradient procedure implemented within the Gaussian 03W program. Optimized geometries of \mathbf{L}^1 and \mathbf{L}^2 are presented at Fig. 1.

All the parameters were allowed to relax and all the calculations were converged to optimized geometries which correspond to a true energy minimum as revealed by the lack of imaginary values in the wave number calculations. The ^1H and ^{13}C NMR chemical shifts of Schiff bases were calculated in CDCl_3 using the GIAO method. The each vibrational modes of the studied compound were characterized by their potential energy distributions (PED) which were calculated by using SQM-FF program [34].

3. Results and discussion

Schiff-base ligands (\mathbf{L}^1 – \mathbf{L}^2) were prepared by a simple condensation reaction in 1:2 M ratios of 1,8-diamino-*p*-menthane and thiophene/furan-2-carboxaldehyde. The structural determinations of the ligands were done with the help of elemental analysis, ^1H

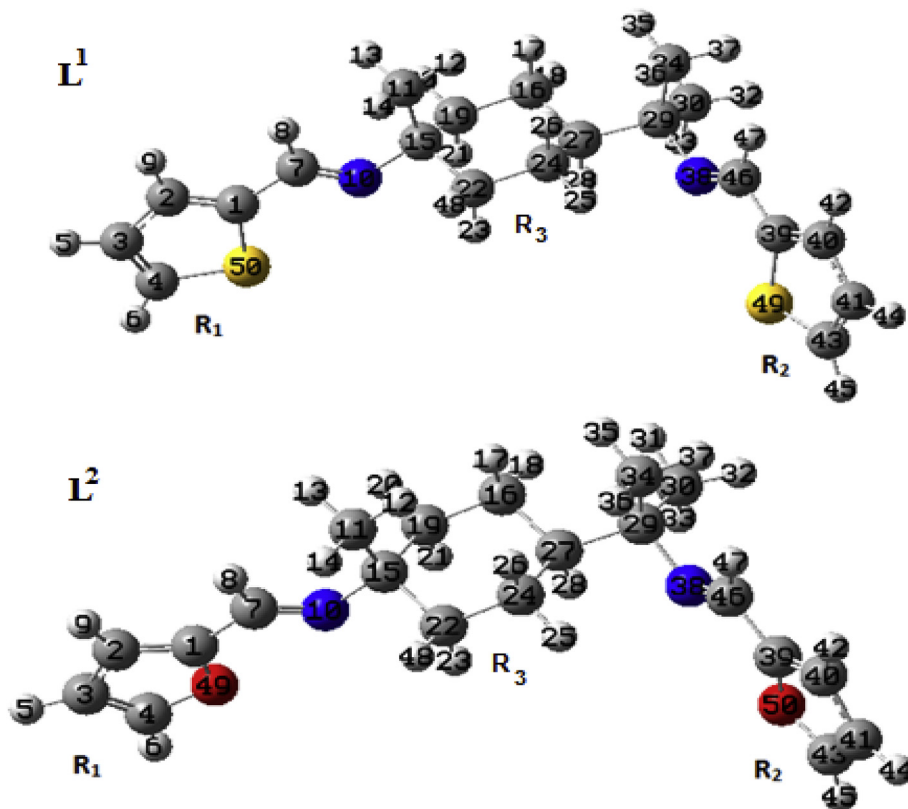


Fig. 1. Optimized geometries of L^1 and L^2 at B3LYP/6-311++G(d,p) level.

NMR, ^{13}C NMR, UV–vis, FT-IR and LC-MS spectrum. Optimized geometries, chemical shifts, vibrational analysis, electronic parameters and nonlinear optical (NLO) properties were investigated by theoretical studies by using Gaussian 03 software package. The metal complexes were also characterized by several spectroscopic methods, conductivity and magnetic measurements. The spectroscopic data suggest that Schiff bases behave as SNNS and ONNO chelators to give a copper (II) complex in tetragonal geometry. The antibacterial activities of Schiff bases and their Cu(II) complexes were tested against Gram positive bacteria and Gram negative bacteria by using microdilution method (as MIC values in mM).

3.1. NMR calculations

The NMR spectrum (^1H , ^{13}C) of L^1 and L^2 were obtained in d_6 -DMSO. In order to facilitate the interpretation of the NMR spectrum, quantum-chemical calculations were performed using B3LYP/6-311G++(d, p) basis set in d_6 -DMSO phase. Isotropic shielding tensors of ^{13}C were changed into chemical shifts by using a linear relationship suggested by Blanco et al. [35]. The experimental and computed chemical shift values are shown in Table 1. The ^1H NMR and ^{13}C NMR spectrum of the ligands in d_6 -DMSO are given in Fig. 2. In ^1H NMR spectrum, the signals appearing at 8.47 ppm and 8.36 ppm (calculated 8.44 ppm and 8.39 ppm) for L^1 , 8.17 ppm and 8.04 ppm (calculated 8.12 ppm and 8.01 ppm) for L^2 are assigned as singlet peak belonging to the hydrogen of the azomethine groups (C(5)H=N and C(13)H=N). The signals for aromatic protons are observed in the range of 7.59–7.11 ppm (calculated 7.32–7.08 ppm) for thiophene ring and 7.79–6.59 ppm (calculated 7.48–6.53 ppm) for furan ring. Aliphatic protons (H-7, H-12 protons) for L^1 appeared at 1.85 ppm and 1.08 ppm were calculated at 1.79 ppm and 1.23 ppm, for L^2 appeared at 2.16 ppm

and 1.17 ppm were calculated at 2.18 ppm and 1.17 ppm, respectively. In ^{13}C NMR spectrum, ligands exhibit the characteristic resonance due to azomethine (C(5)H=N) carbon which appears around 188.86 ppm and C(13)H=N carbon which appears around 187.26 ppm (calculated at 189.20 ppm and 187.00 ppm) for L^1 (Fig. 2), C(5)H=N carbon which appears around 165.81 ppm and C(13)H=N carbon which appears around 165.80 ppm (calculated at 153.52 ppm and 153.41 ppm) for L^2 [24]. The signals appear around 182.35–165.66 ppm (computed at 181.80–162.00 ppm) due to thiophene ring in L^1 and 153.43–111.75 ppm (computed at 142.52–112.22 ppm) due to furan ring in L^2 [3].

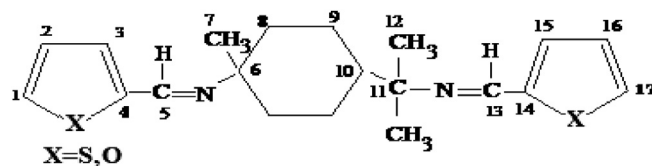
3.2. Vibrational spectrum

Density functional theory makes the frequency values closer to the experimental values due to inclusion of electron correlation. The vibrational band assignments were performed at B3LYP/6-311++G(d,p) theory level combined with scaled quantum mechanics force field (SQMFF) methodology to compare the experimental and calculated vibrational frequencies of L^1 and L^2 . The visual check for the vibrational band assignments were also performed by using Gauss-View program. In order to enable assignment of the observed peaks, we have analyzed the some important characteristic vibrational frequencies and compared our calculated results for L^1 - L^2 ligands with their experimental data as presented in Tables S1 and S2 (Supporting information).

3.2.1. C–H, CH_3 and CH_2 vibrations

The characteristic C–H stretching vibrations of heteroaromatic structures occur above 2900 cm^{-1} [37–40]. In the present study, 3388 – 3262 cm^{-1} for L^1 and 3098 – 3071 cm^{-1} for L^2 are assigned to aryl C–H stretching vibrations. For L^1 and L^2 , the calculated

Table 1
The NMR shifts for Schiff bases (L^1 and L^2) as ppm in d_6 -DMSO.



Assign.	L^1		L^2	
	δ (exp.) ^a	δ (calc.) ^b	δ (exp.) ^a	δ (calc.) ^b
C(1)	166.80	164.49	114.04	117.22
C(17)	165.66	162.00	111.75	112.22
C(2)	168.44	169.76	144.64	144.97
C(16)	182.35	181.80	153.43	142.52
C(3)	188.86	189.20	165.81	153.52
C(15)	187.26	187.00	165.81	153.41
C(4)	99.44	97.12	61.03	63.13
C(14)	60.43	58.21	22.42	17.80
C(5)	67.34	65.20	24.24	41.82
C(13)	62.58	63.12	20.18	21.12
C(1)H,	7.59 (d, 1H),	7.32	7.79 (m, 2H)	7.48
C(17)H,				
C(2)H,	7.11 (m, 2H)	7.08	6.59 (m, 2H)	6.53
C(16)H,				
C(3)H,	7.42 (m, 2H)	7.25	6.86 (m, 2H)	6.74
C(15)H,				
C(5)H=N,	8.47 (s, 1H),	8.49–8.39	8.17 (s, 1H),	8.12–8.01
C(13)H=N,	8.36 (s, 1H)		8.04 (s, 1H)	
C(7)H ₃ -C(12)H ₃	1.85–1.08 (m, 18H)	1.79–1.23	2.16–1.17 (m, 18H)	2.18–1.17

^a s:singlet, d:doublet, m:multiplet.

^b σ Transform into d using equations given in Refs. [35]; $\delta^{13}\text{C} = 175.7 - 0.963 \sigma^{13}\text{C}$ and $\delta^1\text{H} = 31.0 - 0.970 \sigma^1\text{H}$.

frequencies 3138–3101 cm^{-1} and 3102–3071 cm^{-1} are assigned to C–H stretching vibrations, respectively. The C–H in plane bending vibrations usually occurs in the 1400–900 cm^{-1} region. And also, C–H in plane bending vibrations for L^1 and L^2 were observed at 1383–1348 cm^{-1} , 1079–1015 cm^{-1} and 1322–1265 cm^{-1} , respectively. The bands at 3115 cm^{-1} and 2936 cm^{-1} correspond to the asymmetric and symmetric stretching vibrations of CH_3 group for L^1 . Similar results were observed for L^2 (2967 cm^{-1} and 2930 cm^{-1} , respectively). Asymmetric and symmetric stretching vibrations of CH_2 group were also observed at 2967–2869 cm^{-1} and 2958–2909 cm^{-1} for L^1 and L^2 . Computed values for CH_3 and CH_2 groups can be seen from Tables S1 and S2.

3.2.2. C–S and C–O vibrations

C–S stretching vibration were observed at 867 cm^{-1} , 869 cm^{-1} and 873 cm^{-1} by Mei-Rong et al. for 3-(4-fluorophenyl)thiophene, 3-(4-nitrophenyl)thiophene and 3-(4-cyanophenyl)thiophene, respectively [41]. In the present study, the C–S stretching vibrations were observed at 855 cm^{-1} and 828 cm^{-1} . Similarly, C–O stretching vibrations were observed at 1079 cm^{-1} and 904 cm^{-1} .

3.2.3. C=C stretching

In general, the aromatic C=C stretching vibrations occur in the range 1650–1400 cm^{-1} [42]. For six-membered aromatic rings, there are two of three bands in this region due to skeletal vibrations, the strongest usually being at about 1500 cm^{-1} [8]. The C=C aromatic stretching vibrations for L^1 and L^2 were observed at 1583–1383 cm^{-1} and 1556 cm^{-1} , respectively.

3.2.4. C=N vibrations

The infrared spectrum of the ligands show sharp peaks at functional region due to C=N bond stretching vibrations at 1637 and 1631 cm^{-1} for L^1 and L^2 , respectively. The calculated values of other group vibrations show good agreement with the experimental results as seen in Tables S1 and S2.

3.3. LC-MS spectra

All the molecular ions; $[\text{M}]^+$, $[\text{M}+\text{H}]^+$ or $[\text{M}-\text{H}]^-$ of Schiff bases were detected under the LC-MS(ES) condition. The molecular ion peaks are observed at m/z (%intensity): 359.1 (%100) $[\text{M}+\text{H}]^+$ for L^1 , 324.9 (%60.9) $[\text{M}-\text{H}]^+$ and 325.9 (% 14.9) $[\text{M}]^+$ for L^2 . By the removal from one azomethine bonding, the residual groups give the fragments at 258.1 (%23.1) and 276.1 (%100) for L^1 - L^2 ligands [3,24,25].

3.4. Frontier molecular orbital analysis and absorption spectra

The frontier molecular orbitals (HOMOs and LUMOs) and energy level of the molecules (L^1 and L^2) have been calculated by using B3LYP/6-311++G(d,p) method. As shown in Fig. 3 and Table 2, the difference between HOMO and LUMO energy levels of the molecules are 4.88 and 4.71 eV for L^1 and L^2 , respectively.

L^1 and L^2 ligands exhibited absorption peaks in the UV–vis region. The absorption peaks are observed at 270 nm for L^1 and 280 nm for L^2 . It can be proposed that these peaks are equal to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. 3D plots of the HOMO and LUMO shapes and their corresponding energy levels for the title

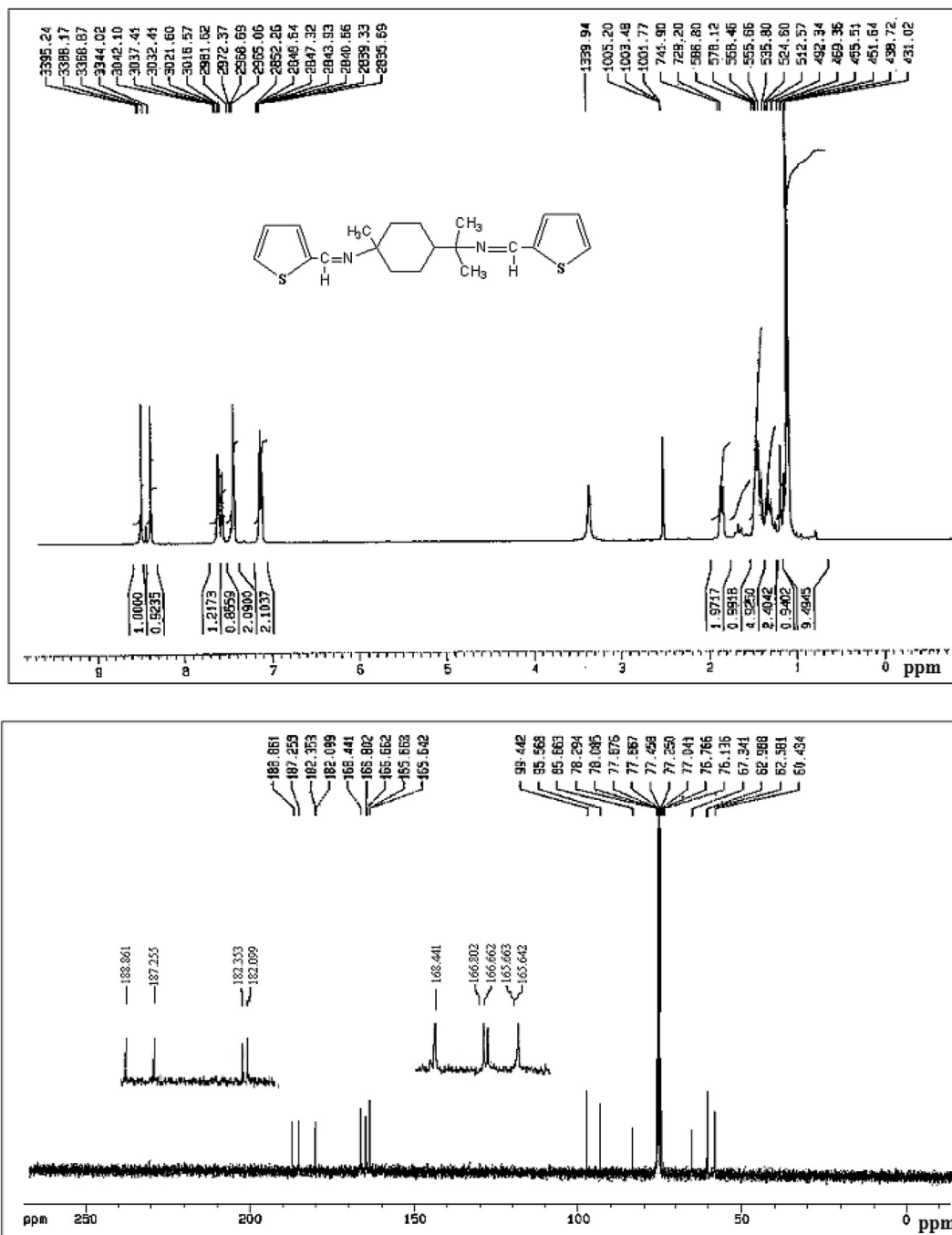


Fig. 2. ¹H NMR and ¹³C NMR spectra of **L**¹.

compounds are shown in Fig. 3. The calculated electronic transfer peaks using B3LYP/6-311++G(d,p) basis set for **L**¹ and **L**² are at 293 nm and 295 nm belong to electronic transfers occurred between HOMO and LUMO, respectively. The greater calculated absorption wavelengths of the compound have slight red shifts compared with the corresponding experimental ones.

3.5. Nonlinear optical (NLO) activity

In the last two decade, highly NLO active molecular materials are attracting wide interest because of their potential applications in optoelectronic devices of telecommunications, information

storage, optical switching signal processing [43,44] and THz wave generation [45]. The THz region, which lies in between microwaves and infrared region of the electromagnetic spectrum, offers diverse applications such as wireless communications, inspection of drugs, spectroscopy and imaging [46]. Due to measures in the field of technology, there is an increasing interest in designing new organic materials with desired nonlinear optical properties.

The dipole moment (μ), the static polarizability (α_0) and first static hyperpolarizability (β_{tot}) are related directly to the nonlinear optical (NLO) activity of molecular structures (Table 3). NLO activities of the molecules have also reverse relationship with their biological activities.

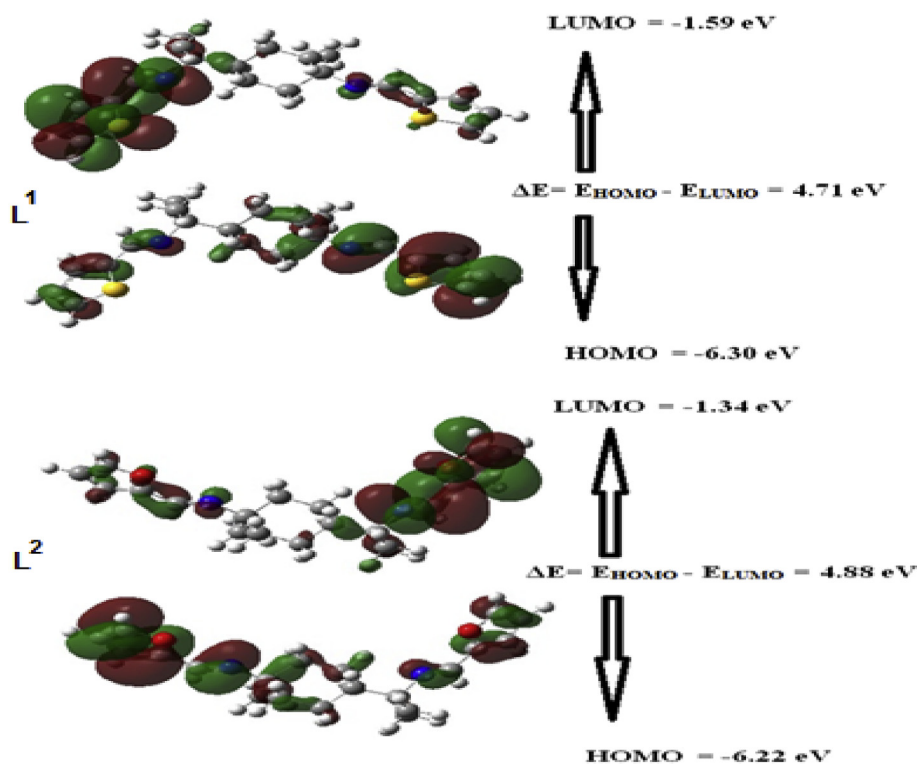


Fig. 3. Molecular orbital surfaces and energy band gaps between HOMO and LUMO orbitals ($E_{\text{HOMO-LUMO}}$) for L^1 and L^2 .

Table 2

Molecular orbital energies of L^1 and L^2 with DFT B3LYP/6-311++G(d,p) method.

Energies	L^1	L^2
HOMO (a.u.)	-0.22864	-0.23164
LUMO (a.u.)	-0.04930	-0.05841
HOMO -1 (a.u.)	-0.23148	-0.23457
HOMO -2 (a.u.)	-0.24938	-0.25314
LUMO +1 (a.u.)	-0.04645	-0.05581
LUMO +2 (a.u.)	-0.01172	-0.01257

1 a.u. = 27.2116 eV.

Table 3

The electric dipole moment μ (D), the mean polarizability $\langle\alpha\rangle$ ($\times 10^{-24}$ esu) and the first hyperpolarizability β_{tot} ($\times 10^{-33}$ esu) of L^1 and L^2 by DFT B3LYP/6-311++G(d,p) method.

Parameter	L^1	L^2	Parameter	L^1	L^2
μ_x	0.16	-0.25	β_{xxx}	586.89	657.30
μ_y	-0.05	1.93	β_{xxy}	-2952.64	1073.29
μ_z	-2.00	-1.69	β_{xyy}	-1549.10	820.54
M	2.01	2.58	β_{yyy}	-2275.86	1477.88
α_{xx}	55.21	59.71	β_{xxz}	-1442.66	-816.85
α_{xy}	0.96	0.69	β_{xyz}	696.30	485.80
α_{yy}	37.26	41.47	β_{yyz}	-753.76	-607.71
α_{xz}	1.92	2.12	β_{zzz}	139.88	-53.51
α_{yz}	1.35	-1.94	β_{yzz}	147.44	40.52
α_{zz}	31.60	35.30	β_{zzz}	-374.93	-149.67
$\langle\alpha\rangle$	41.36	45.49	β_{tot}	5753.72	3350.19

α : 1 a.u. = 0.1482×10^{-24} esu.

β : 1 a.u. = 8.6393×10^{-33} esu.

The calculated values of the polarizabilities and the hyperpolarizabilities from Gaussian 03 output were converted from atomic units into electrostatic units (α : 1 a.u. = 0.1482×10^{-24} esu; β : 1 a.u. = 8.6393×10^{-33} esu) [47]. The total static dipole moment, μ ,

is defined as; $\mu = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{1/2}$. The calculations of static polarizability (α_{ave}) and first static hyperpolarizability (β_{tot}) from the Gaussian output have been stated in detail previously [48] as follows:

$$\langle\alpha\rangle = 1/3 (\alpha_{xx} + \alpha_{yy} + \alpha_{zz})$$

$$\beta_{\text{tot}} = [(\beta_{xxx} + \beta_{xyy} + \beta_{xzz})^2 + (\beta_{yyy} + \beta_{yzz} + \beta_{yxx})^2 + (\beta_{zzz} + \beta_{zxx} + \beta_{zyy})^2]^{1/2}$$

The calculated first static hyperpolarizability (β_{tot}), mean polarizability ($\langle\alpha\rangle$) and the ground state dipole moment (μ) of Schiff bases were computed to be 5.7537×10^{-30} esu, 41.36×10^{-24} esu, 2.01 Debye for L^1 and 3.3502×10^{-33} esu, 45.49×10^{-24} esu, 2.58 Debye for L^2 . The first static hyperpolarizabilities of L^1 and L^2 are 15.4 and 9 times larger than that of urea (0.3728×10^{-30} esu).

3.6. Structure of the metal complexes

Molar conductivities of the metal complexes measured in MeOH or DMF/HAc solvents confirm the 1:2 electrolytic natures of Cu(II) complexes. Magnetic measurements show the paramagnetism for the metal chelates and the magnetic moment (μ_{eff}) values obtained lie in the range 1.88–2.24 B.M. corresponds to the unpaired electrons of high spin Cu(II) complexes [3,25]. The monomeric structure of Cu(II) Schiff base complexes is exhibited in Fig. 4.

UV–vis spectral data along with magnetic susceptibility measurements gave adequate support in establishing the geometry of the metal complexes. In general, the electronic absorption spectra of the azomethine complexes show intense high-energy absorption bands at ca. 230–348 nm. The high energy absorption bands, which are also found in the free ligands, are assigned as $\pi \rightarrow \pi^*$ transitions in the azomethine groups, while the low-energy absorption bands

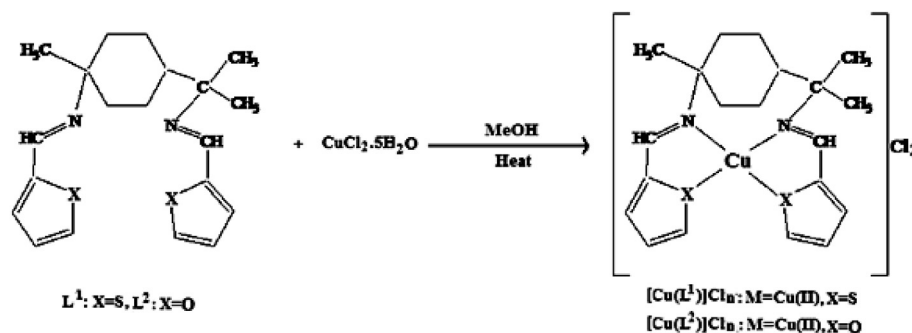


Fig. 4. Monomeric structure of Cu(II) complexes.

at 448 nm for Cu(II)- L^1 and 620 nm for Cu(II)- L^2 tentatively assigned as $d\pi(Cu) \rightarrow \pi^*$ (diimine) metal to ligand charge transfer (MLCT) transitions with in the visible region. The coordination geometries of Cu(II) central ions are that of a distorted tetrahedral with tetradentate diimine ligands [49,50].

IR spectrum of the free Schiff base are compared with that of the Cu(II) complexes in order to determine the coordinating sites of the ligand to the metal ion. In the spectra of the metal chelates, the sharp $\nu_{(C=N)}$ vibrations between 1630 and 1659 cm^{-1} are shifted to lower frequencies indicating chelating through the azomethine-N. This type of coordination by aromatic rings has already been reported as: The $\nu_{(C-S-C)}$ vibrations between 715 and 718 cm^{-1} and $\nu_{(C-O-C)}$ vibrations between 1012 and 1045 cm^{-1} are shifted to higher wave numbers by the chelation, which means that, the shifts are due to coordination of the ligands to metal ions through the thiophene-S and furan-O [51–53].

The mass spectra of complexes were taken at 70 eV and molecular ion with counter chlorine ions was not observed clearly. In the MS spectra of $[Cu(L^1)]Cl_2$, the molecular ion peaks $[Cu(L^1)]^{2+}$ by the removal of 3CH₃ and counter ions is observed at 378.9 (0.9%). In the mass spectra of $[Cu(L^2)]Cl_2$ complex, the molecular ion peak with counter ions is detected at 461.1 (14.0%). The fragment by the removal of 3CH₃ from the molecular ion is observed at 416.1 (9.2%) and the fragment by the removal of counter ion from the molecular ion is observed 388.2 (3.8%), respectively.

3.7. Biological activity

Schiff bases and Cu(II) complexes were investigated for their antibacterial activities against Gram positive bacteria: *B. subtilis*, *Y. enterocolitica*, *B. cereus*, *L. monocytogenes*, *M. luteus* and Gram negative bacteria: *E. coli*, *Pseudomonas aeruginosa*, *S. dysenteriae*, *S. typhi*, *K. pseudomonas* by microdilution method (as MIC values in mM) [54]. The biological activity results are exhibited in Table 4. It was observed that, the Schiff bases and their complexes have moderate activity against Gram positive bacteria than Gram negative bacteria. All the tested compounds are highly active against

B. cereus. Cu(II) complexes are better antibacterial agents than Schiff bases as expected. Chelation reduces the polarity of the metal ion because of the partial sharing of its positive charge with the donor groups and a possible π -electron delocalization system. Meanwhile, the increment of the lipophilic character of the complexes may be responsible for their potent biological activities. The lipids and polysaccharides are main fragments of the cell walls and membranes, which are responsible for the metal interactions. The permeation of complexes through the lipid layer of the cell membranes blocks some cellular enzymes, which play a vital role in various metabolic systems of these microorganisms like Tweed's chelation theory [55]. Metal chelations are not the only reason for their antibacterial activities. The higher toxicity of the metal complexes can be explained by the involvement of a metal ion in the normal cell processes [56]. The interaction of metal ions with cellular constituents is due to the structures containing a variety of functional donor groups as imine-N, thiophene-S, furan-O etc. that can act as metal-binding ligands [57].

4. Conclusions

In this study, tetradentate Schiff bases (L^1 and L^2) and copper(II) complexes have been synthesized and structurally characterized by using spectroscopic methods, magnetic and molar conductivity measurements. Vibrational analysis of L^1 and L^2 were also performed by using SQM-FF method with the great match between experimental and calculated vibrational wavenumbers. The nonlinear optical (NLO) activities having importance in optoelectronic applications were calculated with Gaussian 03 software package by using DFT approaches. L^1 and L^2 molecules exhibit absorption peaks in the UV–Visible region and their absorption peaks are observed at 270 nm corresponding to $n \rightarrow \pi^*$ and 280 nm corresponding to $\pi \rightarrow \pi^*$ transition, respectively. While Schiff bases and their complexes have moderate activity against Gram positive bacteria than Gram negative bacteria, all the tested compounds are highly active against *B. cereus*. The biological activity results present that Cu(II) complexes are better antibacterial agents than free Schiff

Table 4
Antibacterial activity results of the compounds (as MIC in mM).

Compound	Gram positive bacteria					Gram negative bacteria				
	BS	YE	BC	LM	ML	EC	PA	SD	ST	KP
L^1	0.468	0.468	0.234	0.936	0.468	0.936	0.936	0.468	0.936	0.936
L^2	0.520	0.520	0.260	0.520	1.040	0.520	0.520	1.040	1.040	1.040
$[Cu(L^1)]Cl_2$	0.171	0.686	0.343	0.343	0.343	0.343	0.686	0.686	0.343	0.686
$[Cu(L^2)]Cl_2$	0.371	0.371	0.186	0.371	0.371	0.742	0.742	0.742	0.371	0.742

Gram positive bacteria: BS: *Bacillus subtilis*, YE: *Yersinia enterocolitica*, BC: *Bacillus cereus*, LM: *Listeria monocytogenes*, ML: *Micrococcus luteus*.

Gram negative bacteria: EC: *Escherichia coli*, PA: *Pseudomonas aeruginosa*, SD: *Shigella dysenteriae* type, ST: *Salmonella typhi*, KP: *Klebsiella*.

bases.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.molstruc.2016.05.002>.

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