Bull. Chem. Soc. Ethiop. **2023**, 37(2), 335-346.
© 2023 Chemical Society of Ethiopia and The Authors
DOI: https://dx.doi.org/10.4314/bcse.v37i2.7

ISSN 1011-3924
Printed in Ethiopia
Online ISSN 1726-801X

SYNTHESIS, CHARACTERIZATION, THEORETICAL STUDY AND BIOLOGICAL EVALUATION OF SCHIFF BASE AND THEIR La(III), Ce(IV) AND UO_2(II) COMPLEXES

N.M. El-Barasi[1], S.F. Algazale[1], M.M. El-Ajaily[2], A.A. Maihub[3], M.M. Miloud[4], T.H. Al-Noor[5], Hayfaa A. Mubarak[6] and Mohanad Mousa Kareem[7*]

[1]Chemistry Department, Faculty of Art and Science, Benghazi University, Tawkara, Libya
[2]Chemistry Department, Faculty of Science, Benghazi University, Benghazi, Libya
[3]Chemistry Department, Faculty of Science, Tripoli University, Tripoli, Libya
[4]Chemistry Department, Faculty of Art and Science, Benghazi University, Al-Abiar, Libya
[5]Chemistry Department, Ibn-Al-Haitham College of Education for Pure Science, Baghdad University, Baghdad, Iraq
[6]College of Engineering, University of Babylon, P.O. Box 51002, Hilla, Iraq
[7]Department of Chemistry, College of Science, University of Babylon, P.O. Box 51002, Hilla, Iraq

(Received June 13, 2022; Revised July 8, 2022; Accepted July 8, 2022)

ABSTRACT. A new three metal complexes of La(III), Ce(IV) and UO_2(II) ions have been synthesized based on a Schiff base derived from the condensation of L-histidine and anisaldehyde. All prepared compounds were characterized by different spectroscopic techniques and Density-functional theory (DFT) calculations. The complexes were proposed to have an octahedral structure based on the investigated results. The optimized shape, numbering system, and dipole moment vector of Ligand and La, Ce, and UO_2 (1:1) chelates were investigated. The Schiff base ligand and complexes exhibit moderate action against all of the bacteria tested, with *P. aeruginosa*, *Klebsiella sp.*, and *E. faecalis* respectively being the order of inhibition.

KEY WORDS: 2-Anisaldehyde, Biological activity, DFT, L-Histidine, Metal complexes, Schiff base

INTRODUCTION

Amino acids and their derivatives are very useful ligands for coordination properties, and biological significance. Also, their biological uptake due to specific mechanisms of transport [1]. The L-histidine amino acid is a very interesting bioactive amino acid with multiple physiological functions. The transition metals play good roles in biological systems when binding to L-histidine amino acid has a major physicochemical role in several proteins, as the X-ray structural determination studies of metallo proteins like carbonic anhydrase, carboxypeptidase, plastocyanin, or azurin among others have demonstrated [2]. L-Histidine is an important to play a major role in the zinc metabolism acting as the major zinc-binding moiety in serum [3]. Schiff bases [4] formed when any primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine).

Several Schiff bases are reported to possess remarkable antibacterial, antifungal and anticancer activities. In such class of compounds, the C=N moiety is important for biological activity. The number of transition metal complexes have reported by using variety of Schiff base ligands and have studied their different biological activities such as antimicrobial, anticancer, antifungal. Metals have an esteemed place in medicinal chemistry [5]. Transition metal hydroxides of the late transition metals are now relatively common, and play a special role in both the synthesis of new complexes and in important catalytic reactions and many drugs possess modified pharmacological and toxicological properties when administered in the form of metallic

---

*Corresponding author. E-mail: sci.mohanad.mousa@uobabylon.edu.iq

complexes [6, 7]. Here, new La(III), Ce(IV) and UO_2(II) complexes have been synthesized, characterized and studied using various physicochemical techniques, DFT and biological activity.

EXPERIMENTAL

Materials and instrumentation

Anisaldehyde, L-Hisditine $C_6H_9N_3O_2$, acetic acid, ethanol, sodium hydroxide, $La(NO_3)_2.H_2O$, $Ce(SO_4)_2.4H_2O$, $UO_2(SO_4)_2.H_2O$ used in the experiment were acquired from Sigma-Aldrich. The (C.H.N.) elemental analyses of the compounds were made on 2400-CHN elemental analyzer. The molar conductivity was determined in DMF solvent on CMD-650 digital conductivity meter, Benghazi University. The infrared spectra were carried out on IFS-25 DPUS/IR spectrometer. The ^{1}H NMR spectra were obtained in dimethyl sulfoxide (DMSO-d_6) using a Varian INOVA 500 MHz NMR spectrometer; chemical changes are in units (ppm). The electronic and mass spectra were recorded on Perkin-Elmer lambda-365 spectrophotometer and Shimadzu QP-2010 Plus spectrometer, respectively.

Synthesis of Schiff base ligand

Sodium hydroxide (0.40 g) in 30 mL ethanol and L-histidine (1.55 g, 1 mmol) in 20 mL of ethanol were mixed in a 500 mL flask and the mixture was stirred at room temperature. Anisaldehyde (1.36 g, 1mmol) was added to the concentrated mixture. Then 1 mL of acetic acid was added to cold mixture. The obtained product was filtered, washed and dried in desiccator over calcium chloride (Figure 1). The White product yielded 80% of ($C_{14}H_{15}N_3O_3$) [HL], M.Wt. 273, m.p. °C 265-268. The elemental analysis (calc.), found: C% (61.51) 61.90; H% (5.49) 6.02; N% (15.38) 14.9.

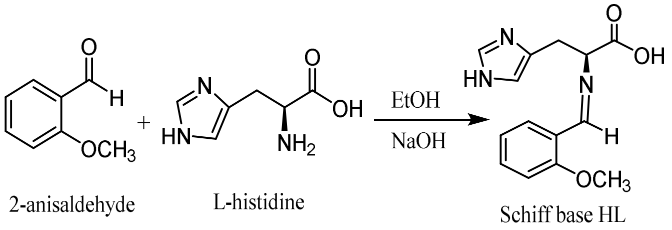


Figure 1. Synthesis of Schiff base ligand [HL].

Synthesis of Schiff base metal complexes

The following Schiff base complexes with La(III), Ce(IV) and UO_2(II) ions were synthesized by adding 2.73 g, 0.01 mol of the Schiff base (HL) in 25 mL of the absolute methanol to 0.01 mol (4.33, 4.04 and 4.29 g, respectively) of the metal salts (La, Ce and UO_2). A few drops of 10% sodium hydroxide solution were added slowly to adjust the pH value at 8 and then the mixtures were refluxed for three hours. The mixtures were filtered and rinsed with hot ethanol multiple times until the filtrates were clear. The obtained new amino acid Schiff base complexes were dried in desiccator under calcium chloride.

Antibacterial activity tests

Three pathogenic bacteria species, including one species of Gram positive bacteria *E. faecalis* and two species of Gram negative bacteria *Klebsiella sp.* and *P. aeruginosa* were collected in the microbiology laboratory of Benghazi Medical Centre (BMC), Libya.

Mueller Hinton Agar (MHA) was prepared by suspending 38 g in 1000 mL of distilled water. The media was sterilized by autoclaving at 121 °C for 15 min. Cool to 45-50 °C, and then pour into sterile Petri plates.

Antibacterial activity Assay

The prepared compounds were tested against three pathogenic bacteria species *E. faecalis*, *Klebsiella sp.* and *P. aeruginosa* by the agar well diffusion method [8, 9]. Tetracycline was used as the standard antibacterial agents. The Schiff base ligand was dissolved in DMF solvent. Petri plates were poured with (MHA) medium and allowed to solidify. The bacterial suspension of each test was evenly spread over the media by sterile cotton swabs. A sterile cork borer (6 mm in diameter) was then used to punch wells (4 wells) in the agar medium. Subsequently, wells were filled with 100 µL of ligand at concentrations of 50, 100 and 150 mg/mL and allowed to diffuse at room temperature for 30 min. The plates were incubated at 37 °C for 24 h. After the incubation the plates were observed for formation of clear inhibition zone around the well indicated the presence of antibacterial activity. The absence of a clear zone around the well was taken as inactivity [10, 11] and the diameter of inhibition zone was measured with a ruler. The experiment was performed in triplicate for each bacteria and tested ligand and the mean zone of inhibition was calculated for each ligand and standard antibiotic.

RESULTS AND DISCUSSION

The analytical data and physical properties of the ligand and its complexes were studied. The data are consistent with the calculated results from the empirical formula of each compound. The analytical data of the complexes confirm the existence of 1:1 [M:L] ratio. The molar conductance measurements were carried out in DMF solution (10^{-3} M). The obtained data reveal the presence of non-electrolytic nature for all complexes at room temperature have low values of 12-16 Ω^{-1} cm^2mol^{-1} that suggest their non-electrolyte nature [12, 13].

Characterization of compounds

The ligand and its metal complexes' infrared spectral data were examined. The infrared spectrum of the Schiff base shows a strong band located at 1581 cm^{-1} assigning to the ν(HC=N) stretching vibrations. This band shifted to lower frequencies 1573-1450 cm^{-1} in the spectra of the complexes indicating the participation of azomethine group in chelation through nitrogen atom [14]. The bands in the range of 3441-3536 cm^{-1} assigned to the existence of water molecules in the mixed ligand chelates. New bands in the range of 617 and 532 cm^{-1} which are not present in the free ligands are assigned to ν(M-O) and ν(M-N) vibrations and the appearance of these bands supports the involvement of oxygen and nitrogen atoms of the azomethine and OH groups of the free ligands in chelation process [15, 16]. Infrared spectra data (cm^{-1}) for prepared compounds: ($C_{14}H_{15}N_3O_3$) HL: 2877 (N-H), 1636 (C=O), 1582 (C=N); $[La(L)(OH)_2(OH_2)]H_2O$: 3441 (H_2O), 3008 (N-H), 1635 (C=O), 1573 (C=N), 617 (M-O), 532 (M-N). $[Ce(L)(OH)_3]H_2O$: 3526 (H_2O), 3132 (N-H), 1635 (C=O), 1450 (C=N), 617 (M-O), 532 (M-N). $[UO_2(L)(OH) (H_2O)]H_2O$: 3526 (H_2O), 3132 (N-H), 1636 (C=O),1520 (C=N), 617 (M-O), 532 (M-N). The ^{1}H NMR (500 MHz, DMSO-d_6, δ ppm) of ligand shows 12.5 for carboxylic-OH, 12.8 (NH-imidazole), 7.70 and 7.13 for CH-imidazole;7.29 and 7.62 for CH-benzylidenimin; 3.8 for CH3; 4.40 for CH-methine; 3.27 for methylene; 8.52 H-benzylidenimin (Figure 2). ^{13}C NMR (125 MHz, δ, ppm): spectrum: 137 (CH), 116.5 (CH), 159 (C), 122 (C), 114 (CH), 125 (CH), 134.0 (CH), 120.5 (CH), 179 (C) C=O, 53.8 (CH_3), 162.4 (CH), 73.5 (CH), 31.4 (CH_2).

[La(OH)$_2$(OH$_2$)]H$_2$O. White; M.Wt. 462.6; m.p. > 300 °C; The Elemental Analysis (Calc.), Found: C% (36.32) 36.00; H% (4.32) 4.08 ; N% (9.08) 9.37.

[Ce(L)(OH)$_3$]H$_2$O. Brown; M.Wt 463; m.p. > 300 °C; The Elemental Analysis (Calc.), Found: C% (36.29) 36.68; H% (4.10) 4.26 ; N% (9.07) 9.00.

[UO$_2$(L)(OH)(H$_2$O)]H$_2$O. Yellow; M.Wt 559; m.p. > 300 °C; elemental analysis (calc.), found: C% (30.01) 30.78; H% (3.40) 3.68; N% (7.51) 7.10. The mass data shows base peaks at m/z = 202, 121, 110 and 82 confirming different fragmentations due to broken some bonds and loss of different atoms.

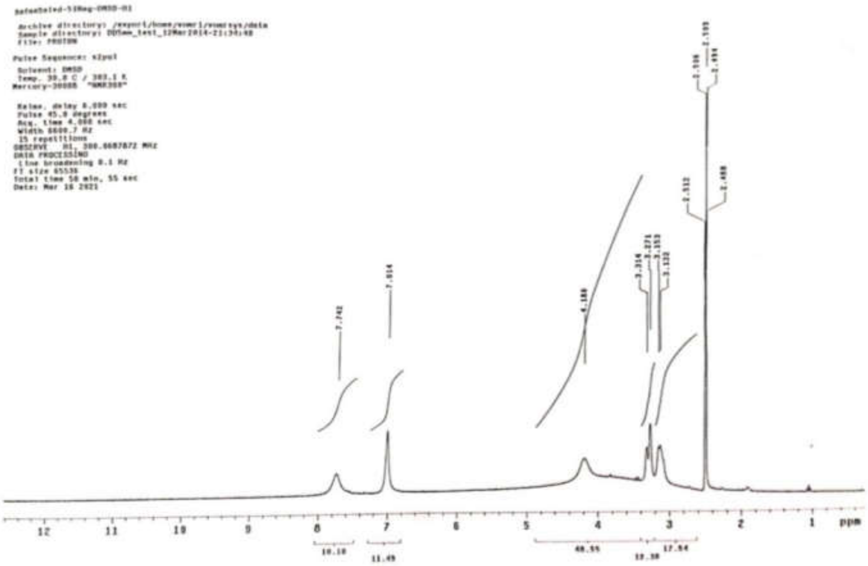


Figure 2. ^{1}H NMR spectrum for Ligand [HL].

Electronic study

The electronic spectrum of the Schiff base (HL) exhibits absorption bands at 283 nm and 331 nm corresponding to $\pi\rightarrow\pi^*$ (phenyl ring) and $n\rightarrow\pi^*$ transition, respectively [16]. The electronic absorption spectrum of La(III) chelate shows three bands at 260 nm, 283 nm and 317 nm. The magnetic moment value of this complex is (0.00 B.M.) indicates the presence of diamagnetic character. Based on these data, an octahedral geometry was suggested [17]. The electronic spectra of the cerium(IV) and UO$_2$(II) complexes display weak bands in the range of 260-303 nm due to f-f transition as shown in Figure 3 [18]. Electronic spectra of the Schiff base and their complexes λ nm (cm^{-1}): (C$_{14}$H$_{15}$N$_3$O$_3$)HL: 283 nm (35336 cm^{-1}) and 331 nm (30211 cm^{-1}); [La(L)(OH)$_2$(OH$_2$)]H$_2$O: 260 nm (38461cm^{-1}), 283 nm (35336cm^{-1}), and 317 nm (3154 cm^{-1}); [Ce(L)(OH)$_3$]H$_2$O: 260 nm (38461 cm^{1-}), 277 nm (36101 cm^{-1}), and 303 nm (33003 cm^{-1}); [UO$_2$(L)(OH) (H$_2$O)]H$_2$O: 260 nm (38461cm^{-1}).

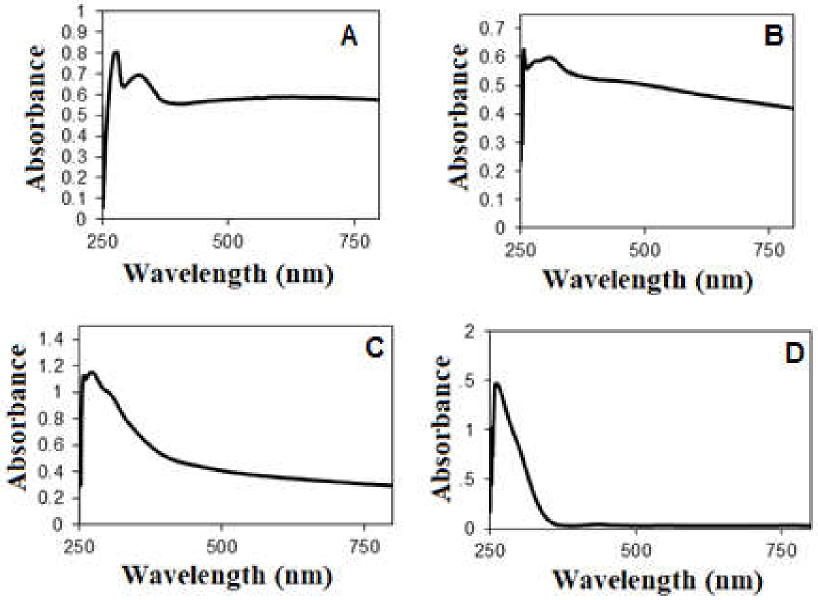
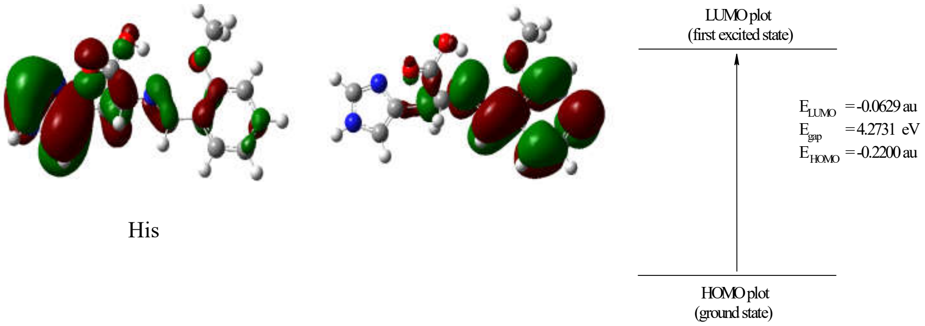


Figure 3. Electronic spectra of Schiff base [A] and its La(III) [B], Ce(IV) [C], UO_2(II) [D] complexes, respectively.

DFT study

The Schiff base ligand and its complexes were optimized by Gauss View 5.0.8 program [19, 20]. The density functional calculations by Gaussian 03 suit programs [21-25], in which B3LYP exchange correlation functional was used with 6-31 G (d, p)/LANL2DZ basis set for carbon, nitrogen, oxygen, hydrogen, and SSD basis set for lanthanum, cerium and uranium metals. HOMO and LUMO charge density were investigated to the ligand and complexes of La(III), Ce(IV) and UO_2(II) resulted E_{gap} = 4.2731, 3.7536, 2,9077, and 3.6421 eV, respectively.

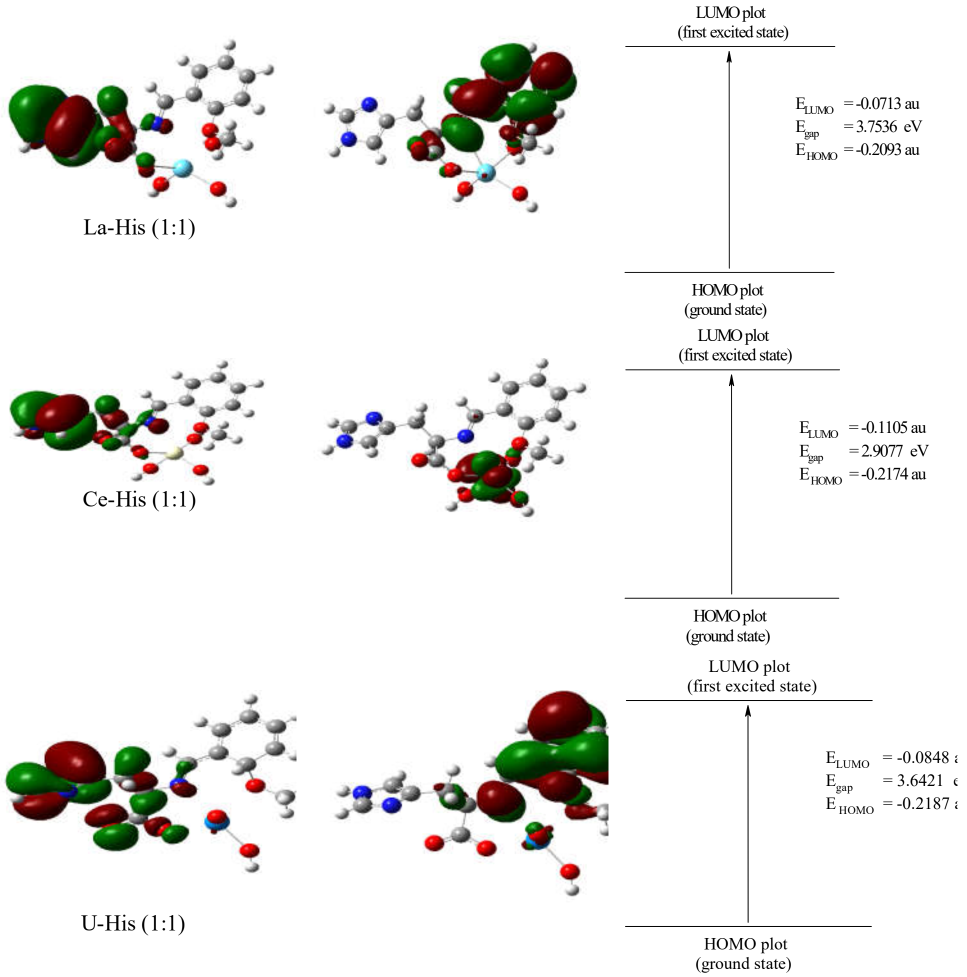


HOMO

LUMO

HOMO and LUMO energy band gab

[A]

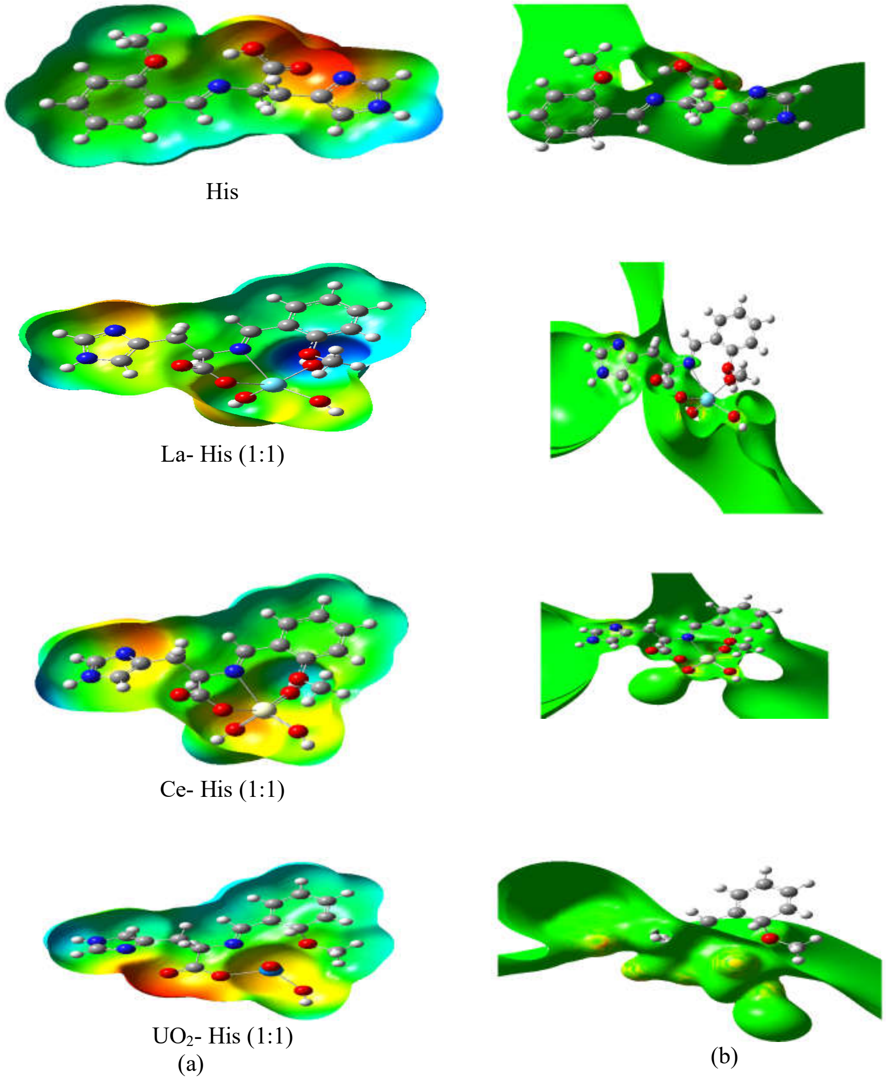


HOMO LUMO HOMO and LUMO energy band gap

[B]

Figure 4. [A] HOMO and LUMO charge density maps of the investigated ligand (His) using B3LYP/6-311G++(d,p) level and [B] HOMO and LUMO charge density maps of the studied chelates using B3LYP/SDD Level.

Surfaces of the ligand's molecular electrostatic potential and electrostatic potential via B3LYP/6-311G++(d,p); La, Ce, and U(1:1) chelates using B3LYP/SDD levels were studied and explained molecular electrostatic potential mapping for ligand and complexes to distinguish the net electrostatic effect established all around a molecule by the total charge distribution (Figures 4 and 5 and Tables 1-3).



His

La- His (1:1)

Ce- His (1:1)

UO_2- His (1:1)

(a)

(b)

Figure 5. Surfaces of the ligand's molecular electrostatic potential (a) and electrostatic potential (b) via B3LYP/6-311G++(d,p); La, Ce, and U(1:1) chelates using B3LYP/SDD levels.

Tables 1-3 show the comparison of the optimized ligand (His) B3LYP/6-311G++(d,p) and its chelates using B3LYP/SDD. It appears that there are differences in the values of the various factors of the four compounds due to the existence of different metals, which confirms the structures of the prepared compounds theoretically.

Table 1. Selected geometric bond lengths, bond angles and dihedral angles of the optimized ligand (His) B3LYP/6-311G++(d,p) and its chelates using B3LYP/SDD.

Ligand/ complexes	Bond lengths (Å)		Bond angles		Dihedral angles	
His	C19-O29	1.352	<C8-C11-O13	113.707	< C17-C18-C19-O29	0.284
	C11-O13	1.344	< C8-C11-O12	123.227	< C18-C19-O29-C30	-179.638
	C8-N14	1.452	<C11-C8-N15	107.895	<C8-N15-C17-C18	-179.309
	C17-N15	1.272	<C18-C19-O29	117.473	<C11-C8- N15-C17	136.358
	C11-O12	1.200	< C19-O29-C30	119.140	<N15-C8-C11-O12	-158.279
La-(His)	C13-O15	1.290	<O15-La35-N16	63.058	<C13-O15-La35-O36	149.646
	O15-La35	2.409	< O15-La35-O38	100.516	< C13-O15-La35-O38	-83.683
	C10-N16	1.471	< O15-La35-O40	144.860	< C13-O15-La35-O30	70.818
	N16-La35	2.775	<N16-La35-O36	17.682	<C10N16-La35-O15	-37.699
	O36-La35	2.252	<O30-La35-N16	61.540	< C10N16-La35-O40	143.519
	O38-La35	2.232	< O30-La35-O15	89.996	<C18-N16-La35-O38	-130.300
Ce-(His)	C13-O15	1.299	< O15-Ce35-N16	63.181	< C13-O15-Ce35-O36	157.519
	O15-Ce35	2.287	< O15-Ce35-O38	89.219	< C13-O15-Ce35-O38	-93.107
	N16-Ce35	2.663	< O15-Ce35-O40	146.981	< C13-O15-Ce35-O30	77.083
	O30-Ce35	2.763	< N16-Ce35-O36	139.617	< C10N16-Ce35-O15	-37.350
	O40-Ce35	2.084	< N16-Ce35-O38	107.504	< C10N16-Ce35-O30	-142.769
	O36-Ce35	2.106	< N16-Ce35-O40	83.988	< C10N16-Ce35-O38	42.545
	O38-Ce35	2.085	< O30-Ce35-N16	64.015	< C10N16-Ce35-O40	139.019
U-(His)	C13-O26	1.311	< O26-U31-N14	65.362	< C13-O26-U31-O32	-78.868
	O26-U31	2.217	< O26-U31-O33	95.099	< C13-O26-U31-O33	92.805
	N14-U31	2.625	< O26-U31-O23	139.010	< C13-O26-U31-O23	2.086
	O23-U31	2.611	< N14-U31-O26	65.362	< C10N14-U31-O23	170.980
	O34-U31	2.142	< N14-U31-O23	73.843	< C10N14-U31-O26	-4.925
	O32-U31	1.779	< N14-U31-O34	177.316	< C10N14-U31-O32	85.119
	O33-U31	1.796	< O32-U31-O33	170.880	< C10N14-U31-O34	140.546

Table 2. Total energy, energy of HOMO and LUMO, energy gap, ionization energy (I, eV), electron affinity (A, eV), absolute electronegativities, (χ, eV), absolute hardness (η, eV), global softness (S, eV^{-1}) chemical potential (π, eV^{-1}) global electrophilicity (ω, eV), additional electronic charge, $\Delta N_{max,}$ and NBO charges calculated for the ligand B3LYP/6-311G++(d,p) and its chelates using B3LYP/SDD.

Parameter	His	La-(His)	Ce-(His)	U-(His)
E_T, a.u.	-0.2200	-0.2093	-0.2174	-0.2187
E_{HOMO}, a.u.	-0.0629	-0.0713	-0.1105	-0.0848
E_{LUMO}, a.u.	4.2749	3.7552	2.90892	3.6436
E_g, eV	5.4641	8.4788	3.2525	10.814
I, eV	5.9866	5.6954	5.9158	5.9512
A, eV	1.7116	1.9402	3.0069	2.3075
χ, eV	3.8491	3.8178	4.4613	4.1294
η, eV	2.1375	1.8776	1.4545	1.8218
S, eV	0.2339	0.2663	0.3438	0.2745
π, eV	-3.8491	-3.8178	-4.4613	-4.1294
(ω, eV)	3.4656	1.6074	7.0750	4.6800
$\Delta N_{max.}$	1.8008	2.0333	3.0672	2.2667
NBO charges				
O12	-0.580	-0.634	-0.633	-0.607
O13	-0.685	-0.812	-0.720	-0.678
O29	-0.506	-0.551	-0.531	-0.556
N15	-0.500	-0.492	-0.462	-0.434
M	-	1.868	1.836	1.650

Table 3. Calculated natural charge, natural population and natural electronic configuration of metals in the studied chelates using B3LYP/SDD level.

Complex	M:L	Natural charge	Core	Natural population			Natural electronic configuration
				Valence	Rydberg	Total	
La-(His)	1:1	1.868	99.9466	127.5500	0.5033	228.0000	[core]$6s^{0.08}4f^{0.15}5d^{0.72}6p^{0.19}5f^{0.01}6d^{0.02}$
Ce-(His)	1:1	0.747	99.913	127.5864	0.5006	228.0000	[core]$6s^{0.10}4f^{0.79}5d^{1.07}6p^{0.23}5f^{0.02}6d^{0.02}$
U-(His)	1:1	1.202	131.6874	128.7343	0.5783	261.0000	[core]$7s^{0.15}5f^{2.60}6d^{1.50}7p^{0.28}$

Based on the foregoing study and results, the complexes have a hexa coordinated structure, as shown in Figure 6.

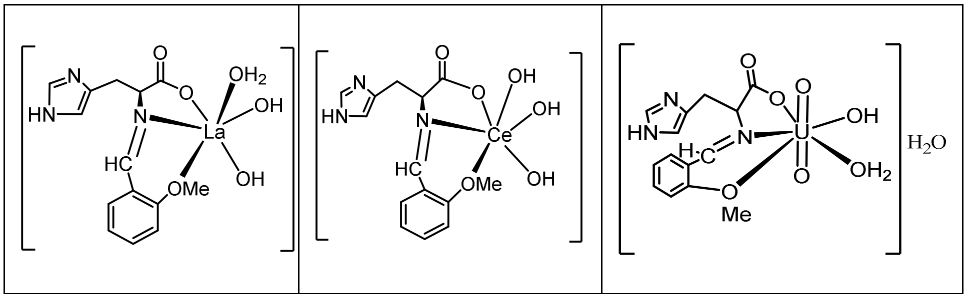


Figure 6. Proposed structure for La(III), Ce(IV) and UO_2(II) complexes.

Antibacterial activity

Antibacterial screening of the synthesized ligand was carried out using three against *E. faecalis*, *Klebsiella sp.* and *P. aeruginosa* using agar well diffusion method. In order to ensure that no effect of solvent a control test was performed with DMF and found inactive in the culture medium. Tetracycline is used as positive control. The antibacterial activity of the Schiff base ligand against pathogenic bacteria species as shown in Figure 7. The results show that the Schiff base ligand has moderate activity against all the tested bacteria and order of inhibition was found to be *P. aeruginosa* > *Klebsiella sp.* > *E. faecalis*. Tetracycline showed highest inhibitory effect on *E. faecalis*, and was moderate effect on *Klebsiella* sp., while was lowest effect *P. aeruginosa*. The lipid membrane surrounding the cell favor the passage of any lipid soluble materials and it is known that lipophilicity is an important factor that controls the antibacterial activity. This increase in lipophilic nature enhances the penetration of Schiff base into the lipid membranes and seizing the growth of the organism [26-30].

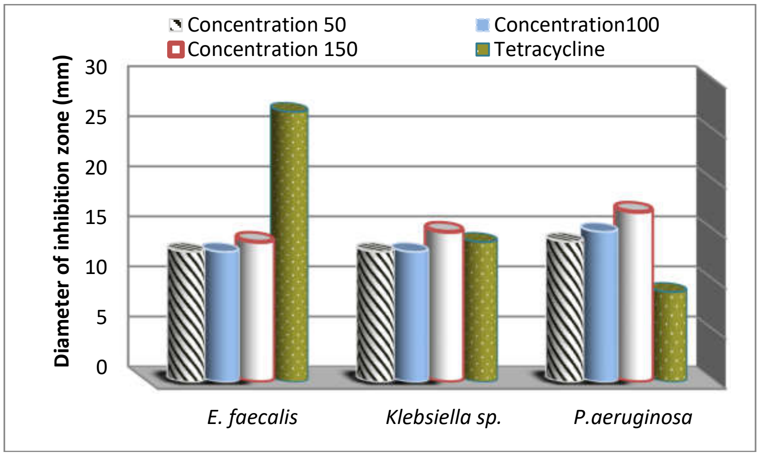


Figure 7. Effect of Schiff base ligand on tested bacterial species.

CONCLUSION

Three novel La(III), Ce(IV) and UO2(II) complexes have been synthesized and characterized using various physicochemical techniques. It has been spectroscopically demonstrated that the Schiff base ligand derived from L-histidine and anisaldehyde coordinated to La(III), Ce(IV) and UO2(II) ions producing an octahedral geometry. DFT studies were also performed to confirm their experimental results. In addition, the antibacterial activity of the Schiff base ligand was tested against some pathogenic bacteria species and the obtained results showed a good activity.

ACKNOWLEDGEMENT

The authors would like to thank their Universities for facilities.

REFERENCES

1. Ortiz, A.; Camacho, C.; Espuñes, T.; Oviedo, I.; Lucas, L.; Carrillo, A.; Ramirez, M.. Novel organotin(IV) Schiff base complexes with histidine derivatives: Synthesis, characterization, and biological activity. *Bioinorg. Chem. Appl.* **2013**, 12, 502713.
2. Casella, L.; Gullotti, M.; Coordination modes of histidine: Coordination structures in the copper(II)-L-histidine (1:2) system. *J. Inorg. Biochem.* **1983**, 18, 19-31.
3. Henkin, R. *Metal-Albumin-Amino Acid Interactions: Chemical and Physiological Interrelationships*, Plenum Publishing: New York; **1974**.
4. Schiff, H.; Mittheilungen aus dem Universitats laboratorium in Pisa: Eine neue Reihe Organischer Basen. *Justus Liebigs Ann. Chem.* **1864**, 131, 118-119.
5. Supuran, C.; Barboiu, M.; Luca, C.; Pop, E. Carbonic anhydrase inhibitors and their therapeutic potential. *Eur. J. Med. Chem.* **1996**, 31, 597-606.
6. More, M.; Joshi, P.; Mishra, Y.; Khanna, P. Metal complexes driven from Schiff bases and semicarbazones for biomedical and allied applications: a review. *Mater. Today Chem.* **2019**, 14, 1-22.
7. Ibrahim, A.A.; Kareem, M.M.; Al-Noor, T.H.; Al-Muhimeed, T.; AlObaid, A.A.; Albukhaty, S.; Sulaiman, G.M.; Jabir, M.; Taqi, Z.J.; Sahib, U.I. Pt(II)-thiocarbohydrazone complex as cytotoxic agent and apoptosis inducer in Caov-3 and HT-29 cells through the P53 and Caspase-8 pathways. *Pharmaceuticals* **2021**, 14, 509.
8. Al-Noor, T.H.; Mohapatra, R.K.; Azam, M.; Abdul Karim, L.K.; Mohapatra, P.K.; Ibrahim, A.A.; Parhi, P.K.; Dash, G.C.; El-ajaily, M.M; Al-Resayes, S.I.; Raval, M.K.; Pintilie, L. Mixed-ligand complexes of ampicillin derived Schiff base ligand and nicotinamide: Synthesis, physico-chemical studies, DFT calculation, antibacterial study and molecular docking analysis. *J. Mol. Struct.* **2021**, 1229, 129832.
9. Hay, P.J.; Wadt, W.R.; Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals. *J. Chem. Phys.* **1985**, 82, 284-299.
10. Rahman, A.; Choudry, M.I.; Thomsen, W.J. *Bioassay Techniques for Drug Development*, Harwood Academic Publishers: Netherlands; **2001**.
11. Frish, M.J.; Trucks, G.W.; Schlegel, H.B. *GAUSIAN 03, Revision E.01*, Gaussian Inc.: Pittsburgh, PA; **2004**.
12. Rafique, S.; Idrees, M.; Nasim, A.; Akbar, H.; Athar A. Transition metal complexes as potential therapeutic agents. *Biotechnol. Mol. Biol. Rev.* **2010**, 5, 38-45.
13. Raman, N.; Joseph, J.; Sakthivel, A.; Jeyvmurudan, R. Synthesis, structural characterisation and antimicrobial studies of novel Schiff base copper(II) complexes. *J. Chil. Chem. Soc.* **2009**, 54, 354-357.
14. Ajayeoba, T.A.; Akinyele, O.F.; Oluwole, A.O.; Synthesis, characterisation and antimicrobial studies of mixed nickel(II) and copper(II) complexes of aroylhydrazones with 2,2'-bipyridine and 1,10-phenanthroline. *Ife J. Sci.* **2017**, 19, 119-132.
15. Abad Al-Ameer, A. Synthesis, characterization and antibacterial evaluation of mixed ligand complexes of 2-phenyl-2-(*o*-tolylamino) acetonitrile and histidine lgand with Co, Cu, Zn divalent metal ion complexes. *Eur. J. Mol. Clin. Med.* **2020**, 7, 2538-2544.
16. Kareem, M.M. Synthesis, characterization and study the physical properties of new 1,2,4-triazoles Mannich-base derivatives. *IOP Conf. Ser.: Mater. Sci. Eng.* **2018**, 454, 012092.
17. El-Sonbati, A.; Diab, M.; Morgan, Sh.; Abou-Dobara, M.; El-Ghettany, A. Synthesis, characterization, theoretical and molecular docking studies of mixed-ligand complexes of Cu(II), Ni(II), Co(II), Mn(II), Cr(III), UO2(II) and Cd(II). *J. Mol. Struct.* **2020**, 1200, 127065.
18. El-Barasi, N.; Miloud, M.; El-ajaily, M.; Mohapatra, R.; Sarangi, A.; Das, D.; Mahal, A.; Parhi, P.K.; Pintilie, L.; Barik, S.; Bitu, Md.; K.-E-Zahan, Md.; Tabassum, Z.; Al-Resayes, S., Azam, M. Synthesis, structural investigations and antimicrobial studies of

hydrazone based ternary complexes with Cr(III), Fe(III) and La(III) ions. *J. Saudi Chem. Soc.* **2020**, 24, 492-503.

19. Obaid, S. Synthesis, spectral and antibacterial activity of mixed ligand from lanthanium(III) complexes of Schiff base ligand with some amino acids. *J. Glob. Pharma Technol.* **2019**, 11, 88-99.
20. *GaussView 5.0*, Gaussian Inc.: Wallingford, CT, USA; **2009**.
21. Al-Amiery, A.H.; Al-Bayati, R.I.; Al-Majedy, Y.K. Novel quinazolinone derivatives: Synthesis and antimicrobial activity. *Int. J. Electrochem. Sci.* **2010**, 14, 1-30.
22. Azam, M.; Al-Resayes, Alam, S.I.; Trzesowska-Kruszynska, A.; Kruszynski, R.; Siddiqui, M.R.H. A new ladder-type dichloro(2,2-dimethyl-1,3-diaminopropane) copper complex: Synthesis, structural studies and selective sensing behavior towards a ketone molecule. *Polyhedron* **2019**, 170, 287-293.
23. Azam, M.; Al-Resayes, S.I.; Trzesowska-Kruszynska, A.; Kruszynski, R.; Shakeel, F.; Soliman, S.M.; Alam, M.; Khan, M.R.; Wabaidur, S.M. Zn(II) complex derived from bidentate Schiff base ligand: Synthesis, characterization, DFT studies and evaluation of anti-inflammatory activity. *J. Mol. Struct.* **2020**, 1201, 127-177.
24. Becke, A.D. Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993**, 98, 5648-5652.
25. Becke, A.D. Correlation energy of an inhomogeneous electron gas: A coordinate-space model. *Phys. Rev. A.* **1988**, 88, 1053-1062.
26. Esfahani, N.M.; Zendehdel, M.; Nia, N.Y.; Jafari, B.; Babadi, M.K. Fabrication and characterization of a new dye sensitized solar cell with a new Schiff base cobalt complex as a redox mediator. *RSC Adv.* **2014**, 4, 15961-15967.
27. Gaballa, A.S., Asker, M.S., Barakat, A.S.; Teleb, S.M. Synthesis, characterization and biological activity of some platinum (II) complexes with Schiff bases derived from salicylaldehyde, 2-furaldehyde and phenylenediamine. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2007**, 67, 114-121.
28. Kareem, M.M.; Abd Alrazzak, N.; Aowda, S.A.; Aljamali, N.M. Synthesis, characterization and biological activity study for new hybrid polymers by grafting 1,3,4-triazole and 1,2,4-oxadiazle moieties onto polyvinyl chloride. *Egypt. J. Chem.* **2021**, 64, 1273-1283.
29. Mohapatra, R.K.; El-ajaily, M.M.; Alassbaly, F.S.; Sarangi, A.K.; Das, D.; Abdussalam, A. A.; Maihub Ben-Gweirif, S.F.; Mahal, A.; Suleiman, M.; Perekhoda, L.; Azam, M.; Al-Noor, T.H. DFT, anticancer, antioxidant and molecular docking investigations of some ternary Ni(II) complexes with 2-[(E)-[4-(dimethylamino) phenyl] methyl eneamino]phenol. *Chem. Zvesti Chem. Pap.* **2020**, 75, https://doi.org/10.1007/s11696-020-01342-8.
30. Eman, J.M.; Kareem, M.M.; Abbas, J.A. Photocatalytic oxidation of butan-2-ol over multi walled carbon nanotubes /cobalt phthalocyanine composites. *Bull. Chem. Soc. Ethiop.* **2022**, 36, 197-207.