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Synthesis, DFT and Molecular Docking Studies of a New Macrocyclic Schiff Base and Its Cu(II) and Ni(II) Complexes

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ABSTRACT

A new Schiff base 6,8,15,17-tetramethyl-7,16-dihydrodibenzo-1,4,8,11-tetraazacyclotetradecine was synthesized by condensation of 1,2-diaminobenzene and pentane-2,4-dione in an alcoholic medium. The synthesized Schiff base and its metal complexes were characterized by micro elemental analysis, magnetic susceptibility, molar conductivity, IR, UV-Vis and NMR spectral data. On the basis of spectroscopic data suggest an octahedral geometry for the Ni(II) complex and a distorted octahedral geometry for the Cu(II) complex. DFT studies at the def2-SVP level show that the HOMO-LUMO energy gap decreases from 4.70 eV (ligand) to 3.80 eV in Cu-complex, indicating enhanced reactivity. Molecular docking with p53 anti-tumor protein DNA revealed a strong intercalation mode at the major groove of DNA.

1. Introduction

The Schiff bases are versatile organic compounds synthesized by the chemical reaction of carbonyl compound with a primary amine under suitable conditions. The general structure of Schiff base is R_1R_2C=N-R_3(R_3=H). The main functional group present in the Schiff base is azomethine or imine(>C=N-). In the Schiff base donor atoms may ne nitrogen, oxygen or sulphur, which provide binding site through non-bonding electrons. Schiff bases sometimes known as privileged ligands have enduring appeal due to a unique blend of structural simplicity and great functional flexibility. Schiff bases stand out for their atom-economic origins in a time when chemical synthesis is increasingly evaluated based on its effectiveness and environmental impact. The versatility of Schiff bases has long served as a foundation for the intersection of coordination chemistry and pharmacology and their diverse biological roles continue to astound researchers. The substances that have the distinctive azomethine linkage are structural mimics of vital biological intermediates rather than merely synthetic ones. Schiff bases exceptional capacity to coordinate with transition metals has made them privileged scaffolds in the hunt for novel therapeutic agents. This chelation frequently works in concert the ligand reduces the metals toxicity and enhances its transport across lipid membranes while the metal ion stabilizes the organic framework. Recent studies shows that the metal Schiff complexes having the capacity to cross the BBB barrier and can be effective against the Oncogenes.

The DNA binding ability of these metal complexes also explored and they showed good result as DNA intercalates. Transition metal Schiff base complexes were used in catalyst, polymer chemistry, dyes, corrosion, anti-microbial, antidiuretic, fluorescence, and anti-inflammatory activities. In-silico study of metal complexes helps in exploring their biological properties [1-5]. Using Molecular-docking study, the binding affinities were determined against the variety of targets and might reveal more insights into the possible mechanisms of drug and target interaction [6]. The molecular docking study of transition metal complexes of pyridine-based ligand showed interaction with calf thymus DNA by the way of intercalative mode [7]. There is a huge demand of such type of metal complexes which can show anticancer, antiviral, antimicrobial, antioxidant and other biological activities.

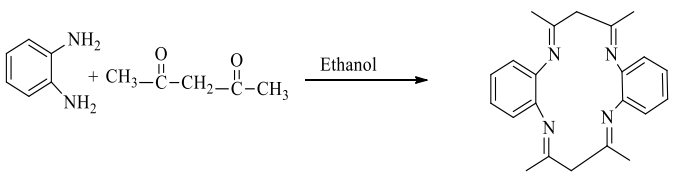
This paper reports the synthesis, characterization, DFT and docking of copper and nickel complexes with tetradentate Schiff base ligand. DFT calculations were done to explore the FMOs of Ligand and its metal complexes and to study the electronic spectra. Molecular Docking was done with p53 antitumor protein (3TS8).

2. Experimental Methods

All the chemicals used for the synthesis of Schiff base and its copper and nickel complexes were of analytical grade. They were used without further purification. The elemental analyzes were recorded on a Carlo-Ebra EA1110 analyzer. The molar conductivity of the synthesized complexes was measured by DMF bridge model PW9501. Hitachi-320 spectrophotometer was used to record the electronic absorption spectra of the complexes. Shimadzu infrared spectrophotometer was used to record the IR spectra of the investigated complexes. The magnetic susceptibility of investigated complexes was measured by Gouy method using Hg [Co (SCN)$_4$] as a calibrant.

2.1 Synthesis of Schiff Base Ligand

The Schiff base 6,8,15,17-tetramethyl-7,16-dihydrodibenzo-1,4,8,11-tetraazacyclotetradecine was synthesized by condensation of 1,2-diaminobenzene (0.01 mol) with pentane-2,4-dione (0.01 mol) in ethanol (25 mL). The reaction mixture was refluxed for 2-3 hours. The reaction mixture was stirred after cooling in crushed ice. The crystal was filtered out, recrystallized in ethanol, washed with distilled water and then dried over anhydrous $CaCl_2$ in a desiccator. The melting point of the ligand was recorded to be 178 °C.



Scheme 1 Synthesis of Schiff base

2.2 Synthesis of Metal (II) Complexes

A solution of 0.01 mol of metal salts (nickel (II) chloride hexahydrate/ copper (II) chloride dihydrate) was added to the ethanolic solution of Schiff base (0.01 mol) with constant stirring. The solution was refluxed for 3-4 hours on a water bath using water condenser. On cooling the solution, a coloured precipitate was formed. The precipitate was filtered, washed

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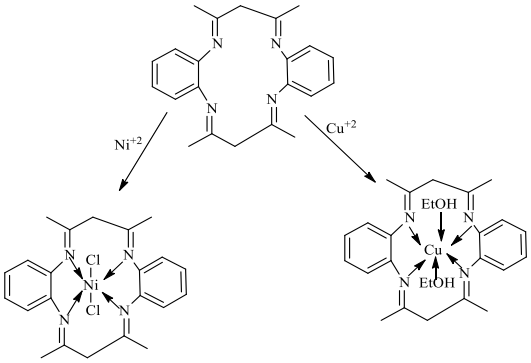
with ethanol and recrystallized from DMF and finally dried over anhydrous $CaCl_2$ in a desiccator. The synthesis route is explained in Scheme 2.



Scheme 2 Synthesis of metal-complexes

3. Results and Discussion

All the synthesized complexes are solid, coloured, and stable at room temperature towards air and moisture. The microanalytical data of the ligand and its metal complexes are shown in Table 1.

Table 1 Micro-analysis of ligand(L) and its metal complexes

Compounds	Elemental analysis: % found (Calcd.)				M.wt.	Colour	m.p.
	C	H	N	M	(Cal)		(°C)
$C_{22}H_{24}N_4$	76.21	6.82	15.98	---	343.8		
	(76.74)	(6.97)	(16.28)		(344)	Yellow	178
$Ni[C_{22}H_{24}N_4Cl_2]$	54.97	5.16	12.14	12.22	472.82	Green	
	(55.73)	(5.06)	(11.82)	(12.39)	(473.69)		280
$Cu[C_{24}H_{30}N_4O]Cl_2$	54.44	6.13	9.75	11.29	569.24	Blue	221
	(54.68)	(6.31)	(9.81)	(11.14)	(570.54)		

3.1 Magnetic Moment and Electronic Absorption Spectra

The electronic absorption spectral data and magnetic moment are shown in Table 2. The electronic spectrum of the Ni(II) complex exhibits three characteristic absorption bands at 8678 cm^{-1}, 14250 cm^{-1} and 25300 cm^{-1} which may be assigned to the spin allowed transitions $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ respectively. The Ni(II) complex exhibits a magnetic moment of 2.94 BM, which is consistent with high-spin octahedral geometry. The Cu(II) complex show one broad and asymmetrical band at 13450 cm^{-1}due to $^2E_g \rightarrow {}^2T_{2g}$ transition. The observed magnetic moment value for copper complex was found to be 1.98 BM which indicates high spin distorted octahedral geometry.

Table 2 Electronic absorption and magnetic moment data of metal complexes

Compounds	Absorption (cm^{-1})	Assignments	Magnetic moment	Geometry
$[Ni(L)Cl_2]$	8678 14250 25300	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$	2.94 BM	Octahedral
$[Cu(L)(C_2H_5OH)_2]Cl_2$	13450	$^2E_g \rightarrow {}^2T_{2g}$	1.98 BM	Distorted octahedral

Table 3 IR data of ligand(L) and its metal complexes (cm^{-1})

Complex	$\upsilon_{(C=N)}$	$\upsilon_{(C-H)}$ Aliphatic	$\upsilon_{(O-H)}$ Ethanol	$\upsilon_{(C-O)}$	$\upsilon_{(M-N)}$	$\upsilon_{(M-O)}$	$\upsilon_{(M-Cl)}$
Ligand(L)	1640	2920	-	-		-	-
$[Cu(L)(EtOH)_2]Cl_2$	1620	2940	3420	1035	485	520	
$[Ni(L)Cl_2]$	1610	2935	-	-	462	-	330

3.2 IR Spectra

The IR spectral data of investigated metal complexes are listed in Table 3. The investigated Schiff base showed strong absorption band at 1640 cm^{-1} is characteristic of azomethine group present in the Schiff base. This band was shifted towards the lower wave number by 20-30 cm^{-1} in the complexes suggested the coordination of azomethine nitrogen atom to the metal ions. A broad band at 3420 cm^{-1} assigned to υ_{OH} vibration and shift in υ_{C-O} at 1035 cm^{-1} suggested coordination of oxygen atom of ethanol to copper ion. The appearance of bands at 462 cm^{-1} and 485 cm^{-1}, which may be assigned to υ_{Ni-N} and υ_{Cu-N} respectively. The appearance of a new band at assigned to the mode of vibration. The appearance of a band at 330 cm^{-1} suggests the υ_{Ni-Cl} in the complex.

3.3 NMR Spectra

A sharp singlet observed at δ 8.35 ppm is attributed to the azomethine protons which confirm the equivalence of the four nitrogen environments in the Schiff base. The protons of the benzene rings appear as multiplets in the region of δ 6.82- 7.54 ppm (Table 4). A highly intense singlet at δ 2.24 ppm attributed to methyl protons of pentane-2,4-dione. Due to the paramagnetic nature of the Cu(II) and Ni(II) ions the NMR spectra of copper and nickel complexes showed significant line broadening and poor resolution.

Table 4 NMR data of ligand(L) and its metal complexes in d_6-DMSO

Group	^1H (δ, ppm)	^{13}C(δ,ppm)	Multiplicity
(–CH=N–)	8.35	160.2	Singlet
Aromatic	6.82 - 7.54	122.5 - 144.8	Multiplet
Methyl ($-CH_3$)	2.24	18.5	Singlet

3.4 Frontier Molecular Orbitals and Electronic Spectra

ORCA software package with Avogadro was used to do the computational analysis of ligand and complexes [8,9]. The DFT calculations were performed at BP86 parameter at def2-SVP level of DFT theory [10-13]. At BP86 parameter the output results are very close to the experimental values so this parameter is considered good for computational calculations. The energy of highest occupied molecular orbital (HOMO) refers to ionization potential and lowest unoccupied molecular orbital (LUMO) refers to electron affinity, which play a key role in the chemical reactivity and stability of compounds [14-20]. The FMO are useful to see the spread of charge density in the molecule [21]. The Frontier Molecular Orbital (FMO) analysis provides a clear picture of the chemical stability and reactivity of the synthesized compounds. The calculated energy gap (ΔE) for the free Schiff base ligand is 4.70 eV. Upon coordination with the metal centers, this gap decreases to 3.80 eV for the copper- complex and 3.90 eV for the nickel-complex. The FMOs are represented in Figs. 1 and 2. In the Fig. 1 the charge density on the ligand (L) is homogenously spread on the pi conjugated system, which showed the planarity of the conjugated system, while in the LUMO the extend of delocalization decreases due to the presence of anti-bonding orbitals. In metal complexes, the spread of charge density in HOMO is more in Cu (II) complex compared to Ni (II) complex, due to which the HOMO is more stabilized in Cu (II) complex as compared to Ni (II) complex. The energy values of FMO are useful to find out the Hardness, softness and electrophilicity properties of molecule [22, 23].

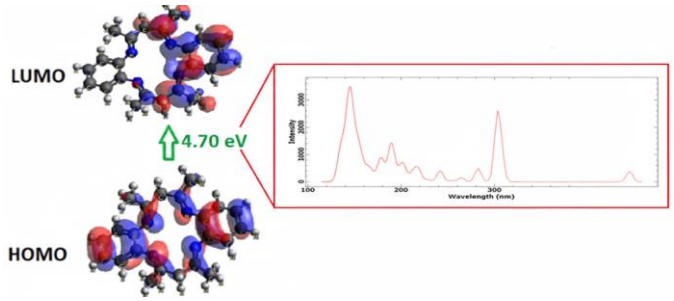


Fig. 1 Calculated energy gap of HOMO and LUMO in ligand (L) with computational UV spectra

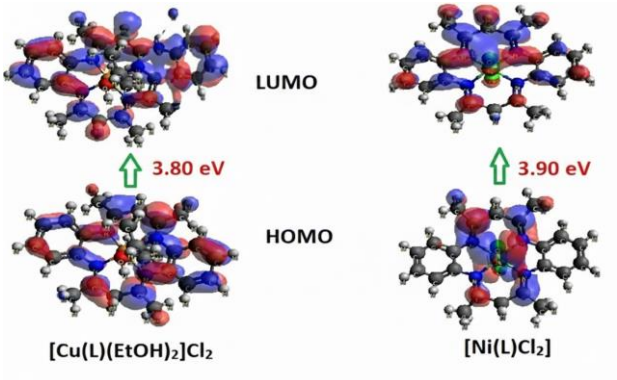


Fig. 2 HOMO-LUMO energy gap in $[Cu(L)(EtOH)_2]Cl_2$ and $[Ni(L)Cl_2]$ complex

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Table 5 Energy of FMOs of ligand (L) and its metal complexes

FMO	Ligand(L)	$[Ni(L)Cl_2]$	$[Cu(L)(EtOH)_2]Cl_2$
HOMO(eV)	-5.85	-5.95	-6.25
LUMO(eV)	-1.15	-2.05	-2.45
ΔE	4.7	3.9	3.8
HD	2.35	1.95	1.9
SOF	0.42	0.51	0.52
EPH	2.61	4.1	5

3.5 Computational UV-Visible Spectra

The nature of the ligand around the metal ion can easily understand from the electronic excitation. Computational UV-visible spectra data and theoretical electronic transitions of the ligand and copper complexes are tabulated in Table 6 and spectra were shown in Figs. 1 and 3. During the theoretical calculations of electronic spectra of Cu (II) complex open shell are deducted which showed that the copper (II) complex is paramagnetic in nature. UV-Visible spectra of Schiff base are containing peak at 241.62 nm due to K-band of the aromatic ring (π-π*) and B-band peak at 282.3 nm (π-π*). The peaks at 444.5 nm are due to n-π* transition of azomethine (-CH=N-) bond. In metal complexes the absorption peaks are shown in the visible region due to the possible MLCT and d-d transitions. The absorption maxima showed that the metal complexes are coloured and the absorption maxima is 628 nm for the $[Cu(L)(EtOH)_2]Cl_2$ complex and 463 nm for the $[Ni(L)Cl_2]$ complex.

Table 6 Theoretical electronic transitions data of ligand and its complexes

Compound	λmax (nm)	Absorbance	Assignment
Ligand (L)	241.6, 282.3	0.11, 0.14	π→π*
	444.5	0.11	n→π*
$[Cu(L)(EtOH)_2]Cl_2$	496.2	0.3	π→π*
	524	0.05	MLCT
	628.3, 715.4	0.29, 0.13	d-d transition
$[Ni(L)Cl_2]$	243.9, 345.3	0.03, 0.08	π→π*
	463.3, 679.6	0.12, 0.03	d-d transition

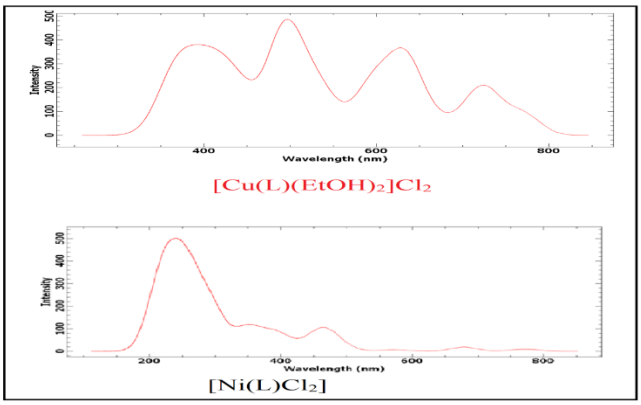

Fig. 3 Computational UV-visible spectra of $[Cu(L)(EtOH)_2]Cl_2$ and $[Ni(L)Cl_2]$ complex

3.6 Molecular Docking with DNA

Docking techniques are useful to show the preferred mode of binding and help in understanding the types of interactions at the binding site. The p53 belongs to DNA repairing genes and the fault in these genes leads to mutations because any mistake in DNA then remains uncorrected [24]. The binding energy for the ligand and its metal complexes are listed in Table 7. The negative values of binding energy for both ligand and its metal complexes showed that the binding are thermodynamically favoured process at the target site. The interactions of the ligand and metal complexes are in the intercalation mode shown in Figs. 4-6. The hydrogen bonding interactions, Vander Waals interactions, hydrophobic interactions, and electrostatic interactions play a vital role at the target site for the binding of ligand and complexes.

Table 7 Binding energy data for the interaction of ligand and its metal complexes

Molecule	BE (kcal/mol)	Nucleotide Targets	Primary Interaction Types
Schiff base (L)	-6.6	G38, G39, G40, A41, T36, T37	Van der Waals, π-π stacking
$[Cu(L)(EtOH)_2]Cl_2$	-8.1	G45, T46, T47, C48, C49	Hydrogen bonding, π-π stacking, Electrostatic
$[Ni(L)Cl_2]$	-6.2	A32, C33, T34	Hydrophobic interactions

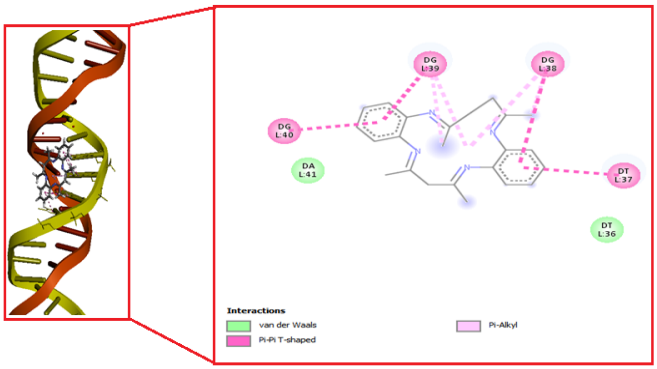

Fig. 4 Interaction at binding site between the ligand (L) with tumor suppressor p53 protein with DNA

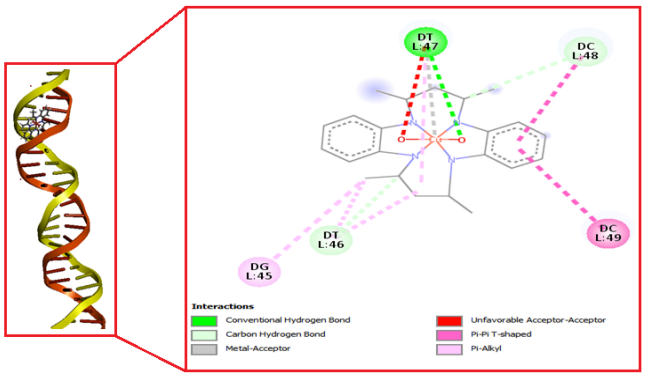

Fig. 5 Interaction at binding site between the $[Cu(L)(EtOH)_2]Cl_2$ with tumor suppressor p53 protein with DNA

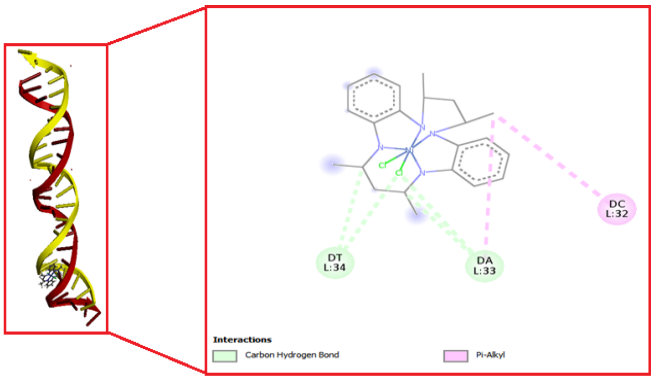

Fig. 6 Interaction at binding site between the $[Ni(L)Cl_2]$ with tumor suppressor p53 protein with DNA

4. Conclusion

The Schiff base 6,8,15,17-tetramethyl-7,16-dihydrodibenzo-1,4,8,11-tetraazacyclotetradecine and its copper and nickel complexes have been synthesized in 1:1 metal ligand ratio. They were characterized by micro elemental analysis, magnetic susceptibility, molar conductivity, IR, UV-Vis, and NMR spectral data. The synthesized Schiff base ligand acts as tetradentate and coordinated through azomethine nitrogen atoms to the metal ion.

On the basis of the magnetic moment, elemental analysis and different spectral data suggested octahedral geometry for nickel complex and distorted octahedral geometry for copper complex. The nature of the ligand environment around the metal ion is well-elucidated through electronic excitation studies. Frontier molecular orbital (FMO) analysis revealed that coordination significantly reduces the energy gap from 4.70 eV in the free ligand to 3.80 eV and 3.90 eV in the Cu(II) and Ni(II) complexes, respectively, enhancing their chemical reactivity and electronic stability.

The docking analysis successfully complements the FMO studies. The reduction of the energy gap upon complexation not only affects the optical properties (UV-Vis) but also enhances the biological efficacy. The Cu(II) complex, with the lowest energy gap of 3.80 eV, showed a slightly higher binding propensity, likely due to its distorted octahedral geometry which allows for better fitting into the DNA major groove compared to the more rigid octahedral Ni(II) complex.

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References

[1] T.K. Bakır, J.B. Lawag, Synthesis and characterization of Schiff base metal complexes and their biological/catalytic activities, Res. Chem. Inter. 46 (2020) 2541 -2559.

[2] M. Sedighipoor, A. H. Kianfar, G. Mohammadnezhad, H. Gorls, W. Plass, A. Abbas M. Borojeni, E. Abdollahi, Synthesis, crystal structure, and spectroscopic characterization of cobalt(III) or nickel(II) Schiff base complexes, Inorg. Chim. Acta. 488 (2019) 182-189.

[3] F. Rahim, M. Taha, H. Ullah, A. Wadood, M. Selvaraj, et al., Synthesis and α-glucosidase inhibition studies of benzimidazole or dihydropyrimidinone derivatives (medicinal chemistry), Bioorg. Chem. 91(10) (2019) 103134.

[4] Basma A. Ismail, Doaa A. Nassar, Zeinab H. Abd El–Wahab, Omyma A.M. Ali, Coordination chemistry of transition metal complexes derived from novel Schiff bases: Synthesis, DFT, and antimicrobial studies, J. Mol. Struct. 1227 (2021) 128487.

[5] E. Moradinia, M. Mansournia, Z. Aramesh-Boroujeni, Bordbar, Immobilization of metal complexes on functionalized magnetic nanoparticles for use as heterogeneous catalysts, Appl Organometal Chem. 33 (2019) e4893.

[6] S.N. Mali, H.K. Chaudhari, Quantitative structure-activity relationship (QSAR) and molecular docking studies of bioactive compounds, Open Pharm. Sci. J. 5 (2018) 23-36.

[7] S.S.A. Fathima, M.M.S. Meeran, E.R. Nagarajan, Structural and spectral investigations of organic-inorganic hybrid materials or specific complex crystals, J. Struct. Chem. 31 (2020) 521-530.

[8] F. Neese, The ORCA program system: A comprehensive review of the software used for quantum chemical calculations, Comput. Mol. Sci. 8 (2018) e1327.

[9] M.D. Hanwell, D.E. Curtis, D.C. Lonie, T. Vandermeersch, E. Zurek, G.R. Hutchison, Avogadro: An advanced semantic chemical editor, visualization, and analysis platform, J. Cheminform. 4 (2012) 17.

[10] D. Becke, Density-functional calculations of molecular bond energies, J. Chem. Phys. 84 (1986) 4524-4529.

[11] J.P. Perdew, Density-functional approximation for the correlation energy of the inhomogeneous electron gas, Phys. Rev. B. 33 (1986) 8822-8824.

[12] E. Bill, E. Bothe, P. Chaudhuri, K. Chlopek, D. Herebian, S. Kokatam, K. Ray, T. Weyhermller, Molecular and electronic structure of octahedral iron complexes, Chem. Eur. J. 11 (2004) 204- 224.

[13] Fleming, Molecular orbitals and organic chemical reactions, First Ed., John Wiley & Sons, Chichester, UK, 2010.

[14] M.M. El-ajaily, A.K. Sarangi, R.K. Mohapatra, S.S. Hassan, R.N. Eldaghare, et al., Structural, spectroscopic, and biological studies of some Schiff base metal complexes: A combined experimental and theoretical approach, Chemistry Select 4 (2019) 9999-10005.

[15] T. Yousef, G.A. El-Reash, R. El-Morshedy, Synthesis, characterization, and antitumor activity of Cu(II) complexes derived from 2-formylpyridin-4-phenyl-3-thiosemicarbazone, Polyhedron 45 (2012) 71-85.

[16] S. Shahraki, H.S. Delarami, M. Saeidifar, Catalase inhibition by two Schiff base derivatives: Kinetics, thermodynamic and molecular docking studies, J. Mol. Liq. 287 (2019) 111003.

[17] G.M. Morris, R. Huey, W. Lindstrom, M.F. Sanner, R.K. Belew, D.S. Goodsell, AutoDock4, and AutoDockTools4: Automated docking with selective receptor flexibility, J. Olson, J. Comput. Chem. 30(16) (2009) 2785-2791.

[18] O. Trott, A.J. Olson, AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading, J. Comput. Chem. 31 (2010) 455-461.

[19] D.S. Biovia, Discovery Studio Visualizer, v17.2.0.16349, Dassault Systems Biovia, USA, 2016.

[20] S. Emamzadah, L. Tropia, T.D. Halazonetis, Crystal structure of a p53 core domain–DNA complex: Insights into DNA binding and transactivation, Mol. Cancer Res. 9(11) (2011) 1493-1499.

[21] V.R. Chandrasekhar, K.M. Palsamy, R. Lokesh, D.T. Thangadurai, Synthesis, characterization and biological evaluation of organotellurium(IV) complexes derived from a Schiff base ligand, Appl. Organomet. Chem. 33(3) (2018) e4753.

[22] M.A. Neelakantan, K. Balamurugan, C. Balakrishnan, L. Subha, DNA/protein binding, DNA cleavage, and cytotoxicity of transition metal complexes of a Schiff base, Appl. Organometal Chem. 32 (2018) e4259.

[23] C. Joerger, A.R. Fersht, The p53 pathway: Origins, node in a network of signaling pathways, and pharmacology, Cold Spring Harb. Perspect. Biol. 2(6) (2010) a000919.

[24] Vladimir J.N. Bykov, Klas G. Wiman, Mutant p53 reactivation by small molecules makes its way to the clinic, FEBS Let. 588(16) (2014) 2622-2627.

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