

Synthesis and Structure-Based Drug Design of 4-(4-Nitrophenylimino)-4-phenylbut-2-en-2-ol and its Ni(II) and Cu(II) Complexes as Potential Treatment for Oral and Genital Thrush

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ABSTRACT

A novel ligand (2Z)-4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol was synthesised by acid-catalysed condensation reaction in ethanol. Ni(II) and Cu(II) complexes of this ligand were also prepared. These synthesised compounds were recrystallised and dried in vacuo. They were characterised by microanalysis, magnetic moment and spectroscopy techniques. Antimicrobial tests were conducted using broth dilution method. Six organisms were tested to determine the Minimum Inhibitory (MIC) and Minimum Microbial (MMC) concentrations. In-silico inhibitory activities of the compounds against the crystal structure of *Candida albicans* protien (Als3 adhesin) were carried-out using Maestro Schrodinger Suite 13.5. Data were analysed using descriptive statistics. They exhibited characteristic $\bar{\nu}_{\text{max}}$ (cm^{-1}) of 3425-3327, 1675-1515 and 555-479 representing very broad OH due keto-enol-tautomerism, C=N + C=C and (M-N/M-O) confirming coordination to the metal ions. The λ_{max} (cm^{-1}) 23,310-14,684 revealed a d-d transition hypsochromic shift for the complexes which are corroborative of a probable six-coordinate octahedral geometry. All these are further supported by the magnetic moment susceptibility values, μ_{eff} , 2.82 B.M for the Ni(II) and 1.83 B.M for the Cu(II) complexes. The antimicrobial activities (mg/mL) were carried out against six organisms, the compounds showed better activity against *Candida albicans*. The docking score of the compounds -4.235, -5.240, -5.159; -3.662, -2.457, -2.283 and -1.586, -2.139, -1.574 together with their amino acids interaction, showed better inhibitory activities than the reference -3.284; -2.155 and -1.526. The synthesised compounds displayed better antimicrobial activities which were confirmed by their inhibition of the active site of the fungus protein on drug-design as potential treatment of oral and genital thrush especially in females.

Keywords: β -Diketone SchiffBase, Coordination, Antimicrobial Activities, *Candida albicans*, Molecular Docking.

INTRODUCTION

Several studies showed that the presence of a lone pair of electrons in a sp^2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance (Nidhi *et al.*, 2025; Mushtaq *et al.*, 2024; Raju *et al.*, 2022; Ceramella *et al.*, 2022), due to the relative easiness of preparation, synthetic flexibility, and the special property of C=N group formed through the condensation of a primary amine with an aldehyde or ketone (Patai, 2003). Schiff bases are generally excellent chelating agents, especially when a functional group like -OH or -SH is present and close to the azomethine group so as to form a five or six-membered ring with the metal ions. Versatility of Schiff base ligands and biological, analytical and industrial

applications of their complexes make further investigations in this area highly desirable.

Molecular docking technique is routinely used in modern drug discovery for understanding the drug-receptor interaction. This technique has frequently been used to predict the binding affinity and orientation of small drug molecules at the target site (Agu *et al.*, 2023; Paggi *et al.*, 2024). This docking study is accurate for structural modelling and correct prediction of activity. Macromolecular docking studies provide the most detailed possible view of drug–receptor interaction and has created a new rational approach.

Candida albicans remains a premier opportunistic fungal pathogen, largely due to its capacity to form drug-resistant biofilms and invade host tissues. Central to these virulence mechanisms is the Agglutinin-Like Sequence 3 (Als3) protein. While Als3 does not directly facilitate the mechanism of action of conventional antifungal drugs, it serves as a critical mediator of virulence and drug resistance. Consequently, Als3 has emerged as a high-priority target for novel immune-therapeutics, vaccine development, and targeted molecular inhibitors (Liu, and Scott 2011, Deng *et al.*, 2021, Edwards Jr *et al.*, 2018 and Sui *et al.*, 2017).

Molecular docking technique is routinely used in modern drug discovery for understanding the drug-receptor interaction. This technique has frequently been used to predict the binding affinity and orientation of small drug molecules at the target site. The two aims of docking studies are accurate structural modelling and correct prediction of activity. Macromolecular docking studies provides the most detailed possible view of drug–receptor interaction and has created a new rational approach (Halgren *et al.*, 2004, Friesner *et al.*, 2004, Isiaka *et al.*, 2024, Adeleke and Adegoke 2020).

Oral candidiasis is one of the most common infections of the oral mucosa. *C. albicans* that accounts for roughly half to over three-quarters of cases, with reported figures ranging from 47% to 84% (Tkaczyk *et al.*, 2025; Vila *et al.*, 2020). It usually develops when host defences or the local environment are disturbed. Wearing removable dentures, uncontrolled diabetes, poor oral hygiene, reduced salivary flow and immunosuppression are the main predisposing factors (Tkaczyk *et al.*, 2025). Genital thrush, or vulvovaginal candidiasis (VVC), similarly is also caused predominantly by *C. albicans*. Up to 75% of women experience at least one episode, and 5–10% go on to develop recurrent disease (Srb *et al.*, 2025). Hyphal transformation or morphological switching, biofilm formation and immune evasion drive its persistence at mucosal sites (Srb *et al.*, 2025).

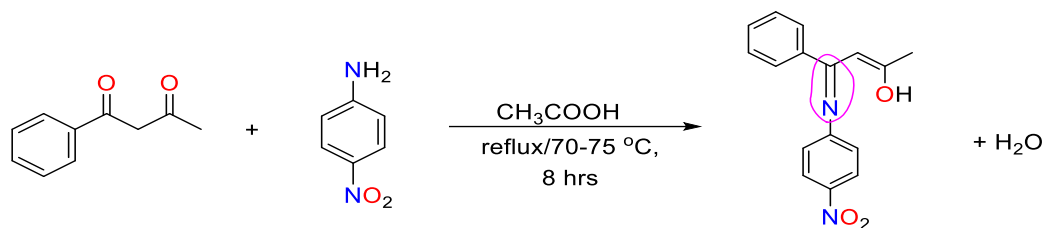
Treatment relies mainly on azole antifungals, but resistance is increasing. In one recent clinical series, *C. albicans* isolates showed up to 30% resistance to azoles, and non-albicans species exceeded 40% (Tkaczyk *et al.*, 2025). Biofilm formation further reduces susceptibility to antifungals (Bhattacharya *et al.*, 2020; Tkaczyk *et al.*, 2025). These limitations motivate the search for new antifungal scaffolds, such as Schiff bases and their metal(II) complexes.

MATERIALS AND METHODS

General Information

All starting materials for synthesis were obtained commercially as reagent grade and used as supplied. Fourier Transform Infrared (IR) spectral data were collected on a Perkin Elmer spectrometer in the range 4000 – 400 cm^{-1} . UV-Vis spectra were recorded on a Spectroquant Pharo 300 Spectrophotometer. ^1H NMR spectra was recorded with a Neo-400 MHz NMR spectrometer. A Stuart Melting Point (SMP10) apparatus was used for melting point determination. Ethylenediaminetetraacetic acid (EDTA) titrimetry was used for the percentage metal determination. Magnetic measurements were carried out using a Sherwood Magnetic Susceptibility Balance. Molecular docking was done with the extra precision (XP) mode of the Glide function of Maestro Schrödinger – with the selected protein receptors obtained from the protein data bank (PDB) website.

Preparation of 4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol, HL, and its Ni(II) and Cu(II) Complexes



4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol, HL

To a hot ethanolic (5 mL) solution of aniline (5.74 g, 0.06170 mol), a hot ethanolic (5 mL) solution of benzoylacetone (10 g, 0.06170 mol) was added dropwise with constant stirring with about three drops of glacial acetic acid. This solution was refluxed at 70-75 °C for 8 h, a yellow-coloured HL was precipitated out. It was filtered, washed with water/ethanol solvent mixture, and dried in vacuo (Adnan, 2013). Yield (71.37 %); **¹H NMR (400 MHz, DMSO-*d*₆)**: δ (ppm) 13.32 (br s, 1H, OH), 8.23 (d, *J* ≈ 9.0 Hz, 2H, Ar-H), 7.95 (m, 2H, Ar-H), 7.54–7.51 (m, 3H, Ar-H), 6.60 (d, *J* ≈ 9.0 Hz, 2H, Ar-H), 6.29 (s, 1H, CH), 2.38 (s, 3H, CH₃). **HR-MS (ESI⁺)**: calculated for C₁₆H₁₅N₂O₃, [M+H]⁺ 283.31, found 283.1077.

Synthesis of Nickel Complex of HL

(0.10 g, 5.287 mmol) of HL₁ dissolved in about 1 mL ethanol was stirred continuously for about an hour at room temperature, in which the solution (0.063 g, 2.643 mmol) of NiCl₂·6H₂O in 1 mL distilled water (M:L = 1:2) was added dropwisely. 2-3 drops of triethylamine was added to each reaction pot to raise the pH and improve the formation of the resulting precipitate. This reaction was allowed to stir for about 3 h and a yellow precipitate was filtered off, washed with ethanol and dried in vacuo.

The Cu complex of HL was prepared under the same condition procedure.

[Ni(L)₂(H₂O)₂].2H₂O; yield (84.95%); **HR-MS (ESI⁺)** calculated for C₃₂H₃₄N₄NiO₈, [M+Na]⁺ 684.34, found 685.4345; [M-4H₂O]⁺ 587.67, found 587.1894; [L₂]⁺ 562.61, found 562.104. **[Cu(L)₂(H₂O)₂].2H₂O**; yield (69.61%); **HR-MS (ESI⁺)** calculated for C₃₂H₃₄N₄CuO₈, [M+Na]⁺ 689.16, found 689.2045; [M-(H₂O)₄]⁺ 593.71, found 593.1571.

Antimicrobial Susceptibility Test (AST)

The antimicrobial screening was carried out in the Department of Pharmaceutical Microbiology, Faculty of Pharmacy, University of Ibadan. The microbial susceptibility of the free organic ligand and its Ni(II and Cu(II) complexes were assessed for their antimicrobial capacity against different pathogenic Gram-negative and Gram-positive bacterial strains and fungal strains. Six microorganisms were used in the screening using a disc diffusion test (4 bacteria and 2 fungi). This test was performed to screen and determine the compounds' potency according to their inhibition zone diameter. A mass of the culture medium (Nutrient agar and Sabouraud Dextrose agar) was weighed and dissolved in distilled water. The mixing was heated to homogenize and sterilize in an autoclave for 15 minutes, brought out to cool and was then poured into the Petri dishes to solidify. The 0.05g of the compounds were weighed and dissolved in 5mL of methanol making a concentration of 10µg/mL, from which serial dilution of two more concentrations was prepared (5µg/mL, 2.5µg/mL). Methanol solvent was used as the negative control. The common antibacterial gentamycin and the antifungal ketoconazole drugs were used as references for comparison.

A colony from a 24 hrs fresh culture of the various organisms was dissolved in 5mL of sterile distilled water which was spread on the prepared culture agar. Sizeable holes were bored on the cultured plate and the different concentrations of the compounds were added into each hole including the positive controls (Gentamycin and Ketoconazole). The Petri dishes were then incubated for 24 hrs for the bacteria and 72 hrs for fungi before the inhibition zone diameters were measured.

Protein Preparation

The protein was prepared using protein preparation wizard of the Maestro Schrodinger suite 2023-1. This was followed by active site prediction which involved and receptor grid generation preparing the active sites for docking. The software was used for the computational studies which included sample preparation, druglikeness, protein preparation, sitemap analysis, and docking. The Adsorption, Distribution, metabolism, Excretion, and Toxicity (ADME-Tox) were carried out to predict the druglikeness of the synthesised compounds. The enzyme was downloaded from the protein database, prepared, optimized, missing loops added, the active site identified, and the receptor grid generated for the binding. Docking studies of the synthesised ligand, its Ni(II) and Cu(II) complexes and the reference compound (Ketoconazole) were carried-out.

Sample Preparation

Ligand (2Z)-4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol, and reference] were prepared using ligprep module and while the complexes ($[\text{Cu}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$ and $[\text{Ni}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$) were prepared using protein preparation wizard.

Docking

The molecular docking was carried out on the prepared ligand, complexes and Als3 adhesin. This was done to get the docking scores and the compound interaction with the amino acids within the active site of the enzyme. The results were analysed using descriptive statistics.

RESULTS

Percentage Metal Analysis

The percentage metal present in the prepared compounds was determined by complexometric titration using EDTA. Both the Ni(II) and Cu(II) complexes have their percentage metal in close agreement with the theoretical values expected for the proposed structures. The results are given in Table 1.

Colour and Percentage Yield

Table 1 showed the analytical data, colours, percentage yield of the prepared ligand, its Ni(II) and Cu(II), and the room temperature magnetic moments (μ_{eff}) of the complexes. All the complexes adopt $[\text{ML}_2] \cdot n\text{H}_2\text{O}$ stoichiometry. The formation of these ligands is confirmed by IR spectroscopy. The synthesised compounds were obtained in various shades of colour different from the colours of the starting materials. The melting points of the synthesised compounds are also distinct and have sharp melting point ranges which signify the purity of the compounds.

Room Temperature Magnetic Moment Susceptibility

The room temperature magnetic moment data for all the synthesised complexes are presented in table 1. Magnetic moments are often used in conjunction with electronic spectra to gain information about the oxidation number and stereochemistry of the central metal ion in coordination complexes. For first row transition metal ions in the free ion state, i.e. isolated ions in a vacuum, all 5 of the 3d orbitals are degenerate. A simple crystal field theory approach to the bonding in these ions assumes that when they form octahedral complexes, the energy of the d orbitals are no longer degenerate but are split such that two orbitals, the $d_{x^2-y^2}$ and the d_{z^2} (e_g subset) are at higher energy than the d_{xy} , d_{xz} , d_{yz} orbitals (the t_{2g} subset). The energy gap is dependent on the position of the coordinated ligands in the Spectrochemical Series (Singh and Singh, 2012). Nickel(II) compounds of tetrahedral and octahedral geometries are usually paramagnetic with values ranging from 3.20-4.10 B.M. and 2.90-3.30 B.M (Woods *et al.*, 2009) respectively due to spin-orbit coupling of $^3A_{2g}$ and $^3T_{2g}(\text{F})$ terms. A lower moment may be due to increase in electron density around the metal which leads to reduction in orbital contribution (Osowole *et al.*, 2012). The room temperature magnetic moments of copper(II) complexes are expected to have 1.73-2.2 B.M. regardless of stereochemistry (Kolawole and Osowole, 2009).

The Ni(II) complex of the ligand had moment of 2.82 B.M. confirming the octahedral geometry. The six-coordinate octahedral geometry of the Cu(II) complex this ligand aligned with the moment value of 1.83 B.M.

Table 1: Physicochemical Data of HL and its Ni(II) and Cu(II) Complexes

Compound	Mol. wt. ($g\ mol^{-1}$)	Yield %	Colour	M.Pt($^{\circ}C$)	%Metal <i>Exp (Cal)</i>	$\mu_{eff}(BM)$
HL	282.3	71.67	Deep Yellow	116-117	-	-
[Ni(L) ₂ (H ₂ O) ₂].2H ₂ O	664.931	84.95	Yellow	126-127	8.77(8.83)	2.82
[Cu(L) ₂ (H ₂ O) ₂].2H ₂ O	669.784	69.61	Blue	146-147	9.13(9.49)	1.83

Infrared spectra of HL and its Ni(II) and Cu(II) complexes

The relevant Infrared spectra of the synthesised compounds are presented in Table 2. The HL showed an expected broad band at $3425\ cm^{-1}$ which was assigned to the intramolecular hydrogen bond of the enol tautomer $\nu(OH)$ group; its complexes showed corresponding band for Ni(II) and Cu(II) between $3427-3353\ cm^{-1}$ respectively with [Cu(L)₂(H₂O)₂].2H₂O at lowest frequency shift due to presence of coordinated water molecule. Appreciable coupling of different vibrational modes is observed in the spectrum of the compounds due to overlap of the vibrational frequencies. The uncoordinated C=N and C=C stretching vibrations in the ligand are observed as three coupled bands around $1675-1557\ cm^{-1}$ (Osohole, 2008) which eventually underwent a bathochromic shift on coordination to the metal ions. The Ni(II) complex had its vibration frequencies around 1659 and $1509\ cm^{-1}$ while Cu(II) complex had the stretching vibrations of $\nu(C=N)+\nu(C=C)$ between $1635-1509\ cm^{-1}$. These shifts indicate coordination of the metal(II) ions to the azomethine-N in the synthesised (Osohole, 2012).

Upon chelation, the intense bands observed in the IR spectrum of the ligand (HL) shifted from $1284\ cm^{-1}$ to lower range of 1275 and $1203\ cm^{-1}$ for the Ni(II) and Cu(II) complexes respectively have been assigned to $\nu(C-O)$ stretching vibrations. This bathochromic shift was an indication of stronger metal-oxygen bonds in the chelate rings due to increased electron delocalisation as a result of weaker M-N interactions (Kolawole and Osohole, 2009). The vibrational frequencies between $558-479\ cm^{-1}$ are assigned to the metal-ligand vibrations, $\nu(M-O)$ and $\nu(M-N)$ modes, evidence for the formation of M-O/M-N bonds (Omoregie and Woods, 2011). The lower this value the stronger the M-N(base) bond.

Electronic Spectra of the Ni(II) and Cu(II) Complexes of HL

The electronic reflectance spectra data for the synthesised compounds are presented in Table 3. The ultraviolet spectrum for the ligand was characterised by two absorption bands at $39,370$ and $31,447\ cm^{-1}$ assigned to $\pi\pi^*$. These bands have been shifted to longer wavelengths in its metal(II) complexes due to coordination (Kumar and Kumar, 2013). →

Nickel(II) complexes can undergo structural switches from four-coordinate square planar to tetrahedral or to six-coordinate octahedral (Sacconi, 1968). The synthesised Ni(II) phenylimine complex displayed three absorption bands at the uv region and the visible d-d transitions around $40,816-14,684\ cm^{-1}$ corroborating of a six-coordinate nickel(II) complex. These bands have been hypsochromically shifted when compared with the ultraviolet spectra transition of the ligand (Osohole *et al.*, 2015). In a cubic environment, copper(II) is susceptible to Jahn Teller distortions, giving rise to unsymmetrical or multiple bands. A maximum of three transitions are predicted in the visible spectra of octahedral complexes of copper(II). Tetrahedral copper(II) complexes rarely exist (Lever, 1980). Cu(II) complex gave two absorption bands at $23,310\ cm^{-1}$ and $14,706\ cm^{-1}$ indicating six-coordinate octahedral arrangement of $^2B_{1g}$ $^2A_{1g}$ and $^2B_{1g}$ 2E_g transitions respectively.

Table 2: Relevant IR Absorption bands (cm^{-1}) of HL and its Ni(II) and Cu(II) Complexes

Compound	$\nu(O-H)$	$\nu_{as}(C=N+C=C)$	$\nu(C-O)$	$\nu(M-N+M-O)$
HL	3425b	1675w, 1575s, 1557s	1284s	558s

$[\text{Ni}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$	3427vb	1659w, 1509s	1203s	479s
$[\text{Cu}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$	3353b	1635vw, 1509vs	1275s	555s, 498s

Table 3: Electronic Reflectance Spectral Data of HL and its Ni(II) and Cu(II) Complexes

Compound	Absorption Region (cm^{-1})	Assigned Transitions	Geometry
Ligand, HL	39,370; 31,447	$\pi \rightarrow \pi^*$	-
$[\text{Ni}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$	40,816; 38,462; 34,250	C.T./ $\pi \rightarrow \pi^*$	Octahedral
	26,455	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{P})$	
	14,684	$^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}$	
$[\text{Cu}(\text{L})_2(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$	38,462	C.T./ $\pi \rightarrow \pi^*$	Octahedral
	23,310; 14,706	d-d	

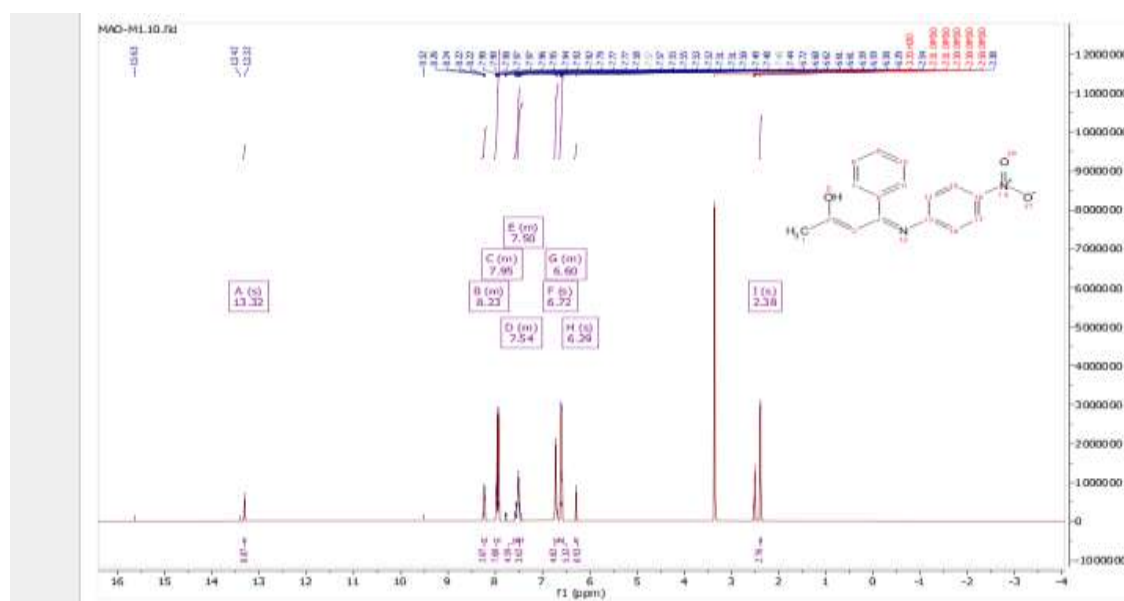


Figure 1: ^1H NMR Spectrum of (2Z)-4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol

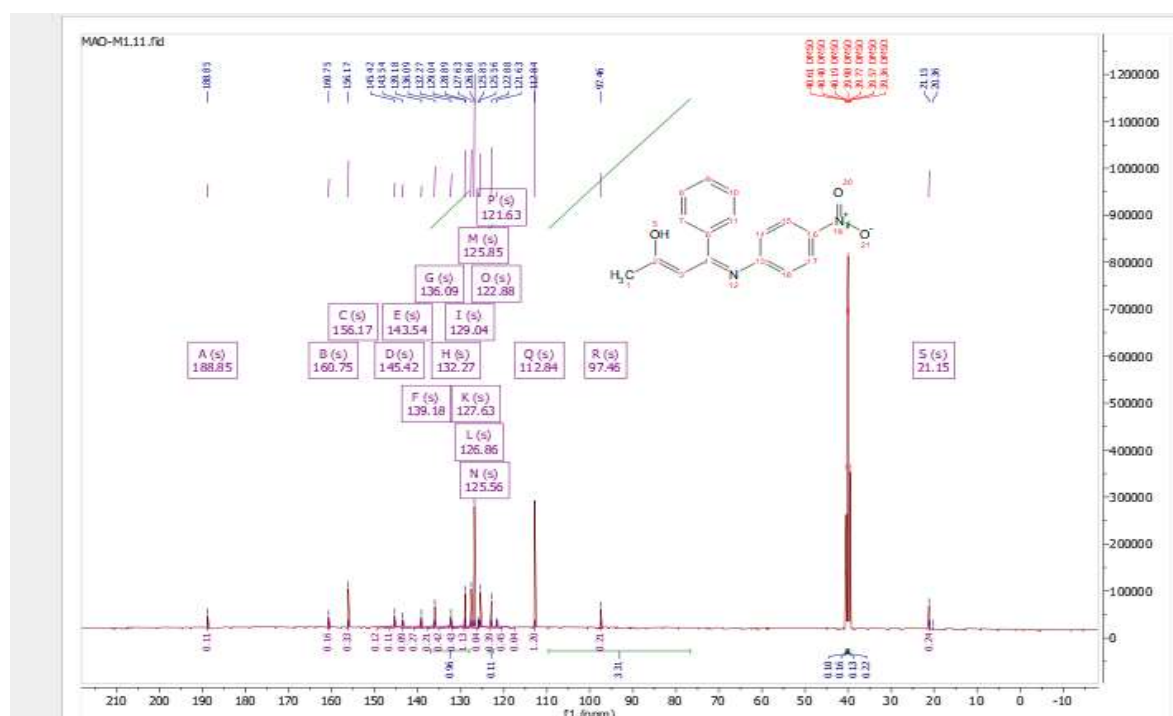


Figure 2: ^{13}C NMR Spectrum of (2Z)-4-(4-nitrophenylimino)-4-phenylbut-2-en-2-ol

Table 4: NMR Data of the Ligand

S/N	δH (ppm)	Multiplicity	Approx. J	Integral	Assignment
1	13.32	br s	—	1H	Enolic OH
2	8.23	d	~ 9.0 Hz	2H	H-2'/H-6' of p-NO ₂ -phenyl
3	7.95	m/d-like	~ 8 Hz	2H	H-2/H-6 of phenyl
4	7.54–7.51	m	~ 8 Hz	3H	H-3/H-4/H-5 of phenyl
5	6.6	d	~ 9.0 Hz	2H	H-3'/H-5' of p-NO ₂ -phenyl
6	6.29	s	—	1H	Vinylic H
7	2.38	s	—	3H	C=C–CH ₃

Antimicrobial activity of HL, its Ni(II) and Cu(II) Complexes

Figure 3 displayed the antimicrobial activity of these synthesised compounds. These compounds were subjected to antimicrobial test and confirmed that they have great activity against the micro-organism strains (*Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Aperginillus niger*). The ligand displayed an appreciable activity than some of the complexes except with *Candida albicans*.

Generally, increased activity is expected for the metal chelates and this can be explained on the basis of chelation theory (Prashanthi *et al.*, 2008). The orbital of each metal ion is made so as to overlap with the ligand orbital. Increased activity enhances the lipophilicity of complexes due to delocalization of pi-electrons in the chelate ring (Abdel-Rahman *et al.*, 2014). In some cases increased lipophilicity leads to breakdown of the permeability barrier of the cell (Cukurovali *et al.*, 2002).

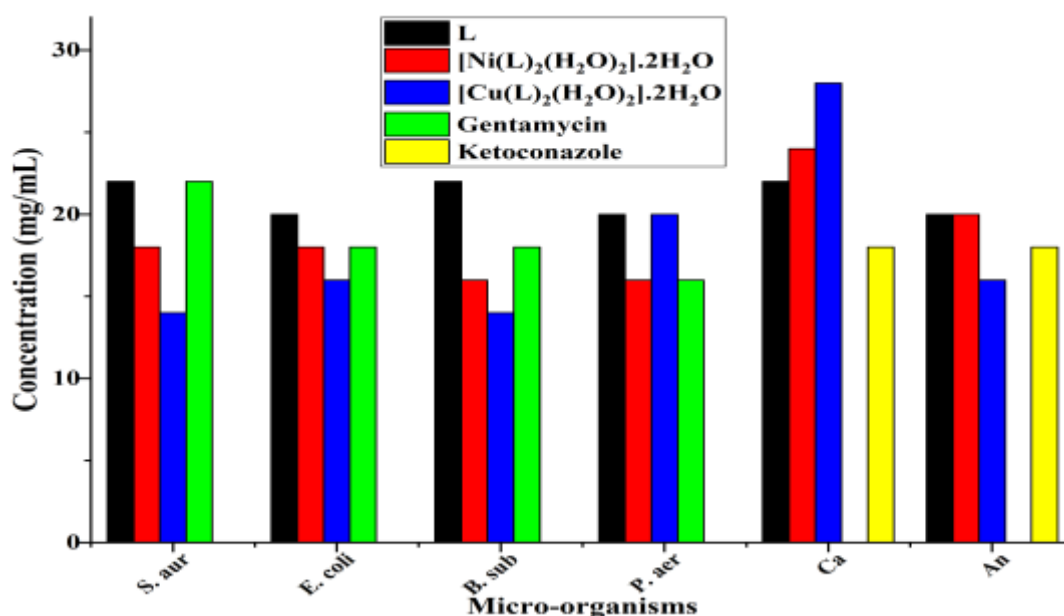


Figure 3: Chart showing the Antimicrobial Activities of the Synthesised Compounds

Sitemap Analysis

The protein displayed three active sites after the preparation. These active sites were then prepared for docking process. Two active sites predicted for 4LEB were more philic than phobic while the last one was more phobic. This means that the predicted active site will interact more with the polar components of the compounds than the non-polar components. The Dscore also showed that ligand will be better located in the

sitemap one than in other sites. This confirmed that the ligand can inhibit the adhesin of *candida albicans* better than the complexes and the reference. The ligand gave just one conformer likewise the complexes.

Table 5: Sitemapping Analysis Data

S/N	SiteScore	Size	Dscore	Volume	Phobic	Philic	Residue
1	1.074	100	1.087	279.545	0.545	1.032	ChainA: 20,21,22,23,26,27,28,119,159,160,161,165,166,167,168,169,170,182,224,225,226,293,295;
							ChainB: 3,4,5,6,7
2	0.756	47	0.732	264.796	0.251	0.906	ChainA: 18,19,21,59,60,61,62,63,64,65,81,82,83,172,174,175,269,297;
							ChainB: 6,7
3	0.577	20	0.564	57.281	0.593	0.521	Chain A: 3,4,5,6,38,39,40,43,44

Ligand Docking

The results obtained from the ligand docking showed that HL had better docking score compared to the reference Ketoconazole as shown in Table 6 below. Although the complexes have lower docking scores but could perform better once disintegrated in the living system. HL also has better amino acid interaction and hence could compete favorably for the active site with the reference.

Table 6: Sample Docking Results

Sitemap	Compound	Docking Scores
1	HL	-4.235
	[Cu(L) ₂ (H ₂ O) ₂].2H ₂ O	-0.252
	[Ni(L) ₂ (H ₂ O) ₂].2H ₂ O	-1.14
	Reference	-3.784
2	HL	-5.24
	[Cu(L) ₂ (H ₂ O) ₂].2H ₂ O	-2.584
	[Ni(L) ₂ (H ₂ O) ₂].2H ₂ O	-2.45
	Reference	-2.155
3	HL	-5.159
	[Cu(L) ₂ (H ₂ O) ₂].2H ₂ O	-2.881
	[Ni(L) ₂ (H ₂ O) ₂].2H ₂ O	-3.504
	Reference	-1.526

Drug-likeness

The drug-likeness of the synthesized ligand compared to the reference showed that the synthesized ligand has a potential of being administered orally. This was owing to its lower molecular weight, similar PSA, partition coefficient, hydrogen bond donor and acceptor etc as shown in table 7 below.

Table 7: Drug-likeness of the synthesized ligand and reference

S/N	Ligand	Mol Wt	Donor HB	Acceptor HB	QPlogPo/w	%HOA	PSA	ROF
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1	HL	282.298	1	2.75	3.258	96.083	67.985	0
2	Reference	531.438	0	8.25	4.483	95.088	68.3	1

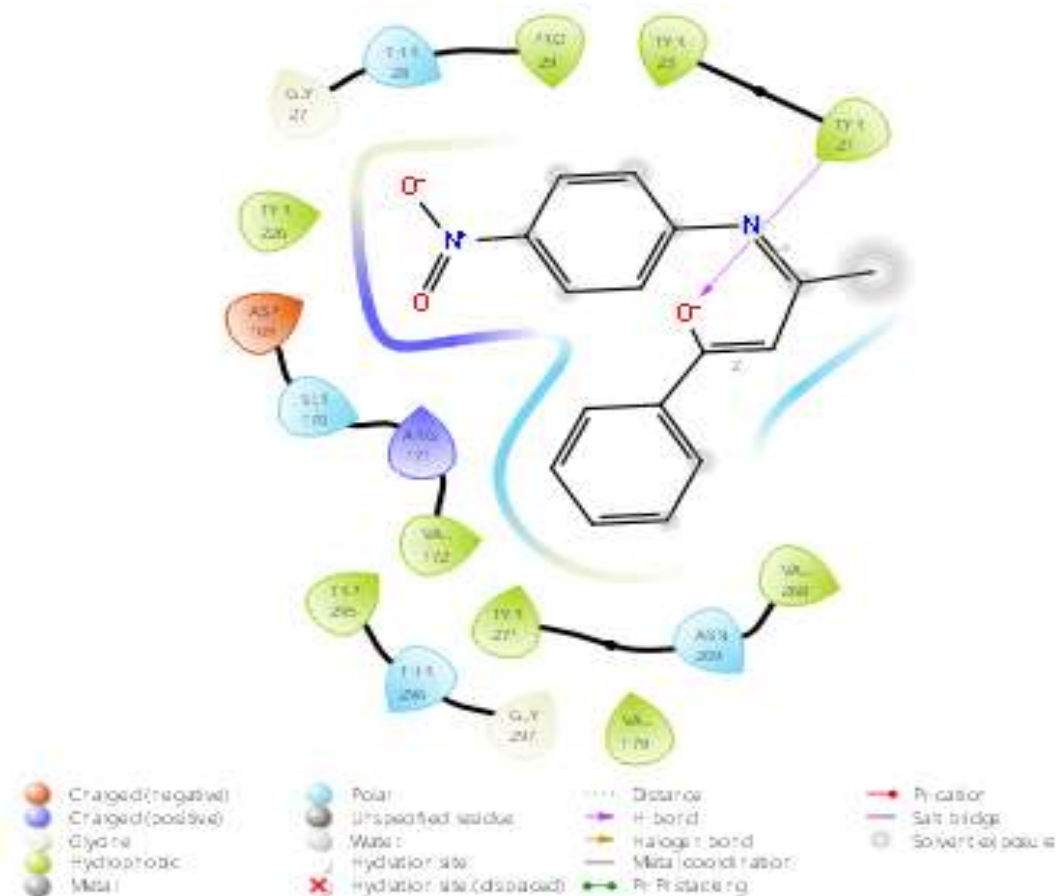


Fig 4: 2D image of HL interaction with protein

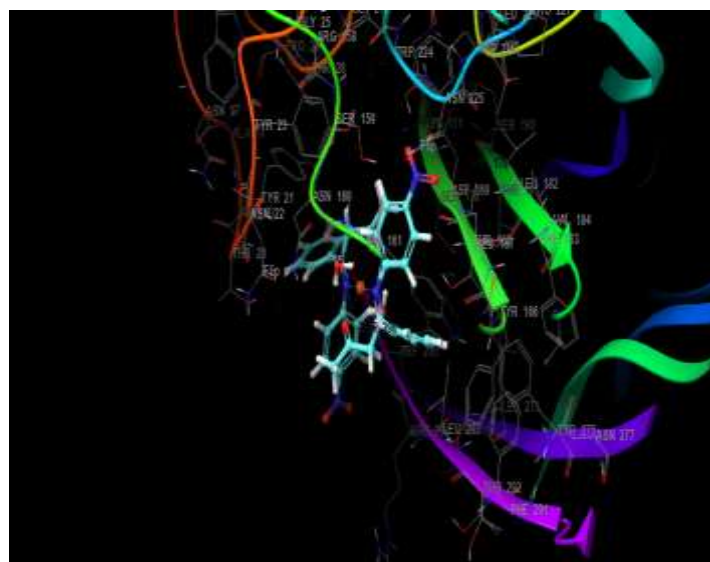
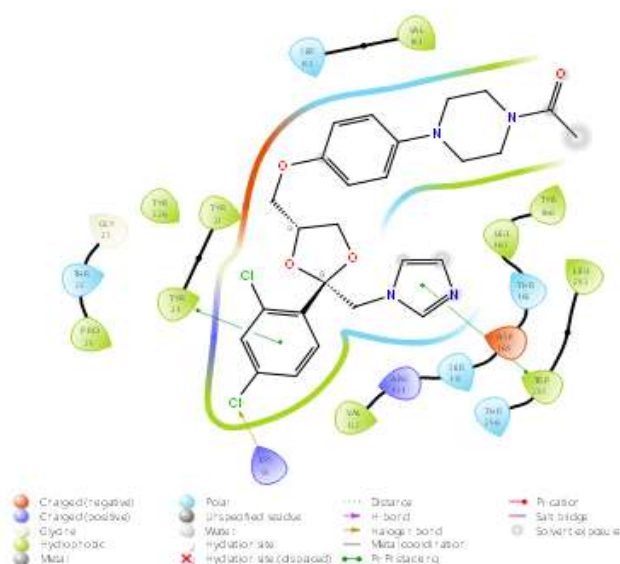


Fig 5: 2D and 3D images of Reference interaction with protein

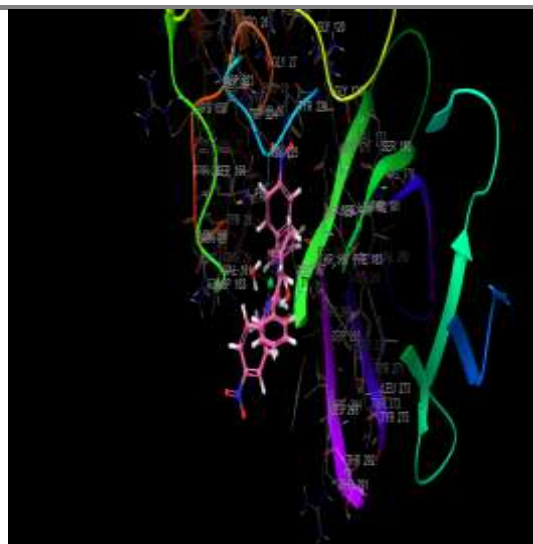
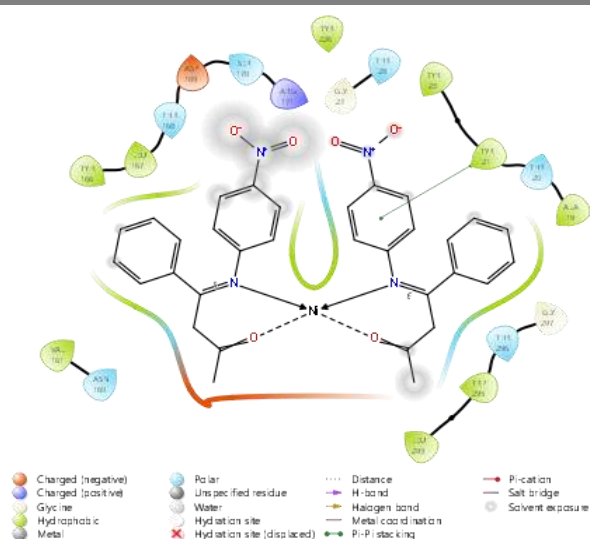


Fig 6: 2D and 3D images of Ni(II) Complex interaction with protein

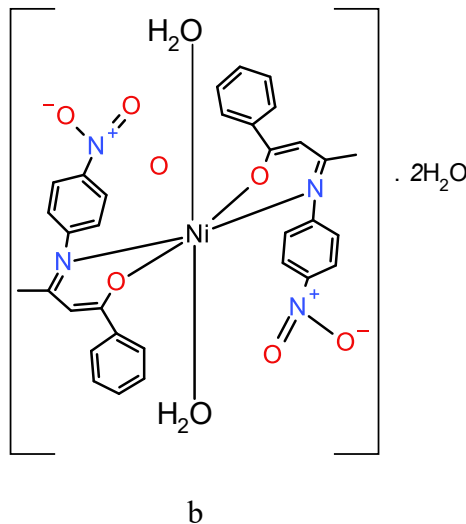
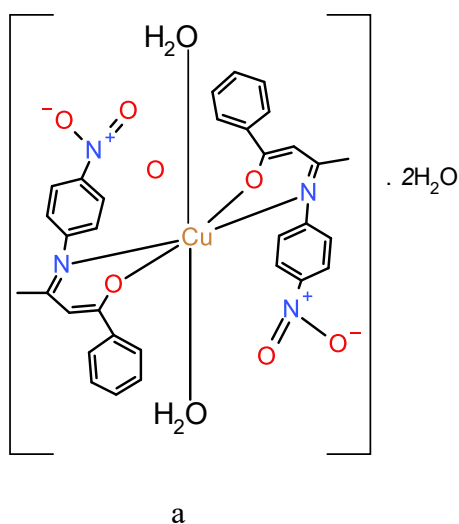


Figure 7 (a) and (b): Structures of the Synthesised Ni(II) and Cu(II) Complexes

CONCLUSION

The novel phenylimine-ligand synthesised ligand behaved as a bidentate compound which coordinated through the azomethine-N and the enolic-O with Ni(II) and Cu(II) ions resulting in complexes displaying octahedral geometry.

The compounds gave very good antimicrobial activity against six different micro-organisms tested especially *Candida albicans*. This was corroborated by the computational analysis which involves the Docking and Scoring for predicting binding affinity and specificity on *Candida albicans* adhesion active sites. However, these compounds, particularly the ligand, could be developed as potential lead compound in the production of drugs for the treatment of oral and genital thrush.

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