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Research Article

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Synthesis, crystal Structure, computational analysis, and biological evaluation of a mononuclear copper(II) Schiff base complex

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Abstract

A mononuclear copper(II) Schiff base complex, bis(2-((E)-(isobutylimino)methyl)phenoxy)copper(II), was synthesized via a one-pot condensation of salicylaldehyde and isobutylamine with copper(II) acetate. The complex was characterized by UV-Vis, FT-IR, high-resolution ESI mass spectrometry, thermogravimetric analysis (TGA), and single-crystal X-ray diffraction (SCXRD). SCXRD analysis revealed an orthorhombic crystal system (space group *Pbca*) with a distorted tetrahedral geometry ($\tau_4 = 0.431$) and a CuN_2O_2 coordination sphere. EPR spectroscopy in methanol revealed a well-resolved axial anisotropy with $g_{\parallel} = 2.1958 > g_{\perp} = 2.0538 > 2.0023$, confirming an unpaired electron in the $3d_{x^2-y^2}$ ground state and providing evidence for the distortion in geometry. The UV-Vis spectrum displayed characteristic $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, along with a ligand-to-metal charge-transfer (LMCT) band at 361 nm. FT-IR analysis confirmed the presence of an azomethine (C=N) stretch at 1620 cm^{-1} . Mass spectrometry verified the intact protonated molecular ion at $m/z = 416.1534 [\text{M}+\text{H}]^+$. TG/DTA showed high thermal stability up to 176°C , followed by a single-step thermal decomposition, leaving a 2.4% residue at 410°C . Density functional theory (DFT) calculations yielded a HOMO–LUMO energy gap (ΔE) of 2.15 eV. Hirshfeld surface analysis (HSA) identified dominant intermolecular $\text{H}\cdots\text{H}$ (79.2%) interactions. In vitro antimicrobial assays showed notable activity against bacteria (*S. aureus* and *E. coli*) and fungi (*C. albicans* and *C. tropicalis*).

Keywords: Copper(II) complex, EPR spectroscopy, Geometry index (τ_4), TD-DFT study, antimicrobial activity

1. Introduction

In 1864, Hugo Schiff described the condensation of an aldehyde with an amine to form a Schiff base [1]. These compounds, characterized by the azomethine (C=N) functional group, offer significant advantages as ligands due to their easy synthesis and coordination with diverse metal ions [2]. Schiff bases containing nitrogen (N) and oxygen (O) donor atoms serve as effective chelating agents for transition metals, often forming coordinatively saturated complexes [3]. Schiff bases derived from aromatic aldehydes are more stable than those from aliphatic aldehydes, which are more prone to decomposition and polymerization. This enhanced stability is attributed to the extended conjugation within the aromatic systems [4].

Considerable research has focused on synthesizing copper(II) complexes with coordination numbers of four to six [5, 6]. Bioinorganic interest in imine-copper complexes has grown vastly because those containing N and O donor atoms (from bidentate, tridentate, and tetradentate ligands) play vital roles in biological systems [7]. Compounds derived from aromatic aldehydes, such as 2-hydroxybenzaldehyde, exhibit strong affinity for copper [8, 9]. This chelation propensity facilitates the formation of stable, well-defined metal–ligand assemblies with diverse properties, including antibacterial [10–17], antifungal [18,19], anticancer [20–23], and cytotoxic [24–26] activities. The robust thermal stability and volatility of transition-metal Schiff base complexes make them suitable as volatile precursors for chemical vapor deposition (CVD) [27, 28].

The structural evaluation and physicochemical characterization of Schiff base metal complexes are essential steps before exploring their potential applications in the biomedical and pharmaceutical sectors [29-31]. In the pharmaceutical industry, thermogravimetric analysis (TGA) is a vital tool for evaluating thermal degradation pathways and kinetics, as

well as for drug quality assurance [32-37]. It enables rapid identification of active pharmaceutical ingredients (APIs) and can be used to optimize the final product formulation by assessing material characteristics [38-42]. Hirshfeld surface analysis (HAS) and density functional theory (DFT) calculations are employed to elucidate ligand–metal interactions and evaluate molecular reactivity [43, 44]. Studies have demonstrated that DFT can accurately compute electron distributions and predict the reactivity of bioactive complexes [45, 46].

In this study, a novel mononuclear copper(II) complex, bis(2-((E)-(isobutylimino)methyl)phenoxy)copper(II), was synthesized and thoroughly characterized. We report its structural determination by single-crystal X-ray diffraction (SCXRD), UV-Vis, FTIR, mass spectrometry, and TG/DTA analyses. Additionally, HSA and electrostatic potential (ESP) calculations were performed to elucidate key intermolecular features, and DFT calculations were used to determine the optimized geometric configurations. The complex was biologically evaluated for antimicrobial activity.

2. Experimental

2.1 Materials

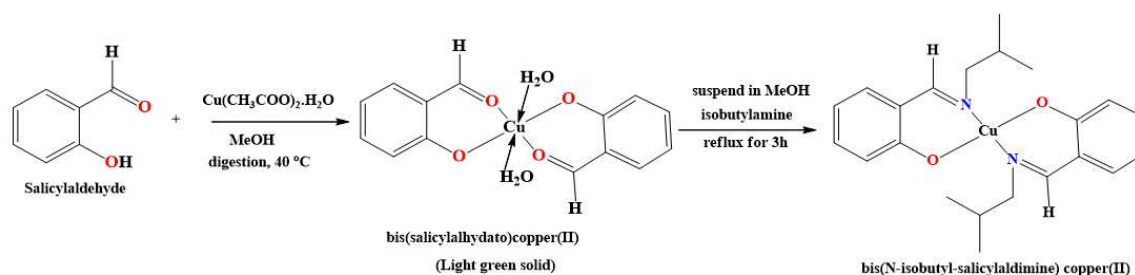
Copper acetate monohydrate (Avra, 98%), salicylaldehyde (Merck, 98%), and isobutylamine (TCI, >98%) were obtained and used without further purification in synthesizing the copper(II) complex. Solvents, including methanol and chloroform (Avra, India), were distilled before use.

2.2 Synthesis of bis(2-((E)-(isobutylimino)methyl)phenoxy)copper(II) complex

The synthesis of bis(2-((E)-(isobutylimino)methyl)phenoxy)copper(II) was carried out in two steps (Scheme 1). In the first step, the parent complex, bis(salicylaldehyde)copper(II), was prepared by mixing a methanolic solution of copper acetate (1.99 g, 0.01 mol) with

salicylaldehyde (2.5 mL, 0.02 mol) in a 1:2 molar ratio under constant stirring at room temperature. The resulting green precipitate was immediately digested for 30 minutes at 60 °C in a water bath, then filtered, washed with methanol, and vacuum dried [47].

In the second step, the parent complex (0.5 g, 0.01 mol) was suspended in 10 mL of methanol and warmed to 40 °C. Isobutylamine (1.5 mL, 0.02 mol) was added dropwise to the suspension, yielding a brown mixture. The reaction was refluxed for 6 hours, after which the solution was allowed to evaporate slowly at room temperature. After 24 hours, dark brown, needle-shaped crystals suitable for single-crystal X-ray diffraction analysis were obtained. The Schiff base metal complex was further characterized, and the spectral results are detailed below. Yield = 78% (2.981 g)



Scheme 1. Synthesis of copper(II) complex

2.3 Physicochemical characterization

The absorption spectrum was recorded on a PerkinElmer Lambda 950 UV-Vis spectrophotometer. The FTIR spectrum was obtained using a Bruker Alpha-P instrument over the 4000–400 cm^{-1} range. The mass spectrum was obtained using a Waters Xevo G2-XS QTOF mass spectrometer coupled with a Waters ACQUITY UPLC H-class system, operating in positive electrospray ionization (ESI+) mode. The X-band EPR spectra were recorded at 77 K on a JEOL JES-X3 spectrometer in frozen methanol and the parameters are, microwave frequency of 9424.685 MHz, power of 0.995 mW, field center of 329.372 mT (width ± 100.0 mT), modulation frequency of 100.0 kHz (width 0.35 mT), sweep time of 30.0s, time

constant of 0.03s, and 2 scan accumulations. Non-isothermal TG/DTA measurements were performed using a Hitachi STA7200 thermal analyzer under a dynamic argon atmosphere (flow rate: 12 dm³ h⁻¹) with a linear heating rate of 10 °C min⁻¹ over the temperature range of 40–500 °C. Surface morphology and elemental composition were analyzed using a ZEISS HR-SEM equipped with a LaB₆ source and coupled to a ZEISS smart EDX spectrometer. Bulk samples were mounted on aluminum stubs with carbon tape and analyzed at 20.00 kV. Quantitative composition was determined using an automated, standardless eZAF matrix-correction software routine.

2.4 Single-crystal X-ray diffraction study

Single-crystal X-ray diffraction data were collected on a Bruker D8 VENTURE dual-source diffractometer equipped with a PHOTON II detector, using MoK α radiation ($\lambda = 0.71073$ Å). A suitable crystal was selected with a Leica polarizing microscope, mounted on a fiber loop, and optically centered on the goniometer. Unit cell determination, data collection, and data integration were performed using the Bruker APEX4 suite [48]. A semi-empirical multi-scan absorption correction was applied using the SADABS program [48]. The structure was solved by intrinsic phasing with SHELXT [49] and refined by full-matrix least-squares on F² with SHELXL-2018/3 [50, 51], integrated within the WinGX interface [52]. Geometric calculations were performed using PLATON [58], and molecular graphics were generated using ORTEP-3 [53]. All hydrogen atoms were placed in geometrically idealized positions and refined with isotropic thermal parameters.

2.5 Computational Studies

All calculations were performed using the Gaussian 09 program package, with GaussView used for visualization. Ground-state geometries were fully optimized using the hybrid B3LYP functional in combination with the 6-311G(d,p) basis set for non-metal atoms (C, H, N, and O) and the LanL2DZ effective core potential (ECP) for the copper (Cu) center.

Frequency calculations were performed on the optimized structures to ensure the absence of imaginary frequencies, confirming that the structures are true global minima. Excited-state properties were subsequently determined via time-dependent density functional theory (TD-DFT) at the same level of theory [54]. To account for solvation effects, both DFT and TD-DFT calculations employed the conductor-like polarizable continuum model (CPCM) with dimethyl sulfoxide (DMSO) as the solvent. The fractional contributions of molecular fragments to the molecular orbitals were determined using GaussSum [55]. Hirshfeld surface analysis and 2D fingerprint plots were generated from the experimental crystallographic information file (CIF) data using CrystalExplorer [56]. Harmonic vibrational frequency calculations confirmed that the optimized geometry of the copper(II) complex is a true local minimum on the potential energy surface, as no imaginary frequencies were observed; the resulting thermochemical parameters are detailed in Table S1.

2.6 Biological studies

The antimicrobial activity of the Cu(II) complex was evaluated using the agar well diffusion method against *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923), *Candida albicans* (ATCC 10231), and *Candida tropicalis* (ATCC 4563). Four concentrations (100-400 µg/mL) of the test compound in 20 µL of dimethyl sulfoxide (DMSO) were evaluated against *S. aureus* and *E. coli*. Bacterial cultures were inoculated into sterile nutrient broth and incubated for 24 h. Sterile Mueller-Hinton Agar (MHA) plates were prepared and allowed to solidify. The standardized inoculum (0.1%) of each test organism was standardized to a 0.5% inoculum and spread uniformly over the agar surface using sterile swabs. Subsequently, 6-mm wells were aseptically bored into the agar. Each well was filled with 20 µL of the respective concentration, and the plates were incubated at 37 °C for 24 h. Antibacterial efficacy was determined by measuring the diameter of the clear zones of

inhibition surrounding the wells in millimeters. Results were compared with the positive control (Streptomycin) and the negative control (DMSO) [57].

For antifungal activity testing, fluconazole and DMSO served as the positive and negative controls, respectively. Following the same well diffusion protocol, *C. tropicalis* and *C. albicans* were cultured in Sabouraud dextrose (SD) broth for 24–48 h. Standardized fungal inocula were spread across sterile SD agar plates, and 6-mm wells were prepared under aseptic conditions. After loading 20 μ L of the test solution into each well, the plates were incubated at 37 °C for 48 h. The antifungal effect was quantified by measuring the clear inhibition zones around the wells, and all data were compared to the established controls [58].

3.0 Result & Discussion

3.1 Absorption spectral analysis

The electronic transitions of the copper(II) complex were investigated using UV-Vis spectroscopy. As shown in the absorption spectrum (Fig. 1), the first set of bands at 225, 240, and 270 nm are attributed to intra-ligand $\pi \rightarrow \pi^*$ transitions originating from the conjugated aromatic rings [59]. The third band at 301 nm arises from $n \rightarrow \pi^*$ transitions involving the non-bonding lone pairs of the azomethine nitrogen atoms ($C=N$) [60]. Additionally, the broader, well-defined absorption band observed at 361 nm is assigned to a ligand-to-metal charge transfer (LMCT) transition of the Cu(II) Schiff base complex [61].

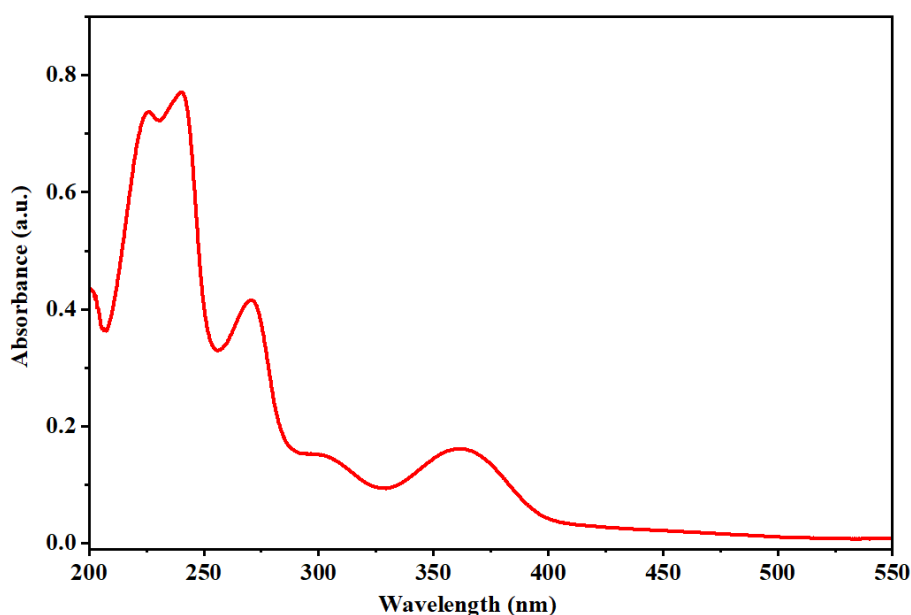


Fig. 1 Electronic absorption spectrum of copper(II) complex recorded in methanol solvent.

3.2 FTIR spectrum of Cu(II) complex

The FTIR spectrum (Fig. 2) of the synthesized complex shows a sharp peak at 1620 cm^{-1} , corresponding to the $\nu(\text{C}=\text{N})$ stretch. This confirms successful condensation and coordination of the azomethine group, forming a metal-ligand framework through the imine nitrogen [62]. The absence of prominent bands above 3000 cm^{-1} indicates complete deprotonation and coordination of the phenolic hydroxy ($\text{Ph}-\text{OH}$) group from the salicylaldehyde precursor. Weak bands at 2990 cm^{-1} are attributed to aromatic and aliphatic $\text{C}-\text{H}$ stretching [63]. The phenolic $\text{C}-\text{O}$ stretch appears at 1192 cm^{-1} . Furthermore, new metal-ligand bands at 527 and 575 cm^{-1} are assigned to $\nu(\text{Cu}-\text{O})$ and $\nu(\text{Cu}-\text{N})$ stretching, respectively.

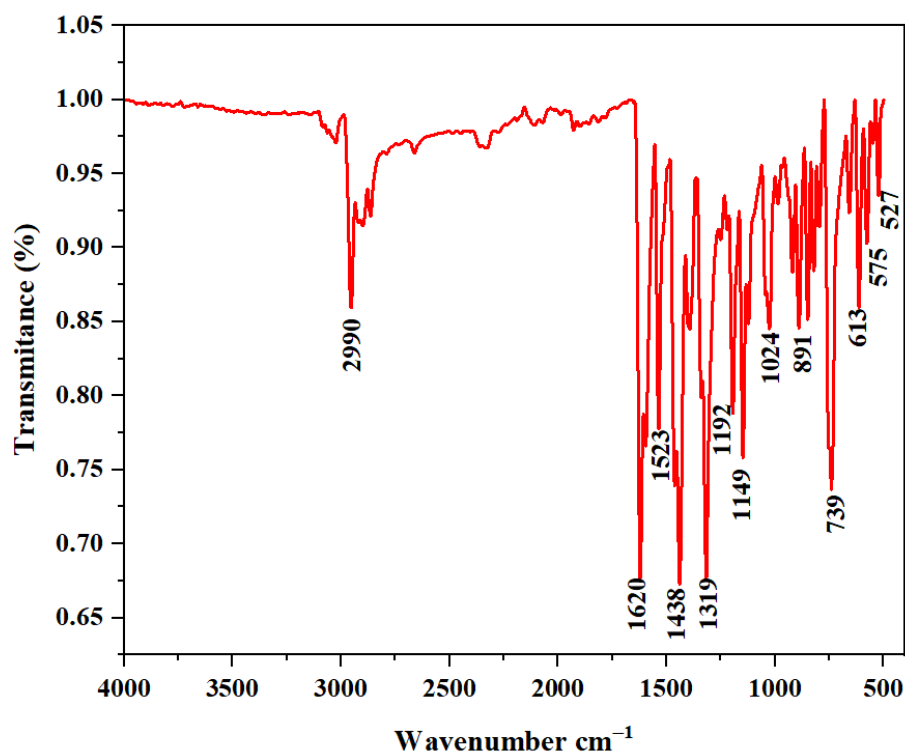


Fig. 2 FTIR spectrum of Cu(II) complex

3.3 Mass spectral analysis of Cu(II) complex

This high-resolution mass spectrum (Fig. S1) illustrates the in-source fragmentation pattern of the copper(II) complex, with peak intensities reflecting the relative stabilities of the coordinated ligands and their fragments. The protonated molecular ion $[M+H]^+$ peak is observed at m/z 416.1534, in excellent agreement with the theoretical mass of 415.14 calculated for $C_{22}H_{30}N_2O_2Cu$. A characteristic isotopic (^{65}Cu) cluster appears at m/z 418.1519. A peak at m/z 178.1228 is attributed to the in situ-generated ligand fragment $[L+H]^+$ (N-isobutyl-salicylalimine), while a minor signal at m/z 239 is assigned to the fragment $[ML]^+$. Furthermore, a peak at m/z 438.1351 confirms the formation of the sodium adduct $[M + Na]^+$ [64].

3.4 EPR studies on Cu(II) complex

The X-band electron paramagnetic resonance (EPR) spectroscopy of the Cu(II) complex (d^9 , $S = 1/2$) was recorded in methanol solution at 77 K to investigate the coordination geometry and electronic structure. The EPR spectrum (Fig. 3) shows well-defined axial anisotropy [65], allowing precise determination of principal g-tensor components ($g_{\parallel} = 2.1958$ and $g_{\perp} = 2.0538$). The tensor relationship $g_{\parallel} > g_{\perp} > 2.0023$ indicates a ground-state electronic configuration where the unpaired electron resides predominantly within the copper $d_{x^2-y^2}$ orbital ($^2B_{ig}$ spectroscopic state) [66]. The increase in directional g-values combined with the characteristic axial line shape confirms a distorted tetrahedral geometry around the Cu(II) ion, which is typical for bis-chelated Schiff base complexes with bulky alkyl substituents.

Both directional g-values exhibit a positive shift from the free electron value ($g_e = 2.0023$) due to the expected spin-orbit coupling mixing from low-lying excited states. Within the Cu(II) coordination geometry, the $g_{\parallel}$ factor is a reliable probe to evaluate the nature of the

metal-ligand bond; a value significantly under the purely ionic threshold of 2.30 (here, $g_{\parallel} = 2.1958$) reflects substantial covalent character in the Cu-N and Cu-O bonds [65]. Further, the calculated effective magnetic moment ($\mu_{\text{eff}} = 1.78$ BM, calculated at a frequency = 9424.685 MHz and a field of 320.34 mT), derived using the average tensor value of $g_{\text{avg}} = 2.10$, aligns well with the standard experimental range of 1.75 to 2.20 BM observed for mononuclear Cu(II) complexes [67,68].

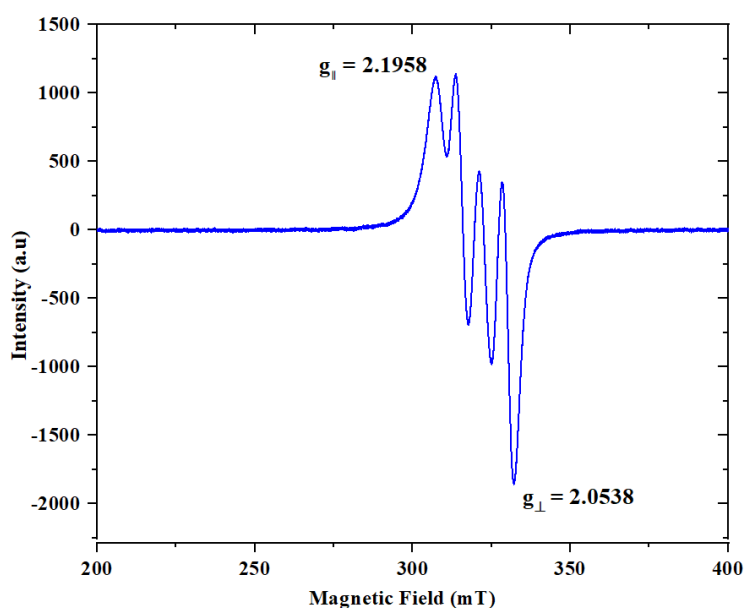


Fig. 3. The X-band EPR spectrum of the Cu(II) complex recorded in methanol solvent at 77 K ($\nu = 9424.68$ MHz). The annotated principal tensor components ($g_{\parallel} = 2.1958$ and $g_{\perp} = 2.0538$) showcase an axially symmetric, distorted tetrahedral coordination sphere.

3.5 Thermogravimetric analysis (TGA)

The simultaneous TG/DTA pattern of the copper(II) complex, recorded over a temperature range of 40 – 420 °C under a dynamic argon atmosphere, is illustrated in Fig. 4. The TG curve remains at a plateau up to 176 °C with a negligible mass loss of only 1.5%, demonstrating high thermal stability. The absence of any weight loss step below 150 °C

indicates that no lattice or coordinated water molecules are present in the copper(II) complex. This observation is strongly corroborated by the DTA curve, which exhibits no endothermic peaks within this temperature range. The higher thermal stability of the complex is attributed to the effective coordination of the azomethine nitrogen atom (C=N) to the metal center. The exclusion of aqua-ligand coordination can be ascribed to the steric hindrance imposed by the bulky isobutyl moieties [69]. Beyond the stable plateau, the complex undergoes a sharp, single-step thermal decomposition from 176 – 317 °C, corresponding to a major mass loss of 94.8% and leaving a 3.7% residue at 317 °C. Continuous heating up to 410 °C results in a final stable residue of 2.4%, which is assigned to a carbonaceous residue [58], as observed in structurally related complexes. Additionally, the sharp endothermic peak observed in the DTA curve confirms that the complex exhibits a well-defined melting point in the range of 161–163 °C prior to decomposition.

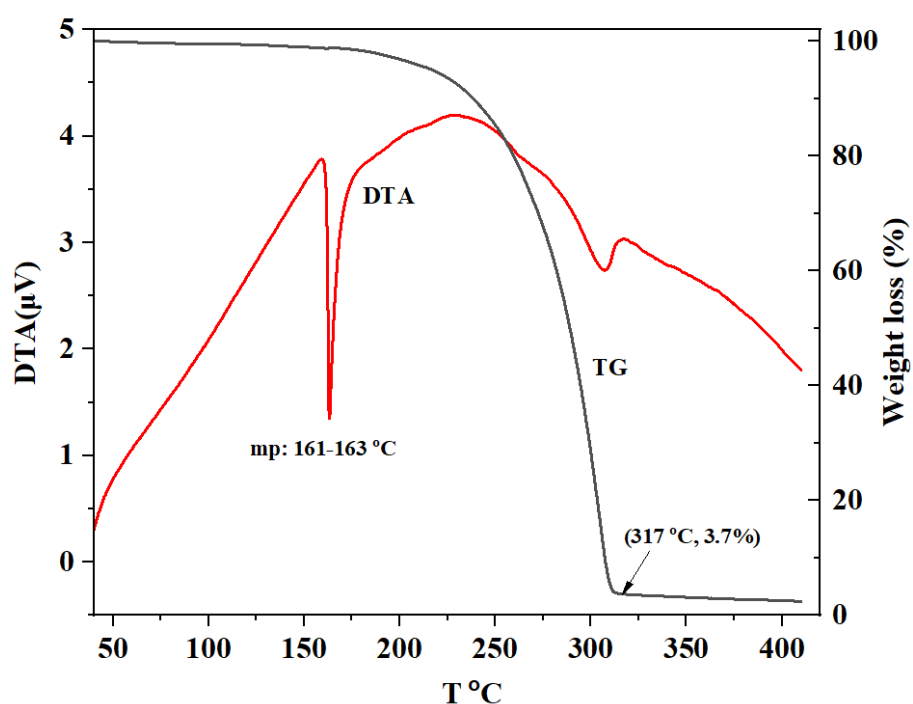


Fig. 4. Simultaneous TG/DTA of copper(II) complex recorded at a linear heating rate of 10 °C/min under an argon flow rate of 12 dm³ h⁻¹.

3.6 Crystal structure description (SCXRD)

Single-crystal X-ray diffraction analysis reveals that the mononuclear copper(II) complex crystallizes in the orthorhombic system in space group *Pbca*, with one complete molecule constituting the asymmetric unit ($Z = 8$). The copper(II) complex is formed by bidentate coordination of the imine nitrogen (N) and phenolic oxygen (O) atoms from two mono-anionic Schiff base ligands, resulting in a four-coordinate CuN_2O_2 coordination sphere. The crystal data are summarised in Table 1 and selected bond lengths and angles are listed in Table 2, and the corresponding ORTEP diagram of the complex is shown in Fig. 5. The complex features a distorted-tetrahedral geometry around the Cu(II) center, coordinated by two oxygen atoms [O(1) and O(2)] and two imine nitrogen atoms [N(1) and N(2)] from the symmetry-independent Schiff base ligands. The ligands adopt a *cis* orientation, resulting in a characteristic butterfly-like molecular conformation as shown in Fig. 6. This arrangement is further stabilized by strong intramolecular $\text{C-H}\cdots\text{O}$ hydrogen-bonding interactions, as illustrated in Fig. 7. The lipophilic, bulky isobutyl groups of both ligands are oriented on the same side of the molecule (*cis* to each other).

To quantify the structural deviation of the four-coordinate copper center from the standard polyhedron, the geometry deviation index (τ_4) [70] was calculated from the two largest valence angles: $\text{N}(1)\text{--Cu}(1)\text{--N}(2) = 150.43(16)^\circ$ and $\text{O}(2)\text{--Cu}(1)\text{--O}(1) = 148.74(15)^\circ$. The resulting τ_4 value of 0.43 confirms a distorted tetrahedral coordination environment around the copper(II) center. This geometry arises from severe steric clashing induced by the bulky *N*-isobutyl substituents, which forces a pronounced flattening twist out of the chelate plane. This structural distortion rationalizes the observed electronic properties in EPR spectrum recorded in methanol, where the elevated $g_{\parallel}$ parameter (2.1958) and axial tensor line shape serve as evidence for this distorted tetrahedral geometry. The $\text{Cu}(1)\text{--O}(2)$ and $\text{Cu}(1)\text{--O}(1)$ bond lengths are 1.879(3) and 1.884(3) Å, respectively, while the $\text{Cu}(1)\text{--N}(1)$ and $\text{Cu}(1)\text{--N}(2)$

bond lengths are 1.962(4) and 1.968(4) Å. These bond distances are intermediate between single and double bonds, indicating electronic delocalization throughout the molecular structure, as reported for related copper(II) complexes [71], often driven by unequal occupation of the metal *d*-orbitals.

The observed bond angles of 127.0(5)° [C(6)-C(7)-N(1)] and 127.1(5)° [C(17)-C(18)-N(2)] are consistent with the expected *sp*² hybridization of the azomethine carbon atoms. The presence of electron-donating isobutyl groups attached to the nitrogen atoms increases the electron density on the donor atoms via inductive effects or hyperconjugation [72]. The Schiff base ligand frame displays a high degree of planarity, as evidenced by the small torsion angle of 3.0(8)° for C(1)-C(6)-C(7)-N(1), indicating extended π -electron delocalization across the entire aromatic core. Concurrently, the imine groups maintain a strictly trans geometry across the core double bonds, with a C(6)-C(7)-N(1)-C(8) torsion angle of 179.9(4)°. To quantify the spatial layout of the peripheral framework, the single-bond conformations anchoring the alkyl groups were evaluated; torsion angles of 116.2(5)° for C(9)-C(8)-N(1)-C(7) and 117.8(5)° for C(20)-C(19)-N(2)-C(18) confirm a gauche (GA) conformation [73], indicating that the bulky isobutyl groups project prominently out of the principal azomethine plane.

The structural integrity and specific spatial conformation of the copper(II) complex are further reinforced by prominent non-classical intramolecular hydrogen-bonding interactions. As depicted in Fig. 7, the aliphatic protons of the N-isobutyl groups engage in cross-ligand interactions with the coordinated phenolate oxygen centers of the opposing ligand arm, forming well-defined C(8)–H(8B)⋯O(2) and C(19)–H(19B)⋯O(1) bridges. These intramolecular contacts exert an attractive force that holds the bulky alkyl substituents in a tight cis arrangement. This cooperative clamping effect not only mechanically locks the

butterfly-like conformation of the complex but also assists the pseudo-Jahn–Teller effect in driving the significant structural flattening observed at the four-coordinate copper(II) core.

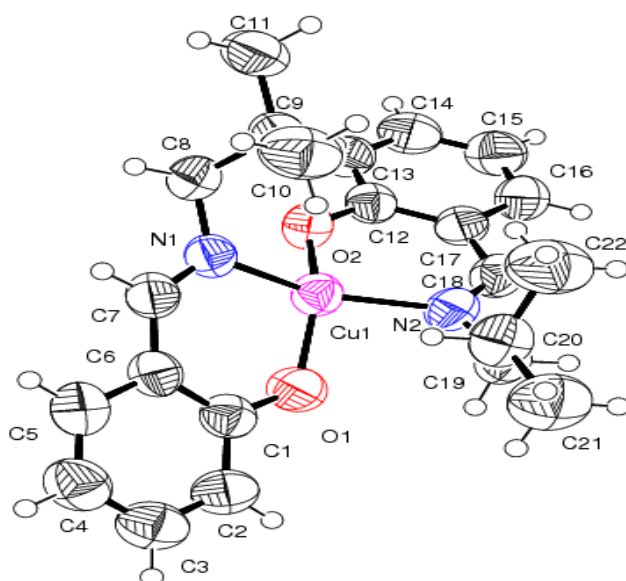


Fig. 5. The ORTEP diagram of the Cu(II) complex drawn using thermal ellipsoids constructed with 50% probability.

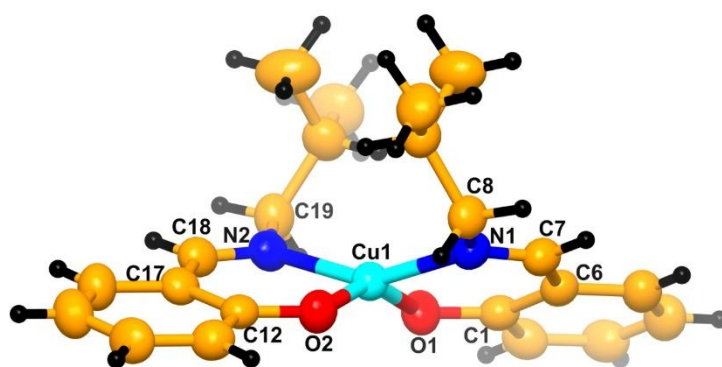


Fig. 6. The *cis*-oriented, butterfly-like molecular conformation of the copper(II) complex.

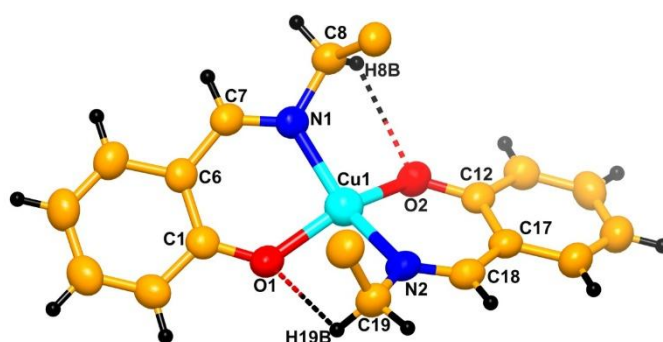


Fig. 7. The core of the complex showing intramolecular C–H $\cdots$ O hydrogen-bonding interactions. Methyl groups on the iso-butyl substituents are omitted for clarity.

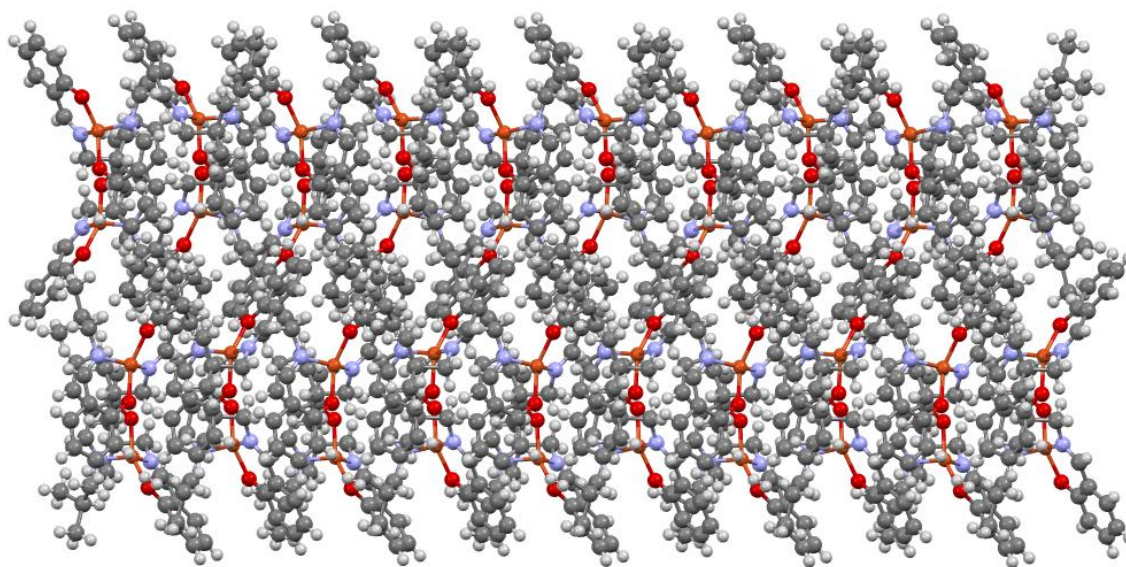


Fig. 8. Supramolecular crystal packing diagram of the copper(II) complex showing the alternating polar metallacycle networks and interlocked hydrophobic isobutyl bilayers.

The crystal packing diagram (Fig. 8) reveals an alternating layered architecture within the orthorhombic lattice. The molecules assemble into parallel columns, with the polar CuN₂O₂ coordination cores and aromatic rings aligning to form stabilized channels. Projecting outward, the bulky, lipophilic N-isobutyl side chains interlock in a "zipper-like" interdigitation, creating hydrophobic bilayers that segregate the polar rows. This packing efficiently stabilizes the three-dimensional matrix through a combination of van der Waals interactions and close hydrophobic contacts (Fig. 8), without trapping any lattice solvent.

Table 1. Crystal data of copper(II) complex

Crystal data	
Empirical formula	C ₂₂ H ₂₈ CuN ₂ O ₂
Formula weight	416.00
Temperature	296(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions (Å)	a= 18.5741(4) b= 9.9640(2) c= 23.0778(5)
Volume(Å ³)	4271.06(16) Z
Z	8
Density (calculated) Mg/m ³	1.294
Absorption coefficient(mm ⁻¹)	1.577
F (000)	1752
Crystal size (mm ³)	0.159 x 0.058 x 0.032
Theta range for data collection	4.511 to 66.987°
Index ranges	-22<=h<=22, -11<=k<=11, -27<=l<=27
Reflections collected	55781
Independent reflections	3796 [R(int) = 0.0926]
Completeness to theta	66.987° 99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7453 and 0.6480
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3796 / 0 / 249
Goodness-of-fit on F^2	1.159
Final R indices [I>2sigma(I)]	R1 = 0.0565, wR2 = 0.1482
R indices (all data)	R1 = 0.1007, wR2 = 0.2166

Extinction coefficient	0.00071(18)
Largest diff. peak and hole	0.492 and -0.593 e.Å ⁻³

Table 2. Selected bond lengths [Å] and angles [°] for the copper(II) complex.

Bond length [Å]	Experimental		Theoretical	
Cu(1)–O(2)	1.879(3)		1.947	
Cu(1)–O(1)	1.884(3)		1.947	
Cu(1)–N(1)	1.962(4)		2.010	
Cu(1)–N(2)	1.968(4)		2.010	
C(7)–N(1)	1.285(6)		1.290	
C(18)–N(2)	1.291(6)		1.290	
C(1)–O(1)	1.319(6)		1.300	
C(12)–O(2)	1.319(5)		1.940	
Bond angles [°]	Experimental		Theoretical	
O(2)–Cu(1)–O(1)	148.74(15)		154.48	
N(1)–Cu(1)–N(2)	150.43(16)		159.47	
O(1)–Cu(1)–N(1)	94.83(15)		92.32	
O(2)–Cu(1)–N(2)	94.29(15)		92.32	
O(2)–Cu(1)–N(1)	93.77(14)		92.18	
O(1)–Cu(1)–N(2)	92.88(16)		92.18	
C(7)–N(1)–Cu(1)	123.3(3)		123.73	
C(18)–N(2)–Cu(1)	123.2(3)		123.73	
C(1)–O(1)–Cu(1)	127.5(3)		129.03	
C(12)–O(2)–Cu(1)	128.8(3)		129.03	
C(6)–C(7)–N(1)	127.0(5)		127.94	
C(17)–C(18)–N(2)	127.1(5)		127.94	
Torsion angles [°]				
C(1)–C(6)–C(7)–N(1)	3.0(8)	C(9)–C(8)–N(1)–C(7)	116.2(5)	
C(6)–C(7)–N(1)–C(8)	179.9(4)	C(20)–C(19)–N(2)–C(18)	117.8(5)	

3.7. Morphological and Elemental Composition Studies (SEM-EDX)

To investigate the bulk surface topography, grain boundaries, and elemental contributions of the Cu(II) complex, high-resolution scanning electron microscopy (HR-SEM) was performed. The SEM micrographs detailing the morphology at various magnification levels are presented in Fig. 9 and b. At medium magnification (Fig. 9a), the complex displays a microcrystalline surface dominated by large, well-defined, flat crystalline blocks, decorated with finer micrometer-sized particulate clusters that adhere tightly to the surface. The high-magnification image (Fig. 9b) reveals that the bulk powder consists of highly homogeneous, aggregated submicron particles with smooth, round grains. The structural homogeneity indicates a uniform crystallization pathway during the one-pot synthesis, confirming that the bulk materials maintain a consistent phase matching the discrete SCXRD geometry.

The corresponding EDX spectrum (Fig. S2) recorded at an accelerating voltage of 20.00 kV confirms the elemental composition and phase purity of the bulk sample. It shows the main constituent elements of the Cu(II) complex, exhibiting sharp, well-defined characteristic X-ray emission lines for carbon (K_{α} at ~ 0.28 keV), nitrogen (K_{α} at ~ 0.39 keV), oxygen (K_{α} at ~ 0.52 keV), and copper (L_{α} at ~ 0.93 keV and K_{α} at ~ 8.04 keV). The quantitative eZAF [74] analysis results are summarized in Table 3. The empirical bulk elemental distribution yielded values of 73.9 wt% (82.7 at%) for carbon, 8.4 wt% (8.0 at%) for nitrogen, 8.7 wt% (7.3 at%) for oxygen, and 9.0 wt% (1.9 at%) for copper. No additional X-ray peaks from elemental impurities or residual starting agents were detected within the instrument's sensitivity limits. Therefore, the homogeneous distribution of all four elements confirms the phase purity and bulk quality of the Cu(II) complex.

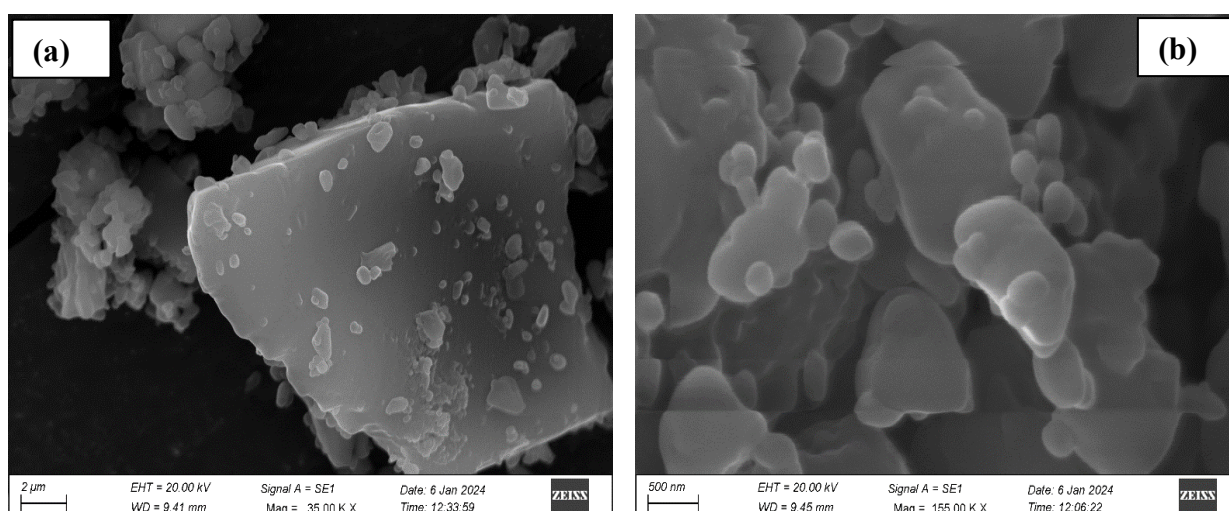


Fig. 9. The HR-SEM micrographs of the Cu(II) Schiff base complex: (a) overview of microcrystalline blocks at 35,000X (2 μ m), and (b) close-up view showing aggregated sub-micron grains at 155,000X (500 nm).

Table 3. EDX elemental quantification for the Cu(II) complex

Element Line	Weight %	Atomic %	Net Intensity
C K	73.9	82.7	1391.7
N K	8.4	8.0	54.1
O K	8.7	7.3	144.6
Cu K	9.0	1.9	333.2
Total	100.0	100.0	

3.8 Hirshfeld Surface Analysis (HSA)

To transition from the discrete internal geometry of the Cu(II) complex to its macroscopic assembly, the spatial boundaries and packing forces of the crystal lattice were evaluated. While SCXRD maps the specific atom-to-atom coordinates of the symmetric unit, it does not describe the cooperative, non-covalent forces responsible for crystal packing. Therefore, to quantitatively map the nature, distribution, and relative strength of the intermolecular interactions governing the crystal packing of the mononuclear copper(II) complex, Hirshfeld surface analysis (HSA) was performed using CrystalExplorer. The calculations were carried out directly on the experimental crystallographic data imported from the refined structural CIF file.

The calculated Hirshfeld surface volume of the asymmetric unit is 782.31 $\text{\AA}^3$, and the corresponding surface area is 551.79 $\text{\AA}^2$. The spatial arrangement shows a structural asphericity (Ω) of 0.744 and a globularity factor (G) of 0.616, reflecting a moderately stretched, anisotropic molecular profile consistent with the highly distorted, cis-oriented,

butterfly structure of the complex. The normalized contact distance (d_{norm}) surface map was generated using a standardized colour scale ranging from -1.6706 au (red) to -0.2862 au (blue), where red zones identify contacts shorter than the sum of the atomic van der Waals radii, blue zones highlight long-distance isolations, and white patches represent equilibrium boundaries matching standard van der Waals separations (Fig. S3). Distinct red spots visible on the d_{norm} surface map correspond primarily to close contacts of non-classical intramolecular C–H $\cdots$ O hydrogen bonds that mechanically anchor the bulky alkyl side chains. Concurrently, the curvature map exhibits broad green patches separated by thin blue boundaries, indicating a lattice environment dominated by close, soft hydrophobic stacking and well-filled alkyl shell interfaces.

To determine the contribution of individual reciprocal interatomic contacts to bulk crystal packing, the total Hirshfeld surface was deconvoluted into two-dimensional (2D) fingerprint plots, with d_i and d_e spanning 0.8929 to 2.70 Å (Fig. 10). Quantitative analysis shows that packing is dominated by H $\cdots$ H interactions, which account for 79.2% of the total Hirshfeld surface. In the 2D matrix, this interaction appears as a prominent, sharp central spike that splits symmetrically at the base, down to a closest approach of $d_i \approx d_e \approx 0.9$ Å, a profile characteristic of densely packed, interlinked aliphatic chains in the peripheral isobutyl moieties. The next most significant contributors are the combined C $\cdots$ H/H $\cdots$ C contacts, which make up 17.3% of the surface. These interactions appear as a pair of reciprocal side wings, representing close spatial contacts between the π -clouds of the aromatic phenolate rings and neighbouring aliphatic protons. The polar O $\cdots$ H/H $\cdots$ O contacts account for a minor 2.9%, appearing as sharp, symmetric low-distance tracks that underpin the non-classical hydrogen-bonding framework. Other individual atom-to-atom contacts (such as C $\cdots$ C, N $\cdots$ N, and O $\cdots$ O) contribute negligibly to the overall surface area, confirming that bulk lattice stability is driven primarily by a dense network of nonpolar van der Waals forces and hydrophobic interlinks.

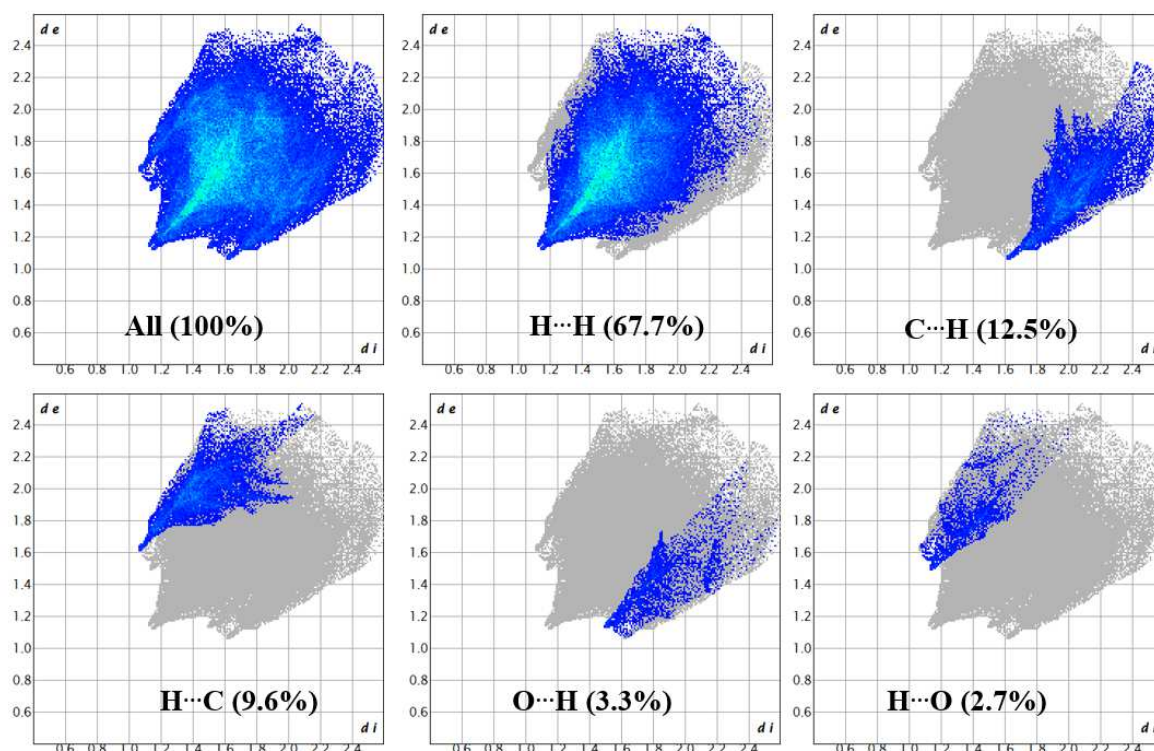


Fig. 10. Two-dimensional (2D) fingerprint plots showing the total and individual deconvoluted intermolecular contacts H $\cdots$ H, C $\cdots$ C, C $\cdots$ H, H $\cdots$ C, O $\cdots$ H, and H $\cdots$ O for the Cu(II) complex.

3.9 Frontier Molecular Orbital (FMO) Analysis

The DFT-optimized structure (Fig. S4) shows excellent spatial correlation with the single-crystal X-ray diffraction structure. The calculated geometric parameters show good agreement with the experimental values obtained from SCXRD (Table 2). The theoretical metal-ligand bond lengths (Cu–O_{calc} = 1.947 Å; Cu–N_{calc} = 2.010 Å) are slightly elongated relative to the experimental parameters (Cu(1)–O(2) = 1.879(3) Å; Cu(1)–N(1) = 1.962(4) Å), a typical trend attributed to the omission of solid-state intermolecular lattice packing constraints in gas-phase DFT calculations. The two largest coordination angles around the central copper are theoretically predicted at 154.48° (O–Cu–O) and 159.47° (N–Cu–N), successfully reproducing the distorted tetrahedral environment caused by the bulky peripheral *N*-isobutyl chains.

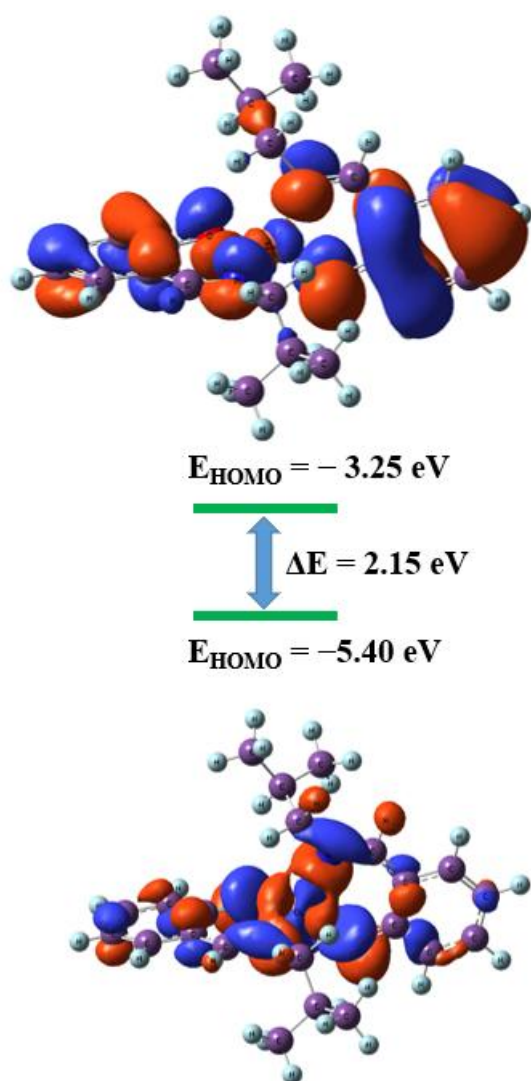


Fig. 11. Calculated frontier molecular orbital energy transition of the copper(II) complex.

The frontier molecular orbital energy gap (ΔE) is a critical descriptor governing intermolecular interactions, electronic charge-transfer processes, and overall chemical stability. As illustrated in Fig. 11, the calculated highest occupied molecular orbital energy (E_{HOMO}) of the copper(II) complex is -5.40 eV , while the lowest unoccupied molecular orbital energy (E_{LUMO}) is -3.25 eV . The resulting narrow frontier orbital energy gap of $\Delta E = 2.15 \text{ eV}$ indicates that the complex has a distinct soft character, rendering it highly polarizable and chemically reactive [75]. The spatial orbital distributions show that the

HOMO electron density is predominantly localized over the coordinated phenolate rings and the core CuN₂O₂ chelate ring system, with contributions from the filled metal *d*-orbitals [88, 89]. In contrast, the LUMO shows a significant shift, with high electron density concentrated over the azomethine (C=N) groups and extending across one of the aromatic ligand wings. This spatial separation between the HOMO and LUMO donor-acceptor centers facilitates low-energy electronic transitions that perfectly match the experimental ligand-to-metal charge-transfer (LMCT) bands observed in the UV–Vis spectrum.

To gain a deeper understanding of the complex's chemical reactivity and chemical-biological interactions, global chemical descriptors were derived from the FMO energies (Table S2). The complex exhibits low global hardness ($\eta = 1.075$ eV) and a correspondingly high global softness ($\sigma = 0.465$ eV⁻¹). In conceptual DFT, this soft, highly polarizable character indicates that the electron cloud of the coordinated framework can readily deform upon approaching a biomolecular matrix. This electronic flexibility lowers the kinetic barrier for the complex to engage in charge-transfer interactions with microbial targets. Furthermore, the complex has a high absolute electronegativity ($\chi = 4.325$ eV) and a pronounced global electrophilicity index ($\omega = 8.70$ eV). This electrophilic nature indicates that the copper(II) complex acts as a potent electron acceptor, enabling it to readily target nucleophilic centers, such as functional thiol (–SH) groups in enzymes or nitrogenous bases in nucleic acids in cellular environments, thereby disrupting vital metabolic pathways. The calculated permanent dipole moment of 4.25 D is a key physical determinant of the complex's in vitro biological efficacy. This substantial molecular dipole enables strong long-range electrostatic and dipole-dipole interactions with the polar lipid heads of microbial cell membranes [76].

4.0 Molecular Electrostatic Potential (MEP) Mapping

To visualize the nucleophilic and electrophilic reactive centers across the complex, the molecular electrostatic potential (MEP) was projected onto the total electron density

isosurface. As illustrated in Fig. 12, the electrostatic potential is mapped on an electronic boundary scale ranging from -7.391×10^{-2} a.u. (deep red, nucleophilic) to $+7.391 \times 10^{-2}$ a.u. (deep blue, electrophilic).

The MEP topography shows that the most intense negative potential (deep red zones) is localized directly over the coordinated phenolate oxygen atoms. This high electron density identifies these oxygen atoms as the primary nucleophilic centers capable of participating in targeted hydrogen bonding or interacting with electropositive targets in cellular media [77]. Conversely, the imine nitrogen (C=N) atoms and the conjugated aromatic framework exhibit neutral green/yellow hues, indicating balanced electron density. The outer aliphatic regions of the peripheral N-isobutyl groups are surrounded by light blue and cyan envelopes, confirming that the terminal alkyl protons remain mildly electropositive. This distinct bipolar spatial mapping, featuring highly concentrated nucleophilic oxygen cores surrounded by neutral, hydrophobic outer alkyl shells, facilitates strong long-range electrostatic alignment with polar cellular structures, thereby enhancing the complex's membrane-targeting capability.

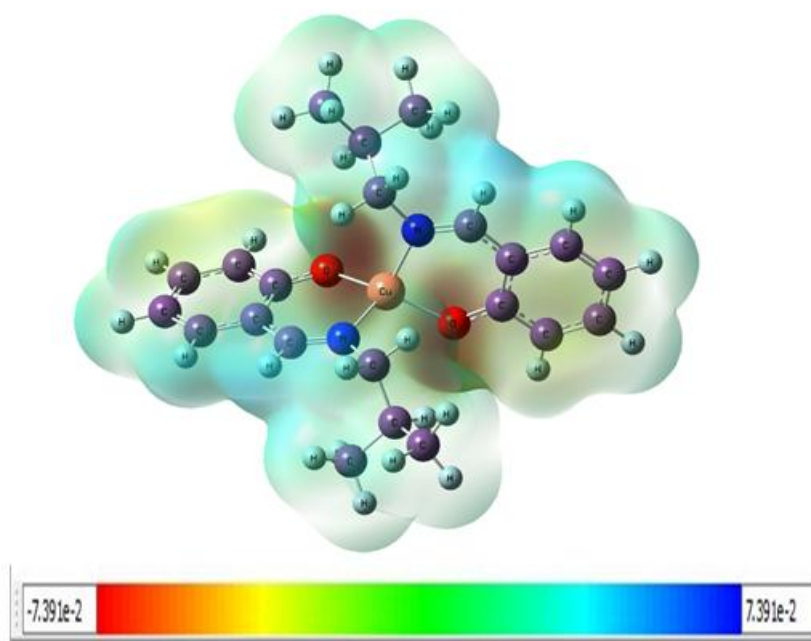


Fig. 12. Molecular electrostatic potential (MEP) surface map of the copper(II) complex showing the potential distribution ranging from -7.391×10^{-2} to $+7.391 \times 10^{-2}$ a.u.

4.1 Electronic Absorption Spectra and TD-DFT Studies

The experimental electronic absorption spectrum of the mononuclear Cu(II) complex in methanol is compared with the simulated time-dependent DFT (TD-DFT) absorption spectrum (Fig. S5). A comparison of experimental data with theoretical wavelengths (λ_{calc}), oscillator strengths (f), and major molecular orbital (MO) assignments is summarized in Table S3.

The experimentally observed absorption bands at 225 nm and 240 nm are theoretically predicted at 278 nm ($f = 0.18$). This transition is assigned to a localized intra-ligand $\pi \rightarrow \pi^*$ electronic transition across the aromatic rings, primarily governed by a HOMO-6 $\rightarrow$ LUMO transition within the β spin manifold. Spatial mapping of these frontier molecular orbitals (Fig. 13) shows that the β -HOMO-6 (-8.41 eV) density is a pure ligand-centered moiety delocalized over the π -system of a single Schiff base ligand, whereas the β -LUMO (-3.03 eV) functions as a covalent, hybrid metal-ligand anti-bonding orbital [78]. The metal component of the LUMO is dominated by a partially vacant copper $3d_{x^2-y^2}$ orbital, which overlaps with the σ -donor lone pairs of the coordinated phenolate oxygen and imine nitrogen donors. This charge relocation yields a significant transition energy gap of $\Delta E_g = 5.38$ eV.

The experimental bands observed at 271 nm and 301 nm correlate with the calculated band at 329 nm ($f = 0.08$), which is dominated by a HOMO-1 $\rightarrow$ LUMO+1 transition (66%, β). The β -HOMO-1 (-5.95 eV) exhibits widespread lobe distributions spanning both phenolate aromatic cores and non-bonding oxygen lone-pair character, whereas β -LUMO+1 (-1.63 eV) shifts electrons into the extended azomethine conjugation framework, requiring an energy gap of $\Delta E_g = 4.32$ eV. An adjacent transition calculated at 343 nm ($f = 0.12$) shows mixed

spin character, with a HOMO→LUMO+1 promotion (47%) in the α spin state alongside a HOMO → LUMO+2 (33%) in a β spin state [79].

For the α spin component, mapping reveals a clear α -HOMO (−5.75 eV) → α -LUMO+1 (−1.66 eV) vector with an excitation gap of $\Delta E_g = 4.09$ eV. For the accompanying β channel component, the β -HOMO (−5.68 eV) → β -LUMO+2 (−1.62 eV) pathway shows a transition gap of $\Delta E_g = 4.06$ eV, collectively defining localized internal $n \rightarrow \pi^*$ transitions within the coordinating azomethine (C=N) groups. The β -HOMO is a mixed metal-ligand moiety, housing substantial non-bonding metal $3d_z^2$ and $3d_{xy}$ orbital character that mixes with the ligand σ -framework. Its excitation into the unoccupied ligand π^* framework (β -LUMO+2) maps a minor metal-to-ligand charge transfer (MLCT) pathway that tracks electron migration out of the filled metal non-bonding core.

The low-energy absorption band at 361 nm is resolved into an extended electronic envelope. This envelope features a prominent allowed transition at 381 nm ($f = 0.08$) and a lower-energy shoulder predicted at 472 nm ($f = 0.06$). Both underlying transitions originate from a common orbital locus, mapped as a HOMO−4→LUMO transition with contributions of 59% and 26% within the β spin channel, respectively. As shown in the orbital diagrams, the β -HOMO−4 (−7.17 eV) density consists purely of the ligand π -donor framework on the phenolate rings, while the corresponding β -LUMO (−3.03 eV) serves as the metal-centered acceptor state. Spanning a transition gap of $\Delta E_g = 4.14$ eV, these transitions represent a classical LMCT mechanism, in which ligand-centered π -electrons are promoted directly into the antibonding copper $3d_{x^2-y^2}$ valence shell [80]. These details confirm that no frontier orbital behaves as a pure atomic state, highlighting the strong metal-ligand covalency driven by the distorted tetrahedral geometry.

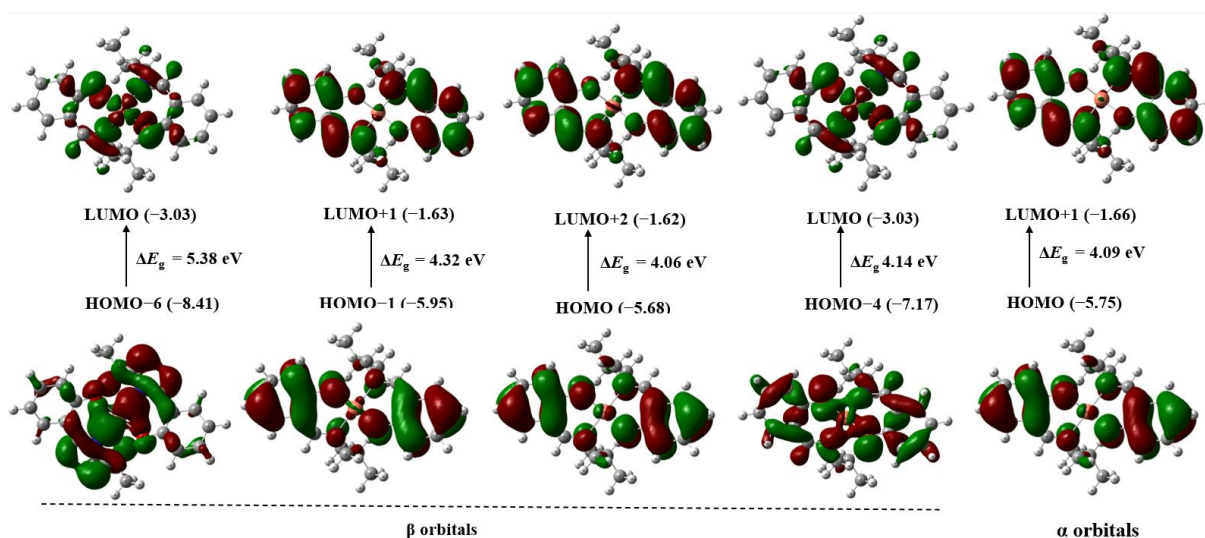


Fig. 13. Spatial orientation and orbital energy transitions of the key frontier molecular orbitals involved in the principal electronic excitations of the copper(II) complex in the β and α spin states. The indicated energies (eV) and transition gaps (ΔE_g) highlight the mixed metal-ligand character that drives LMCT, MLCT, and intra-ligand transitions.

4.2 Antimicrobial study

The results on antimicrobial performance are presented in Table 4 and Figs. S6 and S7. Among the three concentrations tested, 100 $\mu\text{g/mL}$ showed no activity against the two test bacteria (*E. coli* and *S. aureus*). The 200 $\mu\text{g/mL}$ concentration showed inhibition zones of 11 mm and 14 mm against both test bacteria. The 300 $\mu\text{g/mL}$ concentration exhibited more antibacterial activity, as indicated by inhibition zones of approximately 16 mm and 19 mm against *E. coli* and *S. aureus*, respectively. At 40 $\mu\text{g/mL}$, the ZOI values are 18 and 21 mm for *E. coli* and *S. aureus*, respectively. The zones are close to those of standard antibiotics, which were about 21 mm and 24 mm for the respective organisms.

Table 4. Antibacterial and antifungal activity of Cu(II) complex

S. No.	Samples ($\mu\text{g/mL}$)	zone of inhibition (in mm)			
		<i>E. coli</i>	<i>S. aureus</i>	<i>C. albicans</i>	<i>C. tropicalis</i>
1	100	0	0	0	0
2	200	11	14	10	13
3	300	16	19	16	15
4	400	18	21	21	19
5	PC	21	24	25	23

PC: Positive control (Streptomycin for bacteria; Imidazole for fungi). Negative control: DMSO

The complex was screened for its antifungal activity against *Candida tropicalis* and *Candida albicans*. Imidazole was selected as the positive antifungal agent (PC), and DMSO was used as the negative control (NC). Among the four concentrations (100-400 $\mu\text{g/mL}$), the zone of inhibition was 19 mm for *C. albicans* and 21 mm for *C. tropicalis* at 400 $\mu\text{g/mL}$. The results were significant, as the inhibitory zones were comparatively in good agreement with the positive control antifungal agent (Imidazole, 25 and 23 mm, respectively, for both species).

Table 5. Comparative evaluation of the antimicrobial *in vitro* activity (Zone of Inhibition, mm) of the synthesized copper(II) complex against various reported copper(II) coordination compounds.

Ref.	Complexes	Zone of Inhibition (in mm)			
		<i>E. coli</i>	<i>S. aureus</i>	<i>C. albicans</i>	<i>C. tropicalis</i>
[81]	$\text{Cu}(\text{H}_2\text{L}_1) \cdot \text{H}_2\text{O}$	14	11	15	13
[82]	$\text{C}_{22}\text{H}_{29}\text{N}_3\text{O}_5\text{Cu}$	12	14	--	--

[83] $[\text{Cu}_2(\text{H}_2\text{L}_1)\text{Br}\cdot 3\text{H}_2\text{O}]\text{Br}$	11	11	--	--
[84] $\text{C}_{20}\text{H}_{24}\text{N}_4\text{O}_{16}\text{Cu}$	08	12	--	--
[85] $\text{C}_{34}\text{H}_{28}\text{N}_6\text{OC}_{12}\text{Cu}$	16-19	16-19	10-16	--
[86] $\text{C}_{10}\text{H}_{14}\text{N}_3\text{O}_3\text{SCuCl}$	17	12	20	--
[87] $\text{C}_{32}\text{H}_{34}\text{Cu}_2\text{N}_{10}\text{O}_2$	--	--	18	10
[88] $\text{C}_{26}\text{H}_{29}\text{Cu}_2\text{N}_7\text{O}_{11}\cdot 8\text{H}_2\text{O}$	09	11	12	--
[89] $\text{C}_{36}\text{H}_{30}\text{N}_6\text{O}_2\text{Cu}$	19	11	13	--
This work	22	23	19	18

[81]-(diiodosalicylaldehyde with carbohydrazide); [82]-(salicylaldehyde with diethylenetriamine); [83]-(diiodosalicylaldehyde with thiocarbohydrazide); [84]- (EDTA); [85]-(benzaldehyde with 7-chloro-4-Hydrazinoquinoline); [86]- (3-hydroxy-4-methoxybenzaldehyde with N^4 -methylthiosemicarbazide); [87]-(salicylaldehyde with N-benzylethylenediamine); [88]- (Salicylaldehyde with folic acid); [89]-(isatin with tryptamine)
Note: “—” indicates data not reported or not tested in the cited literature.

The *in vitro* antimicrobial efficacy of the mononuclear Cu(II) complex was benchmarked against previously reported analogues (Table 4) [81-90]. The Cu(II) complex shows moderate activity compared with the complexes listed in Table 5 across both bacterial and fungal strains. It produced zones of inhibition against *E. coli* (22 mm) and *S. aureus* (23 mm), which are higher than those of the macrocyclic, multidentate, or thiosemicarbazide Cu(II) complexes, which peak at 8-19 mm [81-86, 88, 89]. Furthermore, the complex exhibited significant activity against *C. albicans* (19 mm) and *C. tropicalis* (18 mm), whereas several complexes reported in the literature remained untested [82-84, 86, 88]. According to Tweedy's chelation theory, coordination reduces the polarity of the central Cu^{2+} ion via charge sharing with N_2O_2 donor atoms, significantly increasing its lipophilic character [90].

5.0 Conclusion

A mononuclear Cu(II) Schiff base complex was synthesized through a one-pot condensation method. Single-crystal X-ray diffraction analysis confirmed that the complex crystallizes in an orthorhombic system and exhibits distorted, flattened tetrahedral coordination geometry driven by the pseudo-Jahn–Teller electronic effect. The bulky, peripheral *N*-isobutyl groups adopt a *cis* orientation on the same side of the coordination sphere, locking into a *gauche* configuration that projects out of the principal azomethine (C=N) plane. This specific butterfly-like conformation is reinforced by a symmetric network of non-classical intramolecular C–H $\cdots$ O hydrogen bonds. X-band EPR spectroscopy provided direct evidence for the distortion in the geometry. Density functional theory (DFT) calculations and molecular electrostatic potential (MEP) mapping confirmed that the complex features high polarizability and a highly concentrated nucleophilic core surrounded by hydrophobic alkyl shells. The Hirshfeld surface analysis via two-dimensional fingerprint plots revealed that the crystal lattice is sustained by dense, interlocked H $\cdots$ H hydrophobic contacts (79.2%). Simultaneously, non-isothermal TG/DTA measurements demonstrated high thermal stability, with a sharp, single-step decomposition yielding a negligible amount of carbonaceous residue. *In vitro* biological screenings demonstrated that the complex possesses notable, dose-dependent antimicrobial efficacy against selected bacterial and fungal pathogens.

Acknowledgments

The CCDC No. 2241173 contains the supplementary crystallographic data. These data are available free of charge from the Cambridge Crystallographic Data Center via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>. The authors acknowledge SAIF at IIT Chennai for a single-crystal X-ray diffraction study. We thank Dr. Selva Kumar R, M.M. Engineering College, for his guidance in computational calculations.

Author contributions: S. A.: Synthesis, characterization, and original draft. S.A.: Conceptualization, data validation, manuscript finalization, and supervision. Both authors reviewed the manuscript.

Data availability

Other data sets created and/or analyzed during the current inquiry are available from the appropriate author upon reasonable request, in addition to the data provided in the CCDC and supporting documentation.

Declarations

Conflict of Interest

The authors declare no conflicts of interest.

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