

NEW COPPER(II) COMPLEX WITH PYRAZINE-CONTAINING TRIPYRIDYLDIAMINE LIGAND: STRUCTURAL FEATURES AND ANTIMICROBIAL PROPERTIES

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ABSTRACT

A novel copper(II) complex, [Cu(H₂dppzda)(NO₃)₂] (1), was synthesized using N,N'-Di(pyridin-2-yl)pyrazine-2,6-diamine (H₂dppzda) as a ligand. Spectroscopic techniques and magnetic measurements were used to describe the complex, and single-crystal X-ray diffraction analysis was used to identify its structure. The X-ray analysis revealed the tridentate coordination mode of H₂dppzda to the copper(II) ion via its pyridine and pyrazine nitrogen atoms in the complex (1). Cu(II) is pentacoordinated with a distorted square pyramidal geometry and a monocoordinated nitrate anion positioned at the apex. The axially symmetric EPR spectrum of complex (1) shows the typical relationship $g_{\parallel} > g_{\perp} > g_e$, which indicates a $d_{x^2-y^2}$ ground electronic state. This finding is supported by results from magnetic susceptibility and electronic spectrum studies, which collectively suggest a distorted square pyramidal arrangement around the central copper(II) ion. The antimicrobial potential of the synthesized ligand and its corresponding complex (1) was rigorously assessed against a panel of pathogens, including *Pseudomonas aeruginosa*, *Mycobacterium phlei*, *Aspergillus niger*, and *Penicillium chrysogenum*. The bioassay results revealed significant microbicidal efficacy for both entities; notably, the Cu(II) complex displayed enhanced potency compared to the uncoordinated ligand, characterized by an inhibition zone of 26 mm at a concentration of 100 µg/mL against *P. aeruginosa*. Beyond their biological profiles, the intrinsic redox activity and sulfur affinity of these types of complexes position them as viable candidates for the sequestration of hydrogen sulfide (H₂S) within reservoir environments and the prevention of oxidative instability in crude oil.

Keywords: modulated oligo- α -aminopyridine ligand; copper complex; hydrogen bonds; supramolecular networks; antimicrobial activity.

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1. Introduction

The heterocyclic compounds have garnered significant attention due to their diverse pharmacological activities. Because of their potent antibacterial and antifungal qualities, pyrazine derivatives are particularly well-liked candidates in medicinal chemistry. Antibacterial, antifungal, antimicrobial, and anti-lung cancer characteristics are only a few of the many biological actions of pyridine derivatives and their substituted analogs [1-3]. These substances frequently cause bacterial and fungal cell death by interfering with essential cellular functions, including the creation

of proteins or cell walls. Pyrazine- and pyridine-based compounds are interesting candidates in the fight against drug-resistant illnesses because of their capacity to fight drug-resistant bacterial and fungal strains [4]. On the other hand, oligo- α -pyridylamines, as heterocyclic ligands containing pyridine and pyrazine heterocycles (Scheme 1), are interesting because multidentate ligands display a variety of coordination mechanisms. The oligo- α -pyridylamine ligands are deprotonated and coupled to the metal in an all-syn configuration in linear extended metal atom chains (EMACs), whereas mononuclear complexes have been shown to have an all-anti configuration [5–11]. The oligo- α -pyridylamines are present in their anti-syn form in the dimer of the free ligand [12]. It is well known that metal

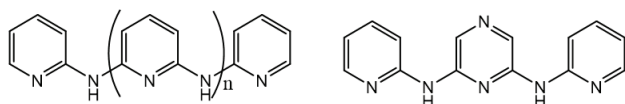
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complexes have various mechanisms of action, such as the exchange or release of ligands, the production of reactive oxygen species (ROS), redox activation, and the catalytic generation of toxic species, all of which are challenging or even impossible to accomplish with organic compounds (ligands) alone [13]. Due to their increased lipophilicity and structural integrity, copper complexes with ligands derived from pyridine or pyrazine are highly proficient at traversing microbial cell membranes and disrupting essential cellular processes [14,15]. Additionally, it is expected that oligo- α -pyridyl/pyrazylamine ligands will exhibit a variety of pharmacological effects, such as anticancer, antibacterial, and antifungal activities, especially in complexes with transition metals that contain highly biologically active pyridine and pyrazine rings. Indeed, coordination polymers of copper(II), mononuclear complexes, and string complexes of nickel(II) with pyrazine-modulated oligo- α -pyridylamine ligands have been shown to exhibit significant biological activity [16–19].

The global rise in antimicrobial resistance among clinically significant pathogens has increased the need for innovative therapeutic structures acting through unprecedented biochemical pathways. Among these new strategies, copper(II)-based biocides are attracting particular attention [20,21]. A standard nutrient medium, peptone-meat extract agar, was used for the cultivation and characterization of test microorganisms [22]. Heteroaromatic architectures incorporating pyrazine nitrogen donors constitute a versatile class of pharmacophores with documented bioactivity across multiple therapeutic indices. Upon chelation to divalent copper, these ligand frameworks typically undergo substantial enhancement in antimicrobial efficacy, an effect mechanistically linked to augmented lipophilicity of the resulting coordination species and facilitated translocation across the hydrophobic domains of microbial envelopes. Beyond biomedical contexts, the petroleum extraction and refining sector confronts substantial operational losses attributable to microbiologically influenced corrosion (MIC) of subterranean infrastructure and biodeterioration of hydrocarbon feedstocks. In this industrial setting, copper(II)-based antimicrobial formulations present a viable technological alternative for biocidal treatment of injection water, pipeline maintenance, and reservoir souring mitigation. Moreover, the thermal robustness and redox tunability of pyrazine-derived metal complexes render them suitable precursors for the design of oxidation catalysts employed in heavy crude upgrading and desulfurization protocols under elevated temperature regimes [23,24].

In this paper, we present our latest research with N,N'-Di(pyridin-2-yl)pyrazine-2,6-diamine ($H_2dppzda$), a tuning ligand from tripyridyldiamine – H_2tpda (Scheme 1). We describe for the first time the synthesis, crystal structure, magnetic, antimicrobial, and antifungal properties of the mononuclear complex $[Cu(H_2dppzda)(NO_3)_2]$ (**1**) of $H_2dppzda$.



Scheme 1.
Oligo- α -pyridylamino ligands
($n=0$, $Hdpa$; $n=1$, H_2tpda)

$H_2dppzda$

2. Experimental

2.1. Materials and instrumentation

All purchased chemicals and solvents were of analytical grade (Aldrich and Sigma) and used as received. Elemental analyses of carbon, hydrogen, and nitrogen were carried out using a CHNSO FlashEA™ 1112 Automatic Elemental Analyzer. The electronic spectra were recorded as Nujol mulls and in methanol solution on a Specord 50 plus, Analytical Jena spectrophotometer, at room temperature. IR spectra were measured by the ATR technique (4000–400 cm^{-1}) on an Agilent Cary 630 FTIR spectrophotometer at room temperature. The magnetic measurement was performed on a SQUID magnetometer with a 500 Oe external magnetic field. The diamagnetic corrections of the molar magnetic susceptibilities were applied using Pascal's constants. The EPR spectrum was recorded for the polycrystalline sample at room temperature on a Bruker BioSpin GmbH spectrometer.

2.2. Crystal structure determinations

A D8-QUEST diffractometer was used to gather X-ray data for $[Cu(H_2dppzda)(NO_3)_2]$ (**1**) at room temperature using Mo $K\alpha$ radiation ($\lambda=0.71073$ Å). The structure was refined using SHELXL-2013 with full-matrix least-squares on F^2 values [26] after being immediately solved with SHELXS-2013 [25]. The refinement of the non-hydrogen atoms was anisotropic. The hydrogen atoms bonded to carbon were considered as riding atoms, keeping a C-H spacing of 0.93–0.96 Å, after being identified on multiple maps. The remaining H atoms were found in a freely refined difference map. The subsequent procedures were employed during our analysis: Bruker APEX2 was used for data collection, the MERCURY program was used for the preparation of molecular graphics [27], and WinGX software was used to prepare publication material [28]. Details concerning collection and analysis are reported in table 1.

Table 1	
Crystal data for (1)	
	1
Formula	$C_{14}H_{12}CuN_8O_6$
Formula weight	451.86
Temperature/K	293
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	12.7758 (19)
b (Å)	11.0776 (17)
c (Å)	12.1797 (17)
β (°)	101.606 (4)
V (Å ³)/Z	1688.5 (4)/4
D_c (Mgm ⁻³)	1.664
Absorption coefficient (mm ⁻¹)	1.35
Crystal size (mm)	0.12 × 0.11 × 0.10
θ range for data collection (°)	2.5–28.4
Reflection collected	46047
Independent reflections	4240 ($R_{int}=0.032$)
R_F , $R_W(F^2)$ ($I>2\sigma(I)$)	0.0313, 0.0778
R_F , $R_W(F^2)$ (all data)	0.0406, 0.0834
GOF	1.07

Syntheses

H₂dppzda was synthesized according to the literature [29].

[Cu(H₂dppzda)(NO₃)₂] (1): After adding a methanolic solution (15 mL) of H₂dppzda (53.8 mg, 0.20 mmol) to a methanolic solution (10 mL) of copper nitrate trihydrate (53.2 mg, 0.22 mmol), the reaction mixture was agitated for a whole day at room temperature. After filtering out insoluble contaminants, the mixture was vacuum-concentrated. Block-shaped black single crystals appropriate for X-ray examination were produced by diffusing ether into the CH₃OH solution (66 mg, 72% yield). IR (KBr) ν/cm^{-1} : 3313 w, 3227 w, 3138 w, 3097 w, 3034 w, 1660 s, 1632 s, 1580 s, 1476 s, 1423 s, 1282 s, 1177 m, 1125 s, 1028 m, 868 m, 764 s, 518 m, 477 m, 432 m; UV/Vis (CH₃OH) $\lambda_{\text{max}}/\text{nm}$ ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) = 203 (3.86×10^4), 259 (1.64×10^4), 312 (1.75×10^4), 378 (1.59×10^4), 412 (1.21×10^4), 680 (0.62×10^2); Elemental analysis (%) C₁₄H₁₂CuN₈O₆ (451.86): calc., C 37.21, H 2.68, N 24.80; found: C 37.29, H 2.79, N 24.69.

2.3. The determination of antimicrobial activity

The antimicrobial activity of the ligand and [Cu(H₂dppzda)(NO₃)₂] complex was evaluated using an agar well diffusion protocol. Stock solutions of 10 mg/mL were prepared by dissolving each complex in dimethyl sulfoxide (DMSO) and stored in a refrigerator at 4 °C until use. The culture medium was prepared by suspending 28 g of commercially available nutrient agar powder in 1 liter of distilled water and then sterilizing by autoclaving at 121 °C for 15 minutes. The panel of test microorganisms consisted of two bacterial species—*Pseudomonas aeruginosa* ATCC 27853 and *Mycobacterium phlei* ATCC 11758—and two fungal species—*Aspergillus niger* ATCC 16404 and *Penicillium chrysogenum* ATCC 10106. Inocula for bacterial cultures were standardized to 10⁸ colony-forming units per milliliter, while fungal spore suspensions were adjusted to 10⁶ spores per milliliter. These standardized microbial preparations were evenly distributed on the surface of solidified nutrient agar plates. Following aseptic punching into the agar, 6 mm diameter wells were filled with 100 μg /mL of test compounds at a working concentration of 100 μg /mL. Following inoculation, fungal plates were maintained at 28 °C for 48–72 hours, whereas bacterial plates were incubated at 37 °C for 24 hours. The diameters of the zones indicating growth inhibition were measured in triplicate using a digital caliper, and the mean values were reported. Ciprofloxacin

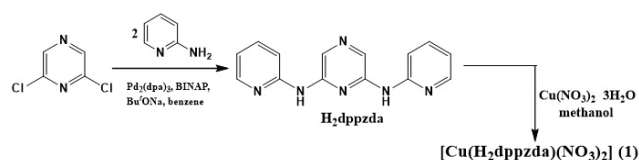
(5 μg per disc) and nystatin (100 international units per disc) were included as reference standards for antibacterial and antifungal activities, respectively. DMSO served as a solvent control, and sterile distilled water was included as a blank control to exclude any environmental or procedural artifacts.

3. Results and discussion

3.1. Syntheses and structures

The ligand N,N'-Di(pyridin-2-yl)pyrazine-2,6-diamine (H₂dppzda) was synthesized according to our previously reported work [30].

The direct reaction of H₂dppzda with Cu(NO₃)₂·3H₂O in methanol produced the complex [Cu(H₂dppzda)(NO₃)₂] (1). Single-crystal X-ray diffraction, elemental analysis, electron spin resonance (ESR), Fourier-transform infrared spectroscopy (FTIR), and UV-Vis spectroscopy were used to characterize the molecule as a mononuclear species (Scheme 2). The complex is also soluble in the majority of organic solvents and stable in air.



Scheme 2.

The synthesis of the H₂dppzda ligand and its complex (1)

Figure 1 shows the crystal structure of [Cu(H₂dppzda)(NO₃)₂] (1). Table 2 lists a selection of bond lengths and angles. The monoclinic space group P2₁/c is where the complex crystallises. With an Addison parameter τ value of 0.37 (where σ = difference between the two biggest angles/60; σ = 1 for ideal trigonal-bipyramidal and σ = 0 for ideal square-pyramidal), the five-coordinated copper(II) atom in (1) has a deformed square-pyramidal geometry. The O(4) atom of the monodentate coordinated nitrate anion and the N(1), N(3), and N(6) nitrogen atoms of the heterocyclic aromatic rings of the ligand define the deformed basal plane of the Cu(II) center in 1. Significant distortion of the basal plane is shown by the nonlinearity of both trans angles, N(1)-Cu(1)-N(6) (169.12(7)°) and N(3)-Cu(1)-O(4) (147.22(6)°). Significant distortion of the basal plane is shown by the nonlinearity

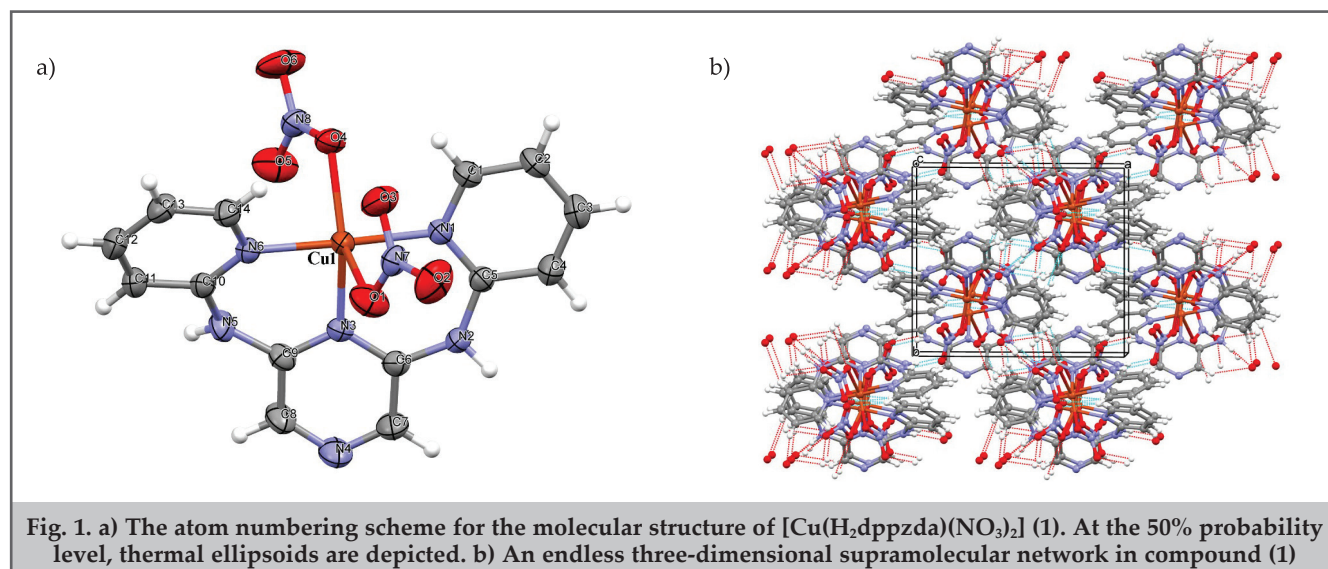


Fig. 1. a) The atom numbering scheme for the molecular structure of [Cu(H₂dppzda)(NO₃)₂] (1). At the 50% probability level, thermal ellipsoids are depicted. b) An endless three-dimensional supramolecular network in compound (1)

of both trans angles, N(1)–Cu(1)–N(6) (169.12(7)°) and N(3)–Cu(1)–O(4) (147.22(6)°). Conversely, the oxygen atom O(1) of the other monodentate coordinated nitrate anion has a significantly long Cu(1)–O(1) = 2.3362 (18) Å bond distance and is situated in the axial position.

The axial Cu–O bond is elongated due to a Jahn–Teller distortion, which is commonly found in Cu(II) complexes with a d^9 electronic configuration [31]. Cu(1)–N(1) = 1.9730(16) Å; Cu(1)–N(3) = 2.0107(16) Å; and Cu(1)–N(6) = 1.9711(16) Å are Cu–N lengths that fall well within the range reported for copper complexes with this kind of ligand [8, 30, 32–35]. As a tridentate N3-donor ligand in compound **1**, H₂dppzda coordinates with the Cu(1) ion in an anti-anti-anti-anti configuration. The two pyridyl groups and one pyrazyl group of the H₂dppzda ligand are nearly planar but exhibit some twisting. The dihedral angles between each pair of neighboring pyridyl (or pyridyl/pyrazyl) planes are 9.07(2)° (Py(N1)–Py(N3)) and 25.92(2)° (Py(N3)–Py(N6)). In the complex (**1**) the nitrogen atoms of amino groups are uncoordinated to Cu(II). Cisoid angles in (**1**) are in the range 84.07(11)° to 122.63(6)°, indicating significant deviation from the square pyramidal structure. The supramolecular network of complex (**1**) is formed through the classical extensive intermolecular hydrogen bonds (HBs) between the amino group and monocoordinated nitrate anions of neighboring molecules (see fig. 1b). Details of all HBs in complex (**1**) can be found in table 3. Complex (**1**) also exhibits C–H...O type non-classical hydrogen bonds, ranging from 2.851(3) to 3.296(3) Å, formed between hydrogen atoms from aromatic rings and oxygen atoms from monocoordinated nitrate anions (table 3). The hydrogen bonds in complex (**1**) significantly influence crystal packing (fig. 1b).

Additionally, complex (**1**) exhibits centroid-centroid distances of 3.6012 (6) Å and, respectively, intermolecular π – π stacking interactions (table 4). For complex (**1**) (Cg (I) = Cg (1); Cg (J) = Cg (1)I; Symmetry code: (i) –x, 1–y, 1–z; Cg(1) = N6–C10–C11–C12–C13–C14), Cg (I) and the perpendicular projection of Cg (J) onto Ring (I) are measured simultaneously at 3.442 Å [36]. The development of supramolecular motifs and the crystal packing of the synthesised complex

are significantly influenced by hydrogen bonding and π – π interactions (1).

3.2. IR, UV-Vis, EPR spectroscopy and magnetic properties

The C=C and C=N vibrations of the pyridyl/pyrazyl groups were identified as the source of the significant absorption bands in complex (**1**)'s infrared spectra, which fell between 1660 and 1423 cm^{-1} . The N–H bonds of amine groups were identified as the group of bands at 3138–3313 cm^{-1} , which demonstrated that the ligand is not deprotonated during complex formation. The novel bands observed at 518 cm^{-1} and 432 cm^{-1} in the IR spectra of compound (**1**) are tentatively assigned to $\nu(\text{Cu–O})$ and $\nu(\text{Cu–N})$, respectively. In complex (**1**), the coordinated nitrate anion displayed distinctive strong vibrations at 1476 cm^{-1} for $\nu_a(\text{NO}_2)$, 1282 cm^{-1} for $\nu_s(\text{NO}_2)$, and 1028 cm^{-1} for $\nu(\text{NO})$. The results obtained are consistent with this compound's X-ray crystallographic study. For various copper(II) nitrate complexes with nitrogen-donor ligands, a similar coordination mechanism of the NO_3^- anion has also been observed (fig. 2) [37].

The electronic spectra of the H₂dppzda ligand and its complex exhibit several absorption bands attributed to $\pi \rightarrow \pi$ and $n \rightarrow \pi^*$ electronic transitions (fig. 3). In comparison to H₂dppzda, which exhibited absorption at 209, 262, and 359 nm, the band at 412 nm for (**1**) can be attributed to a charge transfer between the ligand and the metal center. The charge transfer band at 412 nm of complex (**1**) was found to be affected by solvent polarity changes. This band has a red shift (longer wavelength) and is observed at 433 nm as solvent polarity increases (e.g., methanol to DMF). The result confirms that the charge transfer between the metal and ligand is characterized by a metal-ligand charge transfer (MLCT) band [38].

In the visible part of the electronic spectra, complex (**1**) shows a wide, unresolved, asymmetric weak d–d absorption peak with a maximum at 680 nm. The precise nature of the penta-coordinate geometry can frequently be determined from the arrangement of peaks and their relative intensities [37]. One peak with a lower-intensity, higher-energy

Table 2
Selected bond distances (Å) and angles (°) for **1**

1			
Cu(1)–N(1)	1.9730 (16)	Cu(1)–O(1)	2.3362 (18)
Cu(1)–N(3)	2.0107 (16)	Cu(1)–O(4)	2.0448 (15)
Cu(1)–N(6)	1.9711 (16)		
N(1)–Cu(1)–N(6)	169.12 (7)	N(3)–Cu(1)–O(4)	147.07 (6)
N(1)–Cu(1)–N(3)	94.47 (7)	O(4)–Cu(1)–O(1)	122.63 (6)
N(3)–Cu(1)–N(6)	92.89 (7)	N(1)–Cu(1)–O(1)	84.07 (7)
N(6)–Cu(1)–O(4)	88.10 (7)	N(3)–Cu(1)–O(1)	90.14 (6)
N(1)–Cu(1)–O(4)	90.44 (7)	N(6)–Cu(1)–O(1)	87.65 (7)

Table 3
Hydrogen-bond geometry (Å, °) for complex **1**

D–H...A	D–H	H...A	D...A	D–H...A
C1–H1...O4	0.93	2.28	2.851 (3)	119
C2–H2...O2 ⁱ	0.93	2.39	3.281 (3)	160
C4–H4...O1 ⁱⁱ	0.93	2.51	3.296 (3)	143
C7–H7...O2 ⁱⁱ	0.93	2.40	3.202 (3)	145
C14–H14...O3	0.93	2.51	3.265 (3)	138
N2–H2A...O2 ⁱⁱⁱ	0.86	2.18	2.985 (3)	157
N5–H5...O6 ⁱⁱⁱ	0.86	2.17	3.020 (3)	170
Symmetry codes: (i) –x+1, y–1/2, –z+3/2; (ii) –x+1, –y+1, –z+1; (iii) –x, y–1/2, –z+1/2				

Table 4
The $\pi \cdots \pi$ interactions distances (Å) for [Cu(H₂dppzda)(NO₃)₂] (**1**)

Cg(1)	Cg(J)	Cg–Cg	Perpendicular distance
Cg(1)	Cg(I) ⁱ	3.6012 (6)	3.442
Symmetry codes: (i) –x, 1–y, 1–z; Cg(1) = N6–C10–C11–C12–C13–C14			

shoulder is known to be indicative of trigonal bipyramidal Cu(II) complexes in the visible region of the electronic spectra. However, when a Cu(II) ion displays square-pyramidal coordination, the reverse absorption pattern—a high-energy peak with a low-energy shoulder—is usually observed. Conversely, a broad band in the region of 600–650 nm ($d_{xz}, d_{yz} \rightarrow d_{x^2-y^2}$) indicates square pyramidal (SP) geometry, whereas a single d-d band at $\lambda > 800$ nm ($d_{xy}, d_{x^2-y^2} \rightarrow d_{z^2}$) is characteristic of trigonal bipyramidal (TBP) geometry [39]. Thus, the idea of a square pyramidal structure surrounding Cu(II) centers is supported by the existence of a wide absorption band at about 680 nm in the spectra of (1). The structure of the complex (1) was found to be unchanged by comparing its electronic spectrum in methanol solution and Nujol suspension (in the solid state) (fig. 3b). Similar results were previously obtained when we utilised absorption spectroscopy to investigate the stability of the other copper(II) complexes of the pyrazine-modulated oligo- α -aminopyridine ligand in the solid state and in solution [17,18].

The experimental EPR spectrum of complex (1), which was recorded at room temperature as a solid-state powder, is shown in figure 4. The EPR spectrum of complex (1) exhibits axial symmetry features with two g values ($g_{\parallel} = 2.2481$ and $g_{\perp} = 2.1011$). The results obtained from EPR are in good agreement with the single-crystal analysis data for complex (1). The axially symmetric EPR spectrum of

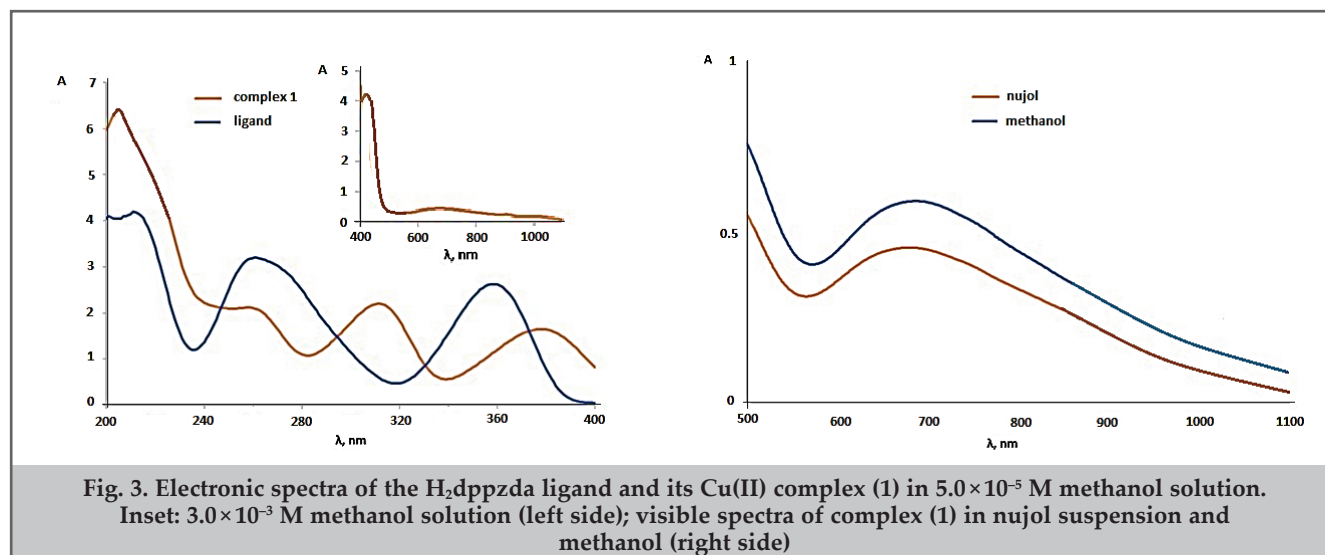
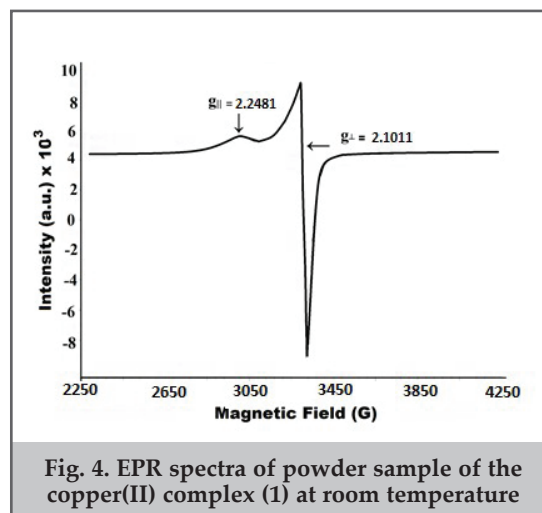
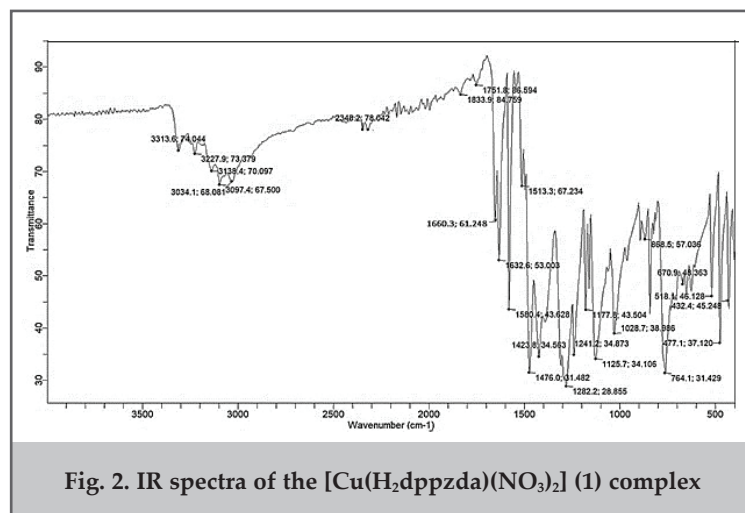
complex (1) exhibits the typical relationship $g_{\parallel} > g_{\perp} > g_e$, where g_e represents the free electron g value of 2.0023. This observation is consistent with a $d_{x^2-y^2}$ ground electronic state [40]. The compound exchange interaction parameter G for (1), defined as $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$, yielded a value of $G = 2.485$. This value suggests significant interaction in the polycrystalline state of complex (1) [41,42].

The room temperature (RT) magnetic moment value, μ_{eff} , for complex (1) aligns with the spin-only value for $S = 1/2$, indicating the presence of one unpaired electron in the $3d^9$ system ($\mu_{\text{eff}} = 1.75 \mu_B$).

3.3. Assessment of antimicrobial activity and growth inhibition

The comparative antimicrobial analysis of the synthesized $[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ complex, which exhibits square-pyramidal geometry, and the free ligand was conducted across various pathogenic strains. The findings demonstrate that incorporation of the metal ion into the coordination sphere significantly enhances the biological activity of the compound.

The Cu(II) complex formed pronounced inhibition zones against *Pseudomonas aeruginosa* and *Mycobacterium phlei*, surpassing the efficacy metrics observed for the free ligand, which suggests that metal coordination significantly potentiates antibacterial activity through enhanced membrane



permeabilization and targeted metal-ion toxicity. Assays conducted on *Aspergillus niger* and *Penicillium chrysogenum* further revealed that the complex effectively retarded fungal colony development, an outcome attributed to its enhanced lipophilicity and consequent improved permeability across cellular membranes, thereby facilitating intracellular accumulation and disruption of vital enzymatic processes. The inhibition zone diameter of 26 mm exhibited by the $[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ complex against *P. aeruginosa* substantiates its superior antimicrobial potency relative to analogous mononuclear systems reported in the literature, positioning this coordination architecture as a promising scaffold for the development of next-generation antimicrobial agents with broad-spectrum activity against both bacterial and fungal pathogens.

3.3.1. Antibacterial and antifungal activities on nutrient agar comparative activity profile

The antimicrobial efficacy of the $[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ complex was systematically benchmarked against the free ligand and established reference standards to elucidate the structure–activity relationship governing its enhanced biocidal properties. Quantitative assessment via the agar well diffusion method revealed that metal coordination profoundly modulates biological activity, with the Cu(II) complex consistently outperforming the non-coordinated ligand across all tested microbial strains (table 5).

The Cu(II) complex showed a clear inhibition zone of 26 mm at a concentration of 100 g/mL when tested against the Gram-negative *Pseudomonas aeruginosa* ATCC 27853, an improvement over that obtained by the free ligand. This increased activity is due to the nature of the lipophilic coordination sphere that may improve entry into *P. Aeruginosa* via outer membrane porin and affect the potential of the cytoplasmic membrane. The Cu(II) complex has strong anti-Mycobacterium activity against the acid-fast bacterium *M. Phlei* ATCC 11758, with a higher zone of inhibition compared to that of the free ligand, although its activity was lower than ciprofloxacin (5 g/disc), the standard antibiotic used in the testing for bacterial species.

In the antifungal domain, assays against *Aspergillus niger* ATCC 16404 and *Penicillium chrysogenum* ATCC 10106 underscored the complex's capacity to retard filamentous fungal growth. The enhanced lipophilicity of the H_2pppzda species, relative to the polar free ligand, promotes partitioning into the lipid-rich fungal cell wall and membrane systems, thereby interfering with ergosterol biosynthesis and inducing oxidative stress through redox cycling of the Cu(II)/Cu(I) couple. Inhibition zones measured following 48–72 hours incubation at 28 °C confirmed that the complex achieves superior mycelial growth suppression compared to both the ligand and

nystatin (100 units/disc) reference standards.

Comparative analysis with analogous mononuclear Cu(II) systems reported in contemporary literature further contextualizes the exceptional performance of the H_2pppzda architecture. The 26 mm inhibition zone diameter observed against *P. aeruginosa* exceeds values typically documented for mononuclear copper (II) complexes incorporating bidentate or tridentate nitrogen donor ligands, which generally range between 14–20 mm under equivalent experimental conditions. This superior potency is rationalized by the unique electronic properties of the N5 coordination environment, wherein the pyrazine and picoline moieties engender enhanced π -delocalization and Lewis acidity at the metal center, thereby intensifying interactions with microbial biomolecular targets.

It is important to highlight the different profiles for bacterial and fungal organisms. Although Gram-negative bacteria had slightly smaller zones of inhibition than Gram-positive (presumably caused by cell wall external lipopolysaccharide coating), the complex was nevertheless very effective. The greater susceptibility demonstrated by fungal strains would be explained by increased cell wall permeability (chitin-based) for hydrophobic metal complexes, and the high susceptibility of the fungal respiratory chains to reactive species generated by the copper ion.

In conclusion, the presented comparative data suggest that coordination of the Hpppzda ligand to Cu(II) results in the development of multi-target antimicrobial activity, greater dependence on lipophilicity-mediated cell membrane penetration, and greater contribution of redox-modulated toxicity compared to the free ligand and analogous mononuclear copper complexes.

3.3.2. Implications for the petroleum industry

The high thermal stability and redox activity of the $[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ complex offer greater potential for use in the petrochemistry industry, where MIC phenomena are predominant in oil reservoirs and pipelines; this copper-based coordination compound can serve as a dual-function inhibitor for both microbial and electrochemical corrosion simultaneously. Moreover, the metal center is found to be good at coordinating sulfur; the complex was capable of nullifying hydrogen sulfide present in crude oil. In the meantime, the potential of the Cu(II)/Cu(I) redox couple can guarantee a sustainable ODS process under mild conditions with acceptable turnover ability.

In recent years, considerable attention has focused on compounds that contain nitrogen-containing fragments, as well as on amides derived from natural petroleum acids. These compounds hold significant potential for developing effective inhibitors against corrosion and salt deposition [43–45].

Comparative antimicrobial activity of ligand, Cu(II) complex, and reference standard

Table 5

Test organism	H_2pppzda (100 µg/mL)	$[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ (100 µg/mL)	Positive control	Solvent control
<i>P. aeruginosa</i>	20 mm	26 mm	Ciprofloxacin (5 µg/disc): 28 mm	DMSO: 0 mm
<i>M. phlei</i>	18 mm	24 mm	Ciprofloxacin (5 µg/disc): 30 mm	DMSO: 0 mm
<i>A. niger</i>	16 mm	23 mm	Nystatin (100 U/disc): 25 mm	DMSO: 0 mm
<i>P. chrysogenum</i>	15 mm	22 mm	Nystatin (100 U/disc): 24 mm	DMSO: 0 mm

Conclusion

A new copper(II) complex with a symmetrical pyrazine-modulated tripyridyldiamine as an N-donor ligand, namely $[\text{Cu}(\text{H}_2\text{dppzda})(\text{NO}_3)_2]$ (**1**), was synthesized and structurally characterized by single-crystal X-ray diffraction analysis. Complex (**1**) exhibits a distorted square pyramidal geometry and functions as a monomer, featuring a monocoordinated nitrate anion positioned at the apex. In complex (**1**), H_2dppzda functions as a tridentate ligand, coordinating to the Cu(II) center in an all-anti configuration. Extensive hydrogen bonding occurs between the amino groups and the monocoordinated nitrate anions of adjacent molecules. This interaction leads to the formation of a three-dimensional supramolecular network within the complex, which contributes to the stabilization of the crystal packing. This study indicates that complex (**1**) is highly effective against both clinically relevant and industrially significant pathogens. The structural modifications facilitated by the N5 coordination sphere provide the complex with strong antimicrobial properties, as well as notable stability against oxidative degradation in petroleum environments. The findings provide a scientific basis for using copper(II)-based metal complexes as multifunctional agents that can help reduce biocorrosion in oil wells.

References

1. Konda, S. G., Khedkar, V. T., Dawane, B. (2010). Synthesis of some new 2-amino-3-cyano-4-aryl-6-(1-naphthylamino)-pyridines as antibacterial agent. *Journal of Chemical and Pharmaceutical Research*, 2, 187–191.
2. Flefel, E. M., Alsafi, M. A., Alahmadi, S. M., et al. (2018). Antimicrobial activities of some synthesized macrocyclic pentaazapyridine and dipeptide pyridine derivatives. *Biomedical Research*, 29, 1407–1413.
3. El-Sayed, H. A., Moustafa, A. H., El-Torky, A. E., Abd El-Salam, E. A. (2017). A series of pyridines and pyridine based sulfa-drugs as antimicrobial agents: design, synthesis and antimicrobial activity. *Russian Journal of General Chemistry*, 87, 2401–2408.
4. Huigens, R. W., Brummel, B. R., Tenneti, S., et al. (2022). Pyrazine and phenazine heterocycles: platforms for total synthesis and drug discovery. *Molecules*, 27(3), 1112.
5. Cotton, F. A., Murillo, C. A., Walton, R. A. (2005). Multiple bonds between metal atoms. Ch.15. 3rd Ed. *New York: Springer*.
6. Ismayilov, R. H., Wang, W. Z., Lee, G. H., Peng, S. M. (2015). Study on a new polydentate pyridylamine and its complexes: synthesis, supramolecular structure and properties. *SOCAR Proceedings*, 1, 74–82.
7. Ismayilova, S. Z., Ismayilov, R. H., Peng, C.-H., et al. (2026). Pyrazine- and picoline-modulated unsymmetrical dipyridylamine and its copper(II) coordination polymers and tetranuclear complex: synthesis, structures and bioactivities. *Journal of Molecular Structure*, 1376, 147100.
8. Wang, W. Z., Wu, Y., Ismayilov, R. H., et al. (2014). A magnetic and conductive study on a stable defective extended cobalt atom chain. *Dalton Transactions*, 43(16), 6229–6235.
9. Ismayilova, S. Z., Ismayilov, R. H., Hamidov, S. Z., et al. (2026). Copper(II) complexes with pyrazine-modulated tetrapyridyltriamine ligands: synthesis, crystal structures, and antimicrobial properties. *SOCAR Proceedings*, 2, 189–197.
10. Ismayilov, R. H., Valiyev, F. F., Tagiyev, D. B., et al. (2018). Linear pentanuclear nickel(II) and tetranuclear copper(II) complexes with pyrazine-modulated tripyridyldiamine ligand: synthesis, structure and properties. *Inorganica Chimica Acta*, 483, 386–391.
11. Ismayilova, S. Z., Guliyeva, L. Sh., Ismayilov, R. H., et al. (2025). Synthesis and structure of the novel mononuclear copper(ii) complex of the unsymmetrical pyrimidine-modulated long-chain hexapyridylpentaamine ligand. *Eurasian Journal of Chemistry*, 30, 4(120), 79–87.
12. Brogden, D. W., Berry, J. F. (2015). Coordination chemistry of 2, 2'-dipyridylamine: the gift that keeps on giving. *Comments on Inorganic Chemistry*, 36(1), 17–37.
13. Andrejević, T. P., Aleksić, I., Kljun, J., et al. (2023). Copper(II) and silver(I) complexes with dimethyl 6-(pyrazine-2-yl)pyridine-3,4-dicarboxylate (py-2pz): the influence of the metal ion on the antimicrobial potential of the complex. *RSC Advances*, 13, 4376–4393.
14. Kumar, S., Dinesha, P., Udayakumar, D., et al. (2024). Synthesis, spectral characterization of novel 2,6-disubstituted-4-oxo-3,4-dihydro-1,3,6-triazine-5-carbonitriles and their molecular docking against selected anti-tubercular targets. *Journal of Molecular Structure*, 1304, 137657.
15. Choudhary, D., Garg, S., Kaur, M., et al. (2023). Advances in the synthesis and bio-applications of pyrazine derivatives: a review. *Polycyclic Aromatic Compounds*, 43(5), 4512–4578.
16. Abbasova, G. G., Ismayilov, R. H., Tagiyev, D. B., et al. (2024). Synthesis, characterization, crystal structure, molecular dynamics simulations, MM-GBSA analysis, and bioactivity studies of pyrazine- and pyrimidine-modulated unsymmetrical dipyridylamide complexes. *Journal of Molecular Structure*, 1315, 138896.
17. Ismayilova, S. Z., Ismayilov, R. H., Tagiyev, D. B., et al. (2025). Copper(II) monohelix complexes with pyrazine-modulated long-chain oligo- α -aminopyridine ligand: synthesis, crystal structures, and bioactivity studies. *Journal of Molecular Structure*, 1347, 143295.
18. Ismayilov, R. H., Valiyev, F. F., Tagiyev, D. B., et al. (2024). Trinuclear nickel (II) string complexes and copper (II) coordination polymer with pyrazine modulated unsymmetrical dipyridylamino ligand: synthesis, structure and bioactivity properties with molecular docking. *Journal of Molecular Structure*, 1307, 137966.

19. Ismayilova, S. Z., Osmanli, M. H., Ismayilov, R. H., et al. (2025). Copper(II) complex with pyrazine- and triazine-modulated tripyridyldiamine ligand: synthesis, crystal structure, magnetic, and antimicrobial properties. *Azerbaijan Chemical Journal*, 4, 23-33.
20. Lister, P. D., Wolter, D. J., Hanson, N. D. (2009). Antibacterial-resistant pseudomonas aeruginosa: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. *Clinical Microbiology Reviews*, 22(4), 582-610.
21. Lemire, J. A., Harrison, J. J., Turner, R. J. (2013). Antimicrobial activity of metals: mechanisms, molecular targets and applications. *Nature Reviews Microbiology*, 11(6), 371-384.
22. MacFaddin, J. F. (1985). Media for isolation-cultivation-identification-maintenance of medical bacteria. Vol.1. Baltimore: Williams & Wilkins.
23. Evans, A., Kavanagh, K. A. (2021). Evaluation of metal-based antimicrobial compounds for the treatment of bacterial pathogens. *Journal of Medical Microbiology*, 70(5), 001363.
24. Li, X., Ai, S., Huang, Y., et al. (2021). Fast and reversible adsorption for dibenzothiophene in fuel oils with metallic nano-copper supported on mesoporous silica. *Environmental Science and Pollution Research*, 28(3), 2741-2752.
25. Sheldrick, G. M. (2008). A short history of SHELX. *Acta Crystallographica*, 64(1), 112-122.
26. Sheldrick, G. M. (2015). Crystal structure refinement with SHELXL. *Acta Crystallographica*, 71(1), 3-8.
27. Macrae, C. F., Sovago, I., Cottrell, S. J., et al. (2020). Mercury 4.0: from visualization to analysis, design and prediction. *Journal of Applied Crystallography*, 53, 226-235.
28. Farrugia, L. J. (2012). WinGX and ORTEP for Windows: an update. *Journal of Applied Crystallography*, 45, 849-854.
29. Wagaw, S., Buchwald, S. L. (1996). The synthesis of aminopyridines: a method employing palladium-catalyzed carbon-nitrogen bond formation. *Journal of Organic Chemistry*, 61, 7240-7241.
30. Ismayilov, R. H., Ismayilova, S. Z., Medjidov, A. A., et al. (2027). Copper(II) complexes of long-chain pyrazine-modulated pentapyridyltetraamine ligand: synthesis, structure, anticancer activity, and molecular docking studies. *Journal of Molecular Structure*, 1379, 147295.
31. Köppel, H., Yarkony, D. R., Barentzen, H. (2009). The Jahn-Teller effect: fundamentals and implications for physics and chemistry. *Springer Series in Chemical Physics*, 97, 915.
32. Ismayilova, S. Z., Huseynova, M. T., Ismayilov, R. H., et al. (2024). Synthesis and properties of CuII complex of benzidine-N,N,N',N' tetraacetic acid. *Azerbaijan Chemical Journal*, 3, 69-75.
33. Guliyeva, E. A. A., Medjidov, A. A., Ismayilov, R. H., et al. (2026). Synthesis, structural characterization and cholinesterase and α -glycosidase inhibition of heterometallic Co-Ni/Zn/Fe maleate complexes. *Polyhedron*, 293, 118138.
34. Ismayilov, R. H., Ismayilova, S. Z., Tagiyev, D. B., et al. (2025). Linear nonanuclear chromium(II) complex with pyrazine-modulated pentapyridyltetraamine ligand: synthesis, structure and properties. *Journal of Molecular Structure*, 1331, 141592.
35. Wang, W. Z., Ismayilov, R. H., Lee, G. H., et al. (2012). Fine tuning of pentachromium(II) metal string complexes through elaborate design of ligand. *New Journal of Chemistry*, 36, 632-637.
36. Zhao, Y., Li, J., Gu, H., et al. (2015). Conformational preferences of π - π Stacking between ligand and protein, analysis derived from crystal structure data geometric preference of π - π interaction. *Interdisciplinary Sciences: Computational Life Sciences*, 7, 211-220.
37. Taha, A. (2003). Spectroscopic studies on chromotropic mixed-ligand copper(II) complexes containing o-hydroxy benzoyl derivatives and dinitrogen bases. *Spectrochimica Acta Part A*, 59, 1611-1620.
38. Vlček, A. A. (1998). Mechanistic roles of metal-to-ligand charge-transfer excited states in organometallic photochemistry. *Coordination Chemistry Reviews*, 177, 219-256.
39. Sain, S., Saha, R., Mostafa, G., et al. (2012). Synthesis and crystal structure of three new copper(II) complexes with a tridentate amine and its Schiff bases. *Polyhedron*, 31, 82-88.
40. Enamullah, M., Haque, I., Resma, A. K., et al. (2005). Square planar vs. pyramidal copper(II)-complexes with benzylal vs. naphthylal-based Schiff bases. *RSC Advances*, 15, 18358-18371.
41. Seenaa, E. B., Sithambaresan, M., Vasudevan, S., Kurup, M. R. P. (2020). Structural and spectral characterization of Cu(II) complexes of N(4)-substituted thiosemicarbazones derived from 2-hydroxyacetophenone: Crystal structure of a dinuclear Cu(II) complex. *Journal of Chemical Sciences*, 132, 149.
42. Joseyphus, R. S., Nair, M. S. (2010). Synthesis, characterization and biological studies of some Co(II), Ni(II) and Cu(II) complexes derived from indole-3-carboxaldehyde and glycylglycine as Schiff base ligand. *Arabian Journal of Chemistry*, 3, 195-204.
43. Ismayilov, T. A., Abbasov, V. M., Ismayilov, I. T., et al. (2025). Effectiveness of propylamide derivatives of ethylenediaminetetraacetic acid against corrosion and salt deposition problems. *SOCAR Proceedings*, 4, 158-166.
44. Bayramov, M. R., Mehdiyeva, G. M., Javadov, M. A., et al. (2025). Study of pyridinium derivatives of 4-isooctylphenoxy-3-propyl- and 2-diethylaminomethyl-4-isooctylphenoxy-3-propyl bromides as acid corrosion inhibitors of steel St.3 in oil production. *SOCAR Proceedings*, 4, 167-172.
45. Abbasov, V. M., Dadashova, N. K., Mursalov, N. I., et al. (2025). Investigation of the inhibitory properties of natural petroleum acid amides in CO₂-containing environment. *SOCAR Proceedings*, 3, 130-136.