

SYNTHESIS, COMPUTATIONAL MODELING, AND ANTIBACTERIAL EVALUATION OF NOVEL ARYLIDENE-2-IMINOTHIAZOLIDIN-4-ONE NI(II), CU(II), AND CR(III) METAL COMPLEXES

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ABSTRACT

A series of nine transition-metal complexes was synthesized from three arylidene-2-iminothiazolidin-4-one ligands and coordinated with Ni(II), Cu(II), and Cr(III) ions. The free ligands were developed through a targeted multistep sequence involving reduction, chloroacetylation, cyclization, and condensation with substituted aromatic aldehydes. Comprehensive structural and thermal characterization utilizing FT-IR, ¹H and ¹³C NMR, UV-Visible spectroscopy, mass spectrometry, PXRD, and TGA confirmed that ligand coordination occurs via nitrogen and sulfur donor atoms. These analyses also established the crystalline nature of the complexes and detailed their multistage thermal decomposition profiles. In vitro antibacterial activity was evaluated against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* using agar well diffusion and broth microdilution assays. The metal complexes demonstrated significantly enhanced antibacterial efficacy compared to the uncoordinated free ligands, exhibiting minimum inhibitory concentration (MIC) values ranging from 12.5 to 100 µg mL⁻¹. Furthermore, molecular docking studies targeting bacterial dihydrofolate reductase (PDB ID: 2W9S) and DNA gyrase (PDB ID: 2XCT) indicated that metal complexation distinctly alters and improves protein–ligand binding interactions. These integrated structural, biological, and computational findings suggest that arylidene-2-iminothiazolidin-4-one transition-metal complexes represent highly promising scaffolds for the development of new antibacterial agents.

KEYWORDS: Antibacterial activity; Molecular docking; Powder XRD; Thiazolidin-4-one; Transition metal complexes

1. INTRODUCTION

The escalating crisis of antimicrobial resistance necessitates the urgent development of novel antibacterial agents. Nitrogen- and sulfur-containing heterocycles [1-3] have garnered considerable interest due to their structural versatility and broad spectrum of biological activities. Specifically, the thiazolidin-4-one scaffold serves as a prominent pharmacophore with proven antibacterial, antifungal, and anti-inflammatory applications. Modifying this thiazolidinone nucleus allows researchers to effectively tune its physicochemical and biological profiles [4–6]. Arylidene-2-iminothiazolidin-4-one derivatives are of distinct interest because their exocyclic C=C linkages and aryl substituents significantly influence the electronic distribution and conformational geometry of the heterocycle.

Synthesized readily via the condensation of 2-iminothiazolidin-4-one with substituted aromatic aldehydes, these derivatives offer a streamlined pathway for structural diversification and structure–activity relationship (SAR) investigations [7-8]. The inherent nitrogen and sulfur donor atoms within thiazolidinone-derived ligands make them highly suitable for transition-metal coordination. This metal complexation fundamentally alters critical parameters such as molecular geometry, charge distribution, lipophilicity, and target binding affinity. As a result, transition-metal complexes featuring heterocyclic ligands are extensively explored for antimicrobial applications [9-12]. While complexes incorporating Cu(II), Ni(II), and other metals demonstrate notable antibacterial activity, their ultimate biological efficacy is heavily dictated by the specific metal ion, oxidation state, ligand architecture, and coordination environment [13–20]. Within this context, Cu(II), Ni(II), and Cr(III) complexes serve as excellent platforms to elucidate the relationship between metal coordination and biological activity. Because specific donor atoms and coordination geometries govern the resulting physicochemical and biological traits [17–24], rigorous characterization is imperative. Techniques including elemental analysis, FT-IR and UV–Visible spectroscopy, molar conductivity, PXRD, and TGA offer critical, complementary insights into the composition, coordination behavior, crystallinity, and thermal stability of these newly synthesized complexes [25–31]. To complement in vitro assessments, molecular docking provides a powerful computational tool to predict interactions between synthesized compounds and key biological protein targets.

These studies map preferred binding orientations and detail essential non-covalent interactions, including

hydrogen bonding, hydrophobic contacts, and pi bond effects. Consequently, such computational approaches are increasingly utilized to evaluate thiazolidinone derivatives and related heterocycles against specific bacterial targets [32–38]. Despite extensive research on general thiazolidinone derivatives and their metal complexes, the specific interplay between metal coordination, ligand architecture, and antibacterial efficacy within arylidene-2-iminothiazolidin-4-one systems remains underexplored. Addressing this gap, the present study details the synthesis of novel Ni(II), Cu(II), and Cr(III) complexes derived from arylidene-2-iminothiazolidin-4-one ligands. Through a robust combination of physicochemical and spectroscopic characterization, PXRD, thermal analysis, molecular docking, and in vitro antibacterial evaluations, this study systematically defines how metal coordination impacts the structural and antibacterial properties of these advanced thiazolidinone-based scaffolds.

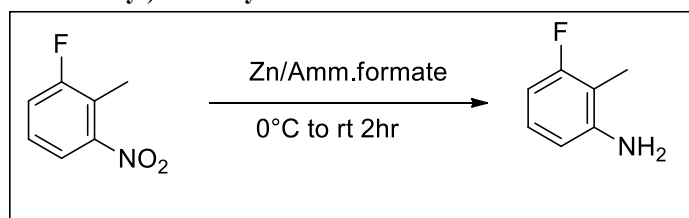
2. EXPERIMENTAL

2.1. Materials and instrumentation

All chemicals and solvents used in the present study were of analytical reagent (AR) grade and were used without further purification. Rhodanine, 2-methyl-3-(methyl)aniline, substituted aromatic aldehydes, chloroacetyl chloride, ammonium thiocyanate, zinc dust, ammonium formate, and the metal salts $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, and $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ were procured from Sigma-Aldrich, Merck, or Spectrochem and used as received. Ethanol, methanol, dimethyl sulfoxide (DMSO), glacial acetic acid, acetone, diethyl ether, and other solvents used for synthesis and purification were of analytical grade. The melting points of the synthesized compounds were determined in open-capillary tubes using a digital melting-point apparatus. The progress of the reactions and the purity of the synthesized compounds were monitored by thin-layer chromatography (TLC) using silica gel precoated aluminium plates with appropriate solvent systems. The developed spots were visualized under ultraviolet (UV) light. FT-IR spectra were recorded in the range of $4000\text{--}400\text{ cm}^{-1}$ using KBr pellets on a Shimadzu FT-IR spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 using a Bruker Avance 400 MHz spectrometer, with tetramethylsilane (TMS) as the internal standard. Chemical shifts (δ) are reported in parts per million (ppm). Electronic absorption spectra were recorded in DMSO solution using a Shimadzu UV-1800 UV–Visible spectrophotometer over the wavelength range of $200\text{--}800\text{ nm}$. Powder X-ray diffraction (PXRD) patterns of the synthesized metal complexes were recorded using $\text{Cu-K}\alpha$ radiation ($\lambda = 1.5406\text{ \AA}$). Thermogravimetric analysis (TGA) was performed under a nitrogen atmosphere at a constant heating rate to investigate the thermal stability and decomposition behavior of the synthesized metal complexes.

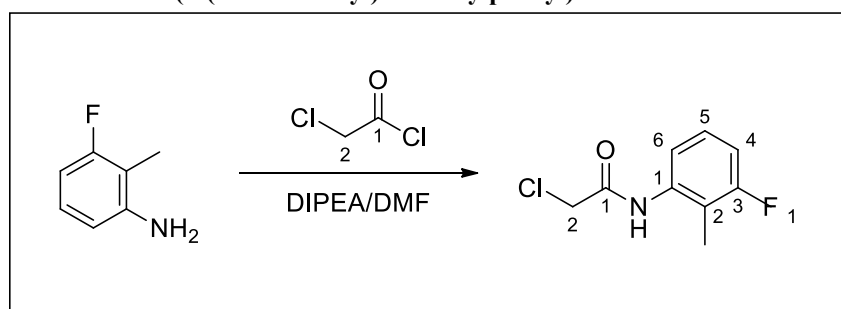
2.2 Synthesis of the Ligands

2.2.1. Synthesis of 3-(Fluoromethyl)-2-methylbenzenamine



To a stirred solution of the nitro compound (1.0 equiv) in methanol (200 mL) was added zinc dust (3.0 equiv) at 0°C , followed by the careful portion-wise addition of ammonium formate (3.0 equiv) at 0°C due to the exothermic nature of the reaction. The reaction mixture was then stirred at room temperature for 2 h, and reaction progress was monitored by TLC using 10% ethyl acetate in hexane as the developing solvent, visualized under UV light, iodine vapor, and ninhydrin. After the reaction was complete, the mixture was filtered through a Celite bed and concentrated under reduced pressure. The resulting crude material was dissolved in dichloromethane (100 mL) and cooled at 0°C for 30 min. The precipitated ammonium formate was removed by decantation, and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 1.20 g of crude material. The crude product was purified by silica gel column chromatography (100–200 mesh) using 40% ethyl acetate in hexane as the eluent to afford 0.80 g of the desired product as a brown solid.

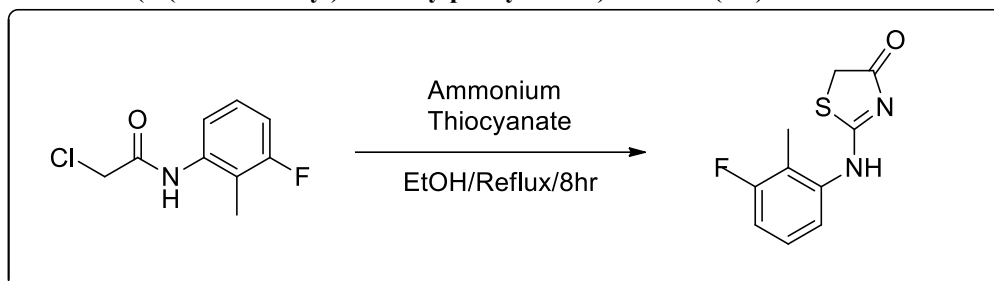
2.2.2. Synthesis of 2-chloro-N-(3-(Fluoromethyl)-2-methylphenyl) acetamide



To a stirred solution of the Step-01 product (1.0 equiv) in dichloromethane (DCM, 100 mL) was added DIPEA (3.0 equiv) at 0°C , followed by the careful addition of chloroacetyl chloride (3.0 equiv) at 0°C due to the

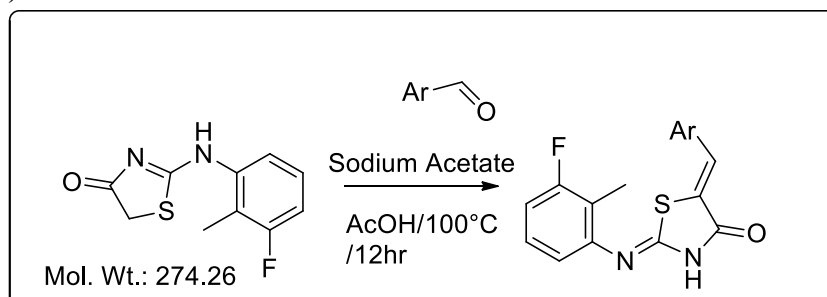
exothermic nature of the reaction. The reaction mixture was then stirred at room temperature for 4 h, and the reaction progress was monitored by TLC using 20% ethyl acetate in hexane as the developing solvent, visualized under UV light and iodine vapor. After completion of the reaction, the mixture was poured into water and successively washed with sodium bicarbonate solution, brine solution, and water. The organic layer was then separated, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 6.0 g of crude material. The crude product was purified by silica gel column chromatography (100–200 mesh) using 8–10% methanol in DCM as the eluent to afford 5.6 g of the final product as an off-white solid.

2.2.3. Synthesis of 2-(3-(Fluoromethyl)-2-methylphenylamino) thiazol-4(5H)-one



To a stirred solution of the **Step-02 product (5.5 g, 1.0 equiv)** in ethanol (80 mL) was added **potassium thiocyanate (KSCN, 2.76 g, 1.5 equiv)**, and the reaction mixture was refluxed for **8 h**. The reaction progress was monitored by TLC using **8% methanol in DCM** as the developing solvent, visualized under UV light and iodine vapor. After completion of the reaction, the mixture was concentrated under reduced pressure to approximately half of its original volume, resulting in the formation of a solid precipitate. The precipitated solid was collected by filtration and washed successively with **water and ethanol (1:1)** to afford **3.9 g of a light-brown solid**. The crude product was further triturated with **hexane (25 mL × 2)** and dried under high vacuum to afford **3.5 g of the final product as an off-white solid**.

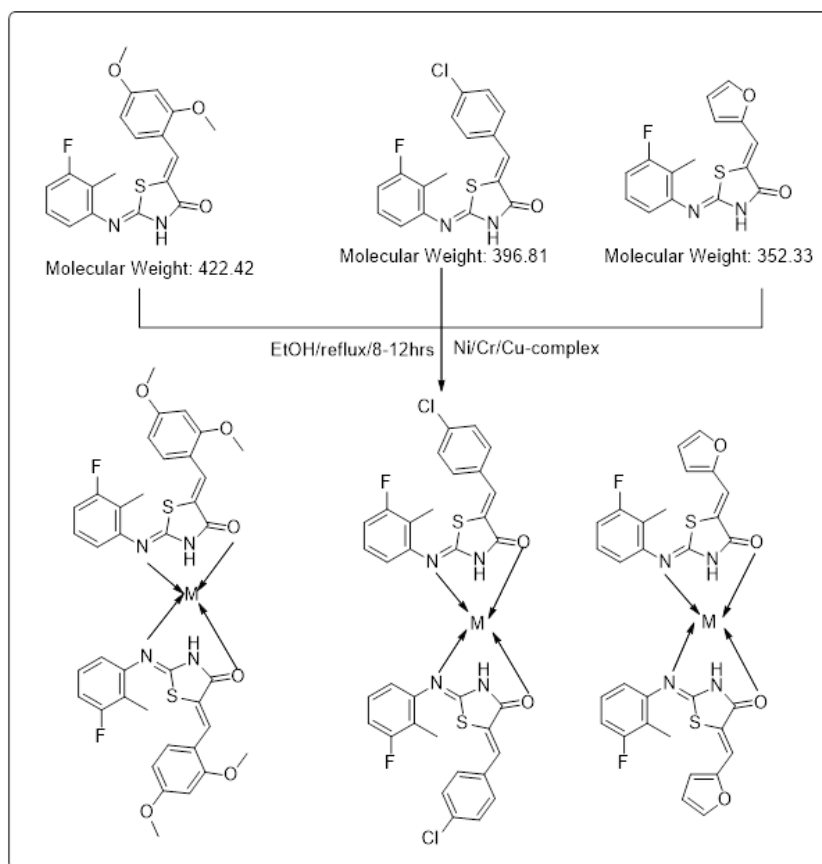
2.3.4. Synthesis (2Z, 5Z)-5-benzylidene-2-((2-methyl-3-(Fluoromethyl)phenyl)imino) thiazoli din -4-one derivatives (7a-c)



To a stirred solution of the **Step-03 product (1.0 equiv)** in glacial acetic acid (AcOH, 20 mL), **sodium acetate (NaOAc, 6.0 equiv)** and the appropriate **substituted aromatic aldehyde (1.2 equiv)** were added. The reaction mixture was refluxed for **8 h**, and reaction progress was monitored by TLC using **50% ethyl acetate in hexane** as the developing solvent, visualized under UV light and iodine vapor. After completion of the reaction, the mixture was poured onto **crushed ice**, and the resulting precipitate was collected by filtration and dried to afford approximately **400 mg of crude product**. The crude material was triturated successively with **hexane (20 mL)**, **a 1:1 mixture of hexane and ethyl acetate**, and **ethanol (3 mL × 2)**. The solid was filtered and dried under vacuum at **60 °C for 20 min** to afford the corresponding purified solid product.

2.3. General Procedure for the Synthesis of Metal Complexes

The metal complexes were synthesized by reacting the appropriate ligand with the corresponding metal salt in a 2:1 ligand-to-metal molar ratio. A hot ethanolic solution of the ligand (2 mmol) was added slowly with continuous stirring to a hot ethanolic solution of the respective metal salt (1 mmol), namely $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, or $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$. The resulting reaction mixture was stirred continuously and refluxed for 4–6 h, while the pH was maintained at approximately 6–7 using dilute ammonia or sodium acetate solution. After the reaction was complete, the mixture was allowed to cool to room temperature, and the resulting colored precipitate was collected by filtration. The precipitate was washed repeatedly with ethanol, followed by diethyl ether, to remove unreacted starting materials and impurities. The obtained complexes were then dried under reduced pressure over anhydrous calcium chloride. The resulting metal complexes were obtained in good yields and were stable under ambient conditions.



2.4. Antibacterial Activity

2.4.1 Antibacterial Protocol

The antibacterial activities of the synthesized ligands 7a–c and their corresponding Ni(III), Cr(III), and Cu(II) complexes were evaluated against two Gram-positive bacterial strains, *Staphylococcus aureus* and *Bacillus subtilis*, and two Gram-negative bacterial strains, *Escherichia coli* and *Pseudomonas aeruginosa*, using the agar well diffusion method. Mueller–Hinton agar was used as the culture medium. The test compounds were dissolved in dimethyl sulfoxide (DMSO), while ciprofloxacin was used as the reference antibacterial agent. Sterile wells were prepared in the inoculated Mueller–Hinton agar plates and filled with the respective test solutions. The plates were incubated at 37 °C for 24 h, and antibacterial activity was evaluated by measuring the diameter of the inhibition zones surrounding the wells in millimetres. The minimum inhibitory concentration (MIC) was determined using the broth microdilution method. Serial dilutions of each test compound were prepared in nutrient broth and inoculated with the respective bacterial cultures. The inoculated samples were incubated at 37 °C for 24 h. The MIC was defined as the lowest concentration of the test compound that completely inhibited visible bacterial growth. All antibacterial experiments were performed in triplicate, and the results are expressed as mean $\pm$ standard deviation (SD) [39–42].

2.5 Molecular Docking Protocol

Molecular docking studies were performed using AutoDock Vina and AutoDock. The synthesized arylidene-2-iminothiazolidin-4-one ligands 7a–c and their corresponding Ni(III), Cr(III), and Cu(II) complexes were considered for docking analysis. The three-dimensional structures of *Staphylococcus aureus* DNA gyrase (PDB ID: 2XCT) and *S. aureus* dihydrofolate reductase (DHFR; PDB ID: 2W9S) were obtained from the Protein Data Bank. The protein structures were prepared by removing non-essential molecules and adding the required hydrogen atoms and partial charges before docking.

The ligands 7a–c were docked against both 2XCT and 2W9S, whereas the corresponding Ni(III), Cr(III), and Cu(II) complexes were docked against 2XCT. Ciprofloxacin and trimethoprim were used as reference inhibitors for 2XCT and 2W9S, respectively. Docking calculations were performed within the predefined binding sites of the respective proteins, and the resulting poses were ranked according to their predicted binding energies. The ligand–protein interactions were subsequently analyzed in terms of hydrogen bonding and hydrophobic interactions [43–46].

2.6 ADME and Drug-Likeness Properties

The predicted absorption, distribution, metabolism, and excretion (ADME) and drug-likeness properties of the synthesized ligands 7a–c were evaluated using the SwissADME web-based platform. The molecular structures of compounds 7a–c were individually submitted to the platform to obtain their corresponding physicochemical and pharmacokinetic parameters. The evaluated parameters included molecular weight (MW), molecular volume

(MV), topological polar surface area (TPSA), predicted gastrointestinal absorption, MLOGP, number of rotatable bonds, hydrogen-bond donors and acceptors, and Lipinski's rule-of-five parameters. Lead-likeness was also assessed using the criteria implemented in SwissADME. The computational predictions were used to compare the physicochemical, absorption, and drug-likeness profiles of ligands 7a–c [47–48].

2.7 Thermogravimetric (TG) and Differential Thermogravimetric (DTG) Analysis

Thermogravimetric (TG) and differential thermogravimetric (DTG) analyses were performed to investigate the thermal stability and decomposition behavior of the synthesized **Ni(II)**, **Cr(III)**, and **Cu(II)** complexes. The TG/DTG curves were recorded over approximately 35–1000 °C under the experimental conditions employed. The onset temperature, DTG peak temperature(s), end temperature, experimental weight loss, and final residue were determined from the corresponding TG/DTG curves.

The observed mass-loss steps were used to evaluate the thermal decomposition patterns of the complexes and to identify the temperature ranges associated with successive decomposition events. The experimental mass losses were compared with the calculated values based on the proposed molecular formulae of the complexes to support their compositions and thermal decomposition behavior [49–51].

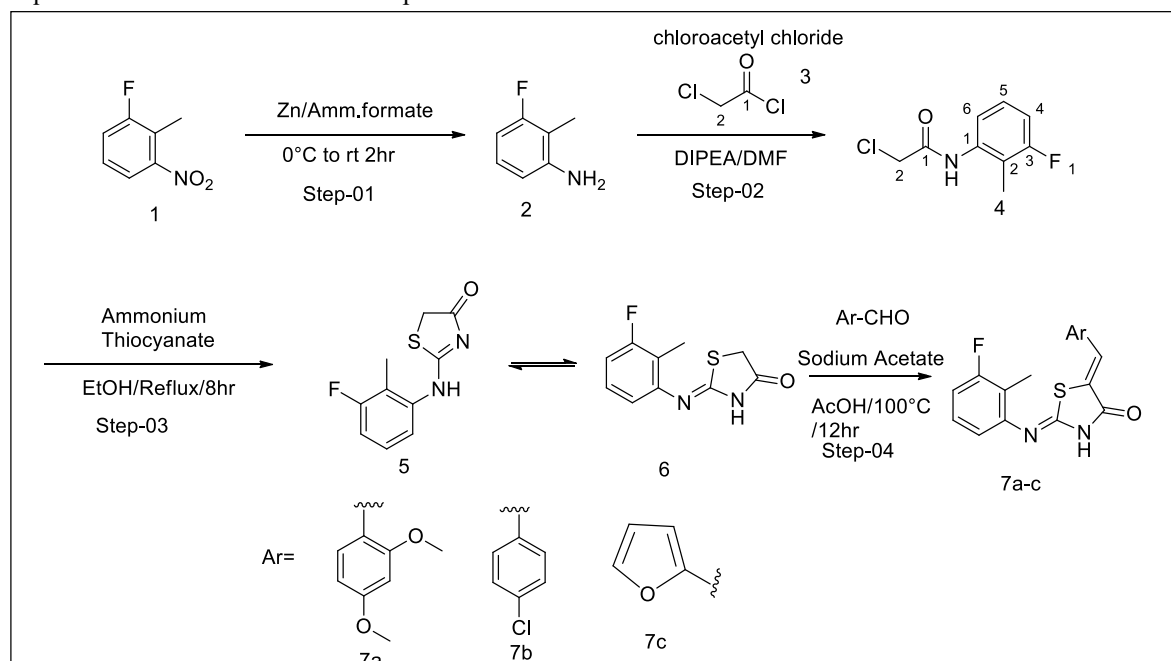
2.8 Powder X-ray Diffraction (PXRD)

Powder X-ray diffraction (PXRD) analysis was performed to investigate the crystalline nature and structural ordering of the synthesized **Ni(II)**, **Cr(III)**, and **Cu(II)** complexes. The diffraction patterns were recorded over the appropriate 2θ range under the experimental conditions employed. The observed diffraction peaks were analyzed in terms of their 2θ positions, interplanar spacing (d), and full width at half maximum (FWHM). The interplanar spacing was calculated from the observed diffraction angles, and the average crystallite size was estimated from the broadening of the diffraction peaks using the Scherrer equation. The PXRD patterns were subsequently used to assess the relative degree of crystallinity and structural ordering of the synthesized metal complexes [52–54].

3.0 RESULTS AND DISCUSSION:

The target arylidene-2-iminothiazolidin-4-one derivatives (7a–c) were synthesized through a multistep synthetic route, as outlined in Scheme 1. The synthesis commenced with the reduction of the corresponding nitro compound to afford 3-(fluoromethyl)-2-methylbenzenamine (2). Subsequent acylation of intermediate 2 with chloroacetyl chloride in the presence of DIPEA afforded 2-chloro-N-[3-(fluoromethyl)-2-methylphenyl]acetamide (3). Cyclization of intermediate 3 with potassium thiocyanate in refluxing ethanol furnished the corresponding 2-iminothiazolidin-4-one intermediate (4), which served as the key precursor for the synthesis of the target derivatives.

In the final step, intermediate 4 underwent a base-promoted Knoevenagel condensation with the appropriate substituted aromatic aldehydes in glacial acetic acid in the presence of sodium acetate to furnish the corresponding arylidene-2-iminothiazolidin-4-one derivatives (7a–c). Variation of the aromatic aldehyde substituents enabled the preparation of analogues containing different substituents on the arylidene moiety. The complete synthetic sequence and reaction conditions are presented in Scheme 1.



Scheme 1- Synthesis (2Z, 5Z)-5-benzylidene-2-((2-methyl-3-(fluoromethyl)phenyl)imino) thiazolidin-4-one derivatives (7a–c)

3.1. Antibacterial Activity

The antibacterial activity of the synthesized ligands and their corresponding **Ni(II)**, **Cu(II)**, and **Cr(III)** complexes

was evaluated against two Gram-positive bacterial strains, *Staphylococcus aureus* and *Bacillus subtilis*, and two Gram-negative bacterial strains, *Escherichia coli* and *Pseudomonas aeruginosa*. The minimum inhibitory concentration (MIC) values obtained by the broth microdilution method are presented in Table 1. The free ligands 7a–7c exhibited moderate antibacterial activity against the tested bacterial strains, with MIC values ranging from 12.5 to 50 $\mu\text{g mL}^{-1}$. Ligand 7a showed MIC values of 12.5, 25, 25, and 50 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, respectively. Ligand 7b exhibited MIC values of 12.5–50 $\mu\text{g mL}^{-1}$, whereas ligand 7c showed MIC values of 25–50 $\mu\text{g mL}^{-1}$. The antibacterial activity of the metal complexes varied considerably depending on the metal ion and ligand structure. Among the Ni(II) complexes, Ni(7c)₂ exhibited MIC values of 25–75 $\mu\text{g mL}^{-1}$, while Ni(7a)₂ and Ni(7b)₂ showed MIC values in the range of 50–75 $\mu\text{g mL}^{-1}$. Thus, under the conditions investigated, complexation with Ni(II) did not result in a consistent enhancement of antibacterial activity compared with the corresponding free ligands. The Cu(II) complexes also displayed variable antibacterial activity. Notably, Cu(7b)₂ exhibited an MIC of 2.5 $\mu\text{g mL}^{-1}$ against *E. coli*, representing the lowest MIC observed among all the synthesized compounds. However, its activity against the other bacterial strains was comparatively weaker, with MIC values of 25, 50, and 75 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, and *P. aeruginosa*, respectively. Cu(7a)₂ and Cu(7c)₂ showed MIC values ranging from 25 to 100 $\mu\text{g mL}^{-1}$ and 50 to 75 $\mu\text{g mL}^{-1}$, respectively. The Cr(III) complexes demonstrated moderate to weak antibacterial activity, with MIC values ranging from 25 to 100 $\mu\text{g mL}^{-1}$. Cr(7a)₂ showed comparatively better activity against *S. aureus* and *B. subtilis*, with MIC values of 25 $\mu\text{g mL}^{-1}$. Cr(7b)₂ exhibited MIC values of 75, 100, 75, and 50 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, respectively. Cr(7c)₂ showed MIC values of 50, 50, 50, and 100 $\mu\text{g mL}^{-1}$, respectively. Ciprofloxacin, used as the reference antibacterial agent, showed MIC values of 12.5, 25, 12.5, and 25 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, respectively. Most of the synthesized compounds exhibited lower antibacterial activity than ciprofloxacin. However, Cu(7b)₂ showed particularly notable activity against *E. coli*, with an MIC of 2.5 $\mu\text{g mL}^{-1}$, which was lower than that of the reference drug under the experimental conditions employed. Overall, the antibacterial results indicate that metal complexation did not uniformly enhance the activity of the ligands. Instead, the antibacterial response depended on both the coordinated metal ion and the ligand framework. The pronounced activity of Cu(7b)₂ against *E. coli* suggests a possible influence of the Cu(II) centre and the structural features of ligand 7b on antibacterial activity. Differences in lipophilicity, molecular geometry, coordination environment, and interactions with bacterial cellular components may contribute to the observed variation in activity. Further biological investigations would be required to establish the precise mechanism responsible for the antibacterial effects of these complexes.

Table 1. Antibacterial activity of the synthesized ligands and metal complexes.

Compound	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
7a	12.5	25	25	50
Ni(7a) ₂	50	50	50	75
cu(7a) ₂	25	75	50	100
cr(7a) ₂	25	25	75	50
7b	12.5	50	50	25
Ni(7b) ₂	50	75	75	50
Cu(7b) ₂	25	50	2.5	75
Cr(7b)₂	75	100	75	50
7c	25	25	50	25
Ni(7c)₂	25	50	50	75
Cu(7c)₂	50	75	75	50
Cr(7c)₂	50	50	50	100
Ciprofloxacin	12.5	25	12.5	25

Antibacterial activity of synthesized ligands and metal complexes

MIC values of compounds against four bacterial strains. Lower MIC values indicate stronger antibacterial activity.

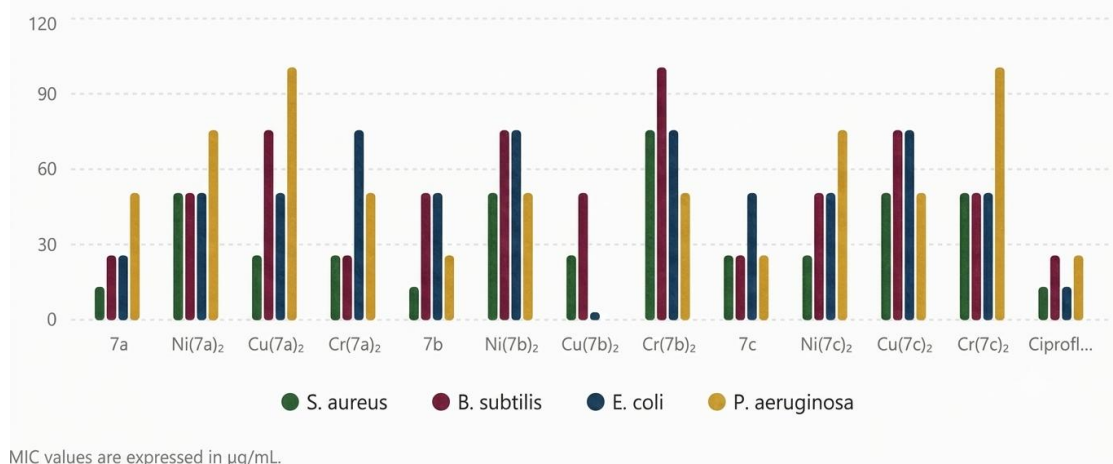


Figure 1. Antibacterial activity (MIC, $\mu\text{g/mL}$) of the synthesized ligands and metal complexes against selected bacterial strains.

3.2. Molecular Docking Studies

Molecular docking studies were performed to investigate the predicted binding modes and protein–ligand interactions of the synthesized compounds. Compounds 7a, 7b, and 7c were evaluated against *Staphylococcus aureus* dihydrofolate reductase (DHFR; PDB ID: 2W9S) and DNA gyrase (PDB ID: 2XCT) using AutoDock Vina. The corresponding metal complexes Ni(7a)₂, Cu(7b)₂, and Cr(7c)₂ were evaluated against DNA gyrase (PDB ID: 2XCT) using AutoDock 4.2. The calculated docking scores and key protein–ligand interactions are summarized in Table 2.

Against DHFR (2W9S), compound 7a exhibited the most favorable calculated docking score of $-9.821 \text{ kcal mol}^{-1}$, followed by 7b ($-9.682 \text{ kcal mol}^{-1}$) and 7c ($-8.950 \text{ kcal mol}^{-1}$). Compound 7a formed hydrogen-bonding interactions with ASN18, THR46, and TYR98, together with hydrophobic contacts involving ILE14, LEU20, ALA43, LYS45, and THR96. Compound 7b showed a docking score of $-9.682 \text{ kcal mol}^{-1}$ and formed a hydrogen bond with THR46, a halogen interaction with ASP27, and hydrophobic contacts involving ILE5, ALA7, ILE14, LEU20, ILE31, PHE92, and THR121. Compound 7c displayed a comparatively less favorable docking score of $-8.950 \text{ kcal mol}^{-1}$ and showed a hydrogen bond with THR46, a halogen interaction with ASP27, and hydrophobic contacts involving ILE5, ALA7, ILE14, LEU20, ILE31, PHE92, and THR121. The recurrence of ILE14, LEU20, and THR46 among the predicted interactions suggests that these residues may contribute to accommodation of the compounds within the predicted 2W9S binding region.

The interaction patterns of compounds 7a–7c with DNA gyrase (2XCT) differed from those observed with 2W9S. Compound 7a showed a docking score of $-6.189 \text{ kcal mol}^{-1}$ and formed hydrophobic contacts involving VAL1045, ALA1089, and ILE1175, together with a hydrogen bond with ARG1033 and a π -cation interaction involving LYS1043. Compound 7b exhibited the most favorable calculated docking score among the three free compounds ($-6.402 \text{ kcal mol}^{-1}$) and formed hydrophobic interactions involving ASP512, ILE516, ARG1033, and HIS1081, accompanied by a hydrogen bond with ASP512. Compound 7c showed a docking score of $-5.935 \text{ kcal mol}^{-1}$ and exhibited hydrophobic contacts involving VAL1045, ALA1089, and ARG1092, together with a π -stacking interaction involving HIS1081. These interaction patterns indicate that the three compounds may adopt different orientations and establish distinct contacts within the predicted DNA gyrase binding region.

The metal complexes Ni(7a)₂, Cu(7b)₂, and Cr(7c)₂ also exhibited distinct interaction profiles with DNA gyrase (2XCT). Ni(7a)₂ showed a calculated docking score of $-9.580 \text{ kcal mol}^{-1}$ and formed a hydrogen bond with GLU435, together with hydrophobic contacts involving LYS460, ASP510, ASP512, and LYS581. Cu(7b)₂ exhibited a docking score of $-9.790 \text{ kcal mol}^{-1}$ and formed two hydrogen-bond interactions involving GLU435 and PRO1080. Cr(7c)₂ displayed the most favorable calculated docking score among the investigated metal complexes ($-10.470 \text{ kcal mol}^{-1}$). It formed hydrogen-bond interactions involving GLY1115, GLN1267, and ASN1269, together with hydrophobic contacts involving PHE1097, MET1113, VAL1268, ASN1269, and ARG1272. The combination of hydrophobic and hydrogen-bonding interactions observed for Cr(7c)₂ provides structural context for its favorable predicted binding pose within the 2XCT binding region. Beyond conventional experimental evaluation, artificial intelligence (AI) and data-driven analytical approaches are increasingly being explored to support systematic data interpretation and evidence-based decision-making in applied research. Such approaches may offer opportunities for integrating experimental observations with computational predictions; however, their relevance to antibacterial metal-complex research requires validation using chemistry-specific datasets and suitable computational methods [55].

Table 2. Molecular docking affinities and protein–ligand interactions of ligands, metal complexes, and reference compounds against 2W9S and 2XCT

Complex	Affinity	Interaction_Type	Interaction_Count	Residues
2W9S_7a	-9.821	Hydrophobic	6	ILE14, LEU20, ALA43, LYS45, THR96
		Hydrogen_Bond	3	ASN18, THR46, TYR98
2W9S_7b	-9.682	Hydrophobic	8	ILE5, ALA7, ILE14, LEU20, ILE31, PHE92, THR121
		Hydrogen_Bond	1	THR46
		Halogen	1	ASP27
2W9S_7c	-8.950	Hydrophobic	8	ILE5, ALA7, ILE14, LEU20, ILE31, PHE92, THR121
		Hydrogen_Bond	1	THR46
		Halogen	1	ASP27
2XCT_7a	-6.189	Hydrophobic	3	VAL1045, ALA1089, ILE1175
		Hydrogen_Bond	1	ARG1033
		Pi_Cation	1	LYS1043
2XCT_7b	-6.402	Hydrophobic	4	ASP512, ILE516, ARG1033, HIS1081
		Hydrogen_Bond	1	ASP512
2XCT_7c	-5.935	Hydrophobic	3	VAL1045, ALA1089, ARG1092
		Pi_Stacking	1	HIS1081
2XCT_Ni(7a) ₂	-9.580	Hydrophobic	4	LYS460, ASP510, ASP512, LYS581
		Hydrogen_Bond	1	GLU435
2XCT_Cu(7b) ₂	-9.790	Hydrogen_Bond	2	GLU435, PRO1080
2XCT_Cr(7c) ₂	-10.47	Hydrophobic	6	PHE1097, MET1113, VAL1268, ASN1269, ARG1272
		Hydrogen_Bond	3	GLY1115, GLN1267, ASN1269

Protein–Ligand Interaction Analysis:

Protein–ligand interaction analysis was performed using PLIP to further characterize the binding modes of 7A–7C with the 2W9S and 2XCT receptors and those of the metal complexes MD1–MD3 with 2XCT. To visualize these binding environments, 2D interaction plots were generated using Discovery Studio Visualizer for the non-metal compounds (7A–7C) and LigPlot+ for the metal complexes (MD1–MD3). The interaction analysis showed that the compounds interacted with the receptors through combinations of hydrophobic contacts, hydrogen bonds, halogen interactions, pi-cation interactions and π -stacking. For 2W9S, 7A formed six hydrophobic interactions involving ILE14, LEU20, ALA43, LYS45 and THR96, together with three hydrogen bonds involving ASN18, THR46 and TYR98. 7B and 7C each showed eight hydrophobic interactions involving ILE5, ALA7, ILE14, LEU20, ILE31, PHE92 and THR121, along with a hydrogen bond involving THR46 and a halogen interaction with ASP27. The recurrence of ILE14, LEU20 and THR46 among the complexes suggests that these residues may contribute to accommodation of the compounds within the 2W9S binding region.

The interaction patterns of 7A–7C with 2XCT were comparatively different from those observed with 2W9S. 7A showed three hydrophobic interactions involving VAL1045, ALA1089 and ILE1175, together with a hydrogen bond involving ARG1033 and a π -cation interaction with LYS1043. 7B formed four hydrophobic interactions involving ASP512, ILE516, ARG1033 and HIS1081, accompanied by a hydrogen bond with ASP512. 7C showed three hydrophobic interactions involving VAL1045, ALA1089 and ARG1092 and an additional π -stacking interaction with HIS1081. These interaction patterns indicate that the non-metal compounds can occupy different regions or adopt different orientations within the 2XCT binding cavity. The docking scores of 7A, 7B and 7C against 2XCT were –6.189, –6.402 and –5.935 kcal/mol, respectively, and the interaction profiles demonstrate that these predicted binding modes are supported by multiple receptor contacts.

The metal complexes displayed distinct interaction patterns with 2XCT. MD1 formed four hydrophobic interactions involving LYS460, ASP510, ASP512 and LYS581, together with a hydrogen bond involving

GLU435. MD2 exhibited two hydrogen bonds involving GLU435 and PRO1080, without additional hydrophobic interactions being identified by PLIP. In contrast, MD3 displayed the most extensive interaction network among the metal complexes, comprising six hydrophobic interactions involving PHE1097, MET1113, VAL1268, ASN1269 and ARG1272, together with three hydrogen bonds involving GLY1115, GLN1267 and ASN1269. The interaction profile of MD3 is noteworthy in view of its most favourable docking score of -10.470 kcal/mol, compared with -9.580 and -9.790 kcal/mol for MD1 and MD2, respectively. The combination of hydrophobic contacts and hydrogen bonding observed for MD3 may contribute to its favourable predicted accommodation within the receptor cavity.

The PLIP analysis provides structural context for the docking results and demonstrates differences between the non-metal compounds and their corresponding metal complexes. The DD compounds showed predominantly hydrophobic interactions with 2W9S, whereas their interactions with 2XCT included additional hydrogen bonding and aromatic or cation-mediated interactions. Metal complexation produced distinct interaction profiles, with MD3 showing the most extensive combination of hydrophobic and hydrogen-bond interactions among the three complexes. The more favourable docking score of MD3 is therefore accompanied by a comparatively diverse interaction network. Nevertheless, the number of detected interactions should not be considered a direct measure of binding affinity, because interaction geometry, distance, orientation and energetic contributions are also important. The combined docking and PLIP results therefore provide a basis for selecting compounds for further structural and experimental investigation.

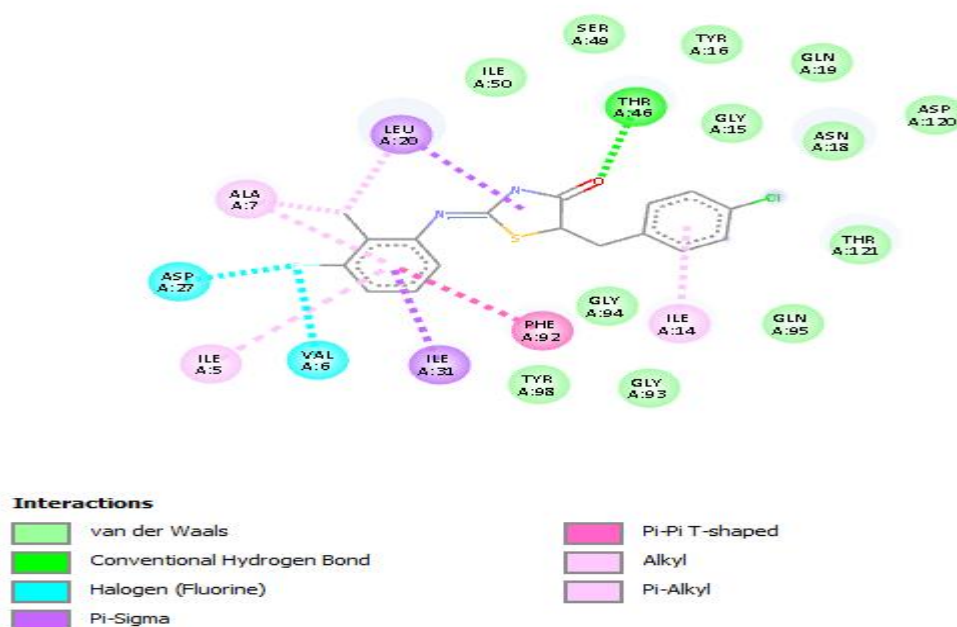


Figure 2- 2D Docking interaction of 7a with 2W9S

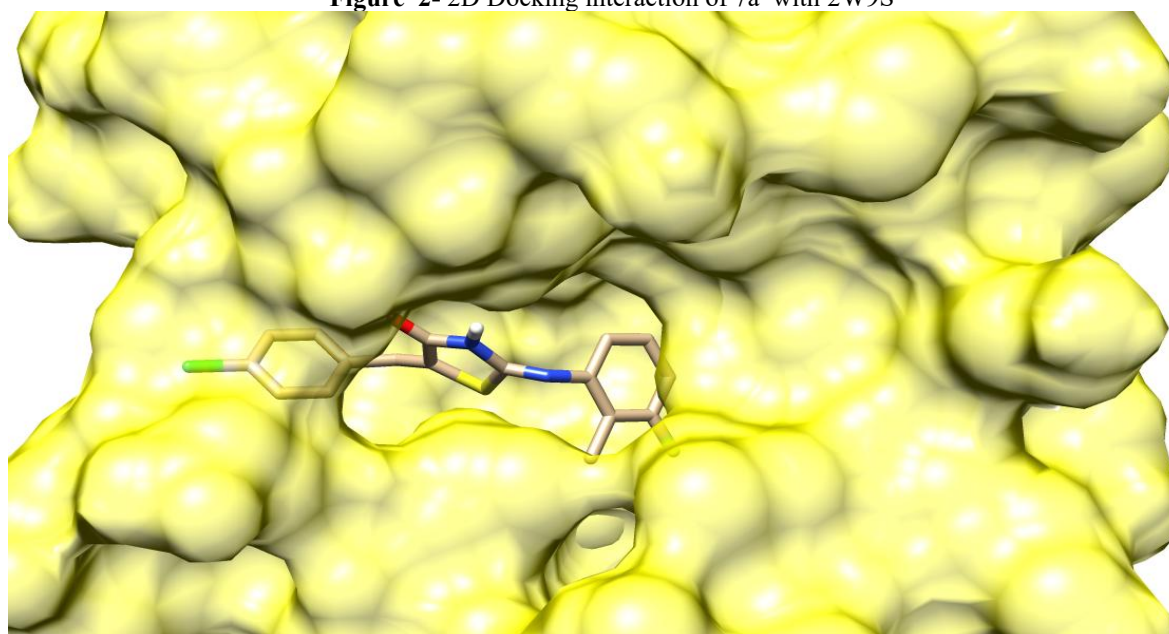


Figure 3- 3D Docking interaction of 7b with 2W9S

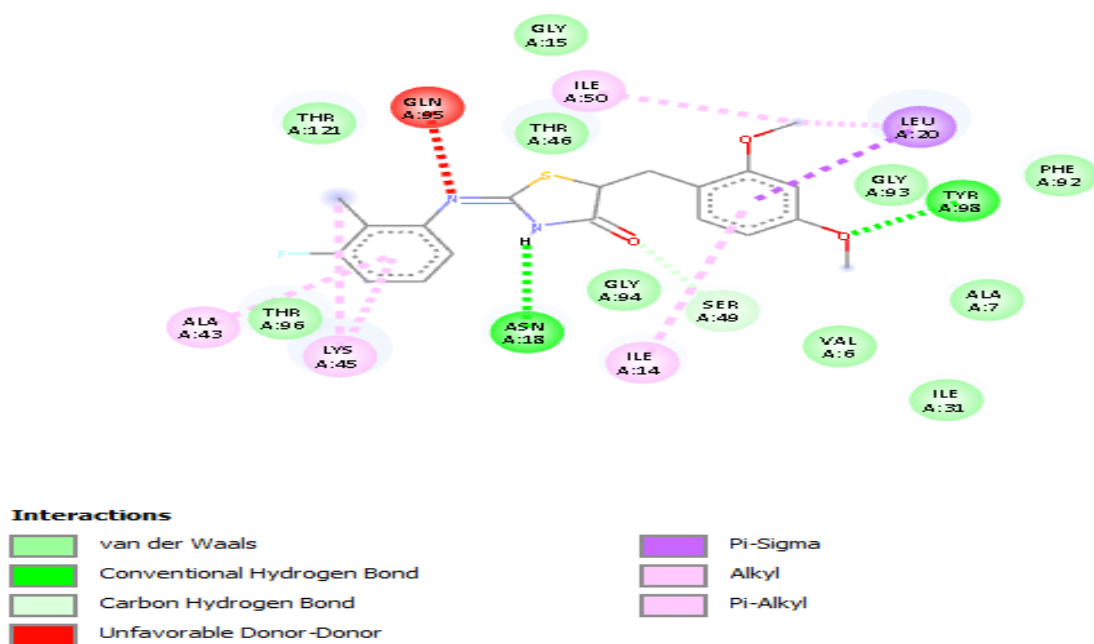


Figure 4- 2D Docking interaction of 7b with 2W9S

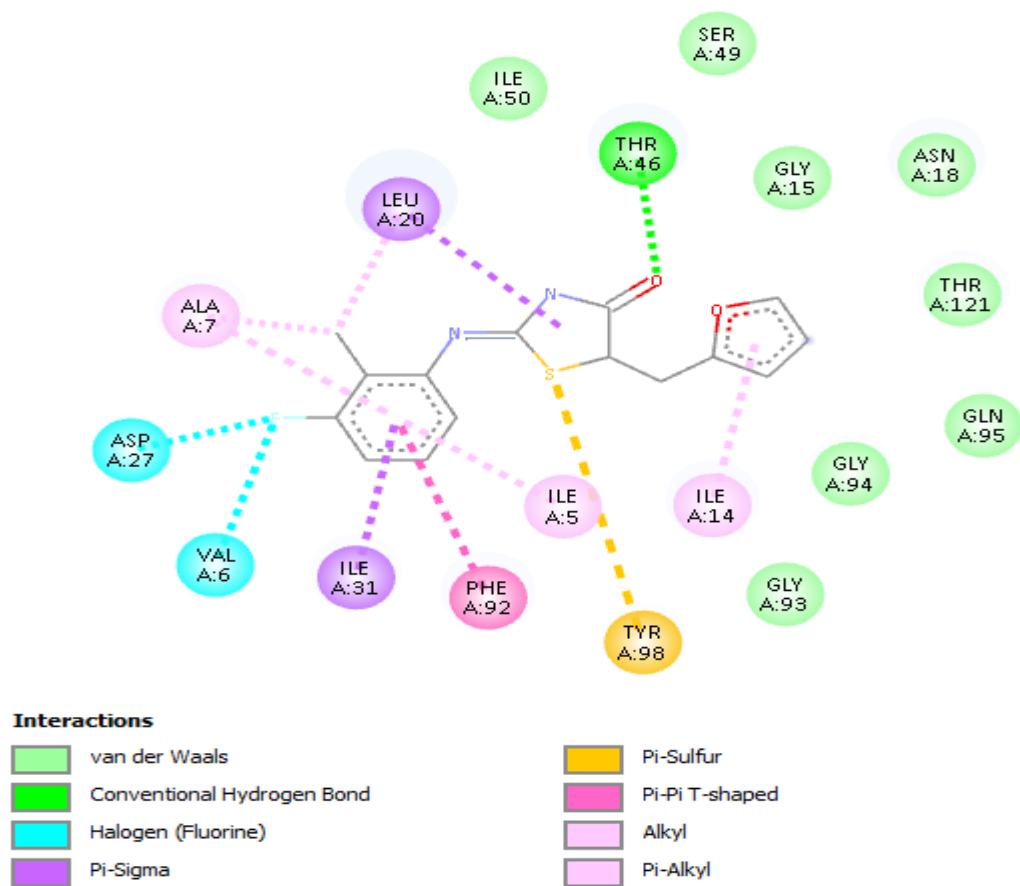


Figure 5- 2D Docking interaction of 7c with 2W9S

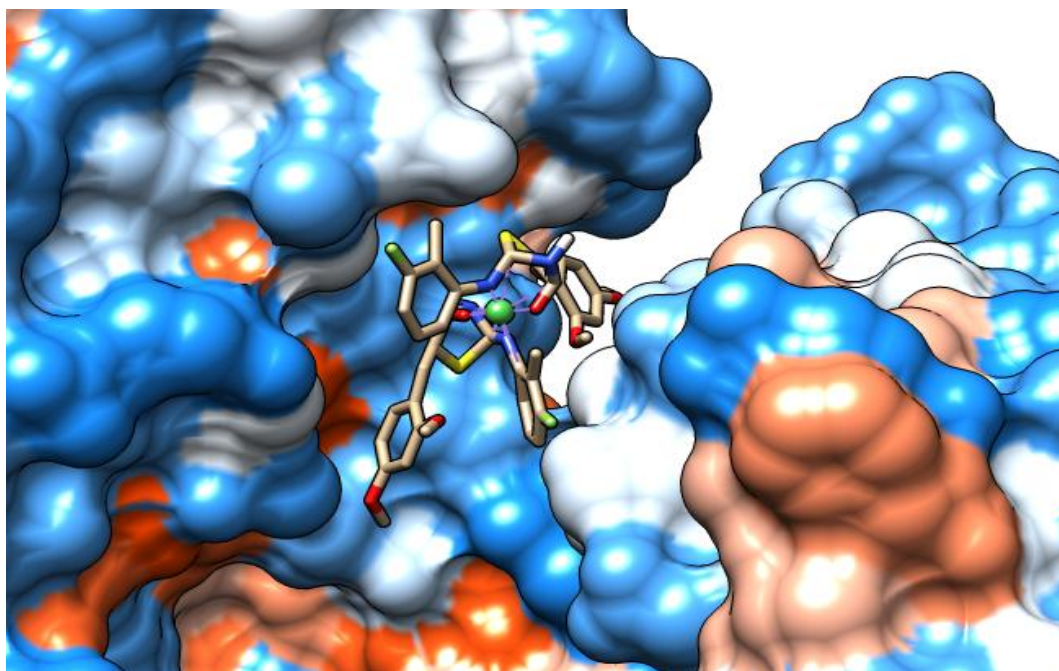


Figure 6- 3D Docking interaction of Ni(7c)2 with 2W9

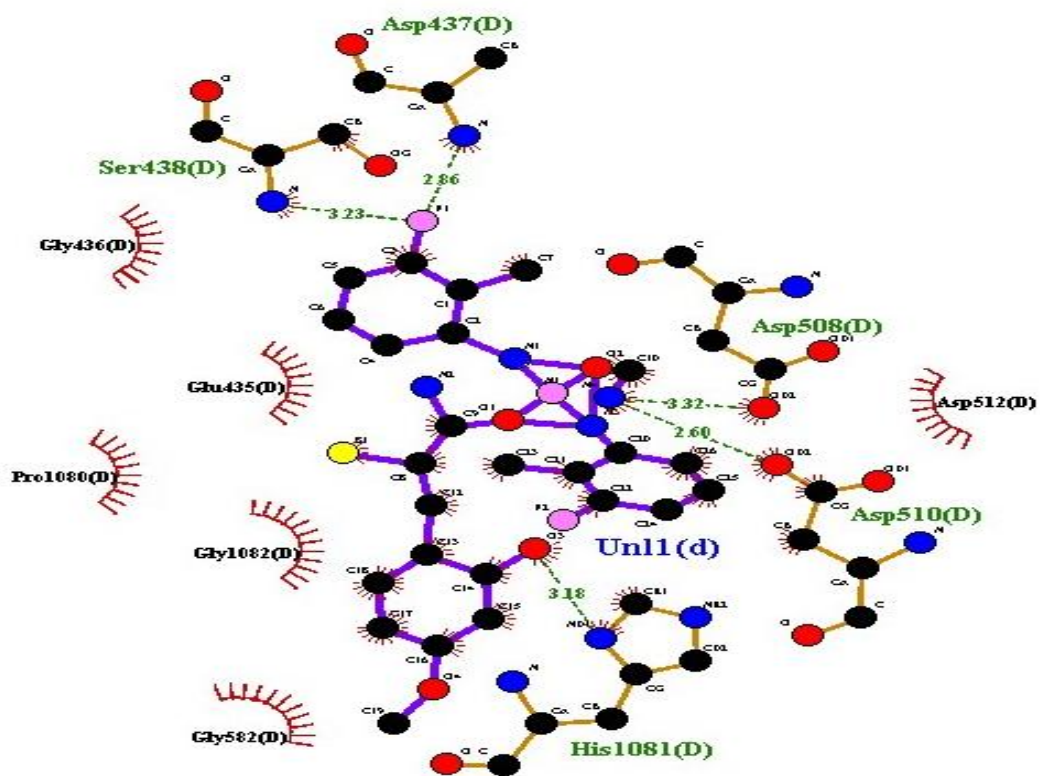


Figure 7- LigPlot interaction of Ni(7a)2 with 2W9S

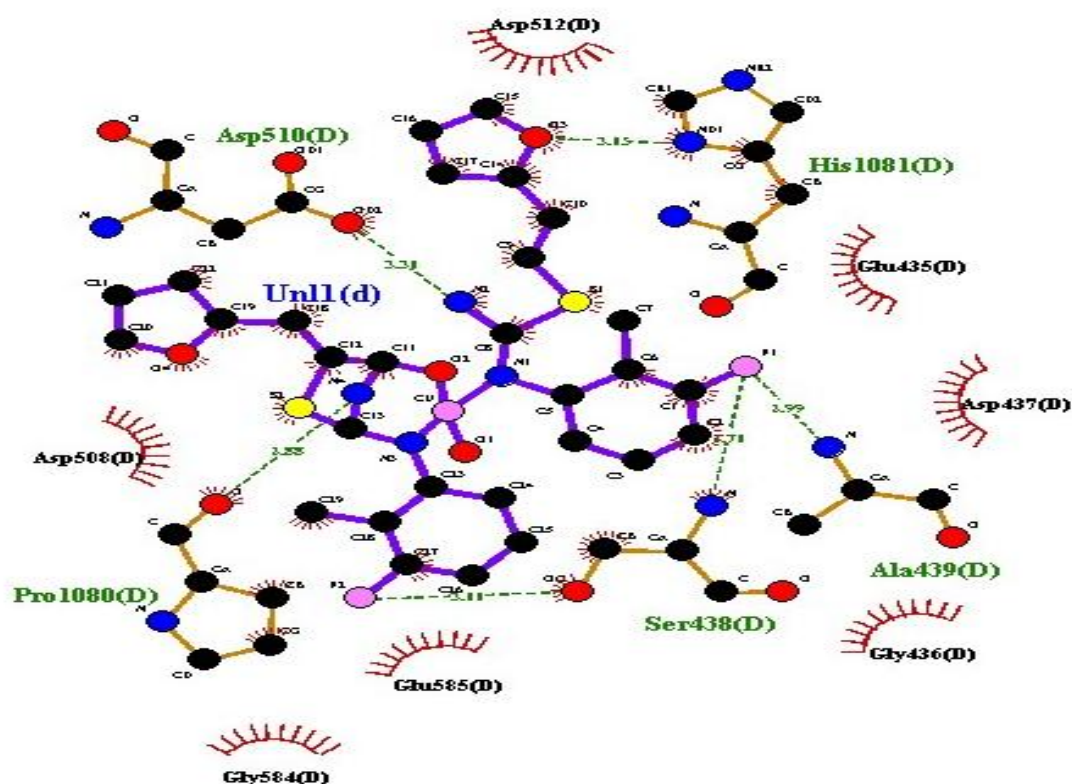


Figure 8- LigPlot interaction of Cr(7b)2 with 2W9S

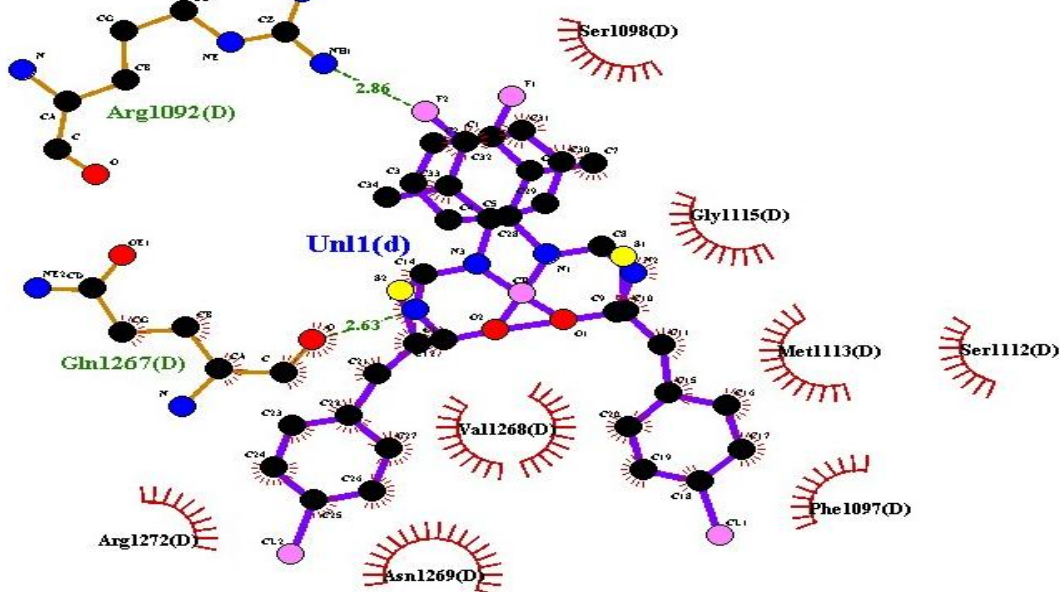


Figure 9- LigPlot interaction of Cu(7c)2 with 2W9S

3.3 ADME and Drug-Likeness Analysis

Table 3. Physicochemical and drug-likeness properties of compounds 8a–8c

Compound	MW	MV	TPSA	% ABS	MLOGP	Rotatable bonds	H-bond acceptors	H-bond donors	Lipinski violations	Leadlikeness violations
7a	372.41	360.723	85.22	79.60	2.85	4	5	1	0	2
7b	346.81	323.762	66.76	85.97	4.03	2	3	1	0	1
7c	302.3	285.38	79.9	81.43	2.23	2	4	1	0	1

	2	6								
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The predicted ADME and drug-likeness properties of 7a, 7b and 7c were evaluated using the SwissADME server. The molecular weights (MW) ranged from 302.32 to 372.41 g/mol, while molecular volumes (MV) ranged from 285.386 to 360.723. 7a exhibited the highest MW (372.41 g/mol) and molecular volume (360.723), whereas 7c showed the lowest values (302.32 g/mol and 285.386, respectively). The topological polar surface area (TPSA) ranged from 66.76 to 85.22 Å², with 7a showing the highest TPSA and 7b the lowest. These values indicate moderate molecular polarity and molecular size across the series, which may contribute to an appropriate balance between polarity and membrane permeability.

The predicted percentage absorption (%ABS) ranged from 79.60 to 85.97%. 7b showed the highest predicted absorption (85.97%), followed by 7c (81.43%) and 7a (79.60%). The MLOGP values ranged from 2.23 to 4.03, indicating moderate lipophilicity. 7b showed the highest MLOGP (4.03), whereas 7c exhibited the lowest value (2.23). 7a contained four rotatable bonds, while 7b and 7c each contained two, suggesting comparatively lower conformational flexibility for the latter two compounds. The hydrogen-bond acceptor count ranged from 3 to 5, while all three compounds possessed one hydrogen-bond donor. These physicochemical characteristics indicate that the compounds possess relatively moderate polarity and lipophilicity, with 7b combining the highest predicted absorption with the highest lipophilicity among the series.

All three compounds showed zero Lipinski violations, indicating compliance with the conventional Lipinski rule-of-five criteria based on the evaluated parameters. With respect to lead-likeness, 7A showed two violations, whereas 7b and 7c each showed one violation. The absence of Lipinski violations, together with the relatively moderate molecular weights, TPSA values and predicted absorption, suggests generally favourable drug-like physicochemical characteristics for the three compounds. Among them, 7b and 7c showed comparatively favourable overall profiles, particularly with respect to lower molecular size, fewer rotatable bonds, high predicted absorption and only one lead-likeness violation. These computational ADME predictions provide preliminary support for further investigation; however, they should not be considered definitive evidence of favourable pharmacokinetics, and experimental ADME, toxicity and biological studies would be required for validation.

3.4 Characterization of synthesized ligands and their metal complexes

3.4.1. Infrared spectral studies

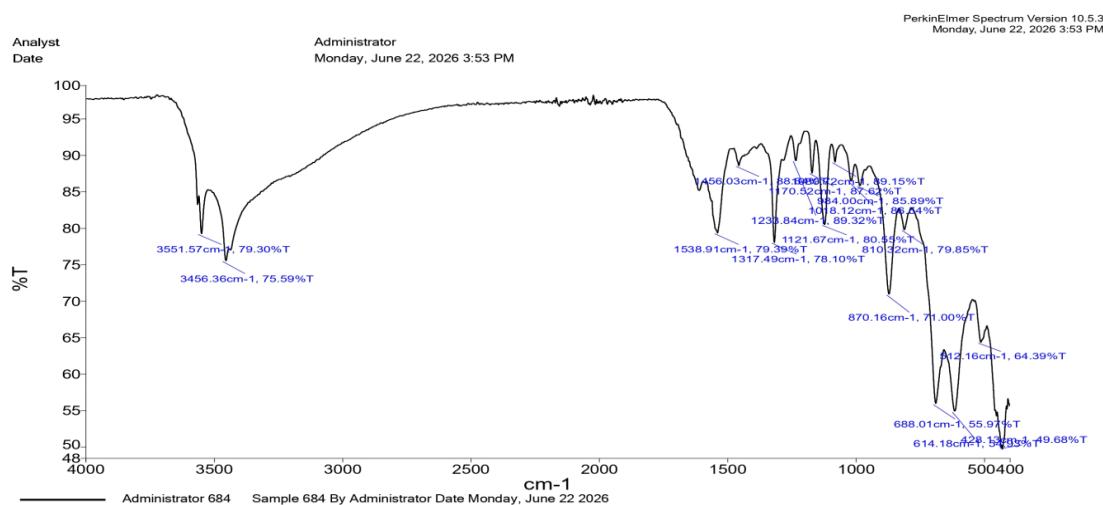
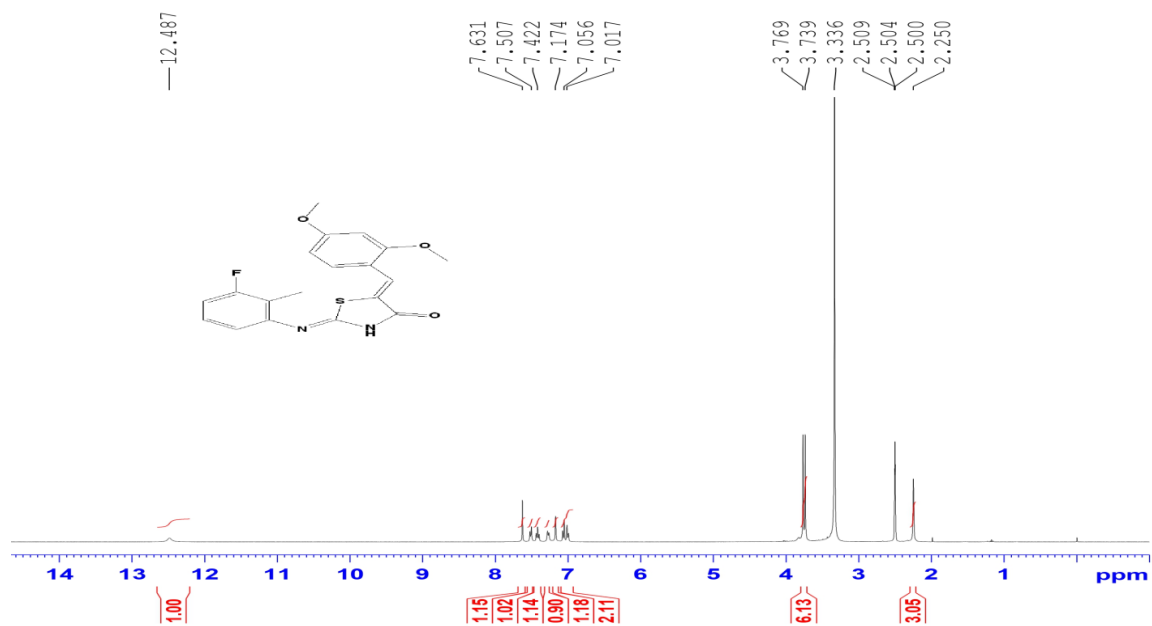


Figure 10- Nickel (7a)₂ complex IR spectrum

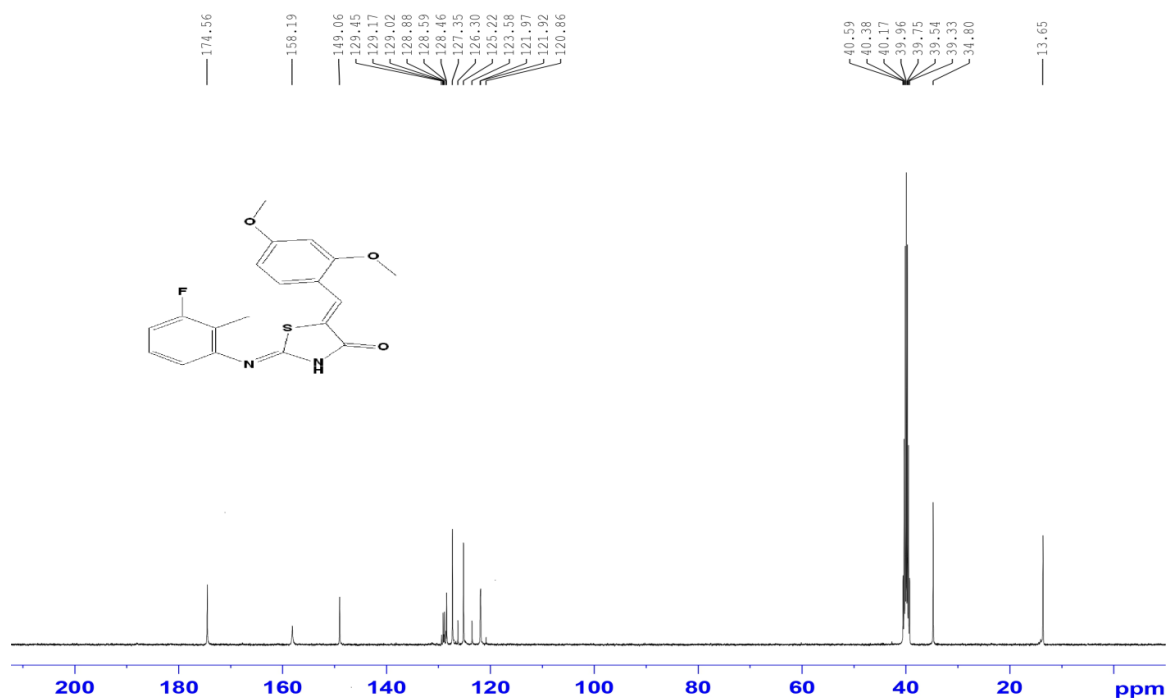
The FTIR spectrum of the synthesized metal complex (Fig. X) provides important evidence for the coordination of the ligand with the metal ion. The spectrum displays prominent high-frequency absorption bands at 3551.57 and 3456.36 cm⁻¹, which are attributed to N–H stretching vibrations. A distinct absorption band at 1538.91 cm⁻¹ is assigned to the azomethine $\nu(\text{C}=\text{N})$ stretching vibration. The observed changes in the positions and intensities of the $\nu(\text{C}=\text{N})$ and C=S/C–N vibrational bands, when compared with those of the corresponding free ligand, suggest the involvement of the imine nitrogen and sulfur donor atoms in metal coordination.

Several absorption bands occurring in the 1317.49–1018.12 cm⁻¹ region can be attributed to coupled C–N and C–S vibrational modes. Further evidence for complex formation is provided by the appearance of new bands in the low-frequency region at 512.16 and 428.13 cm⁻¹, which are tentatively assigned to $\nu(\text{M}–\text{S})$ and $\nu(\text{M}–\text{N})$ stretching vibrations, respectively. These spectral features, together with the shifts observed in the ligand-associated vibrational bands, support the coordination of the ligand to the central metal ion through the N- and S-donor sites.

3.4.2. NMR spectral studies



¹H Spectra of compound 7a



¹³C Spectra of compound 7a

Characterization of step 1

¹H NMR (400 MHz, DMSO-d₆): δ = 6.95–7.15 (m, 3H, Ar–H), 4.85–5.20 (br s, 2H, NH₂), 2.15 (s, 3H, Ar–CH₃), 2.05 (s, 3H, Ar–CH₃). ¹³C NMR (100 MHz, DMSO-d₆): δ = 146–150 (C–NH₂), 135–140 (C–CF₃), 128–135 (aromatic C), 123–126 (q, CF₃), 120–125 (aromatic CH), 17–20 (Ar–CH₃).

Characterization of step 2

¹H NMR (400 MHz, DMSO-d₆): δ = 9.20 (br s, 1H, NH), 7.65 (d, $J \approx 7.8$ Hz, 1H, Ar–H), 7.35 (t, $J \approx 7.6$ Hz, 1H, Ar–H), 7.15 (d, $J \approx 7.7$ Hz, 1H, Ar–H), 3.95 (s, 2H, CH₂Cl), 2.25 (s, 3H, Ar–CH₃). ¹³C NMR (100 MHz, DMSO-d₆): δ = 166.0 (C=O), 145.0 (C–NH), 136.5 (C–CH₃), 132.5 (C–CF₃), 130.0, 126.5, 124.0, 122.5 (Ar–C), 124.0 (q, $J \approx 272$ Hz, CF₃), 42.5 (CH₂Cl), 17.5 (Ar–CH₃).

Characterization of step 3

¹H NMR (400 MHz, DMSO-d₆): δ = 11.80 (br s, 1H, NH), 7.45 (d, $J \approx 7.8$ Hz, 1H, Ar–H), 7.25 (t, $J \approx 7.6$ Hz, 1H, Ar–H), 7.10 (d, $J \approx 7.8$ Hz, 1H, Ar–H), 3.85 (s, 2H, CH₂), 2.20 (s, 3H, Ar–CH₃). ¹³C NMR (100 MHz, DMSO-d₆): δ = 174.0 (C=O), 158.5 (C=N), 145.0, 137.0, 132.0, 129.0, 126.0, 124.0 (q, CF₃), 121.5 (Ar–C), 35.5 (CH₂), 17.5 (Ar–CH₃).

Characterization of 7a-c

Compound 7a

¹H NMR (400 MHz, DMSO-d₆): δ = 12.45 (br s, 1H, NH), 8.05 (s, 1H, =CH), 7.45–7.10 (m, 3H, Ar–H), 7.05–6.85 (m, 3H, Ar–H), 3.82 (s, 3H, OCH₃), 3.78 (s, 3H, OCH₃), 2.18 (s, 3H, Ar–CH₃).

¹³C NMR (100 MHz, DMSO-d₆): δ = 168.5 (C=O), 157.0 (C=N), 149.5, 148.2, 138.0, 135.5, 132.0, 129.5, 127.0, 124.0 (q, CF₃), 121.5, 114.0, 111.0, 56.0, 55.8, 17.5.

Compound 7b

¹H NMR (400 MHz, DMSO-d₆): δ = 12.50 (br s, 1H, NH), 8.05 (s, 1H, =CH), 7.65–7.15 (m, 7H, Ar–H), 2.18 (s, 3H, Ar–CH₃).

¹³C NMR (100 MHz, DMSO-d₆): δ = 168.5 (C=O), 157.0 (C=N), 137.5, 136.0, 132.5, 131.0, 129.5, 128.5, 127.0, 124.0 (q, CF₃), 121.5, 17.5.

Compound 7c

¹H NMR (400 MHz, DMSO-d₆): δ = 12.45 (br s, 1H, NH), 8.10 (s, 1H, =CH), 7.65–7.10 (m, 3H, Ar–H), 7.55 (s, 1H, furan-H), 6.75–6.45 (m, 2H, furan-H), 2.18 (s, 3H, Ar–CH₃).

¹³C NMR (100 MHz, DMSO-d₆): δ = 168.5 (C=O), 157.0 (C=N), 151.5, 143.0, 137.5, 132.0, 129.5, 127.0, 124.0 (q, CF₃), 121.5, 112.0, 108.5, 17.5.

3.5. Powder X-ray diffraction (PXRD) studies

Table.4 PXRD data of the synthesized Cr(III), Cu(II), and Ni(II) complexes

Complex	Major diffraction peaks, 2θ (°)	General PXRD observation
Ni-1	19.92, 22.52, 24.96, 25.76, 26.18, 26.46, 28.78, 31.06, 31.48	Several closely spaced reflections
Ni-2	15.74, 16.26, 18.22, 19.96, 20.46, 30.08, 31.18, 33.04, 35.18, 36.74	Multiple distinct crystalline reflections
Ni-3	16.14, 18.10, 20.38, 22.06, 30.00, 31.14, 32.98, 35.10	Well-defined crystalline reflections
Cr-1	15.30, 18.12, 24.82, 30.08, 31.44, 32.46	Well-defined crystalline reflections
Cr-2	15.38, 18.20, 25.04, 30.18, 32.34, 34.50	Crystalline pattern with multiple reflections
Cr-3	15.46, 18.12, 24.96, 29.48, 30.20, 32.64, 40.68	Well-defined crystalline pattern
Cu-1	15.74, 21.70, 32.14, 33.78, 35.38, 39.88	Distinct, relatively intense reflections
Cu-2	15.64, 20.46, 32.20, 35.38, 39.98, 45.16	Strong and well-resolved reflections
Cu-3	15.68, 21.72, 28.60, 32.12, 33.74, 35.34, 39.88	Multiple well-defined crystalline reflections

Powder X-ray Diffraction (PXRD) Analysis

The powder X-ray diffraction (PXRD) patterns of the synthesized Cr(III), Cu(II), and Ni(II) complexes were recorded to assess their crystalline nature and solid-state structural organization. As shown in Figure 13, all nine complexes exhibit distinct diffraction reflections, confirming the presence of ordered crystalline domains. However, noticeable differences in the positions, number, and relative intensities of the reflections were observed among the complexes, indicating variations in molecular packing and lattice organization.

The Cr(III) complexes exhibited characteristic reflections mainly in the 15–41° 2θ region. Cr-1 showed prominent reflections at 15.30°, 18.12°, 24.82°, 30.08°, 31.44°, and 32.46°. Cr-2 displayed reflections at 15.38°, 18.20°, 25.04°, 30.18°, 32.34°, and 34.50°, whereas Cr-3 exhibited reflections at 15.46°, 18.12°, 24.96°, 29.48°, 30.20°, 32.64°, and 40.68°. The common reflections observed near 15–18° and 30–33° suggest related structural features within the Cr(III) series, while differences in peak distribution and intensity indicate variations in crystal packing. The Cu(II) complexes also showed well-defined diffraction patterns. Cu-1 exhibited characteristic reflections at 15.74°, 21.70°, 32.14°, 33.78°, 35.38°, and 39.88°. Cu-2 showed prominent reflections at 15.64°, 20.46°, 32.20°, 35.38°, 39.98°, and 45.16°, while Cu-3 displayed reflections at 15.68°, 21.72°, 28.60°, 32.12°, 33.74°, 35.34°, and 39.88°. Among the Cu(II) complexes, Cu-2 displayed particularly intense and well-resolved reflections, indicating appreciable crystalline ordering.

The Ni(II) complexes exhibited distinct PXRD profiles compared with the Cr(III) and Cu(II) analogues. Ni-1 showed several closely spaced reflections at 19.92°, 22.52°, 24.96°, 25.76°, 26.18°, 26.46°, 28.78°, 31.06°, and 31.48°. Ni-2 exhibited reflections at 15.74°, 16.26°, 18.22°, 19.96°, 20.46°, 30.08°, 31.18°, 33.04°, 35.18°, and 36.74°, whereas Ni-3 showed characteristic reflections at 16.14°, 18.10°, 20.38°, 22.06°, 30.00°, 31.14°, 32.98°, and 35.10°. The presence of multiple distinct reflections in Ni-2 and Ni-3 further supports their crystalline nature. Overall, the PXRD patterns demonstrate that the synthesized complexes possess ordered crystalline structures, while the differences in diffraction profiles reflect changes in metal–ligand coordination, molecular arrangement, intermolecular interactions, and crystal packing. The PXRD results therefore provide complementary evidence for the formation of structurally differentiated Cr(III), Cu(II), and Ni(II) complexes. Since the present analysis is based on experimental powder patterns without full structural refinement, specific crystal systems and unit-cell

parameters were not assigned solely from the PXRD data.

Powder X-ray Diffraction (PXRD) Patterns of S3 Metal Complexes

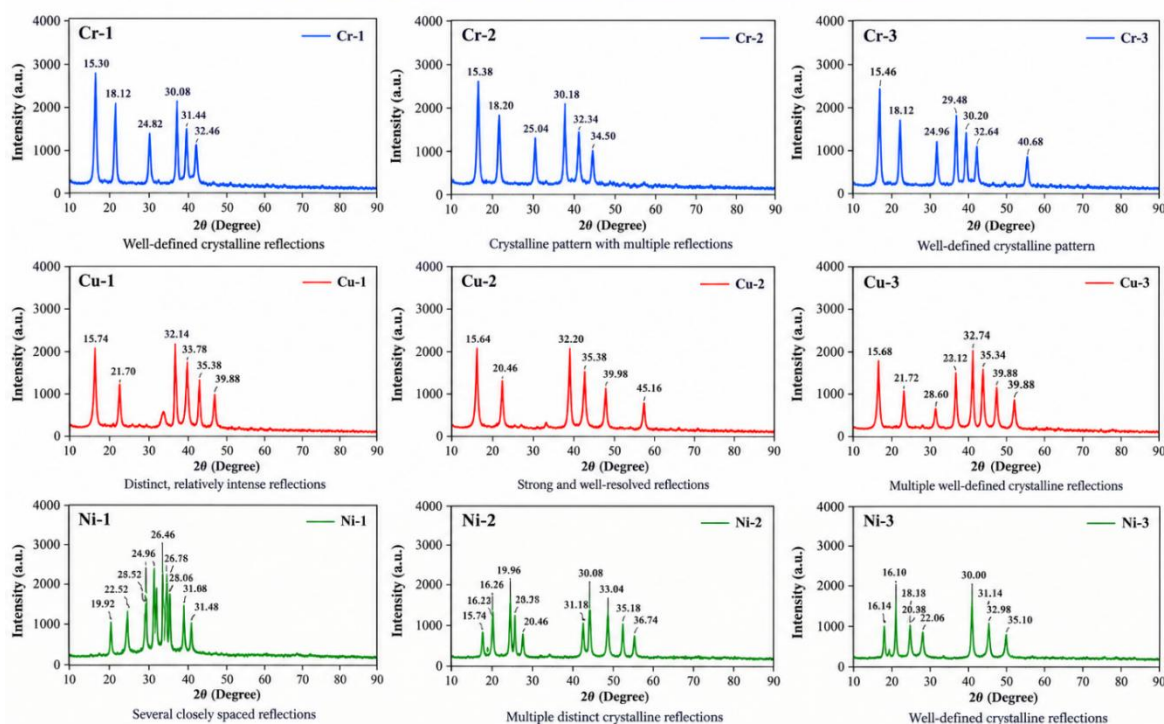


Figure 13. Powder X-ray diffraction (PXRD) patterns of the synthesized Cr(III), Cu(II), and Ni(II) complexes

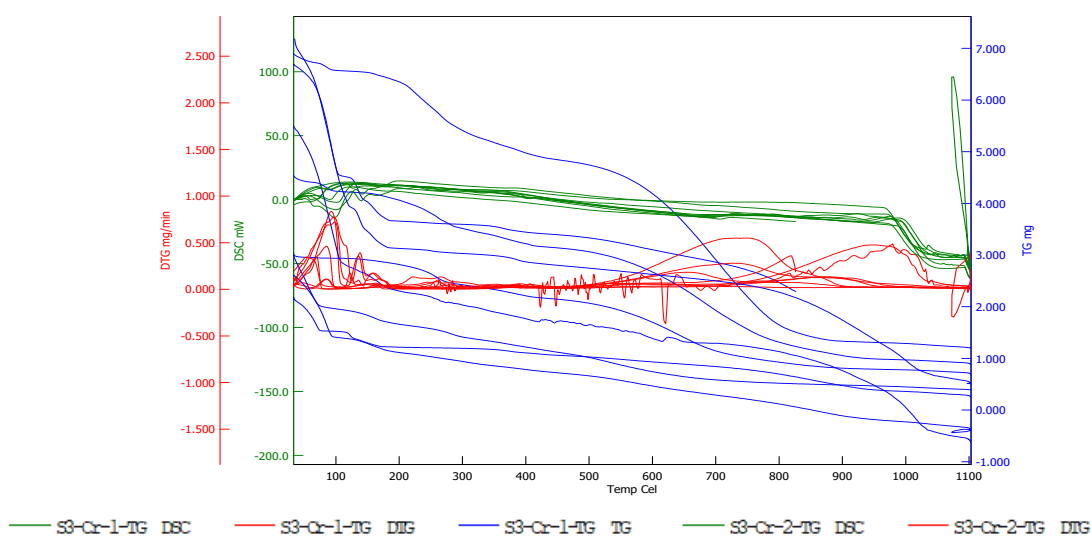
3.6. Thermogravimetric analysis (TGA)

The thermal decomposition behaviour of the S3 metal complexes was investigated by TGA coupled with DTG over 35–1000 °C. All complexes exhibited multistage mass-loss profiles, indicating successive thermal decomposition processes. The corresponding TG/DTG parameters are summarized in Table 5. S3–Cr-1 exhibited three decomposition regions with DTG maxima at 68.8, 122.7, and 859.4 °C. S3–Cr-2 showed a similar profile, with DTG maxima at 93.1, 135.7, and 813.7 °C. S3–Cr-3 displayed a more complex thermal profile, with DTG maxima at 98.6, 441.6, 587.1, 620.3, and 641.5 °C, indicating progressive decomposition over a broad temperature range. S3–Cu-1 and S3–Cu-2 exhibited two major decomposition regions, with DTG maxima at 265.4 and 747.1 °C for S3–Cu-1 and 259.0 and 654.7 °C for S3–Cu-2. S3–Cu-3 showed three decomposition regions with DTG maxima at 84.6, 261.5, and 730.7 °C. The nickel complexes also exhibited multistage decomposition. S3–Ni-1 showed DTG maxima at 53.6 and 538.5 °C, while S3–Ni-2 exhibited maxima at 85.1 and 870.3 °C. S3–Ni-3 showed initial and intermediate events at 96.9 and 138.0 °C, respectively, followed by further high-temperature decomposition. The variation in DTG maxima and decomposition profiles indicates that the thermal behaviour is influenced by the nature of the coordinated metal ion and its coordination environment. Since the hydration/solvation states and final residue compositions were not independently established, individual mass-loss events were not assigned to specific molecular fragments. The thermal behaviour was therefore interpreted conservatively based on the experimentally observed TG/DTG profiles.

Table 5. TGA/DTG thermal decomposition parameters of the S3 metal complexes

Complex	Step	Temperature range (°C)	DTG _{max} (°C)	Assignment
S3–Cr-1	I	35–95	68.8	Initial decomposition
	II	~95–150	122.7	Intermediate decomposition
	III	~150–1000	859.4	Major high-temperature decomposition
S3–Cr-2	I	35–115	93.1	Initial decomposition
	II	~115–160	135.7	Intermediate decomposition

	III	~160–1000	813.7	High-temperature decomposition
S3–Cr-3	I	35~150	98.6	Initial decomposition
	II–V	~150–1000	441.6, 587.1, 620.3, 641.5	Progressive decomposition
S3–Cu-1	I	35~400	265.4	Intermediate decomposition
	II	~400–1000	747.1	Major high-temperature decomposition
S3–Cu-2	I	35~400	259.0	Intermediate decomposition
	II	~400–1000	654.7	Major high-temperature decomposition
S3–Cu-3	I	35~150	84.6	Initial decomposition
	II	~150~400	261.5	Intermediate decomposition
	III	~400–1000	730.7	Major high-temperature decomposition
S3–Ni-1	I	35~100	53.6	Initial decomposition
	II	~100–1000	538.5	Major decomposition
S3–Ni-2	I	35~150	85.1	Initial decomposition
	II	~150–1000	870.3	High-temperature decomposition
S3–Ni-3	I	35~115	96.9	Initial decomposition
	II	~115~180	138.0	Intermediate decomposition



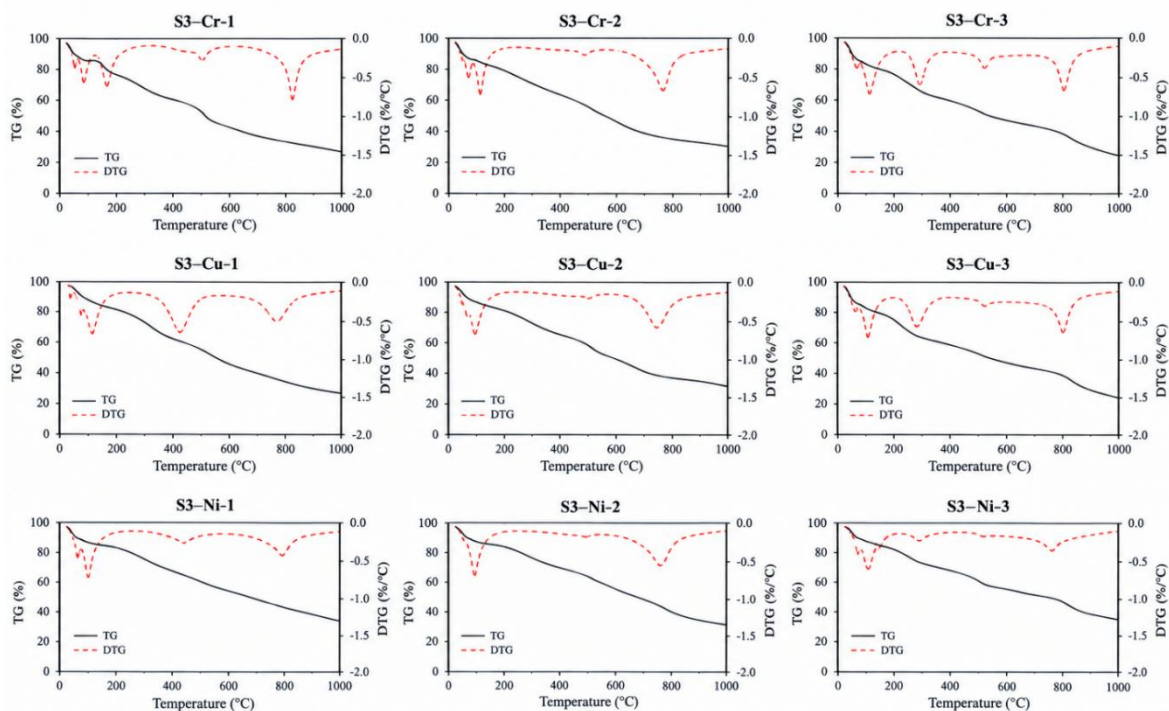


Figure 15. TG/DTG curves of the S3 metal complexes recorded over the temperature range of 35–1000 °C.

4. CONCLUSION

A series of nine Ni(II), Cu(II), and Cr(III) complexes of arylidene-2-iminothiazolidin-4-one ligands 7a–c was successfully synthesized and characterized using elemental analysis, spectroscopic techniques, PXRD, and thermal analysis. The spectroscopic data supported coordination of the ligands through N and S donor atoms, and the complexes were proposed to adopt octahedral geometries. PXRD analysis confirmed the crystalline nature of the complexes, while TGA indicated appreciable thermal stability. The metal complexes exhibited variable antibacterial activity against the tested bacterial strains, with some complexes showing improved activity compared with their corresponding free ligands. Molecular docking studies further revealed favorable ligand–protein interactions, providing additional insight into the possible molecular basis of the observed antibacterial activity. Overall, the experimental and computational findings demonstrate that arylidene-2-iminothiazolidin-4-one metal complexes represent promising scaffolds for further investigation as antibacterial agents.

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