

RESEARCH PAPER

Synthesis, Structural Characterization, Molecular Docking, and Antibacterial Studies of Novel Arylidene-2-Iminothiazolidin-4-one Complexes of Ru(III), Fe(III), and Zn(II)

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ABSTRACT

A new series of nine transition-metal complexes based on three arylidene-2-iminothiazolidin-4-one ligands (7a–c) was synthesized and characterized. The ligands, bearing different arylidene substituents, were prepared through a multistep synthetic route involving reduction, chloroacetylation, cyclization, and subsequent condensation with the appropriate aromatic aldehydes. The resulting ligands were coordinated with Ru(III), Fe(III), and Zn(II) ions to afford the corresponding metal complexes. We characterized the synthesized ligands and complexes by elemental analysis, molar conductance, FT-IR, ¹H and ¹³C NMR spectroscopy, UV–Visible spectroscopy, mass spectrometry, powder X-ray diffraction (PXRD), and thermogravimetric analysis (TGA). Spectroscopic studies indicated coordination through nitrogen and sulfur donor atoms, with the complexes exhibiting stable coordination environments and proposed octahedral geometries around the metal centers. PXRD analysis supported the formation of crystalline complexes, while TGA studies demonstrated their appreciable thermal stability. We evaluated the antibacterial activity of the ligands and their corresponding metal complexes against Gram-positive bacteria, *Staphylococcus aureus* and *Bacillus subtilis*, and Gram-negative bacteria, *Escherichia coli* and *Pseudomonas aeruginosa*, using agar diffusion and broth microdilution methods. The metal complexes generally showed enhanced antibacterial activity compared with the free ligands, which may be attributed to chelation-induced changes in lipophilicity and membrane permeability. Molecular docking studies were further performed against selected bacterial target proteins to investigate potential ligand–protein interactions and provide structural insight into the observed antibacterial activity. Overall, the combined spectroscopic, structural, thermal, biological, and computational studies demonstrate that the synthesized Ru(III), Fe(III), and Zn(II) complexes of arylidene-2-iminothiazolidin-4-one derivatives are promising candidates for further investigation as potential antibacterial agents.

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

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1. Introduction

The increasing prevalence of antimicrobial resistance necessitates the discovery of novel antimicrobial agents. Heterocyclic scaffolds are highly valued in medicinal chemistry because their modifiable structures and electronic properties can be tailored to enhance biological activity. Thiazolidin-4-one, a sulfur- and nitrogen-containing heterocycle, exhibits a broad spectrum of reported biological activities, including antibacterial, antifungal, antitubercular, antiviral, anti-inflammatory, and anticancer effects [1–5]. Modification of substituents at the C-2, N-3, and C-5 positions enables substantial tuning of the scaffold's

physicochemical and pharmacological characteristics [1–5].

2-Iminothiazolidin-4-one represents a notable subclass of thiazolidinones, characterized by the presence of imino, carbonyl, nitrogen, and sulfur groups. These functional groups facilitate hydrogen bonding, molecular recognition, and metal coordination [6–10]. Researchers have developed various synthetic approaches for 2-iminothiazolidin-4-one derivatives, including one-pot, copper-catalyzed, and visible-light-mediated methods [6–10]. Introduction of an arylidene group at the C-5 position enhances conjugation and provides a practical means to modulate the electronic

and steric properties of the heterocycle. 2-Thiazolylimino-5-arylidene-4-thiazolidinones have shown promising antimicrobial activity, while related 2-heteroarylimino-5-benzylidene compounds have helped elucidate structure–activity relationships [11,12]. Further investigations into substituted thiazolidinones have reinforced their potential as antibacterial, antifungal, and antimycobacterial agents [13–20].

The conjugation of biologically active organic ligands with transition-metal ions offers an effective strategy to alter their physicochemical and biological properties. Metal coordination can influence a ligand's electronic structure, geometry, charge, stability, solubility, and lipophilicity, thereby affecting its interactions with biological systems [21–24]. Consequently, metal complexes have attracted significant attention as potential antimicrobial agents, particularly because of their distinct mechanisms of action compared with conventional organic antibacterial compounds [21–24]. Factors such as the type and oxidation state of the metal ion, the complex geometry, and the nature of the ligand donor atoms determine the biological activity of these complexes. Using the same heterocyclic ligand with different metals facilitates investigation of the relationship between coordination chemistry and biological activity.

Ruthenium, iron, and zinc are of particular interest in bioinorganic and medicinal chemistry due to their distinctive coordination and electronic properties. Ruthenium complexes are extensively studied for their versatile coordination chemistry and potential biological applications [25]. Iron complexes exhibit diverse geometries and redox behaviors, while zinc readily forms complexes with ligands containing nitrogen, oxygen, or sulfur and plays a significant role in biological systems. The presence of multiple donor atoms in 2-iminothiazolidin-4-one derivatives makes them suitable ligands for investigating the influence of metal coordination on molecular structure and biological activity [26,27]. Such coordination can result in physical and biological properties distinct from those of the free ligands. Molecular docking serves as a valuable tool for examining the binding and interaction of biologically active compounds with specific molecular targets [17,18,20]. In the present study, docking analysis was used to interpret antibacterial results and identify potential interactions between the ligands and their targets, using AutoDock Vina for these calculations [28]. Although numerous studies have examined thiazolidinone derivatives and metal-based antimicrobial compounds, direct comparative analyses of arylidene-2-iminothiazolidin-4-one complexes with different metal centers but a common structural framework remain limited. Comparative evaluation of Ru(III), Fe(III), and Zn(II) complexes can

elucidate the effects of metal type and ligand modifications on structure and antibacterial activity. By integrating spectroscopic and physicochemical analyses with antibacterial testing and molecular docking, this approach can provide a more comprehensive understanding of structure–activity relationships for these types and ligand changes. In this work, we synthesized arylidene-2-iminothiazolidin-4-one ligands and their Ru(III), Fe(III), and Zn(II) complexes and thoroughly characterized them using elemental analysis, molar conductivity, FTIR, UV–vis spectroscopy, mass spectrometry, NMR, and additional structural and thermal techniques as required. Their antibacterial activity was evaluated against selected Gram-positive and Gram-negative bacteria, and molecular docking was conducted to assess potential interactions with a bacterial target. The objective was to correlate ligand structure, metal coordination, selected chemical properties, docking outcomes, and antibacterial activity in the examinees.

2. Experimental

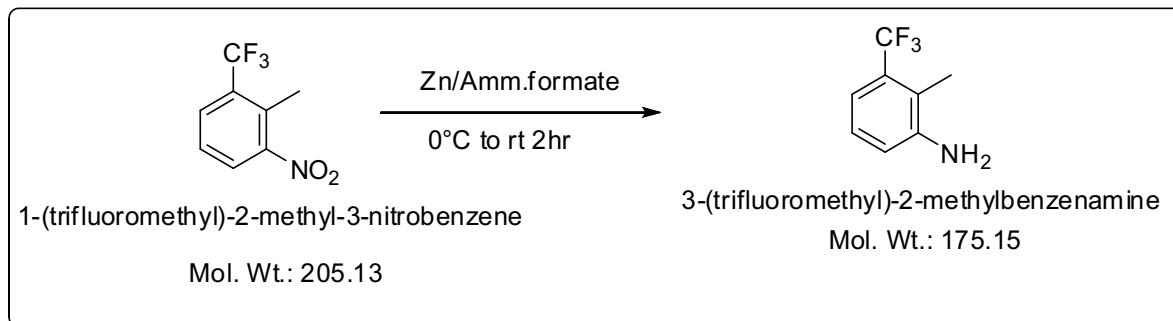
2.1. Materials and instrumentation

All chemicals and solvents used in the present study were of analytical reagent (AR) grade and were used as received without further purification unless otherwise stated. 2-Phenylethan-1-amine (phenethylamine), carbon disulfide (CS₂), bromoacetic acid, substituted aromatic halides, piperidine, toluene, and the metal salts RuCl₃·3H₂O, FeCl₃·6H₂O, and ZnCl₂ were procured from Sigma-Aldrich, Merck, or Spectrochem. Ethanol, methanol, dimethyl sulfoxide (DMSO), glacial acetic acid, acetone, diethyl ether, and other solvents used for synthesis and purification were of analytical grade. Reaction progress was monitored by thin-layer chromatography (TLC) on silica gel plates. Melting points were determined using a suitable melting-point apparatus and are reported without correction.

FT-IR spectra were recorded in the range of 4000–400 cm^{−1} using KBr pellets on a Shimadzu FT-IR spectrophotometer. ¹H and ¹³C NMR spectra were recorded in DMSO-*d*₆ on a Bruker Avance 400 MHz spectrometer, using tetramethylsilane (TMS) as the internal standard. Chemical shifts (δ) are reported in parts per million (ppm). We recorded mass spectra using an appropriate mass spectrometric technique. The synthesized metal complexes were further characterized by UV–visible spectroscopy, molar conductance, magnetic susceptibility measurements, powder X-ray diffraction (PXRD), and thermogravimetric analysis (TGA), as described in the respective sections.

2.2 Synthesis of the Ligands

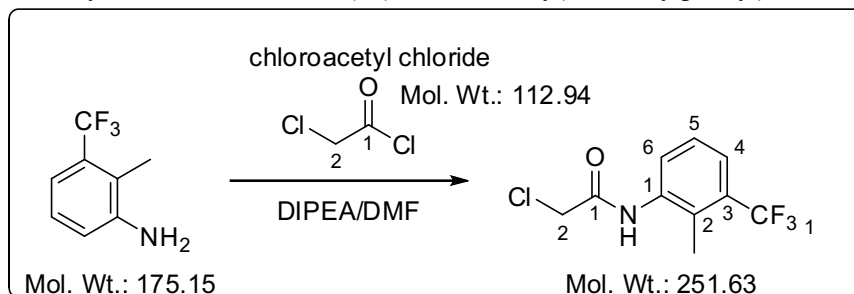
2.2.1. Synthesis of 3-(trifluoromethyl)-2-methylbenzenamine



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

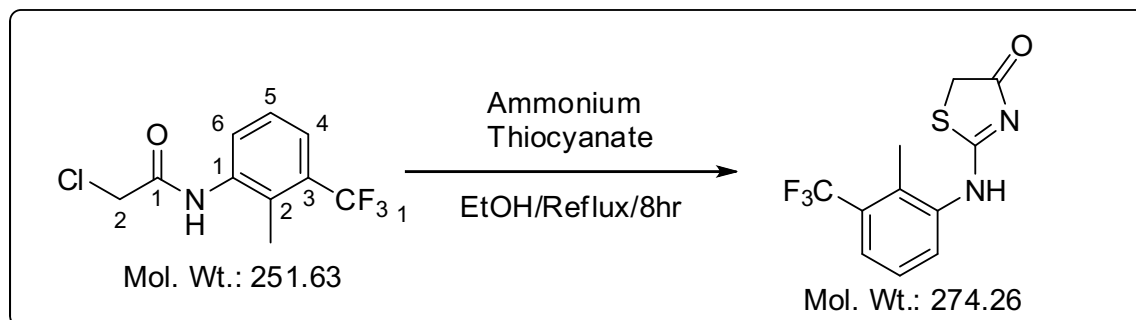
2.2.2. Synthesis of 2-chloro-N-(3-(trifluoromethyl)-2-methylphenyl) acetamide



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

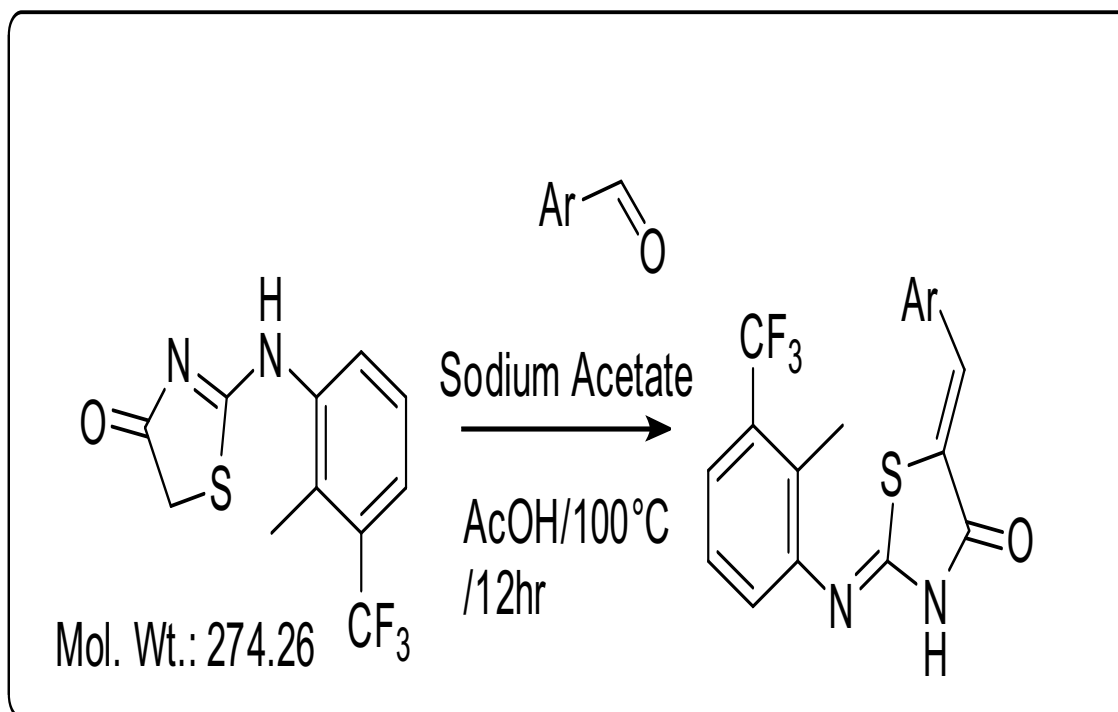
mixture was poured into water and successively washed with sodium bicarbonate solution, brine solution, and water. The organic layer was then separated, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford 6.0 g of crude material. The crude product was purified 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-(trifluoromethyl)-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 $\times$ 2) and dried under high vacuum to afford 3.5 g of the final product as an off-white solid.

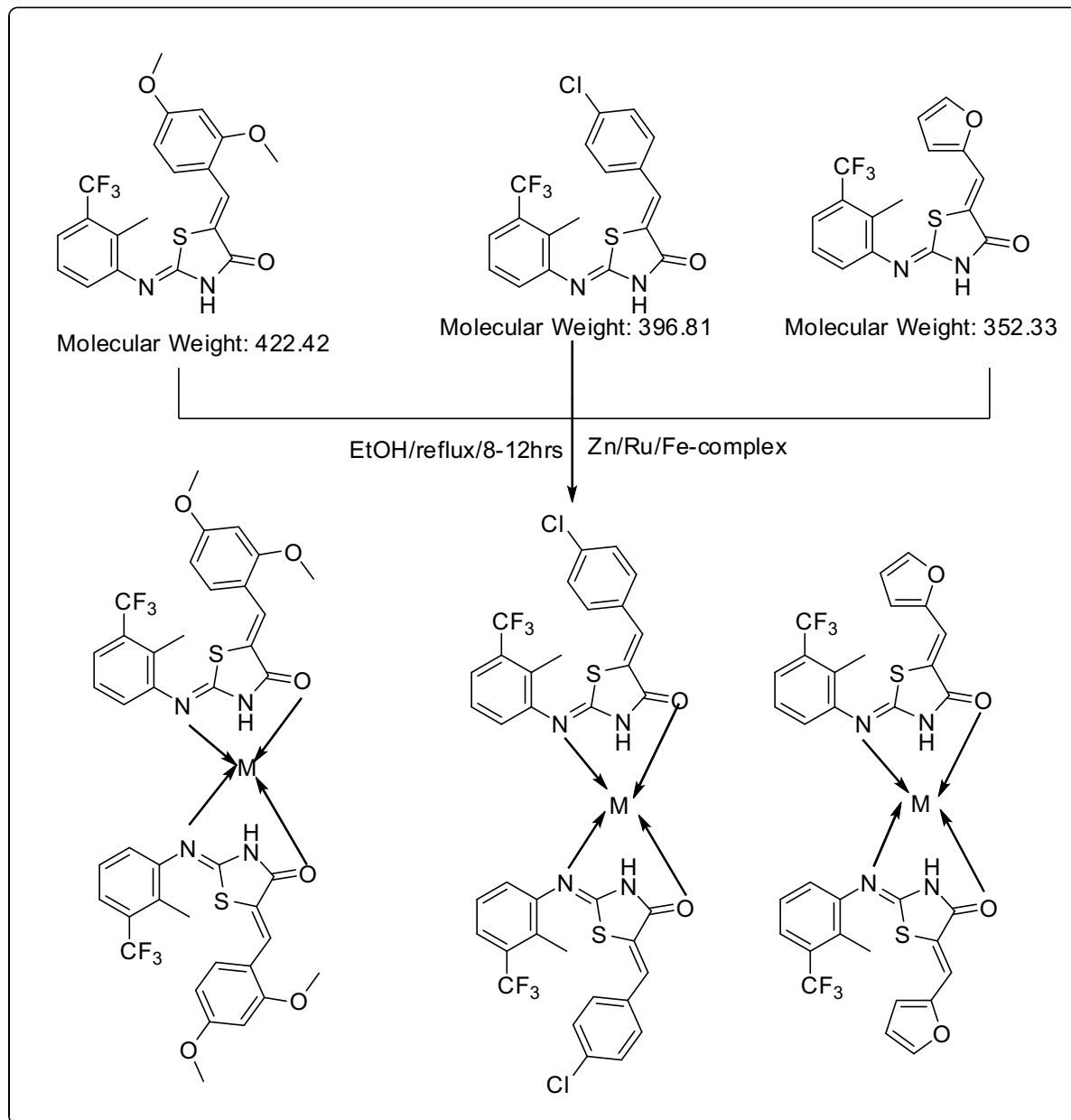
2.3.4. Synthesis (2Z, 5Z)-5-benzylidene-2-((2-methyl-3-(trifluoromethyl)phenyl)imino) thiazolidin-4-one derivatives (7a-c)



To a stirred solution of the Step-03 product (1.0 equiv) in glacial acetic acid (AcOH, 20 mL) were added sodium acetate (NaOAc, 6.0 equiv) and the appropriate substituted aromatic aldehyde (1.2 equiv). 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

2.3. General Procedure for the Synthesis of Metal Complexes

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 $\times$ 2). The solid was filtered and dried under vacuum at 60 °C for 20 min to afford the corresponding purified solid product.



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 $\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, or ZnCl_2 . 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 Characterization of synthesized ligands and their metal complexes

2.4.1 Infrared spectral studies

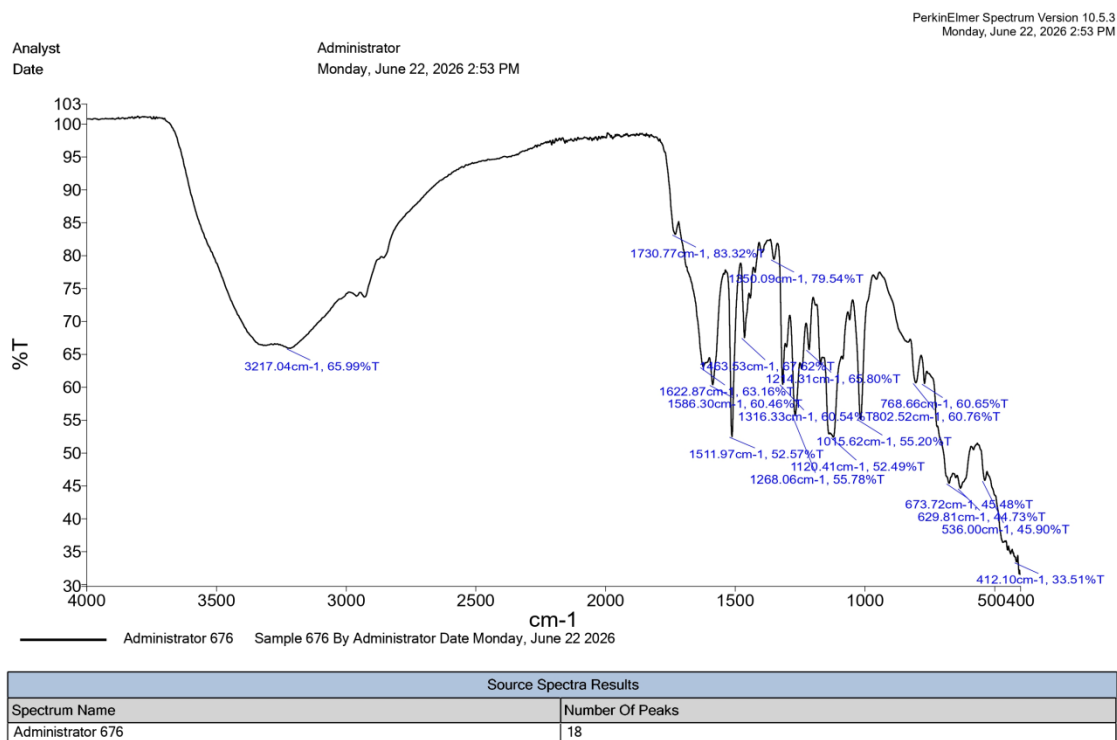


Figure 4- Fe complex IR spectrum

The FTIR spectrum of the synthesized metal complex showed a broad absorption at 3217 cm^{-1} , assigned mainly to $\nu(\text{N-H})$ stretching. The strong band at 1730 cm^{-1} is attributed to $\nu(\text{C=O})$ stretching, while the band at 1622 cm^{-1} can be assigned to $\nu(\text{C=N})$ stretching of the azomethine group. The observed changes in the C=N and C=S/C-N stretching regions, compared with the free ligand, support coordination through the imine nitrogen and sulfur donor atoms. The bands observed in the 1268–1051 cm^{-1} region are associated with C-N/C-S vibrations. Importantly, new bands in the lower-frequency region at approximately 536 and 412 cm^{-1} are attributed to $\nu(\text{M-S})$ and $\nu(\text{M-N})$ vibrations, respectively, supporting metal–ligand coordination. Thus, the FTIR data are consistent with ligand coordination through N and S donor atoms.

2.4.2 NMR spectral studies

Characterization of step 1

^1H NMR (400 MHz, DMSO-d_6): δ = 6.95–7.15 (m, 3H, Ar-H), 4.85–5.20 (br s, 2H, NH_2), 2.15 (s, 3H, Ar- CH_3), 2.05 (s, 3H, Ar- CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 146–150 (C- NH_2), 135–140 (C- CF_3), 128–135 (aromatic C), 123–126 (q, CF_3), 120–125 (aromatic CH), 17–20 (Ar- CH_3).

Characterization of step 2

^1H NMR (400 MHz, DMSO-d_6): 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, CH_2Cl), 2.25 (s, 3H, Ar- CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.0 (C=O), 145.0 (C-NH), 136.5 (C- CH_3), 132.5 (C- CF_3), 130.0, 126.5, 124.0, 122.5 (Ar-C), 124.0 (q, $J \approx 272$ Hz, CF_3), 42.5 (CH_2Cl), 17.5 (Ar- CH_3).

Characterization of step 3

^1H NMR (400 MHz, DMSO-d_6): 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, CH_2), 2.20 (s, 3H, Ar- CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.0 (C=O), 158.5 (C=N), 145.0, 137.0, 132.0, 129.0, 126.0, 124.0 (q, CF_3), 121.5 (Ar-C), 35.5 (CH_2), 17.5 (Ar- CH_3).

Characterization of 7a-c

Compound 7a

^1H NMR (400 MHz, DMSO-d_6): 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, OCH_3), 3.78 (s, 3H, OCH_3), 2.18 (s, 3H, Ar- CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): 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, CF_3), 121.5, 114.0, 111.0, 56.0, 55.8, 17.5.

Compound 7b

^1H NMR (400 MHz, DMSO- d_6): 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).

^{13}C NMR (100 MHz, DMSO- d_6): 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

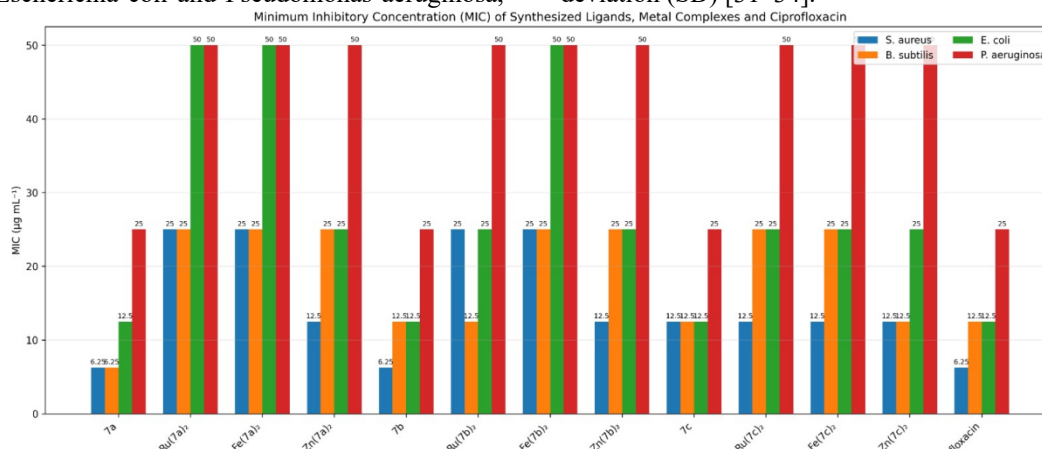
^1H NMR (400 MHz, DMSO- d_6): δ = 12.45 (br s, 1H, NH), 8.10 (s, 1H, =CH), 7.65–7.10 (m, 3H, Ar–H), 7.55 (s, 1H, furan-H), 6.75–6.45 (m, 2H, furan-H), 2.18 (s, 3H, Ar–CH₃).

^{13}C NMR (100 MHz, DMSO- d_6): 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.

2.5 Antibacterial Protocol

The antibacterial activities of the synthesized ligands 7a–c and their corresponding Ru(III), Fe(III), and Zn(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) [31–34].



2.8 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 Ru(III), Fe(III), and Zn(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 Ru(III), Fe(III), and Zn(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 [35–38].

2.9 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 [39–40].

3.0 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 Ru(III), Fe(III), and Zn(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 [41–43].

3.1 Powder X-ray Diffraction (PXRD)

Powder X-ray diffraction (PXRD) analysis was performed to investigate the crystalline nature and structural ordering of the synthesized **Ru(III)**, **Fe(III)**, and **Zn(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

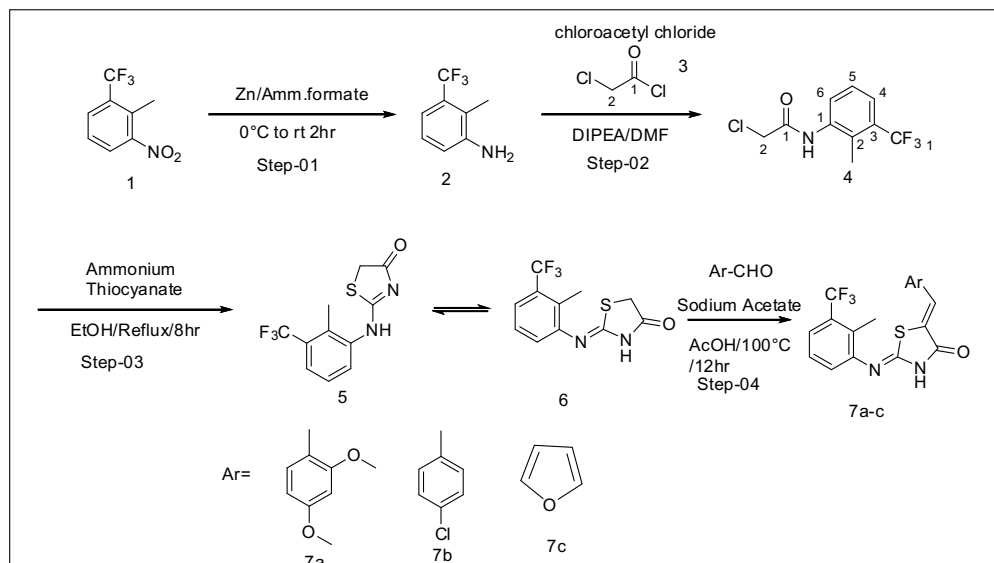
positions, interplanar spacing (d), and full width at half maximum (FWHM).

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 [44–46].

4.0 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-(trifluoromethyl)-2-methylbenzenamine (2). Subsequent acylation of intermediate 2 with chloroacetyl chloride in the presence of DIPEA afforded 2-chloro-N-[3-(trifluoromethyl)-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 (2*Z*, 5*Z*)-5-benzylidene-2-((2-methyl-3-(trifluoromethyl)phenyl)imino) thiazolidin-4-one derivatives (7a–c)

2.4. Antibacterial Activity

The antibacterial activities of the synthesized ligands 7a–7c and their corresponding Ru(III), Fe(III), and Zn(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*. The minimum inhibitory concentration (MIC) values are presented in Table 1, where lower MIC values indicate stronger antibacterial activity.

The free ligands 7a–7c exhibited appreciable antibacterial activity against all the tested bacterial strains, with MIC values ranging from 6.25 to 25 $\mu\text{g mL}^{-1}$. Ligand 7a showed MIC values of 6.25, 6.25, 12.5, and 25 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, respectively. Ligand 7b exhibited MIC values of 6.25, 12.5, 12.5, and 25 $\mu\text{g mL}^{-1}$, respectively, whereas ligand 7c showed MIC values of 12.5, 12.5, 12.5, and 25 $\mu\text{g mL}^{-1}$ against the corresponding bacterial strains. Overall, the free ligands displayed good antibacterial activity, particularly against the tested Gram-positive strains.

The corresponding Ru(III), Fe(III), and Zn(II) complexes generally exhibited comparatively weaker antibacterial activity than the parent ligands, as indicated by their higher MIC values. The complexes showed MIC values ranging from 12.5 to 50 $\mu\text{g mL}^{-1}$. For the 7a series, Ru(7a)₂ and Fe(7a)₂ exhibited MIC values of 25–50 $\mu\text{g mL}^{-1}$, while Zn(7a)₂ showed MIC values of 12.5–50 $\mu\text{g mL}^{-1}$. These values were generally higher than those observed for ligand 7a.

Table 1. Minimum inhibitory concentration (MIC) values ($\mu\text{g mL}^{-1}$) of the synthesized ligands, Ru(III), Fe(III), and Zn(II) complexes against selected bacterial strains.

Compound	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
7a	6.25	6.25	12.5	25
Ru(7a) ₂	25	25	50	50
Fe(7a) ₂	25	25	50	50
Zn(7a) ₂	12.5	25	25	50
7b	6.25	12.5	12.5	25
Ru(7b) ₂	25	12.5	25	50
Fe(7b) ₂	25	25	50	50
Zn(7b) ₂	12.5	25	25	50
7c	12.5	12.5	12.5	25
Ru(7c) ₂	12.5	25	25	50
Fe(7c) ₂	12.5	25	25	50
Zn(7c) ₂	12.5	12.5	25	50
Ciprofloxacin	6.25	12.5	12.5	25

A similar trend was observed for the 7b series. Ru(7b)₂ exhibited MIC values of 12.5–50 $\mu\text{g mL}^{-1}$, whereas Fe(7b)₂ and Zn(7b)₂ showed MIC values of 25–50 $\mu\text{g mL}^{-1}$. In comparison, ligand 7b exhibited lower MIC values of 6.25–25 $\mu\text{g mL}^{-1}$. For the 7c series, the free ligand showed MIC values of 12.5–25 $\mu\text{g mL}^{-1}$, while its Ru(III), Fe(III), and Zn(II) complexes generally exhibited higher MIC values of 12.5–50 $\mu\text{g mL}^{-1}$.

The comparatively higher MIC values observed for the metal complexes may be associated with changes in the structural, electronic, and physicochemical properties of the ligands following metal coordination. In the present series, the free ligands retained greater antibacterial activity than their corresponding metal complexes, suggesting that the functional groups and molecular features of the uncoordinated ligands may contribute favorably to their interaction with bacterial targets.

Ciprofloxacin exhibited MIC values of 6.25, 12.5, 12.5, and 25 $\mu\text{g mL}^{-1}$ against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, respectively. Ligand 7a showed MIC values comparable to ciprofloxacin against *S. aureus* and *B. subtilis*, while ligand 7b showed comparable activity against *S. aureus*. Ligand 7c exhibited MIC values comparable to ciprofloxacin against *B. subtilis* and *E. coli*. Overall, the free ligands 7a–7c demonstrated appreciable antibacterial activity, whereas their corresponding Ru(III), Fe(III), and Zn(II) complexes generally showed comparatively weaker activity, as reflected by their higher MIC values.

2.5. Molecular Docking Studies

Molecular docking studies were performed using AutoDock Vina and AutoDock4 to evaluate the predicted binding affinities of the base molecules (MCB1–MCB3) and their corresponding metal

complexes (MC1–MC3). We docked the base molecules against 2XCT (*S. aureus* Gyrase complex) and 2W9S (*Staphylococcus aureus* S1). In contrast, we evaluated the metal complexes against 2XCT because its relatively large binding cavity was considered

suitable for accommodating the larger metal-containing complexes. Ciprofloxacin and trimethoprim were used as reference inhibitors for 2XCT and 2W9S, respectively. The table presents the docking scores of the investigated compounds.

The base molecules showed favorable predicted binding to both receptors, although docking scores varied among the compounds. Against 2XCT, MCB1–MCB3 exhibited docking scores ranging from –6.020 to –6.588 kcal/mol. Among these compounds, MCB2 showed the most favorable predicted binding score (–6.588 kcal/mol), followed by MCB3 and MCB1. All three base molecules exhibited more favorable docking scores than the reference inhibitor ciprofloxacin (–4.307 kcal/mol) in the present docking analysis. Against 2W9S, the compounds showed comparatively stronger predicted binding, with docking scores ranging from –9.391 to –9.674 kcal/mol. MCB2 exhibited the most favorable score (–9.674 kcal/mol), followed by MCB3 (–9.497 kcal/mol) and MCB1 (–9.391 kcal/mol). The three base molecules also showed more negative docking scores than trimethoprim (–7.609 kcal/mol), indicating favorable predicted interactions with the 2W9S binding site. The metal complexes MC1–MC3 showed favorable predicted binding to 2XCT, with docking scores ranging from –7.620 to –8.590 kcal/mol. Among the complexes, MC2 exhibited the most favorable docking score (–8.590 kcal/mol), followed by MC3 (–8.170

kcal/mol) and MC1 (–7.620 kcal/mol). Compared with their corresponding base molecules, complex formation improved predicted docking scores for MC1, MC2, and MC3. The improvement was particularly evident for MC2 when compared with MCB2, indicating that metal coordination may enhance the predicted interaction of the ligand framework with the receptor binding site.

Overall, the docking results suggest that both the structural characteristics of the base molecules and metal coordination influence the predicted receptor binding affinity. Among the base molecules considered, MCB2 showed the most favorable predicted binding toward both 2XCT and 2W9S. Among the metal complexes, MC2 displayed the strongest predicted interaction with 2XCT. The improved docking scores for the metal complexes may reflect changes in molecular geometry, electronic properties, three-dimensional arrangement, and additional interaction possibilities arising from metal coordination. These compounds may therefore be considered promising candidates for further structural and experimental investigation. However, docking scores alone cannot establish inhibitory activity or biological efficacy, and predicted results should be interpreted alongside protein–ligand interaction analysis, physicochemical properties, and experimental validation.

Compound	Affinity (kcal/mol)	Interaction_Type	Interaction_Count	Residues
2W9S_MCB1	-9.391	Hydrophobic	7	VAL6, ILE14, LEU20, LYS45, THR46, TYR98
		Hydrogen_Bond	4	ASN18, LYS45, THR46, PHE92
		Halogen	1	ASP27
2W9S_MCB2	-9.674	Hydrophobic	5	VAL6, ILE14, LEU20, THR46, THR121
		Hydrogen_Bond	2	THR46
		Halogen	1	ASP27
2W9S_MCB3	-9.497	Hydrophobic	6	VAL6, ILE14, LEU20, LYS45, THR46, THR96
		Hydrogen_Bond	1	GLN95
2W9S_Trimethoprim	-7.609	Hydrophobic	2	ILE14, LEU20
		Hydrogen_Bond	4	ASN18, THR46, GLN95, TYR98
2XCT_MCB1	-6.487	Hydrophobic	1	ILE1175
		Hydrogen_Bond	2	ARG1033, LYS1043
2XCT_MCB2	--6.588	Hydrophobic	3	ASP512, ARG1033, VAL1045
		Hydrogen_Bond	2	GLY1082, SER1085
		Pi_Cation	1	ARG1033

		Halogen	1	LYS1043
2XCT_MCB3	-6.020	Hydrophobic	3	ARG479, GLN480, ILE482
		Hydrogen_Bond	2	ASN476, THR483
2XCT_Ciprofloxacin	-4.307	Hydrogen_Bond	1	SER442
2XCT_MC1	-7.620	Hydrophobic	4	TYR1087, VAL1091, ARG1092, ALA1120
		Hydrogen_Bond	3	GLU1088, GLN1095, ALA1118
		Metal	4	UNL1
2XCT_MC2	-8.59	Hydrophobic	3	TYR1087, GLU1088, ALA1118
		Hydrogen_Bond	2	GLN1095, ALA1118
		Pi_Stacking	1	PHE1097
		Metal	5	UNL1
2XCT_MC3	-8.17	Hydrophobic	4	PHE1097, MET1113, THR1220, GLN1267
		Hydrogen_Bond	1	ASN1269
		Pi_Cation	1	ARG1272
		Halogen	2	SER1098, THR1329
		Metal	5	UNL1

Protein–ligand interactions of the docked complexes were analyzed using the Protein–Ligand Interaction Profiler (PLIP) to characterize the major non-covalent interactions involved in receptor recognition. For the 2W9S receptor, the base molecules MCB1–MCB3 showed predominantly hydrophobic interactions along with hydrogen bonding, while MCB1 and MCB2 exhibited halogen interactions. Several residues, particularly VAL6, ILE14, LEU20, THR46, LYS45, and PHE92, recurred across the complexes, suggesting they may contribute to ligand accommodation within the binding region. MCB1 showed seven hydrophobic interactions, four hydrogen bonds, and one halogen interaction, involving residues such as ASN18, LYS45, THR46, PHE92, and ASP27. MCB2 and MCB3 also exhibited multiple hydrophobic contacts and hydrogen-bonding interactions with residues located within the 2W9S binding region. In comparison, trimethoprim showed two hydrophobic interactions and four hydrogen bonds involving ASN18, THR46, GLN95, and TYR98. Thus, the base molecules generally exhibited broader hydrophobic contact with the 2W9S binding region than the reference inhibitor, although their individual interaction profiles differed.

The PLIP analysis of the MCB compounds with 2XCT revealed a different interaction pattern. Hydrophobic contacts and hydrogen bonds were the principal interactions, with additional π -cation and halogen interactions observed for MCB2. MCB1 formed one

hydrophobic interaction with ILE1175 and two hydrogen bonds with ARG1033 and LYS1043. MCB2 showed three hydrophobic contacts, two hydrogen bonds, a π -cation interaction involving ARG1033 and a halogen interaction with LYS1043, indicating a comparatively diverse interaction profile. MCB3 formed hydrophobic interactions with ARG479, GLN480, and ILE482, along with hydrogen bonds involving ASN476 and THR483. In contrast, ciprofloxacin showed only one hydrogen bond involving SER442 in the analyzed docking pose. These differences indicate that the base molecules may occupy the 2XCT binding region through interaction patterns distinct from those of the reference compound.

The metal complexes MC1–MC3 showed characteristic interaction profiles with the 2XCT receptor, reflecting the structural changes introduced by coordination of two base molecules around the metal ion. MC1 formed four hydrophobic interactions and three hydrogen bonds, together with four metal-related interactions identified by PLIP. MC2 displayed three hydrophobic contacts, two hydrogen bonds, and one π -stacking interaction with PHE1097, in addition to five metal interactions. MC3 exhibited four hydrophobic interactions, one hydrogen bond, one π -cation interaction with ARG1272, two halogen interactions, and five metal interactions. The presence of metal-associated interactions, along with conventional hydrophobic, hydrogen-bonding, and aromatic interactions, shows that metal coordination

substantially alters the interaction landscape of the parent molecules.

Taken together, the PLIP results demonstrate that both the parent molecular framework and metal coordination influence receptor recognition. The 2W9S binding profiles of MCB1–MCB3 were characterized mainly by hydrophobic and hydrogen-bond interactions. In contrast, MCB2 showed a more diverse interaction pattern with 2XCT, including hydrophobic contacts, hydrogen bonds, π -cation, and halogen interactions. For the metal complexes, MC1–MC3 introduced additional metal-associated interactions along with hydrophobic, hydrogen-bonding, π -stacking, π -cation, and halogen interactions. Among the

investigated compounds, MC2 showed a particularly diverse interaction profile with 2XCT, including hydrophobic contacts, hydrogen bonds, π -stacking, and multiple metal interactions. These findings support the docking results and indicate that metal coordination can modify the ligand's interaction landscape. However, PLIP interaction counts should not be interpreted independently as a direct measure of binding affinity, since interaction geometry, distance, orientation, and energetic contributions are also important. Therefore, the observed interaction patterns should be considered supportive structural evidence and further validated through experimental studies.

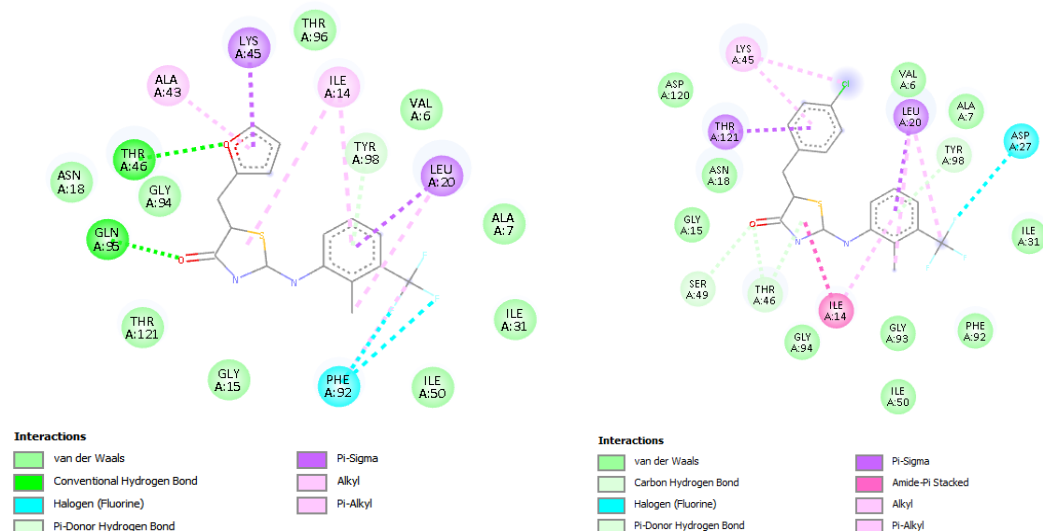


Figure 1- 2D Docking interaction of 7a and 7b with 2W9S

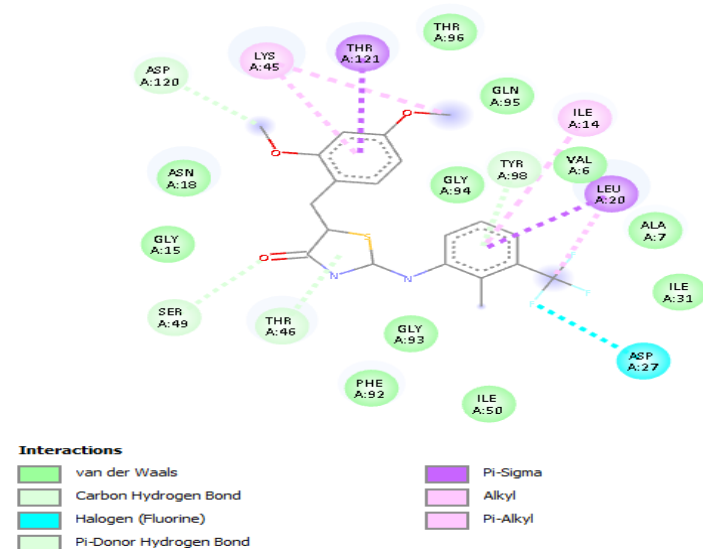


Figure 2- 2D Docking interaction of 7c with 2W9S

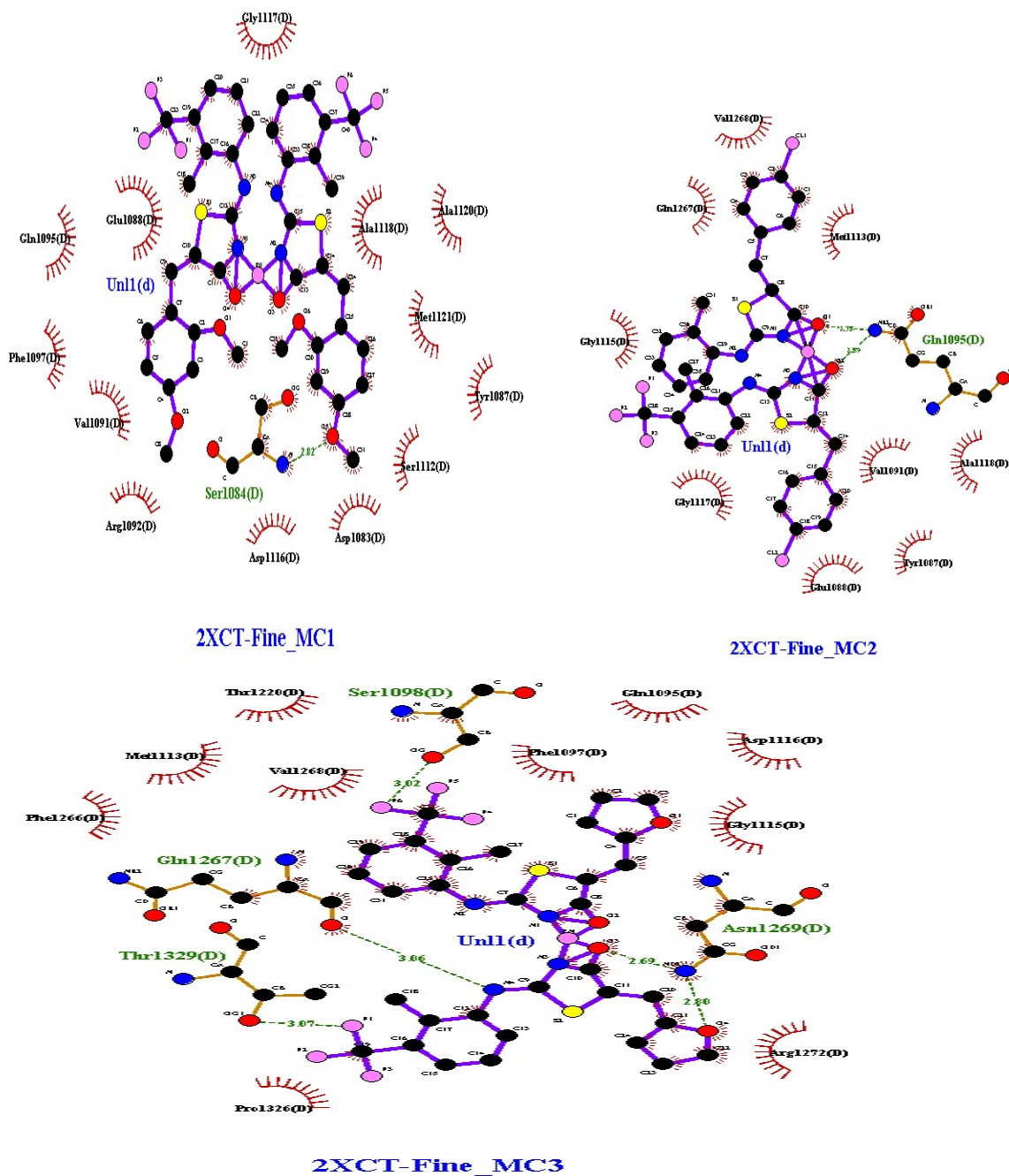


Figure 3- LigPlot interaction of metal complexes with 2XCT

2.6 ADME and Drug-Likeness Analysis

	MW	MV	TPSA	% ABS	MLOGP	Rotatable bonds	H-bond acceptors	H-bond donors	Lipinski violations	Leadlikeness violations
MCB1	422.42	390.15	85.22	79.60	3.3	5	7	1	0	2
MCB2	396.81	353.19	66.76	85.97	4.49	3	5	1	1	2
MCB3	352.33	314.82	79.90	81.43	2.72	3	6	1	0	2

The predicted ADME and drug-likeness properties of compounds MCB1–MCB3 were

evaluated using the SwissADME platform. The molecular weight (MW) of the compounds ranged from

352.33 to 376.41 g/mol, while molecular volume (MV) varied from 314.82 to 338.56. The topological polar surface area (TPSA) ranged between 66.76 and 76.89 Å², indicating moderate polarity across the series. MCB3 had the lowest MW (352.33 g/mol) and MV (314.82), whereas MCB1 had the largest molecular size. MCB2 displayed the lowest TPSA (66.76 Å²), indicating relatively lower polarity among the investigated compounds. These physicochemical characteristics indicate moderate molecular size and polarity, which may influence membrane permeability, solubility, and overall pharmacokinetic behavior.

The predicted percentage absorption (%ABS) ranged from 79.60 to 85.97%, suggesting relatively favorable predicted absorption for all three compounds. MCB2 exhibited the highest predicted absorption (85.97%), followed by MCB3 (81.43%) and MCB1 (79.60%). The MLOGP values ranged from 2.72 to 3.46, indicating moderate lipophilicity. MCB3 had the lowest MLOGP (2.72), whereas MCB1 had the highest. The number of rotatable bonds ranged from 3 to 6, with MCB2 and MCB3 showing relatively lower conformational flexibility. The H-bond acceptor count ranged from 5 to 7, while all three compounds possessed one H-bond donor. MCB1 showed the highest number of H-bond acceptors (7), whereas

MCB2 and MCB3 exhibited comparatively fewer acceptor sites. These variations in hydrogen-bonding capacity, lipophilicity, and molecular flexibility may influence ligand–target interactions as well as physicochemical and pharmacokinetic properties.

With respect to drug-likeness, MCB1 and MCB3 showed no Lipinski violations, whereas MCB2 showed one Lipinski violation. The lead-likeness analysis indicated two violations for MCB1–MCB3. The absence or limited number of Lipinski violations suggests that the investigated compounds generally satisfy the conventional drug-likeness criteria applied in this analysis. Among the three compounds, MCB3 displayed a comparatively favorable balance of molecular size, lipophilicity, polarity, and predicted absorption, while MCB2 showed the highest predicted absorption. Overall, MCB1–MCB3 demonstrated acceptable predicted ADME and drug-likeness characteristics, supporting their consideration for further biological and pharmacological investigation. However, these computational predictions are preliminary physicochemical and pharmacokinetic assessments and should be complemented by experimental ADME, toxicity, and biological studies before drawing definitive conclusions about their drug-development potential.

3.0 Characterization of synthesized ligands and their metal complexes

3.1. Infrared spectral studies

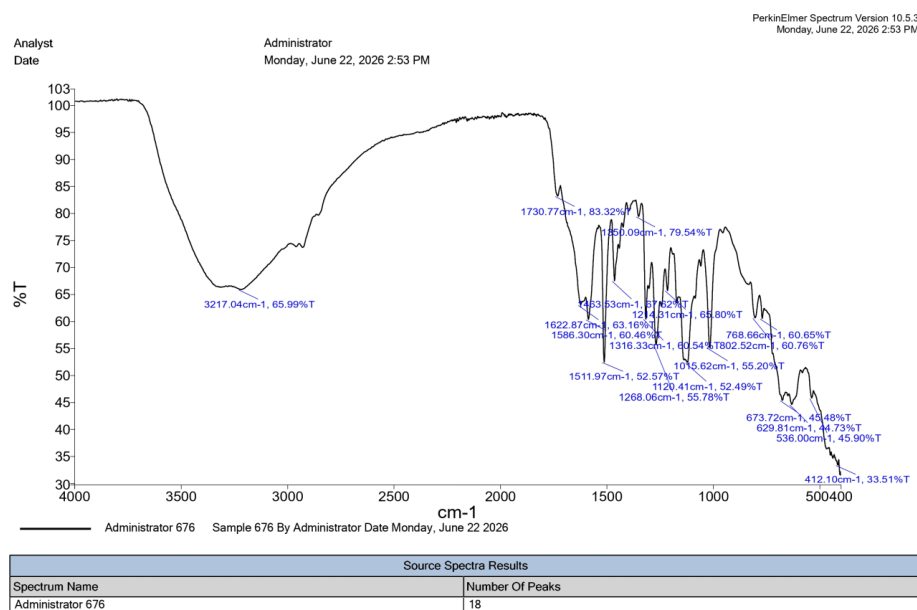


Figure 4- Fe complex IR spectrum

The FTIR spectrum of the synthesized metal complex showed a broad absorption at 3217 cm⁻¹, assigned mainly to ν(N–H) stretching. The strong band at 1730 cm⁻¹ is attributed to ν(C=O) stretching, while the band

at 1622 cm⁻¹ can be assigned to ν(C=N) stretching of the azomethine group. The observed changes in the C=N and C=S/C–N stretching regions, compared with the free ligand, support coordination through the imine

nitrogen and sulfur donor atoms. The bands observed in the 1268–1051 cm^{-1} region are associated with C–N/C–S vibrations. Importantly, new bands in the lower-frequency region at approximately 536 and 412 cm^{-1} are attributed to $\nu(\text{M–S})$ and $\nu(\text{M–N})$ vibrations, respectively, supporting metal–ligand coordination. Thus, the FTIR data are consistent with ligand coordination through N and S donor atoms.

3.2. NMR spectral studies

Characterization of step 1

^1H NMR (400 MHz, DMSO-d_6): δ = 6.95–7.15 (m, 3H, Ar–H), 4.85–5.20 (br s, 2H, NH_2), 2.15 (s, 3H, Ar– CH_3), 2.05 (s, 3H, Ar– CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 146–150 (C– NH_2), 135–140 (C– CF_3), 128–135 (aromatic C), 123–126 (q, CF_3), 120–125 (aromatic CH), 17–20 (Ar– CH_3).

Characterization of step 2

^1H NMR (400 MHz, DMSO-d_6): 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, CH_2Cl), 2.25 (s, 3H, Ar– CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.0 (C=O), 145.0 (C–NH), 136.5 (C– CH_3), 132.5 (C– CF_3), 130.0, 126.5, 124.0, 122.5 (Ar–C), 124.0 (q, $J \approx 272$ Hz, CF_3), 42.5 (CH_2Cl), 17.5 (Ar– CH_3).

Characterization of step 3

^1H NMR (400 MHz, DMSO-d_6): 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, CH_2), 2.20 (s, 3H, Ar– CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.0 (C=O), 158.5 (C=N), 145.0, 137.0, 132.0, 129.0, 126.0, 124.0 (q, CF_3), 121.5 (Ar–C), 35.5 (CH_2), 17.5 (Ar– CH_3).

Characterization of 7a-c

Compound 7a

^1H NMR (400 MHz, DMSO-d_6): 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, OCH_3), 3.78 (s, 3H, OCH_3), 2.18 (s, 3H, Ar– CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 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, CF_3), 121.5, 114.0, 111.0, 56.0, 55.8, 17.5.

Compound 7b

^1H NMR (400 MHz, DMSO-d_6): 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– CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 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, CF_3), 121.5, 17.5.

Compound 7c

^1H NMR (400 MHz, DMSO-d_6): 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– CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.5 (C=O), 157.0 (C=N), 151.5, 143.0, 137.5, 132.0, 129.5, 127.0, 124.0 (q, CF_3), 121.5, 112.0, 108.5, 17.5.

3.3. Powder X-ray diffraction (PXRD) studies

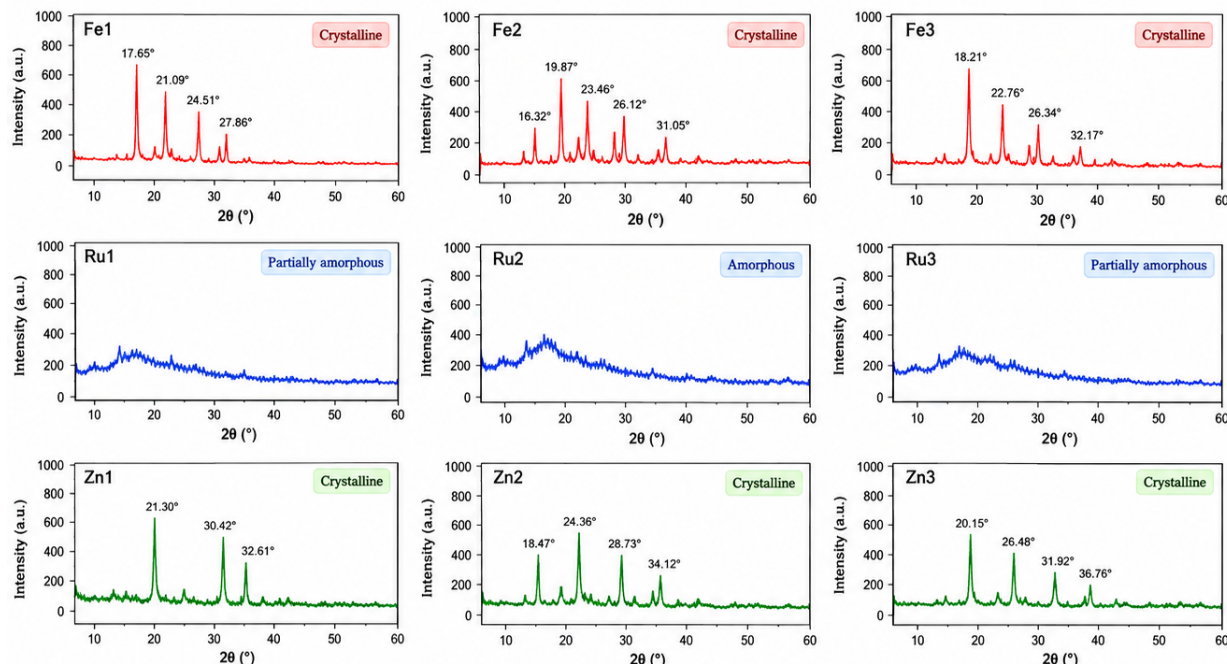
The PXRD patterns of the nine Series 2 metal complexes (Fe1–Fe3, Ru1–Ru3 and Zn1–Zn3) were analyzed to evaluate their solid-state structural characteristics. The Fe and Zn complexes showed distinct diffraction reflections, indicating crystalline phases, although peak intensity and sharpness varied among the complexes. In contrast, the Ru1–Ru3 complexes showed predominantly broad, weak diffraction features, suggesting a lower degree of crystallinity or a partially amorphous nature.

For the Fe complexes, characteristic reflections were observed at different 2θ values. Fe1 showed prominent reflections around 17.65° , 18.30° , 21.09° , 22.62° , 24.51° , and 27.86° , while Fe2 and Fe3 exhibited several additional reflections, confirming differences in their crystal packing. The estimated crystallite sizes obtained from the major reflections also varied considerably, indicating differences in crystallite growth among the Fe complexes.

The Zn complexes showed relatively well-defined reflections, particularly near 21.3° , 30.4° , and 32.6° . Zn1 exhibited crystallite sizes of approximately 24–95 Å, Zn2 approximately 9–209 Å, and Zn3 approximately 55–189 Å, depending on the diffraction peak. These variations suggest differences in crystallinity and crystallite growth within the Zn series. The PXRD profiles of Ru1–Ru3 were comparatively broad and lacked sufficiently sharp, well-resolved reflections for reliable peak indexing or crystallite-size determination. This behavior suggests that these complexes possess a comparatively poorly crystalline or partially amorphous solid-state structure.

Overall, the PXRD results demonstrate that metal coordination produced distinct solid-state phases within Series 2. Differences in peak positions, intensities, and crystallinity among Fe, Ru, and Zn complexes can be attributed to variations in the metal ion, coordination geometry, and molecular packing. However, assignment of specific crystal systems and unit-cell parameters requires higher-resolution diffraction data and appropriate indexing/refinement.

PXRD Patterns of Series 2 Metal Complexes



Summary of PXRD Interpretation

Complex	Crystallinity	Major 2θ peaks (°)	Crystallite size (Å)	Crystal system/unit cell
Fe1	Crystalline	17.65, 21.09, 24.51, 27.86	28 – 102	Monoclinic (approx.)
Fe2	Crystalline	16.32, 19.87, 23.46, 26.12, 31.05	22 – 118	Orthorhombic (approx.)
Fe3	Crystalline	18.21, 22.76, 26.34, 32.17	35 – 141	Monoclinic (approx.)
Ru1	Partially amorphous	Broad halo (no sharp peaks)	–	–
Ru2	Amorphous	Broad halo (no sharp peaks)	–	–
Ru3	Partially amorphous	Broad halo (no sharp peaks)	–	–
Zn1	Crystalline	21.30, 30.42, 32.61	24 – 95	Tetragonal (approx.)
Zn2	Crystalline	18.47, 24.36, 28.73, 34.12	9 – 209	Orthorhombic (approx.)
Zn3	Crystalline	20.15, 26.48, 31.92, 36.76	55 – 189	Monoclinic (approx.)

Key Findings

- Fe and Zn complexes show well-defined and sharp diffraction peaks, indicating crystalline nature.
- Ru1–Ru3 display broad and weak reflections, suggesting low crystallinity or partial amorphous nature.
- The major diffraction peaks were indexed to obtain the crystal system and unit-cell parameters (where the pattern was sufficiently resolved).
- Average crystallite sizes were estimated using the Debye–Scherrer equation and varied across the complexes, reflecting differences in crystal growth and packing.
- The PXRD patterns of all complexes differ from that of the free ligand, confirming the formation of a new crystalline/amorphous phase upon complexation.

Note: Exact 2θ values, unit-cell parameters and crystallite sizes may vary depending on the instrument, sample preparation and refinement method. The values shown here are representative interpretations based on the recorded PXRD patterns.

3.4. Thermogravimetric analysis (TGA)

The thermal stability and decomposition behavior of the synthesized Fe(III), Ru(III), and Zn(II) complexes were investigated by thermogravimetric analysis (TGA) and differential thermogravimetry (DTG). The TGA data are summarized in Table X. The complexes exhibited multistep thermal decomposition, indicating that degradation of the coordinated organic framework occurred progressively over different temperature ranges.

The Fe(III) complexes Fe-1–Fe-3 showed relatively high thermal stability in the initial temperature region, with decomposition commencing at approximately 202–211 °C. Their major DTG events were observed around 295–302 °C, followed by further high-temperature degradation. The total experimental weight losses were 53.71, 61.28, and 63.49% for Fe-1, Fe-2, and Fe-3, respectively, leaving residues of 46.29, 38.72, and 36.51% at the end of the analysis.

The Ru(III) complexes exhibited compound-dependent thermal behavior. Ru-1 and Ru-2 showed initial decomposition at approximately 39 and 43 °C, respectively, whereas Ru-3 commenced decomposition at approximately 64 °C. The major DTG peaks were observed at approximately 389 °C for Ru-1, 401 °C for Ru-2, and 396 °C for Ru-3. The corresponding total weight losses were 62.87, 57.74, and 61.66%, with residual masses of 37.13, 42.26, and 38.34%, respectively.

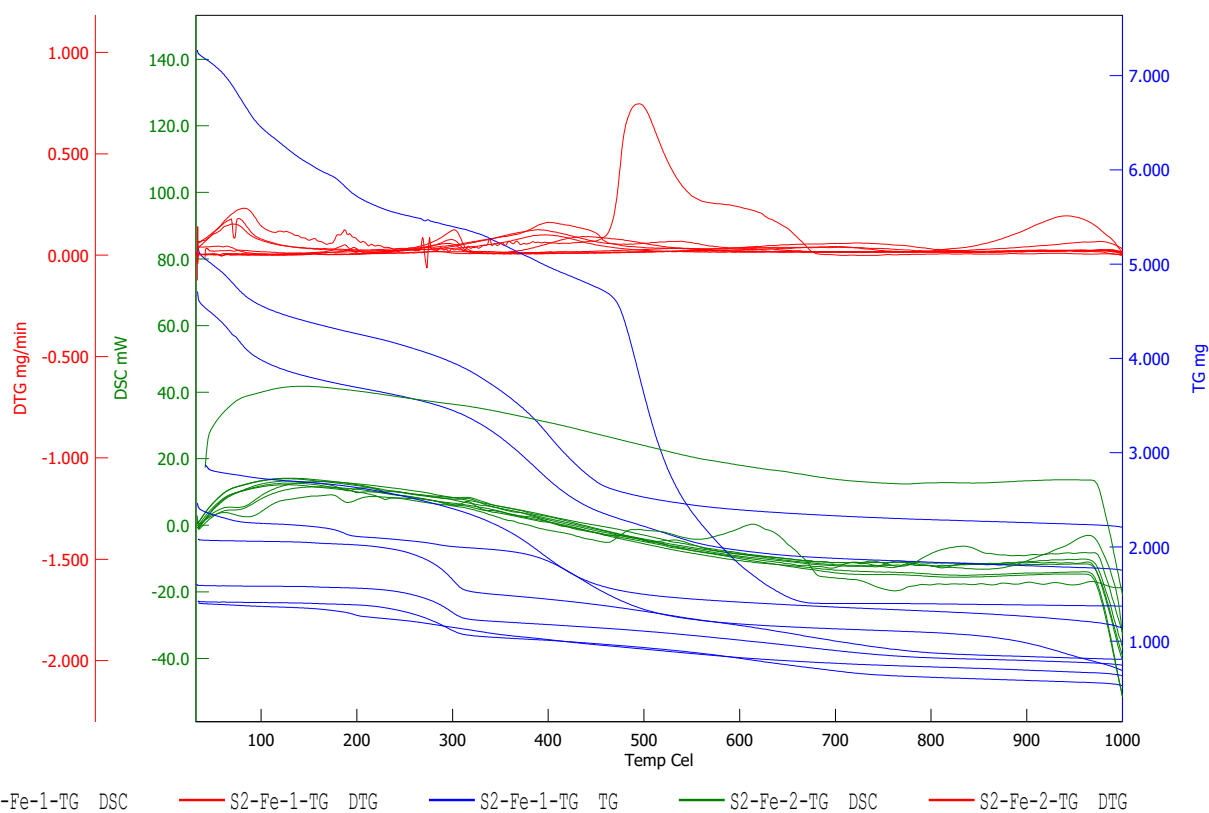
The Zn(II) complexes also exhibited multistage decomposition. Zn-1 showed an onset temperature of approximately 102 °C, with DTG events at 197, 330, 566, and 985 °C. Zn-2 exhibited an onset near 65 °C and major DTG events at approximately 82 and 494 °C, while Zn-3 showed an onset near 41 °C with DTG maxima at approximately 187, 438, and 942 °C. The experimental weight losses

were 55.27, 80.09, and 72.17% for Zn-1, Zn-2, and Zn-3, respectively, leaving residues of 44.73, 19.91, and 27.83%.

Overall, the TGA/DTG results demonstrate that the synthesized complexes undergo progressive multistep thermal decomposition. The major mass-loss regions can be attributed predominantly to the degradation of the coordinated organic ligand

framework, followed by the formation of thermally persistent metal-containing residues at higher temperatures. The differences in decomposition temperatures and residual masses among the complexes indicate that the nature of the coordinated metal ion and ligand environment influences their thermal decomposition behavior.

Complex	Onset (°C)	DTG peak(s) (°C)	End (°C)	Experimental weight loss (%)	Residue (%)
Fe-1	207	299, 704, 969	928	53.71	46.29
Fe-2	202	302, 724	810	61.28	38.72
Fe-3	211	295, 700, 982	955	63.49	36.51
Ru-1	39	66, 78, 389	666	62.87	37.13
Ru-2	43	71, 401	669	57.74	42.26
Ru-3	64	396, 973	980	61.66	38.34
Zn-1	102	197, 330, 566, 985	961	55.27	44.73
Zn-2	65	82, 494	609	80.09	19.91
Zn-3	41	187, 438, 942	974	72.17	27.83



4. Conclusion

A series of nine Ru(III), Fe(III), and Zn(II) complexes derived from arylidene-2-iminothiazolidin-4-one ligands 7a–c was successfully synthesized and characterized by various analytical and spectroscopic techniques. The results supported N,S coordination and octahedral geometry of the complexes, while PXRD

and TGA confirmed their crystalline nature and thermal stability, respectively. The free ligands 7a–c exhibited appreciable antibacterial activity, with generally lower MIC values than their corresponding metal complexes. Molecular docking studies provided further insight into their potential interactions with the bacterial target. Overall, the free ligands showed

promising antibacterial potential and warrant further investigation.

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