

Conventional Liquid-State Synthesis of Glycine-Benzaldehyde Schiff Base Metal Complexes: Methodological Considerations and Antimicrobial Efficacy

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ABSTRACT

Despite growing interest in the emergent solid-state methods, conventional liquid-state reflux remains the main way to synthesize Schiff base transition metal complexes. This study describes a detailed framework for liquid-state synthesis, using the preparation of a glycine-benzaldehyde Schiff base ligand and its Fe (II), Co(II), and Cu(II) complexes as ingredient. The ligand was made by ethanolic reflux with methylamine as a catalyst, and the metal complexes were prepared in methanol at room temperature (30 °C) for 24 hours with a 2:1 ligand-to-metal ratio. The products were analyzed using FTIR, UV-Visible spectroscopy, X-ray diffraction (XRD), thermogravimetric analysis (TGA), magnetic susceptibility, and antimicrobial screening with agar well diffusion. The ligand was obtained in 88.2% yield and showed a clear azomethine $\nu(\text{C}=\text{N})$ stretch at 1679.2 cm^{-1} . Complex yields followed the Irving-Williams order: Cu(II) (81.6%), Co(II) (76.5%), and Fe(II) (71.2%). FTIR confirmed bidentate N, O-coordination by shifts in the imine band. XRD showed that the Co(II) complex was highly crystalline (494–1247 Å), while the Fe(II) product was nearly amorphous (~53 Å). Magnetic measurements indicated spin-crossover behavior for Fe(II). TGA showed that Cu(II) and Co(II) decomposed gradually above 200 °C, but Fe(II) broke down rapidly near 400 °C. The Co(II) and Cu(II) complexes showed broad-spectrum antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus niger*, and *Candida albicans* at 100 µg/mL. Liquid-state synthesis offers clear benefits, such as thermodynamic control, improved crystallinity through Ostwald ripening, and access to spin-crossover materials. The framework described here can guide others using conventional solution-based synthesis in coordination and medicinal inorganic chemistry.

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INTRODUCTION

Schiff bases, characterized by the azomethine functional group ($-\text{C}=\text{N}-$), represent one of the most extensively studied classes of ligands in coordination chemistry since Hugo Schiff's original report in 1864 (Schiff, 1864). The condensation of primary amines with carbonyl compounds produces ligands of considerable versatility, capable of stabilizing transition metal ions across a wide range of oxidation states and coordination geometries (Qin *et al.*, 2013). When derived from amino acid precursors such as glycine, Schiff bases acquire additional donor functionality from the carboxylate moiety, enabling bidentate chelation and the formation of thermodynamically stable five-membered metallacycles (Abu-Dief & Mohamed, 2015).

The synthesis of Schiff base metal complexes has traditionally been done using liquid-state methods (LSM), wherein the preformed ligand and an appropriate metal salt are dissolved in a suitable solvent, typically ethanol, methanol, or their aqueous mixtures and refluxed for extended periods ranging from several hours to days (Abdel-Rahman *et al.*, 2017; Sani *et al.*, 2022). This approach remains the gold standard in coordination chemistry for various convincing reasons. Solution-phase reactions proceed

under homogeneous conditions that maximize molecular collision frequency, secure efficient heat transfer, and drive reactions toward thermodynamic equilibrium (Garnovskii *et al.*, 1993). The solvent medium facilitates the dissolution of both organic ligands and inorganic metal salts, overcoming solubility barriers that would otherwise prevent reaction in the solid state. Moreover, slow crystallization from solution often yields products of high crystallinity suitable for single-crystal, X-ray diffraction, the definitive technique for establishing molecular connectivity and three-dimensional geometry (Vigato & Tamburini, 2004).

The choice of solvent in liquid-state synthesis actively influences reaction kinetics, product morphology, and even the electronic framework of the resulting complexes (Reichardt & Welton, 2011). Protic solvents such as methanol and ethanol can participate in hydrogen-bonding interactions with ligand donor atoms, potentially labilizing certain coordination sites and assisting ligand exchange processes. The dielectric constant of the medium affects ion-pairing equilibria along with can modulate the relative stability of different coordination isomers (Tümer *et al.*, 2007). These solvent effects supply the synthetic chemist with additional parameters for tuning reaction outcomes.

Transition metal ions of the first row, particularly iron, cobalt, and copper, occupy a privileged position in bioinorganic and medicinal chemistry. These metals act as essential cofactors in numerous metalloenzymes, participating in electron transfer, oxygen carriage, and substrate activation (Rafique *et al.*, 2010). Their incorporation into Schiff base frameworks generates complexes with documented antimicrobial, anticancer, and antioxidant activities (Thakur *et al.*, 2024). The biological activity of such complexes is rationalized by Tweedy's chelation theory, which proposes that metal coordination reduces the polarity of the ligand donor atoms, increases π -electron delocalization over the chelate ring, and enhances lipophilicity, therewith facilitating passive diffusion across microbial membranes (Tweedy, 1964).

Despite the emergence of mechanochemical and other solvent-free synthetic methodologies aligned with green chemistry principles (James *et al.*, 2012), liquid-state methods continue to dominate both research laboratories and industrial production of coordination compounds. A complete understanding of LSM protocols, including their mechanistic underpinnings, practical issues, and characteristic product profiles, continues to be essential for practitioners in the field. This study provides a detailed methodological account of conventional liquid-state synthesis, exemplified by the preparation and characterization of a glycine-benzaldehyde Schiff base and its Fe(II), Co(II), and Cu(II) complexes by evaluate the antimicrobial activity against clinically relevant bacterial and fungal pathogens.

MATERIALS AND METHODS

Reagents and Instrumentation

All chemicals were of analytical reagent grade and used without further purification.

Synthesis of the Schiff Base Ligand

The Schiff base ligand was synthesized by condensation of benzaldehyde with glycine in a 1:1 molar ratio, adapting the method of Xavier and Srividhya (2014). Benzaldehyde (20 mmol, 2.12 g) and glycine (20 mmol, 1.50 g) were dissolved in 50 mL of absolute ethanol in a 100 mL round-bottom flask equipped with a magnetic stir bar. Methylamine solution (0.5 mL, 40% aqueous) was added as a catalyst. The reaction mixture was heated under reflux at 80 °C for 4 hours, during which the solution developed a deep yellow coloration indicating imine formation. Upon cooling to room temperature, the crude product precipitated as a purple crystalline solid. The precipitate was collected by vacuum filtration, washed with cold ethanol (3 × 10 mL) to remove unreacted starting materials, and recrystallized from hot ethanol. The purified ligand was dried in a vacuum desiccator over anhydrous silica gel for 48 hours and stored in an amber vial.

General Procedure for Liquid-State Synthesis of Metal Complexes

All metal complexes were prepared using a 2:1 ligand-to-metal molar ratio, following the general protocol described by Umar *et al.*, (2025). The Schiff base ligand (1 mmol, 0.172 g) was dissolved in 100 mL of absolute methanol in a 250 mL round-bottom flask with continuous magnetic stirring until complete dissolution was achieved. Separately, the appropriate metal chloride salt (2 mmol) was dissolved in 50 mL of absolute methanol. The metal salt solution was added dropwise to the ligand solution at room temperature with

constant stirring. The reaction mixture was stirred continuously for 24 hours at room temperature, during which a colored precipitate formed. The solid product was collected by vacuum filtration, washed with cold methanol (3 × 10 mL), and dried in a desiccator over silica gel for 48 hours.

Physicochemical Characterization

Percentage Yield

was calculated as (actual yield / theoretical yield) × 100%, based on theoretical yields based on the limiting reactant (ligand). Syntheses were performed in triplicate, and mean yields are reported.

Solubility

was assessed qualitatively in distilled water, methanol, ethanol, acetone, chloroform, n-hexane, diethyl ether, and DMSO at room temperature (30 °C) using 10 mg of compound per 2 mL of solvent. Results were recorded as soluble (S), partially soluble (PS), or insoluble (IS) after 30 minutes of standing.

Magnetic Susceptibility

was determined at room temperature. The effective magnetic moment (μ_{eff}) was calculated from the molar susceptibility after diamagnetic correction using Pascal's constants. The number of unpaired electrons was inferred by comparison with spin-only values (Figgis & Hitchman, 2000).

XRD Crystallite Sizes

were estimated using the Debye-Scherrer equation: $t = K\lambda / (\beta \cos \theta)$, where $K = 0.9$ (shape factor for spherical crystallites), $\lambda = 1.5406 \text{ \AA}$ (Cu K α), β = full width at half maximum in radians, and θ = Bragg angle (Holder & Schaak, 2019).

Antimicrobial Activity Assessment

In vitro antimicrobial activity was evaluated using the agar well diffusion method against four test organisms: *Staphylococcus aureus* (ATCC 25923, Gram-positive), *Escherichia coli* (ATCC 25922, Gram-negative), *Aspergillus niger* (ATCC 16404), and *Candida albicans* (ATCC 10231) (Umar *et al.*, 2025).

Stock solutions (100 $\mu\text{g/mL}$) of the ligand and metal complexes were prepared in DMSO. Mueller-Hinton agar plates were inoculated with standardized microbial suspensions adjusted to 0.5 McFarland standard ($\sim 1.5 \times 10^8$ CFU/mL). Wells of 6 mm diameter were punched aseptically using a sterile cork borer, and 100 μL of each test solution was dispensed into the wells. Ciprofloxacin (10 μg) served as the positive control for bacterial strains, fluconazole (25 μg) for fungal strains, and DMSO as the negative control. Bacterial plates were incubated at 37 °C for 24 hours; fungal plates at 28 °C for 48 hours. Zones of inhibition were measured in millimetres using a transparent ruler. All tests were performed in triplicate, and results are expressed as mean $\pm$ standard deviation.

Statistical Analysis

All experiments were conducted in triplicate. Results are expressed as mean $\pm$ standard deviation. One-way analysis of variance (ANOVA) with Tukey's post hoc test was used to compare antimicrobial activities among complexes, with $p < 0.05$ considered statistically significant was used for all analyses.

RESULTS AND DISCUSSION

Synthesis and Physical Properties

Table 1: Physical Properties of the Schiff Base Ligand and Its Metal Complexes Produced Via the Liquid-State Method

Samples	Color	% Yield	Melting Point	Solubility	Molecular mass (g/mol)
Ligand (HL)	Purple	88.2 ± 1.5	190–230	S / SS	-
[Fe(L)Cl]·H ₂ O	Pink	71.2 ± 2.1	135	IS / S	12.4
[Co(L) ₂ (H ₂ O) ₂]	Blue	76.5 ± 1.8	110	S / S	15.8
[Cu(L) ₂ (H ₂ O)]	Pale green	81.6 ± 1.2	135	S / SS	10.6

S = soluble; SS = slightly soluble; IS = insoluble. Yields are mean ± SD (n = 3).

The Schiff base ligand, obtained as a purple crystalline solid in 88.2% yield (mp 190–230 °C), exhibited solubility consistent with its zwitterionic, hydrogen-bonded structure, freely soluble in DMSO, slightly soluble in water. The wide melting range is typical for amino acid-derived Schiff bases (Al Zoubi *et al.*, 2020). Metal complexes were isolated with yields that follow the Irving–Williams stability order for divalent first-row transition metals: Cu(II) (81.6%) > Co(II) (76.5%) > Fe(II) (71.2%) (Table 1). This trend confirms that the 24 h stirring period allowed thermodynamic equilibration, with the Cu(II) complex benefiting from Jahn–Teller

stabilization in an octahedral field (Irving & Williams, 1953; Miessler *et al.*, 2014). The liquid-state environment thus imparts predictable, thermodynamically controlled product distributions, a practical advantage over kinetically trapped solid-state reactions (Gutten & Rulíšek, 2013).

Molar conductance values for all complexes (10^{-3} M in DMSO) were below $20 \Omega^{-1}\text{cm}^2\text{mol}^{-1}$, confirming their non-electrolytic nature. This is consistent with the proposed inner-sphere coordination of chloride (Fe) or water (Co, Cu) ligands, with no free counterions (Geary, 1971).

FTIR Spectroscopic Characterization

Table 2: FTIR Absorption Bands (cm⁻¹) Data

Samples	$\nu(\text{C}=\text{N})$ Free Ligand (cm ⁻¹)	$\nu(\text{C}=\text{N})$ Complex (cm ⁻¹)	$\Delta\nu$ (cm ⁻¹)	$\nu(\text{C}-\text{O})$ (cm ⁻¹)	Coordination Mode
Ligand (HL)	1679.2	-	-	1179.7, 1108.9	-
[Fe(L)Cl]·H ₂ O	-	1586.0	-93.2	1094.4	N,O-bidentate
[Co(L) ₂ (H ₂ O) ₂]	-	1584.1-1604.6*	-74.6/-95.1	1151.7, 1105.2	N,O-bidentate
[Cu(L) ₂ (H ₂ O)]	-	1595.3	-83.9	1099.6	N,O-bidentate

*Merged with $\nu(\text{C}=\text{C})$ aromatic envelope.

The free ligand exhibited a sharp $\nu(\text{C}=\text{N})$ band at 1679.2 cm^{-1} , diagnostic of successful Schiff base condensation (Nakamoto, 2009). Upon complexation, this band underwent a significant bathochromic shift of $74\text{--}95 \text{ cm}^{-1}$ (Table 2), appearing as a broadened absorption merged with the aromatic $\nu(\text{C}=\text{C})$ envelope at $1584\text{--}1605 \text{ cm}^{-1}$. The magnitude of this shift is universally accepted as evidence for azomethine nitrogen coordination, resulting from σ -donation of the nitrogen lone pair into vacant metal d-orbitals, which weakens the C=N bond (Fayek *et al.*, 2025). New $\nu(\text{C}-\text{N})$ bands ($1332\text{--}1418 \text{ cm}^{-1}$) further support metal–nitrogen bond formation. Concomitant shifts of the carboxylate $\nu(\text{C}-\text{O})$ stretches indicate participation of the

carboxylate oxygen, consistent with a bidentate N,O-chelation mode that forms a five-membered metallacycle, the geometrically most favorable arrangement for an N,O-donor ligand with donor atoms separated by a single carbon (Deacon & Phillips, 1980). This coordination mode underpins the proposed octahedral geometries: two bidentate ligands occupy equatorial or cis-disposed sites, with axial positions filled by chloride (Fe) or water (Co, Cu) (Iqbal *et al.*, 2015). Although far-IR data were not collected, literature values for analogous systems place $\nu(\text{M}-\text{N})$ at $430\text{--}470 \text{ cm}^{-1}$ and $\nu(\text{M}-\text{O})$ at $500\text{--}570 \text{ cm}^{-1}$ (Ji *et al.*, 1998).

X-ray Diffraction Analysis

Table 3: XRD Crystallite Size Data for Liquid-State Synthesized Complexes

Complex	Crystallite Size Range (Å)	Mean Size (Å)	Crystallinity
[Co(L) ₂ (H ₂ O) ₂]	494–1247	871 ± 148	High
[Cu(L) ₂ (H ₂ O)]	383–1119	683 ± 354	Moderate–High
[Fe(L)Cl]·H ₂ O	~53	53 ± 8	Very poor (near-amorphous)

Powder XRD patterns revealed stark differences in crystallinity (Table 3). The Co(II) complex showed sharp, intense reflections with average crystallite sizes of $494\text{--}1247 \text{ Å}$, reflecting a high degree of long-range order. This is attributed to Ostwald ripening during the extended stirring period in methanol: smaller, more soluble crystallites dissolve and redeposit onto larger ones, yielding larger, more uniform particles (Voorhees, 1985). In contrast, solid-state syntheses often produce broader, less intense peaks indicative of reduced crystallinity (Iorhuna *et al.*, 2025). The Cu(II) complex exhibited moderate-to-high crystallinity ($383\text{--}1119 \text{ Å}$) but with a wider size distribution (CV = 51.8%), consistent with structural disruptions introduced by Jahn–

Teller distortion, which generates a distribution of local coordination geometries that complicates uniform lattice formation (Halcrow, 2013). The Fe(II) complex was essentially amorphous, displaying only a broad halo with an average crystallite size of $\sim 53 \text{ Å}$. This near-amorphous character arises from burst nucleation kinetics: rapid precipitation kinetically traps the system in a disordered state before thermodynamically favoured crystal growth can occur (Bonnert & Ilic, 2021). The liquid-state method thus enables Ostwald ripening and high crystallinity when kinetics permit, but does not prevent kinetic trapping when metal–ligand interactions are weak.

Magnetic Susceptibility

Table 4: Magnetic Susceptibility Data for Liquid-State Synthesized Complexes

Samples	μ_{eff} (μ_B)	Unpaired Electrons (n)	Proposed Geometry	Spin State Assignment
[Cu(L) ₂ (H ₂ O)]	1.75	1	Distorted octahedral	—
[Co(L) ₂ (H ₂ O) ₂]	4.15	3	Octahedral	High-spin
[Fe(L)Cl]·H ₂ O	4.50	Mixed (4 → 2)	Octahedral	Mixed-spin/SCO

Room-temperature magnetic moments (Table 4) provided insight into electronic configurations. The Cu(II) complex exhibited $\mu_{\text{eff}} = 1.75 \mu_B$, consistent with one unpaired electron ($S = \frac{1}{2}$) in a Jahn–Teller distorted octahedral field; the slight elevation above the spin-only value ($1.73 \mu_B$) indicates a small orbital contribution via spin–orbit coupling (Christiansen *et al.*, 2000). The Co(II) complex gave $\mu_{\text{eff}} = 4.15 \mu_B$, confirming a high-spin d^7 configuration (${}^4T_{1g}$ ground term) with three unpaired electrons. The value is somewhat lower than the spin-only prediction ($3.87 \mu_B$ for $S = 3/2$), a phenomenon typical of octahedral Co(II) and attributed to partial quenching of orbital angular momentum by spin–orbit coupling and low-symmetry ligand field components (Su *et al.*, 2020).

The Fe(II) complex displayed $\mu_{\text{eff}} = 4.50 \mu_B$, intermediate between purely high-spin ($S = 2$, ~ 5.0 – $5.6 \mu_B$) and low-spin

($S = 0$, diamagnetic) octahedral d^6 configurations. This is characteristic of spin-crossover (SCO) or mixed-spin behaviour, wherein the 5T_2 (high-spin) and 1A_1 (low-spin) states are thermally populated at room temperature (Ksenofontov *et al.*, 2004). The observation of SCO is significant: the N,O-donor ligand field positions Fe(II) near the crossover threshold ($\Delta_o \approx P$), and the liquid-state environment provided sufficient molecular mobility for structural relaxation, allowing both spin states to coexist in equilibrium during crystallization (Kumar *et al.*, 2019). Access to SCO materials is a distinctive advantage of solution-phase equilibration; mechanochemical methods have not yet been shown to reliably produce such electronic configurations (Kumar *et al.* 2023).

Thermogravimetric Analysis

Table 5: TGA Derivative Data Summary for Liquid-State Synthesized Complexes

Complex	TGA Change	Decomposition Type	ΔH (kJ/mol)	T_o (°C)
[Co(L) ₂ (H ₂ O) ₂]	Positive (mass gain)	Low-T adsorption/relaxation	+0.392	215
[Cu(L) ₂ (H ₂ O)]	Positive (mass gain)	Gradual decomposition	+0.305 → +0.008	230
[Fe(L)Cl]·H ₂ O	Negative (mass loss)	Catastrophic decomposition $\sim 400^\circ\text{C}$	−4.538	385

TGA revealed a clear hierarchy of thermal stability correlating with crystallinity (Table 5). The highly crystalline Co(II) complex and moderately crystalline Cu(II) complex underwent gradual, multi-step decomposition, consistent with ordered solids where thermal energy must first overcome lattice forces (Bello *et al.*, 2024). In contrast, the amorphous Fe(II) complex exhibited a catastrophic mass loss near 400°C ($-4.538\%/min$), attributable to rapid breakdown of the

coordinated ligand. Amorphous materials possess higher free energy, lack a stabilizing periodic lattice, and often contain occluded solvent or voids that facilitate thermal degradation (Hancock & Zografi, 1997). The thermal lability of the Fe(II) complex thus directly reflects its near-amorphous structure and the weak ligand field implied by the SCO magnetic properties.

Antimicrobial Activity

Table 6: Antimicrobial Activity of Synthesized Compounds at 100 $\mu\text{g}/\text{mL}$ (Zone Of Inhibition, mm $\pm$ SD, n = 3)

Compound	<i>S. aureus</i> (Gram-positive)	<i>E. coli</i> (Gram-negative)	<i>A. niger</i> (Fungus)	Compound
Ligand	0.00	0.00	0.00	0.00
Fe(II) complex	0.00	0.00	0.00	0.00
Co(II) complex	17.59 ± 0.42	15.47 ± 0.35	26.03 ± 0.67	27.30 ± 0.58
Cu(II) complex	18.00 ± 0.51	19.02 ± 0.44	15.20 ± 0.39	28.00 ± 0.62
Ciprofloxacin (10 μg)	18.94 ± 0.38	14.63 ± 0.29	NT	NT
Fluconazole (25 μg)	NT	NT	13.94 ± 0.31	16.53 ± 0.44

NT = not tested.

The free ligand and the Fe(II) complex were completely inactive against all test organisms at $100 \mu\text{g}/\text{mL}$ (Table 6). In sharp contrast, the Co(II) and Cu(II) complexes exhibited broad-spectrum activity. The Cu(II) complex showed superior antibacterial potency (*S. aureus*: $18.00 \pm 0.51 \text{ mm}$; *E. coli*: $19.02 \pm 0.44 \text{ mm}$), statistically comparable to ciprofloxacin against *S. aureus* ($p = 0.087$). The Co(II) complex demonstrated exceptional antifungal activity, with zones of $26.03 \pm 0.67 \text{ mm}$ against *A. niger* and $27.30 \pm 0.58 \text{ mm}$ against *C. albicans*, significantly exceeding fluconazole ($p = 0.002$ for *A. niger*). One-way ANOVA confirmed significant differences among complexes ($F = 156.4$, $p < 0.001$).

These results compellingly validate Tweedy’s chelation theory (Tweedy, 1964). Metal coordination reduces the polarity of the donor atoms by delocalizing their negative charge over the chelate ring, enhancing lipophilicity and facilitating passive diffusion through microbial membranes (Rogers *et al.*, 2025). The Cu(II) complex likely benefits from its Jahn–Teller labile axial sites, promoting ligand exchange with biological nucleophiles, and from the redox-active Cu(II)/Cu(I) couple ($E^\circ = +0.153 \text{ V}$), which can generate reactive oxygen species via Fenton-type chemistry (Vatagude *et al.*, 2026). The Co(II) complex’s extraordinary antifungal potency suggests a distinct mechanism, possibly involving interference with ergosterol biosynthesis or fungal metalloenzymes (Raman *et al.*, 2007). The complete

inactivity of the Fe(II) complex is attributed to its weak ligand field/mixed-spin configuration (leading to premature ligand dissociation), near-amorphous structure, and pronounced thermal instability, all of which likely compromise its ability to reach intracellular targets intact (Synthesis, Structural, and Biological Studies..., 2005).

Limitations

There are several limitations to this study. We did not obtain single-crystal X-ray structures, so we could not determine exact bond lengths, angles, or intermolecular interactions. In the future, we plan to work with crystallography labs to access single-crystal XRD facilities. We also did not perform variable-temperature magnetic susceptibility tests, which would help fully describe the spin-crossover behavior of the Fe(II) complex, due to equipment limitations. Future studies will try to access variable-temperature magnetometry through equipment upgrades or cooperation. Far-infrared FTIR spectra (600–50 cm^{-1}) were not recorded, so the $\nu(\text{M}-\text{N})$ and $\nu(\text{M}-\text{O})$ assignments are tentative. We plan to include extended-range FTIR measurements in future experiments, possibly by working with institutions that have the right spectrometers. We also lack cytotoxicity data on human cell lines, so we cannot assess the therapeutic indices of the active complexes. Follow-up studies will include cytotoxicity assays using standard mammalian cell lines to check selectivity and safety. Finally, we did not directly study the mechanisms of antimicrobial action, such as ROS generation, membrane disruption, or metal ion release. To address this, we propose targeted biochemical assays and sophisticated spectroscopic evaluations in future work to clarify the exact mechanisms behind the observed antimicrobial effects.

CONCLUSION

Conventional liquid-state reflux methodology remains an necessary tool in the synthesis of Schiff base metal complexes. This study effectively showcased the application of LSM to prepare a glycine-benzaldehyde Schiff base ligand (88.2% yield) and its Fe(II), Co(II), and Cu(II) complexes (71.2–81.6% yield). Thorough characterization confirmed bidentate N,O-coordination with octahedral geometries, while revealing metal-dependent variations in crystallinity (53–1247 Å), thermal stability, and electronic framework that are direct consequences of the solution-phase synthesis environment.

The Co(II) and Cu(II) complexes displayed notable broad-spectrum antimicrobial activity, with Co(II) displaying notable antifungal potency against *A. Niger* (26.03 mm) that significantly exceeded the standard drug fluconazole. The Fe(II) complex displayed mixed-spin/spin-crossover behavior a phenomenon uniquely accessible through thermodynamic equilibration in the liquid state.

This methodological study provides an extensive experimental framework for practitioners utilising conventional solution-based synthesis and explains the mechanistic principles of this approach. It explains the key principles of thermodynamical control, Ostwald ripening, and spin-state equilibration that set liquid-state methods apart from solid-state approaches. While this work focused on a glycine-benzaldehyde Schiff base and certain first-row transition metals, the framework can be applied to many other Schiff base ligands and metal ions. These methods also work for other amino acid-derived systems, different aromatic aldehyde or ketone precursors, and various metal centers, enabling the synthesis of a wide range of coordination compounds. This pliability makes the framework useful for instructors and researchers who want to adapt these

procedures to related systems in coordination chemistry. Future research needs to focus on single-crystal growth, variable-temperature magnetometry, far-infrared spectroscopy, cytotoxicity testing, and studies of antimicrobial mechanisms to address present constraints and help move these compounds toward pharmaceutical use.ew nano-sized Cu(II), Co(II) and Ni(II) chelates based on tri-dentate NOO imine ligands as precursors for metal oxides.

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