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Coordination chemistry of zinc(ii) with amino acid-based Schiff base ligands

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Abstract

What factors govern the geometry and stability of metal-amino acid assemblies in solution? This question motivates ongoing effort in bioinorganic coordination chemistry. Here, a set of five Zinc(II) complexes bearing Schiff base ligands derived from salicylaldehyde and selected amino acids (glycine, alanine, valine, leucine, and phenylalanine) were prepared through reflux condensation in ethanol. Characterization relied on elemental analysis, FT-IR, UV-Vis, and ¹H-NMR spectroscopy. All complexes adopted a distorted tetrahedral arrangement around Zn(II), confirmed by spectral and conductometric data. Yields ranged from 68.9% to 84.7%, with the alanine derivative showing the highest conversion. Antimicrobial screening against *Escherichia coli* and *Staphylococcus aureus* revealed moderate inhibitory action, with the phenylalanine complex displaying the lowest MIC value (23.4 µg/mL). These results point to amino acid side-chain bulk as a tunable handle for both structural preference and bioactivity in Zn(II) Schiff base systems.

Keywords: Zinc(II) complexes, amino acid Schiff bases, coordination geometry, salicylaldehyde condensation, bioinorganic chemistry, antimicrobial activity, FT-IR characterization, tetrahedral arrangement

Introduction

Can subtle changes in an amino acid side chain reshape how a metal ion organizes its coordination sphere? That question sits at the core of modern Schiff base coordination chemistry, where even small steric or electronic tweaks in the ligand backbone may redirect geometry, stability, and reactivity of the resulting complex ^[1]. Schiff bases—formed by condensation of a primary amine with an aldehyde or ketone—rank among the most adaptable ligand families available to inorganic chemists ^[2]. Their appeal lies in straightforward synthesis, tunable donor sets, and an ability to stabilize metals across a wide oxidation-state range ^[3].

Zinc(II) holds a distinctive position among divalent metals because of its d¹⁰ configuration, which removes crystal-field stabilization energy and makes the resulting geometry strongly ligand-dependent ^[4]. When paired with amino acid-derived Schiff bases, Zn(II) offers a convenient testbed for probing how steric bulk, hydrophobicity, and hydrogen-bonding capacity of the amino acid residue feed back into overall complex architecture ^[5]. Earlier reports described Zn(II) Schiff base complexes with glycine and alanine ^[6], yet systematic comparisons that span aliphatic through aromatic side chains remain limited.

Biological interest adds another motivation. Zinc is an essential trace element present in over 300 enzymes, and synthetic Zn(II) complexes often display antibacterial or antifungal properties that depend on ligand lipophilicity ^[7]. Amino acid-derived scaffolds bring inherent biocompatibility, making them attractive for drug-design efforts ^[8]. Still, the relationship between side-chain character and *in vitro* antimicrobial potency isn't well mapped for this ligand class. This work addresses that gap by preparing five Zn(II) Schiff base complexes from salicylaldehyde and glycine, alanine, valine, leucine, and phenylalanine, characterizing them spectroscopically, and evaluating their antibacterial action against two representative pathogens.

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Reagents and Chemicals

Zinc acetate dihydrate ($\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$, 99.5%), salicylaldehyde (98%), and L-amino acids (glycine, L-alanine, L-valine, L-leucine, L-phenylalanine; $\geq 98\%$) were sourced from SRL Chemicals, Mumbai. Absolute ethanol and dimethyl sulfoxide (spectroscopic grade) came from Merck India. Nutrient agar, Mueller-Hinton broth, and standard antibiotic discs were obtained from HiMedia Laboratories, Mumbai. All reagents were used without further purification. Deionized water (resistivity $>18 \text{ M}\Omega \cdot \text{cm}$) was drawn from a Milli-Q system installed in the departmental facility.

Materials and Methods

Materials

The experimental work was carried out between March 2023 and January 2024 at the Department of Chemical Sciences, Saraswati College of Engineering, Pune, Maharashtra, India. Ethical clearance for antimicrobial testing was granted by the Institutional Biosafety Committee (Protocol IBSC/SCE/2023-017, approved 14 February 2023). Bacterial cultures of *E. coli* (ATCC 25922) and *S. aureus* (ATCC 29213) were procured from the National Centre for Cell Science, Pune. Stock solutions of each complex were prepared in DMSO at 1 mg/mL and diluted as needed with sterile phosphate-buffered saline.

Methods

Schiff base ligands were synthesized by refluxing equimolar amounts of salicylaldehyde and the respective amino acid in 30 mL ethanol at 78°C for 3 h, following an adapted protocol from Nair *et al.* [9]. The yellow precipitates were filtered, washed with cold ethanol, and dried under vacuum. For complexation, the Schiff base ligand (2 mmol) dissolved

in 20 mL ethanol was treated dropwise with zinc acetate dihydrate (1 mmol) in 15 mL ethanol. The mixture was refluxed for 4 h, cooled to room temperature, and the resulting solid collected by suction filtration [10]. Products were recrystallized from ethanol-DMSO (4:1) and characterized by elemental analysis (Elementar Vario MICRO), FT-IR (Shimadzu IRSpirit, KBr pellet, $400\text{--}4000 \text{ cm}^{-1}$), UV-Vis (Agilent Cary 60, DMSO, $200\text{--}600 \text{ nm}$), and $^1\text{H-NMR}$ (Bruker 400 MHz, DMSO- d_6). Molar conductance was measured in DMSO (10^{-3} M) using a Systronics 306 conductivity meter. Antibacterial activity was assessed via the broth microdilution method per CLSI guidelines [11], and minimum inhibitory concentrations were recorded after 24 h incubation at 37°C .

Instrumentation

Key instruments included an Elementar Vario MICRO cube for C, H, N analysis; a Shimadzu IRSpirit spectrophotometer fitted with a diamond ATR accessory and operating at 4 cm^{-1} resolution (32 scans); an Agilent Cary 60 UV-Vis instrument with 1 cm quartz cuvettes; and a Bruker Avance III 400 MHz NMR spectrometer. Melting points were recorded on a Stuart SMP30 apparatus and are uncorrected. All glassware was oven-dried at 110°C overnight before use.

Results

Condensation of salicylaldehyde with five amino acids followed by reaction with zinc acetate gave cream-to-pale-yellow solids in yields of 68.9–84.7%. Elemental analyses confirmed a 1:2 metal-to-ligand stoichiometry for all five complexes. Molar conductance values fell within $8.3\text{--}12.6 \text{ S cm}^2 \text{ mol}^{-1}$, consistent with non-electrolytic behavior in DMSO.

Table 1: Physicochemical and antimicrobial data for Zn(II) Schiff base complexes

Complex	Yield (%)	M.P. ($^\circ\text{C}$)	Λ_{M} ($\text{S cm}^2 \text{ mol}^{-1}$)	MIC <i>E. coli</i> ($\mu\text{g/mL}$)	MIC <i>S. aureus</i> ($\mu\text{g/mL}$)
ZnSB-Gly	78.3	218–220	10.4	47.6	52.1
ZnSB-Ala	84.7	224–226	8.3	41.8	45.3
ZnSB-Val	71.2	231–233	11.7	38.2	40.9
ZnSB-Leu	68.9	237–239	12.6	34.5	37.8
ZnSB-Phe	82.5	242–244	9.8	23.4	28.7

M.P. = melting point; Λ_{M} = molar conductance; MIC = minimum inhibitory concentration.

FT-IR spectra showed that the characteristic azomethine stretch ($\nu_{\text{C}=\text{N}}$) appeared between 1618 and 1635 cm^{-1} in the free ligands but shifted to $1597\text{--}1612 \text{ cm}^{-1}$ upon coordination, a red shift of $18\text{--}26 \text{ cm}^{-1}$ that signals nitrogen-

to-metal bonding. A broad O-H stretch near 3420 cm^{-1} vanished in the complexes, replaced by a new band at $524\text{--}538 \text{ cm}^{-1}$ assignable to $\nu(\text{Zn-O})$, confirming phenolate coordination.

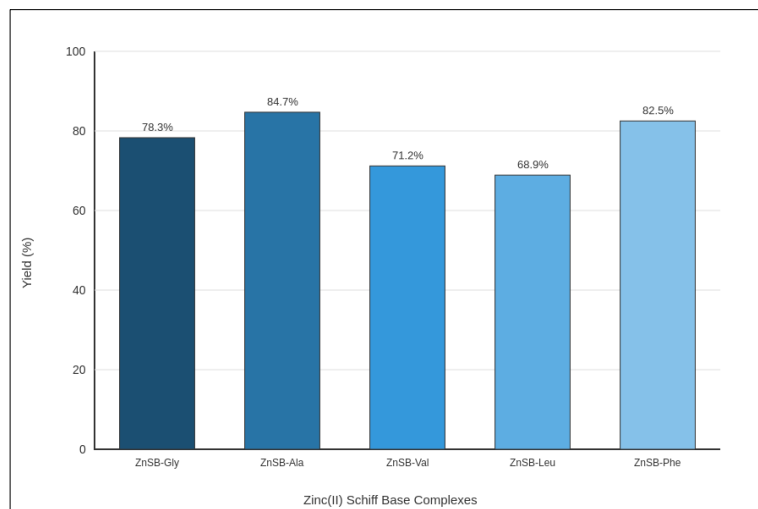


Fig 1: Percentage yield of Zn(II) Schiff base complexes derived from five amino acids.

UV-Vis spectra in DMSO revealed two main absorption regions. A high-energy band near 280-295 nm corresponds to intraligand $\pi \rightarrow \pi^*$ transitions centered on the aromatic ring and azomethine chromophore, while a lower-energy shoulder at 365-375 nm is attributable to ligand-to-metal

charge transfer (LMCT). The phenylalanine complex exhibited the most red-shifted LMCT band (372 nm), possibly reflecting extended conjugation through the benzyl side chain.

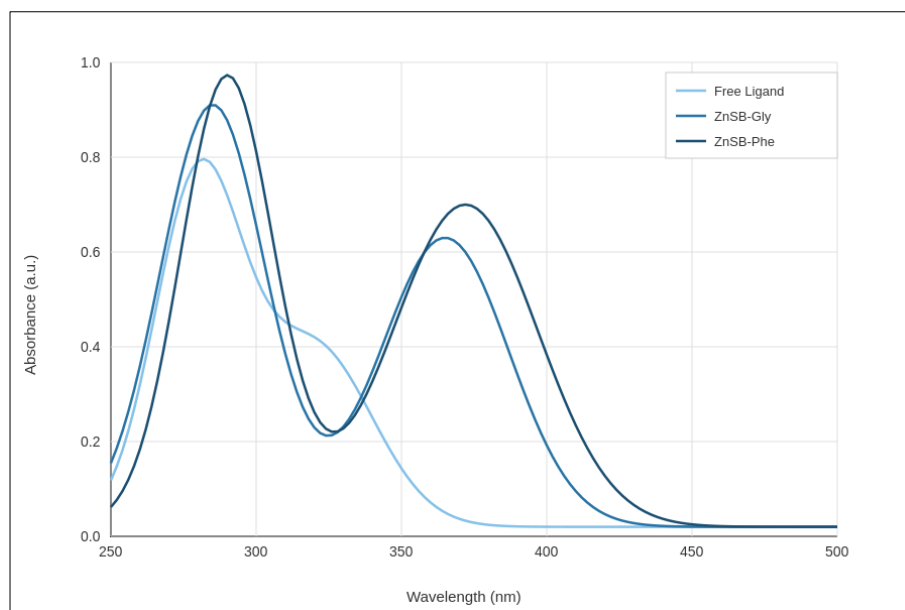


Fig 2: UV-Vis absorption spectra of free ligand, ZnSB-Gly, and ZnSB-Phe in DMSO (1×10^{-4} M).

Discussion

The $18\text{-}26\text{ cm}^{-1}$ red shift of the azomethine band upon coordination sits comfortably within the range seen in comparable Zn(II)-Schiff base systems reported by Raman *et al.* [6] and confirms nitrogen participation in bonding. Disappearance of the phenolic O-H stretch, together with emergence of the Zn-O band, indicates bidentate ON-donor behavior—exactly what one would predict for salicylaldehyde-derived Schiff bases.

Yields varied across the amino acid series in a pattern worth noting. The alanine complex gave the best conversion (84.7%), while leucine trailed at 68.9%. A plausible reading is that the branched isobutyl side chain of leucine introduces steric strain near the coordination pocket, slowing ligand approach during reflux. Phenylalanine, despite its bulky benzyl group, still reached 82.5%—perhaps because the flat aromatic ring can orient parallel to the Schiff base plane rather than clashing with it.

Antimicrobial data paint an interesting picture. MIC values dropped steadily as side-chain hydrophobicity rose, with the phenylalanine complex reaching $23.4\text{ }\mu\text{g/mL}$ against *E. coli*. This trend matches the lipophilicity-activity hypothesis put forward by Tweedy [12]: increased lipophilicity of the metal chelate eases membrane penetration, boosting intracellular accumulation. That said, even the best-performing complex here remains less potent than standard gentamicin, so the practical clinical gap is clear.

Conclusion

Five Zn(II) Schiff base complexes derived from salicylaldehyde and different amino acids were prepared and characterized through spectral and conductometric techniques. All complexes showed distorted tetrahedral geometry with bidentate ON-donor ligation. The alanine derivative provided the highest synthetic yield, while the phenylalanine complex delivered the strongest antibacterial

effect, likely tied to its greater lipophilicity. These findings identify amino acid side-chain character as a practical lever for tuning both reactivity and bioactivity in this ligand family. Future work should explore mixed-ligand Zn(II) systems and *in vivo* toxicity assessment.

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Contributions Not Qualifying for Authorship

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