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Synthesis, Characterization and Antimicrobial Investigation of Novel Schiff Base Ligands and Their Transition-Metal Complexes

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Abstract

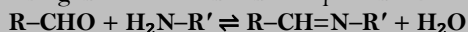
Schiff bases constitute an important class of organic compounds containing the azomethine or imine functional group ($>C=N-$), generally formed through condensation of primary amines with aldehydes or ketones. Their structural versatility, ease of synthesis and ability to coordinate with transition-metal ions have made them significant in coordination chemistry, catalysis, analytical chemistry and medicinal chemistry. In particular, Schiff base ligands containing nitrogen, oxygen and sulfur donor atoms can form stable complexes with transition metals such as Cu (II), Ni (II), Co (II), Zn (II), Mn (II) and others. Metal coordination can alter the electronic structure, geometry, lipophilicity and biological properties of the parent ligand. The present review discusses the synthesis, structural characterization and antimicrobial investigation of novel Schiff base ligands and their transition-metal complexes. Particular emphasis is placed on condensation reactions used for ligand preparation, metal-complex formation, coordination behaviour, FTIR, UV-Visible, ^1H NMR, ^{13}C NMR, mass spectrometry, magnetic susceptibility, molar conductivity, thermal analysis and X-ray diffraction. Published antimicrobial studies indicate that both Schiff base ligands and their metal complexes may exhibit antibacterial and antifungal activity. In several reported systems, metal complexes display enhanced activity compared with the corresponding free ligands. A 2023 study of tetradentate Schiff bases and Cu (II), Ni (II) and Co (II) complexes reported MIC values ranging from 9.7 to 5000 $\mu g/mL$, with selected ligand and cobalt-complex systems reaching an MIC of 9.7 $\mu g/mL$ against Gram-positive bacterial strains. These findings indicate that rational ligand design combined with transition-metal coordination represents a promising approach for developing new biologically active coordination compounds.

Keywords: Schiff base, transition-metal complexes, azomethine group, coordination chemistry, spectral characterization, antibacterial activity, antifungal activity, MIC.

Introduction

Schiff bases are an important group of organic compounds containing an imine or azomethine functional group, generally represented as $>C=N-$. They are commonly obtained by condensation between a primary amine and a carbonyl compound such as an aldehyde or ketone, accompanied by elimination of water.

The general reaction can be represented as:



The carbonyl compound may be an aromatic or aliphatic aldehyde or ketone, while the amine component can contain additional functional groups capable of participating in metal coordination. Consequently, Schiff bases may function as monodentate, bidentate, tridentate or tetradentate ligands.

The imine nitrogen contains a lone pair of electrons that can participate in coordination with a metal ion. Additional donor atoms such as phenolic oxygen, alcoholic oxygen, pyridine nitrogen, thiol sulfur or heterocyclic nitrogen can enhance the chelating ability of the ligand. This structural flexibility has made Schiff bases highly important in coordination chemistry.

Schiff bases and their metal complexes have been investigated for catalytic, optical, analytical and biological applications. Their transition-metal complexes are particularly important because metal coordination can alter molecular geometry, electronic distribution and biological activity. Reviews of Co (II), Ni (II) and Cu (II) Schiff-base complexes emphasize their continuing importance in pharmacological and coordination-chemistry research.

Recent studies demonstrate the breadth of this field. Kumari and co-workers synthesized a 1,2,4-triazole-containing Schiff base and its Ni (II), Cu (II), Zn (II) and Cd (II) complexes and evaluated them against bacterial and fungal organisms. Another 2024 study reported a quinoline Schiff base and Cu (II), Ni (II) and Co (II) complexes, characterized by multiple spectroscopic techniques and evaluated against *Bacillus subtilis*, *Escherichia coli* and *Candida albicans*.

The present article therefore reviews the synthesis, characterization, coordination behaviour and antimicrobial properties of novel Schiff base ligands and their transition-metal complexes.

Objectives of the Study

The principal objectives of the present study are:

1. To understand the fundamental chemistry and synthesis of Schiff base ligands.
2. To examine the formation and coordination behaviour of Schiff bases with transition-metal ions.
3. To discuss the spectroscopic, physicochemical and thermal techniques employed for structural characterization.
4. To examine antibacterial and antifungal properties of representative Schiff base ligands and their metal complexes.
5. To analyse structure–activity relationships and the influence of metal coordination on antimicrobial properties.

Research Methodology

The present work is a descriptive and analytical review based on published scientific literature. Recent peer-reviewed research concerning synthesis, structural characterization and biological evaluation of Schiff base ligands and transition-metal complexes was examined.

Particular attention was given to Cu (II), Ni (II), Co (II), Zn (II) and related transition-metal systems. Characterization techniques including FTIR, UV–Visible spectroscopy, ^1H NMR, ^{13}C NMR, mass spectrometry, elemental analysis, magnetic susceptibility, molar conductivity, thermogravimetric analysis and X-ray diffraction were considered.

Antimicrobial results were evaluated with reference to commonly investigated microorganisms and quantitative parameters such as minimum inhibitory concentration (MIC) and inhibition zones. Since the present article is review-based, no numerical value is represented as an original laboratory result. Numerical experimental results are explicitly attributed to the corresponding published studies.

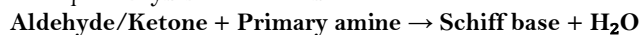
Discussion

Synthesis and Chemistry of Novel Schiff Base Ligands

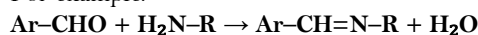
The synthesis of a Schiff base is generally based on nucleophilic addition of a primary amine to the carbonyl carbon of an aldehyde or ketone, followed by dehydration to generate the C=N linkage.

1. Condensation Reaction

A simplified synthetic reaction is:



For example:



Ethanol or methanol is frequently employed as a reaction medium. Depending upon the reactants, the mixture may be heated under reflux to facilitate condensation. Removal of water can favour product formation.

The selection of aldehyde and amine determines the donor atoms and overall coordination behaviour of the final ligand. Salicylaldehyde derivatives are particularly useful because they introduce a phenolic oxygen adjacent to the imine group. The resulting ligand can coordinate through both azomethine nitrogen and phenolic oxygen.

Hydrazine-type Schiff bases provide further coordination possibilities because they contain additional nitrogen atoms. Heterocyclic components such as quinoline, pyridine, pyrazole, triazole and thiophene can likewise introduce additional donor centres.

For example, a 2024 study synthesized a Schiff base containing 1,2,4-triazole and 4-(benzyloxy)benzaldehyde units and subsequently prepared Ni (II), Cu (II), Zn (II) and Cd (II) complexes. Single-crystal analysis and spectroscopy established the structural characteristics of the ligand.

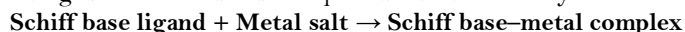
Another 2024 study prepared a quinoline Schiff base by condensation of 3-formyl-2-hydroxyquinoline-5-carbonitrile with 1-tosylhydrazine, followed by preparation of Cu (II), Ni (II) and Co (II) complexes.

Thus, careful selection of carbonyl and amine components enables rational design of Schiff base ligands with desired donor sets and coordination properties.

Synthesis and Coordination Behaviour of Transition-Metal Complexes

After synthesis and purification, a Schiff base ligand can be reacted with suitable transition-metal salts. Common metal ions include Cu (II), Ni (II), Co (II), Zn (II) and Mn (II).

The general reaction can be represented schematically as:



Metal chlorides, acetates and nitrates are commonly employed. The ligand-to-metal ratio may vary depending on the denticity of the ligand and coordination requirements of the metal.

1. Coordination through the Azomethine Group

The azomethine nitrogen is one of the principal coordination sites. Coordination decreases electron density around the imine functionality and can therefore alter the vibrational frequency associated with C=N.

2. Coordination through Oxygen and Other Donor Atoms

If the ligand contains phenolic –OH groups, deprotonated phenolic oxygen may coordinate strongly with a transition-metal ion. Heterocyclic nitrogen and sulfur atoms can provide additional donor sites.

Consequently, Schiff bases may act as:

Monodentate → one donor atom

Bidentate → two donor atoms

Tridentate → three donor atoms

Tetradentate → four donor atoms

Kumari et al. reported bidentate coordination behaviour in their triazole-containing Schiff base system. Their Ni (II), Cu (II), Zn (II) and Cd (II) complexes were synthesized with different ligand-to-metal ratios.

A 2023 study synthesized a tetradentate ONNO Schiff base and complexes with Cu (II), Co (II), Ni (II), Mn (II) and Cd (II). Spectroscopic and magnetic data suggested octahedral structures for several complexes and a tetrahedral structure for the Cd (II) complex.

Another study of a pyrazole-containing Schiff base reported octahedral geometries for Co (II), Ni (II) and Zn (II) complexes and a square-planar geometry for the Cu (II) complex.

These examples demonstrate that the geometry of a Schiff base complex depends upon ligand denticity, metal-ion electronic configuration, stoichiometry and coordination environment.

Spectroscopic and Physicochemical Characterization

A combination of analytical techniques is necessary for reliable structural characterization of Schiff base ligands and their metal complexes.

1. FTIR Spectroscopy

FTIR spectroscopy is particularly important for identifying the azomethine C=N group and examining metal coordination.

Formation of a Schiff base is supported by appearance of an imine-related C=N absorption and changes associated with the starting carbonyl and amino groups.

On complexation, shifting of the C=N stretching frequency provides evidence that the azomethine nitrogen participates in coordination. Changes in phenolic C–O bands can similarly support oxygen coordination.

Low-frequency bands attributed to M–N and M–O vibrations may provide additional evidence for metal–ligand bonding.

2. Nuclear Magnetic Resonance Spectroscopy

¹H NMR and ¹³C NMR are valuable for characterizing free ligands and diamagnetic metal complexes.

The azomethine proton generally produces a characteristic signal whose position depends on the ligand structure. Phenolic –OH, aromatic and aliphatic protons provide further structural information.

¹³C NMR can identify the imine carbon and other chemically distinct carbon atoms. Paramagnetic metal complexes, however, can produce broadened or shifted NMR signals, so other techniques become particularly important.

3. UV–Visible Spectroscopy

UV–Visible spectroscopy provides information regarding electronic transitions.

Free Schiff base ligands generally display $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions associated with aromatic and imine systems. Transition-metal complexes may additionally exhibit d–d transitions and charge-transfer bands.

Electronic spectra, together with magnetic susceptibility measurements, can help determine whether a complex is square planar, tetrahedral or octahedral.

4. Mass Spectrometry and Elemental Analysis

Mass spectrometry provides molecular-mass and fragmentation information. Elemental analysis helps verify the proposed empirical composition by comparing experimental carbon, hydrogen and nitrogen percentages with theoretical values.

5. Molar Conductivity and Magnetic Measurements

Molar conductivity helps determine whether a metal complex behaves as an electrolyte or non-electrolyte in solution.

Magnetic susceptibility provides information about the number of unpaired electrons and can assist assignment of oxidation state and geometry.

6. Thermal Analysis and X-Ray Diffraction

Thermogravimetric analysis (TGA) and differential thermal analysis provide information about thermal stability, coordinated water and decomposition patterns.

Hezam et al. reported that different tetradentate Schiff-base complexes began decomposition at different temperatures: several compounds at approximately 250 °C, Cu-containing complexes at 200 °C and one Ni-containing complex at 300 °C.

Single-crystal X-ray diffraction provides the most direct structural information when suitable crystals are available. Powder XRD can also contribute to structural and phase analysis.

Table 1. Major techniques for characterization of Schiff base metal complexes

Technique	Principal information obtained
FTIR	C=N formation and M–N/M–O coordination
¹ H NMR	Proton environment and ligand structure
¹³ C NMR	Carbon environment and imine carbon
UV–Vis	Electronic and d–d transitions
Mass spectrometry	Molecular mass and fragmentation

Elemental analysis	Empirical composition
Molar conductivity	Electrolytic/non-electrolytic behaviour
Magnetic susceptibility	Magnetic properties and geometry
TGA/DTA	Thermal stability and decomposition
XRD	Crystalline structure and geometry

A recent Cu (II), Zn (II) and Ni (II) Schiff-base study similarly used FTIR, UV–Vis, ^1H NMR, ^{13}C NMR, TGA-DTA and powder XRD for structural characterization.

Antibacterial and Antifungal Investigation

The antimicrobial activity of Schiff bases and their transition-metal complexes is an important area of bioinorganic chemistry.

Typical bacterial test organisms include Gram-positive species such as *Staphylococcus aureus*, *Bacillus subtilis* and *Staphylococcus epidermidis*, and Gram-negative species such as *Escherichia coli* and *Pseudomonas aeruginosa*. Fungal organisms such as *Candida albicans* are also commonly investigated.

1. Antimicrobial Testing Methods

Two common methods are:

Disc or agar diffusion method: Activity is expressed as the diameter of the inhibition zone, usually in millimetres.

Broth microdilution method: Activity is expressed as MIC, usually in $\mu\text{g/mL}$. MIC represents the lowest tested concentration preventing visible microbial growth under specified conditions.

The broth microdilution method was used in a 2023 study of tetradentate Schiff bases and their Cu (II), Ni (II) and Co (II) complexes. The synthesized compounds were tested against three Gram-positive bacteria, three Gram-negative bacteria and a fungus.

2. Antibacterial Activity

Metal coordination frequently changes antimicrobial behaviour. However, the degree of improvement varies according to the ligand, metal and microorganism.

In the study by Hezam et al., the synthesized compounds displayed MIC values between **9.7 and 5000 $\mu\text{g/mL}$** . The ligand L2 and its cobalt complex L2-Co showed particularly strong activity against *S. epidermidis* and *S. aureus*, reaching an MIC of **9.7 $\mu\text{g/mL}$** .

A 2023 study of a tetradentate ONNO ligand and Cu (II), Co (II), Ni (II), Mn (II) and Cd(II) complexes likewise found dose-dependent antimicrobial behaviour; the Cd (II) complex showed the highest antibacterial activity within that reported series.

An Indian Journal of Chemistry study published in 2024 evaluated a quinoline-derived Schiff base and Cu(II), Ni(II) and Co (II) complexes against *B. subtilis*, *E. coli* and *C. albicans*, reporting stronger antimicrobial action for the metal complexes than the free ligand.

3. Antifungal Activity

Schiff base complexes can also exhibit antifungal activity. The 2024 triazole-containing Schiff-base study screened its ligand and metal complexes against *C. albicans* in addition to bacterial species.

Table 2. Selected published antimicrobial findings for Schiff base systems

Schiff base system	Metal complexes	Microorganisms / assay	Published result
Tetradentate ligands L1/L2	Cu (II), Ni (II), Co (II)	Gram-positive, Gram-negative bacteria and fungus	MIC range 9.7–5000 $\mu\text{g/mL}$
L2 / L2-Co	Co (II) complex	<i>S. epidermidis</i> , <i>S. aureus</i>	MIC as low as 9.7 $\mu\text{g/mL}$
ONNO tetradentate Schiff base	Cu (II), Co (II), Ni (II), Mn (II), Cd (II)	Bacterial/fungal strains	Cd (II) complex most active in reported series
Quinoline Schiff base	Cu (II), Ni (II), Co (II)	<i>B. subtilis</i> , <i>E. coli</i> , <i>C. albicans</i>	Metal complexes reported more active than ligand
Thiophene-derived SNN ligand	Cu (II), Co (II), Ni (II)	Bacterial/fungal strains	Reported order: Cu (II) > Co (II) > Ni (II) > ligand

Note: Results originate from different experimental studies and assay conditions and therefore should not be treated as a direct head-to-head comparison.

Structure–Activity Relationship and Future Prospects

The biological behaviour of Schiff base metal complexes depends on several interconnected factors: the nature of the ligand, donor atoms, metal ion, oxidation state, geometry, lipophilicity and stability.

Chelation is frequently invoked to explain enhanced activity of some complexes. Coordination can redistribute electron density and modify the polarity and lipophilicity of the metal–ligand system, potentially altering interactions with microbial membranes or biological targets. However, enhanced activity after complexation is not universal and must be experimentally established for each system.

The metal itself is also important. Cu (II), Ni (II), Co (II), Zn (II) and other ions have different electronic configurations and coordination preferences. Therefore, complexes formed from an identical ligand can display different biological behaviour.

Modern research increasingly combines experimental antimicrobial screening with molecular docking, density functional theory and ADMET calculations. Kumari et al., for example, combined antimicrobial evaluation with docking against protein receptors associated with *E. coli*, *S. aureus*, *P. aeruginosa* and *C. albicans*, along with computational and ADMET analyses.

Future research can follow the pathway:

Ligand design → Schiff base synthesis → Metal complexation → Spectral characterization → Geometry determination → Antimicrobial screening → MIC determination → SAR → Molecular docking → Cytotoxicity/ADMET → Lead optimization

Importantly, antimicrobial activity alone does not establish therapeutic suitability. Future studies should assess mammalian-cell cytotoxicity, selectivity, aqueous stability, pharmacokinetic behaviour and mechanism of action.

Conclusion

Schiff base ligands and their transition-metal complexes represent a versatile and scientifically important class of coordination compounds. Schiff bases can be readily synthesized through condensation of primary amines with aldehydes or ketones, resulting in formation of the characteristic azomethine (>C=N-) group.

The presence of azomethine nitrogen together with oxygen, sulfur or heterocyclic nitrogen donor atoms enables formation of stable complexes with transition metals such as Cu (II), Ni (II), Co (II), Zn (II) and Mn (II). Depending upon ligand denticity and the electronic characteristics of the metal ion, square-planar, tetrahedral and octahedral geometries may be obtained.

Reliable characterization requires multiple complementary techniques, particularly FTIR, UV-Vis, ¹H NMR, ¹³C NMR, mass spectrometry, elemental analysis, molar conductivity, magnetic susceptibility, TGA and XRD.

Published antimicrobial studies demonstrate that Schiff base ligands and their transition-metal complexes can possess significant antibacterial and antifungal properties. In one well-defined 2023 series, MIC values ranged from 9.7 to 5000 µg/mL, with L2 and L2-Co reaching 9.7 µg/mL against selected Gram-positive organisms. Other recent studies likewise report that metal complexation can enhance antimicrobial activity relative to the corresponding free ligand in particular systems.

Thus, integration of Schiff base synthesis, transition-metal coordination, comprehensive structural characterization, standardized antimicrobial evaluation and structure-activity analysis represents a promising approach in bioinorganic and medicinal chemistry. Further research involving toxicity, selectivity, mechanism-of-action studies and in vivo evaluation will be essential for determining whether promising complexes can progress toward practical therapeutic applications.

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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