



## Biological Study and synthesis of Schiff bases metal complex using ionic liquid/green method

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### Abstract

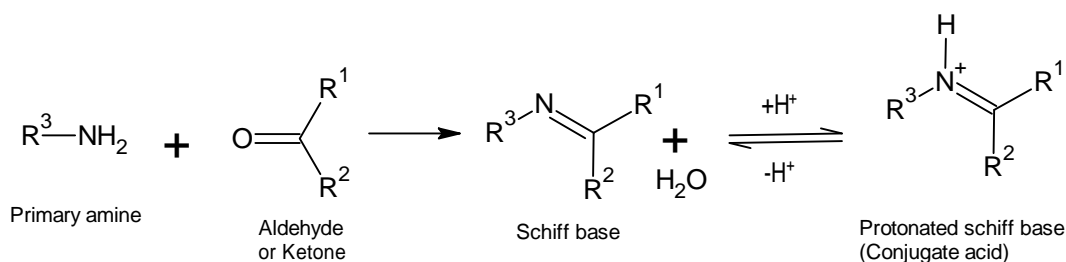
As a green chemistry approach for synthesizing organic molecules, the use of microwave to expose reactants with or without solvents is explored here. Analytical, inorganic, and organic chemists all employ Schiff bases (SBs) in their work. The need for SB synthesis is further emphasized by a broad variety of pharmacological and biological functions, including analgesic, antiproliferative, antiviral, anti-inflammatory, antibacterial, antipyretic, and antifungal activities. In a variety of processes particularly when there is moisture present, several Schiff base complexes have good catalytic activity. The study of these compounds' coordination behavior has significantly increased because of the impact that specific metals have on their biological properties and its inherent chemical significance as multidentate ligands. The overview of the synthesis of SBs and its metal compounds Schiff bases and its metal complexes using various green methods and ionic liquid techniques is discussed here. Examples of the most promising applicable SBs and its metal compounds from many fields are included in this overview.

**Keywords:** *Biological activities, Green chemistry, Ionic liquid method, Metal complexes, Schiff bases.*

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## 1 Introduction

A Schiff base is a nitrogen analogue of an aldehyde or ketone wherein the carbonyl group (CO) has been swapped out for an imine or azomethine group structurally [1]. Any primary amine may react with an aldehyde or a ketone to produce a Schiff base under appropriate circumstances.



**Fig. 1: Common concept for establishing SBs [2]**

Drug design techniques often use organic reactions involving the condensation of two or more molecules to create new compounds with novel biological properties [3]. Schiff bases are the result of condensation reactions involving primary amines along with artificially produced ketones or aldehydes. Schiff bases play a key role in a variety of industrial and catalytic processes as well as a wide range of biological functions. They may also stabilize metal ions in different oxidation states [4, 5]. The nitrogen lone pair of electrons in azomethine ( $N = CH$ ) bonding in their structure is what causes stable complexes to form with metal ions [6]. In several crucial biochemical processes, bioinorganic chemistry, supramolecular chemistry, and molecular magnetism, such stable compounds play a significant role [7]. Imine complexes possess a variety of biological characteristics, such as antibacterial, antiviral, antifungal, and anticancer activities [8]. They are widely explored as antimalarial drugs and are used to treat medicine resistance in cancer. They could also be used to immobilize enzymes [9].

Numerous Schiff base ligands and its complexes have been studied for their intriguing and significant characteristics, including their photochromic properties, their capability to

reversibly bind oxygen, their ability to complex with some toxic metals, and their catalytic properties in the hydrogenation of olefins. However, other Schiff base complexes have excellent biological action and biological modelling applications [10].

### 1.1 Green chemistry

A more modern approach to studying organic synthesis as well as drug design methods is known as "green chemistry" [11]. It is that area of chemistry that deals with tools, methods, and apparatuses and offers considerable economic and environmental advantages over traditional synthetic techniques [12]. The present focus on green chemistry has posed several challenges for organic synthesis, from which it is necessary to construct contemporary reaction conditions that entail reducing the usage of organic solvents or harmful compounds [13].

In contrast to conventional approaches, many of the processes used by green chemists use solvent-free reactions, simplify workup procedures, reduce reaction time, improve selectivity, and streamline purification operations [14]. The first synthesis of Schiff bases (imines) was documented by Hugo Schiff in the 19th century. An aldehyde with an azomethine  $-N=CH-$  group in place of a  $C=O$  group is referred to as a Schiff base. Typically, it is created when primary amines and aldehydes react [15].  $RCH=NR_1$  (R & R<sub>1</sub> characterizes alkyl or aryl substituents) is the common chemical expression for Schiff bases [16].

### 1.2 Ionic liquid method

Ionic liquids (ILs) are "ionic materials" with low melting temperatures (below 100°C), often made up of massive, typically asymmetric organic cations and inorganic or organic anions. When used in place of conventional molecular solvents, ionic liquids (ILs) have a variety of unique physicochemical and solvation features that may be tailored for purposes and often produce fascinating results [17]. Additionally, the majority of ILs have low vapor pressure [18] and great thermal stability [19]. They are known as neoteric solvents or green solvents because of these appealing characteristics. Due to their large electrochemical window, high ionic conductivity [20], and wide temperature range of the liquid state, ILs have received a lot of attention in recent years. Additionally, by altering their cation and anion pairing, ILs'

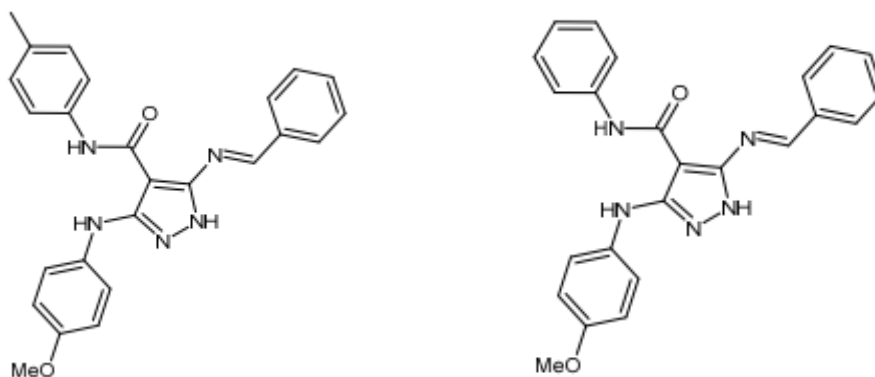
physical characteristics, including density, melting temperature, polarity, Lewis acidity, viscosity, and enthalpy of vaporization, may all be adjusted [21]. The improved reaction kinetics that an IL-based solvent solution often demonstrates allows for the efficient use of both time and energy [22]. These characteristics make ILs an effective substitute for traditional media in chemical processes as well as a new generation of solvents for catalysis, environmentally friendly reaction media, and organic synthesis [23]. Functionalized ionic liquids (FILs), which include various functional groups in the cationic moiety, have recently attracted the attention of numerous researchers [24]. Both the cationic and anionic moieties of the FILs may be changed as needed for applications such as greater catalytic stability and decreased catalyst leaching, etc. by readily functionalizing the cation in a single chemical step [25].

### 1.3 Schiff Bases with Antibacterial Activity

Gram-negative, Gram-positive, *E. coli*, *Pseudomonas aeruginosa* as well as *Bacillus cereus*, were inactive against two series of schiff base derivatives containing anthracene/pyrene units, as disclosed by **Gumu et al. (2020)** [26]. Tetracycline (30 µg) and streptomycin (10 µg) discs were used as positive controls in these studies, which were carried out using the disc diffusion technique. Agarose gel electrophoresis, which measures how DNA molecules respond to changes in mass, charge, and shape, was also used to investigate DNA binding activities. Free DNA travels more quickly across the gel because it is smaller than bound DNA because of the chemicals binding to calf thymus DNA (CT-DNA). It should be noted that compounds 5 and 6, respectively, “(E)-2-((anthracen-1-ylimino)methyl)quinolin-8-ol and “(E)-2-((pyren-1-ylimino)methyl)pyridin-3-ol”, were observed to be bounded stable to CT-DNA and had antibacterial action against *E. coli* and *Bacillus cereus*.

Three SBs were synthesized, and their antibacterial activity was assessed using the disc diffusion test in a study by **Warad et al. (2020)** [27]. In comparison to gentamicin, the compounds had little action. “2-(piperazin-1-yl)-N-(thiophen-2-ylmethylene)-ethanamine (17)” [28] was the most intriguing molecule. Compared to *P. aeruginosa* (IZD = 16 mm) and gentamicin (IZD = 25 and 24 mm, respectively), the most susceptible isolates to this substance were methicillin-resistant *S. aureus* (MRSA) and Gram-positive *S. aureus*.

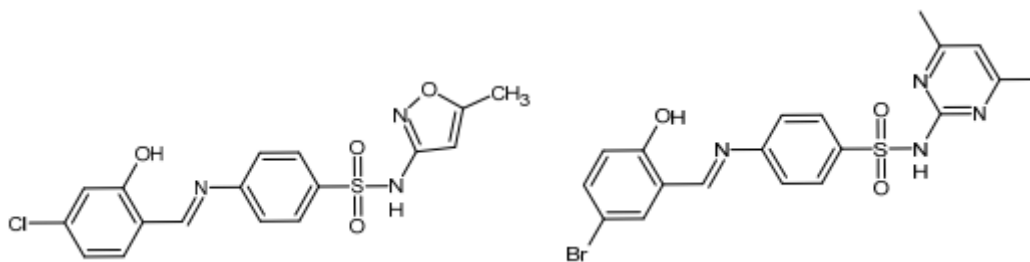
**Hassan et al. (2019)** [29] demonstrated the antibacterial efficacy of "5-(benzylideneamino)-3-(4-methoxyphenylamino)-N-phenyl-1H-pyrazole-4-carboxamides" against MDRB (multidrug-resistant bacteria). Particularly, compound 1 had comparable activity to the reference against the Gram-positive *E. faecalis* (MIC = 7.81  $\mu\text{g/mL}$ ), that causes serious infections in humans whereas compounds 2 through 3 were more effective than ciprofloxacin against the *S. epidermidis* (15.62  $\mu\text{g/mL}$  versus MIC = 7.81  $\mu\text{g/mL}$  of ciprofloxacin) [30].



**Fig. 2. Compound 1 and 2**

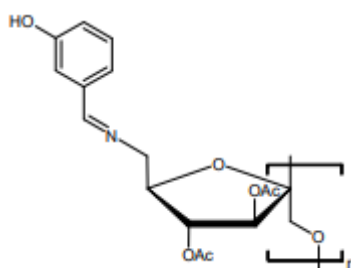
#### 1.4 Schiff base with antifungal activity

Worldwide reports of severe fungal coinfections and a variety of COVID-19-related candidemia outbreaks in hospital critical care units have been made as of 2020 [31]. A multispecies panel strains of *Candida* was used to assess the SBs of sulphonamides first (*Candida albicans* NCPF3179, and NCPF3281 *C. auris* TDG1912, *Candida tropicalis* NCPF8760, *Candida krusei* NCPF3876, *Candida glabrata* NCPF8018, and *Candida parapsilosis* NCPF3209). MIC values for compound 3 against virtually all strains were noteworthy, falling between 4 and 32  $\mu\text{g/mL}$  (compared to fluconazole's  $0.5 \geq 128 \mu\text{g/mL}$ ). As a result, it was examined against a wider range of MDR (multi-drug resistance) *C. auris* strains (TDG2211, NCPF8977, TDG2512, TDG2506, TDG1102, NCPF8971, and NCPF8984), and its antifungal properties was approved with MICs of 4–16  $\mu\text{g/mL}$ , that are incredibly low when you consider that in four cases, TDG2211, TDG1102, TDG2506, and NC. Only on the expanded panel did compound 4 exhibit the same outcomes as compound 40.



**Fig. 3. Compound 3 and 4**

To increase the biological activity of inulin, **Chen et al. (2020)** [32] reported a structural alteration of inulin by SBs. According to Guo's technique [33], antifungal investigations conducted on three different types of plant pathogenic fungus (*Phomopsis asparagi*, *Fusarium oxysporum* f. sp. *cucumerium* Owen, and *Botrytis cinerea*) revealed that synthesized inulin derivatives have a wide antifungal range. The IIs (Inhibitory Index) of compound 5 were 93%, 83%, and 82% against *F. oxysporum* f. sp. *cucumerium* Owen, *B. cinerea*, and *P. asparagi*, respectively, at 1.6 mg/mL. compound 5 can quickly enter cells owing to its lipophilic properties brought on by the presence of the benzene ring and acetyl groups, which causes apoptosis. Additionally, through interacting with cellular components, the novel inulin compounds altered with Schiff bases demonstrated a superior metal binding property, inhibiting microbial development.



**Fig. 4. compound 5**

23 cinnamyl SBs were created, and there in vitro antifungal effectiveness was evaluated by **Magalhes et al. (2020)** [34]. Six of them demonstrated antifungal properties against strains of *Cryptococcus* species in particular as well as *Candida* sp., *Aspergillus* sp., and *Fonsecaea*. Fluconazole, on the other hand, proved ineffective against all *Cryptococcus* strains, regardless of species. It was found that fluconazole had a MIC more than two times lesser

against all strains of *C. neoformans* (1.4  $\mu\text{g/mL}$  and MIC = 1.33  $\mu\text{g/mL}$  in that order), versus fluconazole, 5.2  $\mu\text{g/mL}$ ) and that the compounds 6 and 7 did not significantly harm human kidney, lung, or RBCs, all of which had selectivity indices over 10.

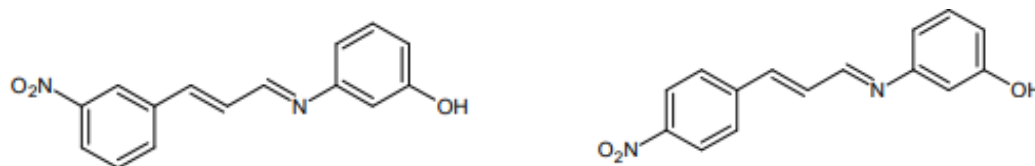
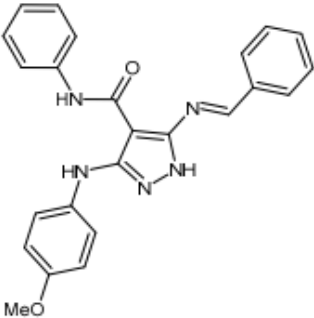
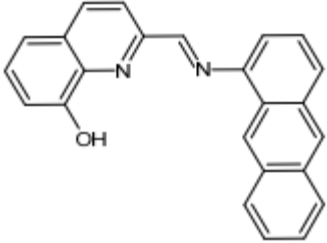
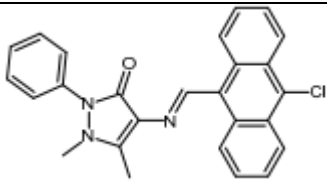
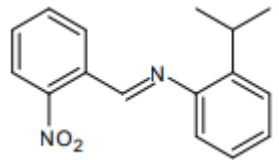


Fig. 5. compound 6 and 7

Table 1. Schiff bases with antimicrobial properties			
Compound	Structure	Antimicrobial properties	References
<b>Antifungal activity</b>			
23 cinnamyl Schiff base (6)		MIC=1.33 $\mu\text{g/mL}$ ( <i>C. neoformans</i> ) MIC = 1.33 $\mu\text{g/mL}$ ( <i>C. gatii</i> )	[34]
Schiff base of “2-amino-4, 6-dimethylpyrimidine”		IZD (Inhibition zone diameter) = 21 mm ( <i>C. albicans</i> )	[35]
23 cinnamyl Schiff base (7)		MIC = 3.2 $\mu\text{g/mL}$ ( <i>C. neoformans</i> ), MIC = 8.0 $\mu\text{g/mL}$ ( <i>C. gatii</i> )	[34]
Schiff base of “2-amino-4, 6-dimethylpyrimidine”		IZD = 19 mm (mm) ( <i>A. niger</i> )	[35]
“4-(5-bromo-2-hydroxybenzylideneamino)-N-(5-methylisoxazol-3-yl) benzenesulfonamide”		MIC = 16–32 $\mu\text{g/ml}$ ( <i>C. auris</i> TDG1102, TDG2211), MIC = 16 $\mu\text{g/mL}$ ( <i>C. auris</i> TDG2512, TDG2506,	[36]

		NCPF8984, NCPF8977), MIC = 8–16 µg/mL ( <i>C. auris</i> NCPF8971)	
<b>Antibacterial activity</b>			
“5-aminopyrazoles, namely 5-(benzylideneamino)-3-(4-methoxyphenylamino)-N-phenyl-1H-pyrazole-4-carboxamides”		MIC= 7.81 µg/mL ( <i>S. epidermidis</i> )	[37]
“(E)-2-((anthracen-1-ylimino)methyl)quinolin-8-ol”		IZD = 13 mm (13 mm <i>B. cereus</i> )	[29]
“4-(((10-chloroanthracen-9-yl)methylene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one”		MIC= 12.5 µg/ml ( <i>A. niger</i> 9642) MIC=12.5 µg/ml ( <i>S. aureus</i> 23235)	[29]
“(E)-2-isopropyl-N-(2-nitrobenzylidene) aniline”		MIC = 15.625 ( <i>S. thyphymurium</i> ) MIC= 125 µg/Ml ( <i>E. coli</i> )	[38]

### 1.5 Synthesis of “1-{2-(2-hydroxy-5-chlorobenzylamine) ethyl}-3-methylimidazolium tetrafluoroborate”.

**Sinha et al. (2020) [39]** synthesised "1-2-(2-hydroxy-5-chlorobenzylamine) ethyl-3-methylimidazolium tetrafluoroborate", a Schiff base supported by ionic liquid and characterized by several analytical (molar conductance, element analysis, and magnetic susceptibility measurements) and spectroscopic (UV-Visible, SEM, PXRD, ESI-MS, FT-IR,



<sup>1</sup>H NMR, and <sup>13</sup>C-NMR) techniques. Tetra coordinated as well as hexacoordinated structures were ascribed to the synthesized metal complexes based on this spectral data and spectra. The complexes' molar conductance revealed their (1:2) electrolytic character. The Schiff base ligands and its complexes were evaluated for in vitro antibacterial activity against several naturally accessible gram-positive and gram-negative bacteria to determine their inhibitory potentials. Cu(II) complex created the maximum inhibition zone in *Klebsiella pneumoniae* plates whereas *Bacillus cereus* plates produced the least inhibition zone.

### 1.6 Synthesis of “1-{2-(2-hydroxy-5-nitrobenzylideneamino)ethyl}-3-ethylimidazolium tetrafluoroborate”

**Sinha et al. (2019) [40]** synthesized new Co(II), Ni(II), and Cu(II) metal complexes from the Schiff base “1-(2-hydroxy-5-nitrobenzylideneamino)ethyl-3-ethylimidazolium tetrafluoroborate”, which was supported by an imidazolium ionic liquid. These complexes were then characterized using a variety of analytical and spectroscopic methods, including elemental analysis (CHN analysis), UV Tetra coordinated 1:2 metal-ligand stoichiometry for the metal complexes was proposed based on these spectroscopic and analytical findings. The complexes' molar conductance measurements demonstrated their electrolytic character. To evaluate their potential for inhibition, the produced complexes and the ligand were tested for in vitro antibacterial activities against Gram-positive and Gram-negative bacteria. The complexes were quite successful in fighting off the tested organisms.

### 1.7 Synthesis of “4-chloro-2-{(E)-[(4-fluorophenyl) imino] methyl}phenol” (C<sub>13</sub>H<sub>9</sub>ClFNO)

**Ommenya et al. (2020) [41]** synthesized the Schiff base ligand, "4-chloro-2-(E)-[(4-fluorophenyl) imino] methylphenol" (C<sub>13</sub>H<sub>9</sub>ClFNO), to create a novel series of Cu(II), Mn(II), Co(II), Zn(II), and Ni(II), complexes. The condensation reaction between “5-chlorosalicylaldehyde” and 4-fluoroaniline, took place at room temperature. The Schiff base as well as the metal complexes were characterized by elemental composition, UV-Vis, FT-IR, and NMR spectrum data, molar conductivity measurement, and melting temperatures. According to the results of the elemental analysis, the metal complexes that were created had the general formulas [M(L)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>], where M = Mn, Co, Ni, Cu, and Zn and L = Schiff base ligand (C<sub>13</sub>H<sub>9</sub>ClFNO). The "O" and "N" donor atoms of the Schiff base ligand

participated in coordination with the metal (II) ions based on FT-IR, electronic spectra, and NMR data; as a result, a six coordinated octahedral geometry was postulated for all these complexes. The compounds were nonelectrolyte, according to investigations on their molar conductance. Using the disc diffusion technique, the (Schiff base ligand and its metal (II)) complexes were evaluated in vitro for their bactericidal efficacy against Gram-positive (*B. subtilis* and *S. typhi*) and Gram-negative (*E. coli* and *P. aeruginosa*) microorganisms. The metal (II) compound have more antimicrobial action than the free Schiff base ligand, according to the findings of the antibacterial examination.

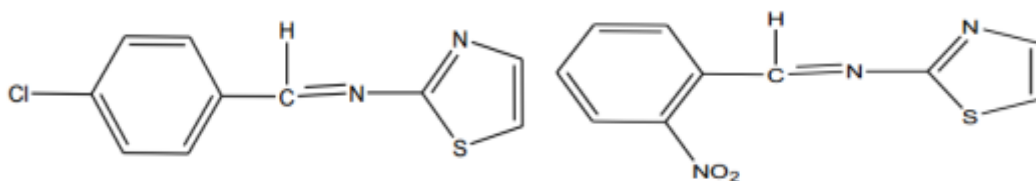
Table 2. Some Schiff base metal complexes synthesis by green method/ionic liquid method			
Compounds	Methods	Antimicrobial activity	References
“1-{2-[(2-hydroxy-5-bromobenzylidene)amino]ethyl}-3-ethylimidazolium tetrafluoroborate”	Ionic- liquid	Gram-negative and positive bacteria are both susceptible to in vitro antibacterial activities.	[42]
“1-(((1H-1,2,4-triazol-3-yl) imino) methyl) naphthalen-2-ol (TMN)”	microwave irradiation technique (green synthesis)	Compound showed antimicrobial activity against bacterial and fungal strain	[43]
“3-(2-hydroxy-3-ethoxybenzylideneamino)-5-methyl isoxazole and 3-(2-hydroxy-5-nitrobenzylidene amino)-5-methyl isoxazole”	condensation	Antibacterial activity showed against against <i>Aspergillus niger</i> and <i>Rhizoptonia solan</i> .	[44]
“1,4-dicarbonyl-phenyl-dihydrazide and chromene-2,3- dione”	Green method	Show slightly lesser properties against <i>Rizoctonia sp.</i> , antifungal activity against <i>Aspergillus sp.</i>	[45]
“N,N-Bis-(2-hydroxyl-5-methoxybenzaldehyde)-mphenylenediamine”	microwave assisted synthesis approach (green method)	Shown antibacterial activity against <i>Bacillus thuringiensis</i> , <i>Bacillus subtilis</i> , <i>Klebsiella pneumoniae</i> and <i>Escherichia coli</i> .	[46]
N-salicylidene-2-aminophenolate dioxidomolybdenum complexes	Ionic- liquid	Catalytic activity	[47]

### 1.8 Ni-Based Transition Metal Complexes with Schiff Bases

### 1.9.1 Schiff - Base Compounds' and its Antimicrobial Activity

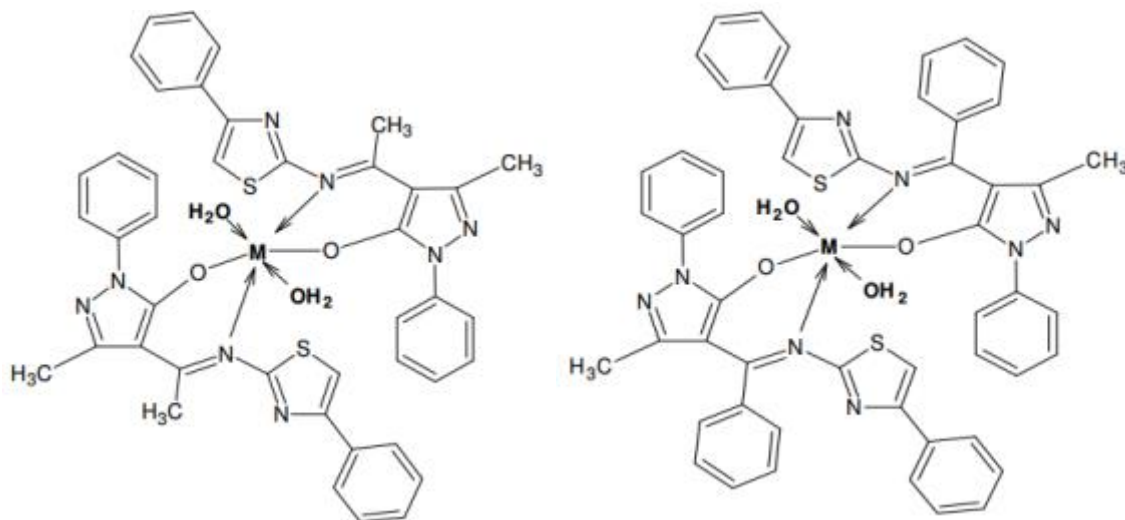
Two novel metal complexes with the general formula  $M(H\alpha ft)_2$  were created by **Hossain et al. [48]** using an asymmetric Schiff base ligand ( $HL = H\alpha ft)_2$  generated from amoxicillin and  $\alpha$ -formylthiophene. The antimicrobial response study points to the  $H\alpha f$  (Ligand) and  $M(H\alpha ft)_2$  complexes as having promised antibacterial properties against 4 experimental harmful bacteria, namely *P. aeruginosa*, *P. vulgaris*, *E. coli*, and *S. aureus*, despite being less effective than the amikacin standard medication.

**Mishra et al. (2012) [49]** produced Schiff base metal complexes of Ni(II), Co(II), and Cu(II) generated from "4-chlorobenzylidene-2-aminothiazole" (CAT) and "2-nitrobenzylidene-2-aminothiazole" (NAT). The Gram-positive bacteria *S. aureus* as well as Gram-negative bacteria *E. coli* as well as the fungus *Aspergillus niger* and *Candida albicans* were tested using the metal complexes of Schiff base. According to the antibacterial results, all pathogenic species were more effectively inhibited by metal complexes than by their Schiff base ligand parents (Figure 6). Additionally, as the concentration rises, the chemicals more strongly suppress bacterial and fungal development.



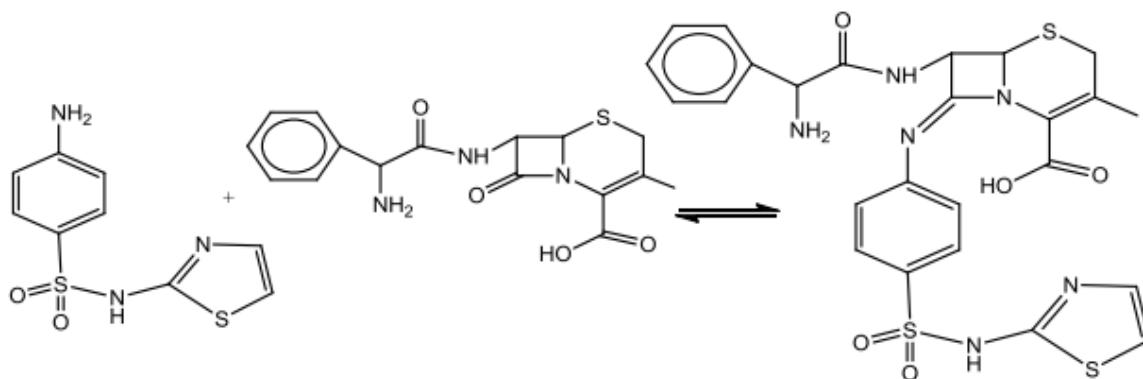
**Figure 6. Structure of Schiff base ligand. (a) “4-chlorobenzylidene-2-aminothiazole” (CAT) (b) “2-nitrobenzylidene-2-aminothiazole” (NAT)**

“2-Amino-4(4'-methylphenyl)-thiazole" and the Schiff base "4-Acyl-1-phenyl-3-methyl-2-pyrazolin-5-ones" were condensed. These Schiff bases combine to create complexes of form  $ML_2 \cdot 2H_2O$  ( $M = Ni, Fe, Mn, Cu$  and  $Co$ ) (Figure 7). The compounds were examined in vitro using the Agar cup assay method for its antimicrobial properties against *E. coli*, a gram-negative bacterium that causes diarrhea, *Bacillus subtilis*, a gram-positive rod that causes general contamination, and *S. aureus*, a gram-positive spore-forming bacteria that causes wound infections [50].



**Figure 7. Schiff base metal complexes' structure.**

**Anacona et al. (2014) [51]** produced transition co-ordination compounds containing a Schiff base (HL) generated from the combination of the antibiotic cephalixin with sulphathiazole. The Schiff base (HL) was created when sulphathiazole and cephalixin antibiotic condensed (Figure 8). *E. coli*, a Gram-negative bacterium, and *S. aureus*, a Gram-positive bacterium, were examined for Schiff base ligand as well as metal complex antibacterial properties using a revised Mueller–Hinton agar media as well as Kirby–Bauer disc diffusion method in normal conditions.



**Figure 8. The process of making a Schiff base ligand**

## Conclusion

Due to their capacity to form metal complexes as well as their pharmacological characteristics, Schiff bases are regarded as a particularly significant family of organic chemicals. The past several years has seen a surge in interest in transition metal complexes containing Schiff bases, partly due to their many biological uses and potential for use in the development of novel medicines. However, more research into the biological effects of these already-created transition metal complexes as well as the creation of novel complexes with additional features are still required. Understanding the characteristics of both metals and ligands may help in the synthesis of highly active compounds since the activity is often improved via complexation. To further understand how these compounds interact with metals, researchers are looking at how they interact with metals and how they interact with other ligands.

## References

1. Abdel-Rahman LH, El-Khatib RM, Nassr LA, Abu-Dief AM, Ismael M, Seleem AA. Metal based pharmacologically active agents: synthesis, structural characterization, molecular modeling, CT-DNA binding studies and in vitro antimicrobial screening of iron (II) bromosalicylidene amino acid chelates. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2014 Jan 3;117:366-78.
2. Abu-Dief AM, Mohamed IM. A review on versatile applications of transition metal complexes incorporating Schiff bases. *Beni-suef university journal of basic and applied sciences*. 2015 Jun 1;4(2):119-33.
3. Ekennia AC, Osowole AA, Olasunkanmi LO, Onwudiwe DC, Ebenso EE. Coordination behaviours of new (bidentate N, O-chelating) Schiff bases towards copper (II) and nickel (II) metal ions: synthesis, characterization, antimicrobial, antioxidant, and DFT studies. *Research on Chemical Intermediates*. 2017 Jul;43(7):3787-811.
4. Osowole AA, Ekennia AC, Achugbu BO, Etuk GH. Synthesis, spectroscopic characterization and structure related antibacterial activities of some metal (II) complexes of substituted trifluorobutenol. *Elixir Appl Chem*. 2013 Jun 12;59:15848-52.
5. Morgan SM, El-Sonbati AZ, Eissa HR. Geometrical structures, thermal properties and spectroscopic studies of Schiff base complexes: Correlation between ionic radius of metal complexes and DNA binding. *Journal of Molecular Liquids*. 2017 Aug 1;240:752-76.
6. Mahmoud WH, Mohamed GG, El-Sayed OY. Coordination compounds of some transition metal ions with new Schiff base ligand derived from dibenzoyl methane. Structural characterization, thermal behavior, molecular structure, antimicrobial, anticancer activity and molecular docking studies. *Applied Organometallic Chemistry*. 2018 Feb;32(2):e4051.
7. Gavey EL, Pilkington M. Coordination complexes of 15-membered pentadentate aza, oxoaza and thiaaza Schiff base macrocycles "Old Complexes Offer New Attractions". *Coordination Chemistry Reviews*. 2015 Jul 15;296:125-52.
8. Ogutu HF, Saban W, Malgas-Enus R, Luckay RC. Synthesis and characterization of 5-and 7-donor Schiff base ligands and spectroscopic evidence for tautomerism: A crystal structure showing tautomeric forms within one ligand. *Journal of Molecular Structure*. 2019 Jun 5;1185:392-402.

9. Boghaei DM, Askarizadeh E, Bezaatpour A. Synthesis, characterization, spectroscopic and thermodynamic studies of charge transfer interaction of a new water-soluble cobalt (II) Schiff base complex with imidazole derivatives. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2008 Feb 1;69(2):624-8.
10. Abdallah SM, Mohamed GG, Zayed MA, Abou El-Ela MS. Spectroscopic study of molecular structures of novel Schiff base derived from o-phthaldehyde and 2-aminophenol and its coordination compounds together with their biological activity. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2009 Sep 1;73(5):833-40.
11. Bhat AR, Wagay MH. Synthesis of Schiff's Base Derivatives using Water as Solvent.(A Green Methodology). *International Journal for Research in Applied Science & Engineering Technology*. 2017;5(11):971-82.
12. Yadav G, Mani JV. Green synthesis of Schiff bases by using natural acid catalysts. *International Journal of Science and Research*. 2015;4(2):121-7.
13. Habibi A, Valizadeh Y, Mollazadeh M, Alizadeh A. Green and High Efficient Synthesis of 2-Aryl Benzimidazoles: Reaction of Arylidene Malononitrile and 1, 2-Phenylenediamine Derivatives in Water or Solvent-Free Conditions. *International Journal of Organic Chemistry*. 2015;5(04):256.
14. Sravanthi M, Kavitha B, Reddy PS. Green route for efficient synthesis of biologically active schiff base ligand derived from 2-hydroxy acetophenone: structural, spectroscopic, antimicrobial and molecular modeling studies. *Int. Res. J. Pharm.* 2019;10(3).
15. Malik S, Nema B. Antimicrobial activities of Schiff Bases: A review. *International Journal of Theoretical & Applied Sciences*. 2016;8(1):28-30.
16. Yadav P, Sarkar A, Kumar A. Synthesis and biological activities of schiff bases and their derivatives: a review of recent work. *Journal of Basic and Applied Engineering Research*. 2019;6(1):62-5.
17. Chiappe C, Pieraccini D. Kinetic study of the addition of trihalides to unsaturated compounds in ionic liquids. Evidence of a remarkable solvent effect in the reaction of ICl<sub>2</sub>. *The Journal of Organic Chemistry*. 2004 Sep 3;69(18):6059-64.
18. Earle MJ, Esperança JM, Gilea MA, Canongia Lopes JN, Rebelo LP, Magee JW, Seddon KR, Widegren JA. The distillation and volatility of ionic liquids. *Nature*. 2006 Feb;439(7078):831-4.
19. Rogers RD, Seddon KR. Ionic liquids--solvents of the future?. *Science*. 2003 Oct 31;302(5646):792-3.
20. Sakaebe H, Matsumoto H. N-Methyl-N-propylpiperidinium bis (trifluoromethanesulfonyl) imide (PP13-TFSI)--novel electrolyte base for Li battery. *Electrochemistry Communications*. 2003 Jul 1;5(7):594-8.
21. Freire MG, Neves CM, Carvalho PJ, Gardas RL, Fernandes AM, Marrucho IM, Santos LM, Coutinho JA. Mutual solubilities of water and hydrophobic ionic liquids. *The Journal of Physical Chemistry B*. 2007 Nov 15;111(45):13082-9.
22. Welton T. Room-temperature ionic liquids. *Solvents for synthesis and catalysis*. *Chemical reviews*. 1999 Aug 11;99(8):2071-84.
23. Sheldon R. Catalytic reactions in ionic liquids. *Chemical Communications*. 2001(23):2399-407.
24. Yi F, Peng Y, Song G. Microwave-assisted liquid-phase synthesis of methyl 6-amino-5-cyano-4-aryl-2-methyl-4H-pyran-3-carboxylate using functional ionic liquid as soluble support. *Tetrahedron Letters*. 2005 May 30;46(22):3931-3.
25. Fei Z, Geldbach TJ, Zhao D, Dyson PJ. From dysfunction to bis-function: on the design and applications of functionalised ionic liquids. *Chemistry--A European Journal*. 2006 Mar 1;12(8):2122-30.
26. GÜMÜŞ A, Okumuş V, GÜMÜŞ S. Synthesis, biological evaluation of antioxidant-antibacterial activities and computational studies of novel anthracene-and pyrene-based Schiff base derivatives. *Turkish Journal of Chemistry*. 2020;44(4):1200-15.
27. Warad I, Ali O, Al Ali A, Jaradat NA, Hussein F, Abdallah L, Al-Zaqri N, Alsalmeh A, Alharthi FA. Synthesis and spectral Identification of three Schiff bases with a 2-(piperazin-1-yl)-N-(thiophen-2-yl)

- methylene) ethanamine moiety acting as novel pancreatic lipase inhibitors: Thermal, DFT, antioxidant, antibacterial, and molecular docking investigations. *Molecules*. 2020 May 11;25(9):2253.
28. Mishra N, Yadav R, Kumar K, Pandey H, Pandey R. Conventional vs Microwave assisted SiO<sub>2</sub>/P<sub>2</sub>O<sub>5</sub> catalyzed synthesis of Schiff bases. In *Journal of Physics: Conference Series* 2020 Mar 1 (Vol. 1504, No. 1, p. 012002). IOP Publishing.
29. Hassan AS, Askar AA, Nossier ES, Naglah AM, Moustafa GO, Al-Omar MA. Antibacterial evaluation, in silico characters and molecular docking of Schiff bases derived from 5-aminopyrazoles. *Molecules*. 2019 Aug 28;24(17):3130.
30. Pozzi C, Ferrari S, Cortesi D, Luciani R, Stroud RM, Catalano A, Costi MP, Mangani S. The structure of *Enterococcus faecalis* thymidylate synthase provides clues about folate bacterial metabolism. *Acta Crystallographica Section D: Biological Crystallography*. 2012 Sep 1;68(9):1232-41.
31. Chowdhary A, Tarai B, Singh A, Sharma A. Multidrug-resistant *Candida auris* infections in critically ill coronavirus disease patients, India, April–July 2020. *Emerging infectious diseases*. 2020 Nov;26(11):2694.
32. Chen Y, Mi Y, Li Q, Dong F, Guo Z. Synthesis of Schiff bases modified inulin derivatives for potential antifungal and antioxidant applications. *International journal of biological macromolecules*. 2020 Jan 15;143:714-23.
33. Guo Z, Li Q, Wang G, Dong F, Zhou H, Zhang J. Synthesis, characterization, and antifungal activity of novel inulin derivatives with chlorinated benzene. *Carbohydrate polymers*. 2014 Jan 2;99:469-73.
34. Magalhães TF, da Silva CM, Dos Santos LB, Santos DA, Silva LM, Fuchs BB, Mylonakis E, Martins CV, de Resende-Stoianoff MA, de Fátima Â. Cinnamyl Schiff bases: synthesis, cytotoxic effects and antifungal activity of clinical interest. *Letters in Applied Microbiology*. 2020 Nov;71(5):490-7.
35. Bhagwatrao Biradar S, Vithal Narte D, Pradip Kale R, Momin KI, Sudewad MS, Tayade KC, Palke DG. Synthesis, spectral and biological studies of DHA Schiff bases. *J. Appl. Organometal. Chem*. 2021;1:41-7.
36. Hamad A, Chen Y, Khan MA, Jamshidi S, Saeed N, Clifford M, Hind C, Sutton JM, Rahman KM. Schiff bases of sulphonamides as a new class of antifungal agent against multidrug-resistant *Candida auris*. *MicrobiologyOpen*. 2021 Aug;10(4):e1218.
37. Whitty-Léveillé L, Tremblay-Cantin JC, Picard-Lafond A, Boudreau D, Reynier N, Larivière D. Core-shell nanoparticles bearing Schiff base ligand for the selective extraction of uranium from REE leach liquors. *Hydrometallurgy*. 2022 Feb 1;208:105780.
38. Erturk AG. Synthesis, structural identifications of bioactive two novel Schiff bases. *Journal of Molecular Structure*. 2020 Feb 15;1202:127299.
39. Sinha B, Bhattacharya M, Saha S. Transition metal complexes obtained from an ionic liquid-supported Schiff base: synthesis, physicochemical characterization and exploration of antimicrobial activities. *Journal of Chemical Sciences*. 2019 Mar;131(3):1-0.
40. Sinha B, Saha S. Imidazolium Ionic Liquid-Supported Schiff Base and Its Transition Metal Complexes: Synthesis, Physicochemical Characterization and Exploration of Antimicrobial Activities. In *Solvents, Ionic Liquids and Solvent Effects* 2019 Sep 9. IntechOpen.
41. Ommenya FK, Nyawade EA, Andala DM, Kinyua J. Synthesis, characterization and antibacterial activity of Schiff base, 4-Chloro-2-[(E)-(4-fluorophenyl) imino] methyl} phenol metal (II) complexes. *Journal of Chemistry*. 2020 Mar 30;2020.
42. Saha S, Basak G, Sinha B. Physico-chemical characterization and biological studies of newly synthesized metal complexes of an Ionic liquid-supported Schiff base: 1-{2-[(2-hydroxy-5-bromobenzylidene) amino] ethyl}-3-ethylimidazolium tetrafluoroborate. *Journal of Chemical Sciences*. 2018 Jan;130(1):1-9.
43. Abdelsalam MM, Hassan AM, Bedair MA, Abd El Naeem G, Elbially ZI. Green Synthesis, Spectral, Thermal Characterization and Biological Activity of Schiff base Ligand Derived from 3-amino-1, 2, 4-triazol and its Metal Complexes. *Organic & Medicinal Chemistry International Journal*. 2019;8(3):49-58.

44. Prashanthi Y, Kiranmai K, Subhashini NJ. Synthesis, potentiometric and antimicrobial studies on metal complexes of isoxazole Schiff bases. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2008 Jun 1;70(1):30-5.
45. Kumar G, Devi S, Johari R, Kumar D. Synthesis, spectral characterization and antimicrobial evaluation of Schiff base Cr (III), Mn (III) and Fe (III) macrocyclic complexes. *European journal of medicinal chemistry*. 2012 Jun 1;52:269-74.
46. Kassim K, Hamali MA. Green synthesis and antimicrobial studies of Ni (II) and Zn (II) dinuclear Schiff base complexes. *International Journal of Engineering & Technology*. 2018;7(3.11):237.
47. Bibal C, Daran JC, Deroover S, Poli R. Ionic Schiff base dioxidomolybdenum (VI) complexes as catalysts in ionic liquid media for cyclooctene epoxidation. *Polyhedron*. 2010 Jan 13;29(1):639-47.
48. Hossain MS, Islam HT, Nuruzzaman M. A Short Review on Antimicrobial Activity Study on Transition Metal Complexes of Ni Incorporating Schiff Bases.
49. Mishra AP, Purwar H, Jain RK, Gupta SK. Microwave synthesis, spectral, thermal and antimicrobial studies of some Co (II), Ni (II) and Cu (II) complexes containing 2-aminothiazole moiety. *E-Journal of Chemistry*. 2012 Jan 1;9(4):1655-66.
50. Hania MM. Synthesis and antibacterial activity of some transition metal complexes of oxime, semicarbazone and phenylhydrazone. *E-Journal of Chemistry*. 2009 Oct 2;6(S1):S508-14.
51. Anaconda JR, Rodriguez JL, Camus J. Synthesis, characterization and antibacterial activity of a Schiff base derived from cephalixin and sulphathiazole and its transition metal complexes. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2014 Aug 14;129:96-102.