

## Acetophenone derived Schiff base and its Fe (III) complex: Synthesis, characterization and biological activity

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Schiff bases are adaptable substances that may be used to create ternary complexes. A test has been conducted to develop an entirely novel Fe(III) compound. In this instance, L-valine served as the secondary ligand, and the primary ligand or Schiff base is made by a condensation reaction between 4-methyl acetophenone and hydroxylamine hydrochloride. Condensation of primary and secondary ligands with iron salt produces a significant complex. The traditional reflux technique has been used to carry out the reaction. The newly created ligand has strong antibacterial efficacy against particular bacterial and fungal species. Researchers may have a big chance here, and one special area of study that will receive future attention is the utilization of biological applications of new molecules that have been synthesized. The medical and pharmaceutical industries benefit greatly from the biological variety of acetophenone derivatives. Valine amino acids also have antibacterial and antifungal properties in addition to these molecules. Elemental analysis, molecular weight estimation, magnetic moment measurement, melting point measurement, spectrum analysis (IR, UV-Vis,  $^1\text{H}$  NMR, mass spectrometry, *etc.*), and X-ray diffraction have been used to characterize the synthesized ligand and complex. The complex that is created is non-electrolytic and paramagnetic. The octahedral geometry of the complexes is suggested by the UV-Vis, FTIR,  $^1\text{H}$  NMR, and mass spectra. Further testing of the synthesized chemicals in biological research against certain bacterial and fungal strains has been carried out. According to the present research, most complexes have been shown to have stronger antibacterial action than ligands. A similar case of the Schiff base complex of Fe(III) has also been studied by some scientists. They have synthesized the monodentate Schiff base and prepared the iron (III) complex by using a similar approach.

**Keywords:** 4-Methyl acetophenone, Hydroxylamine hydrochloride, Schiff bases, L-Valine, Antibacterial, Antifungal

Schiff bases, also known as privileged ligands, are chemical substances created by condensing a primary amine with a carbonyl group. Due to their chelating abilities and capacity to coordinate with a variety of transition, lanthanide, and actinide ions in various oxidation states using their nitrogen and oxygen atoms to form stable complexes, they are considered as a significant class of organic compounds<sup>1,2</sup>. They serve as dyes and pigments, catalysts, steps in the synthesis of organic compounds, and stabilizers for polymers<sup>3</sup>. Additionally, Schiff bases have been demonstrated to possess a wide range of biological activities, such as antifungal<sup>4</sup>, antibacterial<sup>5</sup>, antimalarial<sup>6</sup>, antiproliferative<sup>7</sup>, anti-inflammatory<sup>8</sup>, antiviral<sup>9</sup>, and antipyretic<sup>10</sup> characteristics. Because of the range of ways in which they are bound to metal ions, Schiff base ligands with different donor atoms (such as N, O, S, *etc.*) exhibit extensive biological activity and are of particular interest. Metal ions attached to physiologically active substances are known to boost their activity<sup>11</sup>. Complexes

derived from Schiff bases also have antimicrobial activity, anticancer activity, antioxidant, DNA binding properties, photoluminescence properties, *etc.* Luminescence is produced by the f-f transitions of the metal ion, and the complexes show a narrow and bright band from metal ion emission<sup>12,13</sup>. Upon reviewing the literature, it was discovered that some complexes containing acetophenone derivatives exhibit photoluminescence, and some hydroxylamine compounds exhibit DNA binding properties and antimicrobial activity against gram-positive bacteria, gram-negative bacteria, fungus, and yeasts<sup>14-20</sup>.

A survey of the literature led to the conclusion that acetophenone-based Schiff bases and iron complexes each have many uses in the biological system, thus these substances were utilised in this research to improve the outcome in the area of biology. The primary goal of this article is to investigate how the biological system is affected by the chelation of Schiff base towards Fe (III) ion. Analytical, spectroscopic, magnetic moment and conductance

measurements have been used to characterise a mixed ligand complex of the iron ion. Gram-positive bacteria (*S. aureus* ATCC 25923), gram-negative bacteria (*E. coli* ATCC 25922), and fungi (*C. albicans* ATCC 14053) were all targets of the complex's antimicrobial action.

## Experimental Section

### Materials and Methods

All of the chemicals and solvents were of the analytical variety and came from Sigma Aldrich. The Rast technique was used to determine the molecular weight of compounds, while the CHNX method was used to analyze elements. The melting point device was used to measure the melting point using open capillary tubes. Gouy's Balance Model No. HO-ED-EM-08 and Systronics Direct Reading Conductivity Meter-304, respectively, measured magnetic moment and molar conductance. The Hitachi Perkin Elmer spectrometer model was used to display the  $^1\text{H}$  nuclear magnetic resonance spectra ( $^1\text{H}$  NMR). TMS was employed in this instance as an internal standard in  $\text{DMSO-}d_6$ , and an FTIR spectrophotometer, the Shimadzu-Japan 8400, was used to display spectra.

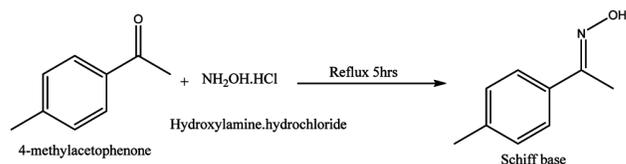
### Synthetic procedure for preparation of Schiff bases

#### Synthesis of Schiff base ( $\text{C}_9\text{H}_{11}\text{NO}$ )

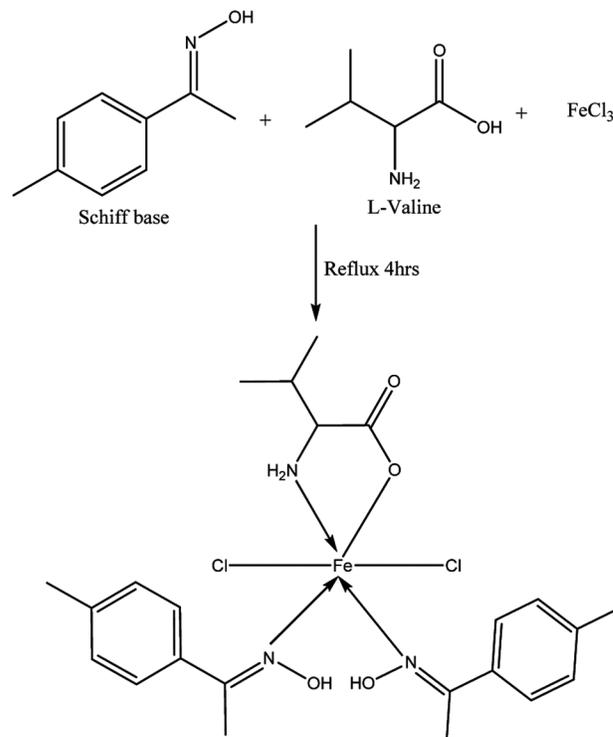
Hydroxylamine hydrochloride (0.69g, 10mmol) was dissolved in ethanol (10 mL), and 4-methyl acetophenone (1.34g, 10mmol) was dissolved in the same amount of ethanol (10 mL). In a 250 mL round-bottom flask, the two solutions were mixed. A small amount of glacial acetic acid and a condensing agent were added to the mixture. The mixture was refluxed using a condenser on the heating mantle for around 4 hours. A Gel-g TLC plate was used to observe the whole synthesis process. The clear TLC we received demonstrated that the product had been created. The liquid was then collected and left overnight on a watch glass. With the use of ethanol, the dry product was recrystallized, yielding colourless Schiff base crystals. The compound's M.P. as measured was  $217.6^\circ\text{C}$  and the yield was 51.38% (Scheme 1).

#### Synthesis of complex ( $\text{FeC}_{23}\text{H}_{32}\text{N}_3\text{O}_4\text{Cl}_2$ )

The complexes were prepared using the traditional standard heating process. The principal ligand was Schiff base, which was produced as a solution (2.98g, 20mmol) in ethanol (10 mL) that was taken as twice



Scheme 1 — Intended procedure for the synthesis of Schiff base.



Scheme 2 — Intended procedure of synthesis of complex

of the secondary ligand. The ethanolic solution (10 mL) of L-valine (1.17 g, 10 mmol) served as the secondary ligand.  $\text{FeCl}_3$  (1.62g, 10 mmol) was utilized to create an iron complex. The primary ligand was combined with the metal ion solution in a 250 mL round bottom flask while being continuously stirred and then added secondary ligand to this mixture. When no precipitation was obtained, the mixture was refluxed for about 4 hours in the heating mantle with the aid of a condenser. Thin-layer chromatography was used to continually monitor the reaction that was taking place. The content was then poured onto the watch glass and left overnight until the final result was ready. The result was a brown-coloured composite. It was re-crystallized using ethanol and then vacuum-dried. The compound's yield was 42.68% and its melting point was  $312.4^\circ\text{C}$  (Scheme 2).

### Antimicrobial Investigation

*Staphylococcus aureus* ATCC 25923 (gram-positive), *Escherichia coli* ATCC 25922 (gram-negative), and *Candida albicans* ATCC 14053 were tested for antimicrobial activity using Kirby-Bauer Well Diffusion techniques at two concentrations (1X, 0.5X) of the test compounds.

Table 1 — Preparation of test sample

S. No.	Compd	Weight (g)	Concentration (mg/mL)
1.	Ligand(C <sub>9</sub> H <sub>11</sub> NO)	0.010	10
2.	Complex(FeC <sub>23</sub> H <sub>32</sub> N <sub>3</sub> O <sub>4</sub> Cl <sub>2</sub> )	0.011	11

### Preparation of test sample

The following compounds were dissolved in DMSO to form a sample to test (Table 1).

### Antimicrobial experiment (Chart 1)

### Results and Discussion

Table 2 and Table 3 provide all material parameters, including physical parameters, element analysis and melting point assessment, and conductance of produced compounds. Table 4 shows the FTIR spectral data, whereas Table 5 gives <sup>1</sup>H NMR data. Table 6 lists the antimicrobial findings.

Table 2 — Physicochemical analytical data of compounds

Compd	Empirical formula	Mol. Wt. Found (Calcd)	Colour/Appearance	m.p. (°C)
Ligand	C <sub>9</sub> H <sub>11</sub> NO	149.08(149.06)	Colourless	217.6
Complex	FeC <sub>23</sub> H <sub>32</sub> N <sub>3</sub> O <sub>4</sub> Cl <sub>2</sub>	541.05(541.03)	Brown	312.4

Table 3 — Elemental analytical data of compounds

Compd	Elemental Analysis Found % (Calcd)					
	C	H	N	O	Fe	Cl
Ligand	72.50 (72.49)	7.37 (7.38)	9.39 (9.37)	10.72 (10.74)	—	—
Complex	51.05 (51.04)	5.91 (5.89)	7.76 (7.78)	11.82 (11.80)	10.32 (10.30)	13.10 (13.06)

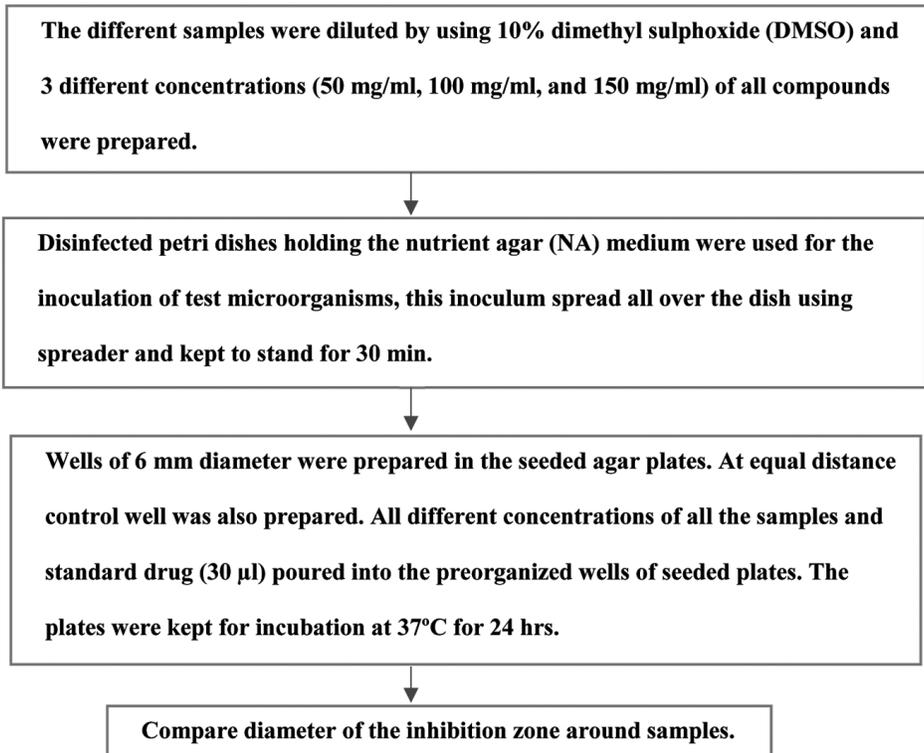


Chart 1 — Antimicrobial experiment

Compd	Table 4 — FTIR spectral data of compounds					
	FTIR bands (cm <sup>-1</sup> )					
	C=C (Str.)	C=C (Bend.)	C=N (Str.)	C=N (Bend.)	Fe-O	Fe-N
Ligand	1397	800	1594	2972	—	—
Complex	1380	748	1514	2920	554	429

Table 5 — <sup>1</sup>H NMR spectral data of compounds (δ, ppm)

Compd	Ar-H	CH <sub>3</sub>	N-H
Ligand	7.12-7.48	1.17	—
Complex	7.11-7.78	1.16	3.46

Table 6 — Antimicrobial activity of compounds against microbes

Compd	Concentration (%)	Inhibition Zone (mm)		
		<i>E. coli</i>	<i>S. aureus</i>	<i>C. albicans</i>
Ligands	50	NA	NA	NA
	100	10	8	6
	150	15	13	3
Complex	50	NA	13	13
	100	6	15	15
	150	13	19	19
Standard	100	32	26	28

NA = No activity, Standard: Cipro (for antibacterial) and Ketoconazole (for antifungal)

### Physicochemical evaluation

The synthesized compounds were found to be pigmented and soluble in ethanol, DMSO, and DMF during physicochemical analysis. The complex's molar conductance ranged from 11.38 to 12.38 cm<sup>2</sup> mol<sup>-1</sup>, which suggests that they are not electrolytic by nature.

### Magnetic moment

The magnetic susceptibility balance technique was used to calculate the magnetic moment of the synthesized compound. The magnetic moment that was detected was indicative of octahedral coordination complexes. The magnetic moment of the complex was measured at room temperature to be 5.97 B.M., which indicates that Fe(III) is in the high spin state for the d<sup>5</sup> electronic configuration.

### UV-Vis spectra

In ethanol, UV spectra in the 200–800 nm region were conducted. To measure the complex's n-π\* or π-π\* transitions, we acquired bands in the range of 250 nm to 550 nm. The complex's n-π\* and π-π\* bands were measured at 270 nm and 250 nm, respectively. Bands in the visible area were found to correspond to the d-d transitions <sup>1</sup>A<sub>1g</sub> → <sup>1</sup>T<sub>1g</sub> and <sup>1</sup>

A<sub>1g</sub> → <sup>1</sup>T<sub>2g</sub>, which further supports the idea that the complexes created during the synthesizing process have an octahedral geometry. The complexes band moved towards a longer wavelength as compared to Schiff bases.

### FTIR data (cm<sup>-1</sup>)

A characteristic stretching frequency was obtained in range 1514-1594 cm<sup>-1</sup> for C=N(Azomethine) for ligand and complex. Other peaks like C=C(str.), C=C(bend), metal-O, and metal-N were obtained at 1380 cm<sup>-1</sup>, 748 cm<sup>-1</sup>, 554 cm<sup>-1</sup>, and 429 cm<sup>-1</sup> respectively for the complex. The metal-O and metal-N frequencies were absent in the FTIR spectra of the ligand. The frequencies of the complex are slightly lower than that of ligands (Fig. S1 and Fig. S2).

### <sup>1</sup>H NMR data (δ, ppm)

<sup>1</sup>H NMR were performed in DMSO-d<sub>6</sub> (Fig. S3 and Fig. S4). Some characteristic peaks were obtained for Ar (C-H), C-H(CH<sub>3</sub>), and N-H at δ 7.11-7.78, 1.16-1.17, and δ 3.46 respectively as represented in Table 5.

### Mass Spectra

The characteristics of certain molecules are ascertained using the mass spectrometer. They are transformed into ions in a mass spectrometer so that they may be influenced and controlled by external magnetic and electric forces. The precise molecular weight and formula of the complexes are demonstrated by the mass spectral fragmentation patterns. The compound's specificity may be seen in the mass spectra (Fig. S5 and Fig. S6). Compounds fragment and show peaks when exposed to electric and magnetic forces. Schiff base and complex have *m/z* values of 150.17 and 541.55 in their spectra, which are identical to their corresponding molecular weights of 149.08 and 541.05 respectively.

### Antimicrobial Study

Using Kirby-Bauer Well Diffusion techniques, antimicrobial activities were investigated against gram-positive bacteria, gram-negative bacteria, and fungal strains (Fig. 1 and Fig. 2), which are tabulated

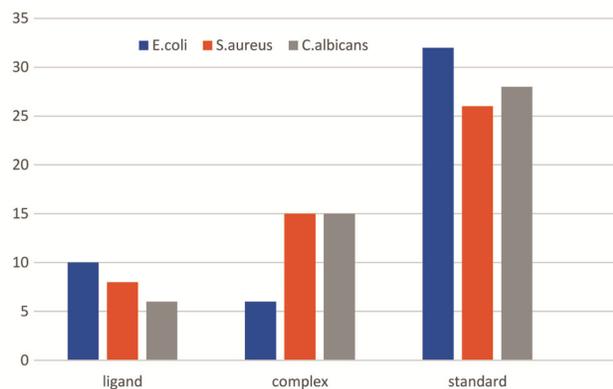


Fig. 1 — Bar diagram representing the antimicrobial activity of compounds

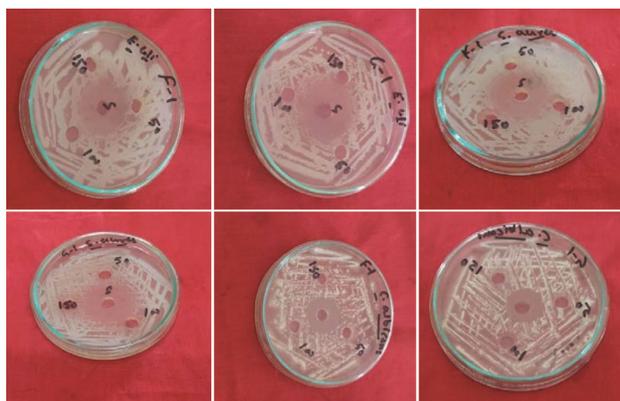


Fig. 2 — Antibacterial and antifungal activity of compounds

in Table 6. All the compounds were biologically active but the complex showed more efficient activity against the microbes.

### Conclusions

An octahedral geometry has been proposed for the synthesized complex. The complex is non-electrolytic in nature and the metal ion exists in the high-spin state with paramagnetic nature. In FTIR spectra of complex, shifting of C=N to lower wave number supports coordination of the C=N group. All synthesized compounds are found to be biologically active. Both Schiff base and complex are less active towards gram-negative bacterial strains but show more activity towards gram-positive bacteria and fungal strains. The complex is more active against the microbial strains than the parent Schiff base from

which the complex is synthesized. In brief, the Schiff base and the complex can be used to synthesize other useful compounds that can be directly employed for the preparation of medicines, industrial products, and agrochemicals.

### Supplementary Information

Supplementary information is available in the website <http://nopr.niscpr.res.in/handle/123456789/58776>.

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