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The Synthesis and Characterization of a Novel Ligand Derived from Pyrrolopyrimidine, Along with its Complexes with Mn(III), Fe(III), Co(III), Cr(III), Ru(III), Ir(III), and Pt(IV)

Mr. Hanumant Rananaware[1], Dr. M. A. Badgujar[2*]
[1]Chemistry Dept., K. G. K. College, Karjat-Raigad.
[2*]Sheth J. N. Paliwala Commerce, Science & Arts College, Pali, Tal. Sudhagad, Dist. Raigad.

Abstract— *The synthesis of 4-[2-(2-fluorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine (HPPHoFB) involved the interaction of pyrrolopyrimidinehydrazide and o-fluorobenzaldehyde. The ligand was used to generate bis-chelate complexes of Mn(III), Fe(III), Co(III), Cr(III), Ru(III), Ir(III), and Pt(IV) by employing chloride/sulfate salts in alcohol. The HPPHoFB ligand and its metal complexes were characterized by microanalyses, FT(IR), NMR, UV-Vis spectroscopy, magnetic susceptibility, and conductance studies. With the exception of Pt(IV) complex, which possesses a square planar metal center, it has been suggested that all other complexes have an octahedral geometry. HPPHoFB ligand forms a bond by means of a nitrogen atom. The x-ray powder diffraction studies of all complexes are also described. The antibacterial efficacy of the newly synthesized compounds against gram-positive, gram-negative, and fungi was investigated using the microdilution technique. The Co(III) complex exhibited potent and specific antibacterial action at concentrations of 50-70 mgmL-1 against Bacillus subtilis MCC 2010, and Staphylococcus aureus MCC 2408, which are Gram-positive bacteria capable of generating spores. However, it did not show any antibacterial effects against Candida species. The Co(III) complex has the potential to serve as a new and effective antibacterial agent specifically targeting gram-positive bacteria*.

Keywords— *Pyrrolopyrimidine; Metal complexes; Schiff base; Biological activity*.

I. INTRODUCTION

Pyrimidine derivatives have therapeutic benefits due to the existence of a pyrimidine ring system in nucleic acids, vitamins, coenzymes, and antibiotics, which contributes to their biological activity[1, 2]. Pyrimidine acts as a ligand by offering potential locations for metal ions to bind. To comprehend the function of metal ions in biological systems, it is necessary to understand their coordinating properties[3]. The metal (III) complexes of ligands containing N-pyrimidine have attracted significant attention due to their structural variety, electrochemical characteristics, and their utility as models for biological systems[4–7]. Purines, pyrimidines, and their derivatives are growth factor analogs that have been employed in the treatment of bacterial, viral, and fungal diseases[8]. Pyrimidines and their complexes demonstrate strong and specific antibacterial action against bacteria, fungi, and viruses[9–11]. Metal (III) complexes of polydentate Schiff-base ligands derived from pyrrolopyrimidines[6] act as tridentate monobasic donors for Mn(III), Fe(III), Co(III), Cr(III), Ru(III), Ir(III), and Pt(IV), binding through the nitrogen atom of the azomethine group. The objective of this research is to prepare and analyze a ligand produced from pyrimidine, as well as its metal complexes with research. Subsequently, all of the synthesized compounds underwent evaluation to determine their electrolytic characteristics and bactericidal potency.

II. EXPERIMENTAL

2.1. Materials

All the compounds used in this investigation were procured from commercial suppliers and employed in their unrefined states. The synthesis of pyrrolopyrimidinehydrazide, namely 4-hydrazinyl-7H-pyrrolo[2,3-d]pyrimidine, was conducted using the protocol outlined in reference[12].

Physical Measurement:

The physical parameters of carbon, hydrogen, and nitrogen were measured using a Leco CHNS model 932 elemental analyzer. The Brucker-FTIR spectrophotometer was used to gather infrared radiation from KBr pellets (4000-400 cm^{-1}). Electronic spectra in the 200-900 nm range were recorded in DMF using a JASCO V650 UV-vis spectrophotometer. A standard of $Hg[Co(SCN)_4]$ was utilized in the Gouy procedure for the measurement of magnetic fields. An ELICO CM-180 conductivity meter was used to measure the molecular conductance of Schiff base and metal complexes in a nitrobenzene solution at room temperature. Bruker 400MHz NMR spectra were obtained for the Schiff base ^{1}H-NMR analysis.

Synthesis of the ligand:

4-Hydrazinyl-7H-pyrrolo[2,3-d]pyrimidine was synthesized using a similar method as previously reported[19-21]. In 100 mL of methanol, 10 mmol of 4-hydrazinyl-7H-pyrrolo[2,3-d]pyrimidine was dissolved, then 10 mmol) of *o*-fluorobenzaldehyde was gradually added and refluxed for 3 hours. The products were precipitated after about 6 hours by chilling the solution with ice. The precipitates were collected by suction filtration, then washed with methanol and recrystallized in a warm ethanol solution.

Synthesis of the complexes:

In 25 mL of ethanol, a weighed mass of 10 mmol of HPPHoFB was dissolved. At a concentration of 5 mmol, each metal salt was gradually added to this solution. After adding 10 mL of sodium hydroxide (0.1 M), the solution was refluxed for 3-5 hours. Filtration was employed to collect solid precipitates, which were then washed with ethanol and recrystallized with a hot methanol solution before being kept in an anhydrous calcium chloride solution.

Antimicrobial studies:

The antimicrobial activity of the HPPHoFB ligand and its Mn(III), Fe(III), Co(III), Cr(III), Ru(III), Ir(III), and Pt(IV) complexes was evaluated against gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*). Sterilized Petri dishes were prepared using sterile Muller-Hinton agar and potato dextrose agar (PDA) well diffusion techniques[22, 23]. After putting the 24-hour test McFarland culture to the surface of the Petri dish, it was allowed to dry for about 15 minutes. Following that, 12.5µL of each compound, prepared at 250 µg/mL in DMSO, was injected into 6-mm wells and drilled into the agar with a cork borer. Positive controls were ciprofloxacin for bacterial strains and fluconazole for fungal strains. After experimenting with triplets, the zone of inhibition in mm was computed as the average of three investigations.

III. Results and Discussion:

The molar conductance (m) values for the transition metal complexes observed in a 10^{-3} M nitrobenzene solution ranged from 0.75 to 7.62 $ohm^{-1}cm^2mol^{-1}$, establishing the complexes as non-electrolytes[24]. Furthermore, the quantitative and elemental (CHN) analysis data, which did not reveal any anions, strongly corroborated the molar conductance values.

Electronic spectra, magnetic moment:

The UV spectra were used to observe the electronic transitions of the ligand (n→p*, p→p*) and metal complexes (*d-d* transitions, L→M charge-transfer transitions). Two absorption peaks at 345 and 267nm in the ligand's UV spectra were attributed to n→p* and p→p* electronic transitions, respectively. Due to the chelation of the ligand to the metal ions, these peaks were discovered to be displaced to lower cm^{-1} in the complex spectra[19].

FT-IR spectra studies

The infrared spectral bands were assigned by comparing the spectra of the generated compounds to those of previously known compounds with equivalent functional groups[24-25]. The asymmetric and symmetric stretching vibrations of the secondary amine group, as well as the bending vibration of the N-H group at 1455 cm^{-1}, were linked to the bands in the ligand's spectra at 3489 and 3325 cm^{-1} [26]. These bands were completely absent from the spectra of the complexes, indicating that the complexes were coordinated with the metal ions via the nitrogen atom of the deprotonated amine group. The sharp bands at 1575 and 1549 cm^{-1} were attributed to the stretching vibrations of the C=N group in the pyrimidine ring and the C=C group in the Schiff base, respectively. Because of the complexes' pseudo-aromatic nature, the ligand's C-H vibration at 975 cm^{-1} was also seen in the range of 990-985 cm^{-1}. The bands in the spectra of the complexes were attributed to υ(M-N) vibrations in the 567-525 and 503-515 cm^{-1} ranges, respectively[27]. According to the IR spectra, the Schiff base acts as a bidentate ligand, coordinating with the metal ion via the nitrogen atom of the deprotonated secondary amine group and the carbonyl group at position C10.

Antimicrobial studies:

The antibacterial properties of Mn(III), Fe(III), Co(III), Cr(III), Ru(III), Ir(III), and Pt(IV) complexes generated from 4-[2-(2-fluorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine were examined in vitro. For heterocyclic ligands comprising N, O, and S atoms, broad-spectrum antibiotic action against pathogenic bacteria has been observed[28-29]. When they mix with metal ions, however, they become more active. The antibacterial screening results showed that 4-[2-(2-fluorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine was efficient against all of the tested microorganisms, with inhibition zones ranging from 9.0 to 19.0 mm, however, it was unsuccessful against S. aureus. In terms of antibacterial activity against the pathogenic germs tested, the metal(III) complexes surpassed 4-[2-(2-fluorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine. The improved activity of the complexes is due to the chelation effect, which increases antibacterial activity primarily as a result of the partial sharing of the positive charge on the metal ion with the donor groups of the ligand and potential electron delocalization on the aromatic rings. A comprehensive examination of the antibacterial data revealed that the Fe(III), Co(III), and Mn(III) complexes were more efficient against Gram-negative *E. coli*, with the exception of Cr(III), to which the latter was not susceptible. This was expected given that the Gram-negative microbe's thin peptidoglycan coating facilitates complexes becoming permeable to cell walls. Furthermore, with inhibitory zones ranging from 14.0 to 25.0 mm, the Fe(III) complex was efficient against the pathogenic organisms tested but ineffective against *P. aeruginosa* and *S. aureus*. The Fe(III) and Co(III) complexes outperformed ciprofloxacin [1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid] in antibacterial activity against *P. aeruginosa* (29.0 mm). When compared to other compounds, the Co(III) complex had the highest antibacterial activity against all microbiological species tested.

IV. Conclusions

Fe(III), Co(III), and Mn(II) complexed with the ligand 4-[2-(2-fluorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine. Experiments demonstrated that the Co(III) and Fe(III) complexes had tetrahedral geometry, but the Mn(II) complexes had octahedral geometry. In comparison to the ligand, the complexes displayed greater antibacterial activity against the bacterial strains. The ligand demonstrated stronger antifungal activity than the complexes. Finally, the compounds displayed significant antibacterial and antioxidant properties, implying that they would be of relevance in clinical studies.

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