https://dx.doi.org/10.4314/dujopas.v10i3a.23
ISSN (Print): 2476-8316
ISSN (Online): 2635-3490
Dutse Journal of Pure and Applied Sciences (DUJOPAS), *Vol. 10 No. 3a September 2024*

Synthesis, Characterization, and Biological Potential of 2-Thiophene Carbaldehyde O-Phenylenediamine Schiff Base and its Cr(II), Mn(II), and Fe(II) Complexes

[1]Habibu Bashir Ado, [2]Naseer Inuwa Durumin iya, [3]Nura Nasiru Rabiu, [3]Baffa Ahmad, [3]Abdulmalik Abdulkadir, [4]Abubakar Abba Muhammad, [4]Shamsu Shuaibu Balah,

[1,3,4]Department of Chemistry,
Rabiu Musa Kwankwaso College of Advanced and Remedial Studies,
Tudun Wada Kano,
Nigeria.

[2]Department of Chemistry,
Federal University Dutse Jigawa State,
Nigeria.

Email: adohabibbashir86@gmail.com

Abstract

A Schiff base was produced through the chemical reaction of 2-thiophene carbaldehyde with o-phenylenediamine. The corresponding metal (II) chlorides were refluxed with the Schiff base to produce the complexes of Cr (II), Mn (II), and Fe (II). These complexes were then characterized by elemental analysis, FT-IR, atomic absorption spectroscopy, solubility, melting/decomposition temperature, and magnetic susceptibility. The vibrational peak at 1622 cm^{-1} in the FT-IR spectral data of the Schiff base was ascribed to the vibration frequencies of azomethine υ(C=N). But in the complexes, it was discovered that the azomethine band shifted between 1614 and 1659 cm^{-1} , suggesting that they were involved in the complexes' creation. The complexes' measured absorption bands in the range of 713–769 cm1 were attributed to the M–N bond, indicating the occurrence of metal–nitrogen bonds. The complexes exhibit non-electrolyte properties attributed to their low molar conductance values ranging from 8.00 to 29 Ohm^{-1} $cm^{-2}mol^{-1}$. The determination of the melting point of the Schiff base yielded 120 °C, while the decomposition temperature fell within the range of 149–160 °C for the complexes, indicating their thermal stability. Analysis of magnetic susceptibility indicated an octahedral geometry for all the complexes, with values ranging from 2.24 to 3.12 BM. The elemental should analysis of both the Schiff base and its metal (II) complexes for C, H, and N indicated a close agreement between observed and calculated percentages, suggesting a consistent 1:2 metal-Schiff base ratio across all complexes. The qualitative analysis of the compounds confirmed the presence of chloride, which was quantified and determined to range from 4.62% to 7.90%. The prepared Schiff base and its metal (II) complexes underwent evaluation for their antibacterial efficacy against Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, and Pseudomonas aeruginosa, as well as their antifungal properties against Candida albicans and Aspergillus niger. The results of the experiments indicated that the metal complexes displayed notable antimicrobial effects.

Keywords: Schiff base, synthesis, characterization, antimicrobial, antifungal

Author for Correspondence

INTRODUCTION

When amines and ketones or aldehydes condense, azomethine groups (-HC=N-) are produced. These compounds are known as Schiff bases. They are remarkable chemical discoveries that have made a significant impact on the advancement of coordination chemistry. They serve as ligands to most of the transition metals forming very stable complexes (Ghosh *et al.*, 2020; Abu-Dief and Mohamed, 2015). With a variety of uses, including radio-immunotherapy, cancer diagnostics and treatment, antiviral medicines, tumor treatment, and catalysts.

Schiff bases have continued to be important in the development of medicinal and industrial chemistry (Abu-Dief and Mohamed, 2015; Noor *et al.*, 2020). On the other hand, sulfa drugs have attracted huge attention due to their therapeutic recognition as they found application in many medical field (Bushra *et al* 2021; Sinem and Marianna, 2019).

Numerous investigations have been conducted on Schiff base transition metal complexes. Abdullahi et al. (2020) synthesized a Schiff base using 4-methyl-o-phenylenediamine and 2-hydroxy-1-napthaldehyde, which was then utilized to produce various metal (II) complexes through refluxing with Metal (II) chloride ions. The ligand and its complexes were characterized using methods such as melting point and decomposition temperature analysis, FTIR spectroscopy, solubility testing, magnetic susceptibility measurements, conductivity assessments, and elemental analysis. The IR spectral data indicated that the Schiff base coordinated with the respective metal(II) ion through the azomethine nitrogen and phenolic oxygen, as evidenced by the shift in the azomethine band v(C = N) from 591cm^{-1} to 1603 and 1581cm^{-1} in the complex spectra. Additionally, the bands at 567 and 563cm^{-1} were attributed to v(M - N), while 729 - 752cm^{-1} were due to v(M - O). The infrared spectra of the metal(II) complexes displayed strong bands at 3443 and 3363cm^{-1}, suggesting the presence of coordinated water in the metal complexes. Molar conductance values of 9.17 and 10.04Ω^{-1} cm^{-1}mol^{-1} indicated that the complexes were non-electrolytes. Furthermore, the ligand and its metal(II) complexes exhibited low solubility in water and most organic solvents, except for DMF and DMSO. The melting point of the ligand and the decomposition temperatures of the metal(II) complexes were within the range 224 to 243 degrees Celsius, respectively, indicating their excellent thermal stability. The magnetic moment values of the metal (II) complexes were determined to be 5.65 and 5.22BM for Mn(II) and Fe(II) complexes, respectively, suggesting their paramagnetic nature. The elemental analysis results indicated a metal to ligand ratio of 1:2. Moreover, antibacterial and antifungal tests conducted on the ligand and its metal(II) complexes revealed moderate activity.

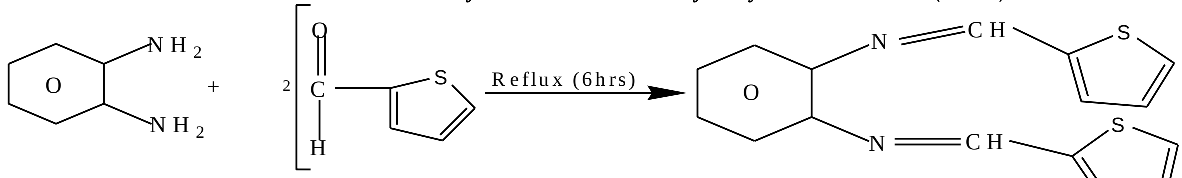
In another study by Bashir and Siraj (2021), a Schiff base was synthesized through the condensation of 2-thiophenecarboxaldehyde and ethylenediamine. Subsequently, Mn(II), Fe(II), and Co(II) complexes of the Schiff base were prepared and characterized based on various parameters including melting point/decomposition temperature, solubility, molar conductance, magnetic susceptibility, elemental analysis, infrared spectroscopic analysis, and UV-visible spectrophotometry. The Schiff base and its complexes were found to be soluble in DMSO, DMF, and certain organic solvents, indicating their non-ionic nature. The decomposition temperatures of the complexes ranged from 173 to 246 degrees Celsius, highlighting the stability of these compounds. All the complexes exhibited low molar conductance values (8.66-25.29Ω^{-1} cm^{-1}mol^{-1}), confirming their non-electrolytic properties. Furthermore, magnetic moment values of the complexes fell within the range of 3.847BM-5.12BM, indicating their paramagnetic characteristics. The IR spectra of the Schiff base displayed an azomethine peak at 1629cm^{-1}, which shifted to lower frequencies (1603 - 1562cm^{-1}) in the complex spectra. Both analytical and spectroscopic data supported the formation of the complexes, with coordination occurring through the nitrogen of the azomethine (-H C =N-) group and the sulfur atom of the thiophene ring. A 1:1 metal to ligand ratio was proposed. The Schiff base and its complexes were evaluated for their in vitro antimicrobial activity against three pathogenic bacteria (Staphylococcus aureus, Streptococcus pneumonia, and Escherichia coli) and two pathogenic fungi (Aspergillus niger and Aspergillus flavus). While the Schiff base exhibited a moderate inhibition zone (6 - 14mm), some of the metal chelates displayed slightly higher inhibition zones (06-17mm) against the bacteria and fungi, but lower than those of the control drugs used (18-30mm).

Synthesis, characterization and antimicrobial activities of Schiff base of 2-thiophene carbaldehyde and o-phenylenediamine it's Cr (II), Mn (II), and Fe (II) complexes have been reported in this paper. The schiff base and it's metal complexes were characterized using various methods.

MATERIALS AND METHODS

Materials
All chemicals and solvents utilized in the study were of analytical grade and were not purified further. The glassware was cleaned thoroughly with detergent, rinsed with distilled water, and then dried in a Gallankamp hot box oven set at 110°C. Weighing was performed on an electric meter balance. Infrared (IR) spectroscopy was conducted using an Agilent Technologies FUR CARY 630 model at the Department of Pure and Industrial Chemistry, Bayero University Kano (BUK), within the ranges of 400–1000 cm^{-1} and 650–4000 cm^{-1} for both the ligand and its metal (II) complexes. The melting points and decomposition temperatures of the ligands and their metal (II) complexes were ascertained using a Gallankamp melting point apparatus. The conductance measurements of the complexes were taken using a Janway 4010 conductivity meter. Magnetic susceptibility was measured with a Sherwood magnetic susceptibility balance. Elemental analysis for carbon, hydrogen, and nitrogen was conducted at the Central Laboratory of Umar Musa Yar'Adua University. The antimicrobial activity tests were performed at the Department of Microbiology, Bayero University, Kano.

Synthesis of the Schiff base
This involved refluxing o-phenylenediamine (0.025 mol/2.7035 g) and 2-thiophene carbaldehyde (0.05 mol/4.67 g) in 50 cm^3 of ethanol for six hours. The mixture was then cooled for 24 hours, resulting in a precipitate, which was filtered, washed with ethanol, and dried in a desiccator over CaCl2 for three days, as described by Aly and Fathala (2020).



ortho phenylene diamine 2 – thiophene carbaldehyde Schiff base

Figure 1:Reaction for the formation of Schiff base

Synthesis of Metal (II) Complexes
After being individually combined with ligand (0.005mol) in 50cm^3 of ethanol, metal (II) salt (0.0025/mol) was refluxed for six hours. After cooling the reaction mixture for a full day, the solid precipitate was cleaned using a combination of acetone and water and allowed to dry for two days over P2O5. (Aly and Fathala, 2020).
Antibacterial Test
The antibacterial activity was assessed against clinical isolates of *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa,* which were sourced from the Microbiology Laboratory culture collection at Bayero University Kano, Nigeria. These isolates were identified at the Department of Microbiology using established microbiological methods outlined by Cheesbrough (2002). The in vitro antibacterial efficacy was evaluated using the Kirby-Bauer disc diffusion assay, as per the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2006). The inoculum was prepared by suspending an overnight bacterial culture in a saline solution (0.85% NaCl) and adjusting it to match the 0.5 McFarland turbidity standard, corresponding to approximately 10^8 cells/mL. This inoculum was evenly spread across the surface of nutrient agar plates, following the method described by Yusha'u and Sadisu (2011).

The Schiff base and its metal complexes were individually dissolved in DMSO to achieve four distinct concentrations (100 µg/mL, 200 µg/mL, 300 µg/mL, and 400 µg/mL) through serial dilution. These solutions were then applied to sterile paper disks (6.0 mm in diameter). A commercial antibiotic, Amoxicillin, was used as a reference standard for comparison. The disks, impregnated with the test compounds and the standard antibiotic, were placed on the bacterial culture, and the plates were incubated at 37°C for 24 hours. After incubation, the zones of growth of inhibition around the disks were observed and measured in millimeters. The diameters of the inhibition zones produced by the ligand and the complexes were compared with those of the standard antibiotic, as described by Yusha'u and Sadisu (2011).

Antifungal Activity Test
Clinical isolates of *Candida albicans* and *Aspergillus niger* were procured from the culture collection maintained by the Microbiology Laboratory at Bayero University Kano, Nigeria. The identification of these isolates was carried out at the Department of Microbiology, employing standard microbiological techniques as detailed by Cheesbrough (2002).
The in vitro antifungal activity was assessed using the Kirby-Bauer disc diffusion assay, in accordance with the guidelines provided by the Clinical and Laboratory Standards Institute (CLSI, 2006). The inoculation method followed the procedure described by Hassan *et al.* (2006). The prepared inoculum was evenly spread onto the surface of solidified Potato Dextrose Agar (PDA) that had been poured into Petri dishes.

The ligand and its metal complexes were individually dissolved in DMSO (Siraj and Ado, 2018) to achieve four different concentrations (100 µg/mL, 200 µg/mL, 300 µg/mL, and 400 µg/mL) per disk, using the serial dilution method. These solutions were then placed on the surface of the Potato Dextrose Agar (PDA) culture medium. The plates were incubated at room temperature for a period of 48 hours. The diameters of the zones of inhibition produced by the ligand and the complexes were measured and compared with those produced by the standard antifungal agent, Nystatin, which served as a reference, as described by Hassan et al. (2006).

RESULTS AND DISCUSSION

Results of the analysis are presented in the tables 1-9 below

Table 1: Physical properties of the ligand and its metal (II) complexes

Compound	Colour	Decomposition temp (^0C)	Melting Point (^0C)	Percentage Yield %
Ligand	Yellow	-	120	90.20%
$[CrL_2Cl_2]$	Brown	160	-	69.73%
$[MnL_2Cl_2]$	Coffee	149	-	78.68%
$[FeL_2Cl_2]$	Antigue brass	150	-	87.75%

L = Ligand

Table 2: Solubility test of the Ligand and its metal (II) Complexes

Compound	Distilled Water	MeOH	EtoH	Chloroform	Acetone	Nitro-Benzene	CCl4	DMF	DMSO	Ether	Pet Ether	Acetonitrile
Ligand	IS	SS	SS	SS	S	SS	IS	S	S	IS	IS	S
$[CrL_2Cl_2]$	IS	SS	SS	SS	S	SS	IS	S	S	IS	IS	S
$[MnL_2Cl_2]$	IS	IS	IS	IS	SS	SS	S	S	S	SS	IS	S
$[FeL_2Cl_2]$	IS	S	S	SS	S	SS	SS	S	S	SS	SS	S

Key:
S = Soluble
SS = Slightly Soluble
IS = Insoluble

L = Ligand: $C_{16}N_2S_2H_{12}$

Table 3: Conductivity measurement of complexes in 1x10m^{-3} DMSO

Complex	Concentration (dm^{-3})	Specific conductance (Ohm-1 Cm-1)	Molar conductance Ohm-1 cm2 mol-1
$[CrL_2Cl_2]$	1×10^{-3}	20×10^{-6}	20
$[MnL_2Cl_2]$	1×10^{-3}	29×10^{-6}	29
$[FeL_2Cl_2]$	1×10^{-3}	8.00×10^{-6}	8

L = Ligand $C_{16}N_2S_2H_{12}$

Table 4: Infrared Spectral Data of the ligand and its metal (II) complexes

Compound	υ (C=N) CM^{-1}	υ (M-N) cm^{-1}	υ (M-Cl) cm^{-1}
Ligand	1622	-	-
$[CrL_2Cl_2]$	1640	477	588
$[MnL_2Cl_2]$	1614	384	492
$[FeL_2Cl_2]$	1659	477	521

L = Ligand $C_{16}N_2S_2H_{12}$

Table 5: Elemental analysis (CHN) of the Ligand and its metal (II) Complexes

Compound	C	H	N
Ligand	64.77 (64.87)	4.05 (4.35)	2.88 (2.67)
$[CrL_2Cl_2]$	54.20 (53.60)	4.07 (3.35)	8.19 (7.82)
$[MnL_2Cl_2]$	53.95 (53.38)	3.84 (3.34)	8.03 (7.78)
$[FeL_2Cl_2]$	54.21 (53.40)	3.57 (3.33)	7.18 (7.77)

L = Ligand $C_{16}N_2S_2H_{12}$
The values in the parenthesis are the calculated ones

Table 6: Magnetic Parameters of metal(II) complexes

Compound	Magnetic susceptibility Xg(erg.G^{-2} g^{-1})	Molar Magnetic Susceptibility Xg(erg.G^{-2} mol^{-1})	B.M (μ_{eff})
[CrL_2Cl_2]	3.80 x10^{-6}	2.72 x10^{-3}	2.97
[MnL_2Cl_2]	3.19 x10^{-6}	2.23 x10^{-3}	2.34
[FeL_2Cl_2].	4.81x10^{-6}	3.45 x10^{-3}	2.87

Table 7: Estimation of chloride in the complexes

Compound	Average weight of AgCl obtained (g)	% chloride calculated
[CrL_2Cl_2]	0.0801	9.9
[MnL_2Cl_2]	0.597	7.38
[FeL_2Cl_2]	0.0611	7.55

Table 8: Antifungal activities of metal (II) complexes against some fungal species

	Candida albican			*Aspergillus niger*		
Compound/conc./(µg/disc)	300	200	100	300	200	100
[CrL_2Cl_2]	16	12	9	14	12	11
[MnL_2Cl_2]	13	10	7	10	6	6
[FeL_2Cl_2]	10	9	9	18	15	12
Nystatin (50mg/ml)	22	23	20	20	20	18

Table 9: Antibacterial activities of metal complexes against some fungal species

Micro Organism	*Escherichia Coli*				*Staphylococcus Aureus*				*Klebsiella Pneumoniae*				*Pseudomonas aeruginosa*			
Compound/Conc./(ug/disc)	400	300	200	100	400	300	200	100	400	300	200	100	400	300	200	100
[CrL_2Cl_2]	13	11	10	10	11	10	6	6	15	13	13	12	15	13	11	10
[MnL_2Cl_2]	15	13	13	12	13	11	11	10	12	12	10	9	13	13	12	10
[FeL_2Cl_2]	14	10	9	9	12	10	6	6	10	10	6	6	12	11	11	9
Amoxicillin (100mg)	29				33				30				31			

DISCUSSION

The synthesis of the Schiff base was achieved through the condensation of 2-thiophene carbaldehyde and o-phenylenediamine, resulting in a yellowish product with a high yield of 92.20% and a melting point of 120°C. Synthesis of metal (II) complexes was done by reacting the Schiff base with the respective metal (II) chlorides, which produced compounds of various colors, as indicated in Table 1. The complexes were obtained with good percentage yields ranging from 69.73% to 87.25%. The decomposition temperatures of the complexes, falling between 149°C and 160°C, suggest that the complexes are relatively stable, as shown in Table 1.

The solubility tests of the metal (II) complexes and the ligand in various solvents, presented in Table 2, revealed that all the complexes and the ligand are soluble in DMSO, DMF, and acetonitrile. However, the Manganese (II) complex showed slight solubility in acetone. The ligand and the Cr (II) complex were insoluble in ether and CCl4, while the Mn (II) complex was soluble in CCl4 and slightly soluble in ether. The Fe (II) complex exhibited slight solubility in both CCl4 and ether.

The molar conductance measurements of the metal (II) complexes in DMSO, detailed in Table 3, were found to be in the range of 8 to 29 Ohm^{-1} cm^{-2} mol^{-1}, indicating a non-electrolytic nature due to the relatively low values (Abdullahi *et el* 2020).

The IR spectral data, outlined in Table 4, showed a vibrational peak at 1622 cm^{-1} for the Schiff base, which was assigned to the azomethine v(C=N) vibration frequency. This peak shifted in the complexes to between 1614 and 1659 cm^{-1}, suggesting the involvement of the azomethine group in complex formation. Absorption bands in the range of 384 to 477 cm^{-1} in the complexes were attributed to M-N bonds, confirming metal-nitrogen coordination. Additionally, bands in the range of 492 to 588 cm^{-1} were associated with M-Cl bond formation.

The elemental analysis results for hydrogen, carbon, and nitrogen in the Schiff base and its metal (II) complexes, shown in Table 5, indicated a close match between the observed and calculated percentages of the elements, suggesting a 1:2 metal-Schiff base ratio in all the complexes.

Magnetic susceptibility measurements at room temperature for the metal (II) complexes, presented in Table 6, showed magnetic moments ranging from 2.34 to 2.97 BM, indicating that the compounds are paramagnetic with an octahedral geometry, consistent with literature values for similar octahedral complexes (Bashir and Siraj 2021).

The qualitative tests for the presence of chloride in the complexes, summarized in Table 7, confirmed the presence of chloride, with estimates ranging from 7.38% to 99%.
The complexes demonstrated good antifungal activities against various fungal species, particularly at higher concentrations, as shown in Table 8.

Similarly, the complexes exhibited good antibacterial activities against different bacterial species, especially at higher concentrations, as indicated in Table 9.

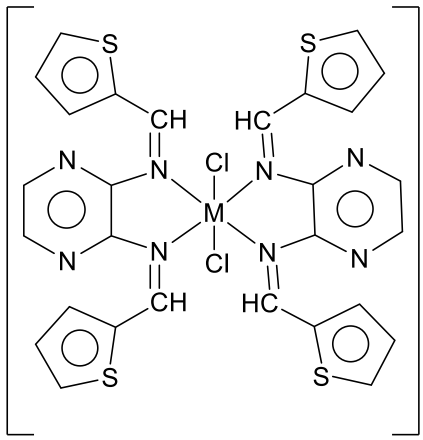


Figure 2: The proposed general structure of the complexes
Where M is Cr, Mn and Fe

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