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SYNTHESIS, CHARACTERIZATION, ANTIOXIDANT, CRYSTALLOGRAPHIC STUDIES OF HETEROCYCLIC SCHIFF BASES AND THEIR BIOLOGICAL EVALUATION

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ABSTRACT

The Schiff bases derived from equimolar quantity of ortho substituted aldehyde and primary amine (aromatic amine, Aromatic heterocyclic amine) were prepared via condensation reaction. These Schiff bases were used as ligands to form stable complexes with metal acetate, such as Cu (II), Ni (II), Co (II), Fe (II), Cd (II). The synthesized Schiff bases act as deprotonated tetradentate for the complexation reaction with metal ion. The Schiff bases were characterized by ^{1}H NMR, FTIR SEM, and spectral analysis and furthermore, the entire synthesized product was screening for their biological activity Antioxidant activity.

KEYWORDS: Schiff bases, Heterocyclic amines, Ligands, Antimicrobial Screening, FESEM.

INTRODUCTION

Schiff bases derived from amine and any aldehyde are important class of compound which co-ordinate to metal ion via the azomethine group (-C=N-) nitrogen.[1] Schiff bases and their metal complexes play an important role in Co-ordination chemistry of transition metalion.[2] There is interest in chemistry of transition metal complex of ligand containing Oxygen, nitrogen, Sulphur, donar atom due to Carcinestic, antitumor, antiviral, antifungal and antibacterial activity, and industrial use.[2-4]

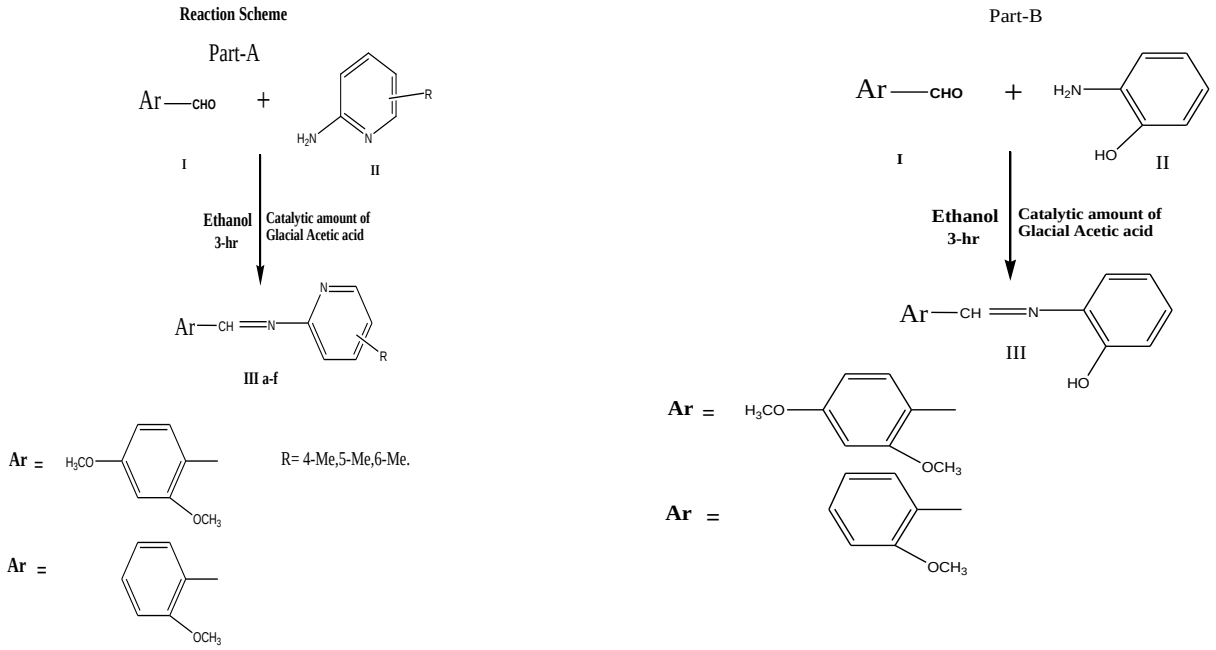
In addition, the presence of nitrogen and oxygen donor atom in the complexes make these compound effectives and stereo specific catalyst for oxidation, reduction hydrolysis other transformation and show biological activity i.e. some drug have increased activity when administered as metal complexes.[2-3] In previous studied have investigated the synthesis and Characterization of various transition metal complexes of novel Schiff bases.[5-14] The complexes of transition metals have been used in solution biometric catalyst for oxygen redox reaction and other oxidative process. Vanadium is physiologically important trace element that found in both anionic and cationic forms with oxidation state ranging from -1 to +5.[15-19] The physic-chemical properties of vanadyl (IV) complex have been used to treat both insulin dependent type-1 and non-insulin-independent type-2.Schiff base important class of compound in medicinal and pharmaceutical fields. They have biological activity including antibacterial, antifungal activity.[20-23] Similarly pyridine derivatives are preferred for long time for variety of biological activities such as CNS depressant, anticancerous , antibiotic, anticonvulsant and may other. Radiolabelled bimolecules are potentially useful tools for cancer diagnosis that are well for tumor for cancer imaging or cancer therapy. Some application of this radionuclide complex or Schiff base with favorable cell membrane permeability have been exploited cancer multidrug resistance.[24]

MATERIAL AND METHOD

All the Reagent used for the synthesis of Ortho substituted Heterocyclic Schiff bases were purchase from Sigma Aldrich A.R. Grade and solvent like Anhydrous ethanol were purified by standard distillation method. The FTIR characterization was recorded on model no. Schimadzu FTIR 8400 S. Spectrometer using KBr pellets and ^{1}H NMR spectra were obtained in $CDCl_3$ Solvents and all above synthesized heterocyclic Schiff bases were tested for their microbiological activity.

General Procedure for Synthesis of Schiff Bases

Schiff bases were prepared by taking equimolar quantity of ortho substituted benzaldehyde (0.01M) and heterocyclic primary aromatic amine (0.01M) in ethanolic solvent in presence of catalytic amount of dilute HCl. The reaction mixture was heated at reflux with stirring for 4-5 hours and then pours the reaction mixture in ice cold water then coloured solid was collected by filtration and recrystallized from ethyl alcohol.



RESULT AND DISCUSSION

Spectroscopic data

I) (E)-N-(2-Methoxybenzylidene)-4-Methyl Pyridine-2-amine.

Yield (70 %); M.P 100-102 ^{0}C; IR (KBr, cm^{-1}): 1285-1240 (OCH_3), 1566 (C=C), HC=N, 1612. (CH_3) (2922.16). ^{1}H NMR ($CDCl_3$, 500 MHz); δ; 6.33-8.35 (m, 7H, Ar-H), 1.22 (s,3H,CH_3). 9.4(S, 1H CH). Elem Anal.calcd for $C_{14}H_{14}N_2O$; C,74.31; H,6.24; N,12.38; O,7.07%; Found C,74.33; H, 6.23; N,12.40; O,7.03 %.

II) (E)-N-(2-Methoxybenzylidene)-5-Methyl Pyridine-2-amine.

Yield (70 %); M.P 105-107 ^{0}C; IR (KBr, cm^{-1}): 1285-1247 (OCH_3), 1566 (C=C), HC=N, 1610. (CH_3) (2922.16). ^{1}H NMR ($CDCl_3$, 500 MHz); δ; 6.34-8.35 (m, 7H, Ar-H), 1.22 (s, 3H,CH_3). 9.5(S, 1H CH). Elem Anal.calcd for $C_{14}H_{14}N_2O$; C,74.31; H,6.24; N,12.38; O,7.07%; Found C,74.32; H, 6.26; N,12.39; O,7.04 %.

III) (E)-N-(2-Methoxybenzylidene)-6-Methyl Pyridine-2-amine.

Yield (70 %); M.P 80-82 ^{0}C; IR (KBr, cm^{-1}): 1280-1247 (OCH_3), 1565 (C=C), HC=N, 1615. (CH_3) (2923.16). ^{1}H NMR ($CDCl_3$, 500 MHz);δ; 6.44-8.45 (m,7H,Ar-H), 1.23 (s,3H,CH_3). 9.4(S, 1H CH). Elem Anal.calcd for $C_{14}H_{14}N_2O$; C,74.31; H,6.24; N,12.38; O,7.07%; Found C,74.37; H, 6.27; N,12.36; O,7.05 %.

IV) (E)-N-(2,4, dimethoxybenzylidene)-4-Methyl Pyridine-2-amine

Yield (70 %); M.P 92-94 ^{0}C; IR (KBr, cm^{-1}): 1263-1247 (OCH_3), 1569 (C=C), HC=N, 1620. (CH_3) (2920.16). ^{1}H NMR ($CDCl_3$, 500 MHz);δ; 6.47-7.84 (m,7H,Ar-H), 1.59 (s,3H,CH_3). 9.2(S,1H CH). Elem Anal.calcd for $C_{15}H_{16}N_2O_2$; C,70.29; H,6.29; N,10.93; O,12.48%; Found C,70.26; H, 6.27; N,10.95; O,12.46 %.

V) (E)-N-(2,4, dimethoxybenzylidene)-5-Methyl Pyridine-2-amine.

Yield (70 %); M.P 108-110 ^{0}C; IR (KBr, cm^{-1}): 1263-1247 (OCH_3), 1568 (C=C), HC=N, 1623. (CH_3) (2918.16). ^{1}H NMR ($CDCl_3$, 500 MHz);δ; 6.45-7.88 (m,7H,Ar-H), 1.55 (s,3H,CH_3). 9.3(S, 1H CH). Elem Anal.calcd for $C_{15}H_{16}N_2O_2$; C,70.29; H,6.29; N,10.93; O,12.48%; Found ,70.27; H, 6.28; N,10.96; O,12.45 %.

VI) (E)-N-(2,4, dimethoxybenzylidene)-6-Methyl Pyridine-2-amine.

Yield (70 %); M.P 95-97 ^{0}C; IR (KBr, cm^{-1}): 1264-1245 (OCH_3), 1560 (C=C), HC=N, 1625. (CH_3) (2916.15). ^{1}H NMR ($CDCl_3$, 500 MHz); δ; 6.44-7.89 (m, 7H, Ar-H), 1.56 (s, 3H,CH_3). 9.4(S, 1H CH). Elem Anal.calcd for $C_{15}H_{16}N_2O_2$; C,70.29; H,6.29; N,10.93; O,12.48%; Found ,70.28; H, 6.26; N,10.95; O,12.46 %.

VII) (E)-2-(2-Methoxybenzylidene amino) phenol.

Yield (70 %); M.P 92-94 ^{0}C; IR (KBr, cm^{-1}): 1263-1246 (OCH3), 1570 (C=C), HC=N, 1635. (CH_3) (2918.14). ^{1}H NMR ($CDCl_3$, 500 MHz); δ; 6.46-7.87 (m, 7H, Ar-H), 3.96 (s, 3H, OCH_3). 9.2(S, 1H CH). Elem Anal.calcd for $C_{14}H_{13}NO_2$; C,73.99; H,5.77; N,6.16; O,14.08%; Found, 70.96; H, 5.76; N,6.15; O,14.06 %.

VIII) (E)-2-(2,4, dimethoxybenzylidene amino) phenol.

Yield (70 %); M.P 105-107 ^{0}C; IR (KBr, cm^{-1}): 1265-1245 (OCH3), 1572 (C=C), HC=N, 1640. (CH_3) (2917.13). ^{1}H NMR ($CDCl_3$, 500 MHz); δ; 6.47-7.88 (m, 7H, Ar-H), 3.94 (s, 3H,OCH_3). 9.3(S, 1H CH). Elem Anal.calcd for $C_{15}H_{15}NO_3$; C,70.02; H,5.88; N,5.44; O,18.66%; Found ,70.03; H, 5.87; N,5.42; O,18.65 %.

The **^{1}H NMR** Spectrum of synthesized heterocyclic Schiff base (III-a-III-h) show important peak for the

azomethine HC=N is 9.4 S, H.The peak Observed at multiplate for aromatic proton (6.95-8.35 M and show methoxy peak observed at 3.95 S 3H OCH_3.

FTIR

IR spectra gives valuable information about different functional group present in synthesized ligand i.e. (III-a to III-h) from the data obtained. Absence of characteristic band of C=O and $–NH_2$ confirm the formation of proposed azomethine group and show frequency of HC=N at 1612 cm^{-1}. The alkyl aryl ether i.e. ortho substituted methoxy showed in the range of 1285-1240 cm^{-1}. The strong peak for (C=C) unsaturation was confirmed by the observed peak in the region 1566 cm^{-1} and 750 cm^{-1} presence of aromatic ring has been identified.

FESEM

The synthesized heterocyclic Schiff bases were screening for scanning electron microscope for the purpose of understanding the crystal structure of heterocyclic azomethine group.SEM also detect by comparing the different kind of material and we also to make more efficient material for solar panel to collect sun-ray.

The synthesized heterocyclic Schiff's base was obtained in crystalline form so that it will characterized by the hope to understand nature of crystal and crystal structure.

Biological Activity: The Antibacterial and antifungal activity of the synthesized heterocyclic Schiff bases have been done with help of Disc diffusion method at Disc size 6 mm concentration100 mg/ml using bacterial strain of gram positive and negative bacteria i.e.(*S.Aures.E.Coli*) respectively and fungi species i.e.(*A.niger, C.Albicans*). The zone of inhibition is measured in mm and compared to standard drug Chloramphenicol and Amphotericin-B. The synthesized heterocyclic Schiff bases shown antibacterial antifungal activities summarize in table no.1.

Method Used and Concentration of Compound

Agar diffusion assay [Disc diffusion method, Disc size 6 mm] stock solution [1000 microgram per ml] of each compound was prepared in distilled water. Assay carried out by taking concentration 100 microgram per disk. disk. Hi-media antibiotics disk: Chloramphenicol (10 microgram/ disk), moistened with water are used as standard.

Zone of Inhibition

The Synthesized heterocyclic Schiff's bases i.e. ligand shown antibacterial antifungal activities summarize in given table.

Table.

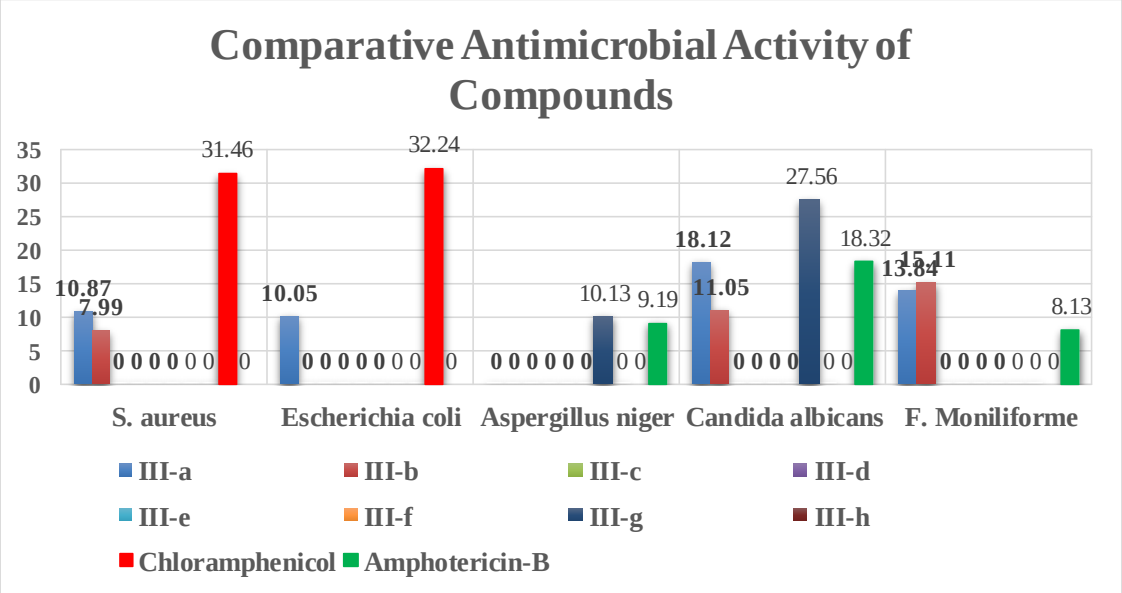
Sr. No.	Sample code	*S.aures*	*E.coli*	*A.niger*	*C.albicans*	*F.moniliforme*
1)	III-a	10.87	10.05	Nil	18.12	13.84
2)	III-b	7.99	Nil	Nil	11.05	15.11
3)	III-c	Nil	Nil	Nil	Nil	Nil
4)	III-d	Nil	Nil	Nil	Nil	Nil
5)	III-e	Nil	Nil	Nil	Nil	Nil
6)	III-f	Nil	Nil	Nil	Nil	Nil
7)	III-g	Nil	Nil	10.13	27.56	Nil
8)	III-h	Nil	Nil	Nil	Nil	Nil
	Chloramphenicol	31.46	32.24	NA	NA	NA
	Amphotericin B	NA	NA	9.19	18.32	8.13

The comp(III-a) and (III-b) was found to show moderate activity than standered so the zone of inhibition of synthesized heterocyclic Schiff bases is **10.87** mm and **7.99** mm respectively against ***S.aures*** and (III-b) they also show moderate activity against ***E.coli*** than its standard so its zone of inhibition is **10.05** mm against Chloramphenicol.

Some synthesized comp i.e. III-g was found to show potent antifungal activity than its standard against **Amphotericin-B** so its zone of inhibition is **10.13** mm and its standard **9.19** mm and some comp i.e. III-a, III-b and III-g was found to show moderate to excellent activity than its standard so zone of inhibition is **18.12**, **11.05**, and **27.56** mm respectively. Against Amphotericin-B and its zone is **18.32** mm.

The comp III-a and III-b was found to show potent activity against ***F.Moniliforme*** its zone of inhibition **13.84**,**15.11** mm respectively and its standard is **8.13** mm as shown in graph-1.

Comparative Analysis of Antimicrobial Activity



Graph. 1: Comparative study of zone of inhibition.

Antioxidant Activity (Free Radical Scavenging Activity)

All synthesized heterocyclic Schiff bases are screening for their in vitro free radical scavenging activity by the DPPH method.

A Schiff base ligand derived from aromatic substituted aldehyde and heterocyclic primary amine their antioxidant activity was screened by DPPH method and they do not response to above activity. The ability of Schiff bases to scavenge free radical is an important property and Antioxidant thus play an important role to protect the human body against damage by reactive oxygen species to determine the DPPH radical scavenging activity % radical scavenging activity was calculated using the following formula.

$$\text{DPPH radical scavenging activity (\%)} = 1 - \left[\frac{\text{As 517of Sample}}{\text{As 517 of control}}\right] * 100$$

Metal complex was prepared by using metal acetate and heterocyclic Schiff bases. The Anti-oxidant activity of the complexes can be attributed to the electron withdrawing effect of the metal ions which facillates the release of hydrogen to reduce the DPPH radical.

CONCLUSION

This study concluded that among synthesized heterocyclic Schiff bases i.e. ligand were from the condensation of ortho Para substituted benzaldehyde and heterocyclic primary amine to form azo heterocyclic Schiff bases that is ligand to shows Co-ordination ability with various transition metal such as Ni,Cu, Fe, Co, Cd, to form stable complexes. And these Schiff bases were found to show the potent antifungal activity against *Candida albicans* and show the moderate to good activity against bacteria i.e. *Staphylococcus aures* and *Escherichia coli*.

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REFERENCES

1. K. Arora, K. P Sharma. Synth. Reaction. Inorganic. met-org, chem., 2002; 32: 913.
2. C. Celik, M. Tumer, S. Serin. Synth. Reaction. Inorganic met-org.chem, 2002; 32: 1839.
3. R.Ramesh, M.Sivagamasundri, Synth.Reaction.Inorganic.met-org Chem. 2003; 33: 899.
4. R.C.Maurya, R. Verma, T.Singh. Synth. Reaction. Inorg. Met-org Chem, 2003; 33: 309.
5. I. Sheikhshoari. J. Coord. Chem, 2003; 56: 463.
6. L. F. Lindoy, W. E. Moody, D. Taylor. Inorg. chem, 1978; 16: 224.
7. N. A. Patwardhan, S. Gopinathan, C. Gopinathan, India J. Chem, 1978; 16: 224.
8. R. C. Maurya, P.Patel, S. Rajput. Synth. Inorg. met-org. Chem, 2003; 33: 817.
9. E. Canpolat, M. Kaya, J. Coord. chem, 2004; 57: 1217.
10. S. A. Sharma, H. Omara. Spectrosc. Left, 2001; 34: 49.
11. S. Satapathy, B. sahoo. J. Inorg. Nucl. Chem, 1970; 32: 2223.
12. K. P. Deepa, K. K. Arvindkhan. Synth. React. Inorg. met-org. Chem, 2000; 30: 1601.
13. E.canpolat, M.Kaya, J.Coord.Chem, 2005; 58: 1063.
14. M.A.Hundekar, D.N.Sen, Indian J.Chem.Sec A, 1984; 23: 477.
15. D.G.Barceloux, Vandium, J.Taxicol, Clin.Taxicol.37:265-278 (1984).
16. I. G. Macara, Trend Biochem. Sci., 1980; 92-94.

17. D. Rehdar. Angew chem. Int. Ed. Engl, 1991; 130: 148-167.
18. A. W. Kianfer and S. Mohebbi, J. Iran. Chem. Soc, 2007; 4: 215-220.
19. H. Sakkurai, A. Tamura, J. Fugono, H. Yasui and T. Kiss, Coord, Chem. Rev. 2003; 245: 31-37.
20. A.A.Azza. Abu-hussen, Synthesis and spectroscopic Studies on ternary bis- Schiff base complexes having oxygen/nitrogen donars. J. Coord. Chem, 2006; 59: 157-176.
21. M.S.Karthikeyan, D.J.Prasad, B.Poojary, K.S.Bhat, B.S.Holla, & N.S kumara,. Synthesis and biological activity of Schiff base and Mannich base bearing 2,4-dichloro-s-fluorophenyl moiety, Biorg, Med, Chem, 2006; 14: 7482-7489.
22. R.Mladenova, M.Ignatova, N.Manolova, T Petrova and Raskkovi, Preparation, Characterization and biological activity of Schiff base compound derived from 8-hydroxy quinoline-2-Carboxyaldehyde and Jeff amine ED.rur.Polym.J., 2002; 38: 989-1000.
23. O.M Walsh, M.J. Meegan, R.M. Prendergast, and T.A. Nakib. Synthesis of 3-acetoxyazetidin-2-ones and 3-hydroxyazetidin 2-ones with antifungal and antibacterial activity. rur.j.Med.Chem, 1996; 31: 989-1000.
24. S.S.Jurisson and J.D. Lydon potential Technetium small molecule radiopharmaceuticals Chem.Rev., 1999; 99: 2205-2218.