Original Article

2-(((4h-1,2,4-Triazol-4-Yl)Imino)Methyl)Phenol Derived Schiff Bases And Their Pharmacological Importance

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Abstract

A facile method has been developed for the synthesis of Schiff bases derived from 4-Amino-1,2,4-triazole with 2-Hydroxybenzaldehyde (Salicylaldehyde) and their complexes with the Mn(II) and V(III) have been synthesized. Derived Metal complexes shown that they have a greater impact than their parent medications. Elemental analysis, IR, and ESR XRD studies have been used to characterize the prepared complexes. The results of the spectroscopic investigations suggested that the metal complexes' have octahedral geometry and the presence of the azomethine nitrogen group in coordination with the metal ion have been projected. Schiff bases and their derived metal complexes have potent biological potential (Antibacterial).

Keywords: 4-Amino-1,2,4-triazole, conductivity, Schiff base, Spectral studies, Antibacterial Property

1.INTRODUCTION

Schiff bases are aldehyde or ketone like compounds in which the carbonyl group is replaced by an imine or azomethine group.[1-2] These are used as chelating ligands in the field of coordination chemistry and their metal complexes are of great interest for many years.[3] Many Schiff bases and their complexes have been widely studied because of their industrial and biological applications. [4-5]Schiff bases, as an important class of ligands plays an important role in the development of coordination chemistry as they can easily form stable complexes with most of the transition metals.[6] The coordination compounds of transition metals are found to have added a great deal of interesting flexibility in the areas such as biological, industrial, pharmaceutical, catalysis and material chemistry.[7-10] Schiff base–transition metal complexes are one of the most adaptable and thoroughly studied systems.[11-12] These complexes have also applications in clinical[13] and analytical fields.[14]

2. MATERIALS AND METHODS

2.1 Chemicals

All the chemicals used were of GR/AR grade. A pure sample of 4-Amino-1,2,4-Triazole, molecular formula $C_2H_4N_4$ was obtained from Sigma Aldrich Ltd. The metal salt of $MnCl_2$ and VCl_3 were from Hi-media Pharmaceuticals Ltd. Solvents used were ethanol, acetone, and DMF.

2.2 Synthesis of Ligand:

Equimolar mixture of 4-amino-1,2,4-triazole(0.1 mol) and 2-hydroxybenzaldehyde (0.1 mol) in 30 ml of ethanol was refluxed for about 2 hours followed by the addition of few drops of Sulphuric acid. The product, which wasseparated out as a crystalline solid on cooling, was collected and recrystallized from the ethanol. The ligand was titrated against 0.02

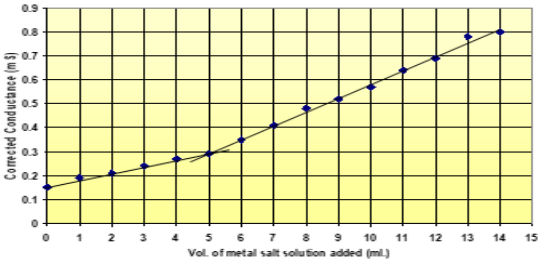


Fig: 1. Conductometric titration (Monovariation method) 4-Amino-1,2,4-Triazole (AT-S) Schiff base with metal Mn(II) salt

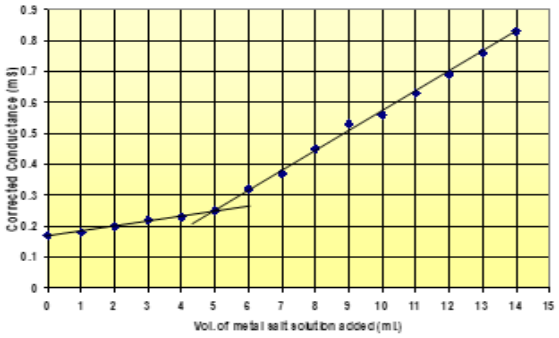
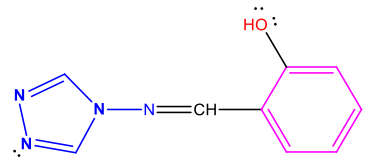


Fig: 2. Conductmetric Titration (Monovariation method) 4-Amino-1,2,4-Triazole (AT-S) Schiff base with metal V(III) salt

M metal solution using mono-variation method and conductance was recorded after each addition of metal salt. Graph is plotted between corrected conductance and volume of added metal salt (fig. 1 and 2). From the equivalence point in the graph, it has been concluded that the complex formation of the ligand and Mn(II) and V(III) metal takes place in the ratio of 2:1 (L: M).



2-(((4*H*-1,2,4-triazol-4-yl)imino)methyl)phenol

Fig.3 Synthesized Schiff Base

2.3 Synthesis of Metal Complexes:

For the synthesis of complexes[15-,16] AT-S-Mn and AT-S-V ligand-metal ratio was determined by conductometric titration using monovariation method on systronics conductivity meter using dip type electrode. 20ml of the ligand (0.01M) was diluted to 200ml using pure ethanol and titrated against metal salt solutions like $MnCl_2.6H_2O$ (0.02M) and VCl_3 (0.02M) in the same solvent. Conductance was recorded after each ml addition of metal salt solution. Graph is plotted **(fig. 4 and 5)** between corrected conductance and volume of metal salt solutions added separately. From the equivalence point in the graph, it has been concluded that the complexes formation of the ligand with the metals $MnCl_2.6H_2O$ and VCl_3 takes place in the ratios of 1:2 (M:L) i.e.; ML_2).Conductmetric titrations support 2:1 (L:M) ratio in the complexes, which was further supported by Job's method of continuous variation[17] as modified by Turner and Anderson[18]

Modified Job's Method

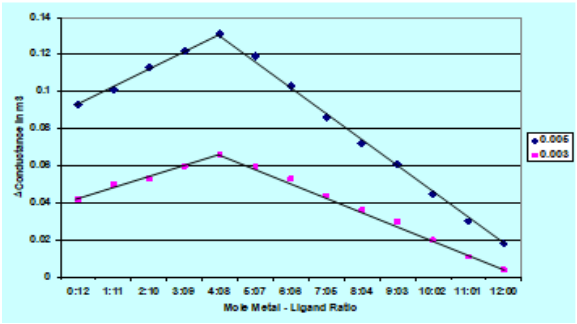


Fig: 4. AT-S with $MnCl_2.4H_2O$

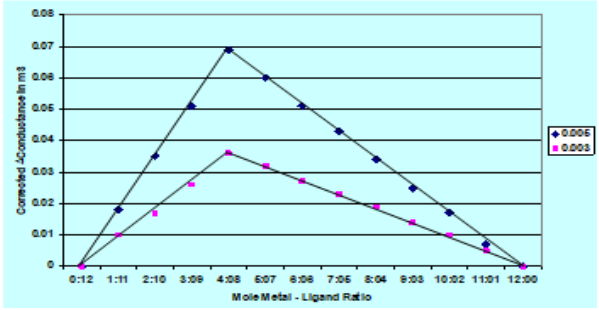


Fig: 5. AT-S with VCl_3

The metal complexes were prepared by mixing 50ml of Schiff base (0.04M) solution in the appropriate metal salts like $MnCl_2.6H_2O$ (0.02M) and VCl_3 (0.02M) in 50 ml Ethanolic solutions each. The resulting solutions were checked for pH

and the pH was adjusted by adding few drops of N/10 NaOH solution. This solutions were refluxed for 2 hours for $MnCl_2.6H_2O$ and 3 hours for VCl_3 the refluxed solutions were kept for 2-3 days. Solid crystalline compound appeared in the reaction mixtures which were filtered, washed with same solvent and dried over fused $CaCl_2$.

2.4 Physical Measurements:

Elemental analysis shows that the 1:2 (M:L) ratio for the synthesized metal complex. The synthesized metal complexes are Daisy and Grass Green in colour and stable at room temperature. The lower values of molar conductance 18.2 $\mathbf{\Omega^{-1} cm^2 mol^{-1}}$ and 15.7 $\mathbf{\Omega^{-1} cm^2 mol^{-1}}$ measured in 10^{-3} M DMF of the complexes indicates that its non-electrolytic nature[23,24]. The low conductivity value is in agreement with low solubility of the complex in water, ethanol, chloroform, acetone and most organic solvents. On the other hand, complexes are soluble in DMSO and DMF and decomposed at higher temperatures (325-330^{0}C For Mn complex and 293-295^{0}C for V Complex). Elemental analysis was performed on Perkin Elmer 24^{O}C Model Elemental Analyzer at Powai, IIT, Bombay. The infra-red spectra of Schiff base and derived complexes were recorded with FT-IR spectrophotometer ModelRZX (Perkin Elmer) using KBr pellets in the range of 400 cm^{-1}-4000cm^{-1} at SAIF, Panjab University Chandigarh. Electronic spectra were also recorded on a UV-VIS-Spectrophotometer Model Synthesis Lambda 750 Perkin Elmer at SAIF, Panjab University, Chandigarh.

2.5 Biological Activity:

Schiff bases and its derived metal complexes were tested against one Gram-positive and one Gram-negative bacterial strains. *The in-vitro* antibacterial activity of the Schiff base and its derived metal complexes was determined by Disc diffusion method[19] against bacterial strains. The test organisms were grown on Nutrient Agar medium in Petri plates and then agar plates were left to solidify at room temperature. After solidification, the disc of Whatman filter paper with 20µL of prepared Schiff base and metal complex solutions was carefully placed with the help of forceps at the center of the Petri dish and then kept at 37±0.1ºC for 24 hours in an incubator. The zone of inhibition was measured.

2.6 X-Ray diffraction studies of Schiff bases and their metal complexes

The x-ray region of the electromagnetic spectrum is probably the most generally useful region for structural studies, analysis and characterization of substances. The X-ray diffraction studies of 4-Amino-1,2,4-Triazole derived Schiff bases and their metal complexes were carried out at MANIT, Bhopal Using Cu target X-ray tube. Following compounds were studied by powder diffraction method. The results have been shown in Figs 6 to 7.

AT-S-V

2theta (θ)	FWHM
1. 16.99058	0.2026
2. 19.74874	0.2198
3. 23.38661	0.22072
4. 26.84089	0.23644
5. 29.31209	0.6476
6. 30.00517	0.52789
7. 34.33973	0.28857
8. 39.3914	0.40515
9. 45.4501	0.23574
10. 55.35828	0.28849

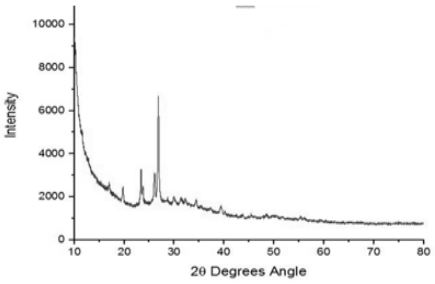


Fig: 6. X-Ray Diffraction Studies of AT-S-V

AT-S-Mn

2theta (θ)	FWHM
1. 16.38738	1.00095
2. 19.29358	0.28046
3. 22.94589	0.20169
4. 23.65892	0.27948
5. 27.18042	0.73257
6. 28.965	0.18363
7. 32.86978	0.39762
8. 34.36339	0.92371
9. 36.52863	0.48134
10. 41.31902	0.32189
11. 43.49296	0.40197
12. 46.99533	0.28881
13. 59.11198	0.02841
14. 62.34357	0.46645

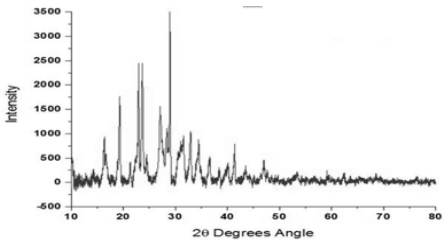


Fig: 7. X-Ray Diffraction Studies of AT-S-Mn

3. RESULTS AND DISCUSSION

The Schiff bases are subjected to elemental analyses. The results of elemental analyses (C, H, N, S) with molecular formula are presented in Table 1. The analytical data for the complexes suggested 1:2 stoichiometry for the entire synthesized complex.

Ligand /Complex	Molecular Weight	Color	M. P (ºC)	Elemental Analysis (%) Found (Calculated)			
				C	H	N	M
At-S $C_9H_8N_4O$	188.18	White	180 ^{0}C	58.21 57.44	4.00 4.25	30.92 29.78	- -
[Mn((At-S)$_2$].H2O $C_{18}H_{18}N_8O_4Mn$	465.32	Daisy	326 ^{0}C	46.95 46.44	3.80 3.87	25.01 24.08	11.70 11.61
[V(At-S)$_2$] $C_{18}H_{14}N_8O_2V$	425.29	Grass Green	294 ^{0}C	49.25 50.80	3.20 3.29	26.00 26.34	11.69 11.76

Table: 1 Elemental analysis of Schiff base and its derived metal complex

3.1 IR Spectral Studies:

The comparative interpretation of Schiff base and derived metal complexes were shown in table 2. The IR spectra of complexes indicates that the Schiff base (ligand) acts as a tridentate ligand, using phenolic oxygen[20] and azomethine nitrogen and nitrogen of triazole ring as donor atoms. The ligand shows the strong band at 3325 cm^{-1} due to phenolic –OH group. This band is absent in the respective metal complexes indicating the involvement of this group in complex formation.[21-22] The IR spectrum of the Schiff base shows a strong band at 1620 cm^{-1} attributed to $^{\nu}$(HC=N) stretching vibrations of the azomethine group, which gets shifted to higher frequency regions 1638 cm^{-1} and 1645 cm^{-1} in the complexes representing involvement of the nitrogen atom of azomethine group.[23-24] The band at 1469 cm^{-1} is due to the $^{\nu}$(C=N) stretching and this frequency shifted to a lower frequency value of 1545 cm^{-1} and 1522 cm^{-1} in the complexes confirming the involvement of the (C=N) inthe coordination with the metal ions[25]. The stretching vibrational band C-O of the ligand lies at 1246 cm^{-1} frequency.[26-27] This band shifts to 1426 cm^{-1} lower frequency side in the complex of Mn(II) and 1373 cm^{-1} a lower frequency side in the complex of V(III).

Ligand/ Complex	(HC=N)	C-O	C=N	OH	Chelate ring
AT-S	1620s	1246s	1469s	3325s	1435s
AT-S-Mn	1638s	1426s	1545s	-	1428s
AT-S-V	1645s	1373s	1522s	-	1415s

Table 2: IR Spectra Value in terms of Wave numbers

3.2 Electronic Spectra

the electronic spectra of Mn(II) complexes displays bands in the range of 26739-26742cm-1, 20701-20745, 19802-19811 and 16000 which can be assigned to $^6A_1g \rightarrow {}^4T_1g$, $^6A_1g \rightarrow {}^4Eg$, $^6A_1g \rightarrow {}^4T_2g$, and $^6A_1g \rightarrow {}^6T_1g$ transitions and V(III) complex are consistent with the formation of an octahedral geometry with the appearance of three bands at 22728, 18518 and 10472 cm^1 corresponding to the transitions. $^3A_2g \rightarrow {}^3T_1g(P)$, $^3A_2g \rightarrow {}^3T_1g(F)$ and $^3A_2g \rightarrow {}^3T_2g(F)$ [28-29].

3.3 Biological Activity

The *in vitro* antibacterial investigation results are given in (Table-3 and Fig 8) respectively. It has been observedthat all compounds exhibited very significant and better antibacterial activity. The free ligand (Schiff base) shows potent activity against *B. subtilis* bacterial strain with inhibition of 10 mm. Among the metal complexes Mn (II) complex show higher antibacterial activity in case of *B.subtilis* with zone of inhibition of 15 mm. The V(III) complex show higher activity in case of *P. aeroginosa* with zone of inhibition of 15 mm. These observations show that both of the metal complexes are more active than the free ligand.

Compound	*B. subtilis*	*p. aeroginosa*
AT-S	10±0.22	13±0.44
AT-S-Mn	15±0.45	14±0.23
AT-S-V	13±0.35	15±0.48
Imipenem	15±0.32	16±0.35

Table: 3- Showing the % Inhibition of Schiff base (AT-S) and its derived metal

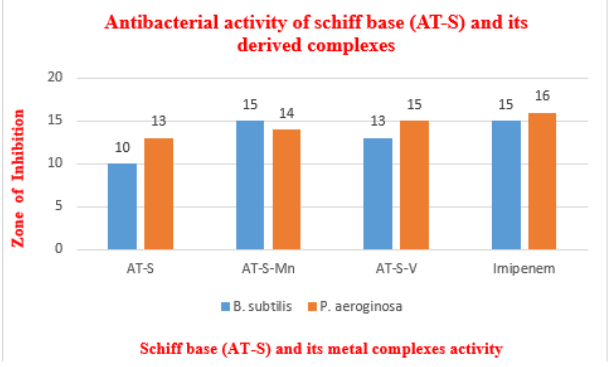


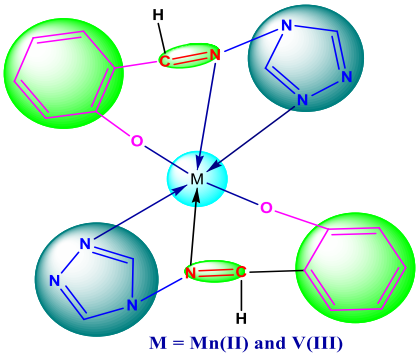
Fig: 8: Antimicrobial Activity of Schiff base (AT-S) and derived metal complexes

3.4. X-Ray diffraction studies of Schiff bases and their metal complexes

X-ray diffraction of the Schiff bases and metal complexes derived from these Schiff bases are entirely different (figs 5 to 6). All the reflections in the complexes are new ones and the patterns are also new ones and fairly strong which suggests that there is a complete conversion of reactants into products[30-35].

CONCLUSION:

On the basis of above results we conclude that the newly synthesized Schiff base acts as a neutral tridentate ligand coordinating through the oxygen of the phenolic group, the nitrogen of the azomethine group and triazole nitrogen. On complexation, complexes show enhanced biological activities than their parents. On complexation, complexes show enhanced biological activities than their parents.



M = Mn(II) and V(III)

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