



Synthesis, characterization and biological studies of a new Schiff base derived from salicylaldehyde, 4-aminoantipyrine and 2-aminothiazole (SAAPAT) and its metal complexes.

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Abstract: Biologically important Schiff base and their complexes from 3d metals have been synthesized by using salicylaldehyde, 4-aminoantipyrine and 2-amino thiazole. Schiff base and complexes have been characterized by molecular weight determination, magnetic measurement and elemental analysis. based on study geometry, yield, color has been propose. Ligand and their metal complexes are tested antibacterial activity.

Keywords: Amino antipyrine, Amino thiazole, Antibacterial activity, Salicylaldehyde.

Introduction:

A new, efficient and environmental friendly procedure for the synthesis of a series of salicylaldehyde-based Schiff bases and their metal complexes is followed. The work involved the condensation of salicylaldehyde with various amines, both aromatic and aliphatic and the Schiff bases formed were complexed with a transition metals Co, Ni, Cu, Zn. This green synthetic approach was compared with conventional procedure and found to have advantages like good yield and reduction in reaction time and byproducts. The synthesized Schiff bases and their complexes were characterized by FTIR. The antibacterial activity of complexed and noncomplexed Schiff bases were compared against Escherichia coli and the complexes is found to have better antibacterial activity.

A Schiff base is a nitrogen analogue of an aldehyde or ketone in which the C=O group is replaced by C=N-R group. It is usually formed by the condensation of an aldehyde or ketone with a primary amine². In general mechanism of synthesis of Schiff bases, an amine reacts with a carbonyl compound by nucleophilic addition. This forms a hemiaminal, followed by a dehydration to produce imine. Schiff bases have a large number of synthetic uses in organic chemistry. Schiff bases appear to be an important intermediate in a number of enzymatic reactions.

Schiff base complexes have attracted wide attention due to their important role in analytical chemistry, organic synthesis, refining of metals, electroplating and photography⁶. The nature of metal ion determines the properties of the complexes. Schiff bases can acts as a potential site for biologically active compounds. Various transition and inner transition metals form complexes with bi, tri and tetra dentate Schiff bases containing nitrogen and oxygen donor atoms^{7, 8}. Several studies have revealed that by condensation of salicylaldehyde with different primary amines and their metal complexes showed potential antibacterial

activity. The antibacterial potency of Schiff bases increased upon chelation/complexation against tested bacterial stain.

It is worthwhile to mention here that the synthesis of these Schiff bases known in the literature involves use of methanol/ethanol as solvent in large amount, and processes requires large reaction time. We here report a green and efficient method for the synthesis of Schiff bases in which less amount of solvent is used. The easy workup, facile conditions, fast reaction rate and good yield of the reaction makes the present methodology attractive.

Experimental

Materials

Chemicals like salicylaldehyde, 4-aminoantipyrine and 2-aminothiazole was provided by Sigma Aldrich Company and they were used as supplied. All metal (II) salts were used as chlorides. The FTIR spectra were recorded on a Bruker IFS55 spectrometer using KBr pellets.

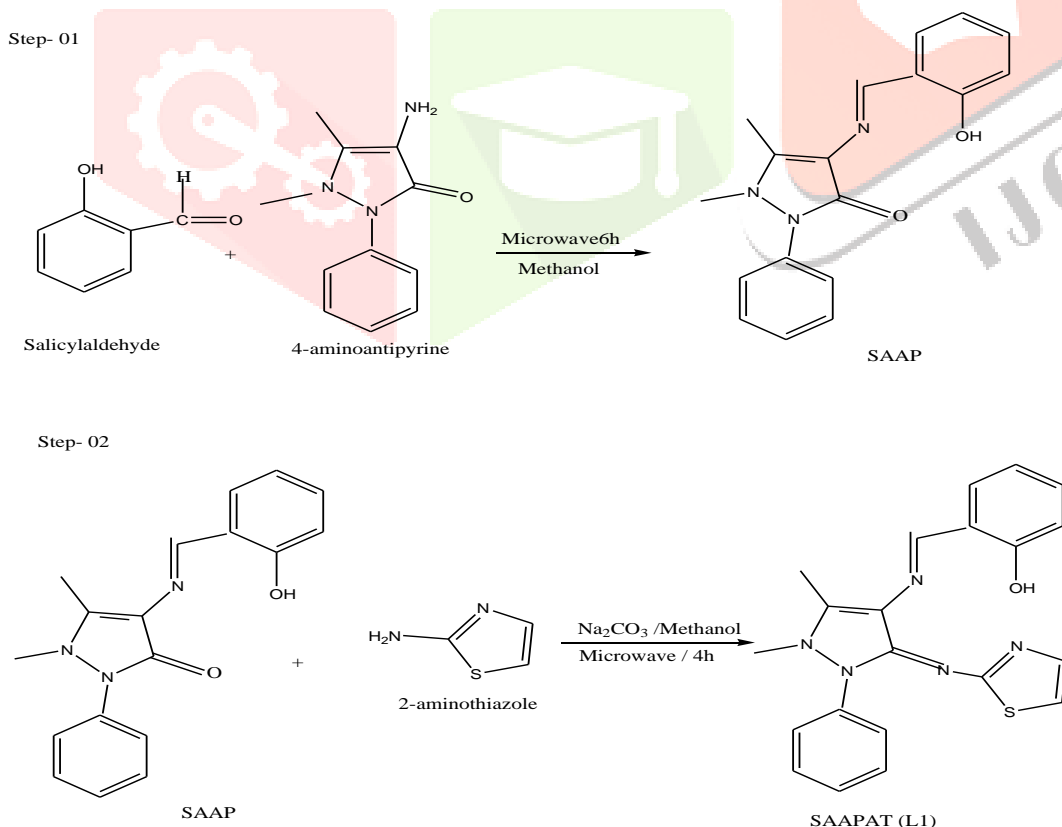
3.1 General Procedure for the synthesis of Schiff base and its metal complexes

Step 1 synthesis of SAAP

The Schiff base¹ (SAAP) was prepared by refluxing equimolar quantities of salicylaldehyde and 4-aminoantipyrine in hot methanol for 6 h with constant stirring. The precipitate was filtered and washed with ethanol.

Step 2 Synthesis of Schiff base, SAAPAT

An methanolic solution of SAAP (0.01 mol) was added to an methanolic solution of 2-aminothiazole (0.01 mol) and the resultant mixture was microwaved for 6- 10 h after adding anhydrous sodium carbonate. The sodium carbonate filtered off from the reaction mixture after completion of the reaction and the solvent was evaporated. The solid separated was filtered and recrystallized from ethanol. The route for the synthesis of the Schiff base ligand is given in (Scheme 3.1)

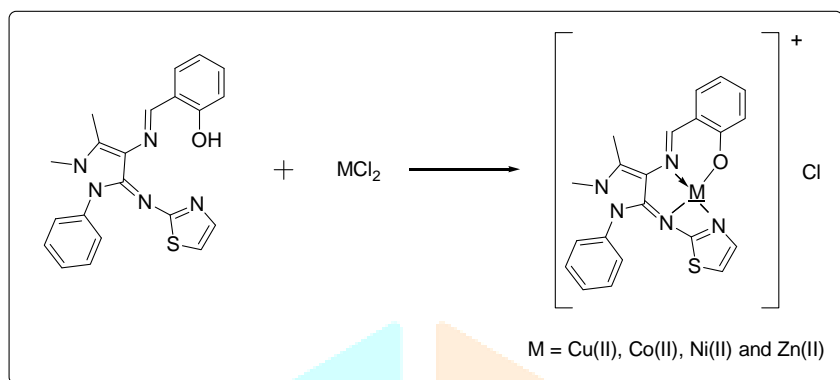


Scheme 3.1

Schematic route for the synthesis of Schiff base SAAPAT 4.2.3 Synthesis of metal complexes using

SAAPAT

An methanolic solution of metal (II) chloride (2 mmol) was stirred with an methanolic solution of the Schiff base (2 mmol) containing a few drops of triethylamine. The above mixture was magnetically stirred and refluxed for 4 h. The resulting solution was reduced to one-third on a water bath. The solid complex precipitated was filtered off and washed thoroughly with ethanol and dried in *vacuum* .



Result and discussion

The Schiff base ligand and its complexes have been synthesized and characterized by spectral and elemental analytical data. The Schiff base is soluble in all common organic solvents but not in water. All the complexes are stable at RT, soluble in DMF, DMSO and MeCN but insoluble in water.

Elemental analysis and molar conductivity measurements

The analytical data for the ligand and the complexes together with some physical properties are summarized in **Table 3.1** The analytical data of the complexes correspond to the general formula $MLCl$, where $M = Cu(II)$, $Co(II)$, $Ni(II)$ and $Zn(II)$; $L = C_{21}H_{19}N_5OS$. The magnetic susceptibilities of the complexes at RT are consistent with square-planar geometry around the central metal ion.

conductivities of $10^{-3}M$ solutions at RT were measured. The higher conductance values ($120-144 \Omega^{-1}cm^2 mol^{-1}$) of the complexes indicate their electrolytic nature.

Table 3.1 Physical and analytical data of the synthesized Schiff base and its

complexes

Compound	Empirical Formula	Yield (%)	Colour	Found (Calculated) (%)				Formula weight	μ_{eff} (B.M.)	χ_{M} (cm ² mol ⁻¹)
				M	C	H	N			
SAAPAT(L ¹)	C ₂₁ H ₁₉ N ₅ O ₅ S	70	Brown	-	64.26 (64.76)	4.24 (4.92)	17.25 (17.98)	389.4	-	-
[CuL ¹] Cl	[CuC ₂₁ H ₁₈ N ₅ O ₅] Cl	66	Black	12.66 (13.04)	51.89 (51.74)	3.14 (3.72)	14.17 (14.37)	487.4	132	1.71
[CoL ¹] Cl	[CoC ₂₁ H ₁₈ N ₅ O ₅] Cl	72	Red	12.22 (12.21)	52.42 (52.24)	3.37 (3.76)	14.34 (14.50)	482.8	120	3.52
[NiL ¹] Cl	[NiC ₂₁ H ₁₈ N ₅ O ₅] Cl	70	Green	12.14 (12.16)	52.35 (52.26)	3.25 (3.76)	14.05 (14.51)	482.6	138	4.20
[ZnL ¹] Cl	[ZnC ₂₁ H ₁₈ N ₅ O ₅] Cl	56	Brown	13.17 (13.36)	51.20 (51.55)	3.59 (3.71)	14.17 (14.31)	489.3	144	Diamagnetic

Antibacterial activity

The Schiff base ligand and its complexes have been screened for their antibacterial activity against various pathogenic bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus*. *Tetracycline* was used as the standard for bacterial studies.

The zone of inhibition (diameter in mm) values of the compounds against the growth of microorganisms are summarized in It has been observed that the metal complexes have a higher activity than the free ligand. Probably this may be due to the greater lipophilic nature of the complexes. The increase in antibacterial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity effect of the metal and ligand. Such increased activity of the metal complexes can be explained on the basis of Overtone's concept¹⁶ and Tweedy's chelation theory¹⁷. According to Overtone's concept of cell permeability the lipid membrane that surrounds the cell favours the passage of only lipid soluble materials due to which liposolubility is an important factor which controls the antimicrobial activity. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelate ring and enhances the lipophilicity of the complex. The increased lipophilicity leads to breakdown of the permeability barrier of the cell and thus retards the normal cell processes.

Table 3.2 Antibacterial activity data for the Schiff base and its complexes

Compound	<i>E. coli</i>			<i>P. aeruginosa</i>			<i>B. subtilis</i>			<i>S. aureus</i>		
	20µg	40µg	60µL	20µg	40µg	60µg	20µg	40µg	60µg	20µg	40µg	60µg
SAAPAT (L ¹)	10	11	13	9	10	11	10	11	12	-	14	15
[CoL ¹]Cl	10	14	15	14	17	17	11	12	14	-	12	13
[CuL ¹]Cl	15	17	21	-	13	14	10	15	20	15	17	20
[NiL ¹]Cl	10	13	17	14	19	19	-	12	13	-	-	10
[ZnL ¹]Cl	11	13	15	14	19	19	10	12	14	-	12	14

Conclusion:

The ligand and all complexes were synthesized are of good yield. The effect of ligand coordination with different 3d metals also showed. On the basis of elemental analysis, IR, NMR data structural geometry of above complexes are determined as tetrahedral and square planar a geometry. Ligand biological activity is found to be different than their metal complexes and more effective.

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