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Synthesis, characterisation, antibacterial and antifungal studies on metal complexes with Schiff bases of benzothiazole

Devdatta V. Saraf, Seema I. Habib*, Prafullkumar A. Kulkarni

P.G. Research Center, Department of Chemistry, Yeshwant Mahavidyalaya, Nanded-431602 (MS) India.
Department of Chemistry, G. M. Momin college, Bhiwandi-421302. (MS) India.

Abstract : Four metal complexes of Schiff bases have been synthesized by the reaction of Schiff bases (L_3 and L_4) with the Co and Fe metal acetates. All the metal complexes are ML_2 type where M=Metal and L= Ligand. The elemental analysis suggests the stoichiometry to be 1:2. Magnetic susceptibility data coupled with electronic spectra suggest octahedral structure for the complexes. The structural features have been determined from IR, UV-Vis, ^{1}H NMR, Thermal and XRD spectral analysis. The Schiff bases and its metal chelates were screened for their antimicrobial activity and the metal chelates were found to posses better activity than that of the respective Schiff base.
Keywords : Schiff bases, Co (II) and Fe (III) Metal complexes, spectral analysis and antimicrobial activity.

Introduction

Schiff bases derived from an amine and aldehyde are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively(Arora & Sharma,2003)[1] These complexes are play an important role in the development of coordination chemistry (Sousa et al.,2003;Kou et al.,2004)[2,3]. Thiazole derivatives have been found a number of uses in medicinal and pharmaceutical fields (Malik & Rajeev, 1982)[4]. Some of them have been showed to have antitumor activity (Bradshaw ,2002;Ioaizaperez,2002 and Racane,2006)[5,6,7] anticandidous (Sidoova et.al,1997)[8] Parkinson's disease (Alain et.al,1997)[9] antihistaminic and anti inflammatory (Abignente et.al,1983)[10].Benzothiazole have also shown significant effect against cancer (Swarnkar et.al, 2007)[11] and antibacterial agent (Lednicar & Matcher,1997; Karia & Parsania,1999)[12,13] Another area of application of these Schiff bases is analytical chemistry where some of compounds were used as ligand in complexometry topic (Rodriguez et.al, 2004)[14] and catalysts as a corrosion inhibitor in chemical industry (Ramesh & Sivagamasundari, 2003)[15]

Literature survey reveals that a very few work is done on Schiff base transition metal complexes of benzothiazole so we plan to synthesis some new transition metal complexes of benzothiazole Schiff bases.

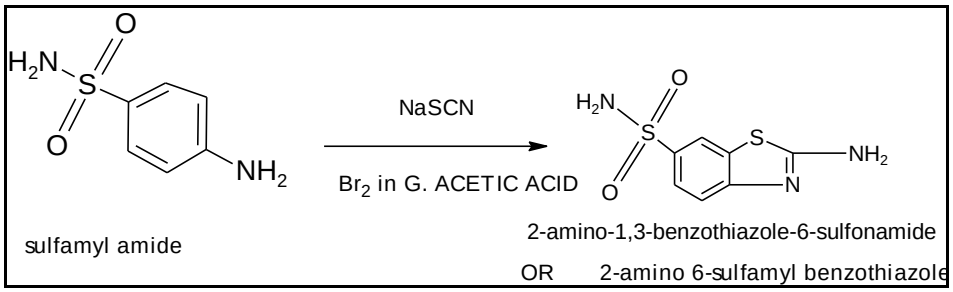
Synthesis of Schiff Bases:

In the present work, we have reported some new Schiff bases synthesized by the condensation of 2-amino-6-sulfamyl benzothiazole and respective hydroxy ketones, aldehydes.

a) Synthesis of Benzothiazole :

Synthesis of benzothiazole was carried out according to the general procedure (Misra,1958, Mebra et.al, 1980)[16, 17]. The method of thiocynation and bromination was adopted. (0.1M) sulfanilamide and sodium thiocyanate (0.2M) in 100 ml glacial acetic acid are mixed together maintaining 0ºC temperature. (0.2M) bromine in acetic acid (25 ml) was added to the above solution drop wise and the mixture was stirred continuously by a mechanical stirrer till the complete addition of bromine. The temperature was maintained below 10ºC. The solid thus obtained after complete addition of bromine was filtered so as to remove excess of bromine and then dissolved in hot water. Again it was filtered and filtrate then treated with alkali like NaOH or KOH for the precipitation of free base. The precipitate thus obtained was filtered, washed and dried. The product was recrystallized from ethanol M.P. 105°C, Yield –40%.

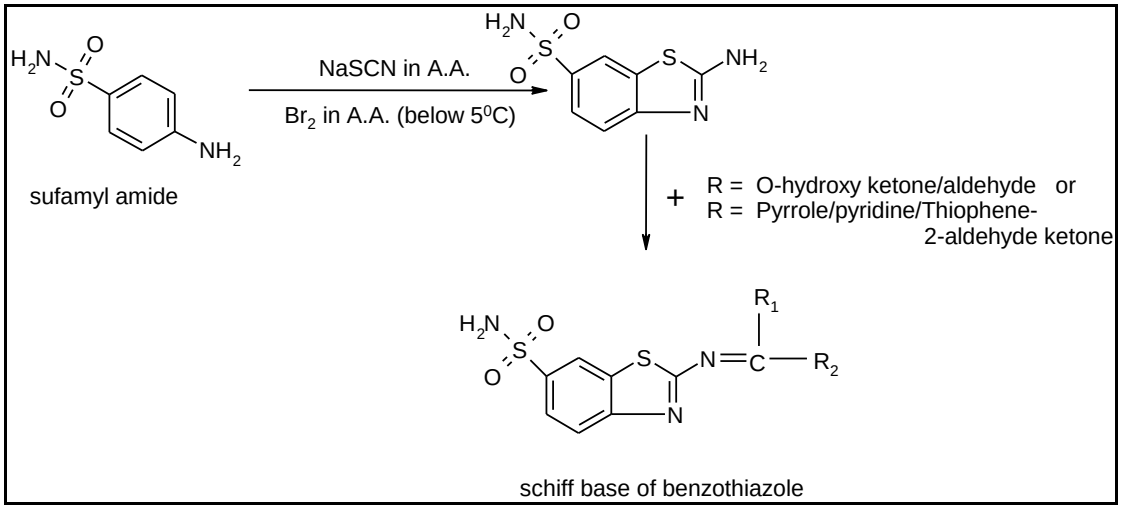
Scheme:



b) Synthesis of Schiff bases:

Schiff bases were synthesized by taking equimolar ethanolic solution of L_3 (pyrrole 2- aldehyde) L_4 (pyridine 2- aldehyde) and 2-amino, 6-sulfamyl benzothiazole were refluxed for 3-4 hours on water-bath. The reaction progress was monitored by TLC. After confirming the completion of the reaction by TLC, the reaction mixture was poured on crushed ice or cold water and the solid separated was then filtered, washed with distilled water and dried, recrystallised from ethanol. The product collected was tested for $–NH_2$ group, >C=O group, -SCN group, -OH group for the sake of the purity of the product.

Scheme:



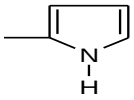
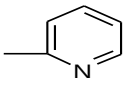
Sr.No.	Compound	Substituents	
		R_1	R_2
1	L_3	H	
2	L_4	H	

Table I-Analytical Data of Co (II) and Ni (II) Complexes

Sr. No.	Comp.	Mol. Formula	Mol. Wt.	Colour	M.P. / D.P. ^{0}C	Elemental Analysis (%)				Mol. Cond. mhos cm^2 mol^{-1}	μ eff. B.M.
						C found (cal)	H found (cal)	N found (cal)	Metal found (cal)		
1	L_3	$C_{12}H_{10}O_2N_4S_2$	306	Pink orange	70	46.87 (47.05)	3.47 (3.26)	18.49 (18.30)	---	----	---
2	L_4	$C_{13}H_{10}O_2N_4S_2$	318	Royal Yellow	40	48.98 (49.05)	3.21 (3.14)	17.77 (17.61)	---	---	----
3.	CoL_3	$Co(C_{12}H_{10}O_2N_4S_2)_2.2H_2O$	707	Puce Red	280-285	40.65 (40.73)	3.43 (3.39)	15.97 (15.84)	8.47 (8.34)	53.82	4.3
4.	CoL_4	$Co(C_{13}H_{10}O_2N_4S_2)_2.2H_2O$	731	Ruddy Brown	285-290	42.56 (42.68)	3.43 (3.28)	15.73 (15.32)	8.35 (8.07)	43.68	4.6
3.	Fe L_3	$Fe(C_{12}H_{10}O_2N_4S_2)_2.2H_2O$	704	Crimson	280-285	40.70 (40.90)	3.72 (3.40)	16.25 (15.90)	8.10 (7.95)	57.38	5.94
4.	FeL_4	$Fe(C_{13}H_{10}O_2N_4S_2)_2.2H_2O]$	728	Windsor tan	225-230	42.77 (42.85)	3.65 (3.29)	15.57 (15.38)	8.15 (7.69)	41.51	5.80

Synthesis of metal complexes:

For the synthesis of Co (II) and Fe (III) complexes, the metal acetates were used. Ethanolic solutions of Schiff bases and respective metal acetate solutions were refluxed in the stoichiometric ratio. The precipitated solid complexes filtered, washed to remove excess base and then dried over fused $CaCl_2$ in vacuum desiccator.

Characterisation of Metal Complexes:

All the metal chelates prepared are stable to air and moisture. These are insoluble in water and in different polar and non polar organic solvents at room temperature. Some complexes are easily soluble and some are sparingly soluble in ethanol, dimethyl sulfoxide (DMSO) and dimethyl formamide (DMF).

The synthesized metal complexes are characterized by elemental analysis, solution conductivity, magnetic susceptibility, electronic and infrared absorption spectroscopy. They are also screened for thermo gravimetric analysis and X-ray powder diffraction analysis.

Magnetic Susceptibility Measurement of Complexes:

Results of the magnetic moment of Co (II) complexes are given in table. Co (II) complexes derived from ligand L_3 and L_4 show magnetic moment in the range 4.3 - 4.6 B.M. at room temperature showing the Octahedral geometry.

Magnetic moment of Fe (III) complexes derived from ligands L_3 and L_4 shows magnetic moment in the range 5.80 – 5.94 B.M at room temperature showing the octahedral geometry are given in table.

Low conductivity values of all the complexes indicated that they are non-electrolytes (Shallary et.al, 1979; Geary, 1971)[18, 19.]

Spectral data of synthesized Schiff bases:

1) L_3:

IR (KBr) ν in cm^{-1}: ~3400-3295(**NH_2,**), 2923- 2855(aliphatic-**C-H** stretch), 1598(**C=C**), 1586(**C=N** azomethine),1519 (**C=N** ring stretch) , 1326(asymmetric stretch -**SO_2**), 1160 (symmetric stretch -**SO_2**) , 910-826 (**C-H** out of plane bend) 780 - 735 (**C-S-C**).

^{1}H-NMR δ ppm: 7.2- 8.3 (m, Ar – **H**), 6.2 (s, = C – **H**), 5 (s, N-**H**), 2.5 (s -N**H_2**).

Mass (M/z) % rel. Intensity: 307.

2) L_4:

IR (KBr) ν in cm^{-1}: ~3330- 3253(-**NH_2**), ~3000 (Ar- **C-H**), ~ 2925 and ~2855 (aliphatic -**C-H**) , 1592 (**C=N** azomethine), 1515 (–**C=N** ring stretch), 1330 (asymmetric strecth -**SO_2**), 1156 (symmetric stretch **SO_2**), 904 and 831 (**C-H** out of plane), 831- 741 (thiazole **C-S-C**).

^{1}H-NMR δ ppm: 7.2 - 8.4 (m, Ar – **H**), 6.2 (s, =C – **H)**, 2.5 (s – C**H_3**)

Mass (M/z) % rel. Intensity: 318

3) Fe L_3:

IR (KBr) ν in cm^{-1}: 3496 (-H2O), 1638 (C=N), 1317 (C-O), 850-728 (C-S-C), 554 (M-N)

4) Fe L_4:

IR (KBr) ν in cm^{-1}: 3510(-H2O), 1647 (C=N), 1527(C-O), 840-726(C-S-C), 560(M-N)

5) CoL_3:

IR (KBr) ν in cm^{-1}: 3551(-H2O), 1631 (C=N), 1301(C-O), 840-723(C-S-C), 556(M-N)

6) Co L_4:

IR (KBr) ν in cm^{-1}: 3496(-H2O), 1638 (C=N), 1527(C-O), 850-730(C-S-C), 564(M-N)

^{1}H NMR Specroscopy:

^{1}H NMR spectra of the corresponding complexes was showed broad peaks due to complex pattern of splitting

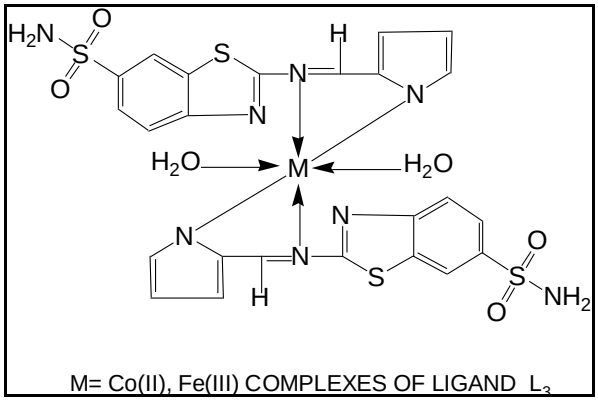
Thermal Analysis

The thermogram of Fe (III) and Co (II) complexes shows the coordination of two moles of hydrated water. Hence from TGA, it is clear that the complexes under study contain two water molecules which are coordinated to central metal ion showing octahedral geometry

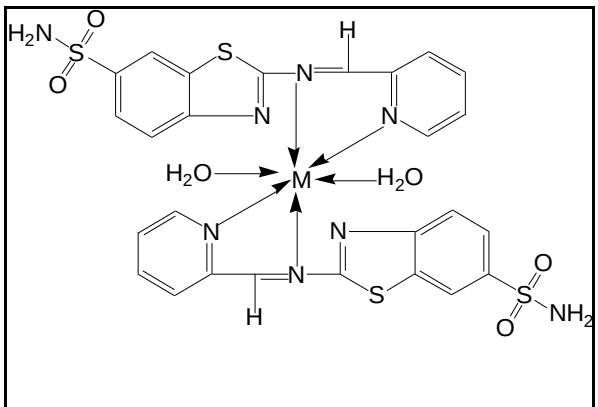
X-Ray Diffraction Study

Diffractogram of Fe (III) with ligand L_3 was scanned in the range 5^0 to 60^0at wavelength 1.540598(A^0). The diffractograms and associated data depict the 2θ value for each peak, relative intensity and inter planar spacing (d-values) had twenty reflections with maxima at 2θ= 35.580^0 corresponding to d value 2.5211A^0 having intensity 1166 cps.

Lattice parameter values as a = b = c and α = β= γ which suggest Cubic Crystal Structure of P type lattice for iron complex of Ligand L_3.



M= Co(II), Fe(III) COMPLEXES OF LIGAND L_3



M= Co(II), Fe(III) COMPLEXES OF LIGAND L_4

Antimicrobial Activity

Antifungal activity was performed by poison plate method. The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with DMSO was prepared as blank (negative control). Similarly a plate with 1% Grysofulvin was prepared as standard reference plate (positive control). Aspergillus niger, Pencillium chrysogenum, Fusarium moneliformе, Aspergillus flavus were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5 ml of 1:100 aqueous solution of teen 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension. The fungal suspension was spot inoculated on the plate's prepared using compound with the help of nicrome wire loop. The plate was incubated at room temperature for 48 hours. After incubation plates were observed for the growth of inoculated fungi. Results were recorded as a growth of fungi (no antifungal activity), reduced growth of fungi (moderate antifungal activity), and no growth of inoculated fungi (antifungal activity).

The cup plate agar diffusion method (Collins, et.al., 1967; Godkar, et.al., 1996)[20,21] was employed for determining the antibacterial activity of the newly synthesised ligands. The antibacterial activity was measured by agar cup method. Nutrient agar (Himedia) was prepared and sterilized at 15 Psi for 15 minutes in the autoclave. It was allowed to be cool below 45^0C and seeded with turbid suspension of test bacteria separately prepared from 24 hours old slant cultures. 3% incula were used every time. The bacterial culture selected where, two gram negative culture viz. Staphylococcus aureus, Bacillus subtilis. This seeded preparation was then poured in sterile Petri plate under aseptic condition and allow it to solidify. Cup of 10 mm diameter were borered in the agar plate with sterile cork borer. 100 µl of compound solution prepared in dimethyl sulphoxide (1%) was added in the cup under aseptic condition with the help of micropipette.100 µl of DMSO was also placed in one of the cup as a blank (negative control). A standard antibiotic disk impregnated with 10 units of pencillin was also placed on the seeded nutrient agar surface as standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 minutes to allow diffusion of the compound from agar cup into the medium. Then the plates were shifted to incubator at 37^0C and incubated for 24 hours. After incubation plates were observed for the zone of inhibition of bacterial growth around agar cup. Results were recorded by measuring the zone of inhibition in milimeters (mm) using zone reader.

Table-II: Antimicrobial Activity

Sr. No.	Compound	Fungal Strain				Bacterial Strain			
		An	**Pc**	**Fm**	**As**	**Ec**	**St**	**Sa**	**Bs**
03	L_3	RG	RG	RG	+ve	20	15	12	20
04	L_4	+ve	+ve	+ve	+ve	18	-ve	20	19
03	CoL_3	RG	RG	RG	+ve	-ve	13	22	-ve
04	CoL_4	RG	RG	+ve	+ve	19	19	27	21
03	FeL_3	+ve	RG	+ve	+ve	17	-ve	25	18
04	FeL_4	RG	RG	-ve	RG	16	-ve	24	16
07	+ve control	+ve	+ve	+ve	+ve	NA	NA	NA	NA
08	Griseofulvin	-ve	-ve	-ve	-ve	NA	NA	NA	NA
07	DMSO	NA	NA	NA	NA	-ve	-ve	-ve	-ve
08	Penicillin	NA	NA	NA	NA	13	22	36	18

Ec-E.coli, St-S.typhi, Sa- S.aureus, Bs-B.subtilis; An-A.niger, Pc-P.chrysogenum, Fm-F.moneliformae, Ca-C.albicans; *-ve: No growth of fungi,+ve; Growth of fungi, RG-Reduced growth, NA-Not Applicable, Zone of inhibition was measured in mm*.

Conclusion

The synthesized Schiff bases showed bidentate nature and gave stable transition metal complexes. All the Schiff base complexes of transition metals under investigation are non-electrolytic in nature. The metal complexes show more potent activity than the corresponding Schiff bases. The electronic spectral data suggest that all Fe (III) and Co (II) complexes of ligands under study have octahedral geometry.

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References

1. Arora, K. and K.P. Sharma, K. P., Studies on Mononuclear Chelates Derived from Substituted Schiff Base Ligands (Part 4): Synthesis and Characterization of a New5-Hydroxysalicyliden-P-Aminoacetophenoneoxime and Its Complexes with Co(II), Ni(II), Cu(II) and Zn(II) , *Synth.React. Inorg. Met.Org.Chem.*, 2003, 32, 913.
2. Sousa, C., Freire, C. and de Castro, B., Synthesis and Characterization of Ni(II), Pd(II) and Cu(II) with heterocyclic compounds , *Molecules,2003*, 8,894.
3. Kou, H. Z., Ni, Z. H., Zhou, B. C. and Wang, R. J., , Synthesis and characterization of Co(II), Ni(II)and Cu(II) complexes containing Heterocyclic Nitrogen donor ligands, *Inorg. Chem.Commun.*, 2004, 7, 1150.
4. Malik, W. U., Rajeev, J., Quantitative Estimation of the Electronic Effects of Substituents in Five-membered Nitrogen-containing Aromatic Heterocycles, *J.Indian, Chem.Soc. ,LIX* , 1982, 558p.
5. Bradshaw, T. D., Preclinical Evaluation of Amino Acid Prodrugs of Novel Antitumor2-(4-Amino-3-Methylphenyl) Benzothiazoles1, *Molecular Cancer therapeutics*, 2002, 1 , 239.
6. Loaizaperez, A. I., Preclinical Evaluation of Amino Acid Prodrugs of Novel Antitumor2-(4-Amino-3-Methylphenyl)Benzothiazoles, *Molecular pharmacology*, 2002, Vol.61, 13p.
7. Racane, L., Antitumour efficiency of novel fluoro substituted 6-amino-2-phenylbenzothiazole hydrochloride salts in vitro and in vivo, *Molecules*, 2006, 11, 328.

8. Sidoova, E., Loos, D., and Bujdakova, H., New anti candidus 2-alky/thio-6-amino benzoyhiazole, *Molecules*, 1997, 2, 36-42
9. Alain, B., Christinsonie, D. M. and Assunta, I., Pharmaceutical compositions containing 2-amino benzothiazoles for treating Parkinson's disease and Parkinson Ian syndromes, *patent CA pharmaceuticals*, 1997, 1,63.
10. Abignente, E., De-Capariis, P., Sacchi, A. and Marmole, E., Synthesis and Antibacterial Activity of Some New Phenothiazine Derivatives, (1983), *Pharm.Co. Ed.Sci.*, 1983, Vol.38, 533p.
11. Swarnkar, P. K., Kriplani, P., Gupta, G. N., and Ojaha, K. G., Microbial transformations of 2-substituted benzothiazoles, *Indian J. Of Chem*., 2007, 4,14
12. Lednicar, D. and Matcher, L. A., The organic chemistry of drug synthesis, A Wiley Inter Science Publication, John Wiley, 1997
13. Karia, F. D., Parsania, P. H., Biologically active Co(II) AND Ni(II) complexes of N-(2-thienylmethylene)-2-aminothiadiazole, (1999), *Asian J. Chem*., 1999, Vol.11,991p.
14. Rodriguez, M. C., Liwes, A. G. and Fernando, D. R., Acenaphtheneqninom thiosemicarbazones and it is transition metal complexes; synthesis, structure and biological activity , Inorg. Biochem., 2004, 98,313.
15. Ramesh R. And Sivagamasundari, M., Synthesis of some new 6-chloro-2-aminobenzothiazole and the study of their biological activities against (2003), *Synth.React. Inorg. Met.Org.Chem*., 33,899.
16. Misra, A. L., 2-amino-6-substituted benzothiazoles as a potential anthelmintics, (1958): *J.Org.Chem*., 23,1388.
17. Mebra, S. C., Zaman, S. and Khan, A. A., Schiff base complexes with transition elements as a corrosion inhibitors, *J. Indian,Chem.Soc.*, 1980, 32,829.
18. Shallary, A. M., Moustafa, M. M. and Bekheit, M. M., Synthesis and spectral studies of Schiff base of 2-amino- substituted thiazoles , *J. Inorg. Nucl. Chem*., 1979, 41, 267.
19. Geary, W. G., Spectroscopy study of Schiff base and their complexes with Ni(II) ,Cu(II) ,Pd(II) and Zn (II), Spectroscopy study of Schiff base and their complexes with Ni(II) ,Cu(II) ,Pd(II) and Zn (II), *Coord. Chem. Rev*., 1971, 7, 81.
20. Collins, C. H., (1967), *Microbiological methods, Butter worth, London*, 364.
21. Godkar, P. B., "*Text Book of Medical Laboratory Technology*", *Bhalani publication House, Mumbai*, India., 1996 326, 332, 382.

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