A Minor Research Project's Final Report

"PHYSICOCHEMICAL AND BIOLOGICAL ACTIVITY STUDIES ON SCHIFF BASE METAL COMPLEXES"

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Final report

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Introduction

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff in 1864. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R^1, where R and R^1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also knows as anils, imines or azomethines. Presence of a lone pair of electrons in an sp2 hybridized orbital of nitrogen atomof the azomethine group is of considerable chemical and biological importance[1-7]. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents,[8-11] especially when a functional group like –OH or –SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations inthis area highly desirable.

Schiff base ligands have been widely studied in the field of coordination chemistry mainly due to their facile syntheses, easily availability, electronic properties and good solubility in common solvents. A large number of Schiff bases and their complexes have been studied for their important properties e.g. their ability to reversibly bind oxygen, transfer of an amino group and complexing ability towards some toxic metals[12-14]. The high affinity for the chelation of the Schiff bases towards the transition metal ions is utilized in preparing their solid complexes. Schiff base metal complexes have been useful to design and develop some models for biological systems. Transition metal complexes which usually contain nitrogen, sulphur /or oxygen as ligand

atoms are becoming increasingly important because these Schiff base can bind with different metal centers involving various coordination sites and allow successful synthesis of metallic complexes with interesting stereochemistry [15-18].

The Schiff bases derived from thiocarbonohydrazide are known to exhibit diverse activities like antibacterial[19],anticarcinogenic20],antiviral [21], herbicidal [22] and antifungal [23]activities

The Schiff bases obtained from o-hydroxyaldehydes have strong ability to form complexes with transition metals and rare earth ions. A number of reviews[24-28] have been published in literature which throw light on physicochemical and biological studies of Schiff base metal complexes.

Thiazoles belong to an important class of organic compound because they are well known as biologically active (antibacterial, antitubercular and antifungal activities) compounds[29-31].

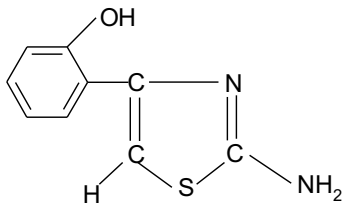
Biological importance of thiazoles and synthetic flexibility of Schiff bases and their selectivity towards metal ions, it is of interest to study physicochemical aspects and biological properties of Schiff bases derived from **aminothiazoles** and their transition metal complexes

2,4-disubstituted thiazoles possess antiflammatory and analgesic activities and were found to be effective on mouse[32]. Vitamin B_{12} and coenzyme cocaboxylase contain thiazolering[33]. Thiazole and its derivatives are also used as thiol flavouring substances. Aminothiazole is an intermediate for dyestuffs, photographic chemicals and pharmaceuticals (example: as a side chain of Cephalosprins. It is parent material for numerous of chemical compounds including sulfur drugs, biocides, fungicides, dyes, and chemical reaction accelerators. Thiazole dyes contain the colour radicals of =C=N- and -S-C= which decide colors to a compound. Thiazole dyes are useful in dying cotton. Benzothiazole derivatives are important in rubber industry. Substituted derivative of benzimidazoles are used as broad-spectrum anthelmintic and preservative.

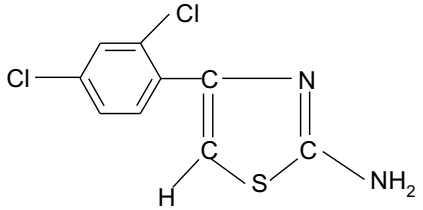
Aminothiazoles and its substituted derivatives form Schiff bases with o-hydroxyaldehydes, which possess a strong ability to form transition metal complexes. Metal complexes of sulphur-nitrogen chelating ligand attract the attention of researchers because of their interesting structural and biological properties. Many studies[34-38]

have described the biological role of metals and chelation The connected metal centers in such biologically active molecules may involve different functions such as oxygen transport, DNA inhibitor, enzymatic activity, electron transfer and lock geometry. All these observation related to the essential role of metal linkage attracted our attention to start research to investigate the factors responsible for this relationship. In our earlier studies, we have reported synthesis and characterization of transition metal complexes of Schiff bases derived from 4-(p-bromophenyl)-2-aminothiazole and substituted salicylaldehyde or 2-hydroxy–1-naphthaldehyde[39]. Literature survey reveals that due to biological significance of thiazoles, there is enough scope to synthesize thiazoles and characterize them by spectral, thermal and x-ray diffraction analysis.

In the present communication we report synthesis, spectral (Uv-Visible, IR, NMR, and Mass), thermal, x-ray diffraction studies and evaluation of antibacterial and antifungal activities of 4-(o-hydroxyphenyl)-2-aminothiazoles (L_1) and 4-(o,pdichlorophenyl)2-aminothiazole(L_2). The thermograms were critically analyzed to estimate kinetic parameters namely E (energy of activation), n (order of reaction), Z (pre-exponential factor), ΔS (entropy of activation) and G (free energy change) using Coats-Redfern, MacCallum-Tanner and Horowitz-Metzger method.



(L_1)



(L_2)

(Fig. 1)

Experimental

All the chemicals used were of Analytical reagent grade. The solvents were purified by double distillation.

A Series of new Schiff bases (derived from 4 –o hydroxyphenyl-2-aminothiazole and R substituted salicylaldehyde or 2- hydroxyl-1- naphtaldehyde, o- vanillin R= H, 5-CH_3, 4-CH_3, 3-CH_3, 5-Cl, 5-Br)

Synthesis of 4-(o-hydroxyphenyl)-2-aminothiazole, physical measurements and testing of biological activity were performed

2.1] Synthesis of 4(o-hydroxyphenyl)-2- aminothiazole / 4-(o, p dichorophenyl)-2-aminothiazole[40]

A mixture of 6.8 g. of p-hydroxyacetophenone or 2,4-dichoroacetophenone, 12.7g. of iodine and 7.6g. Of thiourea was refluxed on water bath for eight hours and again 12 to 16 hours after removal of the condenser. The yield of the final product depends upon the period of heating. The crude reaction product was kept in contact with ether with occasional shaking for 48 hours (to remove the unchanged ketone which otherwise led to a gummy product). On treatment with thiosulphate solution, iodine was finally removed. The resultant product, which was nearly colourless, was boiled (extracted) with water and filtered hot. The filtrate was treated with concentrated ammonia to liberate the base. The product (I) obtained was recrystallised from 50% ethanol.

4-(o-hydroxyphenyl)-2- aminothiazole: M. P.140 °C (obs.) 139 °C (Lit.)

4-(o, p dichorophenyl)-2-aminothiazole: M. P. 159 °C (obs.) 158 °C (Lit.)

2.2 Synthesis of substituted salicyldehydes

The following aldehydes were used for the synthesis of heterocyclic Schiff bases.

1. Salicylaldehyde
2. 5-Methylsalicylaldehyde
3. 4-Methylsalicylaldehyde
4. 3-Methylsalicylaldehyde
5. 5-Chlorosalicylaldehyde

The o-hydroxyaldehydes (Sr. No. 2-5) were synthesized by Duff Reaction[54].

150 g of glycerol and 35 g of boric acid were heated at 170^0C for 30 minutes in a beaker with stirring to expel the water present in the glycerol. An intimate mixture of 50g of phenol and 50 g of hexamine was prepared by grinding the material together thoroughly. The mixture was then added with vigorous stirring to the glycerol-boric acid mixture, previously cooled at 150^0C. The reactants were stirred for 20 minutes, which the temperature was maintained between 150^0C to 165^0C by heating or cooling as necessary. Finally the reaction mixture was cooled at 115 ^{0}C and was then acidified with mixture of 50ml of concentrated sulphuric acid and 150 ml water. The whole mixture was then boiled under current of steam. A solid aldehyde collected was recrystallized from absolute alcohol. The physical constant data is given in table no.2.

Synthesis of 5-bromosaIicylaldehyde:

5-bromosalicylaldehyde was prepared by addition of liquid bromine to an equivalent amount of cold solution of salicylaldehyde in acetic acid. The product was recrystallised from ethanol-water mixture. (M. P. 105°C). was used.

2.3 Synthesis of tridentate Schiff bases:

A solution of o-hydroxyaldehyde in ethanol was added to the ethanolic solution of 4-(o- hydroxyphenyl)- 2- aminothiazole, in equimolar quantity. The mixture was refluxed in a water bath for 30 min. The Schiff base thus formed was filtered at suction, recrystallised from ethanol and dried under vacuum. Purity of the Schiff base was checked by molecular weight determination, elemental analysis and TLC.

Following Schiff bases were prepared.

1. (SB^1) N-(2-hydroxy-1-naphthalidene)-4-(o-hydroxyphenyl)-2-aminothiazole
2. (SB^2) N- (Salicylidene)-4-(o-hydroxyphenyl)-2-aminothiazole
3. (SB^3) N- (3-methylsalicylidene)- 4- (o-hydroxyphenyl)-2-aminothiazole
4. (SB^4) N- (4-methylsalicylidene)-4- (o-hydroxyphenyl)-2-aminothiazole
5. (SB^5) N- (5-methylsalicylidene)- 4- (o-hydroxyphenyl)-2-aminothiazole

2.4 Preparation of metal complexes;

Cobalt (II) Complexes

An ethanolic solution of 0.01 mole of cobalt acetate (Albright and Wilson Ltd., London) was added to the ethanolic solution containing 0.02 mole of o— hydroxyaldehyde and 0.02 mole of substituted 2-aminothiazole or 0.02 mole of the Schiff base. The reaction mixture was then refluxed on a water bath for 30 minutes. On standing overnight the dark red coloured crystals separated, which were filtered, washed with ethanol and dried under vacuum:

Zinc (II) Complexes

0.01 mole of zinc acetate (A. R. grade, B. D. H.) in ethanol was added to the ethanolic solution of 0.02 mole of o-hydroxyaldehyde and 0.02 mole of substituted 2-aminothiazole or 0.02 mole of Schiff base. The mixture was heated on a water bath until the orange coloured crystals began to form. The crystals separated, were washed with hot ethanol and dried under vacuum.

Copper (II) Complexes

0.01 mole of Copper acetate (A. R. grade, B. D. H.) in ethanol was added to the ethanolic solution of 0.02 mole of o-hydroxyaldehyde and 0.02 mole of substituted 2-aminothiazole or 0.02 mole of Schiff base. The mixture was heated on a water bath until the orange coloured crystals began to form. The crystals separated, were washed with hot ethanol and dried under vacuum.

Nickel (II) Complexes

0.01 mole of zinc acetate (A. R. grade, B. D. H.) in ethanol was added to the ethanolic solution of 0.02 mole of o-hydroxyaldehyde and 0.02 mole of substituted 2-aminothiazole or 0.02 mole of Schiff base. The mixture was heated on a water bath until the orange coloured crystals began to form. The crystals separated, were washed with hot ethanol and dried under vacuum.

2.5 Physical Measurements:

Carbon, hydrogen and nitrogen analysis of Schiff bases and the complexes were performed on Carbo –Elba 1106 elemental analyser. Chlorine was estimated by Carius[55] method. Molecular weights were determined by cryoscopic method using benzene as the solvent.

The estimation of cobalt, nickel, copper and zinc was carried out gravimetrically[57] by decomposing the complexes with concentrated sulphuric acid.

Physical constants (melting points) of the Schiff bases and the complexes were measured in sealed glass tubes using paraffin bath.

Ultraviolet and visible region spectra were recorded in chloroform solution on Shimadzo and Beckman DU-2 spectrophotometer using quartz cells at room temperature.

Infrared spectra were recorded in KBr pellets on Perkin-Elmer 783 IR spectrophotometer and Beckman IR-20 spectrophotometer in the range 4000-250 cm^{-1}.

X-ray diffractograms were run in the range of 10-100° on a Philips PW 1710 diffractometer attached with computer alongwith graphical assembly in which CuKα radiation source connected with the tube of Cu-NF 2KV/20 A was used. Thermal measurements were performed by using i) Perkin-Elmer TGS-2 thermogravimetric analyser alongwith TADS computer system, ii) Metler TA 4000 system and iii) Rigaku TAS 100 thermal analyser. The furnace heating rate was 10°C/minute in nitrogen atmosphere.

Electrical conductivity of the complexes in nitrobenzene solution was measured with Philips conductivity bridge model PR 950 with a dip type cell or with a systronics conductivity meter bridge. The bridge was calibrated with a standard solution of potassium chloride.

Magnetic susceptibility measurements were carried out by Gouy method at room temperature. The tube was calibrated by using a $HgCo(CNS)_4$. Diamagnetic corrections were applied using Pascal's constants[58].

2.6 Testing of biological activities:

Minimum Inhibitory Concentration (MIC) tests[59-61] were used to determine the lowest concentration of the Schiff bases and their metal complexes that inhibit the growth of standard stain of sensitive test organisms. The test organisms used were Klebcialla pneumoniae, Staphylococcus aureus, Aspergillus niger and Candida albicans.

Minimum Inhibitory Concentration Tests

Preparation of medium and materials

a) Materials:
    1. Nutrient broth and Sabouraud broth.

2. 24 Hours old culture of S. typhi and C. albicans
3. Sterile test tubes and pipettes.
4. Sterile solution of Schiff bases and their metal complexes (20µg/ml)

b) Composition of nutrient media: Nutrient broth (pH = 7.4)

1. Peptone: l0g.
2. Beef extract: 3g.
3. Sodium chloride: 5g.
4. Distilled water: 1000ml

c) Sabouraud's broth (pH =5.6)

1. Dextrose: 40g.
2. Peptone: 10g.
3. Distilled water: 1000ml.

A measured quantity (5ml) of nutrient / sabouraud's broth was dispensed in test tube (12 x 100 mm) and sterilized by autoclaving at 121°C for 15 minutes.

c) Stock solution of Schiff bases and their metal complexes:

Stock solution of Schiff base and its metal complexes were prepared by dissolving 2 mg of it in 4 ml DMF resulting concentration as 500 µg/ml. 4ml of above stock solution was further diluted to 10 ml using DMF resulting in concentration as 200µg/ml

Method:

Preparation of culture of sensitive test organisms:

Loopfuls of growth of S. typhi was inoculated into sterile flask containing nutrient broth and was incubated at 37°C for 18 hours. Loopfuls of growth of C. albicans was inoculated into sterile flask containing sabouraud's broth and it was incubated at room temperature for 24 hours.

This culture was used for inoculation of the media used for MIC determination.

Serial dilution method[51].

Eight test tubes containing 5 ml of sterile nutrient broth and eight test tubes containing 5 ml of sterile sabouraud's broth were inoculated with 0.02 ml of 24 hours old culture of S. typhi and C. albicans respectively. Different amounts of Schiff bases and their metal complexes were aseptically added with the help of sterile pipettes from stock solution containing 100µg/ml to 5 ml quantities of respective media so as to reach the

concentration from 6 µg /ml to 40 µg /ml. The inoculations were carried out in triplicate. All the test tubes were incubated at 37°C temperature and at room temperature for the tubes included with S. typhi and C. albicans respectively. Nutrient broth test tubes inoculated with S. typhi were observed for presence or absence of turbidity after 48 hours of incubation. Sabouraud's broth test tubes inoculated with C. albicans were observed for presence or absence of growth on the inner wall of the test tube as discrete tiny patches after 5 to 7 days.

The lowest concentration of the Schiff bases and its metal complexes inhibiting the growth of test organisms was determined as MIC value.

3] Synthesis & Characterization of Schiff Bases

We have reported new Schiff bases (HL) derived from 4- (o- hydroxyphenyl)-2-aminothiazole and R' substituted salicyaldehydes and 2-hydroxy-1- naphthaldehyde.

The following Schiff bases were prepared

1. SB^1 N- (2- hydroxy-1-naphthalidene) – 4- (o-hydroxyphenyl) -2- aminothiazole
2. SB^2 N- (salicylidene) -4-(o-hydroxyphenyl) -2- aminothiazole
3. SB^3 N- (3-methyl salicylidene)-4-(o- hydroxyphenyl)- 2- aminothiazole
4. SB^4 N- (4-methylsalicylidence) -4-(o-hydroxyphenyl)-2- aminothiazole
5. SB^5 N- (5- methylsalicylidene)-4-(o-hydroxyphenyl)-2- aminothiazole.

The ligands are characterized with the help of elemental (C,H and N)analysis, spectral analysis (UV- visible, IR and NMR), powder XRD analyses and thermal analysis and testing of biological activity.

Powder X-ray diffraction study of ligands (SB^1 to SB^5) suggested a triclinic crystal system. Various X-ray parameters. (lattice parameters, crystal system, bond angle, volume of the unit cell) have been evaluated by using powder pattern indexing program. TG curve of all ligands $SB^1$to SB^5 have been critically analysed .The Kinetic parameters (E, n, Z, ΔS, G) evaluated by various methods (Coats- Redfern, MacCallum- Tanner and Horowitz- Metzger) are found to be in good mutual agreement. The ligands have been screened for the evaluation of antibacterial activity against S. aureus and K. pneumoniae

and antifungal activity against A. niger and C. albicans. The ligands exhibit good antibacterial and antifungal activities.

Results and discussion

The compounds L_1 and L_2 are crystalline solids and melt at 139 and 158^{0}C respectively. They are soluble in common organic solvents and give satisfactory C, H, N, and S analyses.

Spectral Analysis

Literature survey reveals that 2-aminothiazole shows absorption at 275 nm and other aromatic amino compounds with comparable structures absorb at ~ 300 nm[40]. In the spectra of L_1 and L_2, λmax occurs at around 300 nm and which is in agreement with the earlier reported data.

The compounds L_1 and L_2 exhibit ν (NH2), ν (C=N) and ν (C-S-C) modes[41] at ~3340, ~1620 and ~550 cm^{-1} respectively[42]. They also give band at 1510,1460,1045 cm^{-1} ,characteristic of thiazole nucleus. L_1 exhibits ν (OH) [11] mode at ~3460 cm^{-1}. The IR spectra of L_1 and L_2 are depicted in fig 2 and 3

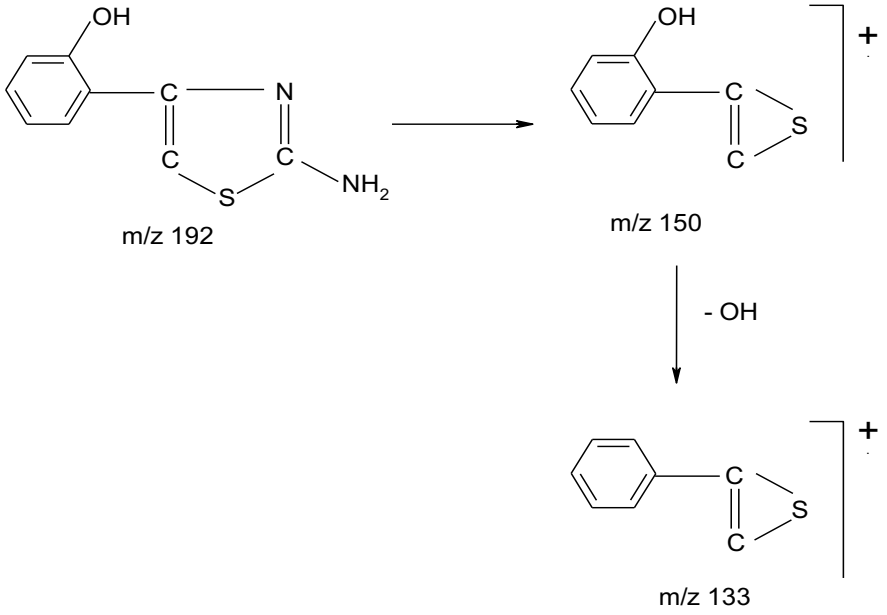
The ^{1}H NMR spectra of L_1 and L_2 were studied for the better understanding of the structures. NMR spectra of L_1 and L_2 are depicted in fig 4 and 5. The spectral data is given below. The NMR spectra are also proved to have considerable diagnostic values when compared with reported[43] related values.

L_1: δ ppm 11.523 (s, 1H, -OH), 5.01 (s, 2H, NH_2), 6.8-6.9(4H,Ar-H,)

L_2: δ ppm 5.054 (s, 2H, NH_2), 7.05-7.79 (3H,Ar-H)

Mass spectra of ligands were recorded for the determination of molecular weights. Mass spectra of L_1 and L_2 are depicted in fig 6 and 7. Mass spectra of L_1 and L_2 show expected molecular ion peaks. Ligand L_1 shows M+ peak at m/z ratio 192 (relative intensity 100%) corresponding to molecular weight of compound and confirms the molecular formula as $C_9H_8ON_2S$ .The molecular ion further undergoes rupture of thiazole ring to give fragment m/z 150(34%). The rupture of thiazole moiety (Scheme 1) is in agreement with the earlier reported data[44]. The fragment having m/z 150 further undergoes loss of

OH group to give fragment having m/z 133 (48%). Other important fragments obtained are mentioned as m/z (relative intensity%): 121(41), 104(33), 90(16), 77(11), 69 (21)



Scheme 1

The ligand L_2 shows molecular ion peak at m/z ratio 244 (relative intensity 100%) corresponding to the molecular weight of the compound and confirms the formula as $C_9H_6N_2SCl_2$.The M^++2 (m/z =246) and M^++4 (m/z = 248) peaks are observed due to two isotopic chlorine. The molecular ion undergoes the rupture of thiazole moiety to give fragment having m/z 202 (58 %). Other important fragments obtained are, m/z (relative intensity%): 174(10), 167(23.8), 132(11.3), 123(18.18), 104(17.0), 87 (11.36), 73(12.27), 45, (12.27).

Thermal analysis

The TG curves indicate that $L_1$and L_2undergo decomposition in two stages. L_1 undergoes mass loss of 50.44 % within temperature range 142-280^{0}C (Stage I) and mass loss of 31% within temperature range 280-800 ^{0}C (Stage II). The DTA curve gives endothermic peaks at 142^{0}C, 274^{0}C and 891^{0}C

L_2 undergoes mass loss of 83.59 % within temperature range 158-262 ^{0}C (Stage I) and mass loss of 8.25% within temperature range 262-600^{0}C (Stage II) .The DTA curve gives endothermic peaks at158.74, 262.58 and 933.70^{0}C.

The residue left at the end, for L_1 (11 %) and L_2 (5.4 %), may be due to formation of thermally stable polymeric product at high temperature[45]. On the ground of initial decomposition temperature, we have proposed order of thermal stability of the ligands as $L_2 > L_1$. It is of interest to note that the chloro substituents have stronger influence on stability of aminothiazole than OH group.

In order to calculate the kinetic parameter viz. E (Energy of activation), n (order of reaction), Z (pre-exponential factor), ΔS (entropy of activation) and G (free energy change), we have used Coats-Redfern (C.R.), MacCallum-Tanner (M.T.) and Horowitz-Metzger (H.W.) method as summarized below

Coats-Redfern Method[46]

$$\log\left(\frac{1-(1-\alpha)^{1-n}}{(1-n)T^2}\right) = \log\frac{ZR}{Eq}\left(1-\frac{2RT}{E}\right) - \frac{}{2.303\,R}\cdot\frac{1}{T} \qquad .....1$$

MacCallum- Tanner Method[47]

$$\log\left(\frac{1-(1-\alpha)^{1-n}}{(1-n)}\right) = \log\frac{ZE}{Rq} - 0.485E^{0.435} - \frac{0.449+0.217E}{T}\cdot 10^3 \qquad .....2$$

Horowitz – Metzger Method

$$\log\left(\frac{1-(1-\alpha)^{1-n}}{(1-n)}\right) = \log\frac{ZRT_S^2}{Eq} - \frac{E}{2.303\,RT_s} + \frac{E\theta}{2.303\,RT_s^2} \qquad .....3$$

Where

α - The fraction decomposed

q - The heating rate

T – Absolute temp

Ts – The temp at half weight loss

The left hand side of equation 1 was plotted against 1/T. By using different value of order of reaction straight line was fitted by regression .The highest value of r, the correlation coefficient, gave the correct value of n. From the value of slope and intercept, E and Z values were calculated. Using E and Z values, the values of Δ S and G were determined. The values of n, E, Z, Δ S and G for L_1 and L_2 are given in table 1 and 2. The values of E for L_1 and L_2 are 17.446 and 21.507 for Stage I, and 3.362 and 2.244Kcal mol^{-1} for Stage II respectively. The values of ΔS are negative for Stage I and II for both the compounds.

X-ray diffraction studies

Thecompound L_1 has been characterized by powder x-ray diffraction study to find the crystal system present. The x-ray diffraction data is given in Table 3 and diffractogram is depicted in fig 10. It shows 52 reflection (2θ) between 10.125 and 60.30 with maximum at $2\theta=10.13^0$ and d=8.7505 A^0.The general procedure and methods of calculations are based on published work[49]. The observed and calculated values of d and θ are quite consistent (Table 2.) In order to evaluate lattice parameters (a, b and c) of the unit cell and volume, we first assumed a triclinic crystal system for the ligand. The cell parameters calculated for the ligands are given in table 2 (a =20.582 b = 8.924A^0, c = 8.4646 A^0; $\alpha = 94.189^0$,$\beta=115.632^0$, $\gamma =101.966^0$) and which are found to be in accordance with those required for a triclinic system[50]where $a\neq b\neq c$ and $\alpha \neq \beta \neq \gamma \neq 90^0$. Thus it may be concluded that the crystal system of L_1 is triclinic. Volume of unit cell= 1336.19 $A^{o\,3}$

The X-ray diffractogram of L_2 (fig. 11) shows 47 reflection (2θ) between 10.67 to 79.12 with maximum at 2θ = 38.82 and d = 5.57 A^0. The x-ray diffraction data is given in Table 4. The cell parameter calculated are a = 8.1851,b = 8.7875A^0, c = 7.0573 A^0 and $\alpha=90.3050^0$, $\beta =97.7880^0$,$\gamma =109.4140^0$. . A triclinic crystal system is proposed for L_2.Volume of unit cell = 473.90 $A^{o\,3}$.

Biological activity

Biological activity of ligands L_1 and L_2 has been evaluated using serial dilution technique[51]. The ligands were tested for antibacterial activity against *S. aureus* and *k. pneumoniae* and antifungal activity against *A. niger* and *C. albicians* in DMF in concentration range 2 - 16 μg / ml .The minimum inhibitory concentration values (MIC values) have been reported. MIC values for L_1 and L_2 lie in the range 8-12 and 4-8 μg/ml for antibacterial and antifungal activity respectively. It is concluded that L_1 and L_2 exhibit pronounced antifungal activity as compared to antibacterial activity. The antibacterial and antifungal activity data are given in Table 5 and 6.

The ligands L_1 and L_2 are colourless crystalline solid, show sharp melting points and are soluble in common organic solvents. Spectral analyses supports the structure proposed for the ligands. XRD studies indicate that the ligands possess a tetragonal crystal system. Thermal studies suggest that the ligand L_2 is thermally more stable than L_1. The ligands exhibit antibacterial activity against S. aureus and k. pneumoniae and antifungal activity against A. niger and C. albicans. The antifungal activity exhibited by the ligands is more pronounced than antibacterial activity.

Table1: Calculation of Kinetic Parameters for ligand L_1

STEP	**KINETIC PARAMETERS**	**Coats-Redfern Method**	**McCallum-Tanner Method**	**Horowitz-Metzger Method**
I	n	0.18	**0.18**	0.45
	E	17.446	17.400	22.432
	Z	2.62×10^{6}	8.189×10^{10}	1.47×10^{7}
	ΔS	-15.2473	-4.8955	-13.522
	G	19.360	18.015	24.129
II	n	0.85	0.45	1.35
	E	3.362	5.723	4.507
	Z	4.50×10^{7}	7.583×10^{3}	6.66×10^{-3}
	ΔS	-12.911	21.601	-35.54
	G	6.056	10.230	11.924

Units: E (Kcal mol^{-1}), Z (S^{-1}), ΔS (JK^{-1} mol^{-1}), G (Kcal mol^{-1})

Table2: Calculation of Kinetic Parameters for ligand L_2

STEP	KINETIC PARAMETERS	Coats-Redfern Method	McCallum-Tanner Method	Horowitz-Metzger Method
I	n	0.47	**0.45**	0.75
	E	21.507	21.329	26.826
	Z	$3.83x10^{6}$	$6.20x10^{12}$	$9.36x10^{11}$
	ΔS	-15.150	-0.8514	-2.44
	G	24.032	22.4715	27.128
II	n	0.73	0.73	
	E	2.244	4.114	4.942
	Z	$2.58x10^{7}$	$1.38x10^{-2}$	$1.03x10^{4}$
	ΔS	-13.240	-34.2573	4.262
	G	4.451	11.419	

Units: E (Kcal mol^{-1}), Z (S^{-1}), ΔS (JK^{-1} mol^{-1}), G (Kcal mol^{-1})

- Table 3 : X ray data of L_1

Peak no.	2 d		2 θ		I/I_{max} %	h k l
	Obs	Cal	Obs	Cal		
1	8.7289	8.7289	10.13	10.13	87.9	0 1 0
2	8.5191	8.5191	10.38	10.38	98.2	-1 1 0
3	8.4420	8.4420	10.47	10.47	72.8	–1 0 1
4	6.1224	6.1224	14.45	14.45	3.7	1 0 1
5	5.7993	5.7993	15.27	15.27	10.0	0 -1 1
6	5.6918	5.6918	15.56	15.56	13.9	0 1 1
7	5.5674	-	15.90	-	46.2	-
8	5.4936	5.5102	16.12	16.07	33.9	-3 1 1
9	5.4218	5.4104	16.33	16.37	46.2	-3 1 0
10	5.3647	5.3565	16.51	16.54	46.8	-2 -1 1

11	5.3246	-	16.64	-	72.1	-
12	4.8372	4.8366	18.33	18.33	60.5	-4 0 1
13	4.7136	4.6453	18.81	19.09	32.9	-4 1 1
14	4.6139	4.6151	19.22	19.22	8.1	-3 -1 1
15	4.4128	4.4339	20.10	20.01	46.2	4 0 0
16	4.3676	4.3644	20.32	20.33	69.8	0 2 0
17	4.3349	4.3077	20.47	20.60	38.2	-4 1 0
18	4.2628	4.2595	20.82	20.84	16.0	-2 2 0
19	4.0835	4.1039	21.75	21.64	36.0	-3 0 2
20	4.0614	4.0580	21.86	21.88	51.8	1 2 0
21	3.9893	3.9964	22.26	22.23	100.0	-1 2 1
22	3.9456	3.9297	22.51	22.61	53.8	3 0 1
23	3.8136	3.8151	23.31	23.30	12.0	0 0 2
24	3.5316	3.5360	25.19	25.16	51.8	-5 1 0
25	3.5186	3.5203	25.29	25.28	72.1	0 –1 2
26	3.4700	3.4719	25.65	25.64	91.3	0 1 2
27	3.4495	3.4543	25.81	25.77	97.4	2 -2 1
28	3.3097	3.3136	26.92	26.88	13.0	-4 -1 2
29	3.0158	3.0211	29.59	29.54	25.2	-5 -1 2
30	2.9926	2.9824	29.83	29.93	27.0	-6 1 0
31	2.9717	2.9662	30.05	30.10	38.7	2 -1 2
32	2.8073	2.8141	31.85	31.77	9.1	-1 3 1
33	2.7108	2.7121	33.01	33.00	10.5	-7 0 2
34	2.5397	2.5370	35.31	35.35	5.1	-7 2 2
35	2.5163	2.5144	35.65	35.68	10.8	-3 3 2
36	2.4943	2.4967	35.97	35.94	9.7	-5 –2 2
37	2.3109	2.3117	38.94	38.93	3.8	-6 3 0
38	2.2725	2.2674	39.63	39.72	5.3	4 1 2
39	2.1923	2.1910	41.14	41.16	6.4	-3 4 0
40	2.1768	2.1781	41.44	41.42	7.8	5 -1 2
41	2.1101	2.1114	42.82	42.79	2.4	1 -4 1
42	2.0386	2.0390	44.40	44.39	6.6	6 -3 1

43	1.9989	1.9982	45.33	45.35	5.1	-2 4 2
44	1.9242	1.9236	47.19	47.21	2.0	-7 4 1
45	1.8860	1.8877	48.21	48.16	3.0	7 -3 1
46	1.8423	1.8409	49.43	49.47	2.9	-7 4 0
47	1.8085	1.8084	50.42	50.42	2.2	-10 1 0
48	1.7877	1.7874	51.04	51.05	1.9	7 0 2
49	1.7302	1.7282	52.87	52.94	1.8	6 3 1
50	1.6975	1.674	53.97	53.97	1.5	-8 –3 1
51	1.5934	1.5925	57.81	57.85	2.9	-1 –5 2
52	1.5336	1.5338	60.30	60.29	1.9	4 4 2
53	1.3464	1.3463	69.79	69.80	1.0	-14 0 1
54	1.3138	1.3142	71.79	71.76	.4	1 6 2
55	1.0846	1.0929	90.50	89.62	1.1	-4 8 2

Refined calculated cell parameters for a triclinic crystal system

a = 20.582 A^0 b = 8.924 A^0 c =8.4646 A^0

$\alpha = 94.189^0$ $\beta = 115.632^0$ $\gamma = 101.966^0$

Volume of unit cell = 1336.19 A^{03}

Table 4: X ray data of L_2

Peak no.	d		2 θ		I/I_{max} %	h k l
	Obs	Cal	Obs	Cal		
1	8.2803	8.2803	10.68	10.68	7.0	0 1 0
2	7.6417	7.6417	11.57	11.57	2.8	1 0 0
3	5.5639	5.5639	15.91	15.91	34.4	-1 0 1
4	5.4549	5.4549	16.24	16.24	42.6	0 –1 1
5	5.2310	5.2310	16.93	16.93	14.6	0 1 1
6	5.1451	5.1451	17.22	17.22	11.6	-1 1 1
7	4.9198	4.8627	18.01	18.23	3.6	1 1 0
8	4.8411	4.8265	18.31	18.37	3.0	1 0 1
9	4.1429	4.1402	21.43	21.44	9.8	0 2 0
10	3.8160	3.8209	23.29	23.26	83.7	2 0 0
11	3.6858	3.6947	24.13	24.07	9.0	-2 1 1
12	3.6020	3.5999	24.69	24.71	10.6	1 –2 1
13	3.4908	3.429	25.50	25.48	8.8	0 0 2
14	3.4417	3.4398	25.86	25.88	14.1	-2 2 0
15	3.1105	3.0972	28.67	28.80	4.9	2 1 0
16	3.0020	3.0045	29.74	29.71	23.6	1 –1 2
17	2.8198	2.8220	31.70	31.68	2.0	-2 1 2
18	2.7514	2.7574	32.51	32.44	0.9	-1 2 2
19	2.6538	2.6630	33.74	33.63	1.0	1 –2 2
20	2.6203	2.6155	34.19	34.25	2.4	0 2 2
21	2.5740	2.5725	34.83	34.85	100.0	-2 2 2
22	2.5665	-	34.93	-	43.5	-
23	2.4916	2.4844	36.01	36.12	6.2	-2 –1 2
24	2.3519	2.3562	38.24	38.16	2.7	1 3 0
25	2.3436	2.3450	38.38	38.35	4.6	2 –2 2
26	2.2165	2.2166	40.67	40.67	0.8	-3 –1 1
27	2.1678	2.1801	41.63	41.38	2.0	2 1 2

28	2.1259	2.1270	42.49	42.46	5.9	-2 0 3
29	2.0586	2.0675	43.94	43.75	1.7	0 –2 3
30	1.9671	1.9622	46.10	46.23	2.4	0 4 1
31	1.9199	1.9212	47.31	47.27	2.1	-3 4 1
32	1.8902	1.8956	48.10	47.95	3.0	-4 3 0
33	1.8470	1.8473	49.29	49.28	5.0	-4 2 2
34	1.8330	1.8308	49.69	49.76	2.0	-1 3 3
35	1.7666	1.7673	51.70	51.68	0.2	-3 -2 2
36	1.7149	1.7166	53.38	53.37	3.6	-3 3 3
37	1.6554	1.6557	55.46	55.45	0.7	3 –1 3
38	1.6052	1.6067	57.35	57.35	0.4	-2 4 3
39	1.5054	1.5050	61.55	61.57	0.9	0 –3 4
40	1.4448	1.4453	64.43	64.41	0.9	-1 6 0
41	1.3880	1.3876	67.42	67.44	3.6	-1 5 3
42	1.3841	1.3842	67.63	67.62	1.8	5 –1 2
43	1.2659	1.2655	74.96	74.98	0.4	-1 3 5
44	1.2291	1.2296	77.61	77.57	1.3	-3 7 1
45	1.2094	1.2098	79.12	79.09	2.8	-1 7 1
46	11.1843	1.1844	81.14	81.13	0.3	-3 –5 2
47	1.0617	1.0618	93.03	93.01	0.3	5 –7 2

Refined calculated cell parameters for a triclinic crystal system

a = 8.1851 Å b = 8.7875 Å c = 7.0573 Å

$\alpha = 90.3050 \quad \beta = 97.7880 \quad \gamma = 109.4140$

Volume of unit cell = 473.90 $Å^3$

Table5:Antibacterial activity data of L_1 and L_2

L_1				L_2			
Quantity of stock solution	Conc. in µg / ml	Growth (+) / inhibition (-) for		Quantity of stock solution	Conc. in µg / ml	Growth (+) / inhibition (-) for	
		Staph aureus	klebsialla pneumoniae			Staph aureus	klebsialla pneumoniae
0.05	2	+	+	0.05	2	+	+
0.1	4	+	+	0.1	4	+	+
0.2	8	+	-	0.2	8	+	-
0.3	12	-	-	0.3	12	-	-
0.4	16	-	-	0.4	16	-	-
control		+	+	control		+	+

Table6:Antifungal activity data of L_1 and L_2

L_1				L_2			
Quantity of stock solution	Quantity of stock solution	Conc. in µg / ml		Quantity of stock solution	Quantity of stock solution	Conc. in µg / ml	
		Aspergillus niger	Candida albicians			Aspergil lus niger	Candida albicians
0.05	2	+	+	0.05	2	+	+
0.1	4	+	-	0.1	4	+	-
0.2	8	-	-	0.2	8	-	-
0.3	12	-	-	0.3	12	-	-
0.4	16	-	-	0.4	16	-	-
control		+	+	control		+	+

It deals with purification of solvents (ethanol, methanol, acetone, chloroform, DMF, etc), synthesis of 4(o-hydroxyphenyl)-2- aminothiazole and 4-(o,p-dichorophenyl)-2-aminothiazole, synthesis of o-substituted salicylaldehyde and 2-hydroxy - 1- napthaldehyde, synthesis of Schiff bases derived from o-hydroxyaldehydes and 4-(o- hydroxyphenyl)- 2- aminothiazole, preparation of metal (Zn^{II}, Cu^{II}, Ni^{II} and Co^{II}) complexes of the above Schiff bases, physical measurements and testing of biological activities.

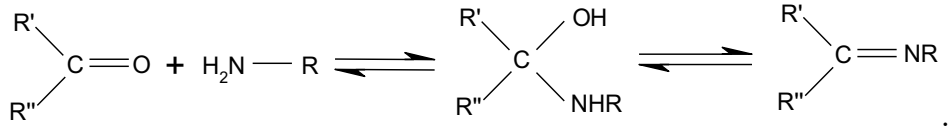
The solvents (ethanol, methanol, benzene, acetone, chloroform, DMF etc.) were purified by the standard procedures available in the literature[52-56].

Table : Physical Constant Data:

Sr. No.	Phenol used	Aldehyde obtained	M. P. / B.P.°C	
			Reported	Observed
1.	p-cresol	5-methylsalicylaldehyde	56	54
2.	m-cresol	4-methylsalicylaldehyde	60	58
3.	o-cresol	3-methylsalicylaldehy de	208	204
4.	p -chlorophenol	5-chlorosalicylaldehyde	99	96
5.	1-Naphthol	2-hydroxy- 1 -naphthaldehyde	82	80

Schiff bases

In last 25 years extensive chemistry has surrounded the use of Schiff bases in inorganic chemistry. Azomethine compounds or Schiff bases are typically formed by condensation of a primary amine and aldehydes or ketones and first reported by Schiff[1] (Equation 1).



……(1)

The resulting functional group, R^1-HC=N-R^2, is called as imine and particularly for binding metal ions via nitrogen atoms lone pair, especially when used in combination with one or more donor atoms to form polydentate chelating ligands. (Ketones, of course, will also form imines of the type$R_1R_2C=NR_3$, but the reactions tend to occur less readily than with aldehydes.) During the past decades, there has been a great deal of interest in the synthesis and characterization of transition metal Schiff base compounds. Schiff bases are becoming increasingly important in the medicinal,

pharmaceutical, dye and plastic industries as well as for liquid-crystal technology and mechanistic investigation of drugs used in pharmacology, biochemistry and physiology[63]. A lot of Schiff base compounds are used as ligands and catalysts in coordination and organic chemistry.

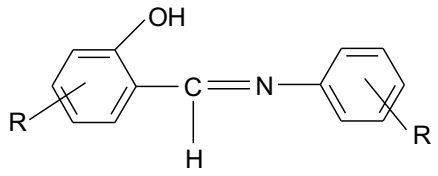
Schiff bases are important in diverse fields of chemistry owing to their interesting properties e.g. thermochromism and photochromism[64-66]. Polydentate Schiff bases containing nitrogen and oxygen donor atoms are useful for catalytic applications[67-68] . The complexes are used as catalysts for water photolysis or for oxygen reduction at modified carbon cathode[69] .

Schiff bases have also been used for analytical purposes in the determination of metal ions and some Schiff base derivatives have been used in the solvent extraction of metals[70][17].

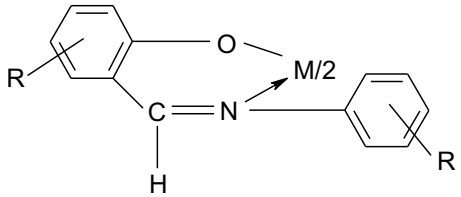
Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds via ring closure, cycloaddition, and replacement reactions[71] . Patai[72] has reviewed all these reaction in excellent manner.

Schiff bases ligands are able to coordinate through nitrogen atom of azomethine group because nitrogen atom of azomethine group is having a lone pair of electrons. In an aprotic medium the lone pairs of electron on the nitrogen atom forms a hydrogen bonded complex with the hydroxyl group. Schiff bases ligands are to coordinate many different metal and to stabilize them in various oxidation states. The have widely studied because of their applications in many fields of fundamental and applied research.

Schiff base are playing a central role as chelating ligands for large number of metal ions. A number of reviews are available on this subject[73-75] . For a Schiff base to act as chelating agent, besides the nitrogen, it must possess an additional appropriately located electron donor group so that five or six membered ring can be formed in order to increase stability of required Schiff base complex. Schiff base (IA) forms complex or chelate (IB) with bivalent metal ion.

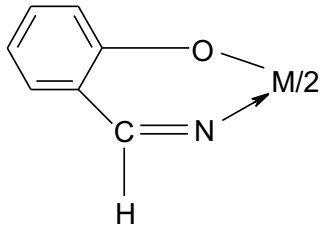


(IA)

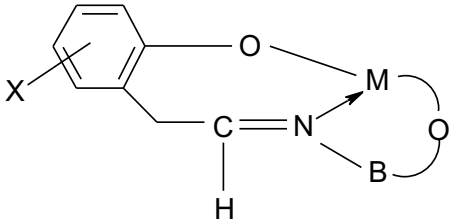


(IB)

Schiff bases are classified as bidentate, tridentate, tetradentate, pentadentate and hexadentate ligands. The stereochemical aspects and changes in the electronic properties of the complexes formed are primarily due to structural variations of the ligand. In the cases of bidentate ligands (II), the structural variations depend upon the central mental ion and steric requirement of R group. The complexes of Cu^{II} and Co^{II} with small R group possess Square planar geometry[76] and show distortion towards tetrahedral structure with R= aryl group[77-78] .



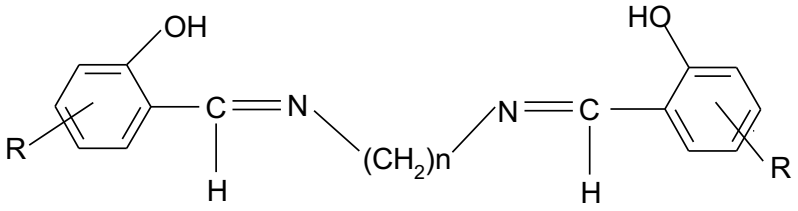
(II)



(III)

The complexes of tridentate Schiff bases (III) gives abnormal magnetic properties depending upon the structural nature of B and the presence or absence of ligand occupying forth co-ordination position.

In case of quadridentate Schiff bases (IV) the stereochemistry of metal complexes depends upon the number of carbon atoms present in the methylene bridge i.e. the value of n, for example the Co^{II} and Cu^{II} complexs with n=2 have square planar geometry, whereas the complexes with n=3 or 4 possess tetrahedral geometry[77-78] .



(IV)

Two Schiff bases 4-[(4-nitrophenyl) azo]-N-propylamine-salicylaldimine [HL^1] and 4-[(4-chlorophenyl) azo]-N-propylamine-salicylaldimine [HL^2] were synthesized from salicylaldehyde and n-aminopropane by Sheikhshoaie[79] .The structures of these compounds were studied by their microanalytical, FTIR, UV-visible studies.

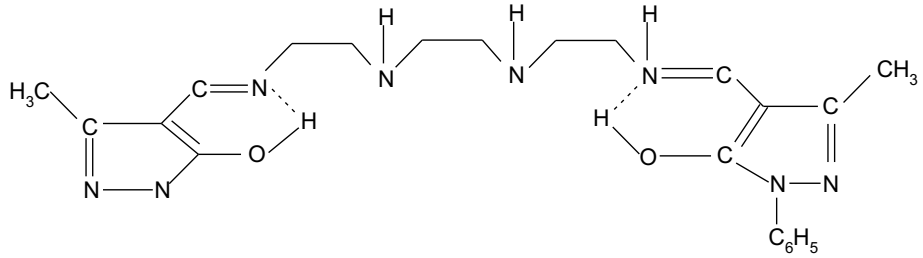
Condensation of 2-toluidine and 3-toluidine with benzaldehyde and substituted benzaldehydes resulted in the formation benzal-2-toluidines and benzal 3-toluidiness

respectively. The products were identified on the basis of elemental and spectral studies and screened in vitro for their antifungal potential against three phytopathogenic fungi and two nematodes by Rai et al[80].

Raman et al[81] prepared a new tridentate Schiff base ligand (HL) by the condensation of salicyaldehyde and p-aminoacetanilide .The compounds were characterized by microanalytical data, IR, UV-vis, ^{1}H NMR and mass spectra. The Schiff base acts as a tridentate monobasic donor, coordinating through the deprotonated phenolic oxygen carbonyl oxygen and azomethine nitrogen atoms.

The ligand tris (hydroxymethyl)-N-(2-oxo-1-naphthalideneamino)methane was prepared by reacting tris (hydroxymethyl)aminomethane with 2-hydroxy-1-naphthaldehyde by Singh et al[82] .The ligand was characterized by UV, IR and NMR spectral studies.

Patel and Thakare[83] synthesized Mn^{III} complexes with hexadentate Schiff bases (V) derived from heterocyclic β- diketones and triethylenetetramine.



(V)

Uses of Schiff bases in organic synthesis

Azomethine are considered to be analogous to carbonyl compounds and the chemical properties of azomethine are similar to those of carbonyl compounds in many respect.

The addition reactions of azomethines are mainly the reactions in which a variety of reagents add to the polarized >C=N- double bond. Therefore both electrophilic and nucleophilic reactions are possible, along with their analogous reactions[84] . A large amount of work[85] is available on the cycloaddition of the >C= N- bond, a number of these reactions are useful in synthetic organic chemistry.

Substitution of azomethine is possible either at carbon or at nitrogen. Many compounds were synthesized by this method and the subject has been reviewed by McCarty[86] .

IR spectral studies of Schiff bases

Abd –Elzaber[87] has studied infrared spectra of Schiff bases derived from o-phenylenediamine with salicyaldehyde & β-hydroxyl napthaldehyde. Due to intramolecular hydrogen bonding between nitrogen of azomethine group (>C=N) and hydrogen of the phenolic OH group, no free OH stretching is observed, but a broad and a weak band in the region of 2900-2700 cm^{1} and phenolic C-O stretching vibrations at 1298 cm^{1} in the Schiff bases.

Tumer[88] et al synthesized Schiff base ligands from vanillin, 4-dimethylaminobenzaldehyde and 3,5-di-t-butyl-4- hydroxybenzaldehyde with N-(pyridyl-3-methoxy-4 hydroxy-5-aminobenzylamine. The ligand coordinate through azomethine N and phenolic O to the metal ions. In same manner N atoms of pyridine and amine are not coordinated to the metal ions.

Kovacic et al[89] have studied IR spectra of Schiff bases derived from o-hydroxy aldehydes. The $\nu_{C=N}$ and ν_{C-O} modes occur at ~ 1630 and 1280 cm^{-1}. Schiff bases have been studied by various authors[90-94] .

Biological activity of Schiff bases

The discovery and development of antibiotics are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases. However, the increasing microbial resistance to antibiotics in use nowadays necessitates the search for new compounds with potential effects against pathogenic bacteria. The most spectacular advances in medicinal chemistry have been made when heterocyclic compounds played an important role in regulating biological activities**.** Extensive investigation in the field of schiff bases have been reported. Their preparation, chemical and physical properties have been described by various workers. Several workers have reported that Schiff bases formed from aromatic aldehydes or ketones are quite stable. Due to the great flexibility and diverse structural aspects of Schiff bases, a wide range of these compounds have been synthesized and their complexation behavior studied. Many Schiff bases are known to be medicinally important and are used to design medicinal compounds.

Thiazole compounds have been found to be associated with diverse antibacterial[95] , antifungal[96][43], antitumour[97] , anticancer[98] , and anthelmintic[99] activities particularly 2- aminothiazole have recently found

application in drug development for the treatment of allergies[100], hypertension[101], inflammation[102], infections[103] and very recently for the treatment of pain[104]. Hence, Schiff bases derived from thiazoleamines are expected to be biologically active compounds. Literature survey revels that Schiff bases exhibit antibacterial, antimicrobial and anticancer activities.

Chohan[105] et al evaluated biological activity of Schiff base derived from condensation of 2-amino-1,3,4- thiadiazole with Furan-, thiophene-, with Furan-, thiophene-, and pyrrole-2, carboxaldehyde against several bacterial strains, such as Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa.

Antimicrobial activity of Schiff bases derived from 2- amino phenol/ 2-aminothiophenol and -1-phenyl -2, 3- dimethyl-4-(4- iminopentan-2-one)- pyrazol-5-one were studied by Raman et al[106]. The above Schiff bases were tested for antibacterial activity against Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumoniae, Salomonella typhi, Pseudomonas aeruginosa, Shigella flexneri, Aspergillus niger and Trichoderma vivid.

Mohan et al studied biological activity of ligands N, N'-o-o- phenylene bis salicylaldimine and its meta and para analogs. Antibacterial activity of the Schiff base was studied against gram positive (Staphylococcus aureus) and gram negative (Escherichia coli) bacteria and antifungal activity on Aspergillus niger and Candida albicans by serial dilution method.

Cukurovali[107] et al studied the biological activity of Schiff base ligands derived from

4-C1-methyl-1-mesitylcyclobutane-3-l) -2-aminothiazole against Bacillus megaterium, Candida albicans, Escherichia coli, Listeria monocytogenes, Micrococcus luteus, Proteus vulgaris, Pseudomonas aeruginosa, Succharomyces cerevisiae and Staphylococcus aureus.

A new Schiff base ligand, 4-[{[4-(benzyloxy) phenyl]-imino} methyl] benzene-1,3-diol(bmbH), has been synthesized by the condensation reaction of p-benzyloxyaniline with 2,4-dihydroxybenzaldehyde in EtOH solution at boiling point by Kurtoglu et al[108].A mononuclear complexs of bmbH bidentate Schiff base ligand with Co(II) acetate, Ni(II) acetate and Cu(II) acetate salts have been synthesized. All the complexes have been characterized by several techniques using elemental analyses, conductivity measurements, IR and electronic spectra. 1H NMR

spectrum of the bmbH ligand was also recoded. The mononuclear Co(II), Ni(II) and Cu(II) complexes of Schiff base ligand, bmbH have a metal/ligand ratio of 1:2 complexes and the ligand coordinates through the N andO atoms. The ligand and its metal complexes were screened for antibacterial and antifungal activities by agar well diffusion techniques using DMF as solvent.

P.G. More et al[109-116] have reported Schiff bases derived from 4- aryl – 2- aminothiazole (aryl = C_6H_5, p- $CH_3C_6H_4$, p- O $CH_3C_6H_4$, p- Br C_6H_4,p-Cl C_6H_4) and R- substituted salicylaldehydes (R= H, 3- Me, 4- Me, 5-Me, 5-Cl, 5-Br) and 2-hydroxy-1- naphthaldehyde.The compounds were characterized by elemental and spectral analysis.

In this chapter we report synthesis and characterization of Schiff bases derived from 4- (o-hydroxyphenyl) -2- aminothiazole and o-hydroxyaldehydes.

1. SB^1 N- (2- hydroxy-1-naphthalidene)-4- (o-hydroxyphenyl) -2- aminothiazole
2. SB^2 N- (salicylidene) -4-(o-hydroxyphenyl) -2- aminothiazole
3. SB^3 N- (3-methyl salicylidene)-4-(o- hydroxyphenyl)- 2- aminothiazole
4. SB^4 N- (4-methylsalicylidence) -4-(o-hydroxyphenyl)-2- aminothiazole
5. SB^5 N- (5- methylsalicylidene)-4-(o-hydroxyphenyl)-2- aminothiazole.

All the ligands are yellow crystalline solids. They possess sharp melting points and are soluble in common organic solvents (alcohol, acetone, chloroform, DMF, etc.)

The elemental analysis data is given in Table 1. All compounds gave satisfactory C, H and N analysis.

UV- visible and IR and spectra

Schiff bases (in Chloroform) show intense absorption band at ~ 400 nm in Uv-visible spectra.The literature survey reveals that 2- aminothiazole shows a absorption band at ~ 275 nm, while other aromatic amino compounds with comparable structures absorb at ~ 300 nm[117-118] . The shifting of absorption band (~400 nm) of the reported Schiff bases towards longer wavelength may be due to extended conjugation in molecule.

The IR Spectrum of ligands show a broad and weak band at ~ 2900 cm^1(instead of strong band at ~ 3100 cm^1 expected for free phenolic OH group) and confirms the intramolecular hydrogen bonded OH[119-120] . In all these Schiff bases there is additional band at ~ 3100 cm^1 due to another free OH (OH group of thiazole moiety)

The $\nu_{C=N}$ & ν_{C-O} modes occur at ~1630 and ~ 1280 cm^{-1} respectively[121]

NMR spectra

NMR spectra of the Schiff bases (SB^1 to SB^8) were recorded for better understanding of structure. The NMR spectral data is given in Table 3 and spectra are depicted in figures 9-16.The assignment of NMR signals show close resemblance with earlier results[122] .

XRD Study of Schiff bases:

Diffractograms of SB^1, SB^2, SB^3, SB^4, SB^5, have been studied for predicting the crystal system. The diffractograms are depicted in fig. 17-24.

Nowadays, large no of techniques[123] have been used for structure determination of molecules. Amongst these techniques X-ray diffractometry (XRD) is important one because it is non-destructive, non-contact, fast and sensitive by powder XRD[124]

Choukimath et al[125] studied the structure of 3–methoxysalicylidene–x-(N-phenylcarbonyl) aceto carboxyhydrazone by X-ray diffraction technique. He indexed the X-ray pattern using software by trial and error method. A tetragonal structure has been proposed for the ligand. The various X-ray parameters such as lattice parameters (a, b, c) of unit cell, bond angle and volume of unit cell have been evaluated.

More and Bhalvankar[126] have reported powder XRD studies of Schiff bases derived from 4- (p-bromophenyl) - 2-aminothiazole and substituted salicylaldehyde and 2-hydroxy-1-naphthaldehyde. The crystal system present in the molecule has been proposed and various X- ray parameters were calculated.

Literature survey reveals that no work has been done on thermal and XRD studies on Schiff bases derived from aminothiazoles and o-hydroxyaldehydes. Therefore in this chapter we have undertaken thermal and XRD studies of thiazole Schiff bases.

We have reported the powder X-ray diffraction pattern of the ligands. One representative ligands (SB^5) are chosen for detailed analysis

The X-rays diffraction data of SB^5 is given in Table 4 and diffractogram is depicted in figure.21 There are 33 reflections between 5.34 to 68.685^0 with maximum of $2\theta = 5.57$ and d= $15.8325A^0$. The general procedures and methods of calculation are based on published work[127-129] . The observed and calculated values of d and θare in good mutual agreement. The lattice parameters (a, b, c) of the unit cell and cell volume were calculated by assuming a triclinic crystal system for the ligand. The cell parameters such as a=8.6232 A^0, b=$9.4755A^0$, c= 10.3723 A^0 and bond angles $\alpha = 110.741^0$ $\beta = 104.338^0$ $\gamma = 97.230^0$ Volume of unit cell = 746.26 $Å^3$ which are required for a triclinic system[130] where $a \neq b \neq c$ and $\alpha \neq \beta \neq \gamma \neq 90^o$. Therefore a triclinic crystal system is proposed for the ligand SB^5.

Thermal analysis:

Thermal stability of ligands can be studied with the help of thermogravimetric analysis patel et al[131] have reported thermal properties of α - oximinoacetoccet-o/p- chloroanidide- β - thiosemicarbazone (OAOCATS/ OAPCATS) and their Cu^{II}, Co, Ni, and Zn complexes. From the TG curves for metal chelate are steeper and that for the ligands are broad. From this it is concluded that metal chelates decompose at faster rate than the ligands. Broido method is used for the calculation of energy of activation (E) (6.22 Kcal /mole for OAO ATS)

Thermograms of ligands SB^1, SB^2, SB^3, SB^4, SB^5 are depicted in figure 25 to32. The data of initial decomposition temperature, decomposition range and % wt. loss are shown in the Table 9.Crystal system present in the molecule has been proposed and various X-ray parameters were calculated.

The TG curves of ligands are critically analysed and various kinetic parameter such as order of reaction (n), energy of activation (E), frequency factor (Z), entropy of activation (ΔS) and free energy of activation (G) have been calculated using Coat-Redfern (CR), Horowitz- Metzger (HM) and MacCallum-Tanner (MT) methods.

A representative ligand SB^4 (R=OH, R'= 4- Me) has been chosen for interpretation (fig.28) . The ligand does not show any loss in weight, when heated upto 180ºc. This indicates the absence of water of crystallization or coordinated water in the molecule. The ligand undergoes decomposition in three stages. It shows 12.91 % weight loss in the temperature of 180.27ºC -251.18 ºC in the first stage, 13.85%

weight loss (251.18º -456.31ºC in the second stage and 52.69% weight loss (456.31ºC- 590ºC) in the third stage.

The values of energy of activation (E) calculated by C.R., M.T.and H.M. methods in the first stage are 26.54, 28.59 and 29.58 kcal/mole respectively. The values of activation energies in the second stage calculated by C.R., M.T. and H.M. methods are 17.85, 20.40 and 21.48 Kcal/ mole respectively. The values of activation energies obtained by different methods for all the three stages are in good mutual agreement. The values of slope, intercept and energy of activation were obtained from plots. The residue remained at higher temperature in all the above Schiff bases may be due to formation of highly thermally stable product[132] .

The ligand SB^1 shows 26.23% weight loss (204.87-312.19) in the first stage, 10.44% weight loss (310-495ºc) in the second stage and 46.32% weight loss (497-595º c) in the final stage. (Fig.25)

The ligand SB^2 shows 14.92% weight loss in the temperature range of 180.0 331ºc in the intial stage, 5.022% weight loss (331-424º C) in the second stage and 54.76% weight loss (424-599ºC) in the final stage (Fig.26)

The ligand SB^3 shows 14.37 % weight loss in the temperature range (219.51-275.60ºc) in the initial stage, 15.96% weight loss (275-565ºc) in the second stage and 51.05% weight loss (565-643ºc) in the final stage (Fig.27)

The ligand SB^4 shows 12.91 % weight loss in the temperature range (180-268ºc) in the initial stage, 13.85% weight loss (268-463ºc) in the second stage and 51.05% weight loss (463-585ºc) in the final stage (Fig.28)

The residue left at the end, for SB^1 (15.20%), SB^2 (19.14%), SB^3 (15.86 %) and SB^4 (19.20 %) may be due to formation of thermally stable polymeric product at high temperature[132-133] [79-80].

The value of kinetic parameters such as (n, E, Z, Δ S and G) obtained by Coats-Redfern, Horowitz-Metzger and MacCallum-Tanner methods are summarized in Table 10 to 12.

On the grounds of initial decomposition temperature we have proposed the order of thermal stability among the Schiff bases as,

$SB^3 >$ SB1 > SB5 > SB4 > SB2 >

Biological activity

The biological activity of Schiff bases SB^1 to SB^5 was studied by using serial dilution technique[81] as described in chapter II. The MIC values for the ligands are given in Table 13. Comparison of MIC values for all above Schiff bases reveals that antifungal activity (against Aspergillus niger and Candida albicans) is more than antibacterial activity shown by same ligands (against Klebcialla pneumoniae and Staphylococcus aureus). The MIC values lie in the range 14-16 μg/ml for antibacterial activity and 12-14 μg/ml for antifungal activity. The biological activity data is given in Table 14. We found that all Schiff bases exhibit antifungal activity better than antibacterial activity.

The antifungal activity is more due to morphological, cytological features and mode of reproduction of the test organisms (Aspergillus niger and Candida albicans). It has round, oval shaped cells. The cell wall weak polymers like mannan and glucan. These polymers are weaker than those present in the cell walls of bacteria and those of filamentous fungi

(chitin, pectin,) due to larger size of yeast cells, the surface area to volume ratio is greater, which might be responsible for adsorption of Schiff bases over the cells

In yeast cell during budding stage, the existing cell wall gets weakened and after formation of bud, it contains newly synthesized material. The yeast cell might be more susceptible to the inhibitory action of Schiff bases, due to these two factors.

In case of bacteria, the organism reproduces by binary fission. During binary fission much of the parental cell wall conserved in daughter cells, which makes them less susceptible to the inhibitory action of Schiff bases.

<u>Complexes of Schiff bases with Ni(II)</u>

In this chapter we report the synthesis of Ni^{II} complexes (NiL_2).(LH=Schiff bases SB^1 to Sb^5). The Complexes are characterized with elemental analysis, molecular weight determination, electronic and IR Spectra, magnetic susceptibility and conductivity measurements and thermal analysis. The complexes possess a 1: 2 (metal: ligand) stoichiometry and an octahedral in nature.

The complexes under study are mentioned below.

1. CN^1 =[N-2-(4- o-hydroxyphenyl thiazolyl)-2-hydroxy-1-naphalideneiminato] Ni^{II}

2. CN^2 = [N-2-(4- o-hydroxyphenyl thiazolyl)-salicylidene iminato] Ni^{II}
3. CN^3 = [N-2-(4- o-hydroxyphenyl thiazolyl)-3-methylsalicylidene iminato] Ni^{II}
4. CN^4 = [N-2-(4- o-hydroxyphenyl thiazolyl)-4-methylsalicylidene iminato] Ni^{II}
5. CN^5 = [N-2-(4- o-hydroxyphenyl thiazolyl)-5-methylsalicylidene iminato] Ni^{II}
6. CN^6 = [N-2-(4- o-hydroxyphenyl thiazolyl)-5-bromosalicylidene iminato] Ni^{II}
7. CN^7 = [N-2-(4- o-hydroxyphenyl thiazolyl)-5-chlorosalicylidene iminato] Ni^{II}
8. CN^8 =[N-2-(4- o-hydroxyphenyl thiazolyl)-3-methoxysalicylideneiminato] Ni^{II}

The complexes are monomeric and nonelectrolyte in nature .The complex coordinate to the central metal atom through N of the azomethine group, oxygen of the phenolic –OH group and N atom of the thiazole moiety (NNO donor set). Various ligand field energy parameters (Racah parameters B and C, Dq, Slater-Condon parameters F_2 and F_4 Slater-Condon-Shortley parameters F^2 and F^4) are calculated from electronic spectra. The Nephelauxatic parameters (h_X) values for the ligands have been calculated for fixing their position in nephelauxetic series.

TG curves of two representative Ni^{II} Complexes CN-I and CN-V have been critically studied. The kinetic parameters (n, E, Z, ΔS and G) calculated by various methods (Coats-Redfern, MacCallum-Tanner and Horowitz-Metzger) are found to be in good mutual agreement. The Complexes are thermally stable.

A variety of stereochemistries were shown by Ni^{II} complexes. Electronic spectral properties of six coordinate (octahedral, tetragonal), five coordinate (high spin and low spin square pyramidal) and four coordinate (tetrahedral, pseudotetrahedral, square planar geometries) of Ni^{II} complexes has been reviewed by A. B. P.Lever[133]

Octahedral Ni^{II} complexes possess two unpaired electron in eg level (t^6_{2g} e^2_g). Three spin allowed transitions are observed with intensities less than 30 l mol^{-1} cm^{-1} in octahedral system as follows

$^3T_{2g} \leftarrow {}^3A_{2g}(\nu_1)$ 7000-13000 cm^{-1}

$^3T_{1g}(F) \leftarrow {}^3A_{2g}(\nu_2)$ 11000-20000 cm^{-1}

$^3T_{1g}(P) \leftarrow {}^3A_{2g}(\nu_3)$ 19000-27000 cm^{-1}

Two forbidden transitions are also quite prominent, one $^1E_g \leftarrow {}^3A_{2g}$(near the second spin allowed transition), and the second $^1T_{2g} \leftarrow {}^3A_{2g}$(between the second and the third spin allowed band).

Jorgenson[2] studied Ni ^{II} complexes. Ni $(H_2O)_6^{+2}$ (pale green complex)[134] exhibits three bands at 8500,13500 and 25300 cm^{-1} and $Ni(NH_3)_6^{+2}$ exhibits bands at 10700, 17500 and 28200 cm^{-1}. From the difference between energies $^1T_{2g}$(F) and $^3A_{2g}$ (F), the Dq values for the above two cases are equal to 850 cm^{-1} and 1070 cm^{-1} respectively.

Ni^{II} complexes with fourteen membered macrocyclic ligand were reported by Chandra et al[135]. The electronic spectrum of the Ni^{II} complex shows two well defined bands at 10800 and 16700 cm^{-1} assignable to $^3A_{2g} \rightarrow {}^3T_{2g}$(F) and $^3A_{2g} \rightarrow {}^3T_{1g}$(F) transitions respectively. The third d-d transition band which may be obscured by the more intense charge transfer band, is calculated to be at 25000 cm^{-1}. The value of ν_2/ν_1 is 1.55 and the ligand field parameters Dq, B and β have been found to be 1080,600 and 0.58 respectively. All these values, together with the magnetic moment (3.00 B.M.)are characteristic of an octahedral geometry for this complex. The complex is found to be paramagnetic high spin and octahedral.

Chandra et. al[136] has prepared Ni^{II}complexes of macrocyclic ligands.1, 5:10, 14-dimetheno-[1,4,8,11]-tetraazatetradeca-1,3,5,6,8,10,12, 14, 15, 17-decane.The electronic

Spectrum of the Ni^{II} complex shows two well defined bands at 10700 and 16450 cm-1 assignable to $^3T_{2g}$ (F) $\leftarrow {}^3A_{2g}$ and $^3T_{1g}$(F) $\leftarrow {}^3A_{2g}$ transitions respectively. The third d-d transition band which may be obscured by the more intense charge transfer band is calculated to be at 24700cm-1. The value of ν_2/ν_1 is 1.54 and the ligand field parameters Dq, B and, β have been found to be 1070 cm^{-1}, 603cm^{-1} and 0.58 respectively. All these values, together with magnetic moments (2.95 B. M.) are characteristic of an octahedral geometry of this complex.

Chandra[136] et al synthesized Ni^{II} complexes with thiosemicarbazones and semicarbazones derived from pyrrole-2- carboxyaldehyde, 2-acetyl furan and 2-acetyl thiophene. The complexes were characterized by elemental analysis, molar conductance, magnetic susceptibility measurements, mass, IR, electronic and EPR spectral studies. The values of magnetic moments for the complexes under study lies

in the range from 2.92-3.98 B. M. Electronic spectra of chloro and nitrato complexes show electronic spectral bands in the range 8580-13000,11000-20000 and 19000-27000 cm^{-1}. These electronic spectral bands may be assigned to the spin allowed transitions $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{1g}$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ corresponding to an octahedral geometry

The nitrate complex of Ni^{II} with ligands L^1,L^3 and L^4 have medium intensity electronic spectral bands around at 9000 cm^{-1} assigned as ν_1. The bands at 10000-16500 cm^{-1} corresponds to ν_2 and it is not split, as the state is orbitally non-degenerates. The ν_3 transition appears at 14000-25000 cm^{-1} indicates tetrahedral geometry.

Some tellurium containing tetraazamacrocyclic complexes of the type RR^1TeL^1, RR^1TeL^2, RR^1TeL^3 and RR^1TeL^4 (where $R=R^1=CH_3$ and $R=R^1=C_6H_5CH_2$) have been prepared via template condensation of 1, 2-diaminoethane or 1, 3-diaminopropane with RR^1TeX_2 and metal salts by Srivastava[137] et al. Elemental analysis, molar conductivity, PMR, IR, Magnetic susceptibility measurements and X-ray photoelectron spectra have characterized the compounds. At room temperature these complexes show magnetic moment in the range 2.94-2.98 B. M. These values correspond to a high spin configuration and show the presence of an octahedral environment around the nickel ^{II} ion in the complexes.

The electronic spectra of the complexes display three absorption bands in the range 9997-10526 cm^{-1}(ε= 36-42 dm^{-3} $mol^{-1}cm^{-1}$)16257-16642cm-1(ε =66-73 dm^{-3} $mol^{-1}cm^{-1}$) and 24867-24876cm^{-1}(ε= 121-127 dm^{-3} $mol^{-1}cm^{-1}$). These bands may be assigned to the three spin allowed transitions: $^3A_{2g} \rightarrow {}^3T_{2g}(\nu_1)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3) respectively, corresponding to an octahedral geometry.

The complexes of the type $[Ni(ACAAP)Cl_2]$, $[Ni(ACAAP)_2]$[138] and [Ni(ACAAP)Cl], where ACAAP is acetylacetone-4-amino-antipyrine) show a broad absorption band in the region 16500-16000 cm^{-1} assignable to $^3T_{2g}$ (F) $\leftarrow {}^3T_1$(F) in tetrahedral geometry .

Square planer Ni^{II} complexes are generally yellow or orange red in colour[139]. The d^8 configuration species form four coordinate diamagnetic square planar complexes with strong ligand field. The complexes exhibit single band in the visible region at 18000-25000 cm^{-1} (intensity 50-500 l mol^{-1} cm^{-1}) and a second intense band at 23000-

30000 cm^{-1} corresponding to ν_2 and ν_3 respectively. Complexes of sulphur containing ligands exhibit additional band in the NIR region[140].

The distinction between the square planar and octahedral or tetrahedral coordination can be done on the basis of the fact that the prior does not absorb below 10000 cm^{-1}. This situation is due to the large crystal field splitting in the square planar complexes. Spectra of single crystal of some complexes have, however exhibited bands below 10000 cm^{-1} and these may be vibrational in nature[141].

Nishida et al[141] studied square planar Ni^{II} complexes of microcyclic Schiff bases. The electronic spectral bands corresponds to transition dxy $\leftarrow$ dyz, dxy $\leftarrow$ dz^2 and dxy $\leftarrow$ dx^2. y^2.

Mitu et al[142] synthesized Ni ^{II} complexes with arylhydrazone ligand formed through the condensation of isonicotinoylhydrazine with 2-aldehyde pyrrole. The spectrum of the Ni^{II} complex contains two bands of absorption at 10101cm^{-1} and 17241 cm^{-1} are assignable to the transition $^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$ respectively. These transitions are characteristic the Ni^{II} ion in an octahedral coordination and this is supported by the value of the magnetic moment of 3.37 B. M. The band of absorption associated to the $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3) transition is concealed by the transition specific to the n$\leftarrow\pi^*$ ligand which exhibits a much higher intensity. For Ni^{II} complex the parameters Dq, B, β have been calculated: Dq=1010cm^{-1}, B=795cm^{-1}, β=0.77.

Some new Ni ^{II} complexes of azodyes derived from 4-amino antipyrine were reported by Nair et al[143]. The electronic absorption spectra of octahedral Ni^{II} complexes show three transitions: $^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3), which are observed at 25000, 17000 and 11000 cm^{-1} respectively. These bands suggest octahedral geometry of the complex.

Badwaik et al[144] synthesized 2-amino-4- (2-hydroxy-5-methylphenyl)-thiazole and its complexes of bivalent metal ions. The complexes were characterized by analytical, magnetic, IR, reflectance spectral data and thermal analysis. The Ni^{II} exhibits three band at 15556, 19230 and 23255 cm^{-1} corresponding to the transitions: $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\nu_1)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3), respectively and the position of the bands indicative of an octahedral structure. The observed magnetic moment of the complex is 3.20 B. M. which is within the expected range for Ni^{II} ion in an octahedral environment.

(B) Ligand field energy parameters of octahedral high spin Ni ^{II} complexes:

The A_{2g} state represents the ground state of octahedral d^8 system. The d^8 configuration gives rise to two quartet terms ^3F and ^3P with ^3F the ground term and ^3P being 15B higher in energy. The action of octahedral will split the ^3F into $^3A_{2g}$. $^3T_{2g}$ states and ^3P goes over into a $^3T_{1g}$ state. Therefore the three spin allowed transitions are expected as $^3T_{2g}$ (F) $\leftarrow {}^3A_{2g}$ (ν_1), $^3T_{1g}$(F) $\leftarrow {}^3A_{2g}$(F)(ν_2) and $^3T_{1g}$(P) $\leftarrow {}^3A_{2g}$ (F) (ν_3) in order of increasing energy. The energies of these transitions will follow following equations.

$$\nu_1 = 10\ Dq$$

$$\nu_2 = \tfrac{1}{2}\ (15B + 30\ Dq) - \tfrac{1}{2}\ \{(15B - 10\ Dq^2) + 12\ B.\ 10\ Dq\}^{1/2}$$

$$\nu_3 = \tfrac{1}{2}\ (15B + 30\ Dq) + \tfrac{1}{2}\ \{(15B - 10\ Dq^2) + 12\ B.\ 10\ Dq\}^{1/2} \qquad (1)$$

The correct positions of the bands and Racah interelectron repulsion parameter B can be determined according to the different fitting methods as described by Konig[28].

a. Fitting the second band

Solving expression of ν_2 in the equation (7) for B we get

$$10Dq = \nu_1$$

$$B = (2\nu_1^2 + \nu_2^2 - 3\nu_1\nu_2)/\ (15\nu_2 - 27\nu_1) \qquad (2)$$

b. Fitting the third band

In this method, ν_3 is used instead of ν, hence we get

$$10Dq = \nu_1$$

$$B = (2\nu_1^2 + \nu_3^2 - 3\nu_1\nu_3)/\ (15\nu_3 - 27\nu_1) \qquad (3)$$

c. Fitting the sum of the second and the third band

If all the three d-d transitions are observed, then the following simple equation can be used,

$$10Dq = \nu_1$$

$$B = (\nu_2 + \nu_3 - 3\nu_1)/\ 15 \qquad (4)$$

d. Fitting the difference between second and the third band

If the difference between second and third is taken as a basis for calculations of B, considerable simplification is possible

$$10Dq = \nu_1$$

$$B = 1/75(3\nu_1 \pm \{25(\nu_3 - \nu_2)^2 - 16\nu_1^2\}^{1/2} \qquad (5)$$

e. Fitting of the second and third band

In few cases, only second and third bands were observed. In such cases determination of 10Dq and B is of importance.

$10\ Dq = 1/34\ [9\ (\nu_2 + \nu_3) \pm \{81\ (\nu_2^2 + \nu_3^2) - 178\ \nu_2\nu_3\}^{1/2}]$ (6)

$B = \nu_2 + \nu_3 - 30\ Dq/\ 15$

Instead of equation (6), an equivalent relation can be used

$10\ Dq = 1/3\ (\nu_2 + \nu_3) - 5B$

$B = 1/510\ \{7\ (\nu_2 + \nu_3) \pm [49\ (\nu_2 + \nu_3)^2 + 680\ (\nu_2 - \nu_3)^2]^{1/2}\}$ (7)

Thermal studies of Ni^{II} complexes

The thermal decomposition of Ni^{II} complex of a novel Schiff base fluorenoneanthranilic acid. The thermal decomposition was studied by TG technique by Thomas et al[145]. The Ni^{II} complex undergoes decomposition in three stages. For the first stage of decomposition of Ni^{II} complex, the values of E (19.19 KJ mol-1), A (5.96x10-1 sec-1) and ΔS (-252.46 J $K^{-1}mol^{-1}$) obtained from Coats-Redfern method with n =1 agree with those obtained from the Mampel equation.

The thermal decomposition of Ni^{II} complex with mercaptobenzothiazole has been studied by Johri et al[146]. The complex was stable upto270^0C. A rapid one-stage decomposition followed upto 615 ^{0} C, giving a black residue, the molecular weight of which corresponds to NiO. The order of reaction and activation energy obtained by employing Coats-Redfern equation are found to be 1 and 366.1(cal/mol^{-1}) respectively are in good agreement

Ni^{II} complexes of 1-amidino-3-phenylthiourea have been prepared and characterized by George[147].The complexes were subjected to thermal analysis. The phenomenological, kinetic and mechanistic aspects of their decomposition have been studied. The Coats-Redfern equation was used for the kinetic studies and various equations were invoked for the mechanistic studies and the Mampel equation gave the best fit.

Jha et al[148] synthesized metal complexes of the type $[M_3(DDDP)_2X_6(H2O)_4]$ [where $M=Mn^{2+}$, Co^{2+} and Ni^{2+}, DDDP=1,5-diamino 2,4-dimethyl 1, 5 diaza 1,4 –penadiene, $X=Cl^-$, NO_3^- ,and ClO_4^-] in neutral medium. The thermal analysis of the complexes show similar pattern of decomposition. Weight loss takes place in one step, 175^0C with exothermal peak in D. T. A. curve which

corresponds to loss of four water molecules, which shows that water molecules are coordinated to metal ions.

Viswanathan et al[149] have been carried out thermogravimetric studies of Mn^{II}, Co^{II}, Ni^{II} and Cu^{II} of N,N'–triethylenediaminebis (3-carboxypropenamide) [$TEBCPH_2$]. The TG studies give valuable information aboat the temperature of inception. The thermal decomposition of the complexes of Mn^{II} and Co^{II} occurs in three stages whereas that of Ni^{II} and Cu^{II} in two stages. The stages of decomposition are attributed to the removal of the ligand from the complex. The residue is due to presence of metal oxide. In addition to this, the kinetic parameters such as energy of activation (E), pre-exponential factor (A) and the entropy of activation (ΔS) have been determined by Coats-Redfern equation. The ΔS has negative value for the first stage of decomposition of nickel^{II}complex and that of other stages of decomposition are positive which indicate that the activated complexes are less ordered in structure compared to the reactants.

More and Bhalvankar[150] have reported powder XRD studies of Schiff bases derived from 4- (p-bromophenyl) - 2-aminothiazole and substituted salicylaldehyde and 2-hydroxy-1-naphthaldehyde. The crystal system present in the molecule has been proposed and various X- ray parameters were calculated.

P .G. More et al[11-157] have reported Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} complexes of Schiff bases derived from 4- aryl – 2- aminothiazole (aryl = C_6H_5, p- $CH_3C_6H_4$, p- O $CH_3C_6H_4$, p- Br C_6H_4, p-Cl C_6H_4) and R- substituted salicylaldehydes (R= H, 3-Me, 4- Me, 5-Me, 5-Cl, 5-Br) and 2-hydroxy-1-naphthaldehyde. The complexes were characterized by elemental(C, H, N and metal) and spectral (uv-visible and IR), magnetic susceptibility and molar conductance measurements and thermal and XRD analysis. The complexes were of ML_2 type and possess an octahedral geometry.

Literature survey reveals that no systematic work has been done on Spectral, thermal, biological studies on Ni^{II} complexes of the Schiff bases derived from 4-(- o-hydroxyphenyl)-2-aminothiazole and o-hydroxyaldehydes. Therefore in this chapter we have undertaken synthesis and characterization of following Ni^{II} complexes of thiazole Schiff bases derived from 4-o-hydroxyphenyl 2-aminothiazole and o-hydroxyaldehydes as mentioned below.

Ni ^{II} complexes of thiazole Schiff bases:

1. CN^1= [N-2-(4- o-hydroxyphenyl thiazolyl)-2-hydroxy-1-naphaylidene iminato] Ni^{II}
2. CN^2= [N-2-(4- o-hydroxyphenyl thiazolyl)-salicylidene iminato] Ni^{II}
3. CN^3= [N-2-(4- o-hydroxyphenyl thiazolyl)-3-methylsalicylidene iminato] Ni^{II}
4. CN^4= [N-2-(4- o-hydroxyphenyl thiazolyl)-4-methylsalicylidene iminato] Ni^{II}
5. CN^5= [N-2-(4- o-hydroxyphenyl thiazolyl)-5-methylsalicylidene iminato] Ni^{II}
6. CN^6= [N-2-(4- o-hydroxyphenyl thiazolyl)-5-bromosalicylidene iminato] Ni^{II}
7. CN^7= [N-2-(4- o-hydroxyphenyl thiazolyl)-5-chlorosalicylidene iminato] Ni^{II}
8. CN^8=[N-2-(4- o-hydroxyphenyl thiazolyl)-3-methoxysalicylidene iminato] Ni^{II}

in nature.

Electronic Spectra

The electronic spectra of the complexes exhibit three bands, which may be assigned as under

$^3T_{2g}(F) \leftarrow {}^3A_{2g}(\nu_1), \sim 8000cm^{-1}$

$^3T_{1g}(F) \leftarrow {}^3A_{2g}(F)(\nu_2) \sim 13500cm^{-1}$

$^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)(\nu_3) \sim 24000cm^{-1}$

and the fourth band at ~26000 cm^{-1}(ε =1000 $mol^{-1}cm^{-1}$) may be due to ligand-metal charge transfer. The electronic spectral data suggested an octahedral geometry for the complexes[1].

The experimental absorption band energies of the Ni^{II} complexes are compared to the transition energies calculated by the various numerical procedures [158](equation 1-7) .For each complex, the experimental results are listed in the first line and the subsequent lines contain calculated transition energies, their deviation from the corresponding experimental value ($\delta\nu = \nu_{cal} - \nu_{exp}$) in cm^{-1}, the values of B and C, Dq, β_{35}, F_2 and F_4 and F^2 and F^4 etc. are also given in subsequent line. The ratio of ν_1, ν_2, ν_3 and Dq/B values. The nephelauxetic parameters values (hx) for the ligands for each numerical method a, b, c and d are given in Table 2.

The Racah parameters C (C=4.709 B), Slater-condon parameters (F_k) Slater-condon-shortley parameters (F^k), nephelauxetic parameters (hx) values for the ligands are calculated by using the methods given in chapter V.

The value of 10Dq is determined directly from the energy (ν_1) of the first spin allowed transitions $^3T_{2g}$ (F) $\leftarrow$ $^3A_{2g.}$ From the table 2 it is observed that of all the compared to other methods[28]. The sequence of δ values is in order δ (a) > δ (d) > δ (b) > δ(c). It is obvious that transition calculated according to method (a) show particularly large differences to the observed band energies, thereby reflecting uncertainty in the energies of second transition $^3T_{1g}$(F) $\leftarrow$ $^3A_{2g}$(F)(ν_2). From the above discussion we can conclude that in case of octahedrally coordinated d^8 ions (Ni^{II}, the method c resulting from fitting the sum of the second and the third band should be preferred, provided all the three d-d transition bands are observed.

The values of B of the complexes (in the range 800-900 cm^{-1}) are less than the free metal ion value (1041 cm^{-1}) and the values of β(0.8-..82) indicates considerable covalent character of theNi-L bond in the complexes. The value of C (4000-4100), β, F_2 (1395-1451) and F_4(109-119), F^2(7.1x10^4) and F^4(5.1x10^4), ν_3/ν_1(2.9), ν_3/ν_2(1.77)and Dq/B (0.9-.10)are in agreement with octahedral geometry of the complexes[159-160].

The hx values for the reported ligands lie in the range 1.2-1.4 cm^{-1} and suggest that the ligands should be placed in between urea and ammonia in the nephelauxetic series[30].

A. B. P, Lever[161] has reviewed the ligand field parameters data of octahedral Ni^{II} complexes [10 Dq values (7500-9000), B(800-900), ν_3/ν_1(2.977), ν_3/ν_2(1.83), ν_2/ν_1(1.624)]

Chandra et al[162] studied octahedral Ni^{II} complexes of thiosemicarbazone derived from 2-acetyl thiophene. The values of ligand field parameters are LFSE (138-139 kJ mol^{-1}), Dq (965-968), β (0.69 -0.74cm^{-1}). These values indicate appreciable covalent character of metal –ligand σ bond.

The Co^{II}, Ni^{II} and Cu^{II} complexes with thiosemicarbazone and semicarbazone derived from 2-acetyl pyridine were studied by Chandra et al[163]. The values of ligand field parameters are LFSE (112-139 kJ mol^{-1}), Dq (780-979 β (0.61-.95cm^{-1}). The value of β lies in the range o.54-0.95. These values indicate appreciable covalent character of metal –ligand σ bond.

Choudhary et al[164] reported octahedral Ni^{II} complexes of Schiff bases derived from substituted quinazoline-4(3H-ones).The values of ν_2/ν_1, Dq/B,B and β

which are1.70,1.0,890 cm-1 and 0.89 respectively are in good agreement with the octahedral geometry of the complexes.

Reddy and Ligappa[165] reported Ni ^{II} complexes of heterodonor ligands. The ligand field energy parameters have been calculated by various fitting procedures. The value of β (.78-.9), ν_2/ν_1(1.8-1.9), B (740-950cm^{-1}) suggest an octahedral geometry of the complexes.

IR spectra

The IR spectra of Ni ^{II} complexes are depicted in fig. 1 and 2.

In order to study the bonding mode of Schiff base to metal ion in the complexes, IR spectra of the free ligands were compared with the spectra of the complexes. The IR spectra of representative Ni^{II} complexes are depicted in fig.1 and 2. Thiazole and phenyl ring vibrations[166] occur at ~1600 m, ~1530 m, ~1480 m, ~1450 m, ~1430 cm^{-1}(m indicates medium absorption band). The ligand exhibit $\nu_{C=N}$ and ν_{C-O} modes at ~1630 and ~1280 cm^{-1}respectively. These values are in agreement with earlier reported data[167]. The new $\nu_{C=N}$ and ν_{C-O} modes in the complexes occur at ~1580 and ~1330 cm^{-1}respectively. The lowering of $\nu_{C=N}$ and shifting of ν_{C-O} towards higher frequency in the complexes as compared to the ligands indicates that coordination to the central metal takes place through oxygen of the phenolic OH and nitrogen of the azomethine group.

The presence of broad and weak non-ligand band ~400 cm^{-1}in the complexes may be due to ν_{Ni-N} andν_{Ni-O} modes[168]. ν_{OH} mode occurs at ~ 2930 cm^{-1}(due to thiazole moiety) in the complexes. IR spectral data is given in Table 3.

Magnetic susceptibility

The magnetic moment data of the present Ni ^{II} complexes is given in Table 1.

Ni^{II} in an octahedral field has an orbitally nondegenerate ground state, $^3A_{2g}(t^6_{2g}\ e_{2g})$ and no contribution from spin-orbit coupling is expected. The measured moments are in the range 2.8-3,3 B. M., very close to the spin-only value, of 2.83 B.M. The value of octahedral complexes slightly above spin-only value arise from slight mixing with the multiplet excited state in which spin-orbit coupling is appreciable.

Figgis[169-170] put forth that magnetic moments of octahedral complexes lie in the range 3.0-3.3 B. M., where as for tetrahedral complexes, they lie in the range

3.6-4.0 B. M. The Ni^{II} square planar complexes are always diamagnetic in nature. The room temperature magnetic moments of the present complexes (Gouy method) lies in the range 3.0-3.2 B. M. and suggests an octahedral geometry for the complexes[171].

Thermal analysis

Two representative Ni^{II} complexes CN-I and CN-V have been chosen for thermal studies. The TG curves of the complexes were critically analysed. The TG curves are depicted in fig. 3and 4. Both the complexes undergo decomposition in two stages. The Ni^{II} complexes doesnot show weight loss upto ~200^0C.The complex CN-I 9.293% weight loss in the temperature range (197- 210^0C), 5.847% weight loss in the temperature range (210-340^0C) in the second stage and 63.58% weight loss in the final stage (fig.3).

The CN-V shows 26.82% weight loss (225-395) in the first stage, 15.72% weight loss (395-495ºc) in the second stage and 43.40% weight loss (497-615º c) in the final stage (fig.4).

The value of kinetic parameters such as (n, E, Z, Δ S and G) obtained by Coats-Redfern., Horowitz-Metzger and MacCallum-Tanner is given in Table. The values of kinetic parameters obtained by all these methods are summarized in Table 4 and 5.The values of kinetic parameters calculated by various methods are in good agreement with each other. The values of energy of activation (E) for both the complexes are sufficiently high[172] and this indicates that both the complexes are thermally stable

Conclusion:

In the light of above discussion it is concluded that these Schiff bases derived from aminothiazole (SB^1-SB^5) are yellow crystalline solids, exhibit sharp melting points and gave satisfactory C, H and N analysis. The spectral (Uv-visible, IR and NMR) analyses supports the structures proposed for the Schiff base. All the Schiff bases are found to be biologically active compounds and exhibit pronounced antifungal activity compared to the antibacterial activity. Powder XRD studies suggest a triclinic system for the ligands. Thermal studies indicate that the ligands are thermally stable.

On the basis of elemental analysis and electronic spectral data coupled with magnetic susceptibility data an octahedral geometry (fig. 6) is proposed for the complexes. The complexes are nonelectrolytic and monomeric in nature. IR study indicates that the coordination to the central atom takes through O of the phenolic OH, N of the azomethine group and N of the thiazole group (ONN donor set).

The electronic spectra analysed in terms of ligand field energy parameters. The lower value of Racah parameters B of the metal complexes compared to that of the free metal ion indicate considerable covalent nature of the metal-ligand bond. The hx (nephelauxetic parameter) indicate that the ligand should be placed between urea and ammonia in the nephelauxetic series.

Thermal study indicates that the complexes are thermally stable. The TG curves of the complexes are sharp a steep whereas the ligands show broad curves. The values of the kinetic parameters calculated by the various methods (C. R., M.T. and H.W) are in good mutual agreement. Structure of the complexes is shown in fig.7

Table : X-ray parameters of Schiff bases

Sr No	Schiff base	a (A^0)	b (A^0)	c (A^0)	α (deg)	β(deg)	γ (deg)	Volume of unit cell A^{03}	Crystal System
1	SB^1	8.4434	10.0282	7.2931	99.708	111.026	120.119	498.52	Triclinic
2	SB^2	8.5546	9.6712	7.151	98.80	109.85	118.13	678.23	Triclinic
3	SB^3	8.6232	9.4755	10.3723	110.741	104.338	97.230	746.26	Triclinic
4	SB^4	8.6232	9.4755	10.3723	110.741	104.338	97.230	746.26	Triclinic
5	SB^5	8.6232	9.4755	10.3723	110.741	104.338	97.230	746.26	Triclinic

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