

ZINC (II) COMPLEXES OF NNO TRI-DENTATE HETEROCYCLIC SCHIFF BASES: SYNTHESIS, THERMAL AND BIOLOGICAL STUDIES**Rajmane S.V. and Ubale V. P.**Department of Chemistry, D.B.F. Dayanand College of Arts and Science, Solapur-413002, Maharashtra, India.
(Email: rajmane.shivaji@gmail.com; vpubale@gmail.com)**ABSTRACT**

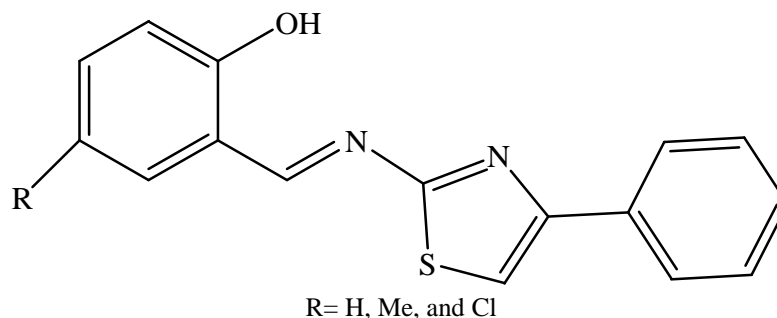
Schiff bases (SB-1 to SB-3) and their zinc (II) complexes derived from 4-phenyl-2-aminothiazole, R substituted salicylaldehyde (R=H, 5-Me, 5-Cl,) and zinc acetate have been synthesized and characterized by elemental, spectral and thermal studies. From the TG curve of complexes various kinetic parameters (n, E, Z, ΔS and G) have been calculated using Coats-Redfern method. The Schiff bases and their zinc (II) complexes were tested for antibacterial activity against *B. subtilis* and *E. coli* and antifungal activity against *A. niger* and *C. albicans* using serial dilution technique. The complexes are monomeric and nonelectrolytic in nature. They possess 1:2 metal: ligand stoichiometry and an octahedral geometry. The coordination to the central metal atom takes place through two nitrogen atoms and bonding through oxygen of the -OH group. The complexes are thermally stable and with high values of energy. The compounds show good antibacterial and antifungal activity.

KEY WORDS: antibacterial and antifungal activity, thermal studies, Zinc(II) complexes.**INTRODUCTION**

Microwave mediated synthesis has played an important role in organic synthesis over the last decade (Lidstrom, 2001; Nilsson, 2006). Seipel et. el. (2008) reported that the microwave assisted reaction times are eighty times faster than the conventional heating reaction times and these reactions are more energy efficient than those which use conventional heating. Microwave heating provides better heating efficiency, high rate of reaction, energy and better quality products and therefore it is of interest to use microwave mediated reactions in organic synthesis. Microwave synthesis of aminothiazoles is of interest in view of green chemistry approach. Kabalka (2006) reported MW promoted synthesis of 2-(N-substituted) aminothiazoles from α -bromoketones. Khrustalev (2008) reported synthesis of 2-amino-4-phenylthiazole under microwave irradiation.

Schiff bases belong to an important class of organic compounds and they undergo a variety of reactions (addition, cycloaddition, substitution and cleavage of C=N bond) (Patai, 1970). A number of reviews (Syamal, 1989; Yamada, 1999) have been devoted to coordination chemistry, which throws light on synthesis and characterization of Schiff base metal complexes. Thiazoles are well known as biological active compounds. They exhibit a wide range of antibacterial and antifungal (Ulusoy, 2002; Kaplancikli, 2004), anti-HIV (Al-Saddi, 2008), hypertension (Tripathi, 2003), anti-inflammatory (Karpov, 2001), anticancer (Baselt, 2008), and anti-convulsant (Karade, 2008) activities. Disubstituted thiazoles possess anti-inflammatory and analgesic (Hadjipavlou, 1993), anti-quorum sensing (More, 2012) activities.

Literature survey reveals that no systematic work has been done on spectral and thermal studies on Schiff bases (SB-1 to SB-3) (figure 1) derived from 4-phenyl-2-aminothiazole with R substituted salicylaldehyde (R=H, 5Me and 5-Cl) and their Zn(II) complexes (figure 2). Therefore we have undertaken synthesis and characterization of Schiff bases derived from 4-phenyl-2-aminothiazole with R substituted salicylaldehyde (R = -H, 5-Me and 5-Cl) and their Zn(II) complexes

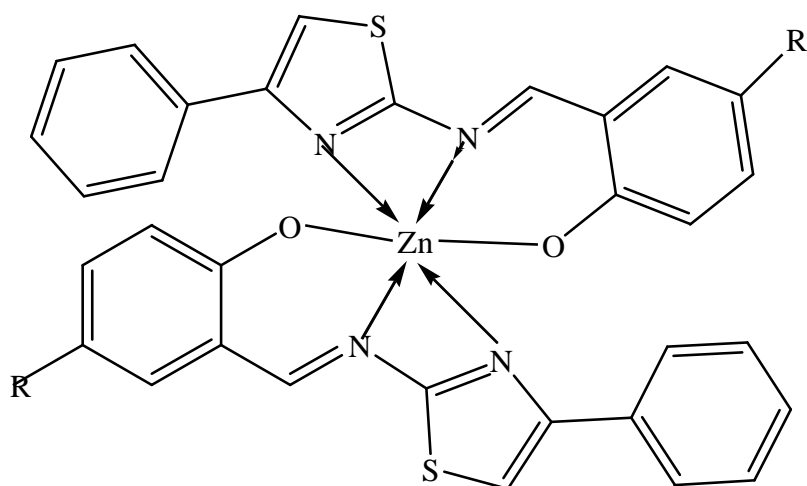


SB-1: N-salicylidine-4-phenyl-2-aminothiazole

SB-4: N-(5-methylsalicylidine)-4-phenyl-2-aminothiazole

SB-6: N-(5-chlorosalicylidine)-4-phenyl-2-aminothiazole

Figure 1: Thiazole Schiff base



SB-Zn-1: R = H,
 SB-Zn-2: R = CH₃,
 SB-Zn-3: R = Cl



Figure 2. Zn (II) complexes with Schiff bases (SB-1 to SB-3)

MATERIALS AND METHODS

All the chemicals used were of A.R. grade. The solvents were dried according to standard procedures and distilled before use. The elemental analyses (C, H and N) were performed using microanalytical technique. Metal contents were determined by gravimetric method. Ultraviolet and visible spectra were recorded in chloroform solution on Shimadzu uv-visible spectrophotometer using quartz cells at room temperature. Infrared spectra were recorded in KBr pellets on Perkin-Elmer 783 IR spectrophotometer in the range 4000-250 cm⁻¹. Thermograms were recorded on V2 4F TA thermal analyzer at the heating rate 1^o C per minute.

Synthesis of 4-phenyl-2-aminothiazole

A 4-phenyl-2-aminothiazole was synthesized by using the method reported by Khurstalev (2008). A mixture of 2-bromoacetophenone (1mmol), thiourea (2mmol) and iodine (1mmol) was stirred well and exposed to microwave irradiations for five minute with 30 sec. pause at 90W. Then 100 ml distilled water was added and exposed to microwave irradiation at 180 W for 5-6 minute with 1 minute pause till the precipitate dissolve. The yellow solution

was filtered. The filtrate was made alkaline by the addition of ammonia solution to separate out product. The product was recrystallised in ethyl alcohol and washed with diethyl ether and dried under vacuum. The purity of compound was tested with TLC.

Synthesis of Schiff bases (SB-1 to SB-3)

Schiff bases (SB-1 to SB-3) were synthesized by reacting 4-phenyl-2-aminothiazole (1mmol) with R substituted salicylaldehyde (R = H, 5-Me and 5-Cl) under microwave irradiation. A mixture of 4-phenyl-2-aminothiazole (1mmol) with R substituted salicylaldehyde (1mmol) (R = H, 5-Me and 5-Cl) stirred well and exposed to microwave irradiation at 90 W for 30 sec. Yellow crystals of the product will separate out. It was recrystallized in ethanol and dried under vacuum. The purity of compounds was tested with TLC.

Syntheses of Zinc (II) complexes

A solution of zinc acetate (0.01 M) in ethanol was added to ethanolic solution of Schiff base (0.02 M). The reaction mixture was heated on water bath for 30 minutes. The reddish yellow shining crystals of ZnII complexes formed were filtered, washed with hot ethanol and dried under vacuum.

Antibacterial and antifungal activity

Schiff bases (SB-1 to SB-3) and their Zn(II) complexes have been tested for the evaluation of antibacterial activity against *B. subtilis* and *E. coli* and antifungal activity against *A. niger* and *C. albicans* in DMSO in the concentration range 1-50 µg/ml by serial dilution technique (Sponer, 1974). Eight test tubes containing 5 ml of sterile nutrient / sabouraud broth were inoculated with 0.02ml of 24 h old culture of bacteria *S. aureus* and *K. pneumoniae* and fungi *A. niger* and *C. albicans* respectively. Different amount of Schiff bases (SB-1 to SB-3) and their Zn (II) complexes in DMSO were aseptically added with the help of sterile pipettes from the stock solution 200 µg/ml to 5 ml quantities of respective media so as to reach the concentration from 1µg/ml to 50µg/ml. All test tubes were inoculated at 37°C and at room temperature for bacteria and fungi respectively. Test tubes inoculated with organism were observed for presence of turbidity after 24h and 48h respectively. The lowest concentration of Schiff bases (SB-1 to SB-3) and their Zn(II) complexes inhibiting the growth of organism were determined as MIC value.

RESULTS AND DISCUSSION

The Schiff bases (SB-1 to SB-3) are yellow crystalline solids having sharp melting points. They are soluble in common organic solvents and gives satisfactory elemental (C, H and N) analyses.

Spectral analysis

UV-visible spectra of the Schiff bases (SB-1 to SB-3) in chloroform exhibit an intense band at ~400nm. UV-visible spectra of 4-phenyl-2-aminothiazole in chloroform exhibit an intense band at 290 nm. The shifting of λ_{max} (~400 nm) of the reported Schiff bases (SB-1 to SB-3) towards longer wavelength may be due to extended conjugation in the molecule (Patai, 1970).

Infrared spectra of the Schiff bases (SB-1 to SB-3) (KBr) exhibit $\nu(O-H)$, $\nu(C=N)$, $\nu(C-O)$ and $\nu(C-S-C)$ modes at ~3400, ~1630, ~1280 and ~665 cm^{-1} respectively. These values are in accordance with the earlier reported values. The $\nu(O-H)$ mode is broad. This may be due to hydrogen bonding between phenolic -OH and nitrogen of the azomethine group (Kovacic, 1967).

¹H NMR data of the Schiff bases and the assignments of NMR signals show close resemblance with the earlier results (Silverstein, 1991).

SB-1: (CDCl₃, TMS, δ ppm) 12.247 (1H, s, Ar-OH), 9.32 (1H, s, benzylidenimin), 6.976-8.293 (10H, m, thiazole and Ar-H); **SB-2:** (CDCl₃, TMS, δ ppm) 2.33 (3H, s, Ar-CH₃), 12.505 (1H, s, Ar-OH), 9.296 (1H, s, benzylidenimin), 6.849-8.293 (9H, m, thiazole and Ar-H); **SB-3:** (CDCl₃, TMS, δ ppm) 12.155 (1H, s, Ar-OH), 9.287 (1H, s, benzylidenimin), 6.986-8.271 (9H, m, thiazole and Ar-H).

Zn^{II} complexes are reddish yellow crystalline solids, melts with decomposition above 200°C and are soluble in chloroform, benzene and DMF. The elemental analysis data shows 1:2 (metal: ligand) stoichiometry. The elemental analyses of Zn (II) complexes gives satisfactory elemental (C, H, N and Zn) analyses. Very low conductivity values (< 10 Ω cm² mol⁻¹) in nitrobenzene suggest the nonelectrolytic nature of the complexes. Molecular weight determination data indicates that complexes are monomeric in nature.

IR spectra

In order to study the bonding mode of Schiff base to metal ion in the complexes, IR spectra of the free Schiff bases were compared with the spectra of the complexes. Thiazole and phenyl ring vibrations (Saydam, 2005) occur at ~1600 m, ~1530 m, ~1480 m, ~1450 m, ~1430 cm^{-1} (m indicates medium absorption band). The Schiff bases exhibit $\nu_{\text{C=N}}$ and $\nu_{\text{C=O}}$ modes at ~1630 and ~1280 cm^{-1} respectively. The new $\nu_{\text{C=N}}$ and $\nu_{\text{C=O}}$ modes in the complexes occur at ~1580 and ~1330 cm^{-1} respectively. The lowering of $\nu_{\text{C=N}}$ and shifting of $\nu_{\text{C=O}}$ towards higher frequency in the complexes as compared to the Schiff base 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 - 430 cm^{-1} in the complexes may be due to $\nu_{\text{C=O-N}}$ and $\nu_{\text{C=O-O}}$ modes (Nakamoto, 1963).

Thermal analysis

The TG curves of the complexes are critically analyzed in order to evaluate various kinetic parameters such as order of reaction (n), energy of activation (E), pre-exponential factor (Z), entropy of activation (ΔS) and free energy of activation (G) using Coats-Redfern (1964) method.

Coats-Redfern Method

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

(where α : fraction decomposed, q: heating rate, T: absolute temperature, n: order of reaction, Z: pre-exponential factor, E: energy of activation).

The representative Zn(II) complex with SB-1 is chosen for studies. The TG-DTA curve is depicted in Fig 3. The TG curves of the complex were critically analyzed. The complex undergoes decomposition in two stages. The Zn^{II} complex does not show weight loss upto ~200^oC and this shows the absence of coordinated water molecule in the complex. The complex show **8.62%** weight loss in stage -I (**307- 341^oC**), and **23.59%** weight loss in stage-II (**360-492^oC**) The **68.05%** residue remained at the end of second stage may be due to formation of zinc oxide.

The value of kinetic parameters such as (n, E, Z, ΔS and G) obtained by *Coats-Redfern method* are summarized in Table 1. The values of energy of activation (E) for both stages of the complexes are sufficiently high and this indicates that the complexes is thermally stable

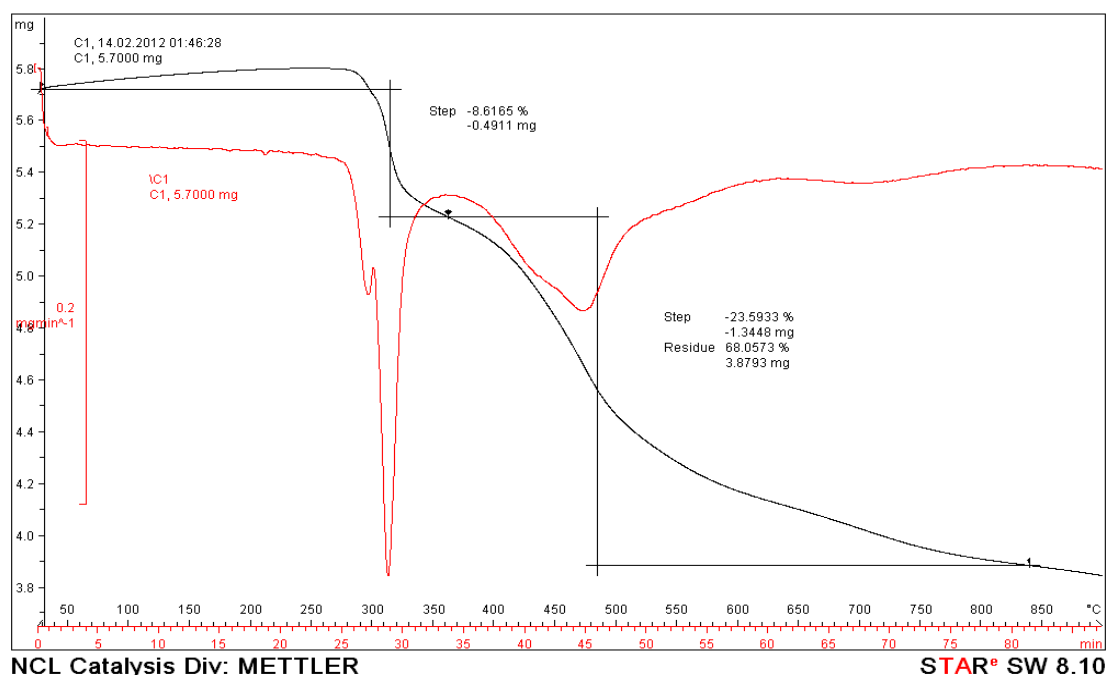


Figure 3. TG-DSC curve of Zn(II) complex with SB-1

Table 1: Kinetic parameters estimated by Coats-Redfern method

Kinetic parameters	Stage-I	Stage-II
N	1.09	1.1
E	75.82	38.82
Z	3.058×10^{25}	1.255×10^8
ΔS	-28.558	-11.717
G	59.15	30.17
Units: E-kcal mol ⁻¹ , Z-S ⁻¹ , ΔS - JK ⁻¹ mol ⁻¹ , G- kcal mol ⁻¹		

Biological Activity

Schiff bases (SB-1 to SB-3) and their Zn(II) complexes have been tested for the evaluation of antibacterial activity against *B. subtilis* and *E. coli* and antifungal activity against *A. niger* and *C. albicans* in DMSO in the concentration range 1-50 µg/ml by serial dilution technique (Spooner, 1974). The MIC values for the Schiff bases (SB-1 to SB-3) lie in the range **16-18 µg/ml** for antibacterial activity and **12-14 µg/ml** for antifungal activity and for their Zn(II) lie in the range **5-20 µg/ml** for antibacterial activity and **4-12 µg/ml** for antifungal activity. Zn(II) complexes shows good microbial activity than Schiff bases. The compounds exhibit good antifungal than antibacterial activities.

Conclusion

All the Schiff bases (SB-1 to SB-3) are yellow crystalline solids having sharp melting points. The spectral analyses (Uv-visible, IR and ¹H NMR) data confirms the structure proposed for the Schiff bases (fig. 1). The Schiff bases are found to exhibit good antibacterial activity against *B. Subtilis* and *E. Coli* and antifungal activity against *A. niger* and *C. albicans*. We found that the synthesis of Schiff base by reacting equimolar amounts of 4-phenyl-2-aminothiazole and R substituted salicylaldehyde (R = H, 5-CH₃ and 5-Cl) under microwave irradiation, is convenient and rapid method giving high yield of the expected product and is 100 times faster than the conventional method of synthesis of Schiff bases.

On the basis of elemental analyses and spectral data an octahedral geometry 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 (Ford, 1968) (ONN donor set). Thermal study indicates that the complex is thermally stable. The TG curve of the complex is sharp and steep whereas the ligands show broad curves. The values of the kinetic parameters calculated by Coats-Redfern method are in good mutual agreement.

ACKNOWLEDGEMENT

The authors are thankful to authorities of D.B.F. Dayanand College of Arts and Science, Solapur, for providing research facilities. One of the authors (SVR) is thankful to UGC – WRO Pune, for providing grants through minor research project.

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