

Research Article

Synthesis, structural and biological studies of complexes of Ti (III) with different Schiff bases

G. Nizami*, S. Ahmad, A. Akhtar

Department of Chemistry, Sir Syed Faculty of Science, Bareilly College Bareilly (UP) 243005.
Mohammad Ali Jauhar University, Rampur (UP) 244901. India.

*Corresponding author's e-mail: gulrezkhurramnizami@gmail.com

Abstract

The complexes of Ti (III) are prepared with the proposed ligands (5-Methyl-2-hydroxyacetophenone-morpholine-N-thiohydrazone, 5-Methyl-2-hydroxyacetophenone-antipyrine, 5-Methyl-2-hydroxyacetophenone-thiosemicarbazone, 2-Hydroxy-5-chloroacetophenone-morpholine-N-thiohydrazone and 2-Hydroxy-5-chloroacetophenone-thiosemicarbazone). These ligands synthesized by the corresponding amino compounds and carbonyl compounds are characterized by molar conductivity, elemental analyses, magnetic susceptibility, electronic spectra, visible spectra, IR spectra and TGA. The adducts have been characterized on the basis of elemental analyses, molar conductance, IR, visible spectra, magnetic susceptibility measurement and TGA. The ligands behave in dibasic Tridentate manner in 5-Methyl-2-hydroxyacetophenone-morpholine-N-thiohydrazone and 2-Hydroxy-5-chloroacetophenone-morpholine-N-thiohydrazone. While 5-Methyl-2-hydroxyacetophenone-antipyrine behaves in monobasic tridentate manner and 2-Hydroxy-5-chloroacetophenone-thiosemicarbazone and 5-Methyl-2-hydroxyacetophenone-thiosemicarbazone behave in tribasic bidentate manner. All the complexes were paramagnetic and have octahedral geometry. The free ligands and their metal complexes have been screened for their *in vitro* biological activities against bacteria, fungi and yeast. The metal complexes show more potent activities compared with Schiff base ligands.

Keywords: Molar conductivity; Elemental analyses; Magnetic susceptibility; Octahedral geometry; Paramagnetic character.

Introduction

Metal complexes of N and S chelating ligands have attracted considerable attention because of their interesting physicochemical properties and pronounced biological activities. The N and S atoms play a key role in the coordination of metals at the active sites of numerous metallobimolecules. Heterocyclic containing thiazole ring is present in a number of pharmacologically and biologically active compounds. Compounds containing Schiff bases derivatives were used as antifungal [1,2], anti-inflammatory [3], anti-HIV [4], anticancer [5], anticarbonic anhydrase [6], diuretic, hypoglycaemic [7], antithyroid [8], antimalarial and in therapeutic fields.

In the present paper the biological screening of free ligands and their complexes against different bacteria, fungi and yeast are reported. In attention to importance of these compounds

many literatures have been published in this field [9,10] Symmetric and asymmetric transition metal complexes of these bases have been developed and used as ligands/ catalysts in many reactions such as epoxidation [11], asymmetric synthesis [12], asymmetric sulfoxidation [13], asymmetric silylcyanation [14] and many other applications [15]. Schiff bases and the relevant transition metal complexes are still found to be of great interest in inorganic chemistry, although this subject has been studied extensively [16,17]. Schiff bases play a central role as chelating ligands in main group and transition metal coordination chemistry [16,18].

The present paper is focused on the synthesis, structural and biological studies of Ti (III) complexes with different Schiff bases like 5-Methyl-2-hydroxyacetophenone-morpholine-N-thiohydrazone, 5-Methyl-2-hydroxyacetophenone-antipyrine, 5-Methyl-2-hydroxyacetophenone-thiosemicarbazone, 2-Hydroxy-5-chloroacetophenone-morpholine-N-thiohydrazone and 2-Hydroxy-5-chloroacetophenone-thiosemicarbazone.

Hydroxy 5-chloro acetophenonemorpholine-N-thiohydrazone and 2-Hydroxy 5-chloro acetophenonethiosemicarbazone. These ligands are prepared in the lab from corresponding amino compounds and carbonyl compounds by the process discussed in methodology. The synthesized complexes were subjected to the biological and structural screening.

The proposed amino compounds are well established biological agents. It may therefore be assumed that their Schiff bases will be potent biological agents and their complexes will also expect to behave in a similar fashion. All the complexes prepared were found to be biological active as antibacterial and antifungal. Therefore the primary novelty of present paper is the biological activity of adducts synthesized first time in the lab. Secondly the present work has been proved to have immense pharmacological importance.

Materials and methods

Chemicals used:

All the chemicals used were of AR grade of equivalent purity. The carbonyl compounds used were 5-methyl 2-hydroxy acetophenone (koach light), 2-hydroxy 5-chloro acetophenone (koach light), pyridine 2-carboxaldehyde (Aldrich) and the amino compounds used were morpholine – N-thiohydrazide (OTTO), Thiosemicarbazide (S.D firm) and 4-amino antipyrine (Glaxo). The metal salts used were $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (Glaxo), MnCl_2 (Glaxo), FeCl_3 (Rankem), V(III) chloride (BDH), oxovandaium sulphate (Flucka). Other chemicals used were ethanol which was purified by distillation in the lab, methanol (Glaxo), nitrobenzene (Glaxo), DMF (Rankem) and DMSO (Glaxo) etc were of highest purity and used as such. The following methods were used for the preparation of the ligands, their complexes and their characterization.

Synthesis of ligands

5-Methyl2-hydroxyacetophenonemorpholine-N-thiohydrazone

1.41gm of morpholine-N-thiohydrazide was dissolved in ethanol and refluxed on water bath for half an hour. Then 1.50 gm of 5-methyl 2-hydroxy acetone was added and refluxed again for about five hrs.

5-Methyl2-hydroxyacetophenone antipyrine

2.06 gm of antipyrine (2, 3 dimethyl 1-phenyl 5-pyrazolone) was dissolved in ethanol and refluxed on water bath for about 25 minutes. Then 1.50 gm of 5-methyl 2-hydroxy acetophenone was added to it and refluxed for about 5 hrs [18].

5-Methyl 2-hydroxyacetophenonethiosemicarbazone

0.91gm of thiosemicarbazide and 1.50 gm. of 5-methyl 2-hydroxy acetophenone was refluxed with ethanol in reflux condenser on water bath for about 5 hours.

2-Hydroxy 5-chloro acetophenonemorpholine-N-thiohydrazone

In reflux condenser 1.41 gm. of morpholine-N-thiohydrazide was dissolved in ethanol and refluxed with 1.70gm of 2-hydroxy 5-chloro acetophenone on water bath for 4 hrs.

2-Hydroxy 5-chloro acetophenone, thiosemicarbazone:

In the presence of ethanol 0.91 gm. of thiosemicarbazide was refluxed with 1.70gm of 2-hydroxy 5-chloro acetophenone in reflux condenser on water bath. After 8 hrs of refluxing, the reaction mixture was kept at room temperature overnight and the orange colored product were filtered, washed with distilled water, diethyl ether and recrystallized from the same solvent. Yield: 85%, mp: 198o, IR (KBr) cm^{-1} : 1631 (C=N, azomethine), 1269 (C–O, phenolic), ^1H NMR (TMS, DMSO- d_6) δ ppm: 9.92 (s, 1H, HC=N, azomethine), 12.82 (s, –OH), 7.60–8.00 (d, 4H, Ar – H), 11.04 (s, NH), 3.48 (s, 3H, OCH₃), 2.30 (s, 3H, CH₃), 5.72 (s, 2H, SO₂NH group), ^{13}C NMR (TMS, DMSO- d_6) δ ppm: 164.66 (HC=N, azomethine), 155.29 (–C–OH, phenolic), 148.51 (C–O–C), 121.69–117.96 (Ar, C=C). The purity of the crystals was checked by determination of its melting point and TLC. The ligands were characterized by determining its elemental analyses and recording its spectra (Table 1).

Preparation of metal complexes

Approximately 250 ml of Titanium (III) Chloride aqueous solution (Containing 15% of TiCl_3) was taken and 4 to 5 gram Titanium metal sponge was added to it. This mixture was cooled over a freezing mixture and dry HCl gas was passed through the solution at a low temperature.

Now the Titanium (III) chloride was covered by a thick layer of toluene which protected it

against oxidation. After saturation with HCl gas the solution was warmed over water bath.

Table 1. Structure of ligands

S. No.	Name of ligands	Structure of ligands
1.	5-Methyl 2-hydroxyacetophenonemorpholine-N-thiohydrazone	
2.	5-methyl 2-hydroxyacetophenoneantipyrine	
3.	5-Methyl 2-hydroxyacetophenonethiosemicarbazone	
4.	2-Hydroxy 5-chloroacetophenonemorpholine-N-thiohydrazone	
5.	2-Hydroxy 5-chloroacetophenonethiosemicarbazone	

The Titanium metal reacted with HCl gas to form $TiCl_4$ which was subsequently reduced to $TiCl_3$ by hydrogen gas produced during the reaction (Table 1). The Titanium (III) chloride in the solution with high concentration was kept inside a freezing mixture for 10 hours, when the dark blue coloured crystals of $TiCl_3 \cdot 6H_2O$ were obtained at the bottom of the flask. The ethanolic solution of the metal salt was gradually added with stirring to a solution of the respective ligand in methanol. The precipitate so obtained was filtered, washed and derived over P_4O_{10} in vacuum desiccators [18].

The metal complexes synthesized were characterized by determination of melting points. The melting points were determined in the lab. For gravimetric Estimation of the metal the complexes were treated with acid mixture and evaporated of dryness and the respective metals were estimated as oxides by the standard methods given in chemical literature. The elemental analyses for C, H, N, and S of the ligands and their respective complexes were carried out at CDRI Lucknow. The magnetic

susceptibility of the ligand was measured by Gouy method at chemistry department Bareilly College Bareilly. $CuSO_4 \cdot 5H_2O$ was used as callibrant. The UV/visible spectra were recorded with the help of Backman-DU at chemistry department Bareilly College Bareilly. The Molar Conductance measurement was carried out at room temperature and 10^{-3} M dilution using conductivity bridge model 910 at chemistry department Bareilly College Bareilly. IR Spectra were recorded at CDRI Lucknow. Thermogravimetric Analyses was carried out at G.N.D. University (Amritsar). Antibacterial and antifungal activities were carried out at IVRI Izzatnagar Bareilly.

Results and discussions

5-Methyl 2-hydroxy acetophenonemorpholine-N- thiohydrazone titanium (III) chloride and 5-chloro2-hydroxy acetophenonemorpholine-N-thiohydrazone titanium (III) chloride complexes were subjected to elemental analyses for C,H, and N. Metal and sulphur were estimated in the lab. This analytical data indicated 1:1 metal-ligand stoichiometry for the complex. The

melting point of the metal complex was much higher than that of the corresponding ligand which indicated the formation of the adduct. The molar conductance of the complex was measured at room temperature and 10^{-3} M dilution.

In DMF and DMSO the values in both solvents indicated 1:1 electrolytic nature of the metal chelate. The magnetic susceptibility of the complex was determined at room temperature by gouy balance using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as callibrant. The observed value of magnetic susceptibility was used to calculate the value of magnetic moment which came out to be 1.69 B.M. [19] This value is slightly less than the calculated value For d1 system like Ti^{+3} . This value indicated octahedral geometry and paramagnetic nature for the nature [20]. The electronic spectrum of the complex exhibited a single band at 21000cm^{-1} with the shoulder at 23000cm^{-1} [21]. This is indicating of d-d electronic transition and octahedral geometry [22].

The IR spectra of the ligand and the complexes were recorded in KBr phase and compared to find out the co-ordination sites. The comparison indicated that both the phenolic $-\text{OH}$ and $\nu\text{C}=\text{S}$ disappeared and a new band appeared at 765cm^{-1} . This suggested the co-ordination of metal ion with the ligand through thiol sulphur and phenolic oxygen via deprotonation in addition to that the lowering of $\nu\text{C}=\text{S}$ in the IR spectrum of the complex by 20cm^{-1} indicated the co-ordination of azomethine nitrogen which is further substantiated. The data of characterization of the ligands is given in the table 2.

The appearance of azine chromophore at 1610cm^{-1} [23], indicated that the ligand is behaving in dibasis tridentate manner co-ordinating through O, N and S atoms. The IR spectrum of the complexes exhibited some new bands. The band at 3410cm^{-1} may be attributed to OH of co-ordinated water. This is further supported by the band at 880cm^{-1} may be due to rocking and wagging modes of co-ordinated water molecules [24, 25]. The inference of IR spectrum regarding the presence of coordinating water molecule is further supported by TGA. The thermogram shows the loss of three water molecules above 150°C . In the far IR region two bands were observed at 560 and 475cm^{-1} which may be assigned to $\nu\text{M}-\text{N}$ and $\nu\text{M}-\text{O}$ vibrations respectively (Table 3).

5-methyl2-hydroxyacetophenoneantipyrene Ti (III) chloride complex: The analytical data C, H, N and metal indicated 1:2 metal ligand stoichiometries for adduct. The difference in the melting-points of ligand and its complex is indicative of the formation of adduct. The molar conductance measurement carried out at room temperature and 10^{-3}M dilution indicated 1:1 electrolytic nature of the complex. The magnetic susceptibility of the complex was determined at room temperature by gouy balance using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as callibrant. The observed value of magnetic susceptibility was used to calculate the value of magnetic moment which comes out to be 1.71 B.M [20]. This value is slightly less than the calculated value for d1 system like Ti^{+3} . This value indicated octahedral geometry and paramagnetic nature for the complex.

The electronic spectrum of the complex in DMF gave one band at 20500cm^{-1} with the shoulder at 19000cm^{-1} . This band appears to have been derived from the transition $2\text{T}_{2g} \rightarrow 2\text{E}_g$ which is characteristic of octahedral geometry. The IR spectrum of the complex and the ligand were compared, which clearly indicate bonding association of the ligand with the metal ion. From IR spectral data it is evident that the ligand is having three donor sites involved in co-ordination with the metal ion. The ligand is therefore acting in monobasic tridentate manner and is bonded to metal ion through azomethine N atom, cyclic carbonyl group of pyrazolone ring and deprotonated oxygen atom of $-\text{OH}$ group. The strong band at 1590cm^{-1} characteristics of the azomethine group in the free Schiff base has shifted to lower frequency of 1570cm^{-1} in the complex indicating that the azomethine nitrogen is one of the co-ordinating atom in the cyclic carbonyl group of the pyrazolone ring of free Schiff indicated the co-ordination of the above group with metal ion [26]. This is further supported by the formation of new band in the IR spectrum of the complex 460cm^{-1} of which are due to $\nu\text{M}-\text{O}$ and $\nu\text{M}-\text{N}$ bands respectively [27]. The IR spectrum of the ligand shows the broad band at 3500cm^{-1} which may be assigned to phenolic group, which disappeared and new band appeared at 1260cm^{-1} indicating bonding of ionized phenolic oxygen to the metal atom [30]. On the basis of above mentioned facts the complex may be tentatively assigned the octahedral geometry.

Table 2. Characterization of complexes

S. No	Name & molecular formula	Colour	mp °C	Elemental analyses					IR peaks					Magnetic moment		Molar conductance
				C%	H%	N%	S%	M%	C=N	C=O	C=S	N-NH	O-H	BM	DMF	DMSO
1	5Methtyl2hydroxyacetophenone-antipyrine Ti(III)chloride complex [Ti(C ₂₀ H ₂₀ N ₃ O ₂) ₂]Cl	Orange pink	352	63.70 (62.99)	5.57 (4.86)	11.15 (10.92)	-	6.38 (5.98)	1570	1620	-	-	1260	1.71	81	86
2	2-Hydroxy 5-chloro acetophenonemorpholine-N-thiohydrazone-[Ti(III)chloride complex [Ti(C ₁₃ H ₁₄ N ₃ O ₂ SCl).3H ₂ O]Cl	Golden yellow	221	34.70 (33.99)	4.45 (3.92)	9.35 (8.93)	7.12 (6.92)	10.69 (9.98)	1570	-	-	-	760	1.76	52	142
3	5-Methtyl 2-hydroxy acetophenonemorpholine Nthiohydrazone Ti(III)chloride complex [Ti(C ₁₄ H ₁₉ N ₃ O ₂ S).3H ₂ O]Cl	Yellow	229	39.70 (38.99)	5.81 (4.02)	9.77 (8.99)	7.44 (7.02)	11.21 (10.90)	1610	-	-	-	765	1.69	62	51
4	5-Methtyl 2-hydroxy acetophenoneantipyrine Ti(III)chloride complex [Ti(C ₂₀ H ₂₀ N ₃ O ₂) ₂]Cl	Purple	310	63.70 (62.99)	5.57 (4.86)	11.15 (10.92)		6.38 (5.98)	1570	1620	-	-	1260	1.71	81	70
5	2-Hydroxy 5-chloro acetophenonethiosemicarbazone [Ti(III)chloride complex [Ti(C ₉ H ₁₀ N ₆ O ₂ S ₂ Cl).3H ₂ O]Cl	Yellow	212	34.70 (33.99)	4.45 (3.92)	9.35 (8.93)	7.12 (6.92)	10.69 (9.98)	1610		830	3280	760	1.70	52	52

Table 3. Structure of complexes

S. No.	Name of complexes	Structures of complexes
1.	5-Methyl 2-hydroxy acetophenonemorpholine-N- thiohydrazone titanium (III) chloride complex	
2	5-Methyl 2-hydroxy acetophenone antipyrine titanium (III)chloride complex.	
3	5-methyl2-hydroxy acetophenoneantipyrineTi(III)chloride complex	
4	5-Methyl-2-hydroxyacetophenonethiosemicarbaz-one Titanium(III) chloride complex	
5	2-Hydroxy5-chloroacetophenonethiosemicarbazone titanium(III)chloride complex	

5-Methyl-2-hydroxyacetophenonethiosemicarbazone Titanium (III)chloride and 5-chloro2-hydroxyacetophenonethiosemicarbazone Titanium(III) chloride

The elemental analyses for C, H, N and gravimetric estimation of the metal suggested 1:2 metal-ligand ratio for the complex. The vast difference in the melting points of the ligand and the complex indicated the formation of the adduct. The molar conductance measured in two solvents, DMSO and DMF at room temperature and 10^{-3} M dilution suggested 1:3 electrolytic natures for the chelate. The magnetic susceptibility of the complex was determined by Gouy balance and the value was used to

calculate the observed spin only value of magnetic moments which come out as 1.73 B.M. The value suggested paramagnetic nature and octahedral geometry for the complex. The electronic spectrum of the complex was recorded in DMF which exhibited a single band at 20500cm^{-1} with the shoulder at 19000cm^{-1} . The band is due to d-d transition $2T_{1g} \rightarrow 2E_g$ for Oh symmetry. The IR spectrum of the ligand and the complex on comparison suggested the coordination through nitrogen atom of azomethine group and sulphur atom of $\nu\text{C}=\text{S}$ group and also deprotonation of $-\text{NH}$ group.

This is further supported by the appearance of non-ligand band at 450cm^{-1} and 270cm^{-1} due

to ν M-N and ν M-S bands respectively. The IR spectrum of the complex shows band at 3310cm^{-1} and 880cm^{-1} which indicated co-ordinate nature of the water present in complex. This is also supported by TGA. The thermogram indicated loss of two water molecules at 180°C . The above mentioned facts suggested octahedral geometry for the complex. In 5-chloro-2-hydroxyacetophenonethiosemicarbazone Titanium (III) chloride the analytical data suggested 1:2 metal-ligand stoichiometries for the complex. The large difference in the melting points of the ligand and its complex indicated the formation of adduct. The molar conductance measurement at room temperature and 10^{-3}M dilution in DMF and DMSO suggested 1:3 electrolytic nature of the complex.

The magnetic susceptibility of the complex was measured at room temperature by Gouy balance using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as callibrant. The observed value of magnetic susceptibility was used to calculate the value of magnetic moment which comes out to be 1.708B.M. This value is slightly less than the calculate value for d1 system like Ti^{+3} ion. The value indicated the octahedral geometry and paramagnetic character of the complex. The electronic spectrum of the complex in DMF gave one band at 2500cm^{-1} with the shoulder at 19000cm^{-1} . This band appears to have been derived from transition $2\text{T}_{2g}-2\text{E}_g$ which is characteristic of octahedral geometry [20].

Infrared spectra of the free ligand exhibited characteristic bands at 3280, 1610, 830, 1045 and 1690cm^{-1} due to $\nu\text{N-NH}$, $\nu\text{C=N}$, $\nu\text{C=S}$ coupled vibrations of $\nu\text{C=S}$ with $\nu\text{N-N}$ and N-C-N deformation respectively. A comparative study of IR spectra of the ligand and complex showed that the bands due to $\nu\text{N-H}$ disappeared in the IR spectrum of the complex indicating elimination of proton from this group. The band due to $\nu\text{C=N}$ registered substantial degrees in the spectrum of metal complex as a results of chelation. The bands due to $\nu\text{C=S}$ was absent from its position in the IR spectrum of the complex indicating change the metal ion. The bands in the free ligand at 3440 and 3320cm^{-1} assignable to asymmetric and symmetric mode of $-\text{NH}_2$ group respectively remain almost at the same position in the IR spectrum of the complex, suggesting non-involvement of this group in co-ordination [28].

Biological studies

Antibacterial Activity

The bactericidal activity was evaluated by the paper disc method. The nutrient agar medium (peptone Beef extract), NaCl and agar-agar and 5mm diameter paper disc of Whatman number-1 were used. The compounds were dissolved in methanol in 500 and 1000 ppm concentrations. The filter paper disc was soaked in different solutions of the compounds dried and then placed in the petriplates already seeded with the test organisms. The plates were incubated for 24-30 hrs at $28 \pm 2^{\circ}\text{C}$ and the inhibition zone around each disc was measured.

Antifungal Activity

The fungi were grown in agar medium (Glucose 20g, starch 20g, Agar agar 20g and 1000 ml water) at $28 \pm 2^{\circ}\text{C}$ and the compounds after being dissolved in 50100 and 200 ppm concentrations in methanol were mixed in the medium. The linear growth of the fungus was obtained by measuring the diameter of colony in Petri plates after four days and the percentage inhibition was calculated by the formula,

$$\% \text{ inhibition} = (C - T) \times 100 / C$$

Where, C=diameter of the fungus colony in control

T = diameter of the fungus colony in test plate.

The ligands and their corresponding complexes were also screened for their antibacterial and antifungal activities against different types of bacteria and fungi. A comparative study of the results of the ligands and their complexes shows that the metal complexes possess 15-40% higher antibacterial and antifungal activities than the parent ligands. In metal complexes, on chelation the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π - electrons over the whole chelate ring. The large ring size of complexes makes them more lipophilic [29].

This increased lipophilicity enhances the penetration of the metal complexes into lipid membranes and block the metal binding sites in the enzymes [30]. Metal complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organisms. This enhancement in inhibiting the growth of bacteria and fungi can also be explained on the basis of their structure.

The azomethine linkage and hetero aromatic moiety in the synthesized complexes exhibit extensive biological activities [31] due to increased lipo solubility of the molecules in crossing cell membrane of these microorganisms.

Conclusions

It is clear from the above discussion that five Ti (III) complexes with following Schiff bases 5-Methyl-2-hydroxyacetophenone morpholine-N-thiohydrazone, 5-Methyl-2-hydroxyacetophenone thiosemicarbazone, 2-Hydroxy-5-chloro acetophenone morpholine-N-thiohydrazone and 2-Hydroxy-5-chloro acetophenone thiosemicarbazone. The synthesis of complexes was confirmed by the vast difference in the melting points of the complexes and the ligands. The ligands and corresponding complexes were characterized by recording their elemental analyses, magnetic susceptibility, molar conductance, visible spectra, IR and TGA. The 5-Methyl-2-hydroxyacetophenone antipyrine behaves in monobasic tridentate manner and 2-Hydroxy-5-chloro acetophenone thiosemicarbazone and 5-Methyl-2-hydroxyacetophenone thiosemicarbazone behave in tribasic bidentate manner. All the complexes were paramagnetic and have octahedral geometry. The ligands prepared and their corresponding complexes were subjected to biological activities. The metal complexes were found to be active as antifungal and antibacterial. The values of biological activity were much higher in the complexes as in ligands. The present work therefore is of highly valuable pharmacological importance.

Acknowledgments

We are thankful to the Chairman, Department of Chemistry, Mohammad Ali Jauhar University, Rampur for providing research facilities, University Grants Commission (India) for financial assistance.

Conflict of interest

Authors declare there are no conflicts of interest.

References

- [1] Chavan AA, Pai NR. Synthesis and biological activity of N-substituted-3-chloro-2-azetidiones. *Molecules*. 2007;12:2467-77.
- [2] Chohan ZH, Ul-Hassan M, Khan KM, Supuran CT. *In vitro* antibacterial, antifungal and cytotoxic properties of sulfonamide derived Schiff's bases and their metal complexes. *J Enz Inhib Med Chem*. 2005;20:183-8.
- [3] Sushilkumar SB, Devanand BS. Synthesis and Anti-inflammatory Activity of [2-(Benzothiazol-2-ylimino)-4-oxo-3-phenylthiazolidin-5-yl]-acetic acid derivatives. *J Korean Chem Soc*. 2003;47:237-40.
- [4] Racane L, Kulenovic VT, Jakic LF, Boykin DW, Zamola GK. Synthesis of bis-substituted amidinobenzothiazoles as potential anti-HIV agents. *Heterocycles*. 2001;55:2085-98.
- [5] Caleta I, Grdisa M, Sermek DM, Cetina M, Kulenovic VT, Pavelic K, *et al*. Synthesis, crystal structure and antiproliferative evaluation of some new substituted benzothiazoles and styrylbenzothiazoles. *Farmaco*. 2004;59:297-305.
- [6] Supuran CT, Scozzafava A. Carbonic anhydrase and their therapeutic potentials. *Exp Opin Ther Pat*, 2000;10:575-600.
- [7] Ogden RC, Flexner CW. *Protease inhibitors in AIDS therapy*. Marcel Dekker, New York: 2001.
- [8] Supuran CT, Scozzafava A, Mastrolorenzo A. Bacterial proteases: Current therapeutic use and future prospects for the development of new antibiotics. *Exp Opin Ther Pat*. 2000;111:221-59.
- [9] Larrow, J.F.; Jacobsen, E.N. Asymmetric processes catalyzed by chiral (salen)metal complexes. *Top Organomet Chem*. 2004; 6:123-152.
- [10] Ambroziak, K.; Szypa, M. A synthesis of unsymmetrical chiral salen ligands derived from 2-hydroxynaphthaldehyde and substituted salicylaldehydes. *Tetrahedron Lett*. 2007;48:3331-3335.
- [11] Zhang W, Jacobsen EN. Asymmetric olefin epoxidation with sodium hypochlorite catalyzed by easily prepared chiral Mn(III) salen complex. *J Org Chem*. 1991;56:2296-2298.
- [12] Spero DM, Kapadia SR. A Novel method for the asymmetric synthesis of, -disubstituted alkylamines *via* Grignard additions to ketimines. *J Org Chem* 1997;62:5537-5541.

- [13] Vetter AH, Berkessel A. Schiff-base ligands carrying two elements of chirality: Matched/mismatched effects in the vanadium-catalyzed sulfoxidation of thioethers with hydrogen peroxide. *Tetrahedron Lett.* 1998;39:1741-1744.
- [14] Guo-Fu Z, Cheng-Lie Y. Asymmetric trimethylsilylcyanation of benzaldehyde catalyzed by novel Ti(IV)-chiral Schiff base complexes. *J Mol Catal A: Chem.* 1998;132:L1-L4.
- [15] Shi M, Wang CJ. Axially dissymmetric binaphthyldiimine chiral Salen-type ligands for catalytic asymmetric addition of diethylzinc to aldehyde. *Tetrahedron: Asymmetry.* 2002;13:2161-2166.
- [16] Temel, H.; Hosgoren, H. New Cu(II), Mn(III), Ni(II) and Zn(II) complexes with chiral quadridentate Schiff base. *Transition Metal Chemistry* 2002, 27, 609-612.
- [17] Hayashi M, Inoue T, Miyamoto Y, Oguni N. Asymmetric carbon-carbon bond forming reactions catalyzed by chiral Schiff base-titanium alkoxide complexes. *Tetrahedron.* 1994;50:4385-4398
- [18] Acikgoz FE. Effect of Chemical and Organic Fertilizer Applications on Lettuce (*Lactuca sativa L. var. crispa*) Nitrate Accumulation. *Asian J Chem.* 2009;21:5421-5426.
- [19] Bermejo MR, Sousa A, Garcia-Deibe A, Maneiro M, Sanmartin M, Fondo J. Synthesis and characterization of new manganese(III) complexes with asymmetrical onsn Schiff bases. *Polyhedron.* 1999;18:511-518.
- [20] Aswale SR, Mandlik PR, Aswale SS, Aswar AS. Synthesis and characterization of Cr(III), Mn(III), Fe(III), Ti(III),YO(IV),Th (IV) , Zr(IV) UO₂ (VI) polychelates derived from bis bidentate salicylaldehyde Schiff base. *Ind J Chem.* 2003;42A:322-326.
- [21] Nizami G, Garg P, Ahmad S. Synthesis and characterization of transition metal derivatives with 5-methyl 2-hydroxy acetophenone morpholine N – thiohydrazone. *Orient J Chem.* 2008;24(3), 1095-1098.
- [22] Biradar NS, Kulkarni VH. A spectroscopic study of tin(IV) complexes with bidentate Schiff bases. *Inorg nucl Chem.* 33:1972:2451-2457.
- [23] Kriza A, Ressi A, Florea S, Maghea A. Transition Metal Complexes of Heterocyclic Ligands. Part I. Complexes with Schiff Base Derived from Amino-dibenzofuran and Salicylaldehyde. *Polish J Chem.* 2000;74:585-588.
- [24] Nakamoto K. *Infrared & Raman Spectra of inorganic & co-ordination compounds (5th Ed.)* Wiley-Interscience, New York 1997.
- [25] Ferro JR. *Low Frequency Vibrations of Inorganic and co-ordination compounds.* Plennm, New York, 1971.
- [26] Soumitra KS, Pandey OP, Akhilesh KS, Mahendra KM, Chandra MT. Synthesis, spectral and antibacterial studies of bis(cyclopentadienyl)titanium(IV)/zirconium(I V) and mono(cyclopentadienyl)titanium(IV) complexes of antipyrine Schiff bases. *J Ind Chem Soc.* 2008;85:247-251.
- [27] Mukhopadyay R, Bhattacharji S, Bhattacharya R. Generation of manganese-(III) versus-(IV) complexes with a conjugated ONS donor set: controlling effect of ligand substituents. *J Chem Soc Dalton Trans.* 1997;13:2267-2272.
- [28] Mazumder UK, Gupta M, Bera A, Bhattacharya S, Karki S, Manikandan L, et al. Synthesis, antitumor and antibacterial activity of some Ru(bpy)₂+2/4-substituted thiosemi-carbazide complexes. *Indian J Chem.* 2003;42A:313-317.
- [29] Vaghasia Y, Nair R, Soni M, Baluja S, Chanda S. Synthesis, structural determination and antibacterial activity of compounds derived from vanilline and 4-aminoantipyrine. *J Serb Chem Soc.* 2004;69:991-998.
- [30] Neelakantan MA, Rusalraj F, Dharmaraja J, Johnsonraja S, Jeyakumar T, Sankaranarayana Pillai M. Spectral characterization, cyclic voltammetry, morphology, biological activities and DNA cleaving studies of amino acid Schiff base metal(II) complexes. *Spectrochim Acta A Mol Biomol Spectrosc.* 2008;71:1599-609.
- [31] Chohan ZH. Antibacterial and antifungal ferrocene incorporated dithiothione and dithioketone compounds. *Appl Organomet Chem.* 2006;20:112-116.
