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Synthesis, Characterization and Antimicrobial Activity of Mn(II), Fe(II), Co(II), Ni(II) and Cu(II) Complexes of Schiff Bases Derived From 2-Amino-4(4'-methylphenyl)-thiazole and Substituted 4-Acetyl-1-phenyl-3-methyl-2-pyrazolin-5-ones

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2-Amino-4(4'-methylphenyl)-thiazole condensed with substituted 4-acetyl-1-phenyl-3-methyl-2-pyrazolin-5-ones to form Schiff base. These Schiff bases from complexes of type $ML_2 \cdot 2H_2O$ (M = Mn, Fe, Co, Ni and Cu). Elemental analysis, magnetic susceptibility, electrical conductance, reflectance and infrared spectral data suggested octahedral structure for the complexes. All the compounds were tested for their antibacterial activity. The result indicates that the growth of the tested organism was inhibited by most of the compounds. These Schiff bases are characterized by elemental analysis, mass spectra, ^{1}H NMR spectra, ^{13}C NMR spectra and FT-IR spectra.

Key Words: 2-Amino thiazole, Schiff base, Transition metals, Spectroscopy, Antibacterial activity.

INTRODUCTION

Thiazole ring unit is a common structural feature in various bioactive molecules[1]. This heterocyclic system has been employed in the preparation of different important drugs required for treatment of inflammations[2], bacterial infections[3] and hypertension[4]. Some of the thiazole analogues are used as fungicides, inhibiting *in vivo* the growth of xanthomonas and as ingredients of herbicides, antischistosomicidal and anthelmintics drugs[5]. Aminothiazoles are known to be ligands of the estrogen receptor and as a novel class of adenosine receptor antagonists[6].

In continuation of our work[7-12] on the metal complexes of Schiff bases, we report here the study of some new, Mn(II), Fe(II), Co(II), Ni(II) and Cu(II) complexes of Schiff bases derived from 2-amino-4(4'-methylphenyl)-thiazole and substituted 4-acetyl-1-phenyl-3-methyl-2-pyrazolin-5-ones. Preparation, characterization and antibacterial activity of above metal complexes with this Schiff bases AMPTACMPO and AMPTAMPMPO are reported here.

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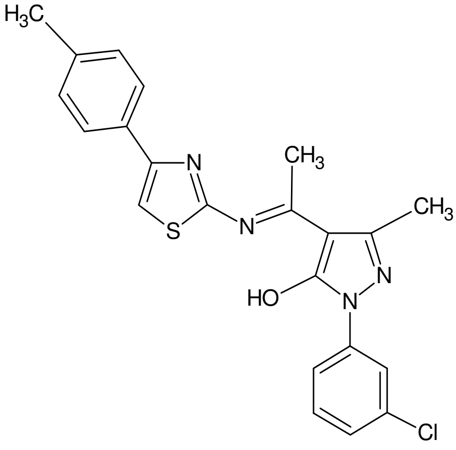
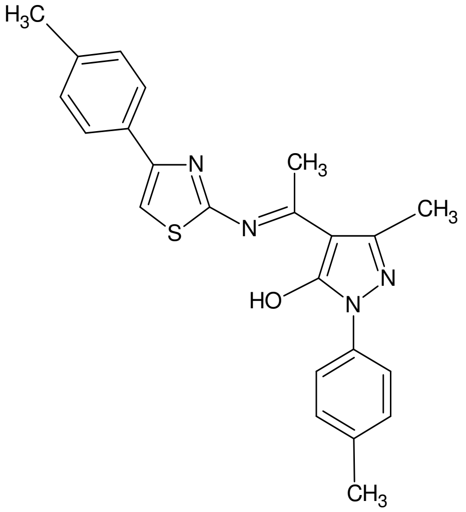


AMPTACMPO

AMPTACMPO = Schiff base of 2-amino-4-(4'-methyl phenyl)thiazole [AMPT] with 4-acetyl-1-(3'-chlorophenyl)-3-methyl-2-pyrazolin-5-one [ACMPO]



AMPTAMPMPO

AMPTAMPMPO = Schiff base of 2-amino-4-(4'-methyl phenyl)thiazole [AMPT] with 4-acetyl-1-(4'-methylphenyl)-3-methyl-2-pyrazolin-5-one [AMPMPO]

EXPERIMENTAL

Electronic spectra were recorded in DMF solution on LAMBDA 19, UV/vis/NIR ("SICART-CVN" at V. V. Nager, Gujarat, India). The mass spectra of all ligands were recorded on the instrument named LCMS-2010A of make Shimadzu. Carbon, hydrogen and nitrogen were estimated on a Thermo fisher (Thermo electron corporation Limited), Flash Elemental Analyzer-1112. The ^{1}H and ^{13}C NMR spectra in deuterated chloroform-$CDCl_3$ of all ligands were recorded on an AVANCE II 400 of make BRUKER spectrophotometer using TMS [$(CH_3)_4Si$] as internal standard. The infrared spectra of the ligands studied in the present work were recorded on the model FT-IR-8300 of Shimadzu in KBr (Zydus Research Center, Ahmedabad, India).

The metal contents in all the complexes were determined gravimetrically as metal oxide by the method reported by Mohanti *et al.*[13]. Carbon, hydrogen and nitrogen were determined micro analytically. Molar conductivities in 10^{-3} M DMF were measured using "Equiptronics EQ-660 digital conductivity meter" and a calibrated conductivity cell at room temperature. Magnetic susceptibilities of the complexes were measured at room temperature (30 °C) using Gouy balance (Sartorius, semi-micro, Sardar Patel University, Vidhyanager, India).

Synthesis of the Schiff base ligands: Analytical grade reagents and pure distilled solvent were used throughout the work. The Schiff bases were prepared by condensation of equimolar amount of AMPT[14] and ACMPO or AMPMPO[15] in minimum quantity of methanol. The reaction mixture was refluxed in rotamental for about 3 h. On cooling the yellow solid compound obtained was filtered, washed with methanol and dried in air.

Synthesis of metal complexes: For the preparation of complexes, an aqueous solution of corresponding metal(II) acetate (0.05 M) and 1:4 dioxane solution of ligand (0.05 M) were mixed in presence of acetate buffer (pH 6.5) and the mixture was digested on sand bath for 0.5 h, cooled and filtered the precipitate and then washed with water and finally with methanol to remove excess metal ions and unreacted Schiff bases. The Schiff bases and their metal complexes were tested for antibacterial activity against *Escherichia coli*, *Salmonella typhi* and *Bacillus subtilis*.

RESULTS AND DISCUSSION

All the complexes are coloured, non-hygroscopic and stable solids. They are insoluble in water, sparingly soluble in all the common organic solvents but fairly soluble in DMF. Analytical and physical characteristics of Schiff base ligands and its metal complexes are given Table-1. The molar conductances of the complexes are in the range of 7.98-16.32 ohm^{-1} cm^2 mol^{-1} and indicate there non-electrolytic nature.

The infrared spectra of the both ligands show ν(O-H) (weakly H-bonded) at 3387 cm^{-1} [16]. The absence of this band in all the metal complexes indicates the removal of proton of hydroxyl group of pyrazolin ring during the chelation. This is further supported by the shift of C-O frequency from *ca.* 1375 cm^{-1} (in ligand) to the higher frequency 1385-1410 cm^{-1} (in complexes)[17]. The sharp intense band at 1624 and 1620 cm^{-1}, respectively in the ligands can be assigned to ν(C=N) (azomethine). A downward shift (Δν = 15-35 cm^{-1}) in ν(C=N) (azomethine) is observed upon coordination indicating that the nitrogen of azomethine group is involved in coordination. All the complexes show broad band in the region 3550-3300 cm^{-1} which may be assigned to ν(O-H) of coordinated water[18]. To account for the octahedral stereochemistry of the metal complexes, the coordination of two water molecules is expected.

The bands at *ca.* 450 cm^{-1} in Mn(II) complexes, *ca.* 470 cm^{-1} in Fe(II) complexes, *ca.* 520 cm^{-1} in Co(II) complexes, *ca.* 550 cm^{-1} in Ni(II) complexes and *ca.* 480 cm^{-1} in Cu(II) complexes may be due to metal-nitrogen stretching vibration[19,20]. A less intense band at *ca.* 1625 cm^{-1} in the spectrum of ligand may be assigned to ν(C=N) (ring)[21]. All the metal complexes do not show shifting in ν(C=N) compared to its respective ligands. This suggests that the nitrogen atom of the ring has not participated in the chelation. However, in water containing chelates, this band is observed as a broad with structure this may be due to coupling of the bending mode of coordinated water molecules with ν(C=N)[22].

Both the ligands show three absorption bands at 35842, 29940, 26041 and 35211, 30769 and 25906 cm^{-1}, respectively. No absorption was observed in the visible region for any of the ligands. In the absence of quantum mechanical calculation, it is not possible to assign the absorption bands for electronic transitions with complete

TABEL-1
ANALYTICAL AND PHYSICAL DATA OF SCHIFF BASE LIGANDS AND COMPLEXES

Ligand/complexes	Colour	m.f.	m.w.	Yield (%)	Elemental analysis, % found (calcd.)						μ_{eff} (BM)	λ_M (ohm^{-1} cm^2 mol^{-1})
					C	H	N	S	Cl	M		
AMPTACMPO	Yellow	$C_{22}H_{19}N_4OSCl$	422.93	76.0	62.03 (62.48)	4.50 (4.53)	12.94 (13.25)	8.26 (7.58)	8.28 (8.38)	–	–	–
Mn(AMPTACMPO)$_2$·2H$_2$O	Creamy	$C_{44}H_{40}N_8O_4S_2Cl_2Mn$	934.81	72.1	56.48 (56.53)	4.28 (4.31)	12.03 (11.99)	6.79 (6.86)	7.70 (7.69)	5.93 (5.88)	5.63	8.22
Fe(AMPTACMPO)$_2$·2H$_2$O	Brown	$C_{44}H_{40}N_8O_4S_2Cl_2Fe$	935.72	71.8	56.52 (56.48)	4.35 (4.31)	12.01 (11.98)	6.80 (6.85)	7.55 (7.58)	5.96 (5.97)	4.92	12.38
Co(AMPTACMPO)$_2$·2H$_2$O	Dark brown	$C_{44}H_{40}N_8O_4S_2Cl_2Co$	937.81	59.8	56.34 (56.29)	4.19 (4.29)	11.88 (11.94)	6.77 (6.83)	7.42 (7.55)	6.35 (6.28)	4.53	16.32
Ni(AMPTACMPO)$_2$·2H$_2$O	Green	$C_{44}H_{40}N_8NiO_4S_2\ Cl_2$	938.56	61.2	56.27 (56.31)	4.36 (4.30)	12.01 (11.94)	6.71 (6.83)	7.42 (7.55)	6.35 (6.25)	2.98	10.31
Cu(AMPTACMPO)$_2$·2H$_2$O	Brown	$C_{44}H_{40}N_8O_4S_2Cl_2Cu$	943.42	65.0	56.08 (56.02)	4.35 (4.27)	11.79 (11.88)	6.78 (6.80)	7.48 (7.52)	6.59 (6.74)	1.86	10.12
AMPTAMPMPO	Yellow	$C_{23}H_{22}N_4OS$	402.51	79.0	68.09 (68.63)	5.44 (5.51)	13.58 (13.92)	7.89 (7.97)	–	–	–	–
Mn(AMPTAMPMPO)$_2$·2H$_2$O	Creamy	$C_{46}H_{46}N_8O_4S_2Mn$	893.97	62.8	61.76 (61.80)	5.12 (5.19)	12.58 (12.53)	7.12 (7.17)	–	6.09 (6.15)	5.79	7.98
Fe(AMPTAMPMPO)$_2$·2H$_2$O	Brown	$C_{46}H_{46}N_8O_4S_2Fe$	897.88	69.4	61.59 (61.74)	5.14 (5.18)	12.60 (12.52)	7.10 (7.15)	–	6.28 (6.24)	5.14	14.09
Co(AMPTAMPMPO)$_2$·2H$_2$O	Dark brown	$C_{46}H_{46}N_8O_4S_2Co$	897.97	58.9	61.42 (61.53)	5.19 (5.16)	12.53 (12.48)	7.11 (7.14)	–	6.58 (6.56)	4.45	13.10

certainty. However, it appears reasonable to assign the bands to $\pi \rightarrow \pi^*$ transitions[23]. The electronic spectra of Mn(II) complexes exhibit three low intense bands, one at 16949 and 17241 cm^{-1}, respectively which may rise due to $^6A_{1g} \rightarrow {}^4T_{1g}(G)$ transition, another at 20080 and 20202 cm^{-1} assigned to $^6A_{1g} \rightarrow {}^4A_{1g}(G)$ transition and the third at 25900 and 26550 cm^{-1} assigned to $^6A_{1g} \rightarrow {}^4A_{1g}, {}^4E_g(G)$ transition for Mn(II) ion in octahedral environment. The μ_{eff} (Table-1) value of the complexes suggests the spin 3d^5 configuration[24]. The electronic spectra of both Fe(II) complexes shows a broad band at 16500 and 16650 cm^{-1}, respectively which may be assigned to the $^5T_{2g} \rightarrow {}^5E_g$ transition. The magnetic moment value 4.92 and 5.14 BM, respectively indicates that the complexes are spin-free and has octahedral geometry[25]. The electronic spectra of Co(II) complexes exhibited absorption bands in the region 8000-10500 and 18000-20000 cm^{-1} corresponding to ν_1 and ν_3 transitions $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)(\nu_1)$; $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)(\nu_3)$. In the present investigation, Co(II) complexes show the absorption bands at 9520, 11494, 17509 and 18039 cm^{-1} corresponding to ν_1 and ν_3 transitions, respectively. These bands are the characteristics of high spin octahedral Co(II) complexes. However, ν_2 band is not observed because of its proximity to strong ν_3 transition. The magnetic measurement of Co(II) complexes display magnetic moment value of 4.76 BM which is in the octahedral range 4.45-4.53 BM[26]. The greenish Ni(II) complexes exhibited three bands at 10350, 15705 and 26240 cm^{-1} as well as three bands at 10550, 15830 and 26450 cm^{-1} which are attributed to the $^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$; $^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(p)(\nu_3)$ transitions, respectively indicating octahedral geometry around Ni(II) ion. Ni(II) complexes showed the magnetic moment value of 3.28 which is in the range of 2.98-3.02 B.M suggesting consistency with their octahedral environment[25]. For the Cu(II) complexes with D_{4h} symmetry, three spin allowed transitions 2B1g → 2A1g (ν_1), 2B1g → 2B2g (ν_2) and 2B1g → 2Eg (ν_3) are possible but the electronic spectra of Cu(II) complexes display two bands at 14695, 21160, 14705 and 21380 cm^{-1}, respectively. There should be third transition but we could not observe the same which may be due to very close energy values of different states. Absence of any spectral band below 10000 cm^{-1} rules out the possibility for tetrahedral structure of the present complexes are also suggestive for distorted octahedral geometry of the complexes[27]. The low molar conductance values in DMF solution for all metal complexes (Table-1) are indicating that the complexes are nonelectrolytes.

Antibacterial activity: The compounds were tested *in vitro* for the antibacterial activity against *Escherichia coli* gram negative bacteria (responsible for diarrhea) (I), *Bacillus subtillis*-gram positive coca (general contaminant)(II) and *Staphylococcus aurous* gram positive spore forming rods (causative agent for wound infection)(III) using Agar cup assay method.

The degree of effectiveness was measured by determining the diameters of the zone of inhibition caused by the compounds. It is observed that the most of the compounds were active against both gram (–) negative and gram (+) positive bacteria (Table-2).

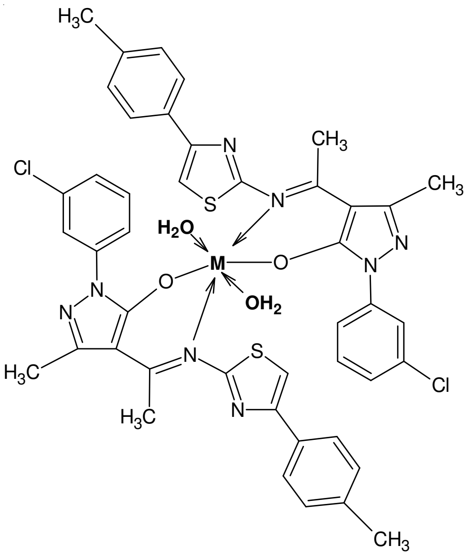
TABEL-2
ANTIBACTERIAL ACTIVITY OF THE SYNTHESIZED SCHIFF BASE LIGANDS AND ITS METAL COMPLEXES

Compound	*E. coli*	*B. subtilis*	*S. aureus*
AMPTACMPO	+	+	+
$Mn(AMPTACMPO)_2\cdot 2H_2O$	++	+	++
$Fe(AMPTACMPO)_2\cdot 2H_2O$	+	++	+
$Co(AMPTACMPO)_2\cdot 2H_2O$	+++	++	++
$Ni(AMPTACMPO)_2\cdot 2H_2O$	++	+++	++
$Cu(AMPTACMPO)_2\cdot 2H_2O$	++	+	++
AMPTAMPMPO	+	+	+
$Mn(AMPTAMPMPO)_2\cdot 2H_2O$	++	++	+
$Fe(AMPTAMPMPO)_2\cdot 2H_2O$	+	+	++
$Co(AMPTAMPMPO)_2\cdot 2H_2O$	+	+++	++
$Ni(AMPTAMPMPO)_2\cdot 2H_2O$	++	+	+++
$Cu(AMPTAMPMPO)_2\cdot 2H_2O$	+	++	+

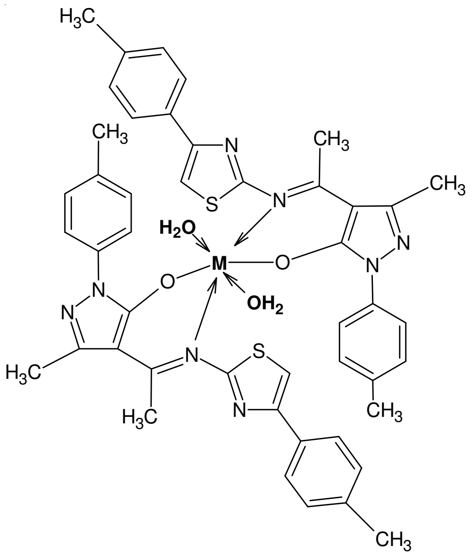
+++: Most effective, ++: Moderate effective, +: Slightly effective, –: Non effective.

Conclusion

On the basis of these results obtained for elemental analysis, infrared spectra and magnetic susceptibility measurements the following structures are proposed for the complex compounds.



(1)



(2)

M = Mn(II), Fe(II), Co(II), Ni(II) and Cu(II)

The synthesized metal complexes in comparison to the uncomplexed Schiff base ligand were screened for their antibacterial activity against pathogenic bacteria species (*E. coli*, *B. subtillis*, *S. aurous*). The activity of the Schiff base complexes became more pronounced when coordinated with metal ions. The biological activity of the complexes follow the order Co(II) = Ni(II) > Mn(II), Fe(III), Cu(II).

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