

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, Spectral Analysis and Antimicrobial Activity of some new transition metal complexes derived from 2, 4-dihydroxy acetophenones

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

Organic Synthesis Laboratory, P.G. Department of Chemistry, Yeshwant Mahavidyalaya, Nanded(M.S.), India.

ABSTRACT

Cu (II), Ni (II), Co (II), Fe (III), Zn (II) and Mn (II) complexes were synthesized from Schiff bases derived from 2-amino pyridine and 2, 4-dihydroxy acetophenone. The Schiff bases and complexes were characterized by elemental analysis and spectral data. The synthesized Schiff bases and their transition metal complexes have been screened for their antimicrobial activity against E.coli, S. typhi, S. aureus, B. subtilis and against various fungi like P.chrysogenum, A. niger, F. moniliformae, and A.Flavus. The complexes show enhanced activity than their corresponding ligands.

Keywords: Schiff bases, transition metal complexes, Spectral study and Antimicrobial activity.

**Corresponding author*

Email: pak9301@yahoo.co.in

INTRODUCTION

Hydroxy acetophenones were used as starting material for the synthesis of chalcones [1] flavones [2] and Schiff bases [3, 4] etc. Schiff bases of hydroxy aldehydes and ketones were widely used in co-ordination chemistry for the preparation of metal complexes [5, 6]. Schiff bases and their co-ordination compounds have been gained importance now-a-days as they are useful in biochemical [7], anti-cancer [8], anti-inflammatory [9], and antipyretic [10], among others. Some of them have been used as complexing agent [11, 12] and powerful corrosion inhibitors [13]. A Schiff base of hydroxy acetophenone and its complexes has a variety of applications in biological, clinical, analytical and pharmacological areas [14-16]. Earlier work has shown that some drugs showed increased activity when administered as metal chelates rather than as organic compounds [17, 18] and that the co-ordinating possibility of hydroxy acetophenone has been improved by condensing with a variety of carbonyl compounds.

Here in this paper we report the synthesis of Schiff bases as ligand and their metal complexes Cu(II), Ni(II), Co(II), Fe(III), Zn(II) and Mn(II). All the synthesized compounds were screened for their antimicrobial activity. Further the structures of synthesized compounds were confirmed by elemental analysis and spectral studies. The structures of the ligands are shown in **scheme-1** and complexes are shown in **scheme-2**.

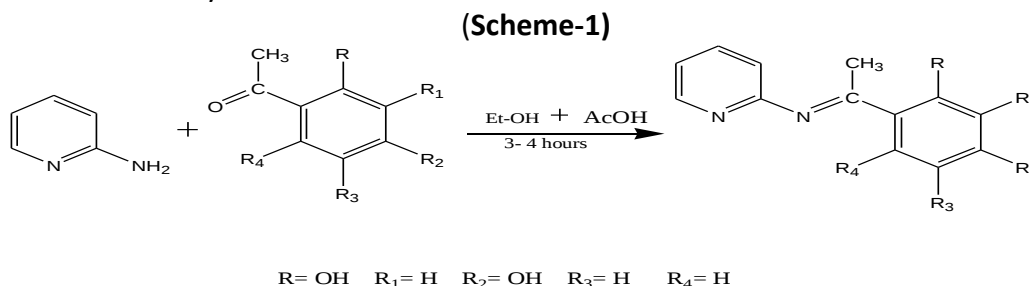
MATERIALS AND METHODS

All the melting points were determined in an open capillary tube and are uncorrected.

Completion of the reaction was monitored by thin layer chromatography on pre-coated sheets of silica gel-G. All the reagents used were chemically pure and are of AR grade. Solvents were dried and distilled before use according to standard procedure [19]. The IR spectra in KBr were recorded on shimadzu spectrophotometer and ^1H NMR spectra were recorded in DMSO on AVANCE 300 MHz spectrophotometer using TMS as an internal standard. (δ ppm).

General procedure for the synthesis of ligands derived from 2-amino pyridine (scheme-1)

An equimolar mixture of 2-amino pyridine and substituted ketone (i.e.0.01mole) dissolved in ethyl alcohol and mixture was refluxed for 3-4 hours. The reaction mixture was then poured into ice cold water the solid separated was filtered washed with water and recrystallised from ethyl alcohol.



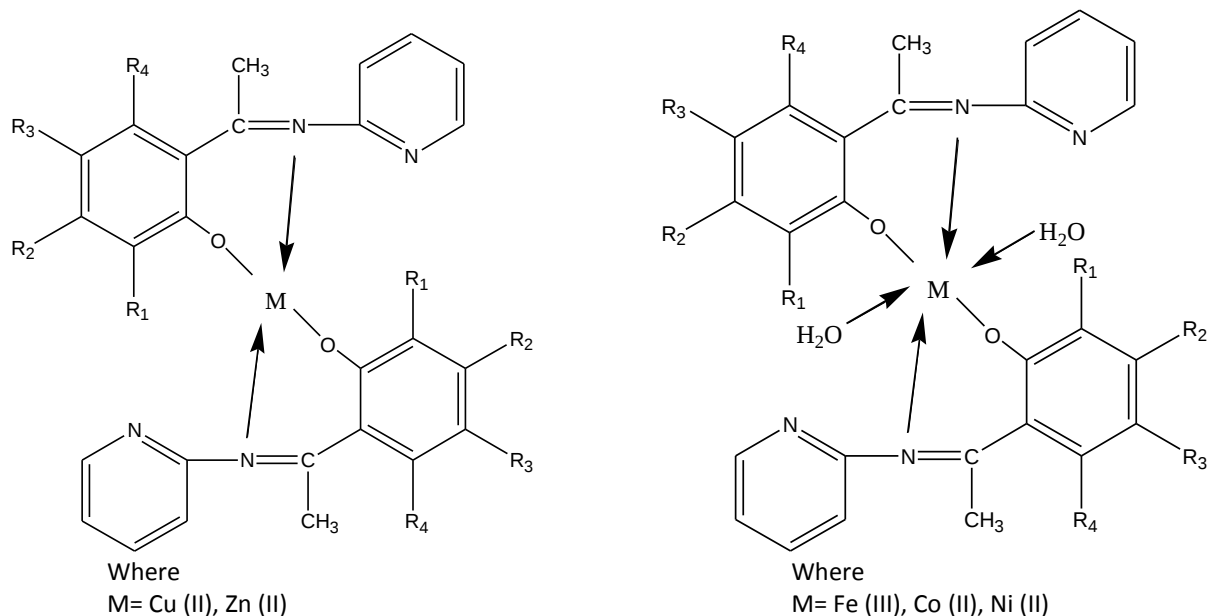
General experimental procedure for the synthesis of metal complexes (Scheme-2)

The ligand (0.02 mole) and the metal salt (0.01 mole) in 50 ml ethanol was refluxed for 2 hours. In all the cases the ligand concentration was slight excess of 1:2 metal ligand molar ratio. After refluxing the solid mass separated filtered through a sintered glass crucible (G4) and the residue was washed several times with hot methanol until the washing were free of the excess of ligand these complexes finally dried under vacuum desiccators over fused calcium chloride.

Table 1: Physical data of synthesized metal complexes

Compound code	Molecular formula	Colour	Decomposition temp. °C	Yield %
L	$C_{13}H_{12}O_2N_2$	brown	232	80
La	$C_{26}H_{22}O_4N_4Cu$	Dark brown	258	68
Lb	$C_{26}H_{26}O_6N_4Co$	Brown	230	64
Lc	$C_{26}H_{26}O_6N_4Ni$	Orange red	268	56
Ld	$C_{26}H_{24}O_6N_4Fe$	Brown	212	72
Le	$C_{26}H_{22}O_4N_4Zn$	Lemon Yellow	256	58
Lf	$C_{26}H_{22}O_4N_4Mn$	Brown	243	60

(Scheme-2)



Molar conductivity measurements were carried out in DMSO on an Elico digital conductometer model 180. The magnetic susceptibility measurements were made on Guoy balance at room temperature using $Hg [Co (NCS)_4]$ as standard.

IR spectra of the metal in KBr pallets in the range of $4000-350\text{ cm}^{-1}$ were recorded making use of FTIR-SCHIMADZU 8400S spectrophotometer.

UV visible spectra in DMF were recorded on a SCHIMADZU multipurpose recording spectrophotometer model 1601 and ^1H NMR spectra were recorded in DMSO on AVANCE 300 MHz spectrophotometer using TMS as an internal standard (δ ppm).

RESULTS AND DISCUSSION

All the complexes are colored solids, soluble in polar solvents like DMF and DMSO. The elemental analysis shows 1:2 (M: L) stoichiometry for all the complexes. The analytical data given in **Table 1**. The metal contents in complexes were analyzed by gravimetric analysis.

All the complexes show low conductance which indicates their non electrolytic nature. The magnetic measurement studies suggest that the Cu (II), Co (II), Mn (II) and Fe (III) complexes exhibit paramagnetic behavior where as the Ni (II) and Zn (II) show diamagnetic behavior.

^1H -NMR Spectra

^1H -NMR spectra of synthesized ligand and its transition metal complexes were recorded in DMSO. The ^1H NMR spectra of complexes show broad signals due to presence of metal ion and the conformation of each signal in the aromatic region is difficult due to complex pattern of splitting.

IR Spectra

The FT-IR spectrum of the free ligand shows four characteristic bands at 3300 cm^{-1} (-OH stretch), 1538 cm^{-1} (C=C Ar .str.), 1644 cm^{-1} (C=N str.), 1248 cm^{-1} (C-O, Ar-OH).

Where as in the IR spectra of complexes there is one more additional absorption band appears at $445\text{--}474\text{ cm}^{-1}$ range due to M-O bond.

Thermal Analysis

The thermogram of Ni(II), Fe(III) Co(II) complexes confirms the presence two moles of coordinated water molecules where as there is absence of coordination of water molecule in Zn(II) and Cu(II) complexes.

Hence from TGA it is clear that the complex under study contains two moles of coordinated water molecules which are coordinated to central metal ion [20].

Magnetic moment

The μ_{eff} . Values at room temperature for Cu (II) complexes are in the range of 1.76-1.88 B.M. usually observed for square planar geometry [21, 22]. Ni (II) and Co (II) complexes have

magnetic moment values in the range of 2.84-3.24 and 4.28-4.94 B.M. respectively. Whereas completely filled 'd' sub-shell the Zn ion complex is diamagnetic in nature.

Electron spin resonance study

From the ESR spectra the values of $g_{\parallel}$ and $g_{\perp}$ have been calculated by Kneubehl's methods [23]. The observed g -values point to the presence of the unpaired electron in the dx^2-y^2 orbital with $g_{\parallel} > g_{\perp}$ characteristic of square planar or elongated tetragonal geometry. The g_{11} obtained for the Cu (II) complexes is less than 2.3 indicating covalent character of the metal-ligand bond [24].

Antimicrobial activity

The antibacterial activity of the compounds was determined by agar diffusion method against various bacteria like *E. coli*, *S. typhi*, *S. aureus*, and *B. subtilis* at various concentrations such as 20, 50 and 100 $\mu\text{g/ml}$. The zone of inhibition was measured in mm and DMSO was used as solvent. Sterile nutrient agar was seeded with test organism and layered in sterile petri plate. After solidification, agar cups were bored with cork borer 0.1 ml of the compound solution was added to the cup with the help of micropipettes, one cup in the plates was filled with solvent. Standard penicillin (10 $\mu\text{g/ml}$) was used as reference drug. The plates were kept at low temperature (4°C) for 20 minutes to allow diffusion of the compound. Then the plates were incubated at 37 °C for 24 hr. After proper incubation the plates were observed for zone of no growth (zone of inhibition of growth) around the cup. Similarly the same compounds were screened for the antifungal activity against different organisms like *P. chrysogenum*, *A. niger*, *F. moniliformae*, and *A. Flavus* by using poison plate method. The compound was mixed with sterile potato dextrose agar medium so as to get final concentration 2%. It was then poured in sterile petri plate and allowed to solidify. Spots of test organisms were placed on the agar surface. A plate without compound was prepared for control. The plates were incubated at room temperature for 48 hr.

After proper incubation plates were observed for growth of the test organisms. The growth indicates that the compound is not antifungal while inhibition of growth of test organism indicates antifungal activity. The antifungal activities of the compounds were compared with standard griseofulvin.

Table-2: Antimicrobial activity of synthesized compounds.

Product	Bacterial strain				Fungal strain			
	Ec	St	Sa	Bs	An	Pc	Fm	An
L ₁	13	12	23	17	-ve	-ve	-ve	-ve
[L ₁ .Cu.H ₂ O]	09	17	12	22	-ve	+ve	-ve	-ve
[L ₁ .Ni(H ₂ O) ₂]	11	08	26	21	-ve	+ve	RG	+ve
[L ₁ .Co(H ₂ O) ₂]	13	-	28	16	+ve	RG	-ve	-ve
[L ₁ Mn]	16	-	-	24	+ve	+ve	-ve	-ve
[L ₁ .Fe(H ₂ O) ₂]	06	08	17	16	-ve	RG	-ve	+ve
[L ₁ Zn]	-	14	23	11	RG	+ve	-ve	+ve
Penicillin	18	20	32	28	-ve	-ve	-ve	-ve
Grisofulvin	NA	NA	NA	NA	-ve	-ve	-ve	-ve

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

The result of antimicrobial data of the ligand and complex shows that the complexes of the schiff bases shows enhanced activity than their corresponding ligand.

CONCLUSION

From the result and the discussion and analytical data it is confirmed 1:2 stoichiometry and the electronic spectral data suggest that the Co (II), Ni (II), Fe (II) complexes have octahedral geometry where as Cu (II), Zn (II) and Mn (II) complexes have square planar geometry.

The antimicrobial study show that the complexes of the corresponding Schiff bases show enhanced activity than their corresponding ligand.

ACKNOWLEDGEMENT

The authors are thankful to the principal Yeshwant Mahavidyalaya, Nanded for providing laboratory facilities. The authors are also thankful to head IICT Hyderabad and IIT Mumbai for providing spectral data and to UGC for sanctioning Maulana Azad National fellowship to Seema Habib.

REFERENCES

- [1] Nalwar YS, Sayyed MA, Mokle SS, Zanwar PR, Vibhute YB. World J Chem 2009; 4(2):123.
- [2] Mokle SS, Sayyed MA, Kottawar, Chopde. Int J Chem Sci 2004; 2(1): 96.
- [3] Raman N, Dhaweethu Raja J, Sakthivel A. J Chem Sci 2007; 119(4):303.
- [4] Jian-ning LIU, Bo-wan WU, Bing ZHANG, Yongchun LIU. Turk J Chem 2006; 30: 41.

- [5] Raman N, Pitchaikani Raja Y, Kulandaisamy A. Proc Indian Acad Sci (Chem Sci) 2001; 113(3): 183.
- [6] Dariusz Pawlica, Marek Marszalek, Grzegorz Mynarczuk, Leslaw Sieron, Julita Eilmes. New J Chem 2004; 28:1615.
- [7] Shah S, Vyas R, Mehta RH. J Ind Chem Soc 1992; 69:590.
- [8] Pandeya SN, Sriram D, Nath G, Declercq E. Eur J Pharma Soc 1999; 9:25.
- [9] More PG, Bhalvankar RB, Patter SC. J Ind Chem Soc 2001; 78:474.
- [10] Kuzmin VE, Artemenko AG, Lozytska RN, Fedtchouk AS, Lozitsky VP, Muratov EN, Mescheriakov AK. SAR & QSAR Environ Res 2005; 16:219.
- [11] Sawodny W, Riederer M E. Urban Inorg Chim Acta 1978; 29:63.
- [12] Oshima S, Hirayama N, Kubono K, Kokusen H, Hyyonjo T. Anal Sci 2002; 1351.
- [13] Agarwala et al. Synthetic Lubricating oil Greases containing Metal Chelates of Schiff bases, US pat 1992; 5:147,567.
- [14] Hitoshi NT, Tamao N, Hideyuki A, Manabu F, Takayuki M. Polyhedron 1997; 16:3787.
- [15] Punniyamurthy T, Kalra SJS, Iqbal J. Tetrahedron Lett 1995; 36:8497.
- [16] Trivedi GS, Desai NC. I J Chem 1992; 31B:366.
- [17] Singh P, Goel R, Singh BP. J Ind Chem Soc 1975; 52:958.
- [18] Mahindra AM, Fisher JM, Rabinovitz. Nature (London) 1983; 303:64.
- [19] a) Sakamoto M, Itose S, Ishimori T, Matsumoto N, okawa H and Sigeo Kida, Bull chem Soc Japan 1990; 63:1830-1831.
- [20] Venugopal P and Krishnakury K. J I Chem Soc 1997; 74:562.
- [21] Nag IK, Das D, and Sinha C. J I Chem Soc 1998.
- [22] Palaniandarar M and Natarajan C. Aust J Chem 1980; 33:737.
- [23] Khulbe RC, Bhoom YK and Singh RP. J Chem Soc 1981; 50:840.
- [24] Kneubuehe FK. J Chem Phys 1960; 33:1074.
- [25] Kivelson D and Neiman R. J Chem Phys 1961; 35:149.