



Synthesis, Characterization and Microbial Activities of Metal Complexes with 2-[N-(2-Hydroxyphenyl)methylidynyl]amino-4,5-dihydronaphtho[1,2d]thiazole Derivatives

VIJAYKUMAR DURG^{1,*}, NIRDOSH PATIL² and K.H. SHIVAPRASAD³

¹Department of Chemistry, Rural Engineering College, Bhalki, Bidar-585 328, India

²Department of Chemistry, Appa Institute of Engineering & Technology, Gulbarga-585 103, India

³Department of Industrial Chemistry, Post Graduate Center Bellary, Gulbarga University, Gulbarga-585 106, India

*Corresponding author: E-mail: vijayakumar_durg@rediffmail.com

(Received: 17 May 2011;

Accepted: 16 December 2011)

AJC-10850

Condensation of substituted salicylaldehydes with primary amine of naphtha-thiazole gave a series of Schiff bases, such as 2-[N-(2-hydroxyphenyl)methylidynyl]amino-4,5-dihydronaphtho[1,2d]thiazole (HL¹); 2-[N-(2-hydroxy 4-methoxyphenyl)methylidynyl]amino-4,5-dihydronaphtho[1,2d]thiazole (HL²) and 2-[N-(3,4-dimethoxy-2-hydroxyphenyl)methylidynyl]amino-4,5-dihydronaphtho[1,2d]thiazole (HL³). All the metal complexes were synthesized by reaction between cobalt(II) chloride, nickel(II) chloride and copper(II) chloride with the ligands (HL¹), (HL²) and (HL³). These Co(II), Ni(II) and Cu(II) complexes were characterized by elemental analyses, conductance measurements, magnetic susceptibility measurements, IR, ¹H NMR and electronic spectral studies. On the basis of magnetic and spectral studies, octahedral geometry was assigned for these complexes. These complexes have been screened *in vitro* for their possible antimicrobial activity.

Key Words: Metal, Complexes, Thiazole, Antimicrobial activity.

INTRODUCTION

A large number of substituted thiazoles are known for their biological activities^{1,2}. It is also believed that the presence of N-C-S linkage is responsible for the amoebicidal, anticonvulsant, fungicidal and antiviral activities^{3,4}. There is growing interest in the studies on the metal complexes of Schiff bases derived from thiazoles, which are biologically important ligands⁵. 1-Tetralone was condensed with thiourea and iodine by Dodson-King method^{6,7} and the resulting 2-amino-4,5-dihydronaphtho[1,2d]thiazole was then treated with substituted salicylaldehyde to get the corresponding Schiff bases, 2-[N-(2-hydroxyphenyl)methylidynyl]amino-4,5-dihydronaphtho[1,2d]thiazole (HL¹)⁷; 2-[N-(2-hydroxy 4-methoxyphenyl)methylidynyl]amino-4,5-dihydronaphtho [1,2d]thiazole (HL²) and 2-[N-(3,4-dimethoxy-2-hydroxyphenyl)methylidynyl]amino-4,5-dihydronaphtho [1,2d]thiazole (HL³). Literature survey has revealed that no attempt has been made to study the bivalent cobalt, nickel, and copper complexes with the above mentioned Schiff bases. The present paper reports the synthesis, characterization and antimicrobial activity of some thiazole complexes of Co(II), Ni(II) and Cu(II) metal ions.

EXPERIMENTAL

All the chemicals and solvents used were of AR grade. Salicylaldehyde was obtained from Sisco-chem. Industries. The metal salts were purchased from commercial sources. Metal contents were estimated using standard methods⁸.

IR spectra of the compounds were recorded on a Beckman IR-20 spectrophotometer in the region 4000-250 cm⁻¹. ¹H NMR spectra were recorded on a Perkin-Elmer 90 MHz spectrometer. The electronic spectra were recorded on an Elico SL 159 spectrophotometer in the 200-1000 nm ranges in DMF solution (10⁻³). Elemental analyses were obtained HERAEUS C, H, N-O rapid analyzer. E.S.R measurements were carried out on a VARAN E-109 GHz. The experiment was carried by taking DPPH as the reference with the field set at 3200 Gauss. Magnetic susceptibilities were determined by the faraday method using a Model 300 Lewis coil force magnetometer of one tesla field strength at room temperature. The instrument being calibrated with Hg[Co(SCN)₄]⁹.

Preparation of ligands: 2-[N-(2-hydroxy-4/5-substituted phenyl)-methylidynyl]-amino-4,5-dihydronaphtho[1,2d]-thiazoles. (HL¹, HL² and HL³): A mixture of 2-amino-4,5-dihydronaphtho[1,2d]thiazole(II) (1.94 g 0.01 mol) and

TABLE-1
PHYSICAL DATA, ELEMENTAL ANALYSES, MAGNETIC MEASUREMENTS AND MOLAR CONDUCTANCE OF METAL COMPLEXES WITH LIGANDS HL¹, HL² AND HL³

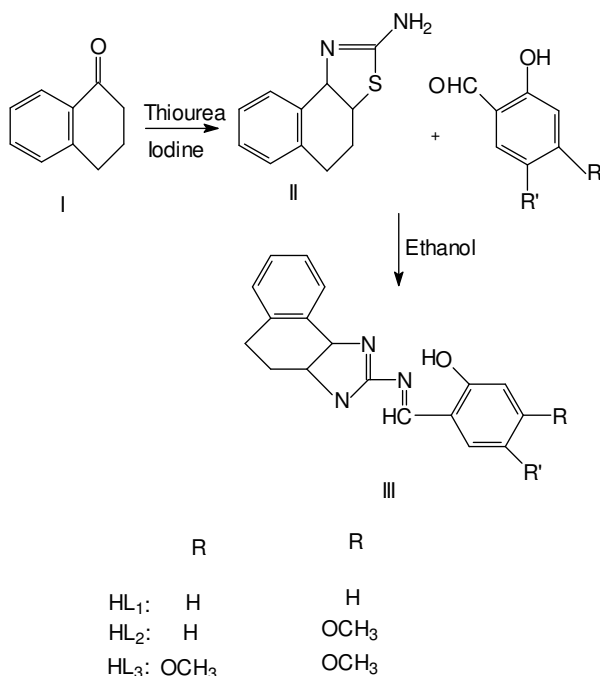
Ligands/complexes ^a	Colour (m.p.) (°C)/yield (%)	Metal (%) found/(calcd.)	μ_{eff} (B.M)	Molar cond. (mho cm ² mol ⁻¹)
HL ¹ (C ₁₈ H ₁₄ N ₂ OS)	Yellow 128 (73)	-	-	-
Co(L ¹) ₂ Co(C ₁₈ H ₁₃ N ₂ OS) ₂	Brown 195 (65)	8.87 (8.81)	4.82	40.00
Ni(L ¹) ₂ Ni(C ₁₈ H ₁₃ N ₂ OS) ₂	Pink 198 (62)	8.83 (8.77)	3.15	32.20
Cu(L ¹) ₂ Cu(C ₁₈ H ₁₃ N ₂ OS) ₂	Yellow 205 (65)	9.39 (9.43)	1.80	43.40
HL ² (C ₁₉ H ₁₆ N ₂ O ₂ S)	Yellow 137 (75)	-	-	-
Co(L ²) ₂ Co(C ₁₉ H ₁₅ N ₂ O ₂ S) ₂	Brown 210 (68)	8.41 (8.45)	4.75	30.85
Ni(L ²) ₂ Ni(C ₁₉ H ₁₅ N ₂ O ₂ S) ₂	Brown 220 (62)	8.37 (8.43)	3.25	45.30
Cu(L ²) ₂ Cu(C ₁₉ H ₁₅ N ₂ O ₂ S) ₂	Yellow 228 (65)	9.12 (9.06)	1.82	35.20
HL ³ (C ₂₀ H ₁₈ N ₂ O ₃ S ₂)	Yellow 137 (75)	-	-	-
Co(L ³) ₂ Co(C ₂₀ H ₁₇ N ₂ O ₃ S ₂) ₂	Brown 210 (68)	7.69 (7.74)	4.77	30.85
Ni(L ³) ₂ Ni(C ₂₀ H ₁₇ N ₂ O ₃ S ₂) ₂	Brown 220 (62)	7.82 (7.76)	3.22	45.30
Cu(L ³) ₂ Cu(C ₂₀ H ₁₇ N ₂ O ₃ S ₂) ₂	Yellow 228 (65)	8.41 (8.34)	1.79	35.20

^aAll the ligands and their complexes showed satisfactory C, H and N analysis

TABLE-2
ELECTRONIC SPECTRAL BANDS (cm⁻¹) AND LIGAND FIELD PARAMETERS OF COMPLEXES

Complex	ν_1	ν_2	ν_3	Dq (cm ⁻¹)	B' (cm ⁻¹)	β	LFSE
Co(H ₂ L ¹)	12425	17650	21515	5223	1562	1.60	18.00
Ni(H ₂ L ¹)	11762	15875	22225	4112	1715	1.64	12.99
Cu(H ₂ L ¹)	12030	15622	22740	-	-	-	-
Co(H ₂ L ²)	13510	19235	20836	5714	1520	1.59	15.40
Ni(H ₂ L ²)	14715	16133	22720	1427	2310	2.23	5.85
Cu(H ₂ L ²)	15622	17235	21745	-	-	-	-

substituted salicylaldehyde (0.01 mol) in absolute ethanol (25 mL) was refluxed for 4 h. The reaction mixture was cooled and the separated solid was crystallized from ethanol (**Scheme-I**).



Scheme-I

Preparation of complexes: A mixture of hot ethanol solution (50 mL) of the corresponding metal salt (0.002 mL) and the ethanol solution of HL¹, HL² and HL³ (0.002 mol) was refluxed for 8 h and solid was separated. The complexes were filtered, washed with hot ethanol and dried in vacuum.

RESULTS AND DISCUSSION

The analytical and physical data of the compounds are given in Table-1. The results of elemental analyses of the complexes correspond to stoichiometry for metal:ligand in 1:2 molar ratios. Molar conductance measurements of these complexes in DMF correspond to nonelectrolytes. IR spectra of ligand show a broad medium intensity band in the region 3450-3300 cm⁻¹ due to phenolic-OH¹⁰, in complexes these bands were not observed due to the complexation through O *via* deprotonation of phenolic-OH. The band in the region 1640-1590 cm⁻¹ is assigned to HC=N group, indicates that the condensation between amino group of thiazole and substituted salicylaldehyde. In ligands, a medium intensity band is observed in the range of 1090-950 cm⁻¹ are assigned to the ν (C-S) vibrations¹¹. The band due to ν (C=N) appears in the region of 1630-1590 cm⁻¹ as a high intensity band in the complexes, indicating that the C=N group is involved in coordination of metal ions through nitrogen. In complexes the bands due to C=N group are shifted to lower frequency by 30-20 cm⁻¹. The magnetic moment of the Co(L¹)₂, Ni(L¹)₂ and Cu(L¹)₂ are 4.82, 3.15 and 1.80 B.M. respectively. The μ_{eff} values are well within the range known for six coordinate octahedral geometry (Table-1). Similarly magnetic moment for the Co(L²)₂, Ni(L²)₂ and Cu(L²)₂ are 4.75, 3.25 and 1.82 B.M. and for the Co(L³)₂, Ni(L³)₂ and Cu(L³)₂ are 4.77, 3.22 and 1.79 B.M. respectively¹². The electronic spectra of the complexes recorded in DMF display three bands at 11760-15620 cm⁻¹(ν_1), 15600-19230 cm⁻¹(ν_2) and 20830-22720 cm⁻¹(ν_3) (Table-2). Six coordinate complexes with O_h symmetry show three spin allowed bands. These bands are due to ⁴T_{1g}(F)→⁴T_{2g}(F)(ν_1), ⁴T_{1g}(F)→⁴A_{2g}(F) (ν_2) and ⁴T_{1g}(F)→⁴T_{1g}(P)(ν_3) for cobalt complexes, ³A_{2g}→³T_{2g}(ν_1), ³A_{2g}→³T_{1g}(F)(ν_2) and ³A_{2g}→³T_{1g}(P)(ν_3) for nickel complexes

and ${}^2B_{1g} \rightarrow {}^2A_{1g}(v_1)$, ${}^2B_{1g} \rightarrow {}^2B_{1g}(v_2)$ and ${}^2B_{1g} \rightarrow {}^2E_g(v_3)$ for copper complexes¹³. Various ligand field parameters have been evaluated for cobalt and nickel complexes (Table-2).

The nephelauxetic parameter, β is readily obtained using the relation $\beta = B(\text{complex})/B(\text{free ion})$, indicate that the complex under study have appreciable covalent character. The value of D_q could be evaluated with the help of the curve transition energies versus D_q by Orgel using the energy level due to transitions ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ respectively. The parameter B was evaluated by using the methods reported earlier¹⁴.

The ESR spectra of the copper complexes as polycrystalline sample have been recorded at room temperature, (ESR chart was calibrated with DPPH). The polycrystalline samples gives one broad isotropic signal centered approximately at 2.023 and 2.040 for the complex $\text{Cu}(L^1)_2$. The observed g values of the $\text{Cu}(L^1)_2$ complex as follows $g_{\parallel} = 2.058$, $g_{\perp} = 2.014$, $g_{av} = 2.028$ and $G = 4.19$. While for $\text{Cu}(L^2)_2$, $g_{\parallel} = 2.052$, $g_{\perp} = 2.024$, $g_{av} = 2.030$ and $G = 4.22$ and $g_{\parallel} = 2.053$, $g_{\perp} = 2.012$, $g_{av} = 2.035$ and $G = 4.41$. The isotropic g values have been calculated Kneubuhl's methods¹⁴ and methods reported earlier. $G = (g_{\parallel}-2)/(g_{\perp}-2)$, which measures the exchange interaction between copper centers in a polycrystalline solid has been calculated. According the Hathaway *et al.*¹⁵, if the G value is greater than 4, the exchange interaction is negligible, while a value of G less than 4 indicates a considerable exchange in the solid complexes. As $G = 4.13$, $G = 4.20$ and $G = 4.41$ for $\text{Cu}(L^1)_2$, $\text{Cu}(L^2)_2$ and $\text{Cu}(L^3)_2$ respectively, indicates the exchange interaction is negligible.

Antimicrobial Activity: The antimicrobial activity of the ligands HL^1 , HL^2 and HL^3 and their metal complexes were determined by agar cup-plate method¹⁶⁻²⁰. The antibacterial activity against *Escherichia coli* and *Pseudomonas aeruginosa* and antifungal activity against *Aspergillus niger* and *Candida albicans*, were screened by the ligands and their metal complexes. The medium was prepared as per the instructions of the manufacturer of dry Mueller Hinton agar powder (Hi-Media). The test ligands and their metal complexes were dissolved in dimethylsulphoxide (DMSO) at a concentration of 100 $\mu\text{g}/\text{mL}$. Ciprofloxacin (100 $\mu\text{g}/\text{mL}$) in DMSO was used as reference standard for antibacterial and flucanazole (100 $\mu\text{g}/\text{mL}$) in DMSO was used as reference standard for antifungal activity²¹⁻²³. The solvent control (only DMSO) was also maintained throughout the experiment. The zones of inhibition are reported in Table-3.

From the Table-3, it is clear that all the ligands (HL^1 , HL^2 and HL^3) show moderate activity against all the antibacterial and antifungal microorganisms. But all the metal complexes show moderate to high active against all the organisms. Among the complexes, all copper complexes [$\text{Cu}(L^1)_2$, $\text{Cu}(L^2)_2$ and $\text{Cu}(L^3)_2$] were found to be most active against all the microbes tested, as compared to their ligands, which due to the faster diffusion of the Cu(II) complexes. Even though the test compounds are less active with reference to the standard drug ciprofloxacin and flucanazole, the data reported in this article may be a helpful guide for the medicinal chemists who are working in the area.

TABLE-3
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY DATA
OF THE LIGANDS AND THEIR COMPLEXES
(ZONE OF INHIBITION IN mm*)

Ligands/ complexes	Antibacterial		Antifungal	
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>A. niger</i>	<i>C. albicans</i>
HL^1	12	14	11	09
$\text{Co}(L^1)_2$	14	17	13	12
$\text{Ni}(L^1)_2$	15	18	14	12
$\text{Cu}(L^1)_2$	20	19	18	16
HL^2	11	13	10	10
$\text{Co}(L^2)_2$	14	16	14	13
$\text{Ni}(L^2)_2$	14	17	13	14
$\text{Cu}(L^2)_2$	21	22	17	17
HL^3	12	14	12	01
$\text{Co}(L^3)_2$	13	16	14	13
$\text{Ni}(L^3)_2$	15	15	14	15
$\text{Cu}(L^3)_2$	22	23	18	18
Ciproflaxacin	27	30	-	-
Flucanazole	-	-	24	23
DMSO	00	00	00	00

ACKNOWLEDGEMENTS

The authors are thankful to Prof. V.H. Kulkarni and S.D. Angadi for helpful suggestions. Our thanks are also due to Prof. N. Goudgaon and Dr. B.B. Lal, Principal, REC, Bhalki, Chairman, Department of Chemistry, Gulbarga University, for providing the facilities.

REFERENCES

- S.R. Pattan, M. Maste and J. Angadi, *Indian Drugs*, **39**, 429 (2002).
- S.A. Javed, N. Siddiqui and S. Drabu, *Indian J. Heterocycl. Chem.*, **13**, 287 (2004).
- H.A. Al-khamees, S.M. Boyami, H.A. Kandil and K. El-Thahir, *Eur. J. Med. Chem.*, **25**, 103 (1990).
- H.D. Joshi, P.S. Upadhyay and A.J. Baxi, *Indian J. Chem.*, **39B**, 967 (2000).
- C.D. Hard and R.J. Mori, *J. Am. Chem. Soc.*, **77**, 5359 (1955).
- R.M. Dodson and L.C. King, *J. Am. Chem. Soc.*, **67**, 2242 (1945).
- A.V. Naidu and M.A. Dave, *Asian J. Chem.*, **12**, 687 (2000).
- A.I. Vogel, *A Textbook of Quantitative Inorganic Analysis*, Longmans Green, London, edn. 4 (1978).
- C.J. Conner, E.S. Sinn, E.J. Cukaskas and B.S. Deaver, *Inorg. Chim. Acta*, **32** (1979).
- B.C. Sharma and C.C. Patel, *Indian J. Chem.*, **8**, 747 (1970).
- A. Kumar, G. Singh, R.N. Handa and S.N. Dubey, *Indian J. Chem.*, **38A**, 613 (1999).
- A.B.P. Lever, *Inorganic Electronic Spectroscopy*, Elsevier Publisher Company, Amsterdam (1968).
- S. Drago, *Physical Methods in Chemistry* (W.B. Saunders Company), p. 530 (1997).
- K. Kneubuhl, *J. Chem. Phys.*, **33**, 1074 (1960).
- B.H. Hathaway, R.J. Dudley and P. Nicholls, *J. Chem. Soc. A*, 1845 (1968).
- R.S. Srivastava, *Inorg. Chim. Acta*, **56**, 256 (1981).
- H.H. Thonberry, *Phytopathology*, **40**, 419 (1950).
- N. Quis and M. Rahman, *Phytotherapy*, **67**, 554 (1996).
- A.B. Aziz, *Science*, **155**, 1026 (1997).
- S. Albart, *Selective Toxicity*, Methuen and Co. Ltd. (1960).
- M.C. Hosur, M.B. Talwar and S.C. Benner, *Indian J. Chem.*, **34B**, 707 (1995).
- S.P. Tripathi, R. Kumar, V. Chatervedi and R.C. Sharma, *J. Indian Chem. Soc.*, **61**, 847 (1984).
- K.C. Stapathy, A.K. Panda, R. Mishra, A.P. Chopdar and S.K. Pradhan, *J. Indian Chem. Soc.*, **79**, 371 (2002).