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SYNTHESIS, CHARACTERISATION & ANTIMICROBIAL STUDIES OF CO(II) & NI(II) COMPLEXES WITH SOME SUBSTITUTED PYRAZOLES DERIVATIVES

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ABSTRACT

We reported here some new biological important metal- dizole complexes of the type ML_2X_2 Where M = Ni (II) and Co (II) , L = 2-(Pyrazol- 1-yl) pyridine (I) , 2- (3,5 – Dimethyl pyrazole -1-yl) 5 methyl pyridine (II) , 2- (3,5- Diphenyl pyrazole-1- yl) pyridine (III) , 2-(3,5- diphenyl pyrazol-1-yl) 5- methyl pyridine (IV) and X = Cl. These complexes have been tested against various bacteria such as Staphylococcus aureus, Escheria coli and Pseudomonas aeruginosa. The complexes show significant antimicrobial activity compared to that of parent compound.

KEYWORDS: **Metal-dizole complexes , various bacteria, and spectral studies.**

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INTRODUCTION

The antibacterial[1,22,26], anti-inflammatory[2] and antitumour[3] activities of anti pyrine based ligands and their metal complexes have drawn the attention of many investigators. Iron complexes were the earliest metal complex used in the treatment of hypochromic anaemia[4,19,20]. In view of this we report here some new biologically important metal–diazole complexes[17,18] of the type ML_2X_2 where M = Ni(II) and Co(II); L = 2–(pyrazol–1–yl) pyridine(I); 2–(3,5–Dimethyl pyrazol–1– yl) 5–methyl pyridine(II); 2–(3,5–Diphenyl pyrazol–1–yl) pyridine(III); 2–(3,5– diphenyl pyrazol–1–yl)–5–methyl pyridine(IV) and X = Cl.[13,14,15,16] We have also studied their spectroscopic characteristics and antimicrobial effect on various bacteria[5,6].

EXPERIMENTAL

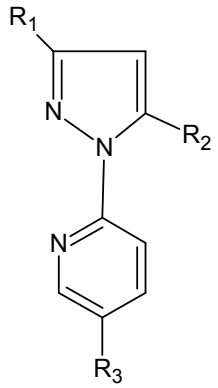
The ligands used in this work were prepared by the method reported by Khan etal[7]. Metal contents of the complexes were determined by first treating the complexes with boiling conc. Nitric acid and then evaporating to dryness repeatedly till the organic matter was destroyed. The residue was dissolved in water and filtered. The filtrate was used for estimation of cobalt and nickel by the pyridine method.[8] Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected.

Table 1.1
Physical and Analytical Data of the Complexes

Complex No. (Molecular Formula)		m.p.(°C)	Mag. Moment (B.M.)	Found (Calc.) %				
				C	H	N	M	Cl
1	($C_{16}H_{14}N_6NiCl_2$)	142–145	2.92	45.60(45.74)	3.20 (3.33)	19.88(20.01)	13.80(13.98)	16.80(16.91)
2	($C_{22}H_{26}N_6NiCl_2$)	170–173	2.85	52.30(52.41)	5.0(5.16)	16.50(16.67)	11.50(11.65)	13.87(14.09)
3	($C_{40}H_{30}N_6NiCl_2$)	166–170	2.95	66.15(66.32)	4.04(4.14)	11.50(11.60)	7.94(8.11)	9.70(9.81)
4	($C_{42}H_{34}N_6NiCl_2$)	188–190	2.83	66.93(67.04)	4.40(4.52)	11.0(11.17)	7.68(7.81)	9.30(9.44)
5	($C_{16}H_{14}N_6CoCl_2$)	156–158	4.25	45.60(45.72)	3.21(3.33)	19.86(20.0)	13.90(14.03)	16.80(16.90)
6	($C_{22}H_{26}N_6CoCl_2$)	167	4.52	52.26(52.38)	5.0(5.15)	16.52(16.66)	11.52(11.69)	13.91 (14.08)
7	($C_{40}H_{30}N_6CoCl_2$)	174–178	4.35	66.38(66.30)	4.0 (4.14)	11.50(11.60)	8.0 (8.14)	9.65 (9.80)
8	($C_{42}H_{34}N_6CoCl_2$)	198	4.55	66.80(67.02)	4.36(4.52)	11.0(11.17)	7.70(7.83)	9.30(9.44)

General method of preparation of metal complexes

To an ethanolic solution (30 ml) of the ligand (2 mmol) was added with stirring an ethanolic solution (20 ml) of the metal chloride salt (1 mmol). The contents were refluxed for 3 hr.[19], The resulting mixture was then cooled, washed with ether (2 × 20 ml) and later reduced to a small volume (15 ml). The concentrated solution was left over–night at room temperature and the product thus formed was separated.[20,21] It was recrystallized from water to get fine crystals (70% yield).



I = $R_1 = R_2 = R_3 = H$
II = $R_1 = R_2 = CH_3$, $R_3 = CH_3$
III = $R_1 = R_2 = C_6H_5$, $R_3 = H$
IV = $R_1 = R_2C_6H_5$, $R_3 = CH_3$

RESULTS AND DISCUSSION

The metal complexes synthesized are crystalline in nature. They are insoluble in water and common organic solvents but are appreciably soluble in dimethylformamide (DMF). The analytical data of the complexes (Table 1) indicate that the complexes have 1:2 (metal:ligand) stoichiometry. The complexes have been found to be electrically non–conducting (7.25 ohm^{-1} cm^2 mol^{-1} in DMF) suggesting that the ligands and the anions are covalently bonded with the central metal atom. The magnetic moments (Table 1.1) for CoL_2Cl_2 fall in the range 4.2–4.5 B.M. expected to contain odd number of electron (d^7–system) and the μeff. Values for Ni(II) complexes are well within the range expected for spin–free octahedral geometry[9–11]. The electronic spectra of all the metal complexes exhibited bands due to d–d transitions (Table 1.2). A strong band around 3000 cm^{-1} in all the metal complexes, was labeled as a charge transfer band, probably associated with the transition of an electron from a non–bonding metal d–orbital to an antibonding ligand π*–orbital. The nickel(II) complexes exhibited three typical bands in the region 2630–3000, 1520–1850 and 900–1100 cm^{-1} corresponding to the transitions $^3A_{2g} \rightarrow T_{1g}(P)$; $^3A_{2g} \rightarrow ^3T_{1g}(F)$; and $^3A_{2g} \rightarrow ^3T_{2g}(F)$. Similarly the cobalt(II) complexes exhibited absorption bands around 3000–3300; 1710–1900 and 835–1100 cm^{-1}; the latter two bands have been assigned to the transitions $^4T_{1g}(F) \rightarrow ^4T_{2g}(P)$ and $^4T_{1g}(F) \rightarrow ^4T_{1g}(P)$ respectively.[6] The first band is already assigned to metal → ligand charge–transfer because of its high intensity.[12–15] A comparative scrutiny of the infrared spectral data of the complexes with those of the uncomplexed ligands gave clues regarding the donor sites of the ligand molecules. A strong and broad band due to ν(C=N) of pyrazole ring, which appeared at 1520 cm^{-1} in the ligands, shifted to higher frequency side (~ 1570– 1585 cm^{-1}) in the spectra of complexes. Furthermore, the appearance of new bands in the regions 300 and 270 cm^{-1} is attributed to ν(M–N) mode, thus confirming that complex formation takes place by coordination of the C=N group to the metal ion.[16–19]

Antimicrobial activity

Antimicrobial action of the compounds under investigation was studied on three bacteria species, *Staphylococcus aureus* (a), *Escherechia coli* (b) and *Pseudomonas aeruginosa* (c). Paper disc diffusion method was adopted to measure the inhibition (–) and growth (+) of the microorganisms. The compounds were tested at concentrations 250, 500 and 1000 μg/ml. DMF was used as the solvent, its final concentration being 0.01 ml/10 ml in the culture medium. (Table 1.3)

Table 1.2
Infrared and Electronic Spectral Data of the Complexes

Complex No. (Molecular Formula)		IR bands (cm^{-1})	λ_{max} (cm^{-1})
1	($C_{16}H_{14}N_6NiCl_2$)	2910, 1570, 1205, 1270, 1910, 275 (M–N)	9530, 15200, 26500
2	($C_{22}H_{26}N_6NiCl_2$)	3128, 1560, (NO_2), 1350, (NO_2), 1290, 290 (M–N)	9525, 17500, 29100
3	($C_{40}H_{30}N_6NiCl_2$)	3080, 3040, 1575, 1280, 920, 280 (M–N)	9530, 16550, 27200
4	($C_{42}H_{34}N_6NiCl_2$)	3130, 3060, 1570, 1490, (NO_2), 1340 (NO_2), 915, 285 (M–N)	10200, 18500, 30000
5	($C_{16}H_{14}N_6CoCl_2$)	3010, 2840, 1580, 1420, 1275, 270 (M–N)	10210, 17100, 29900
6	($C_{22}H_{26}N_6CoCl_2$)	3090, 1585, 1570, (NO_2), 1345, 910, 280 (M–N)	10220, 18550, 31500
7	($C_{40}H_{30}N_6CoCl_2$)	3070, 2805, 1575, 1285, 915, 285 (M–N)	10200, 17700, 30150
8	($C_{42}H_{34}N_6CoCl_2$)	3090, 1570, 1480, (NO_2), 1350, (NO_2), 920, 280 (M–N)	10900, 19000, 32900

Table 1.3
Antimicrobial Activity Data of the Complexes

Complex No.		Conc. (μg/ml)	Microbial species		
			a	**b**	**c**
1	($C_{16}H_{14}N_6NiCl_2$)	1000 500 250	– + +	– + +	– + +
2	($C_{22}H_{26}N_6NiCl_2$)	1000 500 250	– + +	– + +	– + +
3	($C_{40}H_{30}N_6NiCl_2$)	1000 500 250	– – +	– + +	– + +
4	($C_{42}H_{34}N_6NiCl_2$)	1000 500 250	– + +	– – +	– + +
5	($C_{16}H_{14}N_6CoCl_2$)	1000 500 250	– – +	– + +	– – +
6	($C_{22}H_{26}N_6CoCl_2$)	1000 500 250	– + +	– – +	– + +
7	($C_{40}H_{30}N_6CoCl_2$)	1000 500 250	– – +	– + +	– – +
8	($C_{42}H_{34}N_6CoCl_2$)	1000 500 250	– + +	– – +	– + +

Microbial effect (– inhibition, + growth)
a = Staphylococcus aureus
b = Escherechia coli
c = Pseudomonas aeruginosa

The results showed (Table 1.3) that all the metal[20–23] complexes have significant antimicrobial activity at concentration 250 μg/ml, but their toxicity decreases markedly on dilution (at 500 μg/ml and 1000 μg/ml). The metal complexes are more potent against (a), (b) and (c) than the parent compounds. This may be due to the fact that the chelation reduces considerably the polarity of the metal ions in the complexes (due mainly to the partial shairing of its positive charge with the donor group and possible π–electron delocalization over the whole chelate ring system through pπ–pπ or dπ–dπ interactions of the orbitals of the ligand and metal ions). This in turn increases the hydrophobic character of the metal chelate favouring its permeation through lipoid layer of microorganism.[24–26]

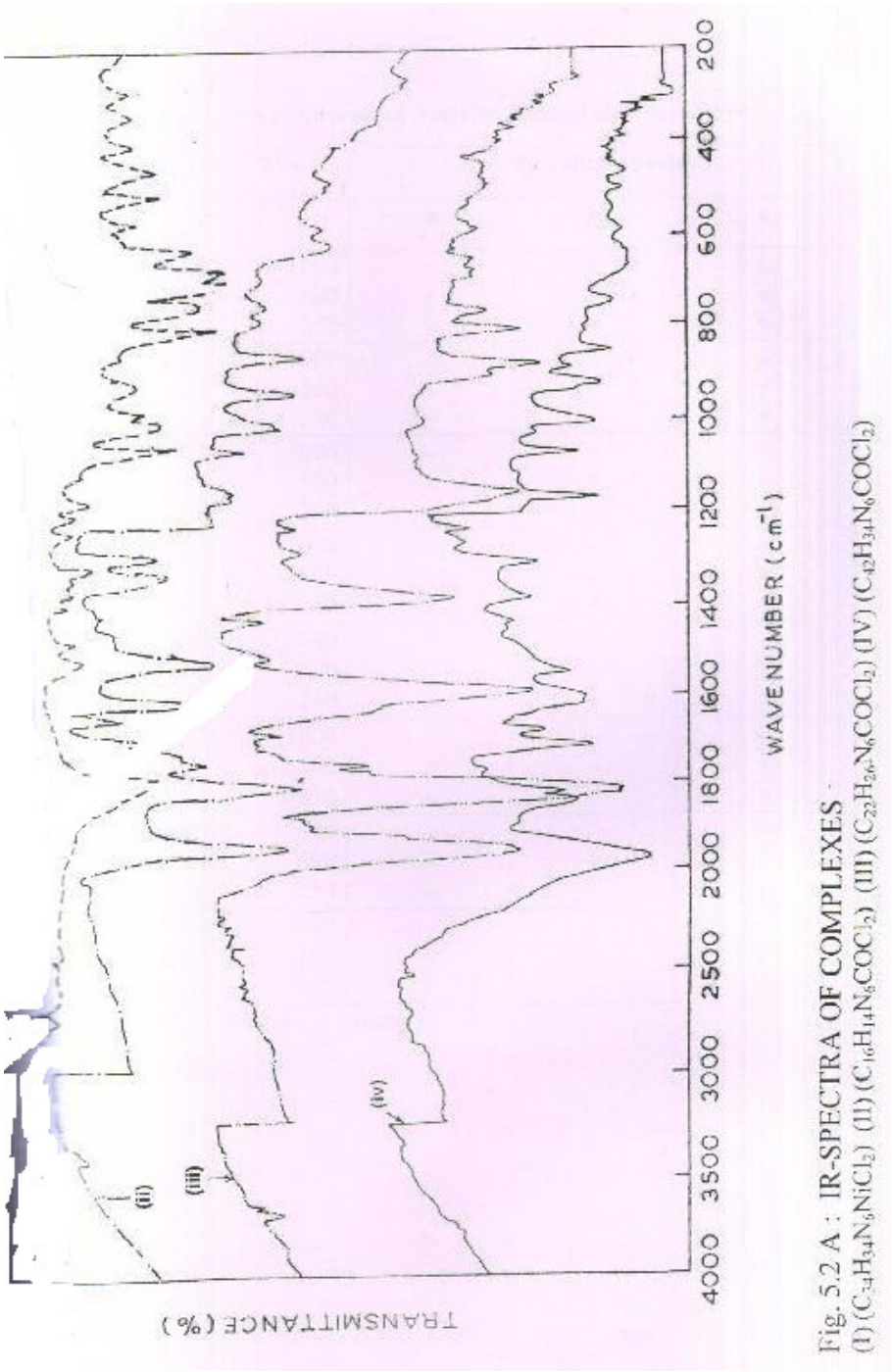


Fig. 5.2 A : IR-SPECTRA OF COMPLEXES
(I) $(C_{34}H_{34}N_6NiCl_2)$ (II) $(C_{16}H_{14}N_6COCl_2)$ (III) $(C_{28}H_{26}N_6COCl_2)$ (IV) $(C_{42}H_{34}N_6COCl_2)$

REFERENCES

1. Alaudeen, M., Abraham, A. & Radhakrishnan, P.K.,Trace elements in animal nutrition ,The role of bacteria in biocoordination chemistry," Proc. Ind. Acad. Sci. 107, 123 (1995).
2. Singh, L., Parashar, R.K., Tripathi, S.P. & Sharma, R.C., Studies of metal ion in biological systems"Curr. Sci. 55, 484 (1986).
3. Alice, C.J. & Prabhakaran, C.P., The bioinorganic chemistry of Nickel" Ind. J. Chem. 29A, 491 (1990).
4. Schwietert, C.W., & Mccue,Antimicrobial studies of some transition metal chelates

with heterocyclic compounds" J.P., Coord. Chem. Rev; 184, 67 (1999).
5. Saha, N. & Kar, S.K.,Synthesis of Co(II),Cu(II) & Ni(II) complexes with para substituted pyrazole derivatives" J. Inorg. Nucl. Chem. 39, 1236 (1977); 41, 1233 (1979).
6. Cleare, M.J.,Antimicrobial studies on transition metal-diazole complexes with some with pyrazoles ring" Coord. Chem. Rev; 12, 349 (1974).
7. Khan, M.A., & Pinto A.A.A.Estimation of transition metal complexes by pyridine" Mh. Chem. III 883 (1980).
8. Vogel, A.I., A Text Book of Quantitative Inorganic Analysis, 3rd Edn. (Longmans, London) 531, (1961).
9. Vleck, A., General methods of preparation of metal complexes with hetrocyclic compounds"Coord. Chem. Rev. 177, 1 (1998).
10. Vleck, A.,Estimation of transition metal complexes with some new biological important metal- dizoles'Coord. Chem. Rev; 200, 933 (2000).
11. Gawelda, W., Johnson, M., Degroof, F.M.F.,Synthesis, characterization,& antimicrobial studies of some pyridine derivative metal-dizoles" Abela, R., Bressler, C. & Chergui, M., J. Am. Chem. Soc. 128, 5001 (2006).
12. Vos, J.G., & Kelly, J.M.,Metal ligand and related Vibration"Dalton Trans. 4869 (2006).
13. Anderson, T.J., Scott, J.R., Millett, F. & Durham, B.,A new class of organosoluble metal chelates containing donar and acceptor moieties for heterocyclic compounds" Inorg. Chem. 45, 3843 (2006).
14. Nickita, N., Belousoff, M.J., Bhatt, A.I., Bond, A.M., Deacon, G.B., Gasser, G., & Spiccia, L,.Synthesis and antimicrobial studies of transition metal dizoles bearing antimicrobial activities" Inorg. Chem. 46, 8638 (2007).
15. Josef, B., Holger, D., & Alexander S.,Synthesis,characterization and antibacterial properties of transition metal complexes derived from pyrazoles" Eur. J. Inorg. Chem. 240 (2000).
16. Allan, J.R., Brown, D.H., Nuttal, R.H. & Sharp, D.W.A.,Novel thermally stable metal dizoles for antibacterial and anti-inflammatory activities" J. Inorg. Nucl. Chem. 27, 1305 (1965).
17. Lever, A.B.P.,Synthesis and characterization of Co (II),Ni(II) and Zn(II) complexes based on 6,6'-disubstituted-2,2'-bipyridine' Inorg. Chem. 4, 763 (1965).
18. Figgis, B.N. & Lewis,Stable anodic Metal dizoles: Synthesis and antimicrobial studies" J., Prog. Inorg. Chem., 6, 67 (1964).
19. Balhausen, C.J., Introduction to ligand fields (McGraw Hill, New York) 256, (1962).
20. Vos, J.G., & Groeneveld, W.L.,The metals ions in biological system" Inorg. Chim. Acta, 24, 123 (1977) .
21. Dorrity, I.A., & Orrel, K.G.,Introduction to Ligand field theory" J. Inorg. Nucl. Chem., 36, 230 (1974).
22. Andrews, J.M.,Electronic Aspects of Biochemistry" J. Antimicrob. Chemother. 48, 5 (2001).
23. Mogilaiah, K., Reddy, N.V. & Reddy, P.R.,Advances in Heterocyclic Chemistry" J. Heterocycl. Chem. 10, 267 (2001).
24. Lidstrom, P., Tierney, J., Wathey, B. & Westman,Purification of Laboratory chemicals" J., Tetrahedron 57, 9225 (2001).
25. Strohmeier, G.A. & Kappe, C.O.,Novel thermally stable triarylamine- containing pyridine bearing transition metal for highly efficient anti-inflammatory materials" J. Comb. Chem. 4, 154 (2004).
26. Andrews, J.M.,Structural and antimicrobial studies on transition metal complexes with pyrazolyl compounds" J. Antimicrob. Chemother. 48, 5 (2001).