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Synthesis, Characterisation, Antifungal and Antibacterial Studies of Nickel(II) and Silver(I) Complexes of Tridentate Bis Benzimidazoles

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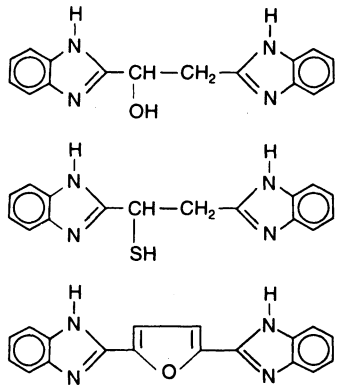
Some biologically active tridentate bis benzimidazoles prepared by the condensation of *o*-phenylene diamine with carboxylic acids such as malic, thiomalic and furan 2,5-dicarboxylic acid and further their 1 : 1 nickel(II) and silver(I) complexes have been described. These ligands and their complexes were characterised on the basis of elemental analyses, conductance measurement, molecular weight determination, IR and (^{1}H and ^{13}C) NMR spectral studies. Spectral data supports distorted octahedral and distorted tetrahedral geometries for nickel(II) and silver(I) complexes respectively. All the newly synthesized ligands and their complexes have been screened *in vitro* for antimicrobial activity against some of the pathogenic fungi and bacteria at different concentrations. Results of this screening have revealed that metal complexes exhibit more enhanced activity than their parent ligands against both the fungal and bacterial strains used.

INTRODUCTION

During recent years, it has been well established that benzimidazoles have versatile biological and pharmacological activities *viz.*, antimicrobial, antitumor, insecticidal, pesticidal, antiviral, antibacterial and antifungal activities[1–10] Interestingly, it is observed that biological activity of these ligands increases on complexation with different transition and non-transition metal ions[11]. In view of this, in present paper, we report the synthesis, characterisation, antifungal and antibacterial studies of Ni(II) and Ag(I) complexes of bis (1-hydroxyethyl), bis (1-mercaptoethyl), bis (2,2′-furyl) benzimidazoles (1a–c).



EXPERIMENTAL

All the chemicals used were of reagent grade and employed after purification. The solvent were dried by the standard procedures.

The ligands bis-(1-hydroxyethyl), bis-(1-mercaptoethyl), and bis-(2-2′-furyl) benzimidazoles were prepared by the reaction of malic, thiomalic and furan 2,5-dicarboxylic acid respectively with *ortho*-phenylene diamine in presence of freshly prepared polyphosphoric acid according to the method described by Heins *et al.*[12] and Vyas *et al.*[13] The purity of the ligands was checked by determination of melting points and by running TLC on silica gel G plates using chloroform-ethyl acetate (1 : 1) mixture. The physical and analytical data of these ligands have been given in Table-1.

Preparation of the complexes

The solutions of nickel(II) nitrate (0.01 mole; 1.45 g)/silver(I) nitrate (0.01 mol; 0.85 g) and each of the ligand derivatives (0.01 mole) in dry ethanol (25 mL) were mixed in a 100 mL round bottom flask. The resulting reaction mixture was refluxed for about 6–8 h on a fractionating column till the solid products start separating out. The product formed was filtered, washed repeatedly with hot ethanol and finally with ether and then dried under reduced pressure. The physical and analytical composition of the complexes formed have been summarised in Table-1.

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF LIGANDS AND THEIR METAL COMPLEXES

Empirical formula of the ligands and complex (Colour)	m.p. (°C)	M. wt. Found (Calcd)	Elemental analysis % Found (Calcd)				
			C	H	N	S	M
1a $C_{16}H_{14}N_4O$ (Whitish)	208	285 (278)	68.89 (69.05)	4.97 (5.07)	19.84 (20.13)	—	—
2a $Ni(C_{16}H_{15}N_5O_5)$ (Pale green)	215	387 (416)	46.05 (46.19)	3.58 (3.63)	16.75 (16.83)	—	14.02 (14.11)
3a $Ag(C_{16}H_{15}N_4O_2)$ (Dull grey)	212	388 (403)	47.58 (47.66)	3.71 (3.75)	13.80 (13.89)	—	26.62 (26.75)
1b $C_{16}H_{14}N_4S$ (Yellowish)	210	282 (294)	65.12 (65.28)	4.72 (4.79)	18.89 (19.03)	10.71 (10.89)	—
2b $Ni(C_{16}H_{15}N_5O_4S)$ (Yellowish green)	216	454 (432)	44.34 (44.47)	3.40 (3.49)	16.12 (16.20)	7.50 (7.42)	13.42 (13.58)
3b $Ag(C_{16}H_{15}N_4OS)$ (Brownish)	209	392 (419)	45.75 (45.83)	3.54 (3.60)	13.28 (13.36)	7.60 (7.64)	25.69 (25.72)
1c $C_{18}H_{12}N_4O$ (Light green)	214	289 (300)	71.82 (71.98)	3.99 (4.02)	18.47 (18.65)	—	—
2c $Ni(C_{18}H_{14}N_6O_8)$ (Bluish green)	218d	480 (501)	43.02 (43.14)	2.75 (2.81)	16.71 (16.77)	—	11.59 (11.71)
3c $Ag(C_{18}H_{12}N_5O_4)$ (Greyish black)	217	447 (470)	45.85 (45.98)	2.49 (2.57)	14.82 (14.89)	—	22.78 (22.94)

IR spectra of ligands and their complexes were recorded as KBr pellets or nujol mulls on a Perkin-Elmer 577 grating IR spectrophotometer. ^{1}N NMR spectra were recorded on a Jeol FX 90Q spectrometer in DMSO-d_6 using TMS as an internal reference. ^{13}C NMR spectra were recorded in dry methanol at 22.89 MHz. Molecular weights were determined by osmotic pressure method. Elemental analysis were carried out by usual methods.

RESULTS AND DISCUSSION

The complexes reported in Table-2 are solids, monomeric and are soluble in DMSO, DMF and chloroform. The low values of molar conductance (10–18 ohm^{-1} cm^2 mol^{-1}) in dry DMF show them to be non-electrolytic in nature.

TABLE-2
ANTIFUNGAL AND ANTIBACTERIAL ACTIVITY OF LIGANDS AND THEIR METAL COMPLEXES

	Antifungal activity Average % inhibition after 96 h (conc. in ppm)									antibacterial activity Diameter of inhibition zone (mm) after 24 h (conc. in ppm)					
	Aspergillus niger			*Fusarium oxysporum*			Candida albicans			Pseudomonas cepacicola (–ve)		Staphylococcus aureus (+ve)		*Escherichia coli* (–ve)	
	50	100	200	50	100	200	50	100	200	500	1000	500	1000	500	1000
1a	36	45	62	35	45	61	35	44	66	6	10	7	11	6	10
2a	46	63	74	45	62	71	44	62	70	8	12	9	11	9	12
3a	50	70	81	49	69	80	50	68	79	10	14	11	16	10	14
1b	37	46	64	34	50	60	34	49	62	8	11	7	10	7	9
2b	45	65	72	46	64	72	44	63	71	9	12	9	11	10	13
3b	51	69	80	50	70	82	49	68	79	11	14	12	15	12	16
1c	35	48	62	34	46	68	30	46	59	7	10	8	12	8	11
2c	45	62	71	43	61	70	40	60	69	9	12	10	13	9	11
3c	54	70	81	52	69	80	52	68	79	10	14	11	15	12	16

In the IR spectra of all the ligand derivatives strong and sharp absorption band at 1610–1605 cm^{-1} assigned to ν(C=N) vibrations of the imidazolyl ring, shifts to lower frequency by 10–12 cm^{-1} in the spectra of corresponding complexes indicating the coordination of the ligands to the metal atom[14] through tertiary nitrogen of the azolyl ring. This further gets support by the formation of ν(Ni—N)[15] and ν(Ag—N)[16] bond in the region 240–237 and 360–355 cm^{-1} respectively.

The bands due to ν_{asym}NH and δNH stretching vibrations at 3200–3150 and 1420 cm^{-1} of the imidazolyl ring remain almost at the same position in the spectra of metal complexes, suggesting the non-coordination and non-deprotonation through this imino group. The absorption bands ascribed to ν_{asym}OH/SH of the ligand moieties observed in the region 3450–3300/2600–2500 cm^{-1} disappears completely in the spectra of metal complexes, indicating the deprotonation and

coordination through these groups in a tridentate fashion. These observations are further supported by the formation of new bands in the region 256–250/232–228 cm^{-1} and 320–316/308–305 cm^{-1} assigned to ν(Ni—O)[17]/ν(Ni—S) and ν(Ag—O)/ ν(Ag—S) vibrations respectively. IR spectra of compounds 2a, b and 3a, b, c exhibited two sharp bands in the region 1500–1485 and 1294–1280 cm^{-1} due to unidentately coordinated —NO_2 groups. Compound 2c also showed two sharp and medium intensity absorption bands in the region 1650–1540 and 1355–1318 cm^{-1} due to bidentately coordinated —NO_2 group[18, 19]. Appearance of broad troughs in the region 3500–3450 cm^{-1} has been assigned ν(OH) vibrations of the water molecule. The δ(HOH) manifests as a shoulder in the region 1635–1615 cm^{-1} and the absorption band at 860–850 cm^{-1} has been assigned to rocking vibrations of coordinated water molecules[20].

In the IR spectra of ligand (1c), the absorption frequency due to >C—O vibrations of furyl ring[21] observed in the region 1235 cm^{-1} shifts to lower wave number by 7–10 cm^{-1} in the spectra of metal complexes 2c and 3c, indicating the coordination through furyl oxygen also, to provide tridentate bonding of the ligand N O N. The other ligand bands of the benzimidazolyl rings are observed nearly in the same region as reported in the literature[22].

The proposed bonding pattern is further supported by (^1H and ^{13}C) NMR spectra. The ^1H NMR spectra reveal the broad signal due to —NH proton at δ 9.3–9.6 ppm in case of the ligands, remains unperturbed and is observed almost at the same position in the spectra of complex derviatives. The —OH/—SH proton signals of the ligands observed at δ 10.1–10.2/4.3–4.5 ppm disappear completely in the spectra of the complexes supporting the above mentioned conclusions. Appearance of broad resonating signals at δ10.8–11.0 ppm may be assigned to OH_2 group of the water molecules respectively. Aromatic protons appearing at δ7.3–8.0 ppm in ligands show slight deshielding on complexation with metal ions. The ^{13}C NMR spectral data show a reasonable shifting of hydroxylic (153.24–154.17), thiolic (159.40–160.15) and pyridyl carbons (145.56–146.42) in the ligands to (150.21–151.63); (155.68–156.82) and (144.17–144.96) in the corresponding complexes, further substantiating the coordination of ligands with metal atom.

All the newly synthesized ligands and their complexes were screened for their antifungal and antibacterial activity against some of the pathogenic fungi and bacteria *viz., Aspergillus niger, Fusarium oxysporum, Candida albicans, Staphylococcus aureus, Escherichia coli* and *Pseudomonas cepacicola.* Aspectic techniques[23] were employed to prepare the culture medium of all the fungi and bacterial tested. The radial growth and paper disc methods were used to evaluate the antimycotic and antibacterial activities. The results of investigation have been presented in Table 2. It is evident from the data that there is a considerable increase in toxicity of complexes as compared to those of the ligands. A possible mode of enhanced toxicity of complexes could be speculated in the light of "Chelation Theory"[24]. Chelation reduces considerably the partial sharing of its positive charge with the donor group and possible π electron delocalisation over the chelate ring.

Further the inferences drawn from these observations reveal that the percentage inhibition increases as the concentration increases and the biocidal activity of silver(I) complexes is slightly more than the corresponding nickel(II) complexes.

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