

SHORT COMMUNICATION

INTERACTION OF 2-(2'-HYDROXY)PHENYLBENZOTHAZOLINE WITH SOME METAL IONS: DETERMINATION OF ITS DISSOCIATION CONSTANT IN AQUO-ORGANIC MEDIA

K. Laxmi, G. Bhargavi, B. Sireesha and Ch. Sarala Devi*

Department of Chemistry, University College for Women, Osmania University, Koti,
Hyderabad 500195, India

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ABSTRACT. Potentiometric titrations were carried out with 2-(2'-hydroxy)phenyl benzothiazoline (HPBT) in various 50%v/v aquo-organic media (dioxan-water, acetone-water, methanol-water, and ethanol-water) and in different percentages of dioxan. The results indicated that the ligand is a monoprotic acid with pK_a corresponding to the hydroxyl group. The pK_a value of HPBT determined in various aquo-organic media followed the regular order of the reciprocal of dielectric constant. The solid metal complexes employing HPBT were synthesized and characterized. Spectral studies of these metal complexes [M(II) = Co, Ni, Cu and Zn] complexes indicated ring cleavage and formation of bis benzylidene disulphide (BBDS) during complex formation.

KEY WORDS: 2-(2'-Hydroxy)phenylbenzothiazoline, Metal complexes, Potentiometric titrations, Dissociation constant, bis benzylidene disulphide

INTRODUCTION

The group N-C-S of benzothiazolines is of considerable chemotherapeutic interest and is responsible for their pharmacological activity [1]. The physiological activity of these compounds is attributable to their ability to chelate traces of metal ions. To understand the acidity of 2-(2'-hydroxy)phenylbenzothiazoline (HPBT), its pK_a value is determined in various aquo-organic solvents, and percentage effects on the dissociation constant were also studied. Since the ligand is prone to ring cleavage under the conditions employed for synthesis of complexes, we studied the structural changes occurring in the ligand upon complexation with IR, NMR, and UV-visible spectroscopic techniques.

EXPERIMENTAL

Potentiometric titrations. The ligand HPBT was synthesized by the reported procedure [2]. All the chemicals used were of AR grade. The proton-ligand dissociation constant of the ligand was determined potentiometrically using the Irving-Rossotti pH titration technique [3]. The pH measurements were made with a Digisun D1-707 digital pH meter, consisting of a combined glass electrode and calomel electrode. The following solutions were titrated potentiometrically against standard carbonate free 0.1 M NaOH containing (i) HNO_3 (4×10^{-3} M) and (ii) HNO_3 (4×10^{-3} M) plus ligand (1×10^{-3} M), at $\mu = 0.1$ M (KNO_3) under an N_2 atmosphere.

Synthesis of complexes and physical measurements. To a hot ethanolic solution of the ligand was added the metal chloride or nitrate solution while stirring. The reaction mixture was refluxed for about 15 hours while maintaining the pH of the solution for complexation by adding

*Corresponding author. E-mail: dr_saraladevich@yahoo.com

few drops of dilute ethanolic ammonium hydroxide to obtain the respective solid metal-ligand complex. The complexes were washed with ethanol and then with water to remove unreacted ligand and metal, followed by petroleum ether and dried under reduced pressure. The metal contents were determined on Perkin-Elmer a 2380 atomic absorption spectrophotometer and C, H and N analyses were carried out on a Perkin-Elmer 240C analyser. Conductivity was measured on Digisun D1 909 instrument at room temperature. IR spectra (KBr) were recorded on Perkin-Elmer 283 spectrophotometer, and ESR spectra on a Joel SE 3X (X-band) instrument. The ^1H NMR spectra were scanned on a Bruker WH 270 MHz NMR spectrometer. Thermogravimetric analysis (TGA) of complexes was carried on a Mettler Toledo Star System in the temperature range 0-1000 °C. Magnetic susceptibilities of the metal chelates were measured at room temperature with Faraday balance Model 7550 of Cahn Instruments Inc Cerritos, CA; USA.

RESULTS AND DISCUSSION

Potentiometric titrations. Potentiometric titrations have been carried out with HPBT to determine its acid dissociation constant at 303 K and 0.1 M (KNO_3) ionic strength (i) in various 50% v/v aquo-organic media viz., dioxan-water, acetone-water, methanol-water and ethanol-water and (ii) in various percentages of dioxan-water media viz., 30%, 40%, 50%, 60%, and 70%. The comparison of free acid curve and acidified ligand curve revealed the presence of one dissociable proton corresponding to the hydroxyl group of the phenyl ring (Figure 1, compound 1). The dissociation constant value in various aquo-organic media is in general influenced by dielectric constant, which is an electrostatic factor [4-9]. The dielectric constant follows the order: methanol-water > ethanol-water > acetone-water > dioxan-water. The dissociation constant value in various 50% v/v aquo-organic media follows the order: dioxan-water > acetone-water > ethanol-water > methanol-water, which is in accordance with the order of reciprocal of dielectric constants [4-9] of the media (Table 1). To understand the percentage effect of organic solvent on the dissociation constant of the ligand, titrations were carried out in various percentages of dioxan-water media viz., 30%, 40%, 50%, 60%, and 70%. A linear relationship between the percentage of organic solvent and pK_a was observed [4-9]. As the mole fraction of the organic solvent increases, the dielectric constant of the medium decreases and hence the pK_a value increases gradually [10-19] (Table 2). The above results reveal that the thiazoline ring moiety is stabilized by the addition of base in various aquo-organic media. If any ring cleavage occurs as the ligand is prone to form its open ring tautomer there should be evidence for release of one more proton, which is not observed. Hence it may be inferred that the ligand is intact in its closed ring form in solution under the experimental conditions.

Table 1. Proton dissociation constant of the HPBT in 50% v/v aquo-organic media at 303 K and 0.1 M (KNO_3) ionic strength.

Medium	Mole fraction	$1/\epsilon$	pK_a
50% v/v Dioxan-water	0.174	0.029	10.65
50% v/v Acetone-water	0.195	0.020	10.52
50% v/v Ethanol-water	0.231	0.019	9.38
50% v/v Methanol-water	0.309	0.018	8.87

Table 2. Proton dissociation constant of the HPBT in varying percentages of dioxan-water media at 303 K and 0.1 M (KNO₃) ionic strength.

Medium	Mole fraction	1/ε	pK _a
30% v/v Dioxan-water	0.083	0.019	9.46
40% v/v Dioxan-water	0.123	0.023	9.64
50% v/v Dioxan-water	0.174	0.029	10.65
60% v/v Dioxan-water	0.240	0.039	11.06
70% v/v Dioxan-water	0.329	0.056	11.65

Characterization of complexes

All the complexes are amorphous, stable to air and moisture, soluble in DMF and DMSO and are found to be non-electrolytes. The elemental analysis of all the complexes indicated a 1:2 (M:L) ratio (Table 3). TGA and DTA studies revealed the presence of coordinated water molecules in all the complexes. From the thermograms of all the complexes it is observed that there is only partial decomposition of complexes even at high temperatures (up to 1000 °C), indicating formation of thermally stable species.

The IR spectrum of HPBT showed peaks corresponding to ν_{NH} (3254 cm^{-1}), ν_{OH} (3100 cm^{-1}), and $\nu_{\text{C-H}}$ (2881 cm^{-1}). The absorption in the lower frequency region for the OH stretching vibration suggests the presence of hydrogen bonding. From the IR spectra of all the complexes it is evident that the ν_{NH} peak observed in the ligand is absent. A new peak observed in the range of 1602-1653 cm^{-1} is attributable to the presence of the C=N group. The disappearance of the OH peak in complexes reveals conclusive evidence for the deprotonation of the ligand upon complex formation involving oxygen in bonding. Since the complexes were prepared by refluxing for about 15 h in ethanol, adjusting pH for complexation, such conditions may lead to cleavage of the thiazoline ring [20-28] and hence formation of either complexes of 2-(2'-hydroxybenzylideneamino)thiophenol (Figure 1, compound **2**) or bis[2-(2'-hydroxybenzylideneamino)phenyl]disulphide (Figure 1, compound **3**). If 2-(2'-hydroxybenzylideneamino)-thiophenol is involved in the formation of corresponding 1:2 complexes, there should be evidence for negatively charged complex ions ML_2^{2-} as the ligand has two dissociable protons (SH and OH protons). But conductivity studies revealed that the metal complexes are non-electrolytes. Therefore, formation of bis-benzylidene disulphide (BBDS) complexes is tentatively predicted.

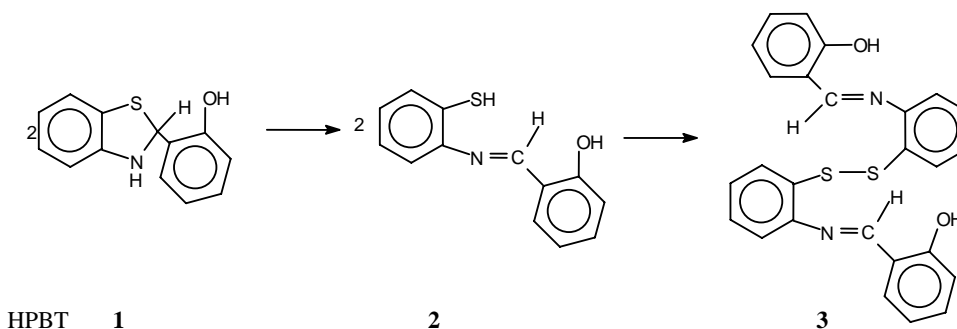


Figure 1. Scheme showing the cleavage of five membered ring of HPBT and resultant dimeric disulphide ligand formation under the experimental condition employed for the synthesis of metal complexes.

Table 3. Physical and analytical data of M(II)-BBDS complexes

No.	Ligand/complex	Colour	m.p. (°C)	μ_{eff} (BM)	Analysis: found (calc.) %			
					C	H	N	M
1	Co(II)-BBDS	Greenish black	Dp	3.21	58.30 (56.84)	4.21 (4.01)	6.65 (5.10)	10.54 (10.74)
2	Ni(II)-BBDS	Green	Dp	Dia	57.64 (60.85)	4.39 (3.51)	5.11 (5.46)	10.85 (11.45)
3	Cu(II)-BBDS	Black	Dp	Zero	56.42 (56.37)	4.31 (3.97)	5.06 (5.06)	11.55 (11.47)
4	Zn(II)-BBDS	Light yellow	Dp	Dia	57.10 (56.18)	3.39 (3.96)	4.79 (5.04)	13.33 (11.79)

Dp: decomposes; Dia : diamagnetic.

Proton NMR spectra of HPBT in DMSO- d_6 recorded peaks at δ 9.8 (s, 1H, OH), δ 6.47- δ 7.4 (m, 8H arom, 1H NH, 1H 2-CH). The OH and NH peaks were identified by their exchange with D₂O. The ¹H NMR spectrum of the zinc complex in DMSO- d_6 recorded chemical shifts at δ 8.8 (s, 1H, CH), δ 6.6- δ 7.6 (m, 8H, arom), indicating loss of NH and OH protons upon complexation. The D₂O exchangeable spectrum of the complex was identical. The signal, recorded at δ 8.8 attributable to the azomethine [22] proton, clearly reveals cleavage of the thiazoline ring, supporting an open ring structure of ligand (Figure 1, compound **3**) in complexes. Thus proton NMR spectral data of metal complexes when compared with the NMR spectral data of the ligand clearly reveal the participation 'O' and 'N' in bonding. Hence it may be concluded that the data from ¹H NMR that substantiate the results observed from IR would support open ring structures in the metal complexes.

The UV-visible spectrum of the Co(II)-BBDS complex showed two absorption bands in the visible region that can be assigned to ⁴T_{1g} → ⁴T_{1g}(P) (16,447 cm⁻¹) and ⁴T_{1g} → ⁴T_{2g} (24,875 cm⁻¹) predicting octahedral geometry. The absorption band observed in UV region (36,630 cm⁻¹) corresponds to the ligand chromophore. By assuming square planar geometry, the absorption at 23,419 cm⁻¹ in the UV-visible spectrum of Ni(II)-BBDS may be assigned as the ¹A_{1g} → ¹A_{2g} transition. The UV-visible spectrum of Cu(II)-BBDS recorded a band in the visible region at 23,809 cm⁻¹. This band is due to transitions in the energy levels that arise from ²D term [29, 30].

The ESR spectrum (X band and Q band) of the Cu(II)-BBDS complex showed three 'g' values, 2.236, 2.067, and 2.025 corresponding to g_x, g_y and g_z respectively, indicating anisotropy.

The magnetic measurements for Cu(II)-BBDS showed zero magnetic moment value though the ESR spectrum indicated the presence of an unpaired electron. This is due to antiparallel alignment [31] of spins on adjacent Cu(II) ions. Thus, these results support a binuclear or polynuclear Cu(II)-BBDS complex. The magnetic moment values of the Ni(II)-BBDS complex reveal that the complex is diamagnetic [32], suggesting a square planar geometry. The magnetic moments measured for Co(II) complex indicate octahedral geometry and the presence of three unpaired electrons.

Thus the interaction of metal ions with HPBT under reflux conditions has resulted in the formation of metal complexes of bis[2-(2'-hydroxybenzylideneamino)phenyl]disulphide due to structural changes in the ligand HPBT. The various structural changes in HPBT upon complexation evident from IR and NMR spectral data clearly support the involvement of disulphide ligand in the complexes. The structures of complexes are assigned tentatively (Figure 2) based on the results obtained from spectroscopic data. However crystallographic characterization is required to ascertain the proposed structures.

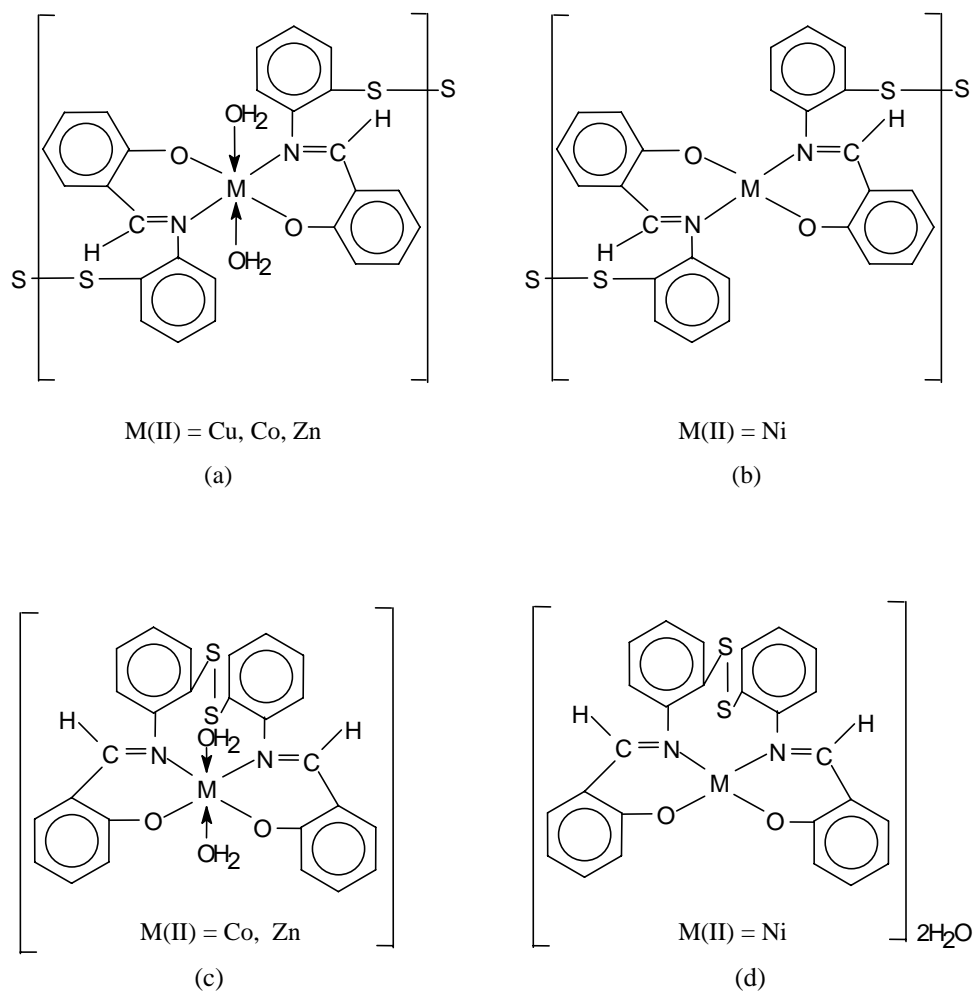


Figure 2. Tentative structures of the complexes.

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