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Synthesis, Characterization and Antimicrobial Activity of Ni(II) Complexes with 2-substituted Benzothiazole Ligands & Amino acids

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ABTRACT

The synthesis and antimicrobial activity of Ni(II) complexes derived from 2-substituted benzothiazole ligands namely 2(2´-aminophenyl)benzothiazole) (APBT), 2(2´-hydroxyphenyl)benzothiazole (HPBT) and 2(2´-merceptophenyl) benzothiazole (MPBT) & Amino acids like Leucine & Isoleucine, are reported here. These complexes have been characterized by IR, ^{1}H-NMR spectral studies, elemental analysis. The ligands & their ternary metal complexes were tested against certain microorganisms to assess their antimicrobial properties. The results indicate that the metal complexes are found more active than the parent ligands.

Keywords: 2-substituted benzothiazole, spectral studies, antimicrobial activity.

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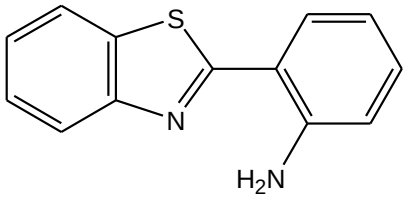
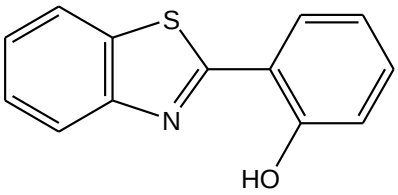
INTRODUCTION

The interest in coordination chemistry is increasing continuously with the synthesis & characterization of large number of transition metal complexes with heterocyclic ligands containing nitrogen, oxygen, sulfur donors [1-4]. Studies of transition metal complexes of benzoxazole, benzimidazole & benzothiazole have gained importance because of their biological significance & it was observed that biological activity of these ligands increases on complexation with metal ion [5-6]. The ligation behaviour of benzimidazole & benzothiazole and their derivatives have been reported by Seth *et al* [7]. Benzthiazole derivatives are key components in the bioactive compounds of both natural & synthetic origin. In addition to their biological importance these ligands are strongly coordinating agent & form stable complexes with various transition metal ion [8]. It is believed that they react selectively toward certain biological system [9], phosphorylated & thiophosphorylated benzothiazole derivatives were also screened for Antifungal activities [10-12].

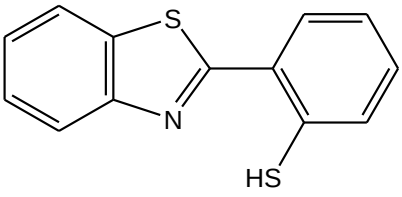
In view of the above mentioned findings we report, herein the synthesis, characterization, and antimicrobial activity of Ni(II) complexes derived from 2-substituted benzothiazole ligands (APBT, HPBT, MPBT) and amino acids (leucine & isoleucine). The ligands used during these investigation are shown in Fig 1.



2(2´-Aminophenyl)benzothiazole (APBT)



2(2´-Hydroxyphenyl)benzothiazole (HPBT)



2(2´-Merceptophenyl)benzothiazole (MPBT)

Figure-1 Structure of the ligands

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MATERIALS AND METHODS

Materials

All the solvents were distilled prior to use. Anthranilic acid, salicyclic acid, thiosalicyclic acid, *O*-aminothiophenol, $NiCl_2.6H_2O$ were purchased from Merck (Germany) and used as such.

Physical Measurements

Microanalysis was carried out at the CDRI Lucknow, India. Infrared spectra were recorded (with KBr pellets) on a Shimadzu 8400 FT-IR spectrophotometer. ^1H NMR spectra were recorded on a JEOL AL 300 MHz FT-NMR spectrometer in $CDCl_3$ using TMS as an internal reference. Molar conductance was measured in 10^{-3}M DMF on a systronics conductivity bridge model 305. Molecular weights were determined by the Rast camphor method. Nitrogen was determined by the Kjeldahl's method and Sulfur was estimated by the Messenger's method. Chloride was determined by the Volhard's method [13]. Ni was estimated by gravimetrically.

Synthesis of ligands

The ligands namely 2(2´-aminophenyl)benzothiazole (APBT), 2(2´-hydroxyphenyl)benzothiazole (HPBT) and 2(2´-merceptophenyl) benzothiazoles (MPBT) were prepared by condensations of O-aminothiophenol (1.25 ml, 0.01 mol) with anthranilic acid (1.37 gm, 0.01 mol), salicylic acid 1.38 g, 0.01 mole), and thiosalicylic acid (1.54 g, 0.01 mole) in polyphosphoric acid (20 ml). Using the methodology previously described [14]. The reaction mixture was heated slowly to 250°C under reflux with constant stirring for 4 h. finally the contents were poured into a large volume of rapidly stirred water. The resultant slurry was made alkaline with 50% NaOH. The crude product was collected by filtration and washed with sufficient amount of water, dried in vacuo and recrystallized from ethanol.

Preparation of Ni(II) Ternary complexes

A solutions of $NiCl_2.6H_2O$ (0.59 g, 0.01 mol) in dry MeOH (25 ml) was added APBT (0.056 g, 0.01 mol) / HPBT (0.0568 g, 0.01 mol) / MPBT (0.060 g, 0.01 mol) and Leucine (0.032 g, 0.01 mol) and Isoleucine (0.032 g, 0.01 mol) in dry MeOH (25 ml). The reaction mixture was refluxed in the presence of a drop of pyridine with constant stirring for 4h, and allowed to stand at room temperature overnight. These were filtered, recrystallized from EtOH and dried *in vacuo*.

Biological evaluation

Antimicrobial Activity

The free ligands (APBT, HPBT, MPBT) and their Ni(II) complexes were screened against pathogenic bacteria, namely *Staphylococcus aureus* (+ve) and *Escherichia coli* Gram (-ve) & Pathogenic fungi, namely *Aspergillus niger* and *Fusarium oxysporium*, to assess their growth

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inhibitory potential as antimicrobial agents. The antibacterial and antifungal activity screening data (table 5 & 6) reveal that the Ni(II) complexes are more potent than the parent ligands (APBT, HPBT, MPBT). The antibacterial and antifungal screening data also reveal that the sulfur containing ligands as well as their Ni(II) complexes are more active than their nitrogen/oxygen containing counterparts [15]. The toxicity increased as the concentrations was increased.

RESULTS AND DISCUSSION

The Ni(II) ternary complexes were synthesized by $NiCl_2.6H_2O$ with 2-substitued benzothiazoles (APBT, HPBT, MPBT) or amino acids (Leu & Ileu) in 1:1:1 molar ratio according to the following equations :-

(i) $MCl_2.6H_2O + \overset{\frown}{N\quad NH_2} + \overset{\frown}{H_2N\quad COOH} \xrightarrow[\text{reflux}]{\text{ethanol}} MCl(\overset{\frown}{H_2N\quad COO})\ (\overset{\frown}{N\quad NH_2}) + 5H_2O + HCl$

M = Ni

$\overset{\frown}{N\quad NH_2}$ = APBT

$\overset{\frown}{H_2N\quad COOH}$ = Amino acids

(ii) $MCl_2.6H_2O + \overset{\frown}{N\quad XH} + \overset{\frown}{H_2N\quad COOH} \xrightarrow[\text{reflux}]{\text{ethanol}} [M(\overset{\frown}{H_2N\quad COO})(\overset{\frown}{N\quad X})(H_2O)_2)] + 4H_2O + 2HCl$

M = Ni

$\overset{\frown}{N\quad XH}$ = HPBT, MPBT

X = O or S

$\overset{\frown}{H_2N\quad COOH}$ = Amino acids

The reaction processed easily and lead to the formation of coloured solids, which are stable to air and moisture. The molar conductance values of 10^{-3} M solutions of these complexes lie in the range 10-15 Ω^{-1} cm^{-1} in dry DMF, indicating their non-electrolyte behaviour. The monomeric nature of these complexes has been confirmed by the molecular weight determination. The analytical data and physical properties of the ligands and their Ni(II) ternary complexes are given in table-1.

The compound has been characterized on the basis of following studies :

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Table-1 Analytical data and Physical Properties of 2-Substituted Benzazoles and their Ni(II) complexes with Leu & Ileu.

S. No.	Compd. & empirical formula	Colour	Molar ratio	M.P. (°C)	Elemental analysis found (Calcd.)						Molecular weight Found (Calcd.)
					C	H	N	S	Cl	Ni	
1.	[NiCl(APBT)(Leu)(H_2O)] $NiC_{19}H_{24}O_3N_3SCl$	Bluish green	1:1:1	224	48.92 (48.76)	5.15 (5.12)	9.01 (8.97)	6.86 (6.85)	7.40 (7.48)	12.44 (12.54)	465.96 (467.97)
2.	[NiCl(APBT)(Ileu)(H_2O)] $NiC_{19}H_{24}O_3N_3SCl$	Bluish green	1:1:1	220	48.92 (48.76)	5.15 (5.12)	9.01 (8.97)	6.86 (6.85)	7.41 (7.48)	12.44 (12.54)	465.97 (467.97)
3.	[Ni(HPBT)(Leu)(H_2O)$_2$] $NiC_{19}H_{24}O_5N_2S$	Light green	1:1:1	260	50.70 (50.60)	5.33 (5.32)	6.22 (6.20)	7.10 (7.11)	-	12.88 (13.01)	450.00 (450.90)
4.	[Ni(HPBT)(Ileu)(H_2O)$_2$] $NiC_{19}H_{24}O_5N_2S$	Light green	1:1:1	255	50.70 (50.60)	5.33 (5.32)	6.22 (6.20)	7.10 (7.11)	-	12.88 (13.01)	450.00 (450.90)
5.	[Ni(MPBT)(Leu)(H_2O)$_2$] $NiC_{19}H_{24}O_4N_2S_2$	Yellowish green	1:1:1	241	52.57 (52.50)	5.52 (5.93)	6.45 (6.91)	7.37 (7.91)	-	13.36 (14.49)	434.00 (404.91)
6.	[Ni(MPBT)(Ileu)(H_2O)$_2$] $NiC_{19}H_{24}O_4N_2S_2$	Green	1:1:1	238	52.57 (52.50)	5.52 (5.93)	6.45 (6.91)	7.37 (7.91)	-	13.36 (14.49)	434.00 (404.91)

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Table-2 IR Spectral data (cm^{-1}) of ternary complexes of Ni(II) of 2-substituted benzothiazole and amino acid.

S. No.	Compd.	ν (C=C)	ν (C=N)	ν (C=O)	ν (NH_2)		ν (O–H)	ν (S–H)	ν (Ni–N)	ν (Ni–S)	ν (Ni–O)	ν (Ni-Cl)
					Asym	Sym						
1.	APBT	1580	1606	1660	3350	3240	-	-	-	-	-	-
2.	HPBT	1578	1605	1658	3348	3235	3340	-	-	-	-	-
3.	MPBT	1585	1610	1675	3355	3240	-	2560	-	-	-	-
4.	[NiCl(APBT)(Leu) (H_2O)]	1582	1608	1670	3354	3238	-	-	449	-	449	315
5.	[NiCl(APBT)(Ileu) (H_2O)]	1582	1606	1659	3351	3234	-	-	446	-	446	319
6.	[Ni(HPBT)(Leu) ($H_2O)_2$]	1580	1605	1665	3345	3225	-	-	456	-	435	-
7.	[Ni(HPBT) (Ileu) ($H_2O)_2$]	1584	1612	1677	3358	3241	-	-	453	-	437	-
8.	[Ni(MPBT)(Leu)($H_2O)_2$]	1577	1603	1664	3344	3224	-	-	439	436	441	-
9.	[Ni(MPBT)(Ileu)($H_2O)_2$]	1578	1604	1669	3351	3256	-	-	437	434	439	-

Table-3 ^{1}H NMR spectral data (ppm) of the ligands (APBT, HPBT, MPBT) and their Ni(II) ternary complexes.

S. No.	Compd.	-NH_2	-OH	-SH	-CH_3	-CH_2	-CH	Aromatic proton
1.	APBT	3.58	-	-	-	-	-	6.52-8.23
2.	HPBT	-	10.32	-	-	-	-	6.79-8.23
3.	MPBT	-	-	3.60	-	-	-	7.06-8.23
4.	[NiCl(APBT)(Leu)(H_2O)]	3.73	-	-	1.30	3.61	3.68	6.69-8.32
5.	[NiCl(APBT)(Ileu)(H_2O)]	3.72	-	-	1.31	3.60	3.67	6.68-8.31
6.	[Ni(HPBT)(Leu)($H_2O)_2$]	3.69	-	-	1.28	3.63	3.66	6.97-8.42
7.	[Ni(HPBT) (Ileu)($H_2O)_2$]	3.68	-	-	1.28	3.63	3.66	6.97-8.42
8.	[Ni(MPBT)(Leu)($H_2O)_2$]	3.75	-	-	1.31	3.60	3.62	7.20-8.50
9.	[Ni(MPBT)(Ileu)($H_2O)_2$]	3.74	-	-	1.31	3.60	3.62	7.19-8.45

Infrared spectra

The broad band at 3340 cm^{-1} due to ν (O-H) phenolic mode of HPBT, disappears in the Ni(II) ternary complexes, indicating the deprotonation of the OH group and coordination of phenolic. Oxygen to the Ni atom with the formations of Ni-O bond. This gets further support by the appearance of bond in the region 435-437 cm^{-1} due to ν (Ni-O) vibration. The IR spectrum of MPBT shows a band at 2560 cm^{-1} due to ν (S-H) (thiophenolic) vibration, which disappears in the Ni(II) ternary complexes, suggesting the deprotonation of -SH group and coordination through thiophenolic sulfur with the Ni atom. It is further supported by the appearance of new band in the region 432-436 cm^{-1} due toν (Ni-S) vibration.

A medium or relatively weak band in the 1605-1610 cm^{-1} region in the IRT spectra of the free ligand (APBT, HPBT, MPBT) is due to ν(C=N) vibration. This band is shifted to lower frequency by 10-20 cm^{-1} in Ni(II) ternary complexes indicate the bonding of the benzothiazola tertiary nitrogen with Ni atom. It is further confirmed by the appearance of bond in the region 436-450 cm^{-1} due to ν(Ni←N) vibrations [16]. The occurance of non-ligand absorption band in the region 315-310 cm^{-1} may be attributed to ν(Ni-Cl) vibration [17].

^{1}H NMR spectra

The ^{1}H NMR spectra of the ligands and their Ni(II) complexes were recorded in $CDCl_2$ (table-3). The ^{1}H NMR spectrum of the ligand APBT exhibit a broad singlet at δ3.17 ppm due to -NH_2 proton, is shifted slightly down field in the metal complexes, suggesting the coordination of nitrogen of the NH_2 group with the metal. The free ligands HPBT show a broad singlet at δ 10.12 ppm due to OH proton. The absence of this signal in the spectra of metal complexes indicates the deprotonation of the OH group and coordination of the phenolic oxygen with the metal. The singlet at δ 3.60 ppm due to a SH proton of the free ligand MPBT, disappears in the spectra of the metal complexes, thereby suggesting the deprotonation of the SH group on complexation with the metal atom. The aromatic protons of the ligands were observed at multiplet at δ 6.98-8.23 ppm. Shifted downfield in their respective Ni(II) complexes, which may be possible due to deshielding on coordination of ligands with metal.

Electronic absorption spectra and magnetic studies

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Table-4 Electronic spectral data and magnetic moments (μ_B) for the Ni(II) ternary complexes of 2-substituted benzothiazole and Leucine/Ileucine.

S.No.	Complexes	Magnetic (μ_B) B.M.	Electronic transition and assignments cm^{-1}		
			$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_1)$	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$
1.	[NiCl(APBT)(Leu)(H_2O)]	3.28	9840	18150	25060
2.	[NiCl(APBT)(Ileu)(H_2O)]	3.30	9845	18155	25055
3.	[Ni(HPBT)(Leu)(H_2O)$_2$]	3.24	9825	18651	25940
4.	[Ni(HPBT)(Ileu)(H_2O)$_2$]	3.25	9827	18655	25245
5.	[Ni(MPBT)(leu)(H_2O)$_2$]	3.27	9730	18220	25050
6.	[Ni(MPBT)(Ileu)(H_2O)$_2$]	3.26	9735	18225	25055

The electronic absorption spectra and magnetic moments of the Ni(II)ternary complexes are given in Table-4. The electronic spectra of Ni(II) ternary complexes were recorded in nujol mull. the ternary nickel(II) complexes display three absorption band at low intensity due to d-d transition in the region 9820 cm^{-1} and 18225 and 25048 cm^{-1} are assigned to the $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\nu_1)$; $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$ and $^3Ag_{2g}(F) \rightarrow {}^3t_{1g}(P)(\nu_3)$ transition [18], respectively. The position of these bands are similar to those reported for nicked(II) complexes with octahedral geometry [19].

The magnetic moments of the ternary nickel(II) complexes have been found in the range 3.24-3.38 BM, which suggests a high-spin state of nickel(II) for these complexes with an octahedral geometry.

CONCLUSION

We have synthesized three biologically active ligands (APBT, HPBT, MPBT) and then prepared their Ni(II) ternary complexes and evaluated their antimicrobial activity. Their structure have been established on the basis of spectral studies. In antimicrobial screening, it has been observed that the antibacterial & antifungal activity increased on complexation. The Ni(II) complexes having sulfur were more active than their oxygen counterparts and the parent ligands. It guides us to synthesize the analogs of substituted benzothiazole ligands, their metal complexes, and to study their biological activity.

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