



Synthesis, Characterization and Antimicrobial activity of Novel Benzimidazole Containing Ligand and Its Metal Complexes

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ABSTRACT

The novel ligand, 2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene)hydrazine carbothioamide (MBITS) was synthesised from 5-methyl-1-(1H-Benzimidazol-1-yl)-2-propanone (MBIP) and Thiosemicarbazone. The metal complexes of MBITS were synthesised from Transition metal ions. The synthesised ligand MBITS and synthesised metal complexes were characterised by elemental analysis, spectroscopic analysis, ratio of metal: ligand and magnetic properties. The ligand MBITS and metal complexes also were screened for Antimicrobial activity.

Keywords: 5-methyl-1H-benzimidazole, Thiosemicarbazone, Metal complexes, Spectral analysis, Magnetic properties and Antimicrobial activities.

INTRODUCTION

Benzimidazole is fused heterocyclic compound, which are associated with various pharmaceutical activities such as antimicrobial, anti-cancer, antiproliferative, anti-diabetic and antibacterial, etc¹⁻⁵. Due to various biological properties, Thiosemicarbazides became significant functional group. The numbers of researches on Thiosemicarbazides were done for and they show excellent pharmaceutical activities⁶⁻⁹. In the treatment of cancer thiosemicarbazides compounds exhibit some significant activities. Thiosemicarbazides compounds are exceptionally discriminated in antitumor activity. The metal chelates of thiosemicarbazides compounds elevated the biological properties^{7,8}. Among

them nitrogen and sulfur-containing compounds, thiosemicarbazides show importance in the field of medicinal chemistry¹⁰. Many scientists have developed a variety of bioactive and pharmacological activities heterocyclic molecules, which contains thiosemicarbazides and thiosemicarbazides moiety¹¹. Thiosemicarbazides generally act as chelating ligands containing which react with transition metal giving complexes, which shows biological activities rather than ligands^{12,13}.

Looking to systematic literature study of benzimidazole and Thiosemicarbazides derivatives, and in continuous of our previous work the present paper comprise the metal complexation study of benzimidazole-thiosemicarbazides clubbed compound The reaction steps is shown in Scheme 1.



EXPERIMENTAL

Laboratory mark chemicals were utilized. Elemental analysis of synthesised compounds were find out by volumetrically by reported process¹⁴. Nicolet-FT-IRspectrometer-760, NMR spectrophotometer-60MHz and LC-MSD-Trap-SL_01046 were utilized for spectral data studies of synthesized BITS (Ligand) and complexes. Magnetic properties find out by Gouy Balance. The antibacterial activities of the synthesized BITS (Ligand) and complexes were detetmined for selected bacteria. Evaluation of antimicrobial activity has been carried out using Broth Dilution method for antimicrobial study¹⁵⁻¹⁷. Similar conditions using Amoxillin and Nystatin were used standard for comparison.

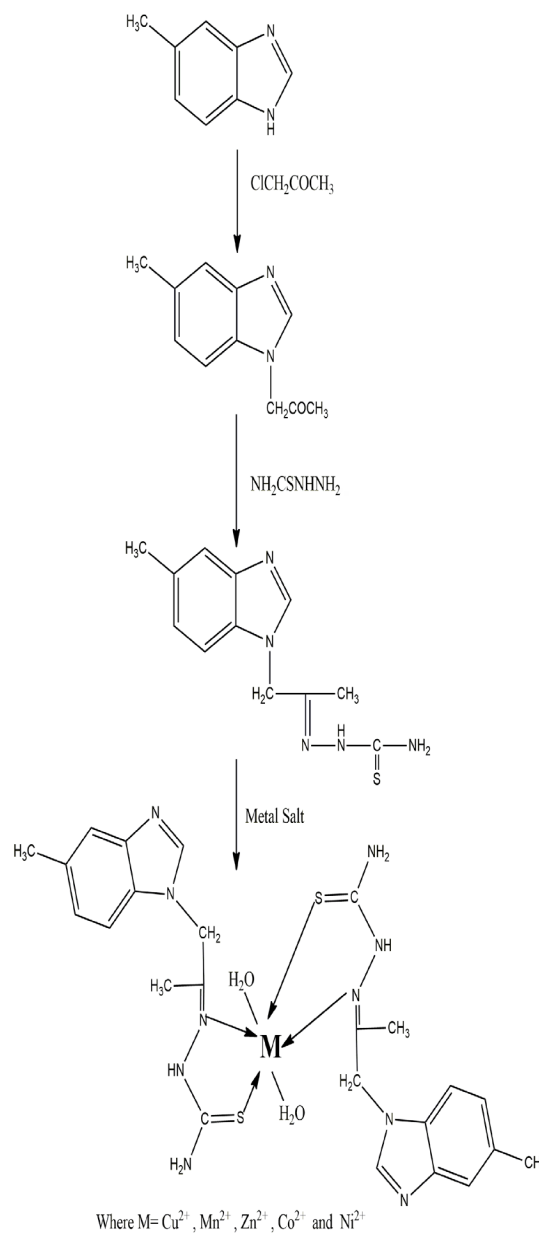
Synthesis of 5-methyl-1-(1H-Benzimidazol-1-yl)-2-propanone(MBIP)

In round bottom flask take a mixture of 5-methyl-1H-benzimidazole (0.01 mole), chloroacetone (0.01 mole) and 150 mL of dry acetone and 35 g of anhydrous potassium carbonate and refluxed this reaction mixture for 7 hours. The product separated out was filter and recrystallized from ethanol^{8,9}. Yield: 74%, m.p.:138°C.Elemental Analysis for $C_{11}H_{12}N_2O$ (188 g/mole): Clac. %C, 70.19; H, 6.43; N, 14.88; Found. %C, 70.1; H, 6.4; N, 14.8. IR Spectral data of IR(cm^{-1}) at 2900, 2852, 1513, 1400(Carbon-H Stra.), 1686 (Carbonyl), 3005 (Ar.Carbon-H Stra.), 1595(-C=N) and 1595, 1452(Aromatic C-C Str.). NMR Signals (δ ppm) at 2.08-2.40 (s, 6H, $-CH_3$), 7.40-8.20 (m, 4H, benzoimidazole C-H) and 4.90-4.92 (s, 2H, $-CH_2-$).

Synthesis of 2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene)hydrazine carbothioamide (MBITS)

Thiosemicarbazides was synthesized by refluxing the solution of thiosemicarbazide (0.03mol) in ethanol and the alcoholic solution of 5-methyl-1-(1H-Benzimidazol-1-yl)-2-propanone (0.03 mol) at 60°C for 5-6 h with continuous stirring. After cooling the compounds were filtered and recrystallized from ethanol^{8,9}. Yield: 76%; m.p.

154°C; Elemental Analysis for $C_{12}H_{15}N_5S$ (261g/mole): Clac. %C, 55.15; H, 5.79; N, 26.80; S, 12.27; Found.%C, 55.1; H, 5.7; N, 26.7; S, 12.2. IR Spectral Features (cm^{-1}) shows at 3376-3274 (N-H Str.), 2905, 2852, 1479, 1400(Carbon-H Stra.), 1686(C=N), 3050(Ar. Carbon-H Stra.) in addition, 741(C=S). NMR Signals (δ ppm) at 1.99-1.77 (s, 3H, C- CH_3), 2.37-2.39 (s, 3H, C- CH_3), 7.20-8.25(m, 4H, Ar C-H), 4.90-4.95(s, 2H, $-CH_2-$), 8.60(s, 1H, $-NH-$) and 3.75-3.72(s, 2H, $-NH_2$). LC-MS: M/z at 261.2(M^+).



Scheme 1. Reaction scheme

Table 1: Analysis of BITS Ligand and Complexes

Ligand and Metal Complex	Mol. Wt.	Color	Yield%	Elemental analysis (%)				
				C% Cald. Found	H% Cald. Found	N% Cald. Found	S% Cald. Found	M% Cald. Found
C ₁₂ H ₁₅ N ₅ S	261	Pale Yellow	72	55.1555.1	5.795.7	26.8026.7	12.2712.2	--
C ₂₄ H ₃₀ N ₁₀ S ₂ Cu ²⁺ .2H ₂ O	622.54	yellow	70	46.3246.3	5.515.5	22.5122.5	10.3110.2	10.2110.2
C ₂₄ H ₃₀ N ₁₀ S ₂ Ni ²⁺ .2H ₂ O	617.71	light green	68	46.6946.6	5.555.5	22.6922.6	10.3910.3	9.519.5
C ₂₄ H ₃₀ N ₁₀ S ₂ Co ²⁺ .2H ₂ O	617.94	red	72	46.6746.6	5.555.5	22.6822.6	10.3810.3	9.549.5
C ₂₄ H ₃₀ N ₁₀ S ₂ Zn ²⁺ .2H ₂ O	624.38	yellowishwhite	73	46.1946.1	5.495.4	22.4422.4	10.2810.2	10.4810.4
C ₂₄ H ₃₀ N ₁₀ S ₂ Mn ²⁺ .2H ₂ O	613.94	white	70	46.9746.9	5.585.5	22.8222.8	10.4510.4	8.958.9

Synthesis of Metal complex of 2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene)hydrazine carbothioamide (MBITS)

The metal chelates of MBITS (i.e. of Cu²⁺, Mn²⁺, Zn²⁺, Co²⁺, Ni²⁺ ions) were prepared in similar manner. The general method for it is as follow.

Add the appropriate metal ion salts (0.001 mol) in 15 mL alcohol/H₂O (50:50) volume into hot 2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene)hydrazine carbothioamide (MBITS) ligand (0.02 mol) in 30 mL alcohol with continuous

stirring than refluxed for one hr in water bath. Next day later, solid colored complexes formed, it were filtered,washed with alcohol.

RESULTS AND DISCUSS

2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene) hydrazine carbothioamide (MBITS) was prepared by condensation of 5- methyl -1-(1H-Benzo[d]imidazol-1-yl)-2-propanone with thiosemicarbazide. The important IR bands of MBITS contains because of thiosemicarbazide.

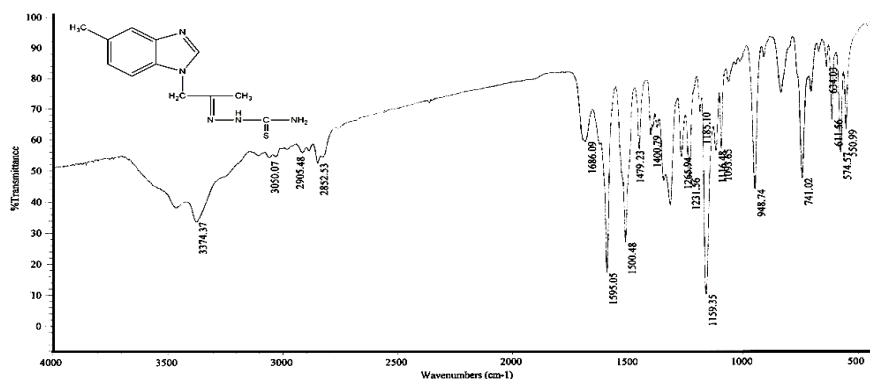


Fig. 1. IR of MBITS

MBITS shows thiosemicarbazide NH at 3.75-3.72 and 8.60. The methylene proton shows singlet at 1.77-1.99 and 2.37-2.39.

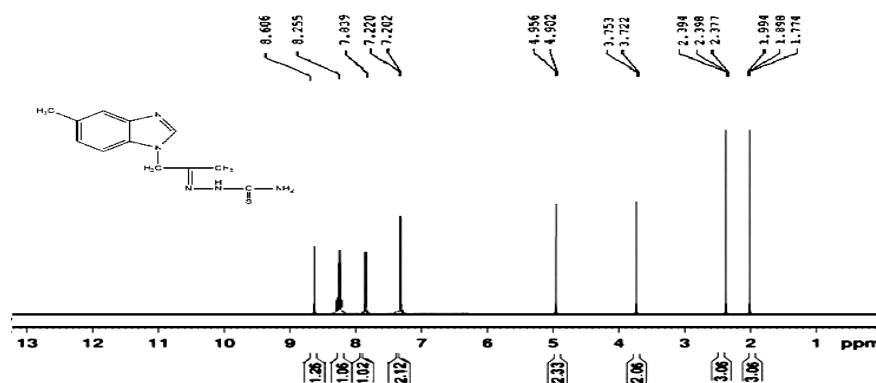


Fig. 2. NMR of MBITS

The presence of IR- band characteristic of metal-nitrogen and metal-Sulpher of indicate making of cyclicmetallic complexes^{18,19}.

Table 1 confirms the synthesised compounds and divalent complexes^{18,19}. The magnetic and reflectance properties of complexes suggest

octa-hedral shape^{18,19} Table 2.

The antibacterial and antifungal properties of MBITS ligand and complexes shows MBITS ligand less effective than complexes, every complexes shows notable toxicity Table 3 and 4.

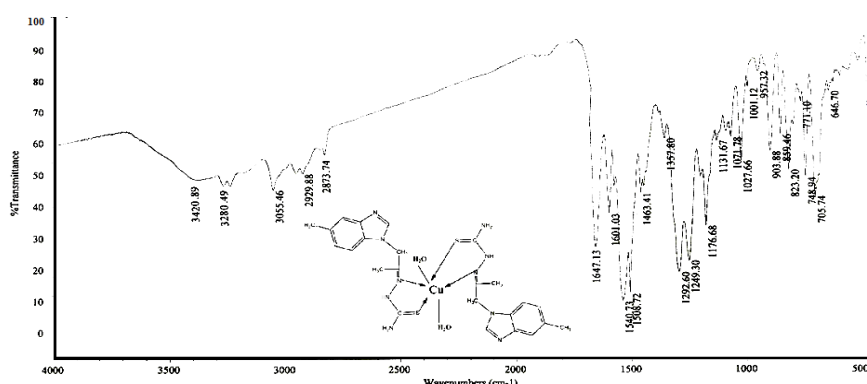


Fig. 3. IR of MBITS-Cu²⁺

Table 2: Magnetic And Reflectance Properties MBITS-Metal Complexes

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm ⁻¹)	Transition
MBITS-Cu ²⁺	2.35	23989 15762	CT ² B _{1g} → ² A _{1g}
MBITS-Ni ²⁺	3.42	22240 15793	³ A _{2g} → ³ T _{1g} (P) ³ A _{2g} → ³ T _{1g} (F)
MBITS-Co ²⁺	4.5	23954 18117 8739	⁴ T _{1g} (F) → ⁶ T _{2g} (u1) ⁴ T _{1g} (F) → ⁴ A _{2g} (u2) ⁴ T _{1g} (F) → ⁴ T _{1g} (P)
MBITS-Mn ²⁺	5.53	23885 18344 16851	⁶ A _{1g} → ⁶ A _{1g} (4Eg) ⁶ A _{1g} → ⁴ T _{2g} (4G) ⁶ A _{1g} → ⁴ T _{1g} (4G)
MBITS-Zn ²⁺	D	-	-

D⁺=Diamagnetic

Table 3: Antibacterial study of MBITS ligand and complexes

Compound	Minimum Inhibitory Concentration (MIC, $\mu\text{g mL}^{-1}$)			
	<i>B. megaterium</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
MBITS	125.5	120	150	150
MBITS-Cu ²⁺	30	25	20	22.5
MBITS-Ni ²⁺	75	105	110	67.5
MBITS-Co ²⁺	55	40	52.5	45
MBITS-Zn ²⁺	35.5	42.5	93.5	100
MBITS-Mn ²⁺	72.5	75	62	140
Amoxicillin	250	150	250	200

Table 4: Antifungal study of MBITS ligand and complexes

Compound	Minimum Inhibitory Concentration (MIC, $\mu\text{g mL}^{-1}$)			
	<i>Penicillium expansum</i>	<i>Botrydoplodia thibromine</i>	<i>Nigrospora Sp.</i>	<i>Fusarium oxysporium</i>
MBITS	100	80.5	65.5	75
MBITS-Cu ²⁺	22.5	20	30	22.5
MBITS-Ni ²⁺	75.5	70	75	50
MBITS-Co ²⁺	75	65.5	82	50.5
MBITS-Zn ²⁺	40	25	42.5	35
MBITS-Mn ²⁺	65	50.5	75	50
Nystatin	300	200	250	200

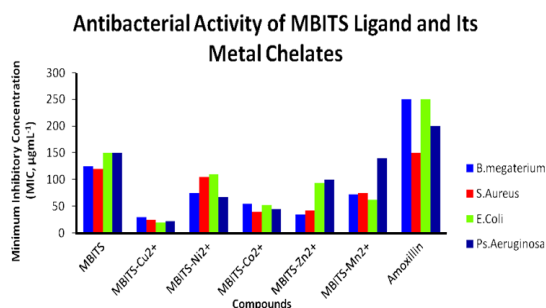


Fig. 3. Antibacterial study of MBITS ligand and complexes

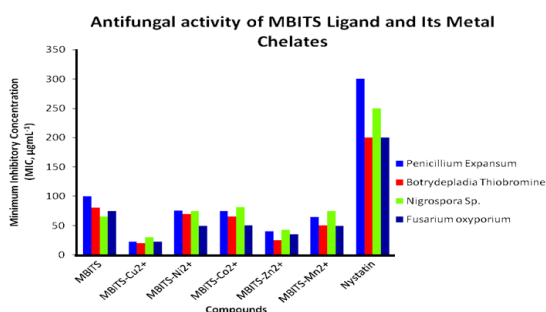


Fig. 4. Antifungal study of MBITS ligand and complexes

CONCLUSION

5-methyl-1-(1H-Benzimidazol-1-yl)-2-propanone (MBIP) react with Thio-semicarbazone afforded novel ligand, 2-(1-(5-methyl-1H-benzimidazol-1-yl)propan-2-ylidene)hydrazine carbothioamide (MBITS). Elemental analysis, IR-NMR spectral analysis, M:L and magnetic properties of MBITS and complexes were characterized. The MBITS and complexes also were displays good antimicrobial activity.

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Conflict of interest

The author declare that we have no conflict of interest.

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