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Synthesis and characterization of some new thiosemicarbazide derivatives and their transition metal complexes

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ABSTRACT

A synthesis of some new thiosemicarbazide like 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide by condensation of 3-bromo-4-hydroxy-5-methoxybenzaldehyde with 4-(4-bromophenyl)thiosemicarbazide is carried out. And their metal complexes were synthesized by condensation of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide and different transition metal chloride salt of Cu(II), Co(II), Ni(II). Their characterization are done by different analytical techniques, such as elemental analysis, ¹H NMR, FT-IR, GC-MS and ESI mass spectroscopy.

Key Words: Thiosemicarbazide, Metal Complexes, Spectral Characterization.

INTRODUCTION

Coordination compounds have been a challenge to inorganic chemist since they were identified in the 19th century. They defy the usual rules of valence at that time and hence called complexes. They play vital role in our lives. Transitions metal complexes with soft or hard donor groups have been used extensively in coordination and organometallic chemistry¹.

In this context, thiosemicarbazones are a class of compounds obtained by condensation of thiosemicarbazide with suitable aldehydes or ketones. In most complexes thiosemicarbazones behave as bidentate ligands because they can bond to metals through sulphur and the hydrazinic nitrogen atoms, although in a few cases they behave as unidentate ligands and bond through only sulphur atom²⁻⁴.

Thiosemicarbazone derivatives are of special importance because of their versatile biological and pharmacological activities. Thiosemicarbazone derivatives have found application in drug development for the treatment of central nervous system disorders, of bacterial infection, as well as analgesic and antiallergic agent. Thiosemicarbazones are potent intermediates for the

synthesis of pharmaceutical and bioactive materials and thus, they are used extensively in the field of medicinal chemistry. Moreover, thiosemicarbazones have found their way into almost every branch of chemistry; commercially they are used as dyes, photographic films, plastic and in textile industry.

Over the years, thiosemicarbazone derivatives have demonstrated wide range of biological activity *viz.* antimicrobial⁵⁻¹⁰, antitumor¹¹⁻¹², sodium channel blocker¹³, anticancer¹⁴⁻¹⁵, antitubercular¹⁶, antiviral¹⁷.

Keeping mind various biomedical application of these class of compounds, we report the synthesis and characterization of Cu(II), Co(II), and Ni(II) complexes of thiosemicarbazide derivative.

EXPERIMENTAL SECTION

All the chemicals were purchased from Merck and were used as received. Melting point of ligand and metal complexes were taken in open capillary and was uncorrected. ¹H NMR spectra was recorded on a Bruker avance II 400 NMR Spectrometer, FT-IR spectra was obtained in KBr pallet in the 4000-400 cm⁻¹ region on a Fourier transform infrared spectrophotometer-8400 Shimadzu, Mass spectra were recorded on a GCMS-QP2010 Shimadzu & micromass Q-T of Micro, elemental analysis was carried out on EURO EA Elemental Analyzer, EA-3000, RS-232.

Synthesis of 1-(3-bromo-4-hydroxy-5-methoxy benzylidene)-4-(4-bromo phenyl) thiosemicarbazide(L)

An equimolar amount of 4-(4-bromophenyl)thiosemicarbazide (0.01 M) and 5-bromo vanillin (0.01 M) were dissolved in 60 ml methanol. The resulting mixture was reflux for 24 hours in the presence of catalytic amount of gl. acetic acid. After completion of the reaction, reaction mixture was poured into crushed ice. The separated product was filtered wash with sodium bisulphite solution and dried at room temperature. Physical data of ligand is shown in table 1.

Synthesis of copper(II) and cobalt(II) complexes

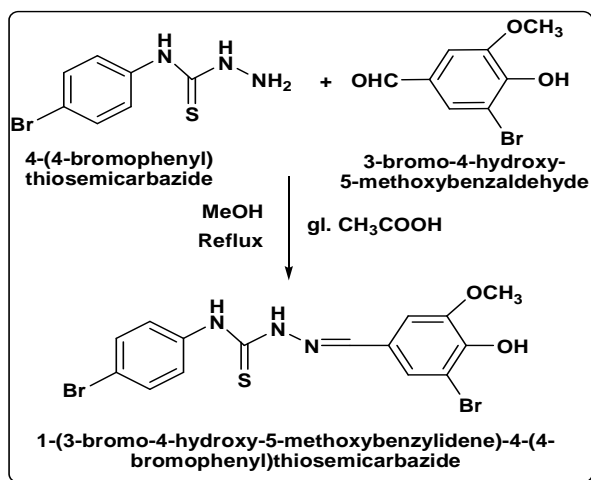
1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thio- semicarbazide (0.02M) was dissolved in 1,4 dioxan than solid M·Cl₂·6H₂O (0.01M)(where M = Cu & Co) was added to reaction mixture. The resulting reaction mixture was refluxed for 24 hours with continues stirring. After completion of the reaction the resulting solid was filtered and wash with cold dioxan and dried at room temperature. Physical data of complex is shown in table 1.

Synthesis of Nickel(II) complex

1-(3-bromo-4-hydroxy-5-methoxy benzylidene)- 4-(4-bromophenyl) thiosemi- carbazide (0.02M) was dissolved in 1,4 dioxan than solid NiCl₂·6H₂O (0.01M) was added to reaction mixture and maintain pH 6.8 to 7 by 40% NaOH. The resulting reaction mixture was refluxed for 5 hours with continues stirring. After completion of the reaction the resulting solid was filtered and wash with cold 1, 4 dioxan and dried at room temperature. Physical data of complex is shown in table 1.

REACTION SCHEME

Step I: Synthesis of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide



Step II: Synthesis of Cu(II), Co(II), and Ni(II) metal complexes of thiosemicarbazide derivative

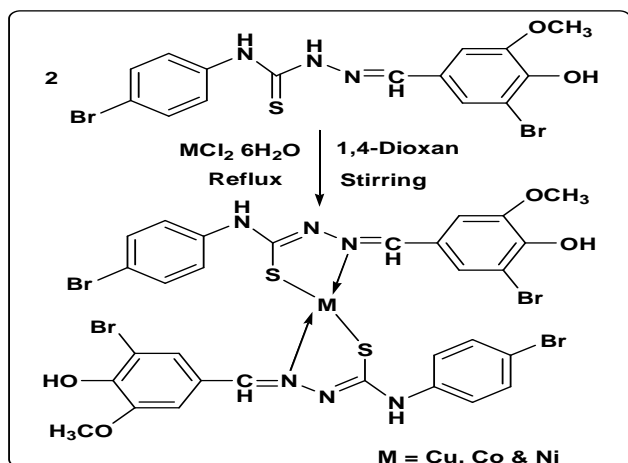


Table 1: The experimental result and physical data of ligand and its complexes

Code No.	Compounds M.F.	M. W. gm/mole	color	M.p. (°C)	Yield (%)	Elemental analysis, % calculated (found)				
						C	H	N	S	Metal
Ligand	C ₁₅ H ₁₃ Br ₂ N ₃ O ₂ S	459.16	Yellow	220	80.0	39.24 (39.13)	2.85 (2.79)	9.15 (9.06)	6.98 (6.90)	-
Ligand +Cu	C ₃₀ H ₂₆ Br ₄ CuN ₆ O ₄ S ₂	981.86	Brown	294	72.26	36.70 (36.61)	2.67 (2.54)	8.56 (8.50)	6.53 (6.41)	6.47 (6.40)
Ligand +Ni	C ₃₀ H ₂₆ Br ₄ NiN ₆ O ₄ S ₂	977	Yellow	320	74.38	36.88 (36.80)	2.68 (2.61)	8.60 (8.48)	6.56 (6.44)	6.01 (5.93)
Ligand +Co	C ₃₀ H ₂₆ Br ₄ CoN ₆ O ₄ S ₂	977.24	Green	274	73.59	36.87 (36.77)	2.68 (2.61)	8.60 (8.53)	6.56 (6.49)	6.03 (5.90)

RESULTS AND DISCUSSION

The 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl) thio- semicarbazide(L) and their metal complexes were subjected to elemental analyses. The results of elemental

analyses (C, H, N, S and M) with molecular formula and melting points are presented in Table 1. The results obtained are in good agreement with those calculated for the suggested formula. The structures of the ligand and metal complexes are also confirmed by IR, MASS and ^1H NMR spectra, which are discussed below.

Mass spectral data confirm the structure of the ligand and their Cu(II), Ni(II) and Co(II) complexes as indicated by the molecular ion peaks corresponding to their molecular weight (Fig. 1, 2 & 3).

The IR spectrum of the ligand showed (Fig. 4) a strong absorption band at 1678 cm^{-1} which was assigned to the azomethine group, $\nu(\text{C}=\text{N})$.¹⁸ The strong band observed at 1288 cm^{-1} & 823 cm^{-1} in the spectrum was due to the $\nu(\text{C}=\text{S})$ & $\delta(\text{C}=\text{S})$.¹⁹ The bands observed at 3495 cm^{-1} and 3315 cm^{-1} were assigned to $\nu(\text{O}-\text{H})$ and $\nu(\text{N}-\text{H})$ vibrations respectively.

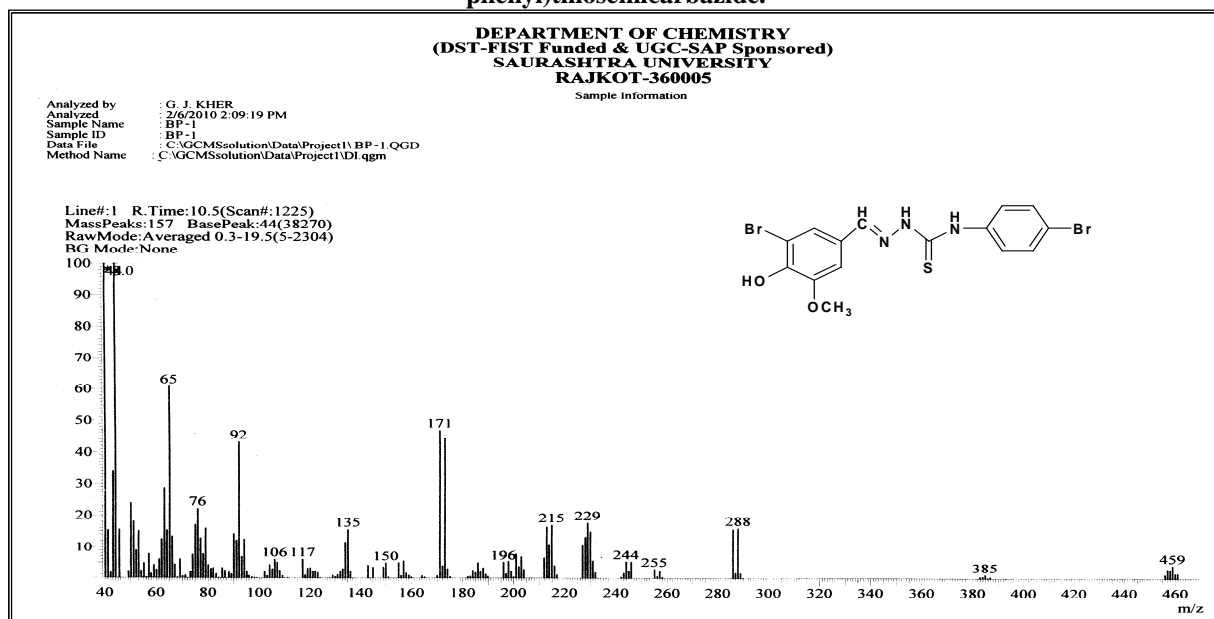
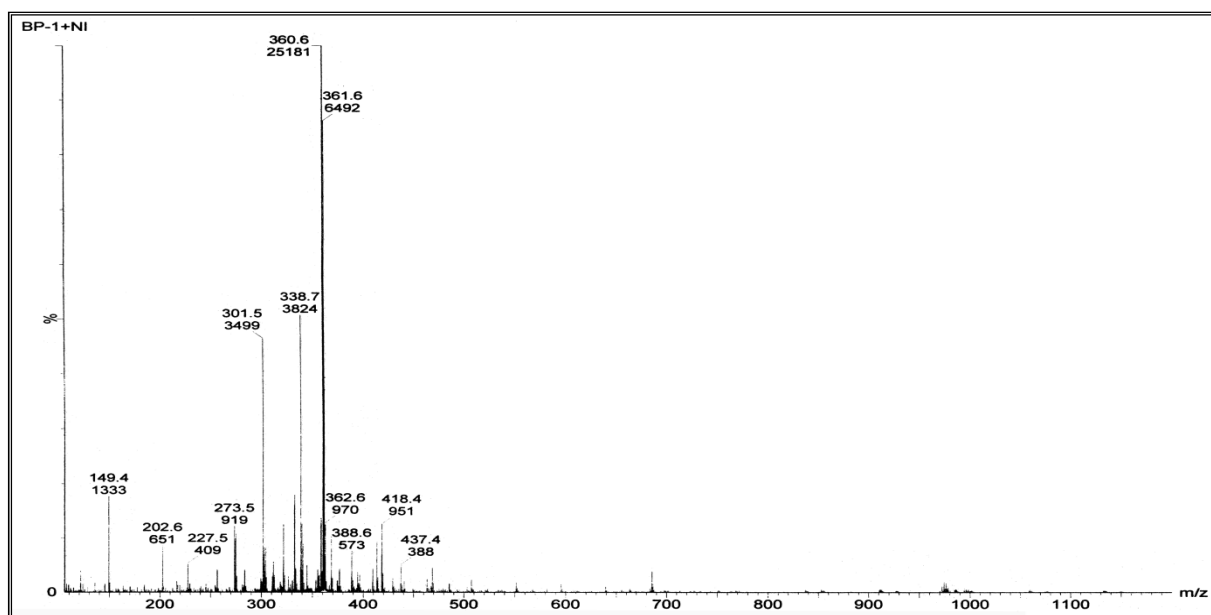
This further indicates that the ligand remained in the thione form. The diagnostic IR spectral bands of the complexes (Fig. 5) are presented in Table (2), together with their tentative assignments. In the spectra of all the complexes, the band due to the azomethine moiety ($\text{C}=\text{N}$) was shifted to a lower frequency, indicating its involvement in coordination with metal ion. The $\nu(\text{C}=\text{S})$ stretching frequency was lowered in the spectra of the complexes, indicating the involvement of the thioketo sulphur in the coordination. These findings are further supported by the appearance of new bands at $495\text{--}524\text{ cm}^{-1}$ and $408\text{--}416\text{ cm}^{-1}$, which are assignable to $\nu(\text{M}-\text{N})$ and $\nu(\text{M}-\text{S})$ vibrations, respectively.

Table 2: IR spectral data (cm^{-1}) of the ligand and their metal complex in KBr pellets

Vibration mode	Frequency in cm^{-1}			
	Ligand	Ligand+Cu	Ligand+Ni	Ligand+Co
$\nu(\text{O}-\text{H})$	3495	3501	3508	3498
$\nu(\text{N}-\text{H})$	3315	3338	3412	3403
$\nu(\text{C}=\text{N})$	1678	1608	1566	1599
$\nu(\text{N}-\text{N})$	1047	1022	1039	1045
$\nu(\text{C}=\text{S})$	1288	1259	1286	1288
$\delta(\text{C}=\text{S})$	823	819	817	833
Ar $\nu(\text{C}-\text{H})$ str.	3147	3134	3105	3107
Ar $\nu(\text{C}=\text{C})$ str	1494	1510	1494	1494
$\nu(\text{C}-\text{Br})$	572	576	561	582
$\nu(\text{M}-\text{N})$	-	524	495	513
$\nu(\text{M}-\text{S})$	-	416	408	412

Table 3: ^1H NMR spectral data of ligand

Signal No.	Signal Position (ppm)	Relative No of Protons	Multiplicity	Inference
1	11.69	1H	Singlet	-NH
2	9.74	1H	Singlet	-NH
3	9.31	1H	Singlet	-OH
4	8.01	1H	Singlet	-CH
5	7.58	2H	Doublet	Ar-H
6	7.54	1H	Doublet	Ar-H
7	7.47	2H	Doublet	Ar-H
8	7.31	1H	Doublet	Ar-H
9	3.91	3H	Singlet	$-\text{OCH}_3$

Figure 1:- Mass spectrum of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide.**Figure 2 & 3: ESI MASS spectrum of nickel complex of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide.**

The ^1H NMR spectra of the 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide(L) in DMSO solutions with assignments are collected in Table (3). The ^1H NMR spectra of the free ligand (Fig. 6) showed besides the aromatic proton signals appearing at 7.58ppm (2H, d), 7.54ppm (1H, d), 7.47ppm (2H, d), 7.31ppm (1H, d), 5-methoxy protons at 3.91ppm (3H, s), the azomethine proton at 8.01ppm (1H, s), secondary amine proton at 11.69ppm (1H, s) and 9.74ppm (1H, s). The phenolic OH proton has a signal at 9.31ppm (1H, s).

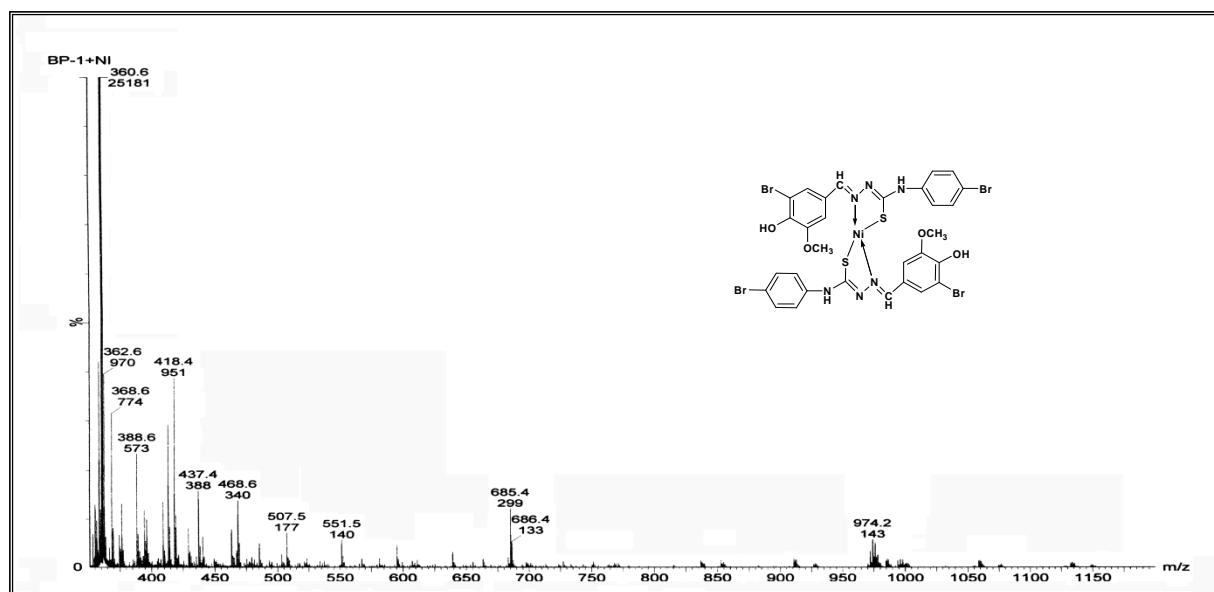


Figure 4: IR spectrum of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide.

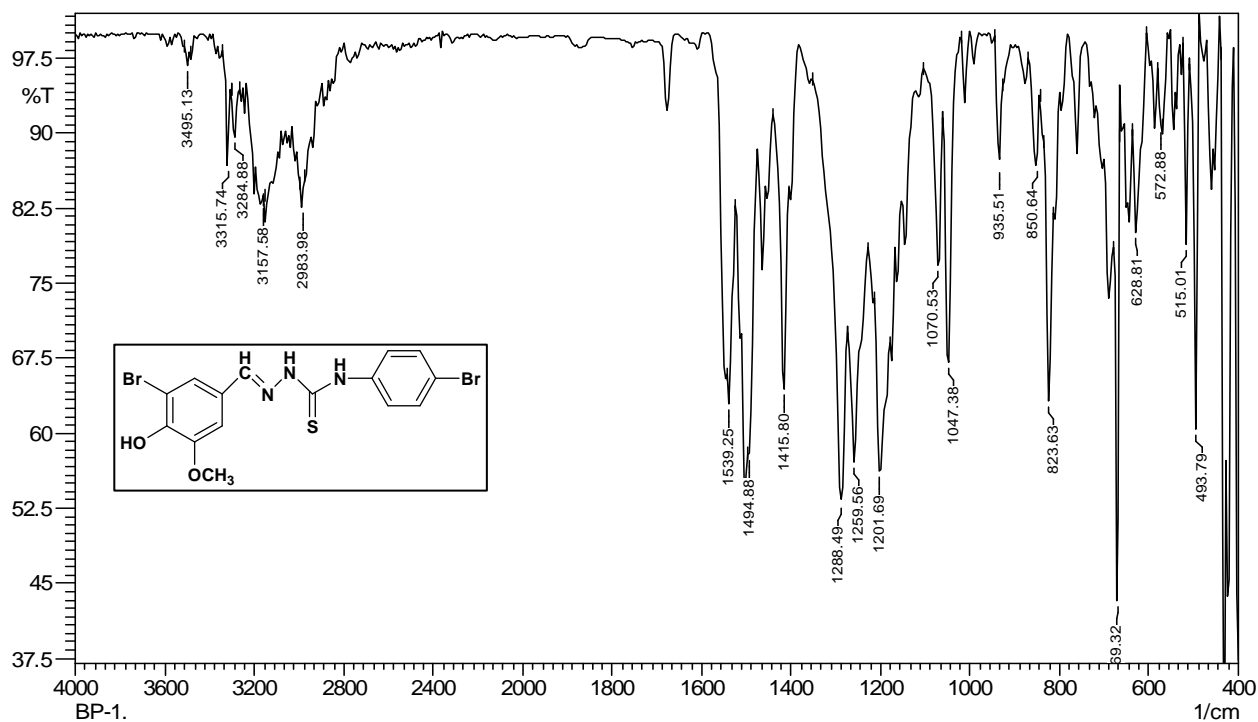


Figure 5: IR Spectrum of Ni-complex of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide.

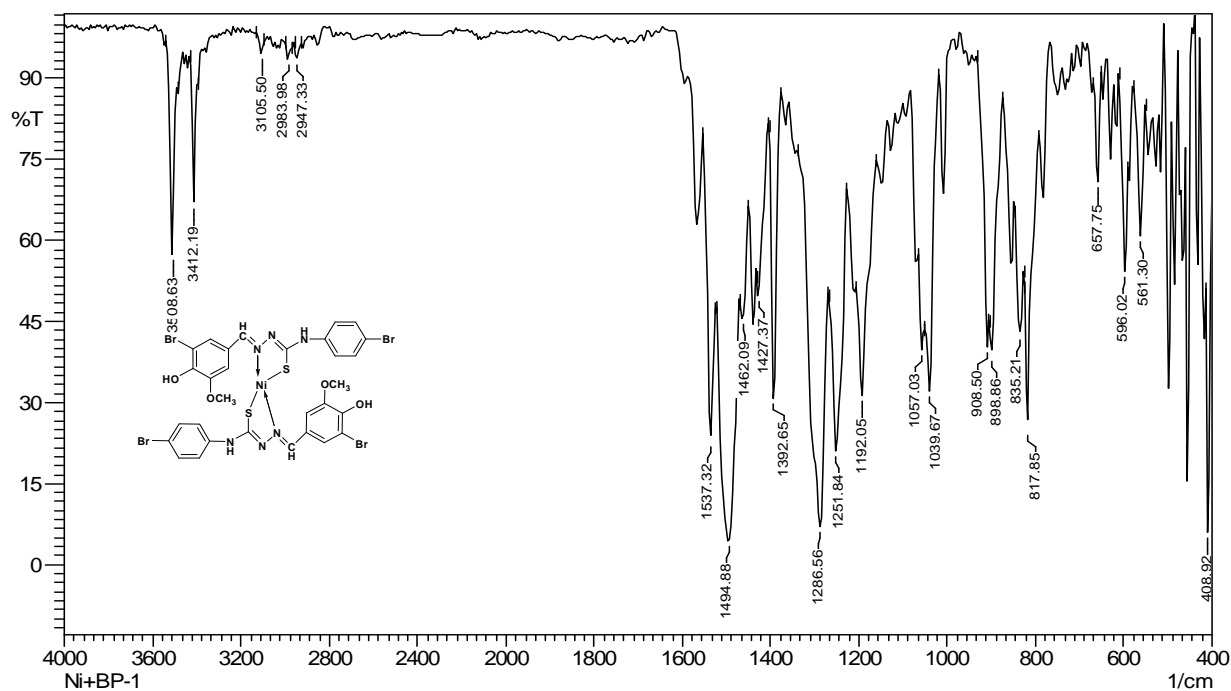
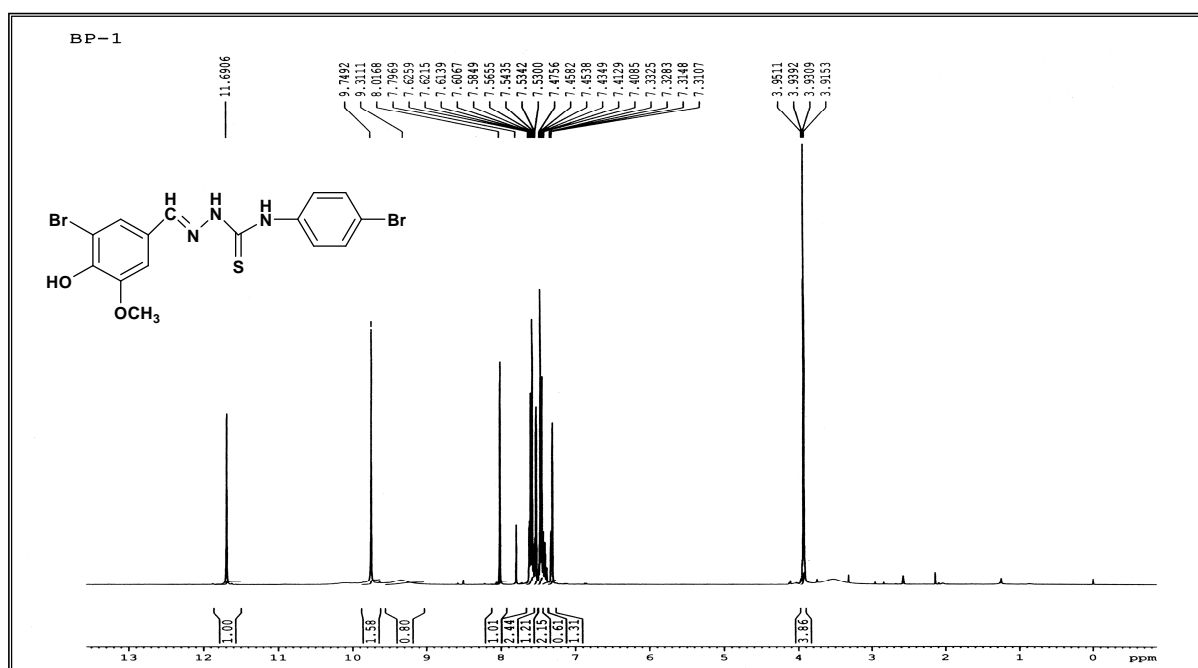


Figure 6: ^1H NMR spectrum of 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide(L).



CONCLUSION

In summary, we present the first report of the synthesis and characterization 1-(3-bromo-4-hydroxy-5-methoxybenzylidene)-4-(4-bromo- phenyl)thiosemicarbazide and its metal complex with cupric ion. The result of the spectrophotometric analysis was in agreement with the proposed formulation.

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