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Microwave Assisted Synthesis, Structural Characterization and Biological Activities of 4-Aminoantipyrine and Thiocyanate Mixed Ligand Complexes

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Abstract

The mixed ligand complexes of Cu(II), Zn(II) and Hg(II) were prepared using 4-aminoantipyrine (4-AAP) and thiocynate ions with microwave irradiation. The prepared complexes were characterized by elemental analysis, conductance measurement, UV-Visible, FT-IR and NMR spectral analysis. The conductivity measurements reveal that the complexes are nonelectrolyte. The elemental analysis showed the formation of 1:2 (metal: ligand) complexes with coordination number 4.The formulae of the complexes are $[Cu(AAP)_2(SCN)_2]$, $[Zn(AAP)_2(SCN)_2]$ and $[Hg(AAP)_2(SCN)_2]$. The antimicrobial and antifungal activities of the complexes were tested with various microorganisms by disc diffusion method. The antimicrobial results indicate that the metal complexes are moderately active compared to the ligand, 4-aminoantipyrine.

Keywords*:* 4-aminoantipyrine, thiocyanate, microwave, antimicrobial, antifunga.

Introduction

Pyrazoles belongs to the five membered heterocyclic system[1]. Some of the synthetic compounds containing pyrazole moiety have been focused in the field of Medicinal Chemistry[2]. One of the pyrazole derivatives, 4-aminoantipyrine has played an important role in Inorganic Chemistry; It forms stable complexes with many transition metal ions. 4-aminoantipyrine and its complexes have applications in analytical, biological and clinical areas[3-4]. Antipyrine derivatives are used as anti-inflammatory[5-6] and chemotherapeutic agents[7]. 4-aminoantipyrine is an intermediate of antipyretic and analgesic drugs[8] and it is also active against a wide range of microorganisms viz *E.coli, Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicance (fungus).*

Material and Methods

4-aminoantipyrine was purchased from Alfa Aesar Company. The metal nitrates and the solvents viz., DMSO, DMF, methanol, ethanol used were of analar grade and used as such.

Instrumental analysis: The elemental analysis of the complexes was carried out by using (Thermo Finnigan make, Flash EA1112 Series Instrument) CHNS (O) analyzer. The molar conductance measurements were conducted using 10^{-3}M solutions of the metal complexes in acetonitrile with Systronic Conductivity Bridge 304 at 30°C. The IR spectra of the complexes were recorded on a Shimadzu FT IR-8400s spectrometer in 4000-400cm^{-1} range with KBr pellet technique. The UV-Visible spectra of zinc and mercury complexes were recorded on Varian, Cary 5000 model UV-Vis Spectrophotometer. ^{1}H- NMR and ^{13}C-NMR spectra of the 4-aminoantipyrine and zinc complex were recorded in DMSO-d6 on a FT NMR 500 MHz Spectrometer using TMS as an internal standard reference. The antimicrobial and antifungal studies of 4-aminoantipyrine and the complexes were done by disc diffusion method.

Synthesis of the complexes: The complexes were synthesized by mixing 4-aminoantipyrine 1.72g, 1.37g, 1.49g (8.30, 6.64, 7.27 mmol) with the respective metal(II) nitrates in methanol medium (4.20 mmol $Cu(NO_3)_2.3H_2O$ (1g); 3.33 mmol $Zn(NO_3)_2.6H_2O$ (1g) and 3.64mmol $HgCl_2$ (1g)). The mixture was heated in a microwave oven for about 10secs. Then potassium thiocyanate 0.54g, 0.43g and 0.47g (8.40, 6.62, 7.23 mmol) respectively in ethanol medium was added and the whole mixture was heated for about 10secs in a microwave oven. The precipitated complexes were filtered, washed with ethanol and dried. The elemental analysis data shows the formation of 1:2 (metal: ligand) complexes. The molar conductance values obtained from 55-58 cm^2 ohm^{-1} mol^{-1} indicates the nature of complexes is nonelectrolyte[9] (figure-1, table- 1).

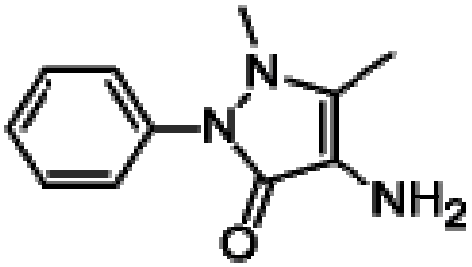

Figure-1
Structure of 4-aminoantipyrine

Table- 1
Analytical data of the complexes: found / (calculated) %

Complexes	Colour	Conductance (ohm^{-1} cm^2 mol^{-1})	Yield	C	H	N	Metal
[Cu $L_2(SCN)_2$]	Green	57.80	65.33	49.10 (49.14)	4.40 (4.43)	19.80 (19.11)	10.82 (10.84)
[Zn $L_2(SCN)_2$]	colourless	58.60	60.07	49.16 (49.15)	4.40 (4.43)	19.14 (19.11)	11.14 (11.16)
[Hg $L_2(SCN)_2$]	Pale yellow	55.10	62.19	39.80 (39.82)	3.56 (3.59)	15.43 (15.48)	27.70 (27.74)

L= 4-Aminoantipyrine

Table- 2
IR spectral data of the ligand and its complexes (cm^{-1})

Complexes	NH_2	C-H Aromatic	C=O	C=C	M-O	M-N	SCN
L	3431	2914	1650	1587	-	-	-
[Cu $L_2(SCN)_2$]	3439	2910	1637	1591	499	450	2083
[Zn $L_2(SCN)_2$]	3456	2929	1637	1575	536	478	2092
[Hg $L_2(SCN)_2$]	3416	2924	1631	1585	501	441	2108

L= 4-Aminoantipyrine

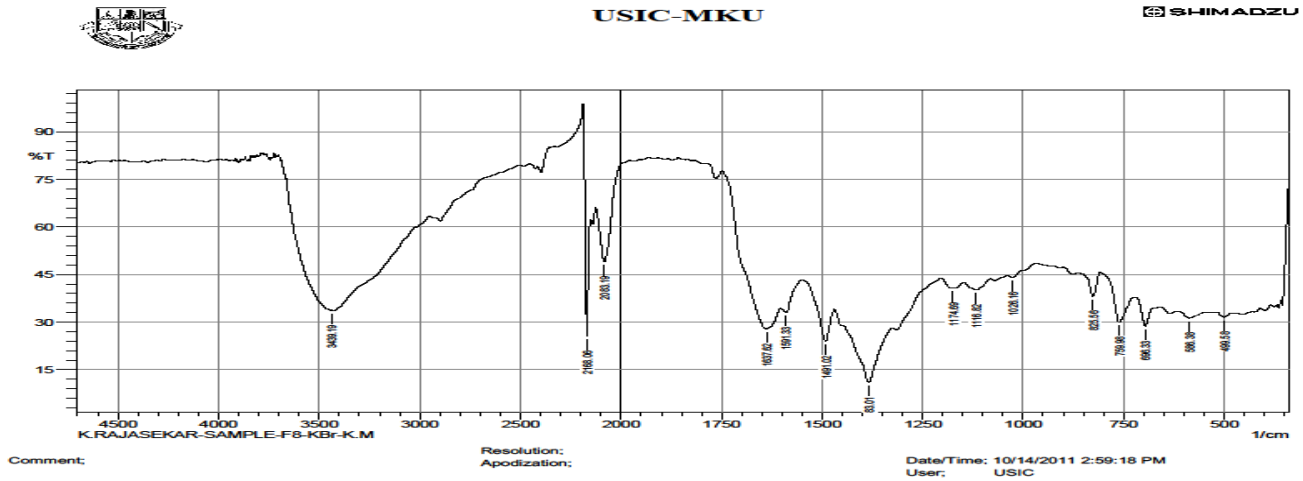

Figure-2
IR Spectrum of copper complex

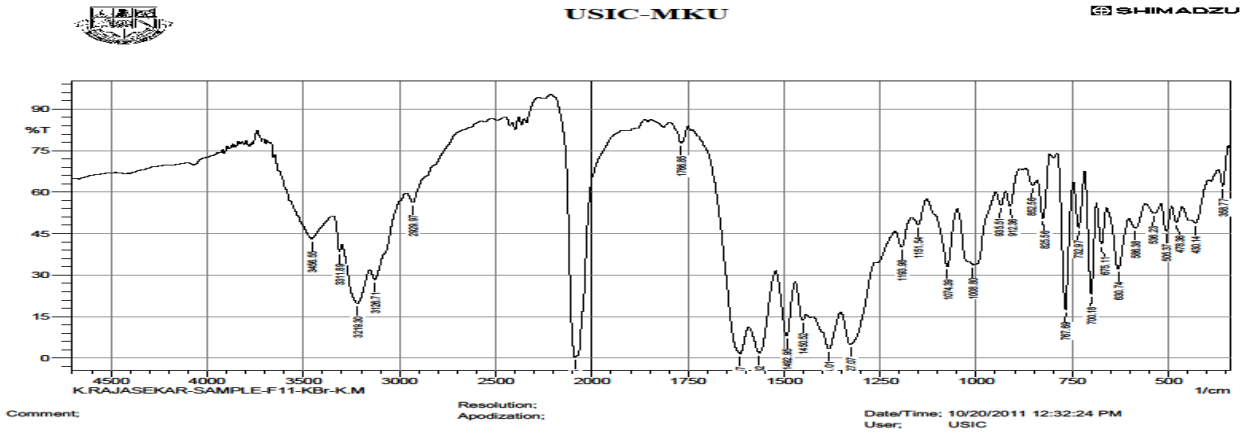

Figure-3
IR spectrum of zinc complex

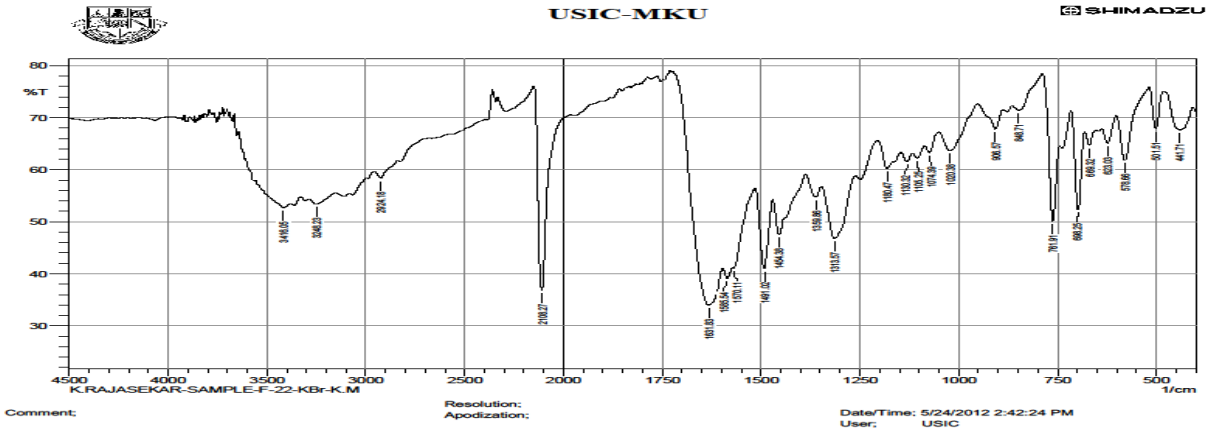

Figure-4
IR Spectrum of mercury complex

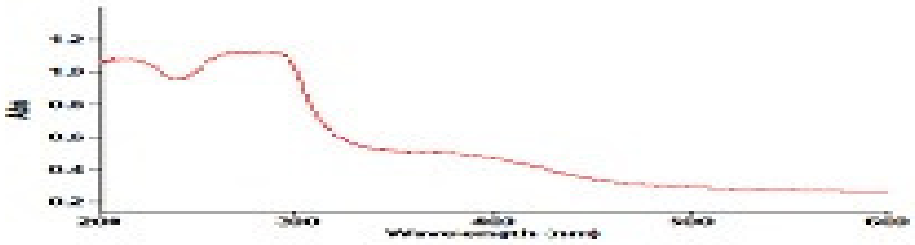

Figure-5
UV-Visible spectrum of zinc complex

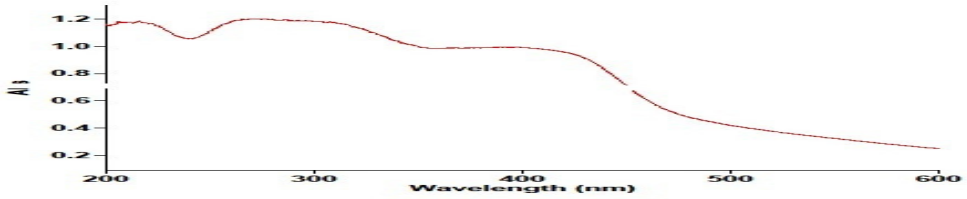

Figure-6
UV-Visible spectrum of mercury complex

Results and Discussion

Infra-red spectra: The IR spectral data of 4-aminoantipyrine and the metal complexes are given in table-2. In the IR spectrum of 4-AAP, the band at 3425 to 3431 cm^{-1} corresponding to the NH_2 group is shifted to 3416 to 3456 cm^{-1} in metal complexes, confirming its entry into the coordination sphere. The value at 1650cm^{-1} in 4-aminoantipyrine due to C=O group gets reduced to 1637 cm^{-1} in the complexes. In all the complexes, frequencies are seen in between 2083cm^{-1} and 2108cm^{-1}, corresponding to the presences of SCN group[10-13]. (Not found in free ligand). The weak band at 490-550cm^{-1} and 440- 480 cm^{-1}which are due to the formation of M-N and M-O coordination bond in complexes[14]. These values indicate the coordination of metal ion through N-atom of ligand 4-aminoantipyrine. Table-2 (figure-2-4)

UV-Visible electronic absorption spectra: The electronic absorption spectra of the zinc and mercury complexes were recorded by diffused reflectance spectra method. The Zn(II) and Hg(II) metal ion in the complexes have (d^{10}) electronic configuration, which is confirmed absence of d-d transition. The electronic spectra of these complexes show metal to ligand charge transfer transition (M→L) at 274nm and 269nm respectively[15-17]and the values are shown in figure- 5 and 6

^{1}H-NMR spectra: The ^{1}H-NMR spectra of 4-AAP and [Zn (4-AAP)$_2$ (SCN)$_2$] show a signal at δ 7.25 to 7.50 ppm which are assigned to the aromatic protons. The peak at δ 3.90 ppm shows the NH_2 protons of 4-AAP.The N-CH_3 and C-CH_3 signals appeared in the region of δ 2.80 and 2.10 ppm respectively. Aromatic Protons appeared in the ligand (4-AAP) get shifted to downfield in the complexes. The different chemical shift values have been shown in table-3.

Table-3
^{1}H-NMR spectral data of the ligand and zinc complex (ppm)

Complexes	NH_2	Aromatic H	N-CH_3	C-CH_3
L	3.90	7.30-7.50	2.80	2.10
[Zn L$_2$(SCN)$_2$]	4.00	7.30-7.50	2.80	2.10

L= 4-aminoantipyrine

Table- 4
^{13}C-NMR Spectral data of the ligand and zinc complex (ppm)

Complexes	Aromatic carbons (C1-C4)	C=O	C-NH_2	C-CH_3	CH_3	N-CH_3	SCN
L	120-130	161	136	121	10	40	-
[Zn L$_2$(SCN)$_2$]	121-129	162	138	135	10	40	120

L= 4-aminoantipyrine

Table- 5
Antimicrobial and antifungal activities results (mm)

Complexes	*Escherichia coli*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Candida albicance(fungus)*
L	10	16	03	14
[Cu L$_2$(SCN)$_2$]	11	11	10	10
[Zn L$_2$(SCN)$_2$]	04	09	10	13

L= 4-aminoantipyrine

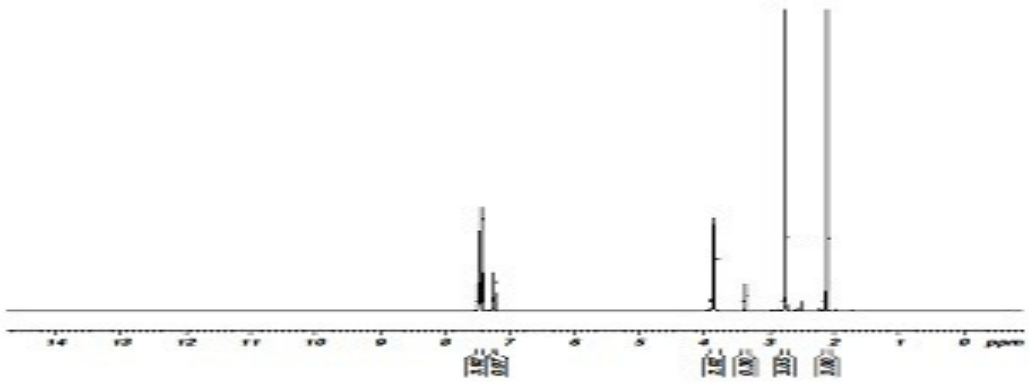

Figure- 7
^{1}NMR Spectrum of 4-Aminoantipyrine

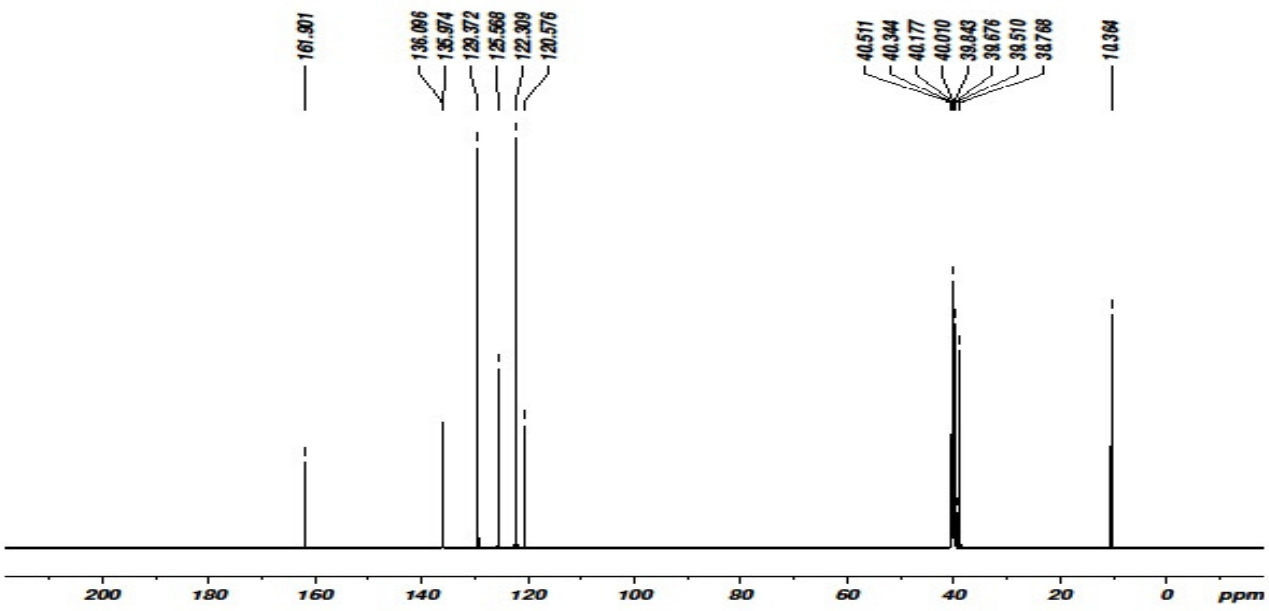

Figure- 8
^{13}C NMR Spectrum of 4-Aminoantipyrine

^{13}C- NMR spectrum: ^{13}C NMR spectral data are presented in Table-4. In the spectrum of 4-AAP the C=O carbon frequency resonated at 161ppm which is present in the same position in complex. The aromatic carbon atoms appeared at120-129 in 4-AAP and zinc complex. There are 11 peaks are observed which is confirmed by the structure of 4-AAP and its entry into the coordination sphere. The signal at δ120 ppm present in the complex corresponds to SCN group. (Figure-7and8)

Antimicrobial and antifungal studies: The antimicrobial and antifungal activities of 4-aminoantipyrine and the complexes were carried out by disc diffusion method. The test solutions were prepared in DMSO, amikacin and Ketokonazole were used as standards. The zone of inhibition was measured in mm and the values of the investigated complexes are given in table-5. The results indicate that the Cu(II) and Zn(II) complexes show moderate activity compared to the free ligand. The ligand is potentially active against *pseudomonas aeruginosa* and *Candida albicance* (fungus). The growth inhibition values are well within the values already reported[18]. (The values of <10mm inactive, 10-16mm moderately active and >16 highly active).

Conclusion

In this study, the complexes of Cu(II), Zn(II) and Hg(II) with 4-aminoantipyrine and thiocyanate ligands were synthesized and characterized. On the basis of elemental analysis, electrical conductivity, UV-Visible, IR and NMR spectral data, the formulae of the complexes are $[Cu(AAP)_2(SCN)_2]$, $[Zn(AAP)_2(SCN)_2]$ and $[Hg(AAP)_2(SCN)_2]$. From the results of antimicrobial and antifungal activities indicate the Cu(II) and Zn(II0 complexes show moderate activities compared to the free ligand.

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