Complexes of Copper Metal with Substituted Acetophenone Thiosemicarbazone and their Spectral, Biological Activities.

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Abstract;- Complexes of Cu have been prepared by reacting metal chloride\sulphate with p-hydroxyacetophenone thiosemicarbazone, p-fluoroacetophenone thiosemicarbazone, p-bromoacetophenone thiosemicarbazone as ligands and their complexes have been screened for their IR, NMR, and antifungal and antibacterial studies.

Keywords- Synthesis, Spectral studies, Copper metal complexes, acetophenone thiosemicarbazone, Antibacterial activity

Introduction-

The Schiff's base and their metal chelates is effective anticancer, antitumor, anti tuberculosis, antipyretic agent as well as anti fertility. Schiff's base possess industrial application as catalysts, dyes, fiber, perfumes an aesthetic, plant growth inhibitors cosmetics corrosion inhibitors, oxygen absorbents, polymers, lubricating agents, for removing metal impurities of oil and drying accelerators.[1 - 4] .The metal complexes with Schiff's base derived from chalcone and thiosemicarbazone have been extensively studied and have exhibited medicinal properties [5].Copper (II) complexes have found possible medicinal uses in the treatment of many diseases including cancer.[6] Semicarbazone of various transition metals have been investigated owing to their coordination capability and pharmaceutical activity [7- 9]. Schiff's bases make them more effective in attaining high coordination structure.[10]

Schiff bases by containing the azomethine group (C=N) as the central structural form have been the subject of prevalent research in the various fields of industry, pharmaceuticals and the synthesis of biologically active organic compounds [11-12]; besides corrosion inhibitors [13]. Recently Schiff bases become an important class of ligands in coordination chemistry[14]. Various method and routes have been developed for the synthesis of Schiff bases such as reflux in ethanolic solution, stirring grinding in mortar, besides microwave irradiation methods.[15] The last one has received increasing interest from researchers.[16] Azo Schiff compounds are new class of chemical compounds they are receiving increasing concern in scientific research.[17] in the present days these derivatives display remarkable applications in each and every field. [18-19]

Since Domagk's original report[20] on the anti-tubercular activity of thiosemicarbazones, the number of papers on the pharmacology of these compounds has expanded dramatically. They have also been found to be active against influenza[21], small pox [22], and certain kinds of tumor[23] and have been suggested as possible pesticides and fungicides[24]. Their activity has frequently been thought to be their ability to chelate with tracer metal.

MATERIALS AND METHODS

The transition metal complexes of substituted acetophenone thiosemicarbazone were derived from the reaction an aqoues solution of metal salt. Acetophenone thiosemicarbazone ligands were prepared by the reaction of substituted acetophenone with thiosemicarbazone in the presence of hot ethanol.

All the transition-ligands 1:2 complexes have been isolated in the solid state, are stable in air, and characterized on the basis of their elemental and spectral data. Thiosemicarbazone ligands behave as bidentate ligands by coordinating through the Sulfur of the isocyanide group and nitrogen of the cyanide residue. The acetophenone thiosemicarbazone ligands and their transition complexes have been screened for their IR, NMR, and antifungal and antibacterial studies.

RESULTS AND DISCUSSION-

The substituted acetophenones were converted into their thiosemicarbazone (2a-d) by reacting them with thiosemicarbazones were then treated with aqueous/ethanolic solution of metal salt to yield their metal complexes (3a-d).

Substituted acetophenones-

In the IR spectra of substituted acetophenone a sharp absorption band from 1780-1650 cm_1 is observed due to acetophenone >C=O and at 1620 cm-1 due to >C=C< stretching vibration. In the 1H NMR spectra of substituted acetophenones.

Substituted acetophenonethiosemicarbazones-

Formation of substituted acetophenones thiosemicarbazone was confirmed by the disappearance of absorption band from 1720-1650 cm-1 due to carbonyl group (>C=O) and appearance of new absorption bands from 3400-3350,3320-2800,and 1200-1045 cm_1 assigned to $–NH_2$, -NH and >C=S stretching vibrations, respectively in their IR spectra. Similarly, in 1H NMR spectra an additional broad singal at δ 2.85 ppm appears due to $–NH_2$ and a sharp singlet at δ 10.82 ppm due to –NH- protons are observed which further support the formation of compounds.(2a-d).

Metal complexes of substituted acetophenone thiosemicarbazone-

In the IR spectra of the ligands and complexes only selected absorption peaks are discussed which are important for ascertaining the doner sites of ligands. In the in spectra of metal complexes of substituted acetophenone-thiosemicarbazones the presence of absorption band at 3380cm-1 due to $–NH_2$ (symmetric) and at 3380cm-1due to-NH_2 (assymmetric) modes remain almost unaltered. This clearly indicates the noninvolvement of this group in complexation reaction [25-26] but slight displacement of these frequencies is due to increased positive charge on nitrogen atom arising from the donation of electron pair from sulfur of thioamide moiety which is involved in chelation.[27-28] Sharp absorption band from 3280-2850cm-1 which was due to NH- in ligands disappear in complexes indicating possible deprotonation on the β-nitrogen after complextion with metal ion [29-33].

A new absorption band in the complexes at 445-432 due to (M-N) confirm the metal nitrogen bond in the complexes.[34]

Experimental-

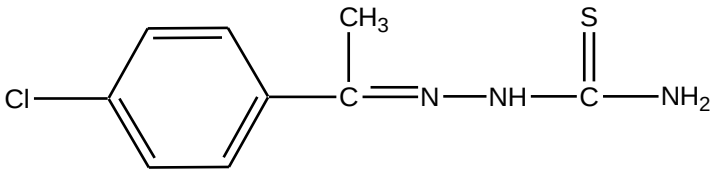
All compounds have been characterized on the basis of spectral (IR, NMR and mass) studies and elemental analysis. IRspectra (400-4000cm-1) were recorded using a KBr. Central drug research institute (CDRI), Lucknow and department of chemistry, university of rajas than, jaipur. 1H NMR spectra were recorded on Brucker spectrometer (300 MHz) at CDRI, Lucknow using $CDCl_3$/DMSO as solvent. TMS was taken as internal standard. Mass spectra were recorded on kratos 30 and 40 mass spectrometer at CDRI, Lucknow. C, H, N and s analysis of these compounds have been done using Coleman C and H analyzer. Melting points were determined in open glass capillaries and are uncorrected. The purity of compounds was checked by TLC using silica gel-G as adsorbent and visualization was accomplished by UV light or iodine adsorption.

All compounds are crystalline dark colored solids, have fairly high melting points and are sparingly soluble in common organic solvents and are insoluble in water.

Synthesis of substituted acetophenone thiosemicarbazones (2a-d)

P-chloroacetophenonethiosemicarbazone-

P-chloroacetophenonethiosemicarbazone was prepared after the method of compainge and Archer.63 p-chlorlacetophenone (2.52g, 20 mmol) was dissolved in ethanol (50ml) in a round bottomed flask and heated on a water bath for 5-10 minutes. This hot solution was treated with a hot ethanolic solution (50 ml) of thiosemicarbazone (1.80g, 20mmol) and refluxed for 4-5 hrs on water bath using reflux water condencer. The change in color of solution indicates the formation of p-chloroacetophenone thiosemicarbazone (2a-d). on cooling the reaction mixture the cream coloured product crystallized out which was filtered off under water suction and further recrystallized from absolute ethanol and finally dried over anhydrous $cacl_2$ in a vacuum desiccator



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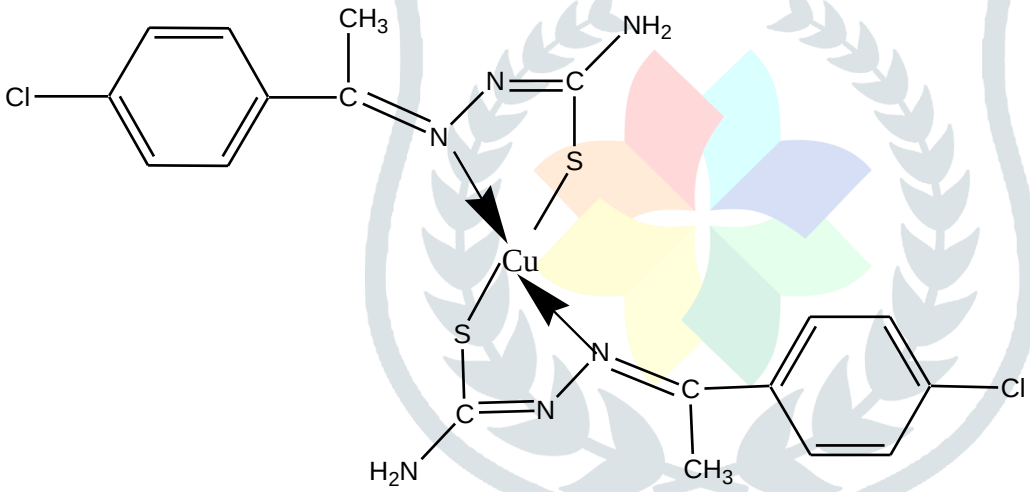
Synthesis of 4-subsitituted acetophenonethiosemicarbazones metal complexes (3a-d)
Bis (p-chloroacetophenonethiosemicarbazone) copper (II)-

P-chloroacetophenonethiosemicarbazone (o.454g, 2mmol) was dissolved in ethanol (20ml) and heated on a water bath. This solution was slowly treated with an aqueous solution of metal salt Cu $(OCOCH_3)_2.H_2O$ (0.200g, 1mmol) in 2:1 molar ratio with strring. Reaction mixture was refluxed on water bath for 1-2 hrs and left overnight to yield the crystalline dark green coloured crystals, which was filtered off under suction washed with water till filtrate become colorless. The product was finally washed with dilute ethanol and dried over fused $cacl_2$ in a vacuum desiccators.



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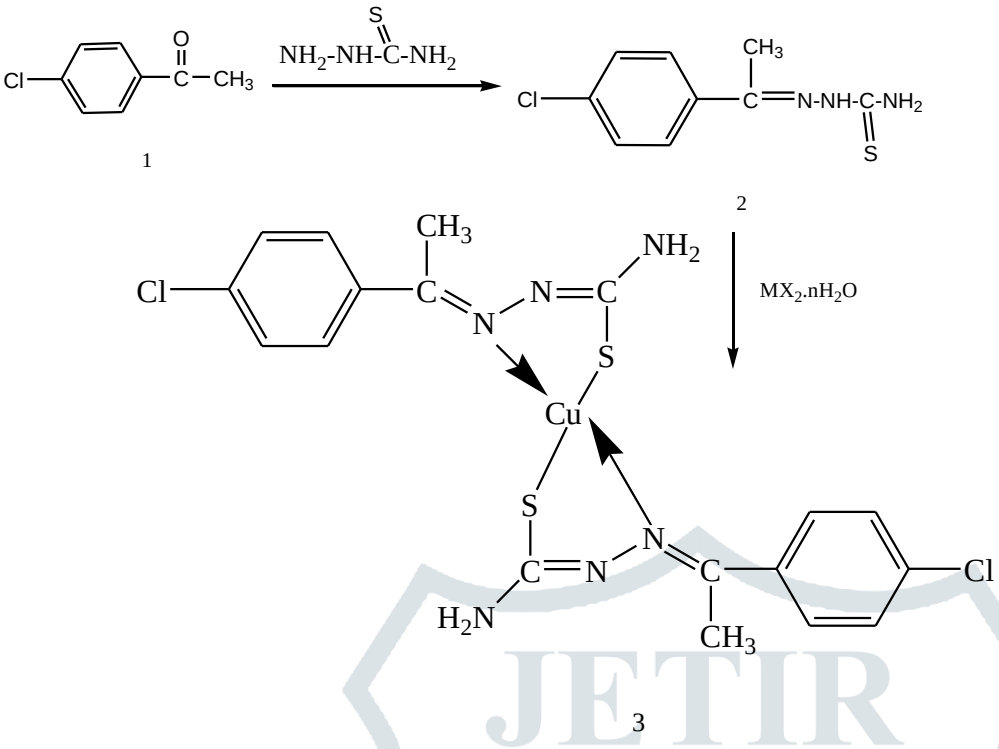

Table -1 analytical and physical data of substituted acetophenonethiosemicarbazones
[Y-Ar-C (CH_3) =N-NH-CS-NH_2]

Comp.	Y	Mol. formula	colour	Mol. Wt.	m.p.	yield	Elemental analysis % (calcd.) C H N S
2a	H	$C_9H_{11}N_3S$	Green	193	170	90	55.91,5.69,21.76,16.58
2b	4-F	$C_9H_{10}FN_3S$	Cream	211	150	85	51.13,4.73,20.12,16.15
2c	4-Cl	$C_9H_{10}ClN_3S$	Brown	227	125	82	72.18,4.45,18.46,74.06
2d	4-Br	$C_9H_{10}BrN_3S$	Cream	272	185	86	38.70,4.12,15.33,12.32

Table -2 analytical and physical data of Cu (II) complexes of substituted acetophenonethiosemicarbazone

[Y-Ar-C (CH_3) =N-NH-CS-NH_2]$_2$ CU (II)

Comp.	Y	Mol. formula	co lour	Mol. Wt.	m.p.	yield	Elemental anylysis % (calcd.) C H N S
3a	H	$C_{18}H_{20}N_6S_2Cu$	Green	440	146	90	47.39,4.41,18.21,14.32
3b	4-F	$C_{18}H_{18}F_2N_6S_2Cu$	Cream	482	153	75	44.65,3.69,17.34,13.17
3c	4-Cl	$C_{18}H_{18}Cl_2N_6S_2Cu$	Brown	227	141	81	40.95,3.45,15.99,12.32

3d	4-Br	$C_{18}H_{18}Br_2N_6S_2Cu$	Cream	272	142	85	31.95,2.95,13.85,10.51

Table -4 Characteristic IR spectral data of substituted acetophenone thiosemicarbazone and their metal complexes

Comp. No.	IR (KBr: ;max cm-1)									
1	2	3	4	5	6	7	8	9	10	11
	$-NH_2$	>NH	Ar-H	>C=N	>C=C<	C-X	>C=S	C-S	N-N	M-N
2a	3320	3290	3010	6120	1450	-	1200	-	810	-
2b	3360	3280	3025	1605	1490	720	1150	-	840	-
2c	3410	3300	3045	1625	1456	560	1190	-	805	-
2d	3390	3265	3026	1620	1480	690	1160	-	845	-
3a	3320	-	3048	1604	1465	-	-	1130	865	440
3b	3310	-	3025	1620	1456	1070	-	1050	842	456
3c	3410	-	3014	1618	1472	650	-	1065	854	450
3d	3410	-	3026	1620	1495	745	-	1060	865	426

Table -5 Characteristic ^{1}H NMR spectral data of substituted acetophenone thiosemicarbazone and their metal complexes

Compd. No.	Mol. formula	^{1}H NMR spectral data (δ,ppm)			
		Ar-H(m)	NH(br)	NH2(s)	-CH=N(s)
2b	$C_9H_{10}FN_3S$	7.8	7.0	2.1	8.5
2c	$C_9H_{10}ClN_3S$	7.3	7.0	2.1	7.2
2d	$C_9H_{10}BrN_3S$	7.65	10.35	2.3	8.5
3b	$C_{18}H_{18}F_2N_6S_2Cu$	6.60	-	2.2	7.2
3c	$C_{18}H_{18}Cl_2N_6S_2Cu$	7.80	-	2.1	7.6
3d	$C_{18}H_{18}Br_2N_6S_2Cu$	7.75	-	2.6	8.9

Table -6 Mass fragments of bis-4-chloroacetophenone thiosemicarbazone copper (II) COMPLEX

Fragment No.	m/z	Relative abundance	Fragment No.	m/z	Relative abundance
1	520	20	20	292	16
2	531	20	21	291	18
3	563	18	22	280	09
4	514	38	23	285	12
5	518	45	24	270	13
6	521	05	25	265	34
7	523	08	26	260	40
8	526	07	27	255	22

9	524	06	28	240	18
10	465	04	29	235	25
11	435	21	30	225	07
12	425	06	31	210	09
13	425	06	32	195	24
14	395	04	33	190	26
15	380	22	34	185	44
16	365	04	35	165	31
17	345	06	36	154	12
18	320	12	37	120	09
19	310	22	38	110	35

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