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Gravimetric determination of the Cu (II) with Schiff bases derived from sulfa drugs and 2-hydroxy, 1-napthaldehyde / benzoyl acetone.

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ABSTRACT

Compounds containing the sulphonamide group have long been used as drugs for diseases like cancer, tuberculosis, diabetes, malaria and leprosy etc. It has now been observed that some of these drugs show increased biological activity when administered in the form of metal complexes. A number of references are now available to show that the condensation products of sulpha drugs with aldehydes, ketones or their derivatives are biologically very active, besides having good complexing ability. The present works deals with the synthesis and preliminary characteristics of various ligands. Here all the ligands are Schiff bases. Schiff bases derived by the condensation 2-hydroxy, 1-napthaldehyde or benzoylacetone with some of the well-known sulpha drugs. After synthesis of such compound the physical properties like MP/BP, elemental analysis and spectral data of IR and NMR will be evaluated.

Keywords: ligands, sulphonamide, complexing, sulpha drugs

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INTRODUCTION

Compounds containing the sulphonamide group have long been used as drugs for diseases like cancer, tuberculosis, diabetes, malaria and leprosy. It has now been observed that some of these drugs show increased biological activity when administered in the form of metal complexes [1-8].

A number of references are now available to show that the condensation products of sulpha drugs with aldehydes, ketones or their derivatives are biologically very active, besides having good complexing ability. Their activity has also been shown to increase on complexation with metal ions. [9-10]

Large numbers of organic compounds like phenones, hydrazones, pheno-neoximes, chalconeoximes etc. have been used reagent for gravimetric and spectrophtometric determination [11-20].Compounds containing the sulphon amide group have long been used as drugs for diseases like cancer, tuberculosis, diabetes, malaria and leprosy. It has now been observed that some of them drugs show increased biological activity when administrated in the form of metal complexes [1-7]. Literature survey reveals that no work has been done Schiff base derived from sulfa drugs as a gravimetric reagent. The work should be continuing in this derection**.**

It was, therefore, considered of interested to synthesize metal (II) derivatives of Schiff bases derived by the condensation 2-hydroxy, 1-napthaldehyde or benzoylacetone with some of the well-known sulpha drugs.

The structures of Schiff base are shown below.

Schiff bases are widely employed in synthetic organic and inorganic chemistry. They were reported to show diverse biological activity [20-24] and have many applications as ligands in coordination chemistry of transition metals [25-28].

Our present work is studies on Schiff bases derived from sulfa drugs and 2-hydroxy, 1-napthaldehyde/ benzoyl acetone as gravimetric reagent for Cu(II), Ni(II), Co(II),Fe (II), and Mn (II).

EXPERIMENTAL

Synthesis of ligands:

All the chemicals used were of analytical grade (Sigma Aldrich Company) which was used without further purification. The melting points were determined on standard melting point apparatus.

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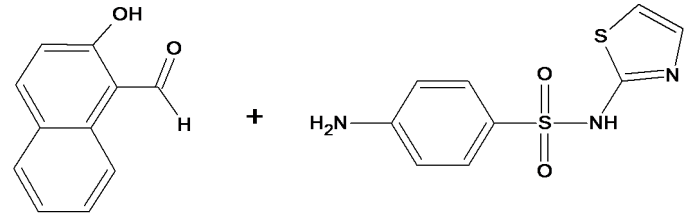
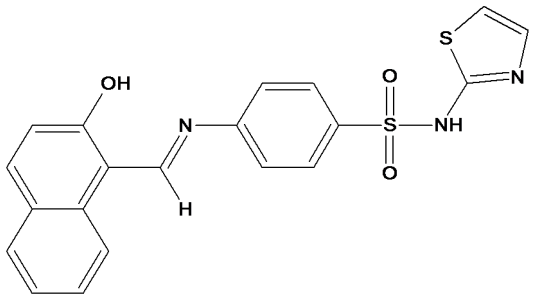
The ligand was prepared by refluxing equimolar amount of 2-hydroxy, 1-napthaldehyde/ benzoyl acetone and sulphdruds. Ethanol/methanol. The reaction mixture was refluxed for 5 hours on water bath. On cooling, crystals of Schiff base separated out with filtration, wash with alcohol, dried and recrystallised from appropriate solvent. (Table 2.1.) The melting point was determined on standard melting point apparatus.

Synthesis of 2-hydroxy, 1-napthaldehyde sulphathiazole (DP1)

The ligand was prepared by refluxing equimolar amount of 2-hydroxy, 1- napthaldehyde and sulphathiazole. 2.083gm (0.0121mole) 2-hydroxy, 1- napthaldehyde and 3.089 (0.0121 mole) sulphathiazole was taken in 80 ml. ethanol. The reaction mixture was refluxed for 5 hours on water bath. On cooling, brown yellow crystals of the 2-hydroxy, 1-napthaldehyde sulphathiazole (DP1) as a Schiff base separated out with filtration, wash with ethanol, dried and recrystallised from acetone. (Table 2.1, 2.2) The melting point was determined on standard melting point apparatus.



2-hydroxy-1-naphthaldehyde 4-amino-*N*-1,3-thiazol-2-ylbenzenesulfonamide



4-{[(1*E*)-(2-hydroxy-1-naphthyl)methylene]amino}-*N*-1,3-thiazol-2-ylbenzenesulfonamide **(DP1)**

Synthesis of benzoylacetone sulphathiazole (DP5)

The ligand was prepared by refluxing equimolar amount of benzoylacetone and sulphathiazole. 1.962gm (0.0121mole) benzoylacetone and 3.089 (0.0121 mole) sulphathiazole was taken in 80 ml. ethanol. The reaction mixture was refluxed for 5 hours on water bath. On cooling, crystals of the benzoylacetone sulphathiazole (DP5) as a Schiff base separated out with filtration, wash

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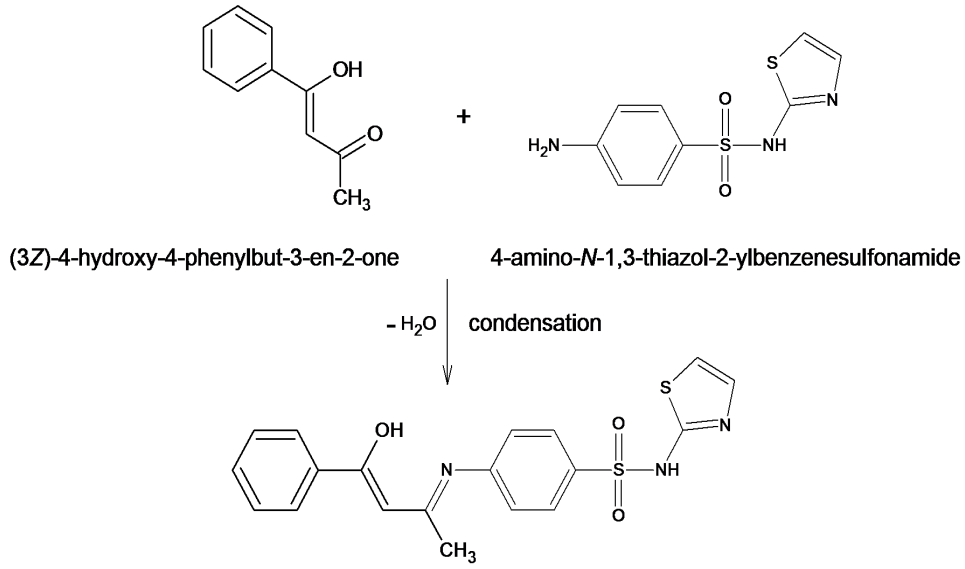
with ethanol, dried and recrystallised from acetone. (Table 2.1, 2.2) The melting point was determined on standard melting point apparatus.



4-{[(1*E*,2*Z*)-3-hydroxy-1-methyl-3-phenylprop-2-enylidene]amino}-*N*-1,3-thiazol-2-ylbenzenesulfonamide **(DP5)**

Gravimetric determination of the Metals

PREPARATION OF METAL CHELATES:

The pure ligands were used in the synthesis of metal complexes. Each ligand was purified with alcohol and ether, filtered and dried. The dried ligand sample was used for the preparation of metal complex.

The synthesis of metal complex comprises the two steps:

(a) Preparation of 0.05 M solution of each metal salt.
(b) Preparation of metal complexes of ligands DP9 and DP29.

PREPARATION OF 0.05 M SOLUTION OF EACH METAL SALTS.

Copper metal salts were used in forms of sulphates. Accurate quantities of sulphates of Cu (II) were dissolved in distilled water with few drops of conc. sulphuric acid to prepare100 ml, 0.05 M stock solution. From this stock solution 10 ml of the metal sulphate solution were used in formation metal complex.

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Gravimetric determination of copper with 2-hydroxy,1-napthaldehyde sulphathiazole (DP9):

10 ml. 0.05 M cupric sulphate solution taken in a clean beaker was treated with ammonium hydroxide solution, till sky blue precipitate was formed just sufficient amount of dilute acetic acid solution was added drop wise to dissolve the precipitate and then the pH of the solution was adjust between 8.0 to 9.0 using ammonium hydroxide solution. The solution was the diluted to 150 ml. and warmed up to 70°C. In this a reagent 2-hydroxy,1-napthaldehyde sulphathiazole methanolic solution was added drop wise when brown precipitate of copper- bis-2-hydroxy,1-napthaldehyde sulphathiazole was obtained.

It was allowed to settle and supernatant liquid was tested for complete precipitation. The precipitate was then digested on a hot water bath at 80-90°C for half an hour. The precipitate was filtered through counterpoised whatman filter papers and washed with hot water, followed by methanolic washings till free from reagent. The precipitates were dried at 120° for an hour and weighed as copper bis 2-hydroxy,1-napthaldehyde sulphathiazole. The results are shown below.

(1) 10 ml. 0.05 M cupric sulphate solution gave 0.4558 gm. copper-bis-2-hydroxy,1 napthaldehy de sulphathiazole
(2) 0.4558 gm. copper-bis 2-hydroxy,1-napthaldehyde sulphathiazole contains
Cu^{+2} = 0.03160 gm (observed)
(3) 10 ml.0.05 M cupric sulphate solution contains 0.03178 gm Cu^{+2} (Theoretical)
Error = -0.00018 gm Cu^{+2}
i.e. error = 0.57

Gravimetric determination of copper with benzoylacetone sulphathiazole. (DP29)

10 ml. 0.05 M cupric sulphate solution taken in a clean beaker was treated with ammonium hydroxide solution, till sky blue precipitate was formed just sufficient amount of dilute acetic acid solution was added drop wise to dissolve the precipitate and then the pH of the solution was adjust between 8.5 to 9.2 using ammonium hydroxide solution. The solution was the diluted to 150 ml. and warmed up to 70°C. In this a reagent benzoylacetone sulphathiazole methanolic solution was added drop wise when brown precipitate of copper-bis-benzoylacetone sulphathiazole was obtained.

It was allowed to settle and supernatant liquid was tested for complete precipitation. The precipitate was then digested on a hot water bath at 80-90°C for half an hour. The precipitate was filtered through counterpoised whatman filter papers and washed with hot water, followed by methanolic washings till free from reagent. The precipitates were dried at 120° for an hour and weighed as copper bis benzoylacetone sulphathiazole. The results are shown below.

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(1) 10 ml. 0.05 M cupric sulphate solution gave 0.4458 gm. copper-bis benzoylacetone sulphathiazole

(2) 0.4558 gm. copper-bis benzoylacetone sulphathiazole contains

Cu^{+2} = 0.03160 gm (observed)

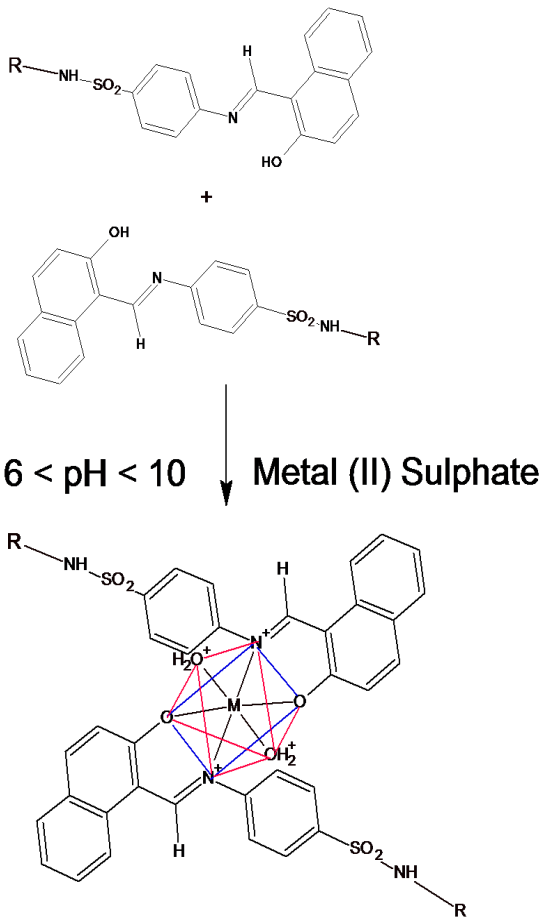
(3) 10 ml.0.05 M cupric sulphate solution contains 0.03178 gm Cu^{+2}(Theoretical)

Error = -0.00018 gm Cu^{+2}

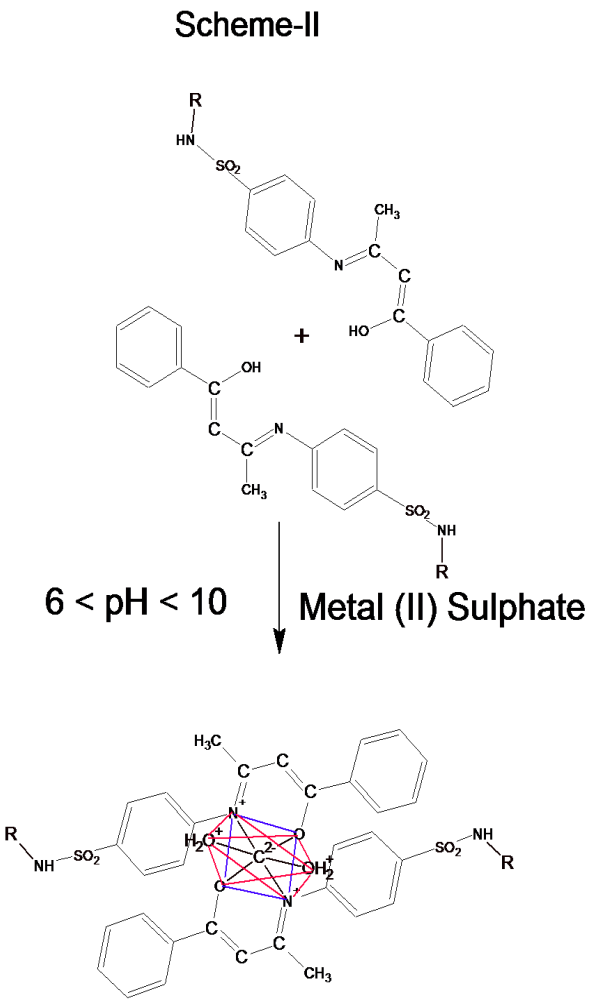
i.e. error = 0.57%

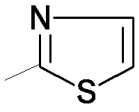
SCHEME: 2.1

Scheme-I



Scheme-II



Where R = 

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Characterization of ligands and Metal Chelates:

The present part deals with the characterization of ligands (i.e. DP1, DP5) and Metal Chelates. (DP9, DP29)

I. Elemental analysis
II. IR spectral studies

ELEMENTAL ANALYSIS.

The general properties of ligands are:

Melting points (^{o}C) of all the compounds were measured by capillary method. All the mp's were uncorrected.

The yields of all compounds reported are of crystallized. All solvents used were distilled and dried. The purity of the compounds was checked by TLC. Column chromatography was performed on silica gel (60-120 mesh).

The C, H and N elements of all the samples were measured by Elemental analyzer Thermofinigan flash1101 EA. The method was adopted as follow:

The C, H, and N contents of all DP1, DP5, DP9 and DP29 derivatives are shown in Tables 3.1,3.2 The data are consistent with the predicted structures of ligands.

INFRARED SPECTROSCOPY:

The anticipated IR spectral frequencies of the 2-hydroxy, 1-napthaldehyde sulphathiazole ligands are given in graph-DP01, benzoylacetone sulphathiazole given in graph-DP05, copper bis 2-hydroxy, 1-napthaldehyde sulphathiazole given in graph- DP09, copper-bis benzoylacetone sulphathiazole given in graph- DP21.

The infrared spectra of selected ligands from are shown in graph- DP1, DP5, DP9 and DP21 The inspection of the infrared spectra of all the ligands reveals following.

Sr.	Group	IR frequencies (Cm^{-1})
1.	- OH / -NH	2700-3600 Broad
2.	- C=N / -C=C-	1500 - 1600
3.	- C-H Stretching (Aromatic)	3000-3100
4.	Tertiary Amines	2300-2400
5.	O=S=O	1335-1375;1155-1170

RESULTS AND DISCUSSION

The yields of 2-hydroxy, 1-napthaldehyde sulphathiazole (DP1) and benzoylacetone sulphathiazole (DP05) 83 % and 82 % respectively. (TABLE-2.1, 3.1) copper bis 2-hydroxy, 1-

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napthaldehyde sulphathiazole (DP09), copper-bis benzoylacetone sulphathiazole (DP29).

Schiff bases derived from sulfa drugs and 2-hydroxy, 1-napthaldehyde and benzoyl acetone reacts with copper metal ion easily and shows error 0.57%. The notable things are that both the ligands 2-hydroxy, 1-napthaldehyde sulphathiazole (DP1) and benzoylacetone sulphathiazole (DP5) give same quantity of chelates. (TABLE-3.2)

The colour of 2-hydroxy, 1-napthaldehyde sulphathiazole (DP1) and benzoylacetone sulphathiazole (DP05) dark yellow and pale yellow respectively. The colour of copper bis 2-hydroxy, 1-napthaldehyde sulphathiazole (DP09) and copper-bis benzoylacetone sulphathiazole (DP29) greenish blue and pale bluish gray respectively.

Table 2.1: The structures of Schiff base and Physical properties of the ligands.

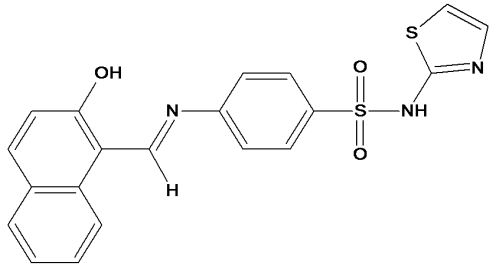
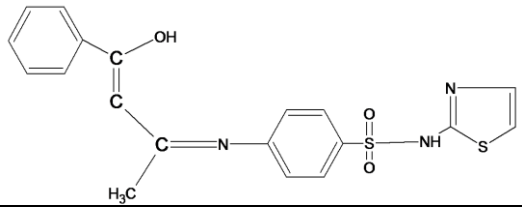
Structure	Name	Mol.wt	MP^{0}C	Yield %
	*DP1*	409.484	97	83
	*DP5*	*399.489*	*166*	*82*

Table 3.1: Characterization of Ligands

Ligand No.	Molecular Formula	Mol. Wt gm/ Mole	Yield %	Elemental Analysis					
				% C		% H		% N	
				Cal.	Found	Cal.	Found	Cal.	Found
DP1	$C_{20}H_{15}N_3O_3S_2$	409.484	83	58.66	58.50	3.69	3.62	10.26	10.22
DP5	$C_{19}H_{17}N_3O_3S_2$	399.489	82	57.12	57.04	4.29	4.23	10.52	10.36

Table 3.2: Characterization of Metal Chelates . $[CuL_2(H_2O)_2]$

Metal Complexes	Molecular formula	M.Wt Gm/mole	%Error in Yield	% Metal analysis		Elemental analysis					
						%C		%H		%N	
				Cal.	Found	Cald.	Found	Cald.	Found	Cald.	Found
DP9	$C_{40}H_{32}CuN_6O_8S_4$	916.528	0.57	6.93	6.8	52.42	52.4	3.52	3.5	9.17	9.1
DP29	$C_{38}H_{36}CuN_6O_8S_4$	896.538	0.57	7.09	7.0	50.91	50.8	4.05	4.0	9.37	9.3

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