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9. Studies on the Synthesis, Characterization and Antimicrobial aspects of Sulfur Donor Ligands and their Boron(III) Complexes

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ABSTRACT

Biological important complexes of phenyldihydroxyborane derived from 1-acetylferrocene carbodithioic acid (LH) have been prepared and investigated using a combination of microanalytical analysis, melting point, electronic, IR, ^{1}H NMR and ^{13}C NMR spectral studies. Phenyl dihydroxyborane interact with the ligand in 1:1 and 1:2 molar ratios (metal: ligand) resulting in the formation of coloured products.

The ligand are coordinated to the boron (III) via the azomethine nitrogen atom and the thiolic sulfur atom. On the basis of above studies for the Boron (III) complexes are tetra coordinated structure for 1:1 and 1:2 complexes have been assigned.

The antimicrobial activities of the ligand and complexes have been screened in vitro against bacteria Pseudomonas cepacicola and Bacillus substilis and fungi Collectatrichum capsici and Fusarium oxysporum.

The complexes have higher activities than the free ligand. The results of these activities indicate the antiandrogenic nature of these complexes.

KEYWORDS

Schiff bases, X-ray powder diffraction studies, hydrazine carbodithioic acid, antimicrobial activity.

1. Introduction:

Synthesis of some new compounds is the need of time but there are many adverse effects associated along with them endangering the human world. Green chemistry is the effort of reducing or eliminating the use of generation of hazardous substance[1]. in the design, manufacture and application of chemical procedures[2] to keep our environment pollution free.

At present, about 25,000 -30,000chemists[3] are using microwave technology to conduct chemical reactions worldwide. It is well known that several Schiff base complexes have anti-inflammatory, antipyretic, analgesic, anti-diabetic, anti-bacterial, anti-cancer and anti-HIV activity [4,5].

Interest in metal complexes of sulfur–nitrogen chelating agents, especially those formed from thiosemicarbazide[6-10], and S-alkyl / benzyl esters of dithiocarbazic acid[11-15], has been stimulated by their interesting physico-chemical properties and potentially useful pharmacological properties.[6,10,12,16]The element boron is a micronutrient for plants and traces of it have also been reported in some bacterial cell. The boron compounds, particularly those with a boron-nitrogen bond find a wide range of applications in different fields. A considerable interest in the studies of compounds containing intra molecular B-N coordination is due to the remarkable degree of hydrolytic and oxidative stability.

2. Experimental:

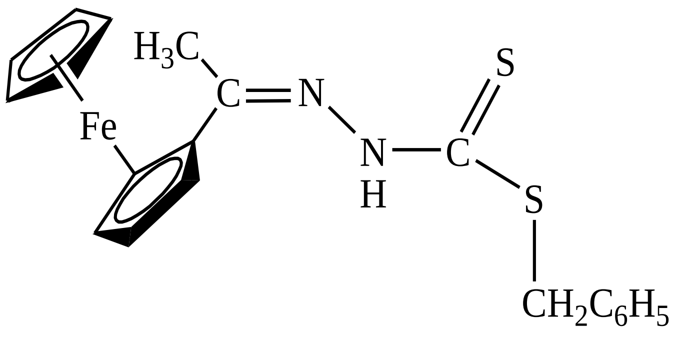
All the chemicals used in the synthesis of the complexes were of A.R. grade. All the solvents were dried and distilled before use.

2.1. Analytical Methods and Physical Measurements

The molecular weights were determined by the Rast camphor method. IR spectra of the ligand and their metal complexes were recorded with the help of Nicolet Megna FT IR 550 spectrophotometer using KBr pellets. The purity of these ligand and their metal complexes was checked by the TLC on silica Gel-G using anhydrous dimethylsulphoxide and benzene (1:1) as solvent. ^{1}H NMR and ^{13}C NMR spectra were recorded in deuterated dimethylsulphoxide (DMSO-d_6) using tetramethylsilane (TMS) as standard on a JEOL AL 300 FT NMR spectrometer. Electronic spectra of the complexes were recorded in DMF on a UV-160 a Shimadzu spectrophotometer in the range 200-600 nm. X-Ray powder diffractograms of the compounds were obtained on a Philip Model PW 1840 automatic diffractogram using Cu(Kα) target with Mg filter. The wavelength used was 1.540598 Å. Nitrogen and sulfur were estimated by the Kjeldahl’s and Messenger's methods, respectively[17]. Carbon and hydrogen analyses were performed at the CDRI, Lucknow.

2.2 Preparation of the Ligand:

The ligand (LH) was prepared by the condensation of 1-acetylferrocene with S-benzyldithiocarbazate in 1:1 molar ratio, respectively as reported earlier[18].



1-Acetylferrocene hydrazinedithio -carbazoaic acid benzyl ester

2.3 Preparation boron azomethine Complexes:

A calculated amount of ligand dissolved in dry benzene was added to the phenyldihydroxyborane in unimolar and bimolar ratios. The reaction mixture was refluxed for several hours on a fractionating column and the progress of the reaction was monitored by the liberation of azeotrope water/ benzene. After the completion of the reaction, excess of the solvent was distilled off and products were dried. The resulting products were washed with dry cyclohexane and then finally dried *in vacuo* for 3-4h. The physical properties and analytical data of these complexes are enlisted in **Table 1.**

3. Results and Discussion:

The reactions of phenyldihydroxyborane with monofunctional bidentate ligand of 1-acetylferrocene refluxing in benzene in 1:1 and 1:2 molar ratios have resulted according to the following equations: 1:1

$$PhB(OH)_2 + N^{\cap}XH \xrightarrow[\text{Dry benzene}]{} [PhB(OH)(N^{\cap}X)] + H_2O$$

1:2

$$PhB(OH)_2 + 2N^{\cap}XH \xrightarrow[\text{Dry Benzene}]{} [PhB(N^{\cap}X)_2] + 2H_2O$$

(Where, $N^{\cap}X$ is the donor set of the ligand molecule and X = O or S) These reactions are quite facile and the resulting complexes are coloured solids and soluble in methanol, $CHCl_3$, DMF, THF and DMSO.

All these newly synthesized complexes are monomeric in nature as indicated by their molecular weight determinations by the Rast Camphor method. The complexes are non electrolytes in nature, because they have low molar conductance values (8-14 ohm^{-1} cm^2 mol^{-1}).

3.1 Electronic Spectra:

The electronic spectra of the ligand show broad maxima in the range 370-360 nm due to the n-π* electronic transitions of the azomethine group, which undergoes a bathochromic shift in the complexes, due to the polarisation within the >C=N chromophore caused by the ligand interactions[19].The bands in the region 285-280 nm due to π-π* electronic transitions of the ligand, undergoes a red shift in the complexes. A band around 395 nm due to n-π* transitions of the azomethine group is observed in the spectra of the complexes which remains absent in the free ligand.

3.2 Infrared Spectra:

The infrared spectra of the ligand show strong band in the region 1620-1590 cm^{-1} due to the >C=N group, which shifts to the higher frequency in the complexes thus showing the coordination of the azomethine nitrogen to the boron atom. The absorption bands at 3410-3140 cm^{-1}, 1610-1580 cm^{-1}, 1010-1015/ 1680-1660 cm^{-1} and 950-940 cm^{-1} are assigned to ν(N-H), ν(C=S)/ν(C=O) and ν(N-N), respectively. The ν(N-H), ν(C=S) and ν(C=O) bands are absent in the complexes, indicating the enolization of the ligand[16] followed by deprotonation during the complexation. The absorption at *ca* 1620 cm^{-1} characteristic of the azomethine (>C=N) group in the spectra of the ligand, gets split into two sharp bands at *ca* 1612 cm^{-1} and 1625 cm^{-1} in 1:2 complexes. This splitting of bands suggests that the azomethine group is in different chemical environments. The shifting of the bands at *ca* 1625cm^{-1} (higher wave number side) suggest the coordination of the azomethine nitrogen to the boron atom, whereas the band at *ca* 1612 cm^{-1} is assigned to the uncoordinated azomethine group. This further gets support by the appearance of the absorption bands in the spectra of the complexes at 1510–1550 cm^{-1} and 1320–1340 cm^{-1}which may be assigned to ν(B←N), and ν(B-O) vibrations, respectively and the bands due to ν(C-S)and ν(C-O) modes at lower frequencies. Two sharp bands at 3485-3455 and 3365-3345 cm^{-1} due to the asymmetric and symmetric vibrations of (NH_2) group remain unchanged in the spectra of the complexes showing the non-involvement of this group in coordination. The characteristic bands of the ferrocenyl group appears at 3080-3070 cm^{-1}, 1450-1445 cm^{-1}, 1120-1110 cm^{-1}, 829-825 cm^{-1} and 480-470 cm^{-1} arising from ν(C-H), ν(C=C), δ(C-H), π(C-H) and (Fe-ring), respectively.

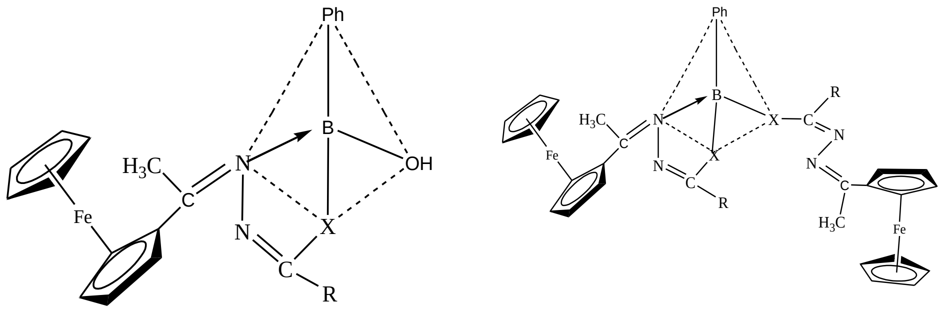
3.3 ^1H NMR Spectra:

The ^1H NMR spectra of the ligand and their complexes were recorded in DMSO-d_6 and the chemical shift values (δ, ppm) are listed in **Table 2.** The methyl proton signal (δ 2.10-2.35 ppm) of the azomethine moiety in the spectra of the ligand gets shifted towards upfield in the complexes. The disappearance of the -NH proton signal (δ 8.34-8.96 ppm) of the ligand in their respective complexes indicates the removal of a proton from the -NH group and the coordination of nitrogen with simultaneous covalent bond formation by sulfur or oxygen with the boron atom. The NH_2 proton signal (δ 2.21-2.42 ppm) remains almost at the same position in the ligand and their complexes, indicating the non-involvement of NH_2 group in the complexes.. In addition, there appears a sharp singlet (δ 6.22-6.62 ppm) giving evidences for the presence of η-C_5H_5 group in all the complexes.

3.4 ^{13}C NMR Spectra:

The ^{13}C NMR spectra of the ligand and their corresponding complexes have also been recorded in DMSO-d_6 **(Table 3).** The chemical shift values of the carbon atoms attached to the azomethine nitrogen, thiolic sulfur and amido oxygen, show considerable shift which further support the proposed coordination in the complexes.

On the basis of the above discussion the following tetra coordinated structures for the derivatives of monobasic bidentate ligand respectively have been suggested.



1:1 Complex **1:2 Complex**

Where X= O and R=NH$_2$,
Fig. 2. Structure of the complexes.

3.5 Antifungal Screening:

The complexes were screened against *Alternaria alternata* and *Fusarium oxysporum* fungi. The antifungal activity of synthesized compounds was evaluated by the "Radial Growth Method".[20]

3.6 Antibacterial Screening:

Various methods are available for the evaluation of the antibacterial activity of different types of compounds. In the present work, activities of synthesized compounds were evaluated by the "Disc-Diffusion Method" using inhibition zone technique[21]. The complexes were screened against *Staphylococcus aureus* and *Xanthomonas compestris* bacteria.

Mode of Action:

The ligand and their corresponding boron complexes were screened against the selected pathogenic fungi and bacteria to examine their growth-inhibiting potential towards the test organism. The results show that these compounds exhibit antimicrobial properties. Boron complexes show more inhibitory effects than the parent ligand (Tables 4 and 5).

The ligand with sulfur and nitrogen donor system might have inhibited enzyme productions since enzymes, which require reactive groups for their activity, appear to be especially susceptible to deactivation by the complexes. The complexes facilitate their diffusion through the lipid layer of the spore membrane to the site of action, ultimately killing them by combining with the reactive groups of certain cell enzymes. The results show that the activity is enhanced by undergoing chelation[22]. It is a well known fact that the concentration plays a vital role in increasing the degree of inhibition. As the concentration increases, the activity increases. The fungicidal activity was better when compared to the bactericidal activity. It is interesting to note that the synthesized boron complexes with ligand have more activity than the ligand. This may be due to the presence of the sulfur atoms in such ligand.

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Table 1 Synthetic and analytical data of organoboron complexes with various $N^{\cap}S$ donor ligand of acetylferrocene.

Sr. No	**Reactants (g)**		**Molar ratio**	**Product and Colour**	**M.P. (ºC)**	**Analyses (%) Found/ (Calcd)**					**Mol. Wt. Found/ (Calcd.)**
	Metal	**Ligand**				C	**H**	N	**S**	M	
1.		$C_{20}H_{20}N_2S_2Fe$ (LH)		Black	220	58.77 (58.82)	5.01 (4.94)	6.81 (6.86)	15.63 (15.70)		390.41 (408.37)
2.	$PhB(OH)_2$	LH	1:1	$[PhB(OH)(L_8)]$ Greyish black	205-207			5.32 (5.47)	12.40 (12.52)	2.02 (2.11)	524.21 (512.29)
3.	$PhB(OH)_2$	LH	1:2	$[Ph\ B(L_8)_2]$ Black	208-210			5.10 (5.21)	14.10 (14.21)	1.10 (1.22)	914.52 (902.65)

Table 2 : ^{1}H NMR Spectral data (δ, ppm) of the ligand and their organoboron (III) complexes.

Compound	**-NH (s)**	**$-NH_2$ (s)**	**$-S-CH_2$ (s)**	**$-CH_3$ (s)**
LH	8.96	-	1.86	2.10
[PhB(OH)(L)]	-	-	1.92	2.28
$[PhB(L)_2]$	-	-	1.94	2.25

Table 3: ^{13}C NMR Spectral data (δ, ppm) of the ligand and their organoboron (III) complexes.

Compound	**Chemical shift values**				
	>C=O / >C=S	**>C=N**	**$-CH_3$**	**Ferrocenyl carbons**	**^{11}B chemical shift**
LH	177.46	168.97	11.54	69.89, 71.26, 73.07, 77.86	-
[PhB(OH)(L)]	175.64	165.91	11.93	69.97, 71.19, 73.25, 77.48	4.24
$[PhB(L)_2]$	174.24	164.89	11.88	69.98, 71.18, 73.19, 77.51	4.26

Table 4: Antibacterial screening data of the ligand and their boron complexes, Diameter of inhibition zone (mm) (conc. in ppm).

Compound	***S. aureus***		***X. compestris***	
	500	**1000**	**500**	**1000**
LH	6	8	6	8
[PhB(OH)(L)]	6	8	7	9
[PhB(L)$_2$]	7	10	7	9
Standard (Streptomycin)	15	17	13	15

Table 5: Fungicidal screening data of the ligand and their boron complexes, (Average % inhibition after 96 hours) (conc. in ppm).

Compound	***Alternaria alternata***			***Fusarium oxysporum***		
	50	**100**	**200**	**50**	**100**	**200**
LH	30	39	64	29	41	68
[PhB(OH)(L)]	32	47	63	33	45	69
[PhB(L)$_2$]	29	43	64	30	45	67
Standard (Bavistin)	90	100	100	86	100	100

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