MICROWAVE SYNTHESIS AND BIOCHEMICAL STUDIES OF BORON(III) COMPLEXES

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Abstract: Microwave assisted synthesis of boron(III) complexes of isobutylmethylketone-benzothiazoline (L_1H) and isobutylmethylketonedithiocarbazate (L_2H) has been reported. The newly synthesized compounds, have been characterized thoroughly by physico-chemical and spectroscopic techniques. The spectral data are consistent with a tetracoordinated environment around the boron atom in which the ligands acts as a monobasic bidentate ligand, coordinating through nitrogen and sulfur atoms. Ligands and their chelates were tested against certain microorganisms to assess their antimicrobial properties and the results are indeed positive.

Introduction

The study of azomethines and their complexes with main group elements and transition elements continue to be of unabated interest for chemists and biologists in order to search for new pharmacological or biologically potent compounds. The interest in chemistry of metal/non-metal complexes of sulfur and nitrogen donor ligands are due to their chemotherapeutic value, which has been increasingly exploited in commercial industries.[1-3] Imines containing sulfur as a donor atom are known to function as potent antimicrobial[4], anticarcinogenic[5] and antineoplastic agents. Boron is an essential element for plants. It plays an important role in plant growth regulatory system. Boron has a unique chemistry. Over the last few years, the design, synthesis and characterization of boron complexes are an area of research, which is undergoing dramatic growth. A novel organoboron compound which not only emits blue electroluminesence but also display isomerism has been reported.[6] Recent study on boron compounds show that they exhibit significant hypolipideamic activity in rodents, specifically lowering serum, cholesterol and triglycerides. The chemistry of organoboron compounds, containing boron-nitrogen and sulfur bond is of interest due to the immense applications of their derivatives in various fields[8]. Organoboron complexes of sulfur / oxygen and nitrogen donor ligands are known to function as microbial agents.[9] Therefore, under these invetigations two sulphur down ligands and their boron complexes have been reported.

Experimental

Chemicals and solvents used were dried and purified by standard methods and moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes.

Preparation of the Ligands

L_1H is prepared by the condensation of isobutylmethylketone with *o*-aminothiophenol in 1:1 molar ratio on a magnetic stirrer in ethanol medium. L_2H is prepred by the condensation of isobutylmethyl ketone with *S*-benzyldithiocarbazate in unimolar ratio. Resulting products were seperated out and recrystallized with the same solvent. L_1H was obtained as a yellow solid, m.p. 92 – 94°C and L_2H was obtained as a light brown solid, m.p. 103 – 105°C.

It is interesting to note that the same reaction could be completed within 3 – 4 minutes under microwave conditions.

Synthesis of the Complexes

Phenylboronic acid and the respective ligands were mixed in 1:1 and 1:2 stochiometric proportions in the presence of dry benzene. The reaction mixture was refluxed for about 10 – 14 hours on a fractionating column and the progress of the reaction was monitered by the liberation of water azeotropically with benzene. The mother liquor was concentrated by removing the excess of solvent under reduced pressure and the resulting products were dried, repeatedly washed with dry cyclohexane and again dried for 2 h to obtain the pure product.

$$PhB(OH)_2 + nN\frown SH \longrightarrow PhB(OH)_{2-n}(N\frown S)_n + nH_2O$$

Where, n = 1 or 2 and NS is the donor set of organic moieties.

It is interesting to note that the same reaction could be completed within 5 – 6 minutes under microwave conditions.

Physical Measurements

The molecular weights were determined by the Rast Camphor method. Nitrogen and sulfur were estimated by the Kjeldahl's and Messenger's methods respectively. Boron was estimated as boric acid in the presence of mannitol using phenolphthalein indicator.

IR spectra were recorded on a FT-IR spectrophotometer in KBr pellets. ^{1}H NMR spectra were recorded on a JEOL FX-90Q spectrometer in $CDCl_3$ using TMS as an internal standard. Conductivity measurements in dry dimethylformamide were performed with a conductivity Bridge type 305.

Results and Discussions

The resulting complexes are coloured solids, soluble in DMF and DMSO. The complexes are monomeric as indicated by the molecular weight determinations. The complexes isolated are presented in Table-2 together with their analytical data.

The IR spectra of L_1H and L_2H, display band due to νNH at ca. 3270 – 3100 cm^{-1}. In the spectra of Boron(III) complexes, band due to NH vibrations disappear, indicating its deprotonation and chelation of nitrogen with boron atom. The νOH band in case of 1:1 boron complexes appear at ca. 3450 cm^{-1}. The coordination of these ligands L_1H and L_2H through azomethine nitrogen and thiolic sulfur further get support by the appearance of new bands at ca. 1555 – 1535 cm^{-1} and 860 – 830 cm^{-1} due to ν (B←N) and ν(B-S) vibrations, respectively.[11] The absence of νSH at 2500 – 2600 cm^{-1} and νC = N at 1600 – 1620 cm^{-1} are indicative of the L_1H structure rather than of the Sehiff base form. A new band at ca. 1600 cm^{-1} in the complexes may be assigned to ν C = N vibrations. The appearance of this band suggests the formation of boron Schiff base derivatives as the benzothiazoline ring rearranges to give the imine form and which then combines with the metal ion.

The ^{1}H NMR spectrum of L_2H showed a sharp singlet at δ 8.49 – 8.95 ppm due to azomethine proton which shifts downfield indicating coordination of l.p. of $e^{(-)}$s of the azomethine nitrogen. The SCH_2 protons in the complex appear at almost the same position as in the present ligand.[13]

The ^{13}C NMR spectra were recorded which were found to be comparable to their respective benzothiazolines.

The ^{11}B NMR spectra in DMSO-d_6 are observed in the range δ 2.03 – 5.09 ppm, which unequivocally suggest a tetracoordinated environment around the boron atom and the presence of a B←N coordinate bond.

Tabic-1: Physical properties and analytical data of the complexes.

Compound	Colour and M.P. (°C)	Yield (%)	Analysis Found (calcd.)			Mol. Wt. Found (Calcd.)
			B	N	S	
L_1H	Yellow 92-94°C	76	-	6.55 (6.75)	15.20 (15.46)	203 (207.33)
$C_6H_5B(OH)(L_1)$	Dark green 219-221°C	62	3.15 (3.46)	4.23 (4.50)	9.97 (10.30)	307 (311.24)
$C_6H_5B(L_1)_2$	Green 200-202°C	67	1.92 (2.15)	5.25 (5.58)	12.50 (12.78)	494 (500.57)
L_2H	Dim brown 103-105°C	89	-	9.65 (9.98)	22.59 (22.86)	269 (280.45)
$C_6H_5B(OH)(L_2)$	Cream 114-116°C	59	3.49 (2.80)	7.78 (7.28)	16.89 (16.68)	381 (384.36)
$C_6H_5B(L_2)_2$	Yellow brown 161-163°C	68	1.36 (1.66)	8.49 (8.66)	19.58 (19.83)	639 (646.80)

Antifungal and Antibacterial Activities

The experimental results show that there is an increase in the toxicity of the complexes as compared to the ligands and the inhibition of the growth of the microrganisms was found to be dependent on the solubility, concentration, fineness of particles and the size of the boron atom.

The enhanced antimicrobial activity of the boron chelates over their corresponding chelating agents may be explained by the chelation theory. Chelation reduces the polarity of the boron ion mainly because of the partial sharing of its positive charge with the donor groups and possible π-electron delocalization over the whole chelate ring. This increase the lipophilic character of the metal complexes, which subsequently favour its permeation through the semi-permeable defences of cell membrane of microorganism and thereby, impairing the normal cell process.[14]

Antifungal Screening

The antifungal activity of both the ligands and their corresponding complexes was evaluated against *Aspergillus niger* and *Fusarium oxysporium* by the agar plate technique. The compounds were dissolved in 25, 50 and 100 ppm concentration in methanol and then were mixed with the medium. The linear growth of the fungus was obtained by measuring the diameter of colony in petri plate after 96 hours and the percentage inhibition was calculated as 100 (C – T) / C, where C and T are the diameters of the fungus colony in the control and test plates, respectively.

Antibacterial Activity

Bacterial activity evaluated by the paper disc plate method. The nutrient agar medium (peptone, beef extract, NaCl and agar-agar) and 5mm diameter paper discs of Whatman No. 1 were used. The compounds were dissolved in methanol in 500 ppm and 1000 ppm concentration. The filter paper discs were soaked in different solutions of the compounds dried and then placed in the petri plates, previously seeded with the test organism *Escherichia coli* and *Staphylococcus aureus*. The plates were incubated for 24 - 30 hours at 28 ± 2°C and the inhibition zone around each disc was measured.

Table-2: Biological activity index.

Compound	Fungicidal % inhibition						Bacterial (diameter)			
	Aspergillus niger			*Fusarium oxysporium*			*Echerichia coli*		*Staphylococcus aureus*	
	25 ppm	50 ppm	100 ppm	25 ppm	50 ppm	100 ppm	500 ppm	1000 ppm	500 ppm	1000 ppm
L_1H	35	43	62	42	54	66	5	6	10	12
$C_6H_5B(OH)(L_1)$	39	50	65	45	56	68	8	14	13	16
$C_6H_5B(L_1)_2$	44	57	75	48	60	71	11	17	14	18
L_2H	38	46	57	40	54	64	6	9	11	13
$C_6H_5B(OH)(L_2)$	41	62	80	43	64	83	8	11	12	15
$C_6H_5B(L_2)_2$	45	66	83	49	68	89	11	13	13	17
Bavistin	61	86	94	68	89	97	-	-	-	-
Streptomycin	-	-	-	-	-	-	1	2	15	17

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