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Mononuclear Boron(III) Complexes of Neo Bidentate Thioimines Derived from Hydrazinecarbodithioic Acid

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Boron chemistry has been intensively studied in the recent past. Although the study of the interactions between transition-metal ions and the phenyl methylene ester derivatives of hydrazine carbodithioic acids has been carried out on a long period, particularly via the formation of adducts, their interaction of Main Group metal ions and the formation of their coordination complexes are subjects of current interest. We have synthesized and isolated a variety of complexes of phenyl dihydroxyborane with substituted dithiocarbazates. The benzene-soluble, high-molecular-weight complexes have been characterized using a wide range of analytical and spectroscopic techniques. The pathogenicity of microbial infections associated with the complexes have been subjected to a variety of biointeraction studies and the results are discussed. Copyright © 1999 John Wiley & Sons, Ltd.

Keywords: organoboron(III) complexes; spectroscopic studies; antimicrobial screening; bajra plant

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INTRODUCTION

The literature includes numerous studies on the metal complexes of dithiocarbazate Schiff bases and a review featuring their geometry and configurations has also appeared.[1–3] The major stimulus for investigating the mononuclear boron(III) complexes of bidentate thioimines derived from hydrazine carbodithioic acid is, from a knowledge of the effects that metal complexes have on N and S/O binding sites, which have prominent roles in biochemical processes in addition to their biological properties.[4–6]

Organoboron compounds are attracting attention currently because of their importance as synthetic intermediates.[7] Dithiocarbazates and their derivatives are sources of important pharmacodynamic significance.[8,9] Organoboron compounds of these ligands have been found to possess conspicuous biological activity.[10] It has been observed that metal chelation apparently plays a definite role in the enhanced activity. Fungicidal and bactericidal activities *in vitro* and *in vivo* of the ligands, along with those of their boron complexes, have been studied using the conventional fungicide, Bavistin and a conventional bactericide, Streptomycin, as the standards for the respective activities. The stereochemical and biochemical aspects of mononuclear boron(III) complexes of bidentate thioimines have been worked out and the findings are presented in this paper.

RESULTS AND DISCUSSION

Reactions of phenyldihydroxyborane with various thioimines were carried out in 1:1 and 1:2 molar ratios in dry benzene. These reactions proceed with the liberation of water azeotropically with benzene (Eqn [1]):

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

where $n = 1$ or 2 and NS is the donor set of organic moieties.

These reactions are quite facile and the resulting complexes are coloured solids, soluble in dimethyl sulphoxide (DMSO) and chloroform. The com-

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Table 1. ^{1}H and ^{11}B NMR spectral data (δ, ppm) of organic moieties and their complexes

Compound	–NH	$-SCH_2$	H⟩C=N	H_3C⟩C=N	Aromatic/Ph–B[a]	^{11}B
T_1H	12.80	5.20	8.50	—	7.68–8.20	—
$PhB(T_1)_2$	—	5.05	8.96	—	7.84–8.35	5.0
T_2H	12.95	4.56	8.46	—	7.12–8.32	—
$PhB(OH)(T_2)$	—	4.48	8.64	—	8.04–6.72	5.09
T_3H	13.20	4.64	8.48	—	6.56–8.26	—
$PhB(T_3)_2$	—	4.96	9.18	—	6.64–8.42	2.03
T_4H	12.9	5.04	8.95	2.48	7.20–8.64	—
$PhB(OH)(T_4)$	—	4.48	9.21	2.72	7.28–8.96	2.20

[a] Merged with aromatic protons.

plexes are monomeric, as indicated by molecular weight determinations.

Infrared spectra

The infrared frequencies for thioimines and their organoboron(III) complexes support the proposed coordination. The use of absorption bands due to the ⟩C=N frequency in identifying the bonding site is somewhat limited because of the complex nature of absorption in the 1550–1630 cm^{-1} region. However, a strong peak of the organic moieties at ca 1600 cm^{-1} shows a substantial increase in the intensity (and a shift in frequency, $\Delta\nu = 10$–20 cm^{-1}) after complexation. This band may be assigned to complex vibrations involving $\nu C=N$, (NH_2) and the aromatic ring.[11] Its shift to a higher frequency is due to an increase in the bond order, showing coordination of the azomethine nitrogen to the boron atom. However, after deprotonation, a new band at approx. 1595 cm^{-1} is assigned to an uncoordinated azomethine group.[12] The spectra of the parent imines show bands due to ν(NH) vibrations in the 3250–3100 cm^{-1} region, which disappear in complexes, indicating deprotonation of the NH group. Another strong band at 1020–1050 cm^{-1} may be assigned to a $\nu(C=S)$ which shows that in the solid state the ligands exist in the thione form. This band disappears in the spectra of complexes, indicating coordination through sulphur. The free organic moieties display a doublet at ~2900 and ~2960 cm^{-1} attributed to symmetric and asymmetric vibrations of the –CH grouping in the $S-CH_2-C_6H_5$ moiety[1] and are reduced to a weak doublet in the spectra of the complexes. The (OH) band in the case of 1:1 complexes appears at *ca* 3450 cm^{-1}. Several new bands in the spectra of complexes appear in the 1560–1540 cm^{-1} and 730–750 cm^{-1} region due to different vibrational modes of B⟶N and B–S bands, respectively.

^{1}H NMR spectra

The ^{1}H NMR spectra of the thioimines and the complexes were recorded in DMSO-d_6 and the chemical shifts (δ, ppm) are recorded relative to DMSO-d_6 (2.54 ppm). The spectral data of the thioimines and their complexes are summarized in Table 1. All the organic moieties exhibit a singlet at = 12.8–13.2 ppm due to the –NH proton. The presence of a –NH proton resonance and the absence of a –SH proton resonance further support the conclusion drawn from the IR spectra, namely the thione nature of the ligands. The disappearance of the signal due to the –NH proton in the spectra of the complexes suggests the involvement of this proton in thioenolization of the ⟩C=S group and subsequent coordination of the sulphur atom after proton replacement. The sharp singlet at δ = 8.46–8.95 ppm due to the azomethine proton shifts downfield, indicating coordination of the lone pair of electrons of the azomethine nitrogen.[13] The $-SCH_2$ protons in the complexes appear at almost the same positions as in the parent imines.

^{13}C NMR spectra

The ^{13}C NMR spectra of parent imines and their complexes $PhB(T_1)_2$, $PhB(OH)(T_2)$ and $PhB(OH)(T_6)$] were recorded in dried DMSO (Table 2). The number of signals found corresponds with the number of magnetically non-equivalent carbon atoms. The heterocyclic moiety carbon signals, especially those of the carbon atoms directly bonded to the heteroatom, undergo slight upfield shifts relative to the other carbon atoms, which remain almost unperturbed. The upfield shift

Table 2. ^{13}C NMR spectral data (δ, ppm) of organic moieties and their complexes

Complex	Thiolo carbon	Azomethine carbon	Aromatic carbons	*B*-Phenyl			
				C_i	C_o	C_m	C_p
T_1H	194.87	163.55	147.25, 135.71, 135.17, 128.08, 127.91, 127.47, 127.31, 126.61, 126.07	—	—	—	—
$PhB(T_1)_2$	188.42	158.32	140.67, 138.07, 130.76, 130.16, 129.14, 128.36, 128.22, 127.32, 126.21	134.80	130.91	127.51	129.82
T_2H	195.05	162.86	147.25, 140.96, 135.60, 134.84, 128.56, 127.85, 127.69, 127.20, 126.50	—	—	—	—
$PhB(OH)(T_2)$	187.48	154.20	141.29, 138.07, 130.17, 129.58, 129.25, 128.01, 127.63, 127.30, 126.12	134.89	131.58	128.50	129.47
T_6H	194.60	164.37	148.58, 136.79, 135.82, 131.43, 128.99, 128.12, 127.42, 127.20, 126.12	—	—	—	—
$PhB(OH)(T_6)$	185.69	157.88	138.61, 132.32, 129.74, 129.63, 129.20, 127.4, 127.09, 126.98, 126.32	132.61	130.12	128.50	129.96

Table 3. Antifungal screening data of the organic moieties and their complexes

Complex	Percentage inhibition after 4 days at 25 ± 2°C											
	Alternaria brassicicola				*Fusarium oxysporum*				*Rhizoctonia bataticola*			
	25	50	100	200	25	50	100	200	25	50	100	200
T_1H	54	63	67	72	23	34	45	56	34	42	50	58
$PhB(OH)(T_1)$	58	65	69	77	28	38	55	60	50	59	65	75
T_2H	60	66	71	74	34	39	50	58	28	32	38	42
$PhB(OH)(T_2)$	63	69	73	76	40	44	55	70	36	41	46	52
T_6H	62	68	74	80	40	48	54	62	30	39	44	48
$PhB(OH)(T_6)$	67	72	75	83	48	56	64	70	36	46	56	68
2-(Methoxycarbamoyl)benzimidazide	82	91	100	100	83	86	100	100	81	84	100	100

Table 4. Efficacy of the organic moieties and their complexes in controlling Rust of bajra

Treatment	PDI in treated plant	Disease control (%)
T_1H	15	60.0
$PhB(OH(T_1)$	8	73.3
T_2H	11	68.7
$PhB(OH(T_2)$	6	78.1
T_3H	17	62.9
$PhB(OH)(T_3)$	7	72.8

of the thiolo carbon and the azomethine carbon in the complexes indicates participation of these groups in coordination to the boron. The identification of new *B*-phenyl signals (C_i, C_o, C_m, C_p) in all the complexes confirms complexation.

^{11}B NMR spectra

The ^{11}B NMR in DMSO-d_6 is observed in the = 2.03–5.09 ppm region (Table 1), which unequivocally suggests a tetracoordinated environment around the boron atom and the presence of a B⟶N coordinàte bond.[14,15] The driving force for the formation of this coordinate bond is the ability of trivalent $PhB(OH)_2$ to accept a pair of electrons from a suitable donor atom (nitrogen in the present case) (Fig. 1).NS = Donor system of ligand

Biocidal screening

Antifungal and antibacterial activities of the organic moieties and their complexes have been evaluated (Tables 3–5). The results show that bioactivity increased on undergoing chelation. The toxicity also increased as the concentration increased. The boron complexes were more toxic than the parent ligands against the same microorganism. However, none of the ligands or boron compounds possessed better inhibitory action than the conventional fungicide 2-(methoxycarbamoyl)-benzimidazide (Bavistin) which was used for comparing the results. On the other hand, some boron compounds were more active against Gram-negative stain bacteria, i.e. *Pseudomonas phaseolicola* and *Xanthomonas campestris* than the bactericide Streptomycin. Overall, the boron compounds were superior to the parent ligands.

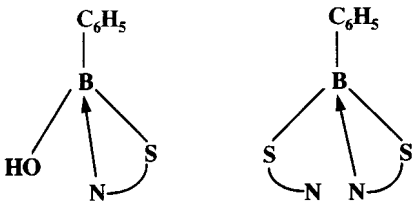


Figure 1 NS = Donor system of ligand

Experiments were conducted *in vivo* in the field on a bajra crop (*Pennisetum typhoides*). Rust disease is caused by the pathogen Puccina penniciti. Disease severity was measured using the Peterson scale.[16] The disease incidence (%) is the area covered on the foliage expressed as a percentage of total foliage affected by the specific disease and was calculated the by Eqn [2].

$$\text{PDI} = \frac{\text{no. of infected plants} \times 100}{\text{total no. of plants observed} \times \text{maximum rating}}$$

The effectiveness of the chemicals was calculated the by Eqn [3]:

$$\text{Disease control (\%)} = \frac{\text{PDI in treated plants} - \text{PDI in untreated plants}}{\text{PDI in untreated plants}} \times 100$$

The activity data reveal that the complexes are superior to the parent moieties. The pathogenicity of the complexes may be ascribed to inhibition of respiration[17] or uncoupling of oxidative phosphorylation and disruption of the cell, thereby affecting the permeability[18] of the cell membrane, resulting in the leakage of cell contents.

Bajra Rust severity was rated using Peterson scale (Table 6)

EXPERIMENTAL

All the reagents were dried and distilled before use. The ligands were prepared by the procedure reported elsewhere[9] and were purified by recrystallization the crystals in the same solvent and drying the crystals under reduced pressure. Their purity was checked by TLC. The abbreviations used for the ligands are given in Table 7.

Preparation of complexes

A calculated amount of phenyldihydroxyborane (0.57–1.28 g) was reacted with various thioimines in unimolar (1.29–2.90 g) and bimolar (2.58–5.80 g) ratios in anhydrous benzene medium. The reaction mixture was refluxed for several hours

Table 5. Antibacterial screening of organic moieties and their complexes

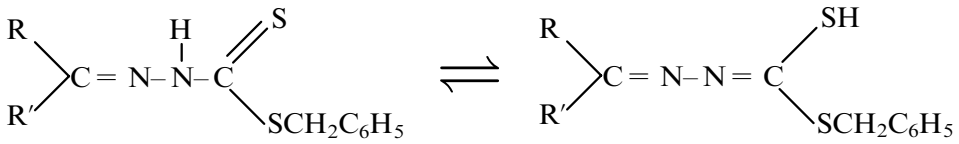
	Diameter of inhibition zone (mm)							
	Pseudomonas phaseolicola (−)		*Escherichia coli* (−)		*Staphylococcus aureus* (+)		*Xanthomonas campestris* (−)	
Complex	500 ppm[a]	1000 ppm	500 ppm	1000 ppm	500 ppm	1000 ppm	500 ppm	1000 ppm
T_5H	6	9	6	8	7	10	4	7
$PhB(OH)(T_5)$	7	10	7	11	8	12	5	9
$PhB(T_5)_2$	10	13	9	13	10	14	7	10
T_6H	4	6	4	5	3	5	3	6
$PhB(OH)(T_6)$	7	10	7	10	7	9	4	7
$PhB(T_6)_2$	6	13	9	14	10	12	7	9
Streptomycin	2	3	17	18	15	17	3	5

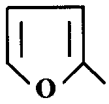
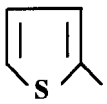
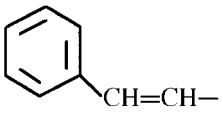
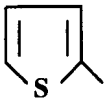
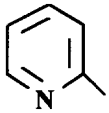
[a] Concentration of the test compound.

Table 6. Peterson scale of disease severity

Scale part	1	2	3	4	5	6	7	8	9	10	11	12
Area of Rust flecks on leaf lamina (%)	1	5	10	20	30	40	50	60	70	80	90	100

Table 7. Ligands used in this study equation



R	R′	Ligand	Abbreviation
	H	(2-Furanylmethylene)hydrazinecarbodithioic acid phenylmethyl ester	T_1H
	H	(2-Thienylmethylene)hydrazinecarbodithioic acid phenylmethyl ester	T_2H
	H	(3-Phenyl-2-propylidene)hydrazinecarbodithioic acid phenylmethyl ester	T_3H
	CH_3	[1-(2-Furanyl)ethylidene]hydrazinecarbodithioic acid phenylmethyl ester	T_4H
	CH_3	[[1-(2-Thienyl)ethylidene]hydrazinecarbodithioic acid phenylmethyl ester	T_5H
	CH_3	[1-(2-Pyridinyl)ethylidene]hydrazinecarbodithioic acid phenylmethyl ester	T_6H

over a ratio head. The completion of the reaction was indicated by the liberation of a benzene–water azeotrope. The complexes were dried under reduced pressure. The resulting product was washed repeatedly with dry cyclohexane and finally dried under vacuum for 3–4 h. All the complexes were then recrystallized in a mixture of benzene and ether (1:1). Their physical and analytical properties are given in Table 8.

Analytical methods and physical measurements

The analytical procedures adopted for the thio-

Table 8. Quantitative analyses and physical properties of organoboron(III) compounds

Compound	Colour	M.p. (°C)	Analysis (%) Found (calcd)			Mol. wt: Found (calcd)
			N	S	B	
$PhB(OH)(T_1)$	Dark brown	134–136	7.25 (7.36)	16.48 (16.86)	2.75 (2.84)	412 (380)
$PhB(T_1)_2$	Brown	157–158	8.67 (8.77)	19.85 (20.08)	1.62 (1.69)	615 (638)
$PhB(OH)(T_2)$	Yellow	167–169	6.95 (7.06)	23.18 (24.27)	2.69 (2.72)	420 (396)
$PhB(T_2)_2$	Lemon yellow	173–175	8.10 (8.35)	28.21 (28.68)	1.58 (1.61)	695 (670)
$PhB(OH)(T_3)$	Yellow	180–181	6.23 (6.72)	14.95 (15.40)	2.32 (2.59)	436 (416)
$PhB(T_3)_2$	Yellow	190–192	7.82 (7.88)	17.97 (18.04)	1.35 (1.52)	729 (710)
$PhB(OH)(T_4)$	Light brown	155–156	6.92 (7.10)	16.08 (16.26)	2.65 (2.74)	432 (394)
$PhB(T_4)_2$	Brown	172–173	7.18 (8.40)	18.75 (19.23)	1.59 (1.62)	682 (666)
$PhB(OH)(T_5)$	Yellow	112–114	6.71 (6.82)	22.37 (23.43)	2.61 (2.63)	382 (410)
$PhB(T_5)_2$	Dark yellow	145–147	7.87 (8.01)	26.83 (27.52)	1.50 (1.54)	673 (698)
$PhB(OH)(T_6)$	Greenish brown	110–112	9.97 (10.36)	15.71 (15.82)	2.61 (2.66)	422 (405)
$PhB(T_6)_2$	Dark green	121–122	12.15 (12.20)	18.59 (18.62)	1.53 (1.57)	713 (688)

imines and their organoboron(III) compounds are outlined below.

IR spectra were recorded on a Perkin-Elmer 577 grating spectrophotometer using KBr pellets. ^{1}H, ^{13}C and ^{11}B NMR spectra were recorded on a JEOL FX 90Q spectrometer. Tetramethylsilane (TMS) was used as the internal reference for ^{1}H and ^{13}C NMR spectra and $BF_3{\cdot}Et_2O$ as the external reference for ^{11}B NMR spectra. Molecular weights were determined by the Rast camphor method. Nitrogen and sulphur were estimated by Kjeldahl's and Messenger's methods, respectively. Boron was estimated as boric acid in the pressure of mannitol using phenolphthalein as an indicator.

Antimicrobial screening

Bioefficacy of the synthesized complexes were tested *in vitro* and *in vivo*. *In vitro*, tests were conducted using the radial-growth method and the paper-disc plate method. *In vivo*, tests were conducted in the field on bajra (Rust) using the percentage disease incidence (PDI) technique.

Antifungal activity (radial-growth method)

Fungi were grown in PDA medium (glucose 20 g, starch 20 g, agar agar 20 g and 1000 ml of distilled water) at 25 ± 2 °C and the compounds, after being dissolved at 50, 100 and 200 ppm concentrations, were mixed in the medium. The medium was then poured into Petri discs and a small disc (0.7 cm) of the fungus culture was cut with a sterile cork-borer and transferred aseptically to the centre of a Petri disc containing the medium with the compound. Controls were kept, in which the culture discs were grown under the same conditions on PDA without the compound. These Petri discs were wrapped in polythene bags and placed in an incubator operating at the same temperature. The linear growth of the fungus was obtained by measuring the diameter of the colony in the Petri discs after four days (96 h) and 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 discs, respectively.

Antibacterial activity (paper-disc plate method)

The nutrient agar medium (peptone 5 g, beef extract 5 g, NaCl 5 g, agar agar 20 g and 1000 ml of distilled water) prepared at 28 ± 2 °C and 5 mm diameter paper discs of Whatman No. 1 were used. The compounds were dissolved in dry methanol at

500 and 1000 ppm concentrations. Filter-paper discs were soaked in different solutions of the compounds, dried and then placed in the Petri discs previously seeded with the test organism. The plates were incubated for 24–30 h at the same temperature and the inhibition around each disc was measured in millimetres.

Percentage disease incidence technique (antifungal activity *in vivo*)

For studying the efficacy of the present ligands, field experiments were laid out in randomized block design with three replications. The bajra plants were raised in each plot. Plants exposed to a standard fungicide, Bavistin [2-(methoxycarbamoyl)benzimidazole] were used in addition as controls (water spray).

Forty five days after sowing, the plants were inoculated artificially, late in the evening, by spraying the conidial suspension, which had been was prepared by crushing infected leaves in water. The initial spray of the each fungicide was given when lesions were first seen and spraying was repeated after 10 days. Disease intensity was recorded 10 days after the second spraying. The data were analysed statistically and disease control (%) was calculated.

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