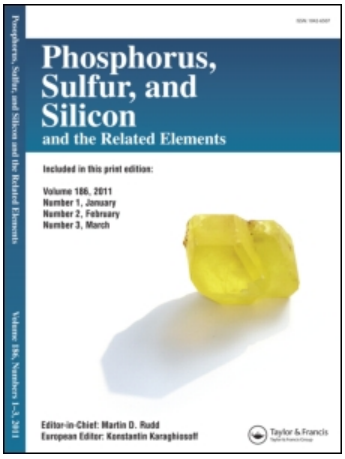

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NOVEL BIOACTIVE THIO- AND SEMICAR-BAZIDE LIGANDS AND THEIR ORGANOSILICON(IV) AND ORGANOTIN(IV) COMPLEXES

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NOVEL BIOACTIVE THIO- AND SEMICARBAZIDE LIGANDS AND THEIR ORGANOSILICON(IV) AND ORGANOTIN(IV) COMPLEXES

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Stereochemical and biochemical aspects of organosilicon(IV) and organotin(IV) complexes with thio- and semicarbazide ligands having NS and NO donor systems are described with the support of elemental analysis, IR, ^{1}H, ^{13}C NMR, ^{29}Si NMR, ^{119}Sn NMR and ^{19}F NMR spectroscopy. From the analysis of these studies the donor sites of ligands are located and the geometries of donor environment around the satin(IV) and silicon(IV) acceptor centres proposed. The ligands and their metal complexes are tested *in vitro* and *in vivo* by a new technique against a number of pathogenic fungal and bacterial strains and the findings are discussed.

Keywords: Silicon(IV) complexes; tin(IV) complexes; thio- ligands; guar blight; spectral studies; biological screening

INTRODUCTION

Considerable efforts have gone into the search for highly active chiral reagents to develop and promote the biocidal activity of different systems. The reason for application of fluoro-organometallic compounds in the pharmaceutical field is due to positive results in microbial activity.[1] This has also been supported by the available literature.[2] It appears that fluorine can alter the activity of molecules or make them specific irreversible enzyme inhibitors.[3] The interest in organosilicon(IV) compounds is due to their versatile applicability in the pharmaceutical industries. Lukevics et. al.[4] reported anticancer properties of several quinoline derivatives. Generally, organosilicon compounds seem to owe

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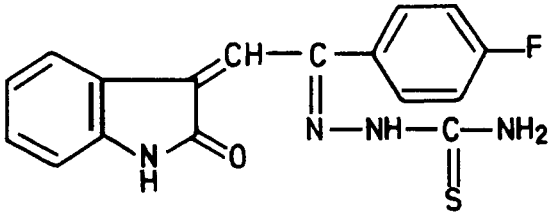
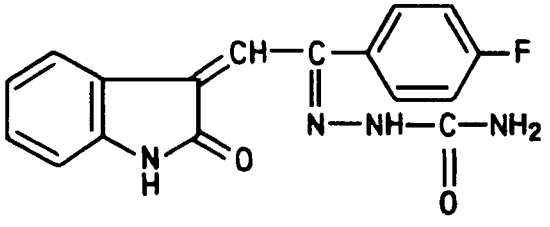
their antitumour properties to the immuno defensive system of the organism.[5] Organotin compounds having the formula R_nSnX_{4-n} have been found to possess significant biological activity and are used as fungicides,[6,7] bactericides, and antitumour[8] agents. Several reports have appeared on the complexes of di and tri-organotin halides with various nitrogen and oxygen/sulphur containing ligands. Encouraged by these findings and our interest in the field of organosilicon and organotin complexes two ligands and their silicon and tin complexes have been prepared and characterized. Ligands and their corresponding metal complexes have also been screened against several pathogens and a comparative account of their activities (ligand vs. complex) and structure activity relationship have been incorporated in the present results.

Ligands used are:



(L_1H)

1,3-Dihydro-3-[2-(4-fluorophenyl)-2-oxo-ethylidene]-2H-indol-2-one-hydrazinecarbothioamide.



(L_2H)

1,3-Dihydro-3-[2-(4-fluorophenyl)-2-oxo-ethylidene]-2H-indol-2-one-hydrazinecarboxamide.

RESULTS AND DISCUSSION

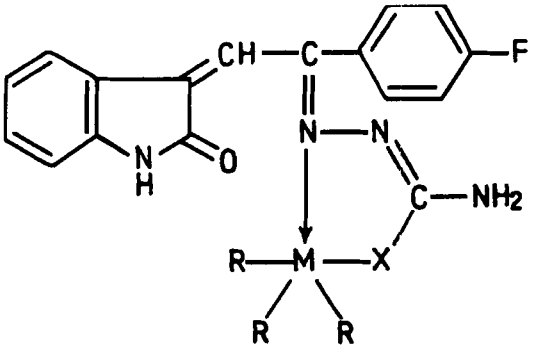
Reactions of organosilicon(IV) and organotin(IV) halides with monobasic bidentate ligands in 1:1 molar ratio in methanol may be represented by the following equations:

$$R_3MCl + NS.Na \xrightarrow{1:1} R_3M(NS) + NaCl$$

$$R_3MCl + NO.Na \xrightarrow{1:1} R_3M(NO) + NaCl$$

(where, M = Si or Sn and R = Me or Ph)

Possible structure of the complexes—



(where R = Me or Ph; X = S or O and M = Sn or Si)

IR Spectra

The IR spectra of complexes do not show any band in the region 3250–3100 cm^{-1} which could be assigned to ν NH. This clearly indicates the deprotonation of the ligands as a result of complexation with the metal atom. Sharp bands at 1620 cm^{-1} and 1615 cm^{-1} are due to ν (>C=N) in the ligands L_1H and L_2H, respectively, which shift to the lower frequency (ca. 15 cm^{-1}) in case of silicon compounds and to higher frequency (ca. 10 cm^{-1}) in the tin compounds, indicating the coordination of the azomethine nitrogen to the metal atoms. A shift of this frequency to the higher[11] and lower[12] wavenumber side as well as no change has also been reported in the literature.[13]

Several new bands are observed in the spectra of the silicon complexes at ca. 620 cm^{-1}, 580 cm^{-1} and 540 cm^{-1} for ν (Si-O),[14] ν (Si←N)[15] and ν (Si-S)[16] vibrations, respectively. These remain absent in the spectra of both the ligands. In case of the tin complexes new bands for ν (Sn-O), ν (Sn←N) and ν (Sn-S) vibrations are observed at ca. 530 cm^{-1}, 420 cm^{-1} and 325 cm^{-1}, respectively.

TABLE I ^{1}H NMR spectral data (δ, ppm) of ligands and their corresponding Organotin(IV) and Organosilicon(IV) complexes

Compound	*NH (ring)*	*NH (free)*	*NH_2*	*> C=N*	*Aromatic*
L_1H	11.08	10.04	3.16	8.08	7.94–7.54
$Ph_3Sn(L_1)$	11.16	–	3.52	8.12	8.12–7.64
$Me_3Sn(L_1)$	11.32	–	3.64	8.24	8.24–7.72
$Ph_3Si(L_1)$	11.24	–	3.46	8.36	8.48–7.96
$Me_3Si(L_1)$	11.84	–	3.72	8.40	8.40–7.56
L_2H	10.04	9.72	3.04	7.16	6.95–6.16
$Ph_3Sn(L_2)$	10.16	–	3.12	7.24	6.56–6.32
$Me_3Sn(L_2)$	10.46	–	3.08	7.56	7.08–6.56
$Ph_3Si(L_2)$	10.54	–	3.16	7.72	7.16–6.72
$Me_3Si(L_2)$	10.72	–	3.52	7.96	7.24–6.96

^{1}H NMR Spectra

The proton magnetic resonance spectral data of hydrazine carboxamide and hydrazinecarbothioamide of the fluoro moiety have been recorded in DMSO-d_6. The chemical shift values relative to the TMS peak are listed in Table I.

The disappearence of -NH proton signals from compounds clearly indicates the deprotonation of the NH group after the substitution reaction.

^{13}C NMR Spectra

The conclusions drawn from the IR and ^{1}H NMR spectra are in agreement with the ^{13}C spectral data regarding the authenticity of the proposed structures. The chemical shift values of the carbon atom attached with the azomethine nitrogen, thiolic sulphur or amido oxygen lends further support to the proposed coordination in these complexes. The ^{13}C NMR spectra of ligands L_1H, L_2H and their metal complexes have been recorded in Table II.

^{19}F NMR Spectra

The ^{19}F NMR spectra of ligand (L_1H) displays a sharp singlet at δ −114.36 ppm. The organometal complexes of these ligands show no change in the position of signals, thus supporting the non-involvement of fluorine in complexation.

^{119}Sn and ^{29}Si NMR Spectra

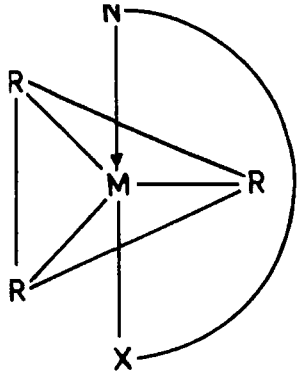
The ^{29}Si and ^{119}Sn NMR spectra of complexes $Ph_3Si(L_1)$ and Ph_3Sn give sharp signals at δ −92.05 and −138.08 ppm, respectively, indicating the penta- coordinated environment around the silicon and tin atoms.

TABLE II ^{13}C NMR spectral data (δ, ppm) of ligands and their corresponding metal complexes

Compound	*Amido/Thiolo carbon*	*Azomethine carbon*	*HNCO (cyclic imide gp)*	*Aromatic carbons*	*M—Me/Ph*
L_1H	178.62	167.66	167.50	148.08, 144.05, 136.25 135.71, 133.22, 132.13	–
$Ph_3Sn(L_1)$	168.34	157.38	165.86	150.10, 141.40, 130.60 131.50, 131.20, 129.80	128.13, 130.04 136.80, 136.92
$Ph_3Si(L_1)$	167.42	148.24	159.48	145.50, 135.07, 129.50 126.30, 127.60, 122.99	130.18, 134.26 133.24, 136.17
L_2H	167.65	162.25	157.32	148.80, 146.51, 132.40 130.10, 129.70, 121.80	–
$Me_3Sn(L_2)$	164.58	152.56	154.04	148.76, 145.07, 135.07 130.60, 129.80, 126.90	18.16
$Me_3Si(L_2)$	159.73	145.50	146.20	143.66, 135.70, 129.64 126.72, 123.52, 122.40	15.56

where M = Sn or Si.

On the basis of the results so far discussed including the analytical as well as spectral data, suitable pentacoordinated trigonal bipyramidal geometry are suggested for the 1:1 metal derivatives.



where, X = S or O; R = Me or Ph and M = Sn or Si.

Pentacoordinated environment in these complexes further gets support by the 1:1 molar reaction of these compounds with pyridine. $Ph_3Si(L_1)$ and $Ph_3Sn(L_2)$ are reacted with equimolar amount of pyridine. The resulting products $Ph_3Si(L_1)$.py and $Ph_3Sn(L_2)$.py were isolated. Their ^{29}Si NMR and ^{119}Sn NMR spectra give signals at δ -124.70 and -310.46 ppm, respectively, and which clearly establish the hexacoordinated environment around the metal atoms in these complexes. However, X-ray crystal structure could not be studied as the complexes are isolated in amorphous powder form.

MICROBIAL ASSAY

Bioefficacies of the synthesized compounds were tested **in vitro** and **in vivo**. **In vitro** test was conducted using spore germination method. Inhibition was measured by using the paper disc technique and food poisoning technique.[18]

In vivo tests were conducted in field conditions, on Guar (Guar blight) and Bajra (rust). Disease severity was measured using the reported standard scale[19] for the same diseases and the Peterson for the rust. The percent disease incidence (PDI) was calculated using the following formula:

$$\text{PDI} = \frac{\text{Sum of the numerical values of leaves/plants} \times 100}{\text{Number of leaves / plants observed} \times 10}$$

The effectiveness of the chemicals were calculated using the following formula

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

The mechanism of toxicity of these complexes to microorganisms may be due to inhibition of energy production or ATP production,[20] for instance by inhibition of respiration or by uncoupling of oxidative phosphorylation. The energy producing processes are located partly in the cytoplasm and partly in the mitochondria. Strong inhibition of such processes will eventually have a drastic microbial effect.

Guar blight: Diseased leaves were graded using the Horsfall and Barratt scale which is as follows:

Scale	*Area affected by the disease*		
1	0%	7	50–75%
2	0–3%	8	75–87%
3	3–6%	9	87–94%
4	6–12%	10	94–97%
5	12–25%	11	97–100%
6	25–50%	12	100% disease

The efficacy of compounds against Guar blight was evaluated using the percent disease incidence technique (PDI).

Treatment	*PDI in treated plants*	*% Disease control*
L_1H	12	57.1
$Ph_3Sn(L_1)$	5	82.1
$Me_3Sn(L_1)$	7	75.0
$Ph_3Si(L_1)$	6	78.6
$Me_3Si(L_1)$	9	67.8
L_2H	14	50.0
$Ph_3Sn(L_2)$	7	75.0
$Me_3Sn(L_2)$	8	71.4
$Ph_3Si(L_2)$	8	71.4
$Me_3Si(L_2)$	10	64.2

Percent disease incidence in untreated plants was

$$= \frac{\text{Sum of the numerical values of plants} \times 100}{\text{Number of plants observed} \times 10}$$

$$= \frac{42 \times 100}{15 \times 10} = 28.$$

RESULTS

All the complexes along with the parent ligands have been tested on Guarblight and rust. The results revealed that activity increased on complexation, i.e., the newly synthesized complexes were found to be more active in inhibiting the growth of pathogens, than the parent ligands themselves.

EXPERIMENTAL

All the chemicals were dried and purified before use and the reactions were carried out with a distillation assembly, fitted with condenser and protected from moisture using $CaCl_2$ drying tubes. Preparation of ligands. Ligand 1,3-dihydro-3-[2-(4-fluorophenyl)-2-oxo-ethylidene]-2H-indol-2-one-hydrazinecarbothioamide was prepared by condensation of reactant with thiosemicarbazide in 1:1 molar ratio in alcoholic medium. The contents were refluxed for 45 minutes, recrystallised from the same solvent and dried under reduced pressure.

Ligand 1,3-dihydro-3-[2-(4-fluorophenyl)-2-oxo-ethylidene] 2H-indol-2-one-hydrazinecarboxamide was prepared by condensation with semicarbazide in presence of sodium acetate in equimolar ratio in absolute alcohol. The contents were refluxed, recrystallised and dried.

Synthesis of Complexes

A calculated amount of sodium salt of ligand in dry methanol was added to the organotin- and organosilicon halides in 1:1 molar ratio. The contents were refluxed over a ratio-head for 16–18 hours and the white precipitate of sodium chloride obtained, was removed under suction. Compounds were dried under reduced pressure for 3–4 hours. These were purified by repeated washing with **n**-hexane and ether. All the compounds were isolated as powdered solids. The details of these reactions and the analysis of the resulting products are recorded in Table III.

Analytical methods and physical measurements. Carbon and hydrogen analysis were performed at the microanalytical laboratory of the department. Nitrogen and sulphur were estimated by Kjeldahl's and Messenger's methods, respectively. Tin and Silicon were determined gravimetrically as SnO_2 and SiO_2. The conductance was measured by conductivity bridge type 304 systronics model and the molecular weights were determined by the Rast Camphor method. IR spectra were recorded on FTIR spectrophotometer, model megna IR -550

TABLE III Physical properties of ligands and their Organosilicon(IV) and Organotin(IV) complexes

Compound	*Analyses %*				
	Colour	*M.P. (°C)*	*Si/Sn Found (calc.)*	*N Found (calc.)*	*S Found (calc.)*
L_1H	Orange	182–185	–	16.15 (16.46)	9.13 (9.42)
Ph_3SnL_1	Brown	203–206	17.12 (17.21)	8.02 (8.12)	4.13 (4.65)
Me_3SnL_1	Brown	186–189	23.08 (23.59)	11.01 (11.16)	6.45 (6.37)
Ph_3SiL_1	Light brown	210 (d)	4.25 (4.69)	9.22 (9.36)	5.18 (5.35)
Me_3SiL_1	Peach	198–201	6.36 (6.85)	13.29 (13.68)	7.41 (7.83)
L_2H	Orange	150–153	–	17.09 (17.27)	–
Ph_3SnL_2	Reddish-brown	195–198	17.12 (17.62)	8.12 (8.32)	–
Me_3SnL_2	Light brown	140–143	24.09 (24.36)	11.15 (11.50)	–
Ph_3SiL_2	Light brown	186–188	4.50 (4.81)	9.23 (9.51)	–
Me_3SiL_2	Orange	135–138	7.02 (7.13)	14.12 (14.24)	–

as nujol mulls using KBr optics. ^1H and ^{19}F NMR spectra were recorded in DMSO-d_6, ^{13}C, ^{119}Sn and ^{29}Si were recorded in methanol, using TMS as the internal/external standard for ^1H, ^{13}C, ^{119}Sn and ^{29}Si NMR spectra and C_6F_6, $(CH_3)_3$ SnCl as the external reference for the ^{19}F and ^{119}Sn NMR spectra, respectively.

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