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Triorganosilicon(IV) Complexes as Biocides: Synthetic, Spectroscopic and Biological Studies of N⌒SH and N⌒OH Fluoroimines and their Chelates

Chitra Saxena and R. V. Singh*
Department of Chemistry, University of Rajasthan, Jaipur-302004, India

A facile synthesis and study of the stereochemistry and biochemical aspects of some triorganosilicon(IV) complexes derived from fluoroimines having N⌒S and N⌒O systems are reported. The fluoroimines were prepared by the condensation of 2-fluorobenzaldehyde and 1-(2-fluorophenyl)ethanone with semicarbazide and thiosemicarbazide. These imines react with triorganosilicon(IV) chlorides to yield compounds having Si—O/Si—S and Si←N bonds. The structures of the compounds have been elucidated by physicochemical and spectral (UV, IR, ^{1}H NMR, ^{13}C NMR and ^{9}F NMR) studies which clearly point to a trigonal bipyramidal geometry around silicon(IV), as the active lone pair of nitrogen is also included in the coordination sphere. In the search for better fungicides and bactericides, studies were conducted to assess the growth-inhibiting potential of the synthesized complexes against various pathogenic fungal and bacterial strains. These studies demonstrate that the concentrations reached levels which are sufficient to inhibit and kill the pathogens.

Keywords: triorganosilicon(IV) complexes; fluoroimines; spectroscopic studies; fungicidal and bactericidal activities

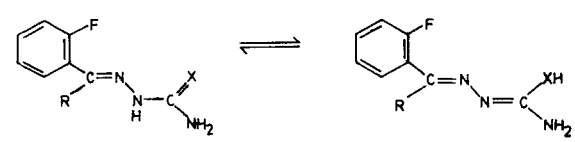
INTRODUCTION

Tetrahedral geometry dominates the structural chemistry of organometallic halides of silicon (R_nMX_{4-n}; $n = 1–3$; R = Me, Ph; M = Si), which exhibit this stereochemistry in all the three phases.[1] However, many five-coordinated silicon halides have also been characterized[2–4] and there are recent examples illustrating the trigonal bipyramidal geometry typically adopted by such compounds. Lukevics *et al.*[5,6] reported anticancer properties for several quinoline derivatives bearing a trialkylsilyl group towards a panel of animal tumour systems including Ehrlich ascites tumour, L5178 leukemia and Lewis lung carcinoma. 2-Trimethylsilylethylthioethylamine inhibited the growth of cancer cells *in vitro* and was highly active *in vivo*.[7,8] Generally, organosilicon compounds seem to owe their antitumour properties to the stimulation of the immunodefensive system of the organism.[9,10]

Fluoroorganometallic compounds are applied in the pharmaceutical field because of their positive results in biological activity.[11] This has also been supported by the available literature.[12] It appears taht fluorine can possibly alter the general activity of substrate molecules or make them specific irreversible enzyme inhibitors.[13]

An objective of the present work is to highlight a systematic study of the stereochemical and biochemical aspects of silicon complexes of fluoroimines. All the complexes, along with their ligands, have been tested *in vitro* against various pathogenic fungi, viz. *Aspergillus niger*, *Fusarium oxysporum* and *Macrophomina phaseolina* and bacteria, viz. *Escherichia coli*, *Klebsiella aerogenous*, *Pseudomonas cepacicola* and *Staphylococcus aureus*. The results of these investigations seem to be promising.

Based on the coordination sites available in the ligand systems, they may be classified as monobasic bidentate as shown in Eqn [1].



R = H or CH_3
X = O or S

[1]

* Author to whom correspondence should be addressed.

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Table 1 Analysis and physical properties of fluoroimines and triorganosilicon(IV) complexes

Compound[a]	Colour	M.p. (°C)	Yield (%)	Analysis (%)[b] N Found (Calcd)	S Found (Calcd)	Si Found (Calcd)	Mol. wt Found (Calcd)
L_1H	Off-white	218	80	23.02 (23.19)	—	—	170 (181)
$Me_3Si(L_1)$	White	224d	62	16.48 (16.59)	—	10.97 (11.09)	278 (253)
$Ph_3Si(L_1)$	Cream	226d	70	9.44 (9.56)	—	6.23 (6.39)	452 (440)
L_2H	White	190	84	21.15 (21.30)	16.18 (16.26)	—	215 (197)
$Me_3Si(L_2)$	Cream	154	68	15.48 (15.60)	11.79 (11.90)	10.26 (10.42)	251 (269)
$Ph_3Si(L_2)$	Light brown	162–164	70	9.07 (9.22)	7.17 (7.04)	6.02 (6.16)	432 (456)
L_3H	White	194	88	21.61) (21.53)	—	—	209 (195)
$Me_3Si(L_3)$	Cream	164–166	70	15.45 (15.72)	—	10.38 (10.50)	250 (267)
$Ph_3Si(L_3)$	White	180	77	9.11 (9.26)	—	6.03 (6.19)	484 (454)
L_4H	White	122	86	20.00 (19.89)	15.03 (15.18)	—	229 (211)
$Me_3Si(L_4)$	Cream	176–179	72	14.67 (14.83)	11.16 (11.31)	9.57 (9.91)	310 (283)
$Ph_3Si(L_4)$	Light brown	220	76	8.83 (8.95)	6.57 (6.83)	5.46 (5.98)	432 (470)

[a] L_1H, 1-(2-fluorophenylmethylene)semicarbazide; L_2H, 1-(2-fluorophenylmethylidene)thiosemicarbazide; L_3H, 1-(2-fluorophenylethylidene)semicarbazide; L_4H, 1-(2-fluorophenylethylidene)thiosemicarbazide.

[b] Satisfactory C and H analyses was also obtained.

EXPERIMENTAL

Adequate care was taken to keep the organosilicon(IV) complexes, chemicals and glass apparatus free from moisture. Clean and well-dried glass apparatus fitted with Quickfit interchangeable standard ground joints was used throughout the experimental work. All the chemicals and solvents used were dried and purified by standard methods.

Preparation of ligands

The fluoroimines were prepared by the condensation of 2-fluorobenzaldehyde and 1-(2-fluorophenyl)ethanone with semicarbazide in the presence of sodium acetate and thiosemicarbazide in equimolar ratios in absolute alcohol. The contents were refluxed for 45 min, recrystallized from the same solvent and dried under reduced pressure. The physical properties and microanalysis of these fluoroimines are recorded in Table 1.

Synthesis of triorganosilicon(IV) complexes

For the preparation of these complexes, triorganosilicon chloride (Me_3SiCl or Ph_3SiCl) and the potassium salt of the fluoroimine in a 1:1 molar ratio were refluxed in dry methanol for about 15–17 h. The white precipitate of potassium chloride, formed during the course of the reaction was removed by filtration and the filtrate was dried under reduced pressure. The resulting product was repeatedly washed with petroleum ether and then finally dried at 40–60 °C/0.5 mm for 3–4 h. The purity was further checked by TLC using silica gel-G. The details of these reactions and the

analyses of the resulting products are recorded in Table 1.

Analytical methods and physical measurements

The analytical procedures and details adopted for the nitrogen and sulphur or oxygen donor fluoroimines and their respective triorganosilicon(IV) complexes are conventional and details are reported in a previous publication.[14]

Biocidal activity

A culture of the test organism was grown on PDA media (starch, glucose, agar-agar and water for fungi) and agar media (peptone, beef extract, agar-agar, NaCl and water for bacteria) for seven days at the optimum temperature for growth. All the glassware used was sterilized in an autoclave before use. The radial growth method and the paper-disc plate method were employed to evaluate the fungicidal and bactericidal activities, respectively.[15]

RESULTS AND DISCUSSION

The substitution reactions of Me_3SiCl and Ph_3SiCl with the potassium salts of the monobasic bidentate fluoroimines have been carried out in a 1:1 molar ratio in dry methanol; they proceed as shown in Eqns [2] and [3].

$$R_3SiCl + N\overset{\frown}{}S.K \rightarrow R_3Si(N\overset{\frown}{}S) + KCl \quad [2]$$

$$R_3SiCl + N\overset{\frown}{}O.K \rightarrow R_3Si(N\overset{\frown}{}O) + KCl \quad [3]$$

R = Me or Ph, $N\overset{\frown}{}S$ or $N\overset{\frown}{}O$ denotes the deprotonated form of fluoroimine

The newly synthesized derivatives are white to light-yellow solids, soluble in common organic solvents and susceptible to moisture. The bonding pattern of these monomeric non-electrolytes (10–15 $\Omega^{-1}\,cm^{-2}\,mol^{-1}$ in dry dimethylformamide) has been deduced on the basis of electronic, infrared and multinuclear NMR (^1H, ^{13}C and ^{19}F) spectroscopic studies.

Spectral studies

UV spectra

The bands around 265 and 305 nm in the ligands remain almost unchanged in the triorganosilicon(IV) complexes and these are assigned to π–π^* electronic transitions within the benzenoid ring[16] and azomethine grouping.[17] However, the band around 370 nm due to n–π^* transitions within the azomethine group is shifted to lower wavelength in the complexes. Such a shift in the n–π^* band is probably due to the donation of the lone pair of electrons by the nitrogen of the fluoro ligand to the central metalloid atom.

IR spectra

On comparing the IR spectra of the ligands and the corresponding silicon complexes, it can be concluded that chelate formation takes place through the sulphur/oxygen and nitrogen atoms of the ligand moieties. In the IR spectra of the ligands, a broad band in the region 3280–3100 cm^{-1} may be assigned to NH stretching vibrations. These bands disappear in the spectra of the resulting derivatives, indicating possible deprotonation of the ligands on complexation and formation of Si—S or Si—O and Si←N bonds. All the ligands display a strong and sharp band at ca 1620 cm^{-1} which is due to the $\rangle C{=}N$ stretching frequency in the free ligands. It shifts to a lower-frequency[18] region (~20 cm^{-1}) in the spectra of the complexes. The appearance of new bands at ca 620 cm^{-1}, 575 cm^{-1} and 545 cm^{-1} in the spectra of the silicon complexes may be assigned to ν(Si—O),[19] ν(Si←N)[20] and ν(Si—S)[21] vibrations, respectively, thus lending support to the proposed coordination in the complexes. Further, medium to strong intensity bands at ca 1430, 1115, 720 and 685 cm^{-1} are due to Si—Ph[22] vibrations. The band in the region 765–750 cm^{-1} may be assigned to Si—CH_3[23] stretching vibrations.

^1H NMR spectra

The mode of bonding discussed above receives further support from ^1H NMR spectral studies. The ^1H NMR spectra of the fluoro ligands and their respective silicon complexes were recorded in DMSO-d_6 and the chemical shift values (δ, ppm) of different protons are listed in Table 2. The disappearance of the NH proton signals of the fluoroimines in the case of the silicon complexes indicates the removal of a proton from the NH group and the coordination of nitrogen, with simultaneous covalent bond formation by sulphur or oxygen with silicon. The azomethine proton and azomethine methyl protons undergo deshielding in the trimethyl- and triphenylsilicon(IV) complexes, supporting the donation of

Table 2 ^{1}H NMR data (δ, ppm) of fluoroimines and their corresponding triorganosilicon(IV) complexes

Compound	—NH (bs)[a]	—NH_2 (bs)	H—C=N / H_3C—C=N or (s)[a]	Aromatic (m)[a]	Si—Me/Ph
L_1H	11.67	2.35	8.42	7.68–6.65	—
$Me_3Si(L_1)$	—	2.36	8.84	7.72–6.78	0.55
$Ph_3Si(L_1)$	—	2.38	8.74	7.80–6.80	6.54
L_2H	11.24	2.16	8.33	7.78–6.70	—
$Me_3Si(L_2)$	—	2.18	8.68	7.84–6.82	0.58
$Ph_3Si(L_2)$	—	2.16	8.76	7.92–6.78	6.48
L_3H	9.30	3.08	1.88	7.52–6.16	—
$Me_3Si(L_3)$	—	3.06	2.14	7.72–6.34	0.78
$Ph_3Si(L_3)$	—	3.04	2.12	7.84–6.44	6.16
L_4H	10.24	3.16	2.12	8.28–6.92	—
$Me_3Si(L_4)$	—	3.16	2.36	8.36–7.08	0.96
$Ph_3Si(L_4)$	—	3.12	2.38	8.38–7.12	6.72

[a] bs, broad singlet; s, singlet; m, multiplet.

a lone pair of electrons by nitrogen to the silicon atom. The presence of new signals in the region δ 0.55–0.96 ppm and δ 6.16–6.72 ppm in the spectra of complexes is due to Me_3Si and Ph_3Si protons, respectively.

^{13}C NMR spectra

The ^{13}C NMR spectra of fluoroimines and their trimethyl- and triphenyl-silicon derivatives, along with the ^{13}C–^{19}F coupling constants for a representative ligand–complex set, L_4H and

Table 3 ^{13}C NMR data (δ, ppm) and ^{13}C–^{19}F compling constants (Hz) of fluoroimines and their respective triorganosilicon(IV) complexes

Compound	Amido or Thiolo	Azomethine	Methyl[a]	Aromatic[a]	Si—Me/Ph
L_1H	175.20	160.24	—	144.18, 129.30, 128.21, 128.85, 127.58, 125.35	—
$Me_3Si(L_1)$	168.24	155.16	—	144.26, 129.41, 128.26 128.82, 125.52, 125.44	16.74
L_2H	179.52	157.38	—	143.66, 127.85, 126.54, 123.34, 122.17, 120.33	—
$Ph_3Si(L_2)$	168.34	148.82	—	143.84, 127.94, 126.49, 123.58, 122.96, 120.64	130.19, 133.24, 137.26, 139.48
L_3H	164.58	156.51	15.88	141.29, 129.64, 129.10 126.72, 123.52, 123.41	—
$Me_3Si(L_3)$	158.36	149.86	16.04	141.48, 129.76, 129.17 126.78, 123.63, 123.58	18.52
L_4H	178.45	147.52	17.34 ($^4J_{CF}$ = 4.88, sd)	131.59 ($^1J_{CF}$ = 155.03, ds), 129.91 ($^2J_{CF}$ = 8.55, sd), 126.50 ($^2J_{CF}$ = 10.99, sd), 124.55 ($^3J_{CF}$ = 3.67, sd), 116.69, 115.72	—
$Ph_3Si(L_4)$	165.23	144.00	16.69 ($^4J_{CF}$ = 4.88, sd)	130.89 ($^1J_{CF}$ = 145.27, ds), 129.64 ($^2J_{CF}$ = 8.55, sd), 127.04 ($^2J_{CF}$ = 10.99, sd), 124.55 ($^3J_{CF}$ = 2.44, sd), 116.48, 115.50	130.51, 132.64, 136.78, 138.56

[a] ds, doublet singlet; sd, singlet doublet.

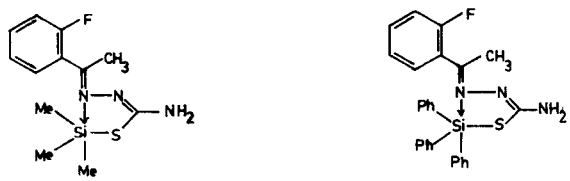

Figure 1 Trigonal bipyramidal geometry of triorganosilicon(IV) complexes

$Ph_3Si(L_4)$, are recorded in Table 3. The marked shifts in the positions of carbon atoms attached to different participating groups in the spectra of complexes compared with the ligands clearly show the bonding of silicon through nitrogen and sulphur/oxygen atoms.

^{19}F NMR spectra

The ^{19}F NMR spectra of 1-(2-fluorophenylethylidene)semicarbazide and 1-(2-fluorophenylethylidene)thiosemicarbazide display a sharp singlet at δ −108.36 and −109.00 ppm, respectively. The triorganosilicon(IV) complexes of these ligands give signals ranging between δ −107.96 and −109.24 ppm, thus suggesting the non-involvement of fluorine in complexation.

Thus, on the basis of the above spectral features, as well as the analytical data, the pentacoordinated trigonal bipyramidal[20] geometry shown in Fig. 1 has been suggested for the triorganosilicon(IV) complexes with 1-(2-fluorophenylethylidene)thiosemicarbazide as the ligand molecule.

Biocidal activity

Fungicidal and bactericidal activities of fluoroimines and their respective triorganosilicon(IV) complexes against pathogenic fungi and bacteria are recorded in Tables 4 and 5.

Mode of action

The degradative enzymes produced by microorganisms are important in host infection, food deterioration and breakdown of organic matter.[24] Enzyme production is here intended to mean both synthesis of the enzyme by the microorganism and activity of the enzyme in the medium after it is produced. Since the triorganosilicon(IV) complexes inhibit the growth of microorganisms, it is assumed that the production of the enzymes is being affected and hence the microorganism is unable to utilize the food for itself, or the intake of nutrients in suitable forms decreases, and consequently the growth ceases. The enzymes which require free sulphydryl groups —SH for activity appear to be especially susceptible to inactivation by ions of the complexes. Due to greater lipoid solubility, the complexes facilitate their diffusion through the spore membrane to the site of action within spores, ultimately killing them by combining with —SH groups of certain cell enzymes.[25] The variation in the effectiveness of different biocidal agents against different organisms as suggested by Lawrence *et al.*[26] depends on the impermeability of the cell.

Table 4 Fungicidal screening data of fluoroimines and their triorganosilicon(IV) complexes

	Average percentage inhibition after 96 h								
	Aspergillus niger			*Fusarium oxysporum*			*Macrophomina phaseolina*		
Compound	50 ppm	100 ppm	200 ppm	50 ppm	100 ppm	200 ppm	50 ppm	100 ppm	200 ppm
Bavistin	91	100	100	86	100	100	82	100	100
L_1H	68	77	80	72	80	84	66	74	78
$Me_3Si(L_1)$	74	86	100	78	90	100	75	88	100
$Ph_3Si(L_1)$	82	100	100	86	100	100	80	100	100
L_2H	70	78	84	74	80	84	69	78	80
$Me_3Si(L_2)$	82	89	100	79	100	100	77	87	100
$Ph_3Si(L_2)$	86	98	100	88	100	100	86	96	100
L_3H	72	78	80	74	79	86	72	81	84
$Me_3Si(L_3)$	76	84	100	80	84	100	86	92	100
$Ph_3Si(L_3)$	90	100	100	94	100	100	91	100	100
L_4H	74	80	86	83	88	92	85	88	92
$Me_3Si(L_4)$	79	88	100	92	100	100	90	96	100
$Ph_3Si(L_4)$	94	100	100	98	100	100	95	100	100

Table 5 Bactericidal screening data of fluoroimines and their triorganosilicon(IV) complexes

	Diameter of inhibition zone (mm) after 24 h							
	Escherichia coli (−)		*Klebsiella aerogenous* (−)		*Pseudomonas cepacicola* (−)		*Staphylococcus aureus* (−)	
Compound	500 ppm	1000 ppm	500 ppm	1000 ppm	500 ppm	1000 ppm	500 ppm	1000 ppm
Streptomycin	17	18	3	5	2	3	15	17
L_1H	4	6	5	7	4	7	7	10
$Me_3Si(L_1)$	5	7	6	9	6	10	9	12
$Ph_3Si(L_1)$	7	10	8	10	7	12	11	14
L_2H	5	8	6	8	6	9	9	12
$Me_3Si(L_2)$	7	11	8	10	8	13	12	15
$Ph_3Si(L_2)$	8	13	9	13	11	14	14	18
L_3H	5	9	6	8	7	10	10	14
$Me_3Si(L_3)$	7	10	7	9	8	11	12	15
$Ph_3Si(L_3)$	8	12	9	11	10	14	14	17
L_4H	7	10	7	10	8	12	12	16
$Me_3Si(L_4)$	9	13	9	12	10	14	14	17
$Ph_3Si(L_4)$	9	14	10	13	12	15	15	18

The toxicity of triorganosilicon(IV) complexes can be well understood by a consideration of chelation theory. Chelation reduces the polarity of the central ion mainly because of partial sharing of its positive charge with the donor groups, and possible π-electron delocalization within the whole chelate ring. This form of chelation increases the lipophilic character of the central atom, favouring its permeation through the lipid layer of the membrane.[27]

In bactericidal activity, it was observed that the complexes were more toxic towards Gram(+) strains as compared to Gram(−) strains. The reason is the difference in the structures of the cell walls. The walls of Gram(−) cells are more complex than those of Gram(+) cells. Lipopolysaccharides form an outer lipid membrane and contribute to the complex antigenic specificity of Gram(−) cells.

Further, the results of bioactivity were compared with the conventional fungicide, Bavistin and the conventional bactericide, streptomycin, taken as standards in either case. It is seen that although the fluoro ligands alone were quite toxic, their activity synergized on undergoing complexation. In fungicidal activity, most of the triorganosilicon(IV) complexes were able to inhibit and kill the pathogens at 100 ppm concentration, whilst 200 ppm concentration proved invariably fatal. None of the fungi was able to withstand this concentration. In bactericidal activity, the complexes exhibited remarkable potential in inhibiting the growth of pathogens. Many of the complexes were found to be even more toxic than the standard.

Thus, it can be postulated that further intensive studies of these complexes in this direction as well as in agriculture could lead to interesting results.

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