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Heterobimetallic penta- and hexa-coordinated organotin (IV) complexes at different temperatures

Rajesh Malhotra[a,*], Jyoti Mehta[a], Kiran Bala[b] & Ashok K Sharma[a]

[a]Department of Chemistry, G J University of Science and Technology, Hisar 125 001, India

Email: malhotra_ksrk@yahoo.co.in

[b]Department of Plant Biotechnology, L P University Jalandhar 144 402, India

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The reactions of triorganotin (IV) chloride with ferrocenyl aroylhydrazone derived from condensation of acetylferrocene and aromatic acidhydrazide yield heterobimetallic penta- and hexa-coordinated organotin(IV) complexes of the type $R_3Sn(L)$ and $R_3Sn(HL)Cl$ (where R=Me, Et or Ph HL=ferrocenyl aroylhydrazone). The ligands behave as bidentate, coordinating through carbonyl oxygen and azomethine nitrogen in keto and enolisation of keto form at low temperature and at room temperature respectively. The isolated complexes have been characterized by elemental analysis, molar conductance, infrared and NMR (^1H, ^{13}C and ^{119}Sn) spectral data. The ligands and their organotin complexes have been evaluated for antifungal activity against *Alternaria alternata, Fusarium oxysporum* and *Rhizoctonia solani*, as well as antibacterial activity against gram negative, (*Escherichia coli*) and gram positive bacilli (*Bacilli subtilis*) at 28°C. The activity of the ligands is enhanced on complexation with triorganotin (IV) chloride.

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Considerable importance has been given to the ligands having nitrogen and oxygen as a donor atoms on account of their biological properties. Extensive study have been carried out regarding the complex formation of hydrazone with transition metals[1,2] and organometallic compounds[3] wherein coordination occurs through the iminic nitrogen to the metal. It is noteworthy that biological activity of the ligand is significantly enhanced on complexation with suitable metal ions[4,5]. Ferrocenyl units have invoked as a bonus in the synthesis of new biologically active compounds[6,7]. Ferrocene based ligands show unexpected biological activity such as new ferrocence-chloroquine analogue[8] and ferrocenic artemisinin derivative[9]. The replacement of aryl group with ferrocenyl moiety improves antibiotic activity in the penicillins and cephalosporins. This effect is thought to be due to the conformational flexibility of the ferrocene backbone in the ligand so it can easily cross the cell membrane. Moreover, it is less toxic than aryl counterpart[10].

Organotin compounds show a wide spectrum of biological activity[11,12] and the activity is essentially determined by the number and nature of the organic moiety bound to tin atom. Mono- and diorganotin complexes are biologically less active, whereas triorganotin complexes usually act as powerful biocides. Trioganotin compounds, R_3SnX, are known for having specific action on mitochondrial oxidative phosphorylation; the activity is independent of the X group but dependent on the nature of R group[13], when R=Me or Et, the compounds are most toxic towards mammals but when R=n-octyl, the compound has low activity. Keeping this in mind, we have synthesized complexes of hydrazones having ferrocene moiety with triorganotin (IV) chloride, R_3SnX, (where R=Me, Et or Ph) and studied the effect of complexation on biocidal activity to explore the possibility of their use as potential biocidal agents.

Experimental

All the operations were carried out in the absence of air and moisture on a vacuum line connected to dry nitrogen supply system. The solvents used were dried by the conventional methods. R_3SnCl (R=Me, Et and Ph) and Cp_2Fe of Aldrich were used as such. The ligands and all the triorganotin (IV) chloride complexes obtained at low temperature and room temperature were analysed for C, H, N on Perkin-Elmer model 2400 while Sn and Cl contents were estimated gravimetrically. ^1H NMR spectra of the ligands and their complexes were recorded on Bruker Avance II 400 NMR spectrometer in $CDCl_3$ containing a few drops of DMSO-d_6 using TMS as an internal standard. The ^{13}C NMR spectra of the compounds were obtained in saturated $CDCl_3$ solution (77.0 ppm) along with ^{119}Sn using TMS as an internal standard and tetramethyl tin as external standard. Infrared spectra were recorded as KBr pellets on Biorad FTS-7 infrared spectrophotometer. Molecular weights of the complexes were determined by

cryoscopic method in dry nitrobenzene. Low temperature was maintained using cryo-cool (model CC-100 II, Neslab, Italy).

Preparation of ligand and complexes

Substituted benzoic acid hydrazides were prepared in good yield by condensing corresponding ester with hydrazine hydrate in ethanol. The ligand ferrocenyl aroylhydrazone (HL) was obtained by refluxing the ethanolic solutions of benzoic acid hydrazides with acetyl ferrocene in 1:1 molar ratio for 6 h. The separated solid was filtered and crystallized from ethanol to give the required ligand (yield 60-70%).

A solution of trialkyl/triaryl tin(IV) chloride (10 mmol) in 20 ml of dry petroleum ether (40°-60°C) was added with constant stirring to a solution of ferrocenyl aroylhydrazone (10 mmol) in 20 ml of the same solvent, under dry nitrogen atmosphere. The reaction mixture was stirred for 2 h and was then left to stand at room temperature for a day, whereupon a yellow microcrystalline solid was obtained (yield 65-75%). The complexes were then filtered, washed with dry petroleum ether and dried under vacuum.

Ferrocenyl aroylhydrazone (10 mmol) dissolved in 30 ml of petroleum ether was cooled to -40° to -50°C and to it was added the required amount (10 mmol) of R_3SnCl (where R=Me, Et or Ph), in the same solvent cooled to -40°C dropwise with constant stirring, strictly under dry nitrogen atmosphere. The reaction mixture was stirred for 2 h at low temperature and then left to stand at room temperature for a day to yield (60-70%) a yellow solid which was separated by adopting the same procedure as discussed above.

Results and discussion

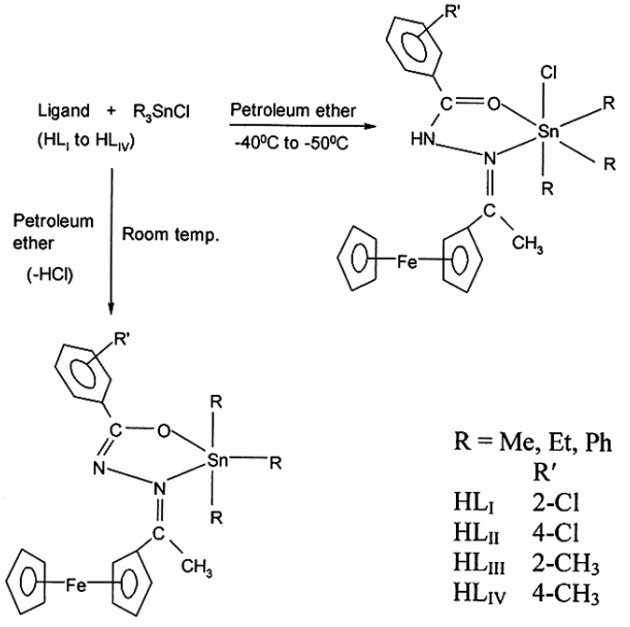
Ferrocenyl aroylhydrazones have been prepared by the condensation reaction of acetyl ferrocene and substituted benzoic acid hydrazide. The homogeneity of the compounds was regularly checked by TLC.

The reaction of triorganotin (IV) chloride R_3SnCl (R=Me, Et, Ph) with ferrocenyl aroylhydrazone in 1:1 molar ratio at -40° to -50°C or at room temperature, in dry petroleum ether afforded the following compounds (Scheme 1).

The analytical data of the complexes obtained at different temperatures are given in Table 1. All the complexes are crystalline solids, insoluble in most of the common organic solvents except in dry DMSO, $PhNO_2$ and DMF. The low molar conductance values (10.0-24.0 Ω^{-1} cm^2 mol^{-1}) in dry DMSO of the triorganotin (IV) chloride complexes isolated at room temperature as well as at low temperature indicates non-electrolytic nature.

IR spectra

The infrared spectra of the complexes were compared with that of the ligands and the coordination sites were ascertained on the basis of shifts in the frequency of various groups and/or from the intensity lowering. The infrared spectra of the ligands showed bands at 3320, 1640-1650, 1600-1605 and 990 cm^{-1} which may be assigned to ν (NH), ν (C=O), ν (C=N) and ν (N-N) respectively. The characteristic bands of ferrocene group which appeared at 3060, 1390, 740 and 470 cm^{-1} in the ligands remained unaltered on complexation. The shift in the absorption bands due to ν C=O and ν C=N in the complexes isolated at low temperature, (-40° to -50°C), to lower frequency by 10-15 and 15-20 cm^{-1} respectively indicates that coordination in keto form has indeed taken place through oxygen and nitrogen of these groups. This fact is in agreement with the fact that 1, 3-diketones coordinate to tin (IV) halides in unenolised from at low temperature[14]. Of the two nitrogens of azomethine group, coordination through N(2) (nitrogen of terminal azomethine group) is suggested as it gives rise to stable five-membered ring with lesser strain as compared to that of four membered ring which would be formed on coordination through other nitrogen. In the complexes



Scheme 1

Table 1—Analytical data of triorganotin (IV) chloride complexes

No.	Comp.	Yield (%)	Found (Calc.) (%)					Mol. wt.
			C	H	N	Sn	Cl	
1.	Me_3SnCl (HL_I)	70	45.2 (45.5)	4.1 (4.48)	4.5 (4.8)	20.3 (20.5)	5.9 (6.1)	595 (580)
2.	Me_3SnCl (HL_{II})	75	45.8 (45.5)	4.1 (4.5)	4.6 (4.8)	20.8 (20.5)	6.2 (6.1)	570 (580)
3.	Me_3SnCl HL_{III})	68	49.0 (49.3)	4.8 (5.2)	5.3 (5.0)	6.1 (6.3)	6.4 (6.3)	545 (559.5)
4.	Me_3SnCl HL_{IV})	72	49.7 (49.3)	5.4 (5.2)	4.8 (5.0)	6.0 (6.3)	6.3 (6.3)	565 (559.5)
5.	Et_3SnCl (HL_I)	72	48.0 (48.2)	5.5 (5.1)	4.8 (4.5)	19.4 (19.1)	5.8 (5.7)	610 (622)
6.	Et_3SnCl (HL_{II})	75	48.6 (48.2)	5.4 (5.1)	4.2 (4.5)	19.4 (19.1)	5.4 (5.7)	640 (622)
7.	Et_3SnCl (HL_{III})	69	51.5 (51.8)	5.5 (5.8)	4.9 (4.7)	19.4 (19.8)	6.1 (5.9)	610 (601.5)
8.	Et_3SnCl (HL_{IV})	67	52.0 (51.8)	5.4 (5.8)	4.4 (4.7)	19.9 (19.8)	5.8 (5.9)	595 (601.5)
9.	Ph_3SnCl (HL_I)	70	57.5 (57.9)	4.5 (4.2)	3.8 (3.7)	15.1 (15.5)	4.6 (4.6)	780 (766)
10.	Ph_3SnCl (HL_{II})	68	58.2 (57.9)	4.5 (4.2)	3.4 (3.7)	15.8 (15.5)	4.8 (4.6)	755 (766)
11.	Ph_3SnCl (HL_{III})	70	61.3 (61.2)	4.3 (4.7)	3.9 (3.8)	15.5 (15.9)	5.1 (4.8)	760 (745.5)
12.	Ph_3SnCl (HL_{IV})	68	61.4 (61.2)	4.9 (4.7)	3.6 (3.8)	15.7 (15.9)	4.9 (4.8)	735 (745.5)
13.	Me_3Sn (L_I)	69	48.2 (48.6)	4.3 (4.6)	5.4 (5.2)	21.6 (21.9)	-	552 (543.5)
14.	Me_3Sn (L_{II})	75	48.9 (48.6)	4.9 (4.6)	5.5 (5.2)	22.0 (21.9)	-	532 (543.5)
15.	Me_3Sn (L_{III})	71	52.3 (52.8)	5.0 (5.4)	5.6 (5.4)	22.4 (22.8)	-	540 (523)
16.	Me_3Sn (L_{IV})	72	52.3 (52.8)	5.7 (5.4)	5.1 (5.4)	22.9 (22.8)	-	532 (523)
17.	Et_3Sn (L_I)	69	51.6 (51.2)	5.0 (5.3)	4.3 (4.8)	20.7 (20.3)	-	594 (585.5)
18.	Et_3Sn (L_{II})	72	51.0 (51.2)	5.6 (5.3)	4.9 (4.8)	20.6 (20.3)	-	578 (585.5)
19.	Et_3Sn (L_{III})	72	55.4 (55.2)	5.7 (6.0)	4.6 (4.9)	21.3 (21.1)	-	576 (565)
20.	Et_3Sn (L_{IV})	60	55.6 (55.2)	6.4 (6.0)	4.7 (4.9)	20.8 (21.1)	-	554 (565)
21.	Ph_3Sn (L_I)	69	60.4 (60.9)	4.6 (4.2)	3.5 (3.8)	16.6 (16.3)	-	740 (729.5)
22.	Ph_3Sn (L_{II})	72	60.4 (60.9)	4.7 (4.2)	3.9 (3.8)	16.2 (16.3)	-	715 (729.5)
23.	Ph_3Sn (L_{III})	70	64.7 (64.3)	4.5 (4.8)	3.5 (3.9)	16.9 (16.8)	-	720 (709)
24.	Ph_3Sn (L_{IV})	70	64.8 (64.3)	4.4 (4.8)	3.6 (3.9)	16.4 (16.8)	-	695 (709)

Complexes 1 to 12 were obtained at -40° to -50°C, while complexes 13-24 were obtained at room temperature.

isolated at room temperature, the bands attributed to v NH and v C=O disappeared, while four new bands in these complexes appeared at about 1620, 1510, 1350 and 1235 cm^{-1} arising from v (C=N-N=C), v (NCO) and v (C-O). This suggests that the ligand was coordinated to tin atom in enolic form after deprotonation. New bands in the regions 416-421 cm^{-1} and 525-530 cm^{-1} was be due to v (Sn-N) and v (Sn-O) modes, thereby supporting coordination through azomethine nitrogen and oxygen of carbonyl group[15].

NMR spectra

The ^1H, ^{13}C and ^{119}Sn NMR spectra of the ligands and their complexes were recorded in $CDCl_3$ containing a small amount of deuterated dimethyl sulphoxide using TMS as an internal standard and tetramethyl tin as external standard respectively. The spectra of the ligands showed a singlet at 4.2 ppm due to five protons of unsubstituted cyclopentadienyl ring of ferrocene, while a double doublet at 4.5-4.7 ppm was observed due to substituted cyclopentadienyl ring. No variation was observed on complexation with organotin (IV) chloride. The presence of singlet due to –NH group was observed at 9.8 ppm and 9.6 ppm in the spectra of both the free ligand and the complexes (isolated at low temperature -40° to -50°C), respectively, thereby suggesting that the ligand was coordinated to tin atom as neutral keto form. The signal due to –NH group was absent in the complexes isolated at room temperature, indicating that the ligand acted as bidentate through deprotonated enol-form (Scheme 1). The multiplets at 6.9-7.4 ppm were due to aromatic protons. Methyl protons due to H_3C—C=N appeared as singlet at 2.1 ppm. Methyl proton attached to tin atom in complexes as singlet at 0.9 ppm, while the triplet and quartet at 0.8 ppm and 1.2 ppm respectively were due to $–CH_3$ and $–CH_2$ protons of ethyl group, attached to tin. The integrated proton ratio for each group was in agreement with the proposed structures.

The ^{13}C NMR spectra of the complexes were recorded in $CDCl_3$ with a few drops of DMSO-d_6. The unsubstituted cyclopentadienyl ring in the ligands showed one peak at 119.6-120.8 ppm, while the substituted cyclopentadienyl ring showed three signals at around 78, 66 and 64.2 ppm. These peaks remained almost unaltered on complexation with triorganotin halide. The signals due to methyl and

ethyl groups attached to tin atom appeared at 9.8-10.0 and 14.2, 16.3 ppm respectively, while ring carbons of phenyl group attached to tin appeared at 144.5, 132.9, 128.8 and 117.6 ppm. The peaks attributed to the carbon of azomethine (C=N) and carbon of carbonyl (C=O) which appeared at 160.2-162.7 and 189.2-191 ppm respectively was shifted downfield by 8-14 ppm upon reaction with triorganotin (IV) chloride. The signal due to carbon of C-O group in complexes isolated at room temperature was observed at 87.4 ppm, suggesting that ligand was bound to the tin atom after deprotonation. This indicates that coordination had taken place through these groups. Not much variation was observed in the signal due to carbon of methyl group of CH_3-C=N, which remained at 19.9 ppm on complexation.

^{119}Sn NMR spectra of all the complexes isolated at room temperature and low temperature, showed a sharp singlet in the range of -179.6 to -203.6 and -316.2 to -342.8 ppm, which is compatiable with penta- and hexa-coordinated geometry respectively around the tin atom[16].

Antimicrobial activity

In vitro growth inhibitory activity against phytopathogenic fungi, viz., *Alternaria alternata, Fusarium oxysporum* and *Rhizoctonia solani* and bacteria, *Escherichia coli* and *Bacillus subtilis* were studied for all the synthesized ligands and their complexes with triorganotin (IV) chloride by adopting the same procedure as reported earlier[17].

Triorganotin (IV) chloride complexes of ferrocenyl aroylhydrazone of type $R_3Sn(L)$ and $R_3Sn(HL)Cl$ were more active than their parent ligands against the same microorganisms under identical experimental conditions. The increased activity of the complexes may be due to the effect of central ion on the normal cell process, which on chelation increases lipophilic character of the central atom. This favours its permeation through the lipid layer of the membrane, thereby resulting in interference with normal cell process;

$Ph_3Sn(L_I)$ was found to be most active and inhibited growth upto 3.25 ppm against *Fusarium oxysporum* and *Rhizoctonia solani*, while $Ph_3Sn(HL_I)Cl$ was active at 3.25 ppm against *Alternaria alternata* and *Fusarium oxysporum*. Triphenyltin (IV) complexes were more potent than the methyl or ethyl counterpart.

The triorganotin complexes isolated at low temperature (-40° to -50°C i.e. $R_3Sn(HL)$ Cl, were more active than the complexes isolated at room temperature, i.e., $R_3Sn(L)$, indicating that complexes having reactive halogen atom tend to hydrolyse to form compounds that have modified activity spectrum. No definite activity pattern was observed with the change in substituents (R′) on the ligands.

Conventional fungicide and bactericide showed inhibition at concentration less than 3.125 ppm. Some of the compounds showed toxicity against *Rhizoctonia solani* and *Alternaria alternata*, comparable to that of conventional fungicide. No compounds show better inhibitory action than bavistin and streptopenicillin used as conventional fungicide and bactericide.

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