APPLIED ORGANOMETALLIC CHEMISTRY, VOL. 7, 655–660 (1993)

Antimicrobial effects of newly synthesized organotin(IV) and organolead(IV) derivatives

Anita Kumari,* J P Tandon† and R V Singh†

* Department of Chemistry, M.D. University, Rohtak-124001, India, and † Department of Chemistry, University of Rajasthan, Jaipur-302004, India

Triorganotin(IV) and triorganolead(IV) derivatives of the types $Me_3Sn(SCZ)$ and $Ph_3Pb(SCZ)$ (where SCZ^- is the anion of a semicarbazone ligand) have been synthesized by substitution reactions of trimethyltin chloride and triphenyl-lead chloride with semicarbazones derived from heterocyclic ketones. The resulting complexes have been characterized by elemental analyses, molecular weight determinations and conductivity measurements. The mode of bonding has been established on the basis of infrared and ^1H, ^{13}C and ^{119}Sn NMR spectroscopic studies. Some respresentative complexes have also been evaluated for their antimicrobial effects on different species of pathogenic fungi and bacteria; the results of these investigations have been reported in the present paper.

Keywords: Triorganotin(IV) complexes, triorganolead(IV) complexes, semicarbazones, antimicrobial studies, NMR

INTRODUCTION

Organotin compounds are toxic to a variety of micro-organisms and find widespread applications in biocidal compositions. In the past few years, organotin compounds of the type R_3SnX such as trimethyltin chloride, tributyltin chloride, triphenyltin chloride and tributyltin oxides have become well known as broad-spectrum biocides, toxic additives in marine biocidal paints, molluscides, fungicides and other types of pesticides.[1] It is noteworthy that trialkyltin compounds dealkylate in natural environments to oxides of tin.[2]

Similarly, a variety of organolead compounds have also been reported to possess fungicidal as well as bactericidal activities.[3–5] Thioacetyl-triphenyl-lead has been proposed for the treatment of acne, while thiobenzyl- and thiophenyl-triphenyl-lead compounds possess anti-inflammatory properties. It has also been suggested that these are suitable for the treatment of various allergies asthma and influenza.[6] Several organolead compounds find use as good algicides, herbicides and also as anticancerous agents.[7–9]. Our continuing interest in the synthesis of fungicides and bactericides has led us to synthesize a new class of organometal derivatives of tin and lead and to study their activity *in vitro*.

EXPERIMENTAL

All the chemicals used were dried and distilled before use. Glass apparatus fitted with Quickfit interchangeable standard ground joints was used throughout these investigations. Moisture was excluded from the apparatus using calcium chloride drying tubes.

Preparation of ligands

The ligands were prepared by condensation of heterocyclic ketones, i.e. 2-acetylpyridine, 2-acetylfuran, 2-acetylthiophene and 3-acetylindole, with semicarbazide hydrochloride and sodium acetate in 1:1:1 molar ratio in absolute ethanol The complexes were purified by recrystallization from the same solvent and analysed before use.

Preparation of complexes

A weighed amount of trimethyltin chloride or triphenyl-lead chloride was dissolved in approximately 30 cm^3 of dry methanol in a 100-cm^3 round-bottom flask. To this was added the calculated amount of the potassium salt of the ligand (Prepared by reaction of the calculated amount of freshly cut potassium metal with ligand in dry methanol) in 1:1 molar ratio. The reaction mixture was refluxed for about 10–14 h on a ratio head, during which the white precipitate of potassium chloride separated out. The contents were

0268–2605/93/080655–06 $08.00

Received 16 November 1992
Accepted 16 June 1993

Table 1 Physical properties and analytical data of semicarbazone complexes of tin and lead

Reactants		Product formed and Colour	M.p. (°C)	Yield (%)	Elemental analysis (%): Found (Calcd)				Mol. wt: Found (Calcd)
Starting material (g)	Ligand (g)				C	H	N	Sn/Pb	
Me_3SnCl	$C_7H_9N_3O_2$	$C_{10}H_{17}N_3O_2Sn$	230	73	36.98	5.26	12.42	35.68	354.24
0.61	0.51	Dark yellow			(36.40)	(5.19)	(12.73)	(35.96)	(329.96)
Me_3SnCl	$C_7H_9N_3SO$	$C_{10}H_{17}N_3SOSn$	192	77	34.44	4.82	12.34	34.15	367.57
0.59	0.55	Creamish			(34.71)	(4.95)	(12.14)	(34.30)	(346.02)
Me_3SnCl	$C_8H_{10}N_4O$	$C_{11}H_{18}N_4OSn$	143	69	38.98	5.46	16.17	34.35	362.13
0.65	0.59	Light brown			(38.75)	(5.32)	(16.48)	(34.74)	(340.97)
Me_3SnCl	$C_{11}H_{12}N_4O$	$C_{14}H_{20}N_4OSn$	270(d)	70	44.63	5.06	14.51	31.13	348.85
0.59	0.64	Reddish brown			(44.37)	(5.32)	(14.78)	(31.32)	(379.03)
Ph_3PbCl	$C_8H_{10}N_3O_2$	$C_{26}H_{24}N_3O_2Pb$	160	73	49.92	3.91	7.28	34.03	628.36
1.22	0.43	Light yellow			(49.66)	(3.83)	(6.95)	(34.26)	(604.67)
Ph_3PbCl	$C_7H_9N_3SO$	$C_{25}H_{23}N_3SOPb$	108	71	48.70	3.87	6.35	33.14	602.22)
0.63	0.24	Dark yellow			(48.37)	(3.73)	(6.77)	(33.37)	(620.73)
Ph_3PbCl	$C_8H_{10}N_4O$	$C_{26}H_{24}N_4OPb$	174	76	50.94	4.21	8.86	33.28	642.68)
1.44	0.54	Off-white			(50.72)	(3.93)	(9.09)	(33.65)	(615.69)
Ph_3PbCl	$C_{11}H_{12}N_4O$	$C_{29}H_{26}N_4OPc$	187	76	53.52	4.21	8.26	31.31	632.84
0.54	0.24	Brown			(53.28)	(4.00)	(8.57)	(31.69)	(653.74)

cooled and the precipitate of potassium chloride so formed was removed by filtration. The mother liquor was concentrated by removing the excess of solvent under reduced pressure and the resulting products were subsequently dried, then repeatedly washed with dry cyclohexane and methanol, and finally dried under vacuum for 3–4 h. The analyses of these new complexes for carbon, hydrogen, nitrogen, tin and lead agreed with the theoretical values within the limits of experimental error (Table 1).

Analytical methods and physical measurements

Carbon and hydrogen analyses were performed in the Microanalytical Laboratory of this Department. Nitrogen was estimated by Kjeldahl's method. Tin and lead were estimated gravimetrically.[10] Molecular weights were determined by the Rast camphor method and conductivity was measured at 32 ± 1 °C with a conductivity bridge (Type 304 Systronics model). Infrared spectra were recorded on a Perkin–Elmer 577 grating spectrophotometer in KBr pellets. The UV-visible spectra of the compounds were obtained on a Pye–Unicam SP-8-100 spectrophotometer in dry methanol. ^1H, ^{13}C and ^{119}Sn NMR spectra were recorded on a JEOL FX 90Q (90 MHz) spectrometer at 89.55, 22.49 and 33.35 MHz, respectively (Tables 2 and 3).

RESULTS AND DISCUSSION

Trimethyltin chloride and triphenyl-lead chloride react with the potassium salts of the semicarbazones (SczH) in 1:1 molar ratios in a dry methanolic medium, resulting in the isolation of $Me_3Sn(Scz)$ and $Ph_3Pb(Scz)$ complexes, respectively. These reactions can be depicted by Eqns [1] and [2].

$$Me_3SnCl + Scz.K \xrightarrow{MeOH} Me_3Sn(Scz) + KCl \quad [1]$$

$$Ph_3PbCl + Scz.K \xrightarrow{MeOH} Ph_3Pb(Scz) + KCl \quad [2]$$

These substitution reactions are quite facile and the resulting products are coloured solids. These are soluble in DMSO, DMF and THF. The molar conductance of 10^{-3} M solutions of the compounds in anhydrous DMF lies in the range 12–15 ohm^{-1} cm^2 mol^{-1} indicating their almost non-electrolytic behaviour. The molecular weight determinations show them to be monomeric in nature. Their physical and analytical properties are given in Table 1.

IR spectra

The infrared spectra of the ligands and their tin and lead complexes were recorded and some important features may be summarized as follows.

A sharp band in the region 1600–1620 cm^{-1} in the ligands can be attributed to $\nu(>\mathrm{C{=}N})$.[11] This band appears at *ca* 1630 ± 10 and 1590 ± 10 cm^{-1} in the corresponding organotin(IV) and organolead(IV) complexes, respectively. The shifting of this band is probably due to the coordination of the azomethine (C=N—) nitrogen atom with the metal atom.

A broad absorption band around 3300 cm^{-1} is observed due to ν(NH)/(OH) stretching of the semicarbazone. This band, however, disappears in the complexes, thereby indicating the bonding of nitrogen and oxygen with the metal atom. Two sharp bands at *ca* 3440 and 3360 cm^{-1}, probably due to the asymmetric and symmetric vibrations of the NH_2 group in the ligand, remain almost unchanged in the spectra of the metal complexes, showing the non-involvement of this group in complexation.[12]

The appearance of new, strong-to-medium-intensity bands in the spectra of the complexes assigned to $\nu(\mathrm{Sn{-}O})$,[13] $\nu(\mathrm{Sn}\leftarrow\mathrm{N})$,[14] $\nu(\mathrm{Pb{-}O})$[15] and $\nu(\mathrm{Pb}\leftarrow\mathrm{N})$[16] vibrations in the region 400–600 cm^{-1}further supports the participation of oxygen and azomethine nitrogen in complexation. The bands observed at *ca* 575 and 550 cm^{-1} in the spectra of tin complexes may be attributed to $\nu(\mathrm{Sn{-}CH_3})_{as}$ and $\nu(\mathrm{Sn{-}CH_3})_{s}$ vibrations, respectively. Further, the bands assigned to $\nu(\mathrm{Pb{-}C_6H_5})_{as}$[18] and $\nu(\mathrm{Pb{-}C_6H_5})_{s}$[19] appear at *ca* 245 and 210 cm^{-1} respectively in the spectra of the lead complexes.

^{1}H NMR spectra

The proton magnetic resonance spectra of the semicarbazone lignads as well as their corresponding metal complexes have been recorded in DMSO-d$_6$ using TMS as the internal standard. The chemical shift values (δ, ppm) of the different protons as shown in Table 2. For the sake of convenience, the spectra of 2-acetylfuran semicarbazone and its trimethyltin(IV) and triphenyllead(IV) derivatives are discussed in detail. The broad signal exhibited by the ligand due to the single NH proton in the N—NH—C grouping at δ 10.91 ppm disappears in the organometallic derivatives, indicating the coordination of nitrogen as well as covalent-bond formation between metal and oxygen due to the deprotonation of the enolic form of the ligand. Further, in the spectra of the complexes, a downfield shift in the position of the —CH_3 and aromatic protons also indicates deshielding as well as the coordination of the azomethine nitrogen to the metal atom. This is probably due to the donation of a lone pair of electrons by the nitrogen to the central metal atom resulting in the formation of a coordinate linkage ($\mathrm{M}\leftarrow\mathrm{N}$). The appearance of signals due to NH_2 protons at about the same positions in the ligand and its complexes shows the non-involvement of this group in coordination. Further, new signals at δ 1.14 and 7.05 ppm in the trimethyltin(IV) and triphenyl-lead(IV) derivatives, respectively are assigned to the protons of methyl and phenyl groups attached to the metal.

^{13}C NMR spectra

The ^{13}C NMR spectral data for 2-AcPyd.SczH and its corresponding tin and lead complexes were recorded in dry DMSO. The considerable shifts observed in the positions of carbon atoms adjacent to atoms involved in complex formation clearly indicate the bonding of the azomethine

Table 2 ^{1}H NMR data (δ, ppm) of ligands and their corresponding metal complexes

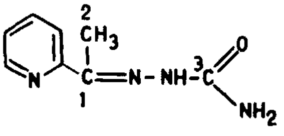
Compound[a]	—NH	—NH_2	$-\underset{CH_3}{\underset{\vert}{C}}{=}N$	Aromatic	Sn—Me/Pb–Ph
2-AcFur.SczH	10.91	2.78	2.16	8.82–7.88	—
2-AcThiop.SczH	10.68	2.43	2.05	8.69–7.04	—
2-AcPyd.SczH	11.21	2.57	1.74	8.21–7.18	—
Me_3Sn(2-AcFur.Scz)	—	2.79	2.25	8.80–7.90	1.14
Me_3Sn(2-AcThiop.Scz)	—	2.45	2.16	8.77–7.22	1.05
Me_3Sn(2-AcPyd.Scz)	—	2.59	1.86	8.34–7.27	1.22
Ph_3Pb(2-AcFur.Scz)	—	2.80	2.38	8.87–7.95	7.05
Ph_3Pb(2-AcThiop.Scz)	—	2.48	2.40	8.86–7.13	—[b]
Ph_3Pb(2-AcPyd.Scz)	—	2.61	1.96	8.40–7.28	—[b]

[a] Abbreviations: Fur, furan; Thiop, thiophene; Pyd, pyridine; Scz, semicarbazone.
[b] Overlapped with aromatic protons.

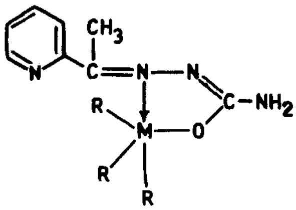
Table 3 ^{13}C NMR data of ligands and their corresponding metal complexes

	Chemical shift values, δ (ppm)				
Compound	1	2	3	Aromatic/Pb—Ph	Sn—Me
2-AcPyd.SczH[a]	157.64	13.26	169.30	145.38, 143.85, 142.67, 126.25, 123.21	—
Me_3Sn(2-AcPyd.Scz)[b]	152.32	12.18	163.48	145.65, 144.13, 142.88, 126.57, 123.73	16.37
Ph_3Pb(2-AcPyd.Scz)[b]	150.28	11.86	161.02	145.90, 144.53, 143.27, 126.85, 124.35, 131.94, 133.66, 135.42, 138.20	—

[a] 2-AcPyd.SczH is



[b] The complexes have the structure



where R = Me or Ph and M = Sn or Pb.

nitrogen and ketonic/enolic oxygen to the metal atom (Table 3).

^{119}Sn NMR spectra

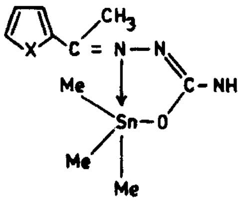
In the ^{119}Sn NMR spectrum of Me_3Sn(2-AcFur.Scz), the signal observed at δ, -155 ppm is in good agreement with previous values for a penta-coordinated state around the tin atom.[20]

On the basis of the results so far discussed, including analytical as well as spectral data, the penta-coordinated structures **I** and **II** may be proposed for the resulting complexes.

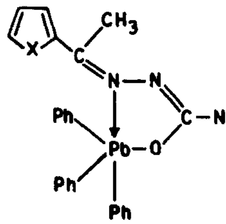
BIOLOGICAL SCREENING

Antifungal activity

The antifungal activity of 2-AcPyd.SczH and 2-AcFur.SczH, along with that of their corresponding trimethyltin(IV) and triphenyl-lead(IV) complexes, has been evalutated against *Alternaria brassicae*, *Alternaria tenuis*, *Aspergillus niger* and *Fusarium oxysporum* by the radial growth method[21] using Czapek's agar medium (sucrose, agar-agar, KCl, KH_2PO_4, $NaNO_3$, $FeSO_4$ and $MgSO_4$). The compounds were directly mixed with the medium in different concentrations. Controls were also run and three replicates were used in each case. The linear growth of the fungus was obtained by measuring the diameter of the fungal colony after seven days (Table 4). The amount of growth inhibition in all of the replicates was calculated by the equation:



(I)



(II)

X = O or S

$$\text{Percentage inhibition} = \frac{(C-T)\times 100}{C}$$

where *C* is the diameter of the fungal colony in the control plate and *T* is the diameter of the fungal colony in the test plate.

Antibacterial activity

The antibacterial activity of 2-acetylthiophene semicarbazone, 2-acetylfuran semicarbazone and their corresponding tin and lead complexes has also been tested against *Escherichia coli* (−), *Staphylococcus aureus* (+) and *Bacillus subtilis* (+) by the inhibition zone technique. All the compounds were dissolved in methanol in 1000 ppm concentration. Paper discs of Whatman No. 1 paper with a diameter of 5 mm, were soaked in these solutions. These discs were placed on the appropriate medium previously seeded

Table 4 Antifungal activity of ligands and their corresponding organotin(IV) and organolead(IV) complexes

	Average inhibition after 7 days (%)							
	Alt. brassicae		*Alt. tenuis*		*Asp. niger*		*Fus. oxysporum*	
Compound	200 ppm	400 ppm	200 ppm	400 ppm	200 ppm	400 ppm	200 ppm	400 ppm
2-AcPyd.SczH	27	32	24	28	35	40	20	28
2-AcFur.SczH	21	28	17	25	29	34	18	24
Me$_3$Sn(2-AcPyd.Scz)	74	88	70	84	81	88	59	68
Me$_3$Sn(2-AcFur.Scz)	70	78	61	74	68	82	71	83
Ph$_3$Pb(2-AcPyd.Scz)	72	84	66	80	73	82	56	67
Ph$_3$Pb(2-AcFur.Scz)	67	77	59	71	63	77	68	80

with organisms in Petri dishes and stored in an incubator at 30 ± 1 °C. The inhibition zone thus formed around each disc containing the test compound was measured (in mm) after 24 h; the results of these studies are shown in Table 5.

The results of the studies reveal that all the compounds are highly active against these pathogens, even at low concentrations, and the inhibition of the growth of micro-organisms was found to be dependent on the concentration of the complexes. Furthermore, all the compounds exert greatest toxicity against the fungus *Aspergillus niger* and bacterium *Bacillus subtilis* but are also least toxic towards the fungus *Fusarium oxysporum* and the bacterium *E. coli*. The results also indicate that the metal chelates are more active than their parent ligands: this may be accounted for by chelation theory.[22] On comparing the influence of the metal ion on the intrinsic fungitoxicity of metal chelates, it has been inferred that organotin(IV) complexes are more active compared with organolead(IV) complexes. The enhanced activity of the complexes may be explained on the basis of their higher solubility and the size of the metal ion.[23]

Table 5 Antibacterial activity of ligands and their corresponding metal complexes

	Diameter of inhibition zone (mm)		
Compound	*E. coli*	*B. subtilis*	*S. aureus*
2-AcThiop.SczH	9	12	10
Me$_3$Sn(2-AcThiop.Scz)	15	19	18
Ph$_3$Pb(2-AcThiop.Scz)	13	18	15
2-AcFur.SczH	6	9	8
Me$_3$Sn(2-AcThiop.Scz)	13	17	14
Ph$_3$Pb(2-AcThiop Scz)	10	15	12

Acknowledgement The financial assistance provided by the CSIR New Delhi in the form of SRF grant no. 9/149(132)/91-EMR-I to AK is gratefully acknowledged.

REFERENCES

1. Smith, P J *Metallurgica*, 1982, 22(3): 161
2. Chapman, A H *Proc. Anal. Chem.*, 1983, 20: 210
3. Dashora, R and Tandon, J P *Acta Cienc. India, Chem.*, 1988, 14(4): 347
4. Dixit, P and Tandon, J P *Phosphorus, Sulfur and Silicon*, 1990, 53: 389
5. Kumari, A, Singh, R V and Tandon J P *Phosphorus, Sulfur and Silicon*, 1993, 66: 195
6. Prokopenko, I, Liatvinov, N N, Klimova, D M, Dmitrieva, R A, Ilin, V P, Mazurina, T L, Pugacheva, O A, Kuznetsova, K K and Kirilkina, T A *Gig. Sanit*, 1989, (2): 9
7. Fernandez-Leborans, G and Antonia-Garcia, M A *Acta Protozool.*, 1988, 27(2): 141
8. Stauber, J L and Florence, T M *Water Res.*, 1989, 23(7): 907
9. Moors, M R and Meredith, P A *Arch. Toxicol.*, 1979, 42: 87
10. Vogel, A I *Quantitative Inorganic Analysis*, ELBS and Longmans Green and Co., London, 1978
11. Degaonkar, M P, Gopinathan, S and Gopinathan, C *Ind. J. Chem.*, 1989, 28A: 678
12. Singh, S V and Singh, R V *Synth. React., Inorg. Met.—Org. Chem.*, 1987, 17: 947
13. Narula, C K and Gupta, V D *Synth. React. Inorg. Met.—Org. Chem.*, 1982, 12: 373
14. Kawakami, K and Okawara, R *J. Organomet. Chem.*, 1966, 6: 249

15. Dashora, R, Singh, R V and Tandon, J P *Ind. J. Chem.*, 1986, 25A: 188

16. Singh, K, Singh, R V and Tandon, J P *J. Prakt. Chem.*, 1989 331: 525

17. Cashion, J D, Domazetis G and James, B D *J. Organomet. Chem.*, 1980, 185: 433

18. Gratz, K, Huber, F, Silvestri, A and Barbieri, R *J. Organomet. Chem.*, 1984, 273: 283

19. Cragg, R H and Taylor, A *J. Organomet. Chem.*, 1975, 99: 391

20. Saxena, A K and Trandon, J P *Polyhedron*, 1983, 2: 443

21. Singh, D, Goyal, R B and Singh, R V *Appl. Organomet. Chem.*, 1991, 5: 45

22. Srivastava, R S *Inorg. Chim. Acta*, 1981, 46: L65

23. Thimmaiah, K N and Lloyd, W D *Inorg. Chim. Acta*, 1981, 106: 1701