Phosphorus, Sulfur, and Silicon, 186:2071–2085, 2011

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426507.2011.557415

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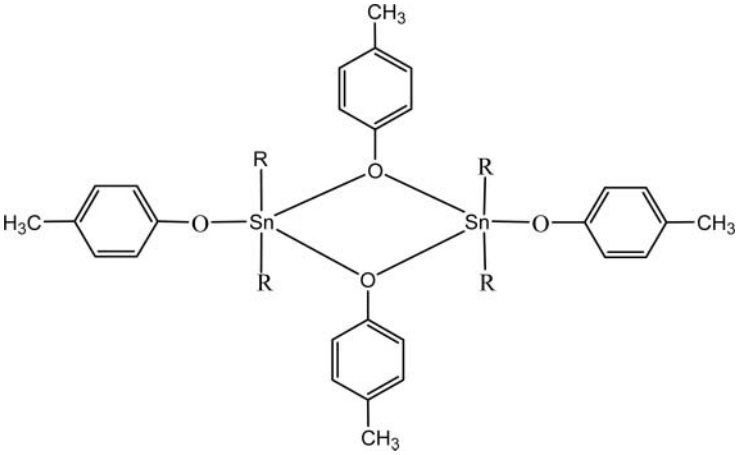
SYNTHESIS, CHARACTERIZATION, AND ANTIBACTERIAL ACTIVITY OF DIORGANOTIN(IV) COMPLEXES OF 4-METHYLPHENOL

Neeraj Sharma and Vijay Kumar
Department of Chemistry, Himachal Pradesh University, Shimla, India

GRAPHICAL ABSTRACT



Abstract *Diorganotin(IV) complexes $R_2Sn(OC_6H_4Me\text{-}4)_2$ (R = Ph, Me, and n-Bu) have been synthesized in good yields by the reaction of Ph_2SnCl_2, $n\text{-}Bu_2SnCl_2$, and Me_2SnCl_2 with $NaOC_6H_4Me\text{-}4$, while complex $n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)$ has been obtained from the reaction of $n\text{-}Bu_2SnCl_2$ with 4-methylphenol in the presence of triethylamine in carbon tetrachloride. The complexes have been characterized by elemental analyses, molar conductance measurements, molecular weight determination, IR, ^1H, ^{13}C, and ^{119}Sn NMR spectroscopy as well as by mass spectrometry. The reactions of the complexes with 2- and 3-cyanoanilines yielded 1:2 coordination compounds authenticated by physicochemical as well as by IR, ^1H, and ^{13}C NMR spectroscopic data. The bases behaved as monodentate*

Received 6 October 2010; accepted 20 January 2011.

Vijay Kumar is grateful to CSIR New Delhi, India, for awarding JRF. The authors thank the Department of Biotechnology, Himachal Pradesh University, Shimla, for providing laboratory facilities (for antibacterial activity), the Department of Science and Technology (DST), Government of India, New Delhi, for providing financial assistance for FT-IR, Sophisticated Analytical Instrument Facility (SAIF), CDRI, Lucknow, for recording mass spectra and elemental analysis, and the Punjab University Chandigarh for recording NMR spectra.

Address correspondence to Neeraj Sharma, Department of Chemistry, Himachal Pradesh University, Summer Hill, Shimla 171005, India. E-mail: neerajsharma_univ@yahoo.co.in

ligands wherein 2-cyanoaniline is bonded through nitrile nitrogen atom, while 3-cyanoaniline is coordinated through amino nitrogen atom. The diorganotin(IV) complexes have also been screened for their antibacterial activity against Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis, Shigella flexneri, Proteus mirabilis, and Pseudomonas aeruginosa. The minimum inhibitory concentration values of these complexes show enhanced activity.

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Dialkyltin/diaryltinchlorides; 4-methylphenol; spectral studies; antibacterial activity

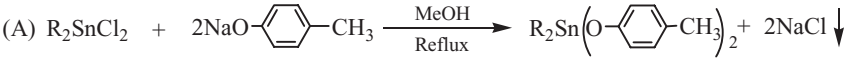
INTRODUCTION

Literature on organotin chemistry abounds with numerous organotin compounds derived from a variety of ligands, predominantly carboxylates,[1,2] peptides,[3–5] Schiff bases,[6,7] dithiocarbamic acids,[8] and hydroxamic acids,[9–12] because of their diverse structural and biological importance. Diorganotin(IV) compounds, in particular, are known as potential antitumor and anticancer agents.[13–17] The potential applications of organotin compounds such as polyvinyl chloride (PVC) stabilizers, catalyst for transesterification reactions,[18,19] polyurethane polymerization, and room temperature vulcanization (RTV) silicone curing agents are also well documented.[20,21] Organotin compounds find use as industrial and agricultural biocides[22–24] owing to their antifungal properties. Of organotin complexes containing tin–oxygen bond, derived from hydroxides, oxides, alkoxides and phenoxides, peroxides, and alkyl peroxides, there are numerous studies concerning organotin alkoxides. The reactions of organotin chlorides with the sodium salt of the appropriate alcohol/phenol[25,26] and organotin oxide with phenols[27] are quite common and are frequently used. However, they do not always provide a successful synthetic route to organotin alkoxides and phenoxides because of the formation of tetraalkyl dialkoxydistannoxanes in the latter reaction.[28,29] A ladder-type structure of tetrabutyl diphenoxydistannoxane $[Sn_4(C_4H_9)_8(C_6H_5O)_4O_2]$ has been reported.[30]

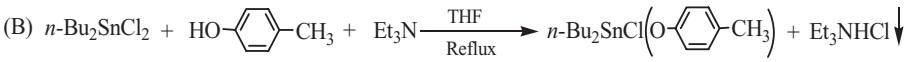
The other synthetic methods employed include the reactions of organotin amines with alcohols and the nucleophilic displacement of alkoxides, hydroxides, or stannyl oxide.[31] The studies on the catalysis of the reaction of organotin phenoxides with diethyl acetylene dicarboxylate have been described.[32] Despite the fact that organotin phenoxides are known to possess antibacterial effects and constitute a potential component of Ziegler-Natta system, only a few reports are encountered on organotin aryloxides.[33] Of the large variety of substituted phenols containing both electron-withdrawing and electron-donating substituents, among methyl-substituted phenols, only 2,6-dimethyl phenol[34] seems to be well studied. Simple *o*-, *m*-, and *p*-cresols, perhaps due to their unique physical properties, have obviously remained rather unexplored. In view of the above observations and in continuation of our previous work on organotin(IV) aryloxide chemistry,[35] we report herein the synthesis of diorganotin(IV) complexes derived from 4-methylphenol, their structural characterization, and Lewis acid behavior in the presence of nitrogen bases. The antibacterial activity of the complexes has also been assayed.

RESULTS AND DISCUSSION

The formation of diorganotin(IV) 4-methyl phenoxides in quantitative yields can be proceeded according to the Equations (A) and (B):



(where R = Ph, n-Bu, and Me)



The elemental analyses (Table 1) confirmed the stoichiometric compositions. The diphenyl, dimethyltin, and dibutyltin(IV) 4-methyl phenoxides are brown, cream colored, light yellow, and white solids, respectively. The complexes exhibit sharp melting points except $Ph_2Sn(OC_6H_4Me\text{-}4)_2$. The complexes are stable under dry conditions and are soluble in most of the common organic solvents. The molar conductance values of 10^{-3} M solutions of the compounds in nitrobenzene suggest that they are nonelectrolytes.[36] The molecular weight determination by Rast's camphor method suggested that they exist as dimers.

FTIR Spectra

The formation of diorganotin(IV) 4-methyl phenoxide complexes was ascertained from a comparison of the IR spectra of the new complexes with that of free 4-methylphenol. The broad absorption band in the region of 3600–3200 cm^{-1} due to υ(OH) mode in free 4-methylphenol was found to be absent in the spectra of the complexes. The absorption bands in the region of 1240–1160 cm^{-1} in free 4-methylphenol ascribed to υ(C-O) mode appeared in the complexes in the region of 1258–1171 cm^{-1}, suggesting the involvement of the phenolic oxygen atom in bonding. The bonding of the phenolic oxygen atom to tin metal was further supported by the appearance of bands at 535–490 cm^{-1} attributed to υ(Sn–O) mode.[1,2] The sharp bands observed at 765–680 cm^{-1} may be assigned to υ(Sn–O–Sn)[37–39] mode, which is indicative of their dimeric nature. The absorption bands observed at 280 and 250 cm^{-1}, 602 cm^{-1}, 601 cm^{-1}, and 545 and 525 cm^{-1} in diphenyl, *n*-butyl, and methyltin(IV) 4-methyl phenoxides may be assigned to υ(Sn–C) mode.[40]

^{1}H NMR Spectra

A comparison of the ^{1}H NMR spectrum of the free ligand with those of the complexes provides further evidences for their formation (Table 2). The ^{1}H NMR spectrum of 4-methylphenol exhibits signals at 5.18, 6.45, 6.79, and 2.20 ppm, which are attributed to the phenolic –OH group, the protons of the aromatic ring (*o*-H and *m*-H), and the protons of the methyl substituent, respectively.[41] The absence of the signal at 5.18 ppm in the complexes confirms the deprotonation of phenolic function. The phenolic ring protons were found to undergo significant downfield shifts in the case of $n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2$ and $n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)$, while moderate downfield shifts have been observed for $Ph_2Sn(OC_6H_4Me\text{-}4)_2$ and $Me_2Sn(OC_6H_4Me\text{-}4)_2$. This may be ascribed to deshielding of

Table 1 Analytical data of diorganotin(IV) complexes

Complex (Molecular formula)	Color	mp/decomp. temp.* (°C)	Yield %	Elemental analysis % Found (Calc.)					Λ_m in $PhNO_2$ (Scm^2/mol)	Mol. Wt. Found (Calc.)
				Sn	C	H	Cl	N		
$Ph_2Sn(OC_6H_4Me\text{-}4)_2$	Brown	230*	82	24.41	64.04	4.50	—	—	2.0	965
($C_{26}H_{24}O_2Sn$)				(24.37)	(64.10)	(4.97)				(488)
n-$Bu_2SnCl(OC_6H_4Me\text{-}4)$	White	73	79	31.52	47.90	6.66	9.37	—	1.5	740
($C_{15}H_{25}ClOSn$)				(31.61)	(47.98)	(6.71)	(9.44)			(376)
n-$Bu_2Sn(OC_6H_4Me\text{-}4)_2$	Light yellow	67	85	26.50	59.00	7.14	—	—	1.3	885
($C_{22}H_{32}O_2Sn$)				(26.55)	(59.09)	(7.21)				(448)
$Me_2Sn(OC_6H_4Me\text{-}4)_2$	Cream- colored	160	80	32.65		5.45	—	—	1.2	718
($C_{16}H_{20}O_2Sn$)				(32.70)	(52.93)	(5.55)				(364)
$Ph_2Sn(OC_6H_4Me\text{-}4)_2{\cdot}2(3\text{-}CNAn)$	White	42	70	16.35		4.93	—	7.64	1.1	—
($C_{40}H_{36}N_4O_2Sn$)				(16.41)	(66.41)	(5.02)		(7.74)		
$Me_2Sn(OC_6H_4Me\text{-}4)_2{\cdot}2(2\text{-}CNAn)$	Brown	170	75	19.70		5.28	—	9.31	0.9	—
($C_{30}H_{32}N_4O_2Sn$)				(19.81)	(60.12)	(5.38)		(9.35)		
n-$Bu_2Sn(OC_6H_4Me\text{-}4)_2{\cdot}2(2\text{-}CNAn)$	Yellow	—	76	17.33	63.18	6.40	—	8.15	1.0	—
($C_{36}H_{44}N_4O_2Sn$)				(17.37)	(63.26)	(6.49)		(8.20)		
n-$Bu_2SnCl(OC_6H_4Me\text{-}4){\cdot}2(3\text{-}CNAn)$	Pale yellow	—	79	19.33	56.85	6.03	5.73	9.10	1.4	—
($C_{29}H_{37}ClN_4OSn$)				(19.40)	(56.93)	(6.10)	(5.79)	(9.16)		

2- and 3-CNAn($C_7H_6N_2$) = 2-cyanoaniline and 3-cyanoaniline.

Table 2 ^{1}H NMR data of diorganotin(IV) complexes

	^{1}H NMR δ (ppm)				
		Aromatic protons			
Complex	-OH	*ortho*	*meta*	Substituent -Me	R-Sn
4-methylphenol	5.18	6.45	6.79	2.20 (s, 3H)	—
$Ph_2Sn(OC_6H_4Me\text{-}4)_2$	—	6.52 (d, 4H)	6.96 (d, 4H)	2.23 (s, 3H)	7.83–7.98 (m,10H)
$n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)$	—	6.50 (d, 2H)	6.98 (d, 2H)	2.26 (s, 3H)	0.87–0.97 (t, 6H) CH_3 1.39–1.50 (m, 4H) $CH_2(\alpha)$ 1.53–1.85 (m, 4H) $CH_2(\beta)$ 1.39–1.50 (m, 4H) $CH_2(\gamma)$
$n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2$	—	6.48 (d, 4H)	6.97 (d, 4H)	2.25 (s, 3H)	0.89–0.95 (t, 6H) CH_3 1.36–1.48 (m, 4H) $CH_2(\alpha)$ 1.50–1.79 (m, 4H) $CH_2(\beta)$ 1.36–1.48 (m, 4H) $CH_2(\gamma)$
$Me_2Sn(OC_6H_4Me\text{-}4)_2$	—	6.70 (d, 4H)	6.99 (d, 4H)	2.26 (s, 3H)	1.18 (s, 6H)

the protons due to a shift of electron density from the ring to the tin metal. The ^{1}H NMR signal of the methyl substituent at the aromatic ring of free 4-methylphenol does not undergo any change on complexation. The resonances of the *n*-butyl, methyl, and phenyl groups attached to tin metal in the respective complexes remain unchanged with respect to the corresponding diorganotin dichlorides.

^{13}C NMR Spectra

A comparison of the ^{13}C NMR spectra (Table 3) of the complexes with that of the free ligand shows that the resonances of the carbon atoms of the phenol ring occurring in the range of 115.3–152.6 ppm for 4-methylphenol are shifted downfield upon complexation, resulting from an electron density transfer from the ligand to tin metal. The carbon resonance of the methyl substituent at 21.1 ppm in free 4-methylphenol does not change upon complexation. The carbon resonances of the organic groups attached to tin also remained unaltered relative to those of the chloride precursors.

The values of $^{n}J(^{119}Sn–^{13}C)$ coupling constants are known to depend on the properties of the ligands in organotin compounds and to increase with an increase of coordination number around tin. The order $^{1}J(^{119}Sn–^{13}C) >> {}^{3}J(^{119}Sn–^{13}C) > {}^{2}J(^{119}Sn–^{13}C)$ is more probable for phenyltin than for alkyltin complexes. The magnitudes of the coupling constants $^{1}J(^{119}Sn–^{13}C)$ for diorganotin(IV) complexes are consistent with four-coordinate geometry around tin. As the coupling constants $^{n}J(^{119}Sn–^{13}C)$ are known to yield important structural information, the C–Sn–C angle in complexes was determined using the

Table 3 ^{13}C NMR data of diorganotin(IV) complexes

	^{13}C NMR δ (ppm)							
Complexes	C_1	C_2	C_3	C_4	C_5	C_6	Substituent -Me	R-Sn
4-methylphenol	152.6	115.3	130.2	130.5	130.2	115.3	21.1	—
$Ph_2Sn(OC_6H_4Me\text{-}4)_2$	154.5	116.4	130.0	131.1	130.0	116.4	21.2	131.2 ($^1J = 535$ Hz)
$n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)$	155.5	115.9	130.7	131.4	130.7	116.0	21.2	C_α:25.2 {$^1J(^{119}Sn\text{-}^{13}C) = 425.0$ Hz} C_β:27.1 {$^2J(^{119}Sn\text{-}^{13}C) = 19.9$ Hz} C_γ:26.9 {$^3J(^{119}Sn\text{-}^{13}C) = 92.6$ Hz} C_δ:13.0
$n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2$	155.4	116.0	130.1	131.1	130.1	116.2	21.1	C_α:25.3 {$^1J(^{119}Sn\text{-}^{13}C) = 418.0$ Hz} C_β:27.2 {$^2J(^{119}Sn\text{-}^{13}C) = 17.0$ Hz} C_γ:27.0 {$^3J(^{119}Sn\text{-}^{13}C) = 90.0$ Hz} C_δ:11.0
$Me_2Sn(OC_6H_4Me\text{-}4)_2$	154.6	116.6	130.7	131.9	130.7	116.8	21.0	4.8 ($^1J = 401$ Hz)

equations given by Howard's (1) and Lockhart (2):

$$\theta(C - Sn - C) = 0.178\ J^1[Sn^{119} - C^{12}] + 14.7 \quad (1)$$

$$\theta(C - Sn - C) = \frac{J^1[Sn^{119} - C^{12}] + 875}{11.4} \quad (2)$$

The C–Sn–C angles of 109.93 °, 114.03 °, 113.42 °, and 111.92 ° found by employing Equations (1) and (2) for diphenyl-, di-*n*-butyl-, and dimethyltin(IV) complexes, respectively, confirm the tetrahedral arrangement around tin.

^{119}Sn NMR Spectra

^{119}Sn NMR spectra of diphenyl-, *n*-butyl-, and methyltin(IV) 4-methyl phenoxides exhibit a single resonance at −118.6, −38.0, −35.9, and 116.5 ppm, respectively, characteristic of tetrahedral Sn(IV) center. The tetrahedral geometry around tin in organotin(IV) 4-methyl phenoxides resulting from ^{1}H, ^{13}C, and ^{119}Sn NMR data is in accord with previous reports[42] that dimeric/polymeric structures are lost in solution.

Mass Spectra

The most important fast atom bombardment (FAB) mass data for *n*-$Bu_2SnCl(OC_6H_4Me\text{-}4)$ and *n*-$Bu_2Sn(OC_6H_4Me\text{-}4)_2$ are given in Table 4 (Schemes

Table 4 Mass spectral data of diorganotin(IV) complexes

n-$Bu_2Sn(OC_6H_4Me\text{-}4)_2$ (M)	*m/z*(%)	*n*-$Bu_2SnCl(OC_6H_4Me\text{-}4)$ (M)	*m/z*(%)
$[\{n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2\}_2 - Me + H]^+$	882 (100%)	$[\{n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)\}_2 + Me]^+$	767 (100.0%)
$[n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2SnBu(OC_6H_4Me\text{-}4)(OPh)]^+$	825 (51.0%)	$[n\text{-}Bu_2Sn(OPh)_2SnBu_2]^+$	654 (91.66%)
$[n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4(OPh)SnBu_2(OPh)]^+$	761 (40.0%)	$[n\text{-}Bu_2SnCl(OPh)_2Bu - H]^+$	631 (30.55%)
$[n\text{-}Bu_2Sn(OPh)_2Sn + H]^+$	541 (48.57%)	$[n\text{-}Bu_2SnCl(OPh)_2Sn]^+$	575 (11.11%)
$[n\text{-}BuSn(OPh)_2 + Na - H]^+$	385 (77.14%)	$[n\text{-}Bu_2Sn\ (OPh)_2Sn - H]^+$	539 (41.66%)
$[n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4) + Na]^+$	364 (80.0%)	$[n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4)Sn + H]^+$	497 (22.22%)
$[n\text{-}BuSn(OC_6H_4Me\text{-}4) + Na]^+$	307 (37.14%)	$[n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)Sn]^+$	461 (11.11%)
$[n\text{-}Bu_2Sn\text{-}H]^+$	233 (25.71%)	$[n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4) + 2Me]^+$	406 (100%)
$[n\text{-}BuSn]^+$	177 (74.28%)	$[n\text{-}Bu_2SnCl(OPhPh) + Na]^+$	385 (41.66%)
$[Sn]^+$	121 (11.42%)	$[Sn(OC_6H_4Me\text{-}4)SnCl]^+$	382 (19.44%)
		$[Sn(OPh)SnCl - H]^+$	367 (16.66%)
		$[n\text{-}Bu_2SnCl + Na - H]^+/[ClSnOSn]^+$	291 (25.0%)
		$[n\text{-}Bu_2SnCl]^+$	269 (33.33%)
		$[SnOSn]^+$	256 (11.11%)
		$[n\text{-}Bu_2SnH]^+$	235 (11.0%)
		$[n\text{-}BuSn]^+$	177 (19.44%)
		[Sn]+	121 (8.3%)

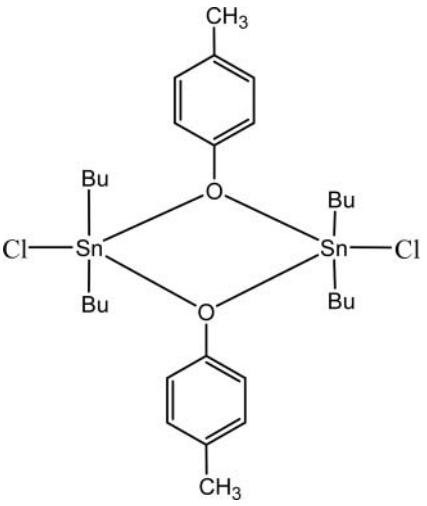


Figure 1 Proposed structure of n-$Bu_2ClSn(OC_6H_4Me\text{-}4)$.

S1 and S2, Supplemental Materials). The complexes do not display a molecular ion peak. The most intense peak at *m/z* 767 and 882 corresponds to $[\{n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4\}_2 + Me]^+$ and $[\{n\text{-}Bu_2Sn(OC_6H_4Me\text{-}4)_2\}_2 - Me + H]^+$ in the respective complexes and indicates a marked tendency of the complexes toward association, suggesting thereby their dimeric nature. The presence of $[n\text{-}Bu_2Sn]^+$ units bridged by 4-methylphenoxo groups is also indicated by the mass spectra. A number of fragment ions observed for the complexes are in accord with the structures deduced from the IR spectra.

Based upon analytical data, IR and mass spectral data dimeric structures (Figures 1 and 2) for the complexes may tentatively be proposed.

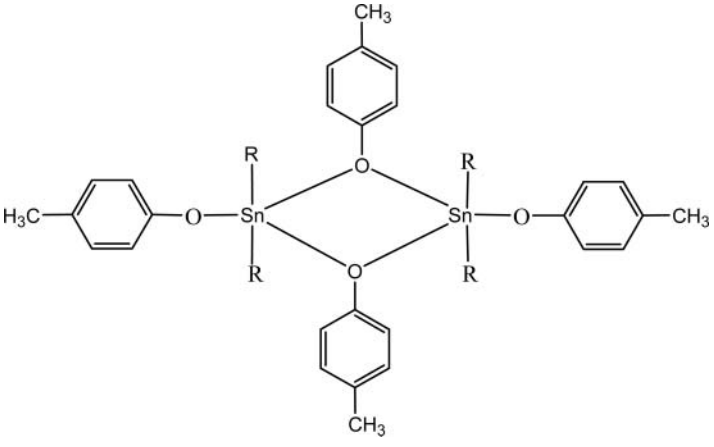


Figure 2 Proposed structure of $R_2Sn(OC_6H_4Me\text{-}4)_2$ (R = Ph, n-Bu, and Me).

Reactions of Diorganotin(IV) 4-Methylphenoxides with 2- and 3-Cyanoanilines

The reaction of diorganotin(IV) 4-methyl phenoxides with two equivalents of 2- and 3-cyanoanilines in absolute alcohol yields 1:2 coordination compounds of composition $R_2Sn(OC_6H_4Me\text{-}4)_2 \cdot 2$ L and $n\text{-}Bu_2SnCl(OC_6H_4Me\text{-}4) \cdot 2$ L (R = Ph, *n*-Bu, and Me, and L = 2- and 3-cyanoaniline), as is indicated by the analytical data (Table 1). The compounds are white to dark brown solids. The molar conductance values of a millimolar solution of the coordination compounds in nitrobenzene showed them to be nonelectrolytes.

The IR spectra of the adducts of 2-cyanoaniline show that the υ(CN) mode occurring at 2212 cm^{-1} in uncoordinated 2-cyanoaniline has moved significantly to higher wave number in the region of 2300–2320 cm^{-1}. The absorption bands due to υ_{asym}NH and υ_{sym}NH modes, which appear at 3457 and 3363 cm^{-1} in free 2-cyanoaniline, remain unchanged. These observations suggest bonding of 2-cyanoaniline through the nitrile group only. It is important to mention here that 2-cyanoaniline is known to coordinate through nitrile as well as the amino group.[43,44]

In the case of the coordination compounds of diorganotin(IV) 4-methyl phenoxides with 3-cyanoaniline, the absorption band due to υCN mode, occurring at 2229 cm^{-1} in free base, shifts insignificantly to lower wave number by approximately 5–8 cm^{-1}, thus excluding the possibility of bonding through nitrile nitrogen atom. On the contrary, the absorption bands due to υ_{asym}NH and υ_{sym}NH mode observed at 3400 and 3323 cm^{-1} in uncoordinated 3-cyanoaniline shift significantly to higher wave numbers and appear at approximately 3470–3460 and 3376–3370 cm^{-1}, respectively, suggesting coordination of 3-cyanoaniline through $–NH_2$ group. It is worth pointing out that the observed trend of shift of the υNH mode in case of 3-cyanoaniline adducts is different from earlier reports,[43] where the bonding through $–NH_2$ group suffers a negative shift. Bonding through nitrogen is further supported by the appearance of bands at 340–280 cm^{-1} assigned to υ(Sn–N) mode[45] and a six-coordinate distorted octahedral environment around the tin atom may be proposed.

^{1}H NMR Spectra

A comparison of the room temperature ^{1}H NMR spectra of the coordination compounds with those of free 2- and 3-cyanoanilines further indicates their formation (Table 5). The ^{1}H NMR spectra of 2- and 3-cyanoanilines exhibit signals at 6.99–7.30 ppm and 7.00–7.32 ppm, respectively, due to the aromatic ring protons. The coordination compounds show the resonances of the aniline ring protons to shift downfield. The resonances due to the protons of the phenol ring in the parent complexes also suffer a slight downfield shift on complexation with bases. The resonances due to the methyl substituent and the phenyl and butyl groups attached to tin remain almost unchanged.

^{13}C NMR Spectra

The ^{13}C NMR spectra of 2- and 3-cyanoaniline display the resonances of the ring carbon atoms at 98.2–148.3 ppm and 115.2–145.8 ppm, respectively. The carbon resonance of the cyano group is observed at 116.0 and 116.5 ppm in the respective bases. The coordination compounds of diorganotin(IV) 4-methyl phenoxides with these nitrogen bases

Table 5 ^{1}H NMR data of coordination compounds

	^{1}H NMR δ(ppm)			
	Aromatic protons			
Complex	Aniline ring	Phenolic ring	Substituent -Me	R-Sn
n-$Bu_2Sn(OC_6H_4Me\text{-}4)_2\cdot 2$(2-CNAn)	7.06–7.35	6.54–6.99	2.23	0.89–0.93 (t, 6H) CH_3 1.38–1.46 (m, 4H) $CH_2(\alpha)$ 1.54–1.79 (m, 4H) $CH_2(\beta)$ 1.38–1.46 (m, 4H) $CH_2(\gamma)$
$Me_2Sn(OC_6H_4Me\text{-}4)_2\cdot 2$(2-CNAn)	7.05–7.35	6.75–6.99	2.26	1.17 (s, 6H)
$Ph_2Sn(OC_6H_4Me\text{-}4)_2\cdot 2$(3-CNAn)	7.07–7.40	6.73–7.01	2.25	7.80–7.95 (m, 10H)
n-$Bu_2SnCl(OC_6H_4Me\text{-}4)\cdot 2$(3-CNAn)	7.03–7.37	6.54–7.01	2.26	0.86–0.97 (t, 6H) CH_3 1.38–1.53 (m, 4H) $CH_2(\alpha)$ 1.53–1.85 (m, 4H) $CH_2(\beta)$ 1.38–1.53 (m, 4H) $CH_2(\gamma)$

show moderate to appreciable downfield shifts of the signals of the aniline ring carbon atoms (Table 6). A slight downfield shift in carbon resonances of the phenol ring compared with those of the parent complexes was also observed for the coordination compounds.

Antibacterial Activity

The antibacterial activity of 4-methyphenol and diorganotin(IV) 4-methyl phenoxides was tested in vitro against *Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis, Shigella flexneri, Proteus mirabilis,* and *Pseudomonas aeruginosa* (Table 7). The results show that the ligand inhibits the bacterial growth at a concentration of 125–250 μg/mL, while *n*-$Bu_2SnCl(OC_6H_4Me\text{-}4)$, *n*-$Bu_2Sn(OC_6H_4Me\text{-}4)_2$, $Me_2(SnOC_6H_4Me\text{-}4)_2$, and $Ph_2(SnOC_6H_4Me\text{-}4)_2$ were found to inhibit at a concentration of 7.81–62.5 μg/mL. Of the four complexes studied, the complexes *n*-$Bu_2SnCl(OC_6H_4Me\text{-}4)$ and *n*-$Bu_2Sn(OC_6H_4Me\text{-}4)_2$ were found to exhibit a significantly enhanced activity at minimum inhibitory concentration (MIC) 7.81–15.62 μg/mL toward all bacteria under study. This enhancement in activity may be due to the coordination of the phenol moiety to the tin atom and an efficient diffusion of the complexes into the bacterial cell.[46,47] The antibacterial activity of these compounds was also compared with the commercial antibiotic streptomycin (See Table S1, Supplemental Materials)

Table 6 ^{13}C and ^{119}Sn NMR data of addition compounds

	^{13}C NMR δ (ppm)													
		Aromatic carbon atoms of aniline					Aromatic carbon atoms of phenol							
Complexes	C_1	C_2	C_3	C_4	C_5	C_6	C_1	C_2	C_3	C_4	C_5	C_6	Substituent -Me	R-Sn
n-$Bu_2Sn(OC_6H_4Me$-4$)_2\cdot$2(2-CNAn)	150.2	100.1	133.0	118.1	132.1	114.1	157.1	117.0	131.2	132.0	131.1	117.2	21.2	C_α : 25.3 C_β : 27.0 C_γ : 27.1 C_δ : 13.0
$Me_2Sn(OC_6H_4Me$-4$)_2\cdot$2(2-CNAn)	150.0	99.8	132.1	117.1	132.0	113.0	154.9	116.8	130.9	132.0	130.9	116.9	21.0	4.4
$Ph_2Sn(OC_6H_4Me$-4$)_2\cdot$2(3-CNAn)	147.1	117.2	112.4	120.0	128.7	117.3	155.1	117.3	131.1	131.8	131.0	117.4	21.1	131.0
n-$Bu_2SnCl(OC_6H_4Me$-4$)\cdot$2(3-CNAn)	148.0	117.0	112.0	119.4	127.9	117.2	155.6	116.4	130.9	131.9	131.1	116.7	21.0	C_α : 25.0 C_β : 27.0 C_γ : 26.6 C_δ : 13.1

Table 7 Antibacterial activity of ligand and diorganotin (IV) Complexes by MIC method in μg/mL

Compound	*E. coli*	*S. aureus*	*S. epidermidis*	*S. flexneri*	*P. mirabilis*	*P. aeruginosa*
4-methylphenol	125	250	125	125	125	250
Ph_2Sn(OPhMe-4)	62.5	62.5	15.62	31.25	31.25	62.5
n-Bu_2SnCl(OPhMe-4)	7.81	15.62	7.81	15.62	15.62	7.81
n-Bu_2Sn(OPhMe-4)$_2$	15.62	7.81	15.62	15.62	15.62	15.62
Me_2Sn(OPhMe-4)$_2$	7.81	7.81	31.25	15.62	15.62	7.81
Streptomycin	31.25	62.5	62.5	62.5	31.25	31.25

CONCLUSION

The dimeric structures for diorganotin(IV) 4-methyl phenoxides are derived from physicochemical, IR, and mass spectral data. The ^{13}C and ^{119}Sn NMR spectra, the C–Sn–C angle, and the coupling constants $^{n}J(^{119}Sn–^{13}C)$ suggest a tetrahedral geometry around the tin atom, indicating that the dimeric structures are lost in solution. The coordination compounds of diorganotin(IV) 4-methyl phenoxides with 2- and 3-cyanoaniline indicate coordination of the bases through the nitrile nitrogen atom in the case of 2-cyanoaniline and through the amino nitrogen atom in the case of 3-cyanoaniline. The new complexes show promising antibacterial activity.

EXPERIMENTAL

Materials

All the solvents used were of analytical reagent (AR) grade and were dried by standard methods. The 4-methylphenol (Merck) was recrystallized from benzene and the purity was checked by its melting point (34 °C–35 °C). Ph_2SnCl_2, *n*-Bu_2SnCl_2, Me_2SnCl_2, and 2- and 3-cyanoaniline were of Merck grade.

Tin in the complexes was determined gravimetrically as SnO_2, while chlorine was determined by Volhard's method. Elemental analyses were performed on Carlo-Erba 1108 Elemental Analyzer. The conductivity measurements in nitrobenzene were made on an Elico Conductivity Bridge type CM-82T. Molecular weights were determined by Rast's camphor method. IR spectra of the complexes were recorded as KBr pellets with a Nicolet-5700 FTIR spectrophotometer. The pellets were prepared in a dry box to avoid the action of moisture. ^{1}H, ^{13}C, and ^{119}Sn NMR spectra were recorded with a Bruker Avance II 400 NMR spectrometer. The FAB mass spectra were recorded with a Jeol SX 102/Da-6000 Mass Spectrometer Data system using argon/xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and *m*-nitrobenzylalcohol (NBA) was used as the matrix.

Syntheses

$NaOC_6H_4Me$-4. To a solution of 4-methylphenol (5 g, 46 mmol) in CCl_4 was added an equimolar amount of sodium metal (1.06 g, 46 mmol). The reactants were stirred at room temperature for 10 h during which a dirty white solid separated out. It was collected by filtration, washed with CCl_4, and dried under vacuum. Yield: 4.8 g, 79%.

$R_2Sn(OC_6H_4Me$-4$)_2$. To a solution of *n*-Bu_2SnCl_2 (1.14 g, 3.7 mmol), Ph_2SnCl_2 (1.29 g, 3.7 mmol), or Me_2SnCl_2 (0.82 g, 3.7 mmol) in methanol was added a methanolic

solution of $NaOC_6H_4Me$-4 (0.98 g, 7.5 mmol). The reactants were then refluxed for 8–10 h, whereupon the separation of a white solid was observed. It was filtered and the filtrate was concentrated by distilling off the solvent. The concentrate was dried under vacuum, whereupon fine cream to pale yellow solids separated out. These were washed with petroleum ether and dried under vacuum.

n-$Bu_2SnCl(OC_6H_4Me$-4). In a typical reaction to a solution of *n*-Bu_2SnCl_2 (0.5 g, 1.6 mmol) in dry tetrahydrofuran (THF) were added equimolar amounts of 4-methylphenol (0.17 g, 1.6 mmol) and triethylamine (0.16 g, 1.6 mmol), dissolved in the same solvent. The mixing of the reactants resulted in the immediate formation of a white solid. The reactants were refluxed for 6 h, to ensure the completion of the reaction. The solid was removed by filtration and the filtrate was concentrated by distilling off the solvent. It was dried under vacuum, whereupon a fine crystalline white solid separated out.

Reactions with 2- and 3-Cyanoanilines

A solution of $Ph_2(SnOC_6H_4Me$-4$)_2$, *n*-$Bu_2(SnOC_6H_4Me$-4$)_2$, *n*-$Bu_2Cl(SnOC_6H_4Me$-4), or $Me_2(SnOC_6H_4Me$-4$)_2$ in absolute ethanol (15 mL) was treated with two equivalents of 2- or 3-cyanoaniline in separate experiments. The reaction mixture was stirred at room temperature for 7–8 h. The addition of acetonitrile to the addition compound of $Me_2(SnOC_6H_4Me$-4$)_2$ with 2-cyanoaniline resulted in the formation of a white solid, while the other compounds were obtained by the addition of petroleum ether. These were then dried under vacuum.

Antibacterial Activity Test

The ligand 4-methylphenol and its diorganotin(IV) complexes were screened in vitro for their antibacterial activity on selected bacteria *E. coli, S. aureus, S. epidermidis, S. flexneri, P. mirabilis, and P. aeruginosa* using the MIC method as recommended by National Committee for Clinical Laboratory Standard (NCCLS).[48] All the samples were tested in triplicate. Experimental details are presented in the Supplemental Materials.

MIC Determination by Two-Fold Serial Dilution

The MIC assay[49] was performed in a 96-well microtitre plate. For MIC assay of each tested drug, a row of 12 wells was used out of which last two wells were taken as control (no drug added). Each of the 10 wells received 100 μL of the Muller-Hinton broth, except the first well, which received 200 μL of broth containing 500 μg/mL concentration of the test drug. From the first well (containing test drug), 100 μL broth was withdrawn with a sterile tip and the same was added to the 100 μL of the broth in the second well; contents were mixed four times. Then, 100 μL was withdrawn from second well and was added to the third well. This way, a range of two-fold serial dilution was prepared (500–0.98 μg/mL). The broth in each of the wells was inoculated with 2 μL of the bacterial culture (*E. coli, S. aureus, S. epidermidis, S. flexneri, P. mirabilis, and P. aeruginosa*) and the contents were mixed by 10 clockwise and 10 anticlockwise rotations on a flat surface. The plate was incubated at 35 °C. The observations for growth of bacteria were recorded after 24 h.

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