CHAPTER 1

A BRIEF REVIEW OF ORGANOTIN(IV) COMPLEXES OF AZO-CARBOXYLIC ACIDS

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1.1 Introduction

The use of tin compounds in a large variety of applications is well known and organotin(IV) carboxylates are well represented in this context, having uses in industry and agriculture [1-3]. In addition, an area of current interest involves the screening of organotin(IV) compounds for potential anti-tumour activity and focuses upon results obtained in the past decade or so, as well as upon other therapeutic applications of tin compounds [4]. A number of early reviews recording advances in the screening for antitumour potential of organotins are available [5-10]. In the recent reviews, published in 1991 and 1994, the structural chemistry of organotin carboxylates was surveyed [11,12]. This survey revealed that there exists a rich structural diversity for these compounds where very different structures are found even though the chemical formulae may be quite similar. In view of these, a number of structures are being reported till today highlighting the interest in this particular class of compound.

1.2 Organotin(IV) complexes of azo carboxylic acid

The organotin(IV) carboxylates derived from azo ligands (Fig. 1.1) have been reported by Majee and Banerjee [13]. This type of ligands is well suited for the preparation of a variety of interesting organotin complexes because the ligands i.e. arylazobenzoic acids with a wide variety of nuclear substituents can be easily prepared by diazotization of the amino benzoic acid followed by coupling with suitable aryl moiety and have a very favourable steric arrangement for the complexation. In this context, a series of triorganotin(IV) derivatives of arylazobenzoic acids were prepared and investigated spectroscopically [13,14] which offered interesting structural possibilities. Their UV spectra recorded in non-polar solvents exhibited a large bathochromic shifts and such shifts were predicted for N→Sn co-ordination (Fig. 1.2). These interaction was found to be absent in co-ordinating solvents as the weak N→Sn bond is replaced by a donor solvent molecule (S) as shown in Fig. 1.3.
Further, when the aryl group contains a donor group in the ortho- position of the coupling moiety, the arylazobenzoato moiety was postulated to function as a terdentate ligand (Fig. 1.4). In view of this, structures of triphenyltin(IV)/ tricyclohexyltin(IV) complexes of $o$-(2-hydroxy-5-methylphenylazo)benzoic acid (Fig. 1.5) and triphenyltin(IV) complexes of $o$-(2-hydroxynaphthylazo)benzoic acid (Fig. 1.6) have been studied by $^{119}$Sn Mössbauer spectroscopy. In addition, triphenyltin(IV) complexes of $o$-(4-dimethylaminophenylazo)benzoic and $o$-(4-hydroxynaphthylazo)benzoic were also investigated (Figs. 1.7 and 1.8).
A few years after, the crystal structure of the triphenyltin(IV) o-(2-hydroxy-5-methylphenylazo)benzoate was determined in the hope that the complex would constitute the first example of a six-coordinated triorganotin(IV) compound. Crystals of the triphenyltin(IV) o-(2-hydroxy-5-methylphenylazo) benzoate (see Fig. 1.5; R = Ph) comprise discrete molecular units, in which the carboxylato group functions as an anisobidentate chelating ligand [Sn-O(1): 2.070(5), Sn···O(2): 2.463(7) Å], thus rendering the tin atom five co-ordinated (Fig. 1.9). The unit-cell projection of the compound reveals that there is no intermolecular carboxylato-bridging. The geometry at the tin atom is intermediate between tetrahedral and cis-trigonal bipyramidal, in which the carboxylato ligand spans equatorial and axial sites. The two C–O bond distances of the carbonyl group are as expected unequal [C–O(1): 1.296(8); C–O(2): 1.224(8) Å]. The structure of the triphenyltin(IV) o-(2-hydroxy-5-methylphenylazo)benzoate complex as shown in Fig. 1.9 is, therefore, the first characterized example of a truly monomeric triorganotin carboxylate. It is interesting to note that, in spite of the bulky phenyl groups attached to tin and the very large steric demands of the arylazobenzoato group which prevent intermolecular bridging, the carboxyl group prefers to function as a chelating ligand giving the five-coordinated structure rather than as a unidentate ligand.
Recently, a series of triorganotin(IV) complexes of formulation $R_3SnO_2CR'$ where $R =$ Me, Et, i-Pr, \(t\)-Bu, and \(c\)-Hex and $R'CO_2$ residue of \(o\)-(2-hydroxy-5-methylphenylazo)benzoic acid, has been investigated in detail [16]. Among these, the structure of triphenyltin(IV) compound was investigated earlier by Harrison et al.[15]. The triphenyltin(IV) compound was again synthesized and upon recrystallization from acetone/methanol (1/9) solution afforded an acetone solvated product. The structure of triphenyltin(IV) \(o\)-(2-hydroxy-5-methylphenylazo)benzoate acetone solvate (2/1) [17] resembles closely that of the unsolvated form as shown in Fig. 1.9 [15]. The Sn atom exists in a distorted tetrahedral geometry with Sn-O(1) being 2.079(5) Å (cf. 2.070(5) Å in the unsolvated form). The Sn...O(2) separation is 2.656(5) Å and is responsible for the expansion of the C-Sn-C angle to 116.9(3)°. There are no close interaction between the solvent acetone molecule and the compound. The same coordination geometry has been reflected in tricyclohexyltin(IV) compound as shown in Fig. 1.9 for triphenyltin(IV) analogue, and with the range of angles subtended at tin being 96.7(2)-120.1(2)°. The Sn...O(2) separation is 2.759(4) Å [16]. On the other hand, trialkyltin(IV) compounds ($R =$ Me, Et, \(t\)-Bu) are polymers [16] and comprise distorted trans-$R_3SnO_2$ trigonal bipyramidal geometries (Fig. 1.10). The carboxylate ligand is bidentate bridging; however, the Sn-O bonds are not equivalent. The disparity in the Sn-O bond distances, [O(1)-Sn-O(2)], increases in the order Me (0.323 Å) < Et (0.350 Å) < \(t\)-Bu (0.415 Å). The intramolecular Sn...O(2) separations are 3.175(4), 3.18(1), and 3.245(3) Å for Me, Et, \(t\)-Bu, respectively.

![Chemical structure](image)

\(R = \text{methyl-}, \text{ethyl- or } n\)-butyl-)

**Fig. 1.10**

The different behaviour, among various triorganotin(IV) compounds, has been ascribed to the steric demands of the tin-bound substituents. A fair correlation was found between the difference in $^{117}$Sn chemical shift between the solution and solid states and, the carbonyl oxygen-tin distance of the triorganotin(IV) compounds, only when the data of triphenyltin(IV) compound, are
omitted. This indicated that the mesomeric effect of the phenyl group does not express its influence to the same extent in the solid and solution states, unlike the inductive effects. The crystal structures of the complexes were correlated with other spectroscopic data. By contrast, a good correlation including triphenyltin(IV) compound was found between the $^{119}\text{Sn}$ Mössbauer quadrupole splitting and the difference in $^{117}\text{Sn}$ chemical shift between the solution and solid states.

Trimethyltin(IV)- [18] and triethyltin(IV)- [19] complexes of $p$-(2-hydroxy-5-methylphenylazo)benzoic acid were also investigated crystallographically. Both the structures are polymeric owing to the presence of bidentate bridging carboxylate ligands. The intramolecular separation of 2.139(3) Å is shorter than the intermolecular Sn...O(2) distance of 2.497(3) Å in Me$_3$Sn compound. In Et$_3$Sn compound, the carboxylate ligands form disparate Sn-O(1) and Sn...O(2) distances of 2.149(4) Å and 2.586(4) Å, respectively. The structures of Me$_3$Sn and Et$_3$Sn resemble closely that found for the ortho- analogue as shown in Fig. 1.10 [16] and structures conform to a common motif, i.e. trans-C$_3$SnO$_2$.

The influence of molecular geometry in halodiorganotin(IV) complexes of the $o$-(2-hydroxy-5-methylphenylazo)benzoic acid was also studied [20]. The crystal and molecular structures of three compounds were presented in which the carboxylate residue has been kept constant and the $R_2$Sn moiety has been altered such that $R$ = Me, ‘Bu and Ph. The crystallographic study show that two distinct motifs are adopted owing to different modes of coordination of the carboxylate ligands. The chlorodimethyltin(IV) complex is dimeric with the two tin atoms being bridged by two ‘O$_2$CR’ anions each of which coordinates a tin atom via one of the carboxylate oxygen atom and the second tin atom via the phenoxide oxygen atom and the complex exists in a zwitterionic form. The tin atom geometry is trigonal bipyramidal, trans-O$_2$SnC$_2$Cl (Fig. 1.11). By contrast to the dimeric structure for chlorodimethyltin(IV) complex, the structures of chlorodi-t-butylin(IV) and chlorodiphenyltin(IV) complexes are monomeric with the tin atoms in cis-O$_2$SnC$_2$Cl trigonal bipyramidal geometries (Fig. 1.12). The ‘O$_2$CR’ anion coordinates the tin atom via the carboxylate oxygen atoms only.
The crystal and molecular structures of two more compounds of the general formula \( R_2Sn(O_2CR')_2 \) are also reported where \( R = 'Bu \) and \( Ph \) [21] (Fig. 1.13). For the \( R = 'Bu \) compound, the tin atom exists in a skew-trapezoidal bipyramidal geometry in which the trapezoidal plane is defined by two asymmetrically chelating carboxylate ligands and the organic residues lie over the weaker Sn…O interactions. A similar coordination geometry is found in the \( R = Ph \) compound which was isolated as a di-chloroform solvate. The chloroform molecules exert an influence on the molecular geometry in that a conformational change in the carboxylate ligand is induced in order to facilitate the formation of intermolecular hydrogen bonds.
Systematic variations in the Sn-ligand parameters in these and related compounds are correlated with the varying Lewis acidity at the tin centres. The replacement of one carboxylate ligand in \([\text{R}_2\text{Sn}(\text{O}_2\text{CR}')]_3\) by a chloride, i.e. yielding \([\text{R}_2\text{Sn}(\text{O}_2\text{CR}')]\text{Cl}\) [20], results in a significant contraction of the Sn-O(2) distance to 2.402(3) Å while maintaining the primary Sn-O(1) interaction constant at 2.105(3) Å. The comparable distances for the \([\text{Ph}_2\text{Sn}(\text{O}_2\text{CR}')]\text{Cl}\) structure are 2.365(3) Å and 2.090(3) Å, respectively [20]. These results are correlated with the enhanced Lewis acidity of the tin centre in the respective \(\text{R}_2\text{SnCl}\) moieties. For the \(\text{R} = \text{Ph}\), substituting a carboxylate ligand in \([\text{Ph}_2\text{Sn}(\text{O}_2\text{CR}')]_3\) with a phenyl group leading to \([\text{Ph}_3\text{Sn}(\text{O}_2\text{CR}')]\) [17] results in Sn-O(1) and Sn-O(2) of 2.079(5) Å and 2.656(5) Å, respectively, a result consistent with the reduced Lewis acidity of the tin atom in \(\text{Ph}_3\text{Sn}\) compared with \(\text{Ph}_2\text{Sn}\). The Lewis acidity of the tin center was found to decreases in the order \(\text{Ph}_3\text{Sn} < \text{Ph}_2\text{Sn} < \text{Ph}_2\text{SnCl} < \text{Bu}_2\text{SnCl}\) for the phenyltin and tert-butylltin compounds, respectively.

More recently, a comprehensive study of organotin(IV) complexes was carried out involving 5-(arylazo)salicylic acid from the point of view of structural motifs and biological applications. A series of triphenyltin(IV) complexes of 5-(arylazo)salicylic acid has provided X-ray quality crystals in which the ligand aryl residue has been varied (aryl = phenyl- [22], 2-methylphenyl- [22], 3-methylphenyl- [22], 4-methylphenyl- [23], 4-methoxyphenyl- [22] and 4-chlorophenyl- [24]), and \(\text{Ph}_3\text{Sn}\) was held constant. The solid state structures of these triphenyltin(IV) complexes were evaluated using \(^{119}\text{Sn}\) Mössbauer and X-ray crystallography. The triphenyltin(IV) complexes adopt a monomeric distorted tetrahedral configuration defined by a \(\text{C}_3\text{O}\) donor set where the carboxylate ligand coordinating in a monodentate mode (Fig. 1.14). The relatively small variations observed for the geometric parameters across the series of
triphenyltin(IV) complexes indicated that the variable substitution in the aryl residue has little influence on the tin geometry.

\[
\text{HO} \quad \begin{array}{c}
\text{N=}
\text{SnPh}_3
\end{array}
\]

\[(R' = H, 2\text{-methyl-}, 3\text{-methyl-}, 4\text{-methyl-}, 4\text{-methoxy-} \text{or} 4\text{-chloro-})\]

Fig. 1.14

Further, one of the tetrahedral triphenyltin(IV) complexes was subjected to the reactivity study towards 2,2'-bipyridine to ascertain the ability of 2,2'-bipyridine to coordinate to the Sn-complex and the resultant changes in the molecular architecture. The crystal structure of the product revealed that the 2,2'-bipyridine moiety does not coordinate to the Sn atom, but forms a cyclic tetrameric adduct of formula \([\text{Ph}_3\text{SnO}_2\text{CR}'(\text{H}_2\text{O})]_2\text{bipy}_2\) \((\text{O}_2\text{CR}' = 5\text{-}(2\text{-methylphenylazo})\text{salicylate})\) through hydrogen bonding between the water ligand of \(\text{Ph}_3\text{SnO}_2\text{CR}'(\text{H}_2\text{O})\) and the 2,2'-bipyridine N atoms (Fig. 1.15) [23].

![Diagram](a)
Fig. 1.15 (a) The molecular structure of Ph₃SnO₂CR'(H₂O).bipy (b) The hydrogen-bonded tetrameric motif in the molecular structure of Ph₃SnO₂CR'(H₂O).bipy, consisting of two Ph₃SnO₂CR'(H₂O).bipy and two bipy molecules.

The trialkyltin(IV) complexes, viz., Me₃ [24], nBu₃ [22,24] were investigated by Sn Mössbauer and Sn NMR spectroscopy. Sn Mössbauer spectroscopy shows that these complexes are polymeric and feature a trans-trigonal bipyramidal geometry with a planar SnR₃ unit and two apical carboxylate oxygen atoms derived from bidentate bridging carboxylate ligands. These trialkyltin complexes dissociate in solution to a tetrahedral species as indicated by Sn NMR data.

In addition, a series of di-n-butyltin complexes involving 5-(arylazo)salicylic acid have been studied in great detail in view of possible biological applications. A systematic investigation of the structures of the di-n-butyltin complexes of 5-(arylazo)salicylic acid was carried out. The carboxylate residue was varied by virtue of changes to the aryl group (aryl = phenyl- [25], 2-methylphenyl- [26], 3-methylphenyl- [25], 4-methylphenyl- [25], 4-bromophenyl- [25] and 4-chlorophenyl- [27]), and the nBu₂ was held constant. In general, the crystallographic results indicated that the complexes adopt a skew-trapezoidal bipyramidal arrangement around the tin atom (Fig. 1.16).
In addition, there are weak bridging intermolecular Sn⋯O contacts in di-n-butyltin(IV) complexes when carboxylate residue is phenyl-, 2-methylphenyl- or 3-methylphenyl- but not in substituents at 4-position (e.g. 4-methylphenyl-, 4-bromophenyl- and 4-chlorophenyl-), where one of the hydroxyl oxygen atoms from a neighbouring molecule coordinates weakly with the Sn atom, thereby completing a seventh coordination site in the extended Sn coordination sphere (Fig. 1.17).
The Sn...O distance is 3.080(2) and 3.439(2) Å in di-n-butylin(IV) complexes when carboxylate residue is phenyl-, 2-methylphenyl- or 3-methylphenyl-. The values are significantly shorter than the sum of the van der Walls radii of the Sn and O atoms. This interaction links the molecules into polymeric chains or head-to-head dimeric units as shown in Fig 1.18.

Fig.1.18 The dimeric unit formed by the weak Sn···O interaction in di-n-butylin(IV) complexes when carboxylate residue is 3-methylphenyl.

The crystal structures of these complexes were correlated with $^{117}$Sn CP MAS NMR and $^{119}$Sn Mössbauer data, while their solution behaviour was evaluated using $^{119}$Sn NMR in non coordinating solvents.

Another interesting report is a dirganotin(IV) complexes containing mixed arylazobenzoates of composition [R$_2$Sn(O$_2$CR')$_2$(O$_2$CR'')] where R = "Bu or Me and O2CR' and O2CR" are two different 5-(arylazo)salicylates. A full characterization of the structures of the complexes in the solid-state was accomplished by single crystal X-ray crystallography [28]. The complexes were found to adopt the usual dicarboxylato structural type with a skew-trapezoidal bipyramidal arrangement around the tin atom as shown in Fig. 1.16.

A sterically congested organotin(IV) complex was obtained by the reaction of sodium 4-(4'-dimethylaminophenylazo)benzoate and {[2-(dimethylaminomethyl)phenyl](diphenyl)}tin chloride [29]. The crystal structure of the complex revealed that the tin atom exists in a slightly
distorted trans-trigonal bipyramidal geometry defined by three *ipso*-carbon atoms of the phenyl groups in equatorial positions, with the intramolecularly bound nitrogen atom for the CH$_2$N(CH$_3$)$_2$ group and the oxygen atom of the carboxylate groups in apical positions (Fig. 1.19).

As a part of a wider study designed to ascertain the reason(s) for the structural variation found in these systems, the reactivity of a few triorganotin(IV)s was studied with a new ligand system e.g. 5-(2'-carboxyphenylazo)salicylaldehyde. The molecular structure of [Ph$_3$Sn(O$_2$CR')(OH$_2$)] (Fig. 1.20) [30] reveals that the carboxylate group coordinate to the tin atom via one of the oxygen atoms only (Sn-O = 2.161(5) Å). The tin atom is also coordinated by a water molecule (Sn-O = 2.527(5) Å) and exists in a trigonal bipyramidal geometry with the three phenyl groups in equatorial positions; the O-Sn-O axial angle is 176.3(2)$^\circ$. The lattice is stabilized by H-bonding contacts as well as charge-transfer interactions. A brief report of a polymeric trimethyltin(IV) compound [Me$_3$Sn(O$_2$CR')]$_n$ is also there in the literature [31]. The tin atom in this compound is fivefold-coordinated, existing in a distorted trigonal bipyramidal geometry (Fig. 1.21). The trigonal plane is defined by the three methyl groups and the axial positions by symmetry related oxygen atoms; Sn-O(1) = 2.174(6) Å, Sn-O(2') = 2.448(7) Å and the tin atom lies 0.1246(7) Å out of the plane in the direction of the more strongly bound O(1) atom.
Further work in this area involving 5-(2'-carboxyphenylazo)salicylaldehyde (systematic name: 2-[(E)-2-(3-formyl-4-hydroxyphenyl)-1-diazenyl] benzoic acid) and related systems constitute the subject matter of the thesis and are described in the forthcoming chapters.

1.3 Biological activity of organotin(IV) azocarboxylates

Triorganotin(IV) o-(arylazo)benzoates [32] (Fig. 1.22) were screened in vitro for their biological activity against several microorganisms. These complexes were found to exhibit considerable activity against *Staphylococcus aureus*, *Bacillus Cereus*, *Sarcina lutea*, *Bacillus pumilus*, *Micrococcus flavus*, and *Bacillus subtilis*.

The activity were correlated on the nature of aryl R', R'', R'''-substituents. The significant inhibition of bacterial growth by triorganotin o-(arylazo)benzoates compared to corresponding o-(arylazo)benzoic acid was explained and mechanism was proposed for arresting bacterial growth. The enzymatic proteins in their relatively rigid planar peptide structure possess carbonyl group capable of forming metal-oxygen bond with the stannyl groups of organotin carboxylate and this bond formation is further augmented by the nearby β-azoic nitrogen and stannyl carboxylate carbonyl oxygens which form bifurcated hydrogen bonds with the peptide N-H groups (N-H...N
= 2.97 Å, N-H...O = 3.29 Å), thus, enhancing the electron density on the peptide oxygen. A stereocomputer simulated molecular model of the mode of attachment of peptide unit (Gly-Gly) with crystallographic structure of triphenyltin(IV) \( o\)-[2-bromo-4-(dimethyl amino)phenylazo]benzoate is shown in Fig.1.23.

Organotin(IV) complexes of 5-(arylazo)salicylic acid have been studied in great detail for evaluating their biological properties. A series of organotin(IV) complexes of formulations \( \text{"Bu}_2\text{Sn}(O_2\text{CR'})_2 \), \( \text{Ph}_3\text{SnO}_2\text{CR'} \) and \( \text{"Bu}_3\text{SnO}_2\text{CR'} (\text{O}_2\text{CR'} = \text{substituted 5-(arylazo)salicylate} \) were subjected to toxicities studies against second larval instar of \textit{Aedes aegypti} mosquito larvae [27]. The results indicate that all the triorganotin(IV) compounds have activities of an order of magnitude higher than for the diorganotin(IV) derivative. The LC\(_{50}\) values (concentration at which the test compounds killed 50% of the tested organisms) for the triorganotin(IV) compounds ranged from 0.53 to 3.50 mg l\(^{-1}\). Also, the data indicated that the tri-n-butyltin(IV) compounds were more effective than the phenyl derivatives. Although the triorganotin(IV) compounds, are not as effective as organophosphorus insecticides [33] in their larvicial effects, their advantages lie in their biodegradability and lack of known resistance by this species of mosquitoes.

In addition, a representative di-n-butyltin(IV) compound of formulation \( \text{"Bu}_2\text{Sn}(O_2\text{CR'})_2 \) (\( \text{O}_2\text{CR'} = \text{substituted 5-(arylazo)salicylate} \), was tested across a panel of human cell lines \textit{viz.}, WIDR (colon cancer), M19 MEL (melanoma), A498 (renal cancer), IGROV (ovarian cancer) and
H226 (non-small cell lung cancer), MCF7 (breast cancer), EVSA-T (breast cancer) to establish the activity [25]. The data clearly show that the di-n-butyltin(IV) compound is more active in vitro than cisplatin and etoposide against all seven human cancer cell lines.

The toxicity studies of tri-n-butyltin(IV) complexes of formulation $^8$Bu$_3$SnO$_x$CR’($O_x$CR’ = substituted 5-(arylazo)salicylate) and the parent 5-(arylazo)salicylic acid were evaluated by using sea urchin early developmental stages as recommended model organisms for toxicity tests [34]. The present report also throw light on the effects of new organotin compounds towards two species of sea urchin, Paracentrotus lividus and Sphaerechinus granularis, in order to compare variation in the impact incidence of contaminant exposure among different species. Biological activity tests of the tri-n-butyltin(IV) complexes demonstrated that the (i) embryos exposed to the tri-n-butyltin(IV) complexes at $10^{-5}$ and $10^{-7}$ M solutions presented blocks and strong developmental anomalies. (ii) embryos treated with free 5-(arylazo)salicylic acid at $10^{-5}$ M concentration stopped to develop at the blastula stage. At $10^{-7}$ M, they developed regularly as the control. (iii) embryos treated with tri-n-butyltin(IV) chloride (positive control) did not develop any more. (iv) sensitivity of $S$. granularis embryos was like that of $P$. lividus. The developmental anomalies can be seen in Figs. 1.24 and 1.25.

![Fig.1.24](image)

**Fig.1.24** Sea urchin control embryos and treated embryos with tri-n-butyltin(IV) compounds. Anomalous embryos exposed to tri-n-butyltin(IV) compounds solutions did not show any significant difference under optical microscopy: $P$. lividus (a) and $S$. granularis (b) anomalous embryos, after incubation in $10^{-5}$ M solution of the compound for 48 h. The blastomeres are of different sizes and are blocked at the two to four-cell stages.
Anomalous embryos exposed to tri-n-butyltin(IV) compounds solutions did not show any significant difference under optical microscopy: *P. lividus* (a) and *S. granularis* (b) anomalous embryos, after incubation in $10^{-7}$ M solution of the compound for 48 h and arrested anomalous embryos.

In conclusion, the tri-n-butyltin(IV) compounds induced high embryonic mortality in *P. lividus* and *S. granularis*; and were as toxic as tri-n-butyltin(IV) chloride independently of the presence of the ligands.

From the foregoing description of the structural chemistry of organotin(IV) azocarboxylates, it is clear that there exists a rich diversity in Sn atom geometry and coordination modes of the azocarboxylates themselves. Such complexes are likely to find wide application in biology, medicine etc.
References


