ORGANOTIN COMPOUNDS: AN INVESTIGATION ON THE SYNTHESIS, STRUCTURES AND PROPERTIES (INCLUDING BIOCIDAL PROPERTIES) OF ORGANOTIN CARBOXYLATES AND RELATED COMPOUNDS

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY

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DECLARATION

I hereby, declare that the work presented in this thesis entitled "Organotin Compounds: An investigation on the Synthesis, Structures and Properties (Including biocidal properties) of Organotin Carboxylates and related compounds" is entirely original and was carried out by me under the supervision of Professor Abhijit Roy, Department of Chemistry, University of North Bengal, Darjeeling for the award of Doctor of Philosophy in Chemistry. The contents of this thesis did not form the basis of award of any previous degree to me or to anybody else.

To the best of my knowledge, the thesis has not been submitted previously for the award of any degree to this university or any other university.

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CONTENTS

CHAPTER 1

ORGANOTIN COMPOUNDS – A SHORT REVIEW ON THE NATURE OF BONDING AND OTHER RELATED PROPERTIES

CHAPTER 2

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL PROPERTIES OF Mn(II), Fe(II), Co(II), Ni(II) AND Cu(II) COMPLEXES OF 3-CYCLOHEXYLPROPANOIC ACID

CHAPTER 3

SYNTHESIS, CHARACTERIZATION AND BIOCIDAL PROPERTIES OF ORGANOTIN(IV) CARBOXYLATES OF CYCLOPROPANE CARBOXYLIC ACID AND 3-CYCLOHEXYLPROPANOIC ACID

CHAPTER 4

SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION, FLUORESCENCE AND BIOCIDAL PROPERTIES OF SOME DIORGANOTIN(IV) COMPLEXES OF SALICYLALDEHYDE THIOSEMICARBAZONE AND RELATED LIGANDS

CHAPTER 5

CYTOTOXIC ACTIVITY OF DIORGANOTIN(IV) COMPLEXES OF SALICYLALDEHYDE THIOSEMICARBAZONES

PREFACE

The thesis entitled "Organotin Compounds: An investigation on the Synthesis, Structures and Properties (Including biocidal properties) of Organotin Carboxylates and related compounds" has aimed to explore the chemistry of simple organotin(IV) carboxylates and other related compounds. The work has been divided in five chapters.

Chapter 1

This chapter gives a brief review on the nature of bonding and other related properties of the organotin compounds.

Chapter 2

This chapter describes the synthesis, characterization and biological properties of Mn(II), Fe(II), Co(II), Ni(II) and Cu(II) complexes of 3-cyclohexylpropanoic acid. The complexes were characterized by IR and elemental analyses. Magnetic moment studies and differential calorimetric analyses were also carried out for these complexes. Antifungal activities of these compounds against two fungal pathogens namely, *Curvularia eragrostidis* and *Alternaria porri* were also studied.

Chapter 3

In this chapter, the synthesis, characterization and biological properties of organotin(IV) complexes of two carboxylic acid ligands, namely, cyclopropane carboxylic acid and 3-cyclohexylpropanoic acid are described. All the compounds have been characterized by IR, (^{1}H, ^{13}C and ^{119}Sn) NMR spectroscopy along with the elemental analyses. The decomposition of a few selected complexes were studied by thermogravimetric analyses(TGA).The solid state structure of dimethyltin(IV) derivative of cyclopropane carboxylic acid was studied by X-ray crystallography. The biological activity of these compounds against four fungal pathogens, namely, *Curvularia eragrostidis*, *Alternaria porri*, *Dreschlerea oryzae* and *Macrophomina phaseolina* of four different crops were investigated. Some of the newly synthesized organotin(IV) carboxylates were screened for their antibacterial activity against

Pseudomonas fluorescens, a fish-pathogenic, Gram-negative bacteria. Phytotoxicities of these new organotin compounds were determined on healthy wheat seeds (variety-Sonalika).

Chapter 4

This chapter describes the synthesis, characterization, fluorescence and biological properties of diorganotin(IV) compounds of Schiff bases derived from salicylaldehyde/substituted salicylaldehyde and thiosemicarbazide. The ligands selected for the study were salicylaldehyde thiosemicarbazone, 5-bromo salicylaldehyde thiosemicarbazone, 5-chloro salicylaldehyde thiosemicarbazone, naphthaldehyde thiosemicarbazone. The complexes with the general formulae $[R_2Sn(OArCH{=}N\text{-}N{=}CSNH_2)]$, where R=Me, n-Bu, Ph and Ar = $-C_6H_4$, $-C_6H_3$(5-Cl), $-C_6H_3$(5-Br) and $-C_{10}H_6$ were characterized by UV, IR, NMR (^{1}H, ^{13}C and ^{119}Sn) spectroscopy and elemental analysis. The solid state structures of some of these complexes were studied by X-ray crystallography. The biological activity of these compounds against four fungal pathogens, namely, *Curvularia eragrostidis*, *Alternaria porri*, *Dreschlerea oryzae* and *Macrophomina phaseolina* of four different crops and a panel of bacteria, namely, *Aeromonas hydrophila*, *Salmonella typhi*, *Salmonella typhimurium*, *Salmonella flexnri*, *Escheria coli*, *Salmonella aureus*, *Bacillus subtilis* and *Lactobacillus rhamnosus* were investigated. The phytotoxic effects of these compounds were also investigated against *Oryzae sativa*, *Lens culinaris* and *Cicer aurantinum*.

Chapter 5

This chapter deals with the cytotoxic effects of the newly synthesized diorganotin(IV) compounds of Schiff bases derived from salicylaldehyde/substituted salicylaldehyde and thiosemicarbazide against a panel of human cell lines, namely, Colo205, Hop62, MCF7, PC3, SiHa, ZR-75-1, A-2780, DWD, K562, DU145, SW 480 and HCT 116. The cytotoxic effect of dibutyltin(IV) salicylaldehyde thiosemicarbazone was also studied against two mouse tumour cell lines namely, EAC and SAR-180 .The results were compared with clinically tested drugs.

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CHAPTER 1

ORGANOTIN COMPOUNDS – A SHORT REVIEW ON THE NATURE OF BONDING AND OTHER RELATED PROPERTIES

1.1 Introduction

The Chemistry of tin has been the subject of extensive research in the last few decades. Tin in the form of a metal and its alloys were known to the ancient people and have greatly affected the course of human history [1]. Tin (atomic number, 50; relative atomic mass 118.70) is an element of group 14 of the periodic table, together with C, Si, Ge and Pb. Tin exists in three allotropic modifications and it can form a variety of inorganic and organometallic compounds. These two classes of compounds have different chemical and physical properties, which make them suitable for different applications in industry, agriculture and elsewhere. Tin as a metal, either as such, or in the form of its alloys and chemical compounds, has an astonishing amount of usefulness. Characteristically, in majority of its applications, only small amount of tin is needed to see its effect. This is generally true for organotin compounds, which during the past few decades have developed into extremely useful industrial commodities. Tin is unsurpassed by any other metal in the multiplicity of its applications. These involve such widely divergent fields as stabilizers for polyvinyl chlorides, industrial catalysts, industrial and agricultural biocides, wood preservatives and anti-fouling agents to mention only the most important applications.

Organotin compounds are defined as those that contain at least one carbon-tin covalent bond, the carbon atom being part of an organic group. The compounds contain tetravalent tin centres and are classified as mono-, di-, tri- and tetraorganotin(IV)s, depending on the number of alkyl (R) or aryl (Ar) moieties. The anion is usually a chloride, fluoride, oxide, hydroxide, a carboxylate or thiolate [2].

1.2 Literature

The first chemist to report the existence of "organic bodies of tin" as they were then known seems to have been E. Frankland [3]. This paper was devoted largely to the reaction which occurred when ethyl iodide and zinc were heated together in a sealed tube. The behaviour of ethyl iodide in contact with metallic tin, at elevated temperatures (150 to 200°C) was also studied. Frankland later showed that the crystals

obtained by the reaction of EtI with Sn at elevated temperatures (Eq.1) were of diethyltin diiodide [4-6].

$$2EtI + Sn \longrightarrow Et_2SnI_2 \quad \ldots\ldots\ldots\ldots (1)$$

In 1852, in an independent work [7], C. Löwig established that ethyl iodide reacted with a tin/sodium alloy to give oligomeric diethyltin. In 1859, Buckton obtained tetraethyltin by treating tin tetrachloride with Frankland's diethylzinc [8]. Letts and Collie showed that tetraethyltin could be prepared (Eq.2) by heating ethyl iodide with a mixture of Zn and Sn powder [9].

$$EtI + Zn/Sn \longrightarrow Et_4Sn + ZnI_2 \quad \ldots\ldots\ldots\ldots (2)$$

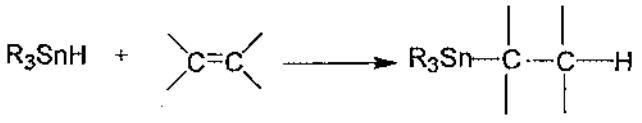
In 1879, Frankland [10] studied the reaction between stannous chloride and diethylzinc, hoping by analogy with results obtained by Buckton [8] simply to displace the chlorides with ethyl groups. The product obtained, however, was Et_4Sn and not Et_2Sn (Eq. 3).

$$Et_2Zn + SnCl_2 \longrightarrow Et_4Sn + ZnCl_2 \quad \ldots\ldots\ldots\ldots (3)$$

As a route to Et_4Sn, this new reaction proved superior to Buckton's original method [8] and remained the method of choice for preparing tetraalkyltins until the early years of 20th century when Pope and Peachey first made use of the reaction of Grignard reagent on tin tetrachloride or alkyltin halides [11]. These types of reactions soon became the standard route to synthesize alkyl- and aryl- tin compounds. Krause and von Grosse summarized this early work in Organometallische Chemie which was first published [12] in 1937.

In 1962, Kuivila and his coworkers showed that the reaction of trialkyltin hydrides with alkyl halides (Eq. 4) was a radical chain reaction involving short-lived trialkyltin radicals $R_3Sn^{\cdot}$ [13]. Subsequently, in 1964, Neumann *et al.* showed that the reaction with non-polar alkenes and alkynes (Eq.5) followed a similar mechanism [14]. These reactions are now the basis of a number of important organic synthetic methods.

$$R_3SnH + R'X \longrightarrow R_3SnX + R'H \quad \text{.....(4)}$$



.....(5)

The use of organotin hydrides in organic synthesis as selective reducing agents was reviewed in 1964 [15] and 1974 [16]. The uses of organotin compounds in organic synthesis have also been reviewed [17].

The first review of organotin compounds was published in 1937 by Krause and von Grosse [12]. Ingham, Rosenberg and Gilman [18] extended the literature up to 1959. Weiss [19] compiled an exhaustive list of organotin compounds covering the literature from 1937 to 1964. Several monographs by J.J. Zuckerman [20], R.C. Poller [21], W.P. Neumann [22] and a multi-author work edited by A.K. Sawyer [23] were published in 1971-72, and progress during the decade 1970-1980 was reviewed by Davies and Smith [24,25]. The preparation, properties and applications of monoalkyltin compounds have been reviewed by Guo Yushen in 1991 [26].

A review by Gielen and Sprecher [27] includes a discussion of organotin structure in which the coordination number of tin is greater than 4; the same topic was treated in an article by Okawara and Wada [28]. Structural aspects of organotin compounds have been reviewed [29] and a comprehensive bibliography of X-ray diffraction studies is available from the International Tin Research Institute [30].The structural diversity of organotin compounds have been attracting the attention of a number of researchers and a multitude of structural types have been discovered [31].

Recently, Nath *et al.* have reviewed organotin(IV) complexes of the amino acids and peptides with special reference to their methods of synthesis, structural, thermal properties as well as their solution studies and biological activity [32].The structures of these complexes were discussed on the basis of IR, electronic, multinuclear (^{1}H-, ^{13}C- and ^{119}Sn -) NMR, X-ray and ^{119}Sn Mössbauer spectral studies.

Synthesis, reactivity, structural aspects and applications of organotin(IV) complexes with phosphorous-based acids have been reviewed by V.K. Jain [33].The applications of these complexes as catalysts, corrosion inhibitors and biocides were also discussed in this review.

An excellent critical review by Beckmann *et al.* [34] has appeared on stannasiloxanes in 2001.Chandrasekhar *et al.* have reviewed the recent progress in the area of organotin assemblies that contain Sn-O bonds [35]. Various kinds of tri-, di- and monoorganotin compounds are described in terms of their preparative methods such as hydrolysis of organotin halides, reactions of suitable organotin compounds with various kinds of substrates such as carboxylic acids, sulphonic acids, oxide transfer reagents etc. The structural characterizations of these compounds by the use of ^{119}Sn-NMR, ^{119}Sn Mössbauer and X-ray crystallography have been presented in considerable detail. The amazing structural diversity present in this family of compounds was discussed [35].

A comprehensive review [2] by L. Pellerito and L. Nagy discusses the properties of organotin(IV) complexes formed with biologically active ligands containing {O}, {N}, {S}, or {phosphorous(O)} donor atoms with various composition and stability. The emergence of new experimental techniques (EXAFS, multinuclear ^{1}H-, ^{13}C-, ^{119}Sn-NMR, ^{119}Sn Mössbauer, etc., spectroscopic techniques) provided useful information about the structure and stability of the complexes formed.

Organooxotin compounds can be assembled by various synthetic methodologies. Although in most instances, organotin oxide and hydroxides are preferred starting materials for organooxotin compounds, Sn-C bond cleavage reactions involving organotin compounds also offer a rational route. A very recent review by Chandrasekhar *et al.* [36] deals with the recent progress in this area and examines various reactions, where Sn-C cleavage occurs. A wide range of products are accessible from this approach and these are beautifully presented in the above-mentioned article.

The work on the use of organotins in agriculture was pioneered in the 1950's and early 1960's by van der Kerk and coworkers who discovered high fungicidal activity of tributyl- and triphenyl- tin compounds [37-40].

In 1989, the results obtained in the wide field of bio-organotin(IV) compounds were surveyed by Molloy [41]. Later Tsangaris and Williams [42] published a paper on Sn (including organotin(IV) compounds), compounds in pharmacy and nutrition. A full listing of reports which have evaluated organotin(IV) compounds in agriculture can be found in the two-part review by Crowe [43,44]. Detailed discussions of organotin(IV) compounds as wood preservatives have been published [45, 46].

In 1973, Atsushi *et al.* [47] in a very important piece of work reported the very high affinity of tin for tumours (highest among group 14 elements). This finding was further confirmed by various workers who prepared tin labelled technetium complexes and used them as imaging agents for tumour localization [48]. Two important reviews covering the literature of anticancer activity of organotin compounds have been published recently [49, 50]. Also, Sartaj Tabassum and Claudio Pettinari in their review article in 2006 provided substantial information on the mode of action of organotins in cancer chemotherapy [51].

1.3 Bonding in organotin compounds

Tin has $5s^2$, $5p^2$ electronic configuration in its valence shell and therefore, two oxidation states i.e., +2 and +4 (due to 'inert s-pair effect') are possible. The ground state for tin is a ^3P state, derived from s^2p^2 configuration [52]. In this state, there are only two unpaired electrons and a covalence of two would be expected. But the tetra-covalent state occurs much more frequently than the divalent state. The four-covalent state is derived from the sp^3, ^5S state of the tin, which is not the ground state but the first excited state.

Essentially, most of the organometallic tin compounds are of the Sn(IV) type [53]. The marked increase in the stability of R_4Sn compounds over R_2Sn compounds demonstrates the effect of increased hybridization. The stability (to heat & oxygen) of

organotin derivatives in tetravalent states is reflected in the vast amount of growing literature about them. By contrast, their bivalent derivatives are much less stable, but these are also beginning to attract attention particularly with sterically demanding ligands {e.g. $CH(SiMe_3)_2$} and π-bonding ligands. These bulky ligands stabilize the compounds in low-coordination geometry, as the congested environment around the metal hinders polymerization due to steric factors [54]. For example, tin(II) cyclopentadienyl, $(C_5H_5)_2Sn$ is a well established compound with tin in the (+2) oxidation state.

1.4 Reactivity of organotin compounds

The tetraalkyl and aryl compounds of main group 14 elements differ from the corresponding derivatives of these elements in neighbouring groups because of their relatively low reactivity. This difference in behaviour is more because of kinetic than thermodynamic factors.

Within group 14, the reactivity of M-C bond in tetra- alkyl and aryl increases progressively from Si to Pb [54] as

- bond energy decreases in the same sequence
- expansion of the coordination number of the metal (M) becomes easier with increasing atomic size and decreasing difference between np and nd orbitals.

$Si(C_2H_5)_4$ $Ge(C_2H_5)_4$ $Sn(C_2H_5)_4$ $Pb(C_2H_5)_4$

Decreasing M-C bond energy →

Decreasing thermal stability →

The electronegativity of tin change with its oxidation number. Tin(II) compounds are generally more ionic than tin(IV) compounds [55].

The general characteristic pertaining to increase in electropositive character with increase in atomic number in a group is also strikingly pronounced among the metals of group 14. Therefore, the Sn-C bond should be polar since tin is electropositive with

respect to carbon and is represented by $C^{\delta-}$-$Sn^{\delta+}$. The polarization of $C^{\delta-}$-$Sn^{\delta+}$ bond makes tin atom more electrophilic and carbon atom attached to tin more nucleophilic. This enhances the reactivity of organotin moieties both towards electrophiles as well as nucleophiles. Reaction of alkyltin chlorides with the appropriate nucleophiles gives the alkyltin alkoxides, amides, thioalkoxides, carboxylates etc. The presence of these electronegative groups on tin renders the metal susceptible to coordination by Lewis bases and simple tetrahedral four-coordination is an exception rather than the rule in such cases [56].

Organotin compounds can undergo Grignard type reactions particularly with carbonyl containing substrates. For instance, allyltin compounds will add across the C=O bond of aldehydes in a manner analogous to that of Grignard reagent [57].

$$Et_3SnCH_2CH{=}CH_2 + RCHO \longrightarrow RCH(OSnEt_3)CH_2CH{=}CH_2 \quad \text{.....(6)}$$

Due to low polarity of C-Sn bond, as in tetraalkyl and aryl derivatives of tin, these are not actually hydrolyzed by water. Hydrolysis however, may be brought about by increasing pressure and temperature and using catalysts such as acid or alkalis which attack 'C' or 'Sn' [58]. A rather unusual feature of the organotin compounds is the ionization of some of the R_3SnX and R_2SnX_2 compounds in water [59].The extremely ready hydrolysis of a fluorocarbon-tin bond in perfluorophenyl trimethyltin has been partly ascribed to the increased susceptibility of tin to nucleophilic attack [60]. The hydrolysis is catalyzed by halide ion.

There is substantial evidence that the d orbitals of the elements of group 14, other than carbon are used in dπ-pπ bonding [59]. A simple example illustrates this phenomenon. With the four acids of the type *p*-$R_3MC_6H_4COOH$, where M=C, Si, Ge or Sn, C is the most electronegative and should enhance the acid strength to the greatest extent. But, it is found that M=C compound shows the lowest acid strength, indicating that dπ-pπ bonding is operative in the other three metal compounds [61, 62]. The tendency to use'd' orbitals in bonding decreases from Si to Sn, since in $(GeH_3)_2S$ and $(GeH_3)_2O$, the Ge-S-Ge and Ge-O-Ge appear to be highly bent [63] whereas in $(SiH_3)_2O$, the Si-O-Si bond angle is around 150° [64]. However, the possibility of dπ-pπ bonding in Sn cannot be completely ignored, atleast with elements of higher atomic numbers,

e.g, Cl, Br, I, etc. This is supported by the higher values of Sn-Cl stretching frequencies in certain tin compounds [65] and Sn–O frequency in $(Ph_3Sn)_2O$ [66].

Reactions of the general type:

are of utmost significance in both theoretical and practical studies in organotin chemistry. Although the reactivity of tin-carbon bonds depends on molecular environment, they are susceptible to attack by a wide variety of reagents so that A-B in the above equation may be a halogen, mineral acid, carboxylic acid, thiol, phenol, alcohol, metallic or non-metallic halide, alkali & alkali metal etc. Tin-carbon bond cleavage not only involves electrophilic attack at 'C' but also nucleophilic assistance at the Sn atom [21].

Among organometallic main group compounds, organotin compounds are quite unique in possessing reasonably labile tin-carbon bonds. While compounds containing Sn-allyl bonds are the most labile, those containing Sn-benzyl and Sn-phenyl substituents are sufficiently reactive. The Sn-alkyl bond cleavage is the most difficult to accomplish and occurs under relatively harsh conditions. Even among Sn-alkyl compounds those containing Sn-methyl cleavage are the most documented. In contrast, those involving Sn-butyl cleavage are very few. The current state of knowledge of these Sn-C cleavage reactions allow these compounds to be utilized extensively as synthons. In view of this, it is expected that in addition to organotin halides, oxides and hydroxide compounds containing Sn-alkyl, Sn-benzyl, Sn-phenyl or Sn-allyl bonds will also be very useful as reactants in synthetic procedures for the construction of rings, cages and clusters [36].

1.5 Structure of organotin compounds

Tin(II) compounds are mostly bent, pyramidal or distorted (due to the presence of a stereochemically active lone pair of electrons which does not participate in bonding and occupies a position directed away from the strongly bonded coordination sites). The structural chemistry of tin(IV) compounds reflects the relative simplicity of the electronic configuration in this oxidation state and is dominated by regular bond

arrangements : tetrahedral, trigonal bipyramidal and octahedral depending on the coordination number. Tin(IV) is remarkable in its capacity to expand its coordination number from four (which is found in most simple organotin compounds like the simple tetraalkyls and tetraaryls) to five, six or seven [67-69].

In organotin derivatives of the type R_nSnX_{4-n} (n = 1 to3), where X is an electronegative group (e.g. halide or carboxylate etc.), the Lewis acid strength of tin is increased and subsequently the Lewis bases form complexes with higher coordination number. The compounds R_3SnX usually yield five-coordinate complexes R_3SnXL which are approximately trigonal bipyramidal, and the compounds R_2SnX_2 and $RSnX_3$ usually form six-coordinate complexes $R_2SnX_2L_2$ and $RSnX_3L_2$ which are approximately octahedral. The groups X, however, by virtue of the unshared electron pairs which they carry, can themselves act as Lewis bases resulting in intermolecular self-association to give dimers, oligomers, or polymers [70]. Nature of the ligands and the steric demands of R, X and L are the factors influencing the self-association [71].

If R or X carries a functional substituent Y beyond the α-position, intramolecular coordination can occur leading to the formation of monomers with 5-, 6-, 7-, or 8- coordinated tin [70]. In fact, even, coordination number 7 which was once regarded an oddity no longer remains to be so given the appropriate type of ligand to interact with the metal; double-armed bis(semicarbazone) and bis(thiosemicarbazone) ligands derived from pyridine belong to this class [72, 73] .

1.6 Applications of organotin compound

1.6.1 Non-biological applications

A major development in recent years has been the increasing use of organotin reagents and intermediates in organic synthesis, exploiting both their homolytic and heterolytic reactivity [74-76]. Another important use of organotin compounds is in the stabilization of PVC [77]. Many organotin compounds are used as homogeneous catalysts in industry [78, 79]. Also, several organostannosiloxanes have been shown to be extremely versatile catalysts for transesterification reactions [80, 81]

1.6.2 Biological applications

Organotin compounds have found a variety of applications in agriculture and medicine. The first organotin compounds to reach commercialization in agriculture (in the early 1960s) were triphenyltin acetate (Brestan*, Hoechst A.G.) and triphenyltin hydroxide (Duter*, Philips Duphar, N.V.) both of which are used widely [82]. Aquatic organisms such as algae, crustaceans, fish and mollusks are sensitive to tri-n-butyltin, triphenyl and tricyclohexyltin compounds leading to the incorporation of these triorganotin units in anti-fouling paints for marine transport vessels [77]. Organotin compounds are also used extensively as preservatives of wood [83] and as agricultural fungicides and insecticides, and in medicine they are showing promise in cancer therapy and in the treatment of fungal infections [84].

To summarize, the basic studies in the field of organotin compounds have been developed due to the success of a large number of modern analytical techniques applied to organotin compounds. Investigations can be performed by general techniques such as UV [21], IR [21, 56], ^{1}H-NMR [85], ^{13}C-NMR [86], mass spectrometry [87] and also by specialized techniques such as ^{119}Sn Mössbauer spectroscopy [21,25] and ^{119}Sn-NMR spectroscopy [88]. ^{119}Sn Mössbauer and ^{119}Sn-NMR Spectroscopy provide complementary information on the structure of the organotin molecules in the solid state and in solution, respectively.

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CHAPTER 2

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL PROPERTIES OF Mn(II), Fe(II), Co(II), Ni(II) AND Cu(II) COMPLEXES OF 3-CYCLOHEXYLPROPANOIC ACID

2.1 Introduction

Metal ions play a pivotal role in the regulation of life processes. They regulate the osmotic phenomenon within the cells and tissues and function as constituent of oxygen carriers. They also act as biocatalysts (enzymes and co-enzymes). Metals like Fe, Cu, V are present in the oxygen carrying system in blood of vertebrates and many invertebrates. The role of Mg in chlorophyll, Zn in the enzymes and Co in vitamin-B_{12} are well-established.

While many metals are essential for different life processes in small amounts, introduction of such metals in larger quantities may destroy those living species. For example, Fe, Cu, Zn and few other elements are required by fungi for proper growth and development. But when Zn or especially Cu are supplied in more than optimal amounts they behave as fungicides. Certain other metals like Ni, Hg and Pb which have no physiological activity can also act as fungicides [1]. Keeping these facts in view, it is of much interest to probe the role of metal complexes as biocides.

Transition metal complexes of Cu, Ni, Cr, Fe etc. are associated with a broad spectrum of activity ranging from biological to commercial applications [2-8].

Several cupric carboxylates are dimeric either in the crystalline state, in solution or in both [9]. Frequently, they are isolated as hydrates or solvates followed by dehydration under vacuum.The application of heat to these complexes may cause slight decarboxylation of the compounds affording anhydrous materials contaminated with small amounts of copper oxide in insufficient quantities to affect the elemental analyses [11]. This contamination of the complexes would significantly affect the magnetic properties [10]. The mode of bonding in dimeric Cu(II) acetate is debatable [10].

The neutral mononuclear copper complexes with the quinolone antibacterial drug oxolinic acid (regardless of the presence or absence of a nitrogen donor heterocyclic ligand 1,10-phenanthroline, 2,2′-bipyridine or 2,2′-dipyridylamine) have been synthesized and characterized with infrared, UV-Visible and electron paramagnetic

resonance spectroscopies. The experimental data suggested that oxolinic acid acts as a deprotonated bidentate ligand and was coordinated to the metal ion through the pyridine and one carboxylate oxygen atoms. The crystal structure of (chloro)(1,10-phenanthroline)(oxolinato) copper(II) has been determined with X-ray crystallography. For all complexes, a distorted square pyramidal environment around Cu(II) was suggested. The EPR (electron paramagnetic resonance) behaviour of (chloro)(1,10-phenanthroline)(oxolinato) copper(II) in aqueous solution indicated mixture of monomeric and dimeric species. The investigation of the interaction of the complexes with calf-thymus DNA was performed with diverse spectroscopic techniques and showed that the complexes were bound to calf-thymus DNA. The antimicrobial activity of the complexes were tested on three different microorganisms. The complexes show a decreased biological activity in comparison to the free oxolinic acid [12].

FT-IR spectra of crystalline alginic acid and its complexes formed by selected transition metal cations were recorded, assigned and discussed in terms of structure of the investigated compounds by Filipiuk *et al.* [13].

Thermal decomposition of transition metal malonates, $MCH_2C_2O_4 \cdot xH_2O$ and transition metal succinates, $M(CH_2)_2C_2O_4 \cdot xH_2O$ (M=Mn, Fe, Co, Ni, Cu & Zn) have been studied employing TG, DTG, DTA, XRD, SEM, IR and Mössbauer spectroscopic techniques by Randhawa *et al.* [14] . After dehydration, the anhydrous metal malonates and succinates decomposed directly to their respective metal oxides in the temperature ranges 310-400°C and 400-525°C respectively. The oxides obtained have been found to be nanosized. The thermal stability of succinates was observed to be higher than that of the respective malonates.

Transition metal complexes of 1-aziridine-carboxylate were synthesized and characterized by Hauck *et al.* [15].

Reaction of copper(II) perchlorate with *p-tert*-butyl-calix[4]arene-1,3-diacid gave mononuclear complex in acetonitrile and dinuclear complex in methanol which was isolated as their pyridine bound adducts. The dinuclear complex exhibited different

characteristics in its EPR and magnetic studies. The reactivity studies clearly indicated that the dinuclear complex had higher catecholase mimetic activity over its mononuclear counterpart owing to its coordination favourability [16].

Few complexes of Fe(III), Co(II), Ni(II) and Cu(II) with uracil, 6-amino uracil, and those with substituted phenyl azo-6-amino uracils containing *o*-methyl, *p*-carboxy and *o*-carboxy substituents and 5,5′-diethyl barbituric acid sodium salt have been synthesized and characterized by elemental analysis, magnetic moment and spectral measurements (IR, UV-Vis, ESR). The IR spectra show that uracil existed in keto-enol tautomerism but 6-amino uracil possessed the keto amino-imine structure with some enol form. The iron complexes were with octahedral geometry while the cobalt complexes were with square planar and octahedral geometries. The square planar copper complexes existed in ligand bridged structures. The nickel complexes were of tetrahedral configuration. In general, the azo group was involved in the structural chemistry of the complexes. The coordination bond length was calculated. The thermal properties (TG and DTA) of the complexes were measured & discussed and the thermodynamic parameters were also evaluated [17].

Copper(II) coordination complexes of bis(1-methylimidazol-2-yl)propionates and bis(1-methylbenzimidazol-2-yl)propionates were synthesized The structures were determined by X-ray crystal structure determination, both molecules forming infinite one-dimensional hydrogen bonded chains. In both structures, the copper atoms were on an inversion center, which resulted in a tetragonally distorted octahedral coordination geometry. The coordination sphere around Cu consisted of four equatorially coordinated imidazole nitrogen atoms and two axially coordinated carboxylate groups. The non-coordinated water molecules of both crystal structures are involved in a one-dimensional hydrogen-bonded network. Two neighbouring octahedrons were connected by two water molecules, each water molecule forming two hydrogen bonds with the non-coordinated oxygen atoms of the carboxylate group. This resulted in the formation of infinite one-dimensional chains [18].

The literature concerning transition metal carboxylates is vast. The author has avoided a comprehensive discussion on the literature rather a very brief glimpse of the literature of the transition metal carboxylates, particularly of simple carboxylic acids

(containing no other donor atoms) is presented here as this forms the subject matter of the thesis.

2.2 Scope and Objective

The main objective was to examine the carboxylic acid namely 3-cyclohexylpropanoic acid as a ligand towards some transition metals as models. This acid and similar acids may then be used to synthesize new organotin compounds for subsequent studies.

2.3 Experimental

2.3.1 Materials

3-cyclohexylpropanoic acid (Lancaster, USA) was used as received from commercial sources. Metal salts (Merck, India) of AR quality were used as received. Methanol (SRL, India) used in the reactions was of AR grade.

2.3.2 Measurements

IR spectra in the range 4000-250 cm^{-1} were recorded on Pye-Unicam SP 300S spectrophotometer as Nujol mulls using CsI optics. Microanalyses were performed at IACS, Jadavpur, Kolkata. Magnetic susceptibility was measured at room temperature on a PAR 155 sample vibrating magnetometer using $Hg[Co(SCN)_4]$ as the calibrant. Differential calorimetric analyses were carried out on a Perkin-Elmer Thermal analyzer from 100-300 °C at a heating rate of 10 °C/min. Metals were estimated using standard methods in our laboratory.

2.3.3 Synthetic procedures

2.3.3.1 Preparation of sodium salt of 3-cyclohexylpropanoic acid

To a methanolic solution (35 ml) of 3-cyclohexylpropanoic acid (3 g, 19.23 mmol) was added dropwise with continuous stirring 0.5 N methanolic NaOH (0.769 g, 38.84 ml, 19.23 mmol) in the presence of phenolphthalein as an indicator. The reaction system was stirred for half an hour. It was then evaporated to dryness leaving behind the crude product of sodium salt of 3-cyclohexylpropanoic acid. The sodium salt thus prepared was recrystallized from methanol and then dried in an air oven at 105 °C for 48 hours.

L^1Na : Yield: 2.73 g, 72.4 %. M.P.: >245 °C (dec.).

Elemental analysis (Calcd. for $C_9H_{15}O_2Na$):

Calcd.: C, 60.67 ; H, 8.42 %.

Found: C, 60.63 ; H, 8.41 %.

IR (cm^{-1}) : $\nu(OCO)_{asym}$ 1570 ; $\nu(OCO)_{sym}$ 1418.

2.3.3.1 Preparation of Mn(II) complex of 3-cyclohexylpropanoic acid(1)

Sodium salt of 3- cyclohexylpropanoic acid (0.632g, 3.55 mmol) was dissolved in methanol (50 ml) and the solution was taken in a 250 ml RB flask fitted with a pressure equalizing dropping funnel and magnetic stirrer. $MnSO_4.H_2O$ (0.300g, 1.775 mmol) was dissolved in 1:1 methanol–water mixture (30 ml) and placed in the dropping funnel & then added dropwise to the solution of sodium salt of 3-cyclohexylpropanoic acid with constant stirring. The flesh coloured product separated out immediately. The product was filtered, washed with methanol (30 ml) and dried in vacuo.

2.3.3.2 Preparation of Fe(II) complex of 3-cyclohexylpropanoic acid (2)

To a solution of sodium salt of 3- cyclohexylpropanoic acid (0.640g, 3.59 mmol) in methanol (40 ml) was added dropwise a 1:1 methanol-water solution (30 ml) of $FeSO_4.7H_2O$ (0.500g, 1.79 mmol) with constant stirring. The brown coloured product

precipitated immediately. The product was washed with methanol (20 ml) and dried in vacuo.

2.3.3.3 Preparation of Co(II) complex of 3-cyclohexylpropanoic acid (3)

To a 1:1 methanol-water solution (20 ml) of $CoCl_2.6H_2O$ (0.350g, 1.47 mmol) was added dropwise with constant stirring a methanolic solution (40 ml) of sodium salt of 3- cyclohexylpropanoic acid (0.524g, 2.92 mmol). A pink coloured product was precipitated .The product was washed with methanol (25 ml) and dried in vacuo.

2.3.3.4 Preparation of Ni(II) complex of 3-cyclohexylpropanoic acid (4)

To a 1:1 methanolic solution (50 ml) of sodium salt of 3- cyclohexylpropanoic acid (0.634, 3.56 mmol) a methanol-water solution (20 ml) of $NiSO_4.7H_2O$ (0.500g, 1.78 mmol) was added dropwise with continuous stirring. The light green coloured product precipitated immediately. The product was washed thoroughly with methanol (30ml) and dried in vacuo.

2.3.3.5 Preparation of Cu(II) complex of 3-cyclohexylpropanoic acid (5)

To the 1:1 methanol-water solution (20 ml) of $CuSO_4.5H_2O$ (0.400g, 1.60 mmol) was added dropwise a methanolic solution (35 ml) of sodium salt of 3-cyclohexylpropanoic acid (0.570g, 3.20 mmol) with constant stirring. A blue coloured product was formed which was washed with methanol (25 ml) and then dried in vacuo.

2.3.4 Fungicidal activity

The fungal strains used were gifts from The Department of Botany, University of North Bengal. The strains were *Curvularia eragrostidis* (a pathogen of tea, *Camellia sineusis*) and *Alternaria porri* (a pathogen of niger, *Guizotia abyssinica)*. These strains were grown on potato-dextrose-agar (PDA, HiMedia, India) medium at 28 ±1 °C.The fungicidal activities were determined following spore germination bioassay as described by Rouxel *et al.* [19]. Purified eluents (10 µl) were placed on two spots 3

cm apart on a clean, grease-free slide and the solvent was allowed to evaporate. One drop of spore suspension (20 µl), prepared from 15 day-old cultures of the fungi, was added to the treated spots. The slides were incubated at 27±1 °C for 24 h under humid conditions in petri plates. Finally, after proper incubation period, one drop of a Cotton Blue-Lactophenol mixture was added to each spot to fix the germinated spores. The number of spores germinated compared with the germinated spores of control (where no chemicals were used) was calculated using an average of 300 spores per treatment. The minimum inhibitory concentration required for complete inhibition was recorded in units of µg/ml.

2.4 Results and Discussion

2.4.1 Synthesis and characterization of transition metal carboxylates

The complexes were prepared in moderate yields by the reaction between the metal salts and 3-cyclohexylpropanoic acid. The complexes are air stable solids having very poor solubility in water and organic solvents. The analytical data correspond to the composition of the complexes and are presented in Table 2.1.

The IR spectra of all the compounds were scanned in the range 4000-250 cm^{-1}. Important vibrational frequencies for structural elucidation are given in Table 2.2. A broad diffused band in the 3500-3200 cm^{-1} region is assigned to OH stretching modes for lattice water present in the complexes [20,21] .In addition, **1**, **3** and **4** displayed bands at 895 cm^{-1}, 897 cm^{-1} and 880 cm^{-1} respectively which can be assigned to the stretching vibration of the coordinated water molecules [22-25]. The carboxylate group displayed two absorbance bands. The denticity of the carboxylate group can be determined with a high level of probability on the basis of the values of $\nu_{asym}(OCO)$ and $\nu_{sym}(OCO)$ and their difference $\Delta\nu$ [26,27]. It is clear from the tabulated values that in all the compounds the carboxylate group is acting as bidentate i.e. the $\Delta\nu \leq 200$ [27] rather than monodentate.

In the case of organotin complexes of 3-cyclohexylpropionic acid also, the ligand was found to coordinate to the organotin moieties in a bidentate fashion except the tri-c-Hex tin derivative where the ligand was behaving as monodentate (see Chapter 3).

The complexes **2** and **5** displayed bands at 1128 and 1164 cm^{-1} corresponding to the presence of SO_4^{2-} group in the coordination sphere as suggested by L. J. Bellamy [28].

The corrected magnetic moment data (Table 2.3) indicate a octahedral geometry for Mn(II), Fe(II), Co(II) and Ni(II) complexes. The value of μ_{eff} = 1.73 B.M. for Cu(II) complex indicates that it is possibly square planar [21,29].

Table 2.1 Physical and analytical data of **1-5**

Complex	Yield	M.pt (°C)	Elemental Composition Found (Calcd.) (%)		
			C	H	M
$[(C_6H_{11}CH_2CH_2COO)_2Mn(H_2O)_2]$ (**1**)	65	173-175	53.58 (53.86)	8.45 (8.47)	13.62 (13.70)
$[(C_6H_{11}CH_2CH_2COO)_2FeSO_4].2H_2O$ (**2**)	58	Started decomposing at 181 °C	43.34 (43.38)	6.81 (6.83)	11.20 (11.22)
$[(C_6H_{11}CH_2CH_2COO)_2Co(H_2O)_2]$ (**3**)	45	Started decomposing at 153 °C	53.29 (53.34)	7.89 (7.90)	14.51 (14.55)
$[(C_6H_{11}CH_2CH_2COO)_2Ni(H_2O)_2]$ (**4**)	42	Started decomposing at 248 °C	53.35 (53.37)	8.39 (8.40)	14.46 (14.50)
$[(C_6H_{11}CH_2CH_2COO)Cu(SO_4)].2H_2O$ (**5**)	67	161-162	30.79 (30.80)	5.39 (5.42)	18.11 (18.12)

Table 2.2 IR spectral data for **1-5**[a]

Complex	$\nu(H_2O)$	$\nu_{asym}(OCO)$	$\nu_{sym}(OCO)$	$\Delta\nu(OCO)$	$\nu(SO_4)^{2-}$
1	3500-3320(mb)	1550(s)	1423(s)	127	-
2	3490-3264(mb)	1535(s)	1430(s)	105	1128(wb)
3	3429(mb)	1561(s)	1434(m)	127	-
4	3370(mb)	1588(m)	1444(s)	144	-
5	3500-3239(mb)	1589(s)	1458(s)	131	1164(mb)

[a]s, strong; w, weak; m, medium; mb medium and broad; wb; weak and broad.

The differential calorimetric analysis of **1** exhibited two peaks at 175.69 °C and 185.21 °C. It is proposed that **1** melted at 175.69 °C ($\Delta H_{melting}$ = 7.21 J/g) and was converted to give a compound (eg. **1a**) which melted at 185.21 °C ($\Delta H_{melting}$ = 1.43 J/g) to form a compound (eg. **1b**). **1b** then started decomposing at 235.69 °C. The enthalpy of first decomposition was calculated to be 3.54 J/g.The complexes **2**, **3** and **4** on heating from 100-300 °C underwent decomposition. The enthalpy of first decomposition was only calculated. **2** started decomposing at 181.24 °C which continued till 217.84 °C. The enthalpy of decomposition was calculated to be 15.02 J/g.The compound **3** also underwent decomposition at from 140 -159.4 °C. The enthalpy of decomposition was calculated to be 9.48 J/g. The onset of decomposition ($\Delta H_{decomposition}$ = 14.33 J/g) for **4** started at 248.46 °C and continued till 258.37 °C. **5** displayed a peak at 162.14 °C corresponding to the melting of the compound ($\Delta H_{melting}$ = 36.79 J/g). **5** after melting gave a compound which underwent decomposition between 244-270 °C ($\Delta H_{decomposition}$ = 17.80 J/g) to give a compound which melted at 273.16 °C ($\Delta H_{melting}$ = 193.46 J/g).

Since all the compounds described above underwent decomposition while heating therefore, no information could be obtained during cooling the compounds. All the

compounds probably decomposed by giving CO_2 off. However, investigations on the decomposed products were not carried out.

Table 2.3 Magnetic moment data[a]

Complex	Magnetic moment (B.M.)	Stereochemistry
1	6.08	octahedral
2	4.98	octahedral
3	4.85	octahedral
4	3.03	octahedral
5	1.73	Square planar

[a] $Hg[Co(SCN)_4]$ as standard

2.4.2 Fungicidal activity of transition metal carboxylates

The results of fungicigal activity of transition metal carboxylates are presented in Table 2.4.The results showed that **5** was most active followed by **4** against the tested fungal strains. Copper fungicides are potentially comparable to organotin compounds, such as triphenyltin acetate and triphenyltin hydroxide [30]. The study undertook revealed that the fungitoxicity of the copper complex was found to be lesser than tributyltin derivative of 3-cyclohexylpropanoic acid and comparable to triphenyltin derivative of 3-cyclohexylpropanoic acid (see Chapter 3).

Table 2.4 Effect of transition metal carboxylates on spore germination

Spore	Complex	MIC[a]
Curvularia eragrostidis	**1**	452
	3	35.62
	4	28.40
	5	21.20
Alternaria porri	**1**	367
	3	50.52
	4	32.36
	5	10.75

[a] Minimum Inhibitory Concentration in μg/ml.

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CHAPTER 3

SYNTHESIS, CHARACTERIZATION AND BIOCIDAL PROPERTIES OF ORGANOTIN(IV) CARBOXYLATES OF CYCLOPROPANE CARBOXYLIC ACID AND 3-CYCLOHEXYLPROPANOIC ACID

3.1 A brief review of organotin carboxylates

In the recent years [1-5], organotin compounds have been the subject of study due to their diversified biological [6-9] and non-biological [10-12] applications along with their interesting structural diversities. The structure of the molecule, coordination number, extent of alkylation and nature of organic groups attached to the tin atom are the main factors deciding the biological activity of the organotin compounds [13-15].Organotin carboxylates comprise one of the most important class of organotin compounds.The chemistry of Organotin carboxylates has attracted much attention owing to their industrial and agricultural importance [16-19] and more recently to their antitumour activity [20]. Consequently there has been considerable interest in their structural characteristics. These compounds may adopt a variety of structural modes depending on the nature of the organic substituent on the Sn atom and/or the carboxylate ligand [21]. The carboxylates are of following types which may either be monomeric or polymeric in the solid state, namely, $R_3SnOCOR'$, $R_2Sn(OCOR')_2$ and $RSn(OCOR')_3$ where R and R' may be same or different alkyl or aryl groups.

3.1.1 Synthesis of organotin carboxylates

Organotin carboxylates are readily synthesized by several routes. The reactions involved in these synthetic routes are extremely general and there does not appear to be any instance where a particular carboxylic acid failed to react with the organotin precursors. Here, attempt has been made to outline the general synthetic methods for the carboxylates of organotins. Attempts are also made to indicate some of the preparatory routes of interesting organotin carboxylates. The review, however, is not comprehensive.

The most general procedure for the synthesis of organotin carboxylates involve the reaction of carboxylic acid with organotin oxides (or hydroxides) [22-24].The reaction is achieved by azeotropic dehydration of the reactants in boiling benzene or toluene, using Dean-Stark apparatus.

$R_3SnOSnR_3 + 2R'COOH \xrightarrow{benzene} 2R_3SnOCOR' + H_2O$ ..... (1)

$R_3SnOH + R'COOH \xrightarrow{toluene} R_3SnOCOR' + H_2O$ .....(2)

$R_3SnOSnR_3 + (R'CO)_2O \xrightarrow{toluene} 2R_3SnOCOR'$ .....(3)

$R_2SnO + 2R'COOH \xrightarrow{toluene} R_2Sn(OCOR')_2$ .....(4)

In a particular synthesis, for example, the water produced in these reactions was alternatively produced by refluxing the reaction mixtures at higher temperatures [25].

$Bu_3SnOSnBu_3 + 2o\text{-}HOC_6H_4COOH \longrightarrow Bu_3SnOCOC_6H_4OH + H_2O$ .....(5)

One of the most convenient and frequently employed method for the synthesis of organotin carboxylates is the reaction between metal carboxylates and organotin halides[26,27] in suitable solvent usually acetone or methanol or CCl_4 or $CHCl_3$.

$R_nSnX_{4-n} + (4\text{-}n)MOCOR' \longrightarrow R_nSn(OCOR')_{4-n} + (4\text{-}n)MX$ ..... (6)

M= Na,K,Ag or Tl; X=halogen

The carboxylates can also be prepared by the reaction of silver salts of carboxylic acids and organotin sulphides [28].

$R_2SnS + 2AgOCOR' \longrightarrow R_2Sn(OCOR')_2 + Ag_2S$ ..... (7)

The cleavage of one or more organic groups from tetraorganotin compounds by carboxylic acids [29] or Hg(I) carboxylates also produces organotin carboxylates.

$R_4Sn + nR'COOH \longrightarrow R_{4-n}Sn(OCOR')_n + nRH$ ..... (8)

$2Me_4Sn + Hg_2(OCOMe)_2 \longrightarrow 2Me_3SnOCOMe + 2Hg$ ..... (9)

In these acidolysis reactions, the cleavage depends on the acid strength, the nature of the organic groups being cleaved and also on the temperature [29, 30]. Vinyl groups are more readily cleaved than the saturated alkyl radicals, but less readily than phenyl [31], and successive groups are lost with increasing difficulty.

An organotin carboxylate $RBu_2SnOCOCH_3$, with different alkyl groups was synthesized by the reaction of $(Bu_2SnX)_2O$ (X=Cl, Br) with Li and subsequent alkylation with RX' (R=Me, Bu; X = Br, I) and $(CH_3CO)_2O$ [32].

Halocarboxylate derivatives of organotin compounds are most conveniently prepared by heating equimolecular proportion of diorganotin dihalides and diorganotin dicarboxylates in an inert solvent (Eq.10) [33] or by the reaction between a diorgaotindihalide(Eq.11) and a metal carboxylate[34].

$$Bu_2SnBr_2 + Bu_2Sn(OAc)_2 \longrightarrow 2Bu_2SnBr(OAc) \quad \text{.....(10)}$$

$$Bu_2SnCl_2 + R'COOK \longrightarrow Bu_2SnCl(OCOR') + KCl \quad \text{.....(11)}$$

Organotin tricarboxylates, $RSn(OCOR')_3$ (R=n-Bu and Ph) are usually prepared from the corresponding organotin trichlorides by the action of Silver salts of carboxylic acids[35].

$$RSnCl_3 + 3R'COOAg \longrightarrow RSn(OCOR')_3 + 3AgCl \quad \text{..... (12)}$$

Organotinhydrides react with carboxylic acids to form the organotin esters with evolution of hydrogen [36]. This reaction is not, however used extensively to prepare organotin esters.

$$Bu_2SnH_2 + 2MeCOOH \xrightarrow{4.5\ hours} Bu_2Sn(OCOMe)_2 + 2H_2 \quad \text{.....(13)}$$

The triorganotin derivatives of 3-ureidopropionic acid of the general formula, $R_3SnOCOCH_2CH_2NHCONH_2$ (R=Ph, n-Bu, c-Hex and *p*–tolyl) have been synthesized by the heating the mixture of Ph_3SnOH and 3-ureidopropionic acid in 1:1 molar ratio in ethanol [37].

The reaction of one molar equivalent of bis(tributyltin)oxide with two molar equivalents each of 2,6-pyridine dicarboxylic acid and dicyclohexylamine in ethanol

solution gave an precipitate of $[(c\text{-}C_6H_{11})_2NH_2][(n\text{–}C_4H_9)_3Sn(O_2C)_2C_5H_3N]$ [38] immediately. The triphenyltin analogue $[(c\text{-}C_6H_{11})_2NH_2][(C_6H_5)_3Sn(O_2C)_2C_5H_3N]$ was prepared from the equimolar reaction between Ph_3SnOH, the acid and the amine.

S.W. Ng *et al.* synthesized monohydrated carboxylate [n-Bu_3Sn(*N*-phthaloylglycin –ate)(OH_2)] and [n-Bu_3Sn(*N*-phthaloylalaninate)(OH_2)] by the condensation of bis(tributyltin)oxide with *N*-phthaloylglycine and *N*-phthaloylalanine respectively in 1:2 molar ratio in the absence of solvents [39].

Triphenyl and tributyltin carboxylates of crotonic acid, 2, 4-hexadienoic acid and 4-nitrocinnamic acids have been prepared by treatment of bis-tributyltin oxide or bis-triphenyltin oxide with one molar proportion of the corresponding acid. Reactions were carried out in benzene or toluene with azeotropic removal of water [40].

μ-oxalatobis(tricyclohexyltin), $\mu\text{-}(O_2CCO_2)[(c\text{-}C_6H_{11})_3Sn]_2$ was obtained is an attempt to prepare $[(CH_3)_4N]^+[(c\text{-}C_6H_{11})_3SnO_2ClO_2]^-$ by the reaction of $[(CH_3)_4N]Cl]$, $(c\text{-}C_6H_{11})_3SnCl$ and $Ag_2O_2CCO_2$ in ethanol by stirring in hot condition [41].

C. Deb and coworkers have shown that alkyl or aryl esters (carbonyl group attached to 1° or 3° carbon atom) may be transesterified to triorganotin carboxylates [42].

$$R'COOR'' + (R_3Sn)_2O \longrightarrow R'COOSnR_3 + R''OSnR_3 \quad \text{.....(14)}$$

Two types of diorganotin(IV) complexes i.e. $[R_2Sn(O_2CCH_2SPh)_2]$ and $\{[R_2Sn(O_2CCH_2SPh_2)_2O\}_2$, R = Me, Et, n-Pr, n-Bu and n-Oct, have been prepared in 1:2 and 1:1 molar ratio (tin : ligand) by refluxing diorganotin(IV) oxide with thiophenoxy acetic acid [43] in a dry benzene – ethanol mixture (3/1 v/v) with azeotropic removal of water.

Recently, a mixed chelate diorganotin compound has been prepared in the reaction with di-n-butyltin oxide with 2,6-pyridinedicarboxylic acid followed by reaction with bis(dicyclohexylammonium) oxalate [44].

The reaction of $RSn(O)OH$ with an excess of carboxylic acid leads to the formation of the hydrolytically sensitive tricarboxylate $RSn(O_2CR')_3$ which under goes hydrolysis to afford the ladder $[(RSn(O)O_2CR')_2\ (RSn(O_2CR')_3]_2$ [45]. In contrast a 6:6 reaction of $RSn(O)OH$ with a carboxylic acid R'COOH afforded a hexametric drum $[RSn(O)O_2CR']_6$ [46].The drums and ladders are also obtained in reactions with diorganotin and triorganotin precursors with carboxylic acids or silver salts of carboxylic acids by Sn-C cleavage reactions [47].

An interesting 2:3 (tin:carboxylate) product, $(n\text{-}Bu_2SnO_2CCCl_3)_2(\mu_2\text{-}OH)(O_2CCl_3)$ has been obtained in 1:2 reaction between $n\text{-}Bu_2SnO$ and CCl_3COOH[48]. In the product, the two Sn units are bridged by a hydroxyl group and a isobidentate carboxylate group. The complex $SnPh_3(O_2CCCl_3).MeOH$ has been prepared by the reaction of Ph_3SnOH and the carboxylic acid in methanol [49]. Synthesis of $SnPh_3(O_2CCl_3)$ without the attached solvent molecule seems to be unusually difficult, although well known for other carboxylates [50,51].In particular, recrystallization of $SnPh_3(O_2CCCl_3)$ in a non-coordinating solvent leads to the diphenyltin compound, $\{[SnPh_2(O_2CCCl_3)]_2O\}_2$.

A compound of the same formulation was also formed by the dearylation of $(SnPh_3)_2O$ with trichloroacetic acid [49].

$$(SnPh_3)_2O \xrightarrow[\text{(ii) recrystallization from dichloromethane - light petroleum}]{\text{(i) trichloroacetic acid, MeOH}} \{[SnPh_2(O_2CCCL_3)]_2O\}_2 \quad \text{.....(15)}$$

However, the product that is formed under the above mentioned condition has different structure. It is not clear whether this is due to solvent effects in the recrystallization or due to the different reaction routes.

The $Bu_2Sn(IV)^{2t}$ complexes formed with ligands containing a carboxylate group(s) are easily prepared by a one-pot method described by Davies *et al.* [52]. In a first step, tetra-n-butyl-di-n-propoxydistannoxane is prepared from Bu_2SnO and n-propanol by refluxing in benzene or in toluene. This distannoxane subsequently reacts at room

temperature with carboxylates. This method [53,54] appears to have two advantages over that in which Bu_2SnO reacts with the carboxylic in refluxing ethanol/ toluene, methanol/toluene; first as the carboxylic acid is added at room temperature, organotin(IV) carboxylates that are unstable at higher temperatures can also be prepared; second, tetra-n-butyl-di-n-propoxydistannoxane is synthesized in water-free medium because the H_2O is eliminated through a H_2O/propanol/benzene azeotrope; hence water- sensitive organotin(IV) carboxylates can be conveniently prepared.

[n-Bu_2Sn(pyridine-2-phosphonate-6-carboxylate)]$_2$ was prepared in very high yield by the reaction of tetra-n-butyl-di-n-propoxydistannoxane, [n-Bu_2Sn(O-Pr-n)OSn(OPr-n)n-Bu_2] (generated *in situ* by the reaction of n-Bu_2SnO with isopropanol in refluxing benzene) with dihydrogen pyridine-2-phosphonate–6–carboxylate in a 1:1 tin/ligand molar ratio at room temperature[55].

A series of diorganotin(IV) compounds were obtained by the reaction of diorganotin(IV) dichloride with 2- pyrazinecarboxylic acid (Hpca) in the presence of sodium ethoxide or triethylamine [56]. Using a 1:1:1 molar ratio of R_2SnCl_2: Hpca: EtONa, trinuclear macrocyclic compounds of the type $[R_2Sn(pca)Cl]_3$ R=Me, n-Bu, Ph, Bz were obtained. With a 1:2:2 ratio, monomeric or polymeric compounds with the general formula $R_2Sn(pca)_2(mH_2O).nH_2O$, m=1 : R=$CH_3$, n=2; m=0: R=n-Bu, n=0 etc. were obtained. Using a 1:2:2 molar ratio of R_2SnCl_2: Hpca: Et_3N, stannate compounds of the type $[Et_3NH]^+[R_2Sn(pca)_2Cl]^-.mH_2O$,m=0 : R=Me; m=0: R= n-Bu etc. were obtained.

The reaction of bis(triphenyltin)oxide, $Ph_3SnOSnPh_3$ and 2,4,6–tris(trifluoromethyl) -benzoic acid, 2,4,6–$(CF_3)_3C_6H_2COOH$ in a 1: 2 stoichiometry, in benzene under reflux conditions afforded the distannoxane $[Ph_2Sn(OH)OC(O)R_f)]_2$, R_f=2,4,6-$(CF_3)_3$ -C_6H_2, in about 94% yield, by means of a facile Sn-C bond cleavage process [57]. The facile Sn-C bond cleavage process occurs as a result of special electronic and steric requirements of the perfluoromesityl carboxylate unit. This is the first example of a Sn-C bond cleaved product in the reaction of $Ph_3SnOSnPh_3$ with carboxylic acid. In contrast, analogous reaction of $Ph_3SnOSnPh_3$ with mesityl carboxylic acid leads to the formation of the normal product, Ph_3SnO_2C-2,4,6-$Me_3C_6H_2$. Also the reaction of

perfluorobenzoic acid C_6F_5COOH with $Ph_3SnOSnPh_3$ leads to the normal product [24]; $Ph_3SnO_2CC_6F_5$.

X-ray quality crystals of the Bis-[(1,7-dicarba-*closo*-dodecaborane-1-carboxylato)-di-n-butyltin]oxide, $\{[1,7\text{-}C_2B_{10}H_{11}\text{-}1\text{-}COO)Bu_2Sn]_2O\}_2$ were synthesized in benzene from a 1:1 condensation of $n\text{-}Bu_2SnO$ with m-carborane-1-carboxylic acid[58].

Reactions of diorganotin(IV) oxides with *o*-anisic acid in a 1:1 and 1:2 stoichiometry in benzene with azeotropic removal of water using Dean-stark trap afforded complexes of the type $\{[R_2Sn(2\text{-}MeOC_6H_4COO)]_2O\}_2$ and $[R_2Sn(2\text{-}MeOC_6H_4COO)_2]$ R=Me, Et, n-Pr, n-Bu respectively[59].

Bis(pentafluorophenylacetato)tetra-n-butyldistannoxane, $\{[n\text{-}Bu_2Sn(O_2CCH_2C_6F_5)]_2O\}_2$; bis(*p*-fluorophenylacetato)tetra-n-butyldistannoxane, $\{[^nBu_2Sn(O_2CCH_2C_6H_4F\text{-}p)]_2O\}_2$ were prepared by the reaction of Bu_2SnO with pentafluorophenylacetic acid and *p*-fluorophenylacetic acid respectively in 1:1 molar ratio by refluxing in 4:1 toluene-ethanol mixture. The water produced in both the reactions was distilled off using a Dean-stark apparatus [60].

The product of the reaction of both ethylene-vinyl acetate copolymers (EVA) and ethylene-methyl acrylate copolymers (EMA) with Bu_2SnO at 200 °C, which leads to the cross-linking of the polymer matrix, is shown to be a dimeric 1-alkoxy-3-acyloxy-distannoxane. The reaction mechanism was studied using model esters(n-octylacetate, n-octadecyl acetate and methyl nonanoate) in absence of solvent at 200 °C. The formation of the main reaction product, $(R\text{-}CO\text{-}O\text{-}(C_4H_9)_2Sn\text{-}O\text{-}(C_4H_9)_2Sn\text{-}OR')_2$ is complete after heating for 25 minutes [61].

Base hydrolysis of $[t\text{-}Bu_2Sn(O_2CCH_3)_2]$ with NaOH yielded hydroxy bridged dinuclear complex $[t\text{-}Bu_2Sn(O_2CCH_3)(\mu\text{-}OH)]_2$, which could also be prepared by the reaction of $(t\text{-}Bu_2SnO)_3$ with acetic acid in 1 : 1 stoichiometry in benzene [62].

Organotin compounds with the general formula $R_2(X)SnL$ (where R= Me, Et, n-Bu, Ph; L= *trans*-3-(2-furanyl)-2-propenoate anion or the *trans*-3-(3-methylphenyl)-2-

propenoate anion; X=Cl) have been prepared by redistribution reactions between R_2SnL_2 and R_2SnX_2 compounds [63].

1,2,3,4-Di-μ-*o*-aminobenzoato-*O*-*O*'-1, 3-bis(*o*-aminobenzoato-*O*)-1,2,4;2,3,4-di-μ_3-oxotetrakis[di-n-butyltin(IV)] was obtained by azeotropic removal of water from the reaction between Bu_2SnO and *o*-aminobenzoic acid in the molar ratio 1:1 in benzene [64].

The complexes $[Me_2(Indo)SnOSn(Indo)Me_2]_2$ and $[Bu_2(Indo)SnOSn(Indo)Bu_2]_2$ were obtained by the azeotropic removal of water produced by the reaction between the respective diorganotin oxide and indomethacin (Hindo) in the molar ratio 1:1 [65].

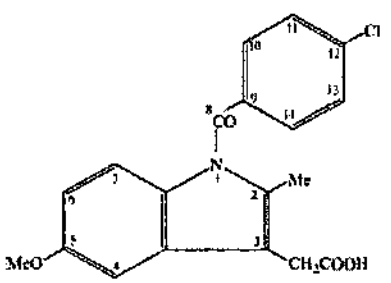


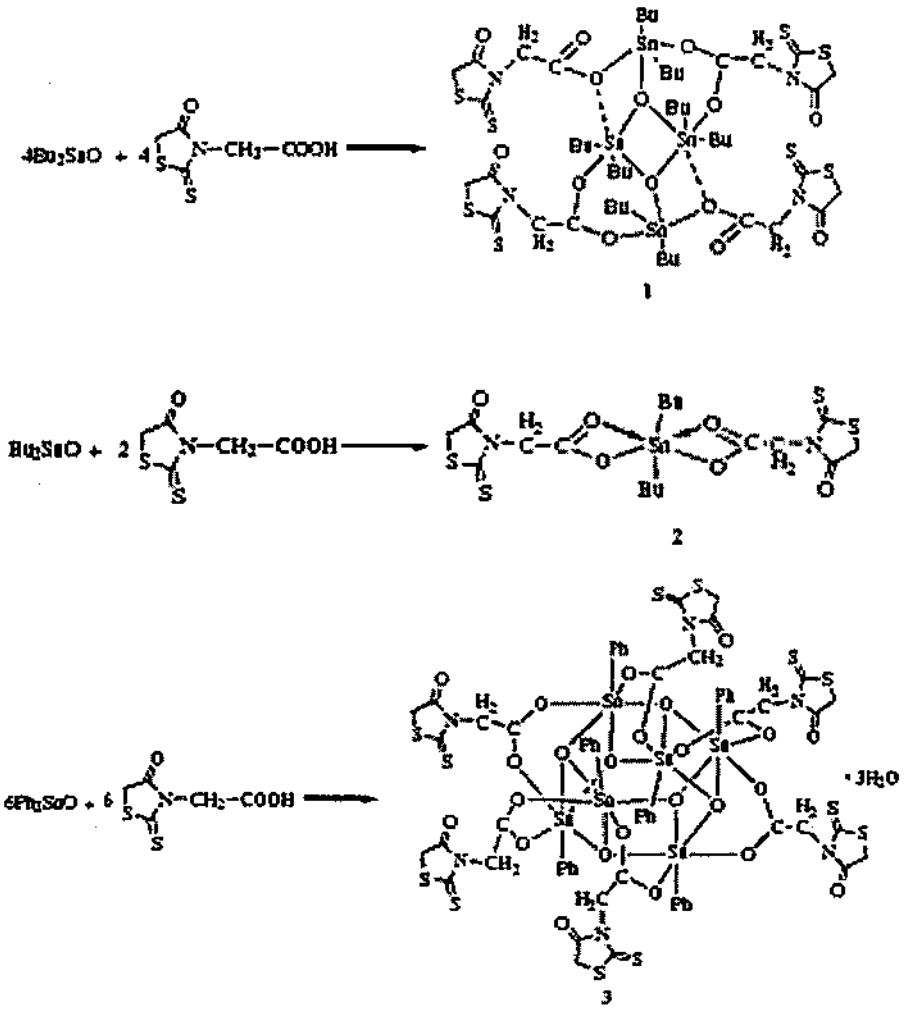
Fig. 3.1 Structure of indomethacin (Hindo) [65].

Diorganotin(IV) derivatives $[R_2Sn(A)_2]$ and $\{[R_2Sn(A)_2]_2O\}_2$ (where A is the dianion of *N*-phthaloyl-**DL**-valine and R= Me, n-Bu, n-Oct) were obtained in moderate yield by the reaction between dialkyltin(IV) oxides with *N*-phthaloyl-**DL**- valine in 1:1 and 1: 2 (Sn: ligand) molar ratio in mixture of dry benzene and absolute ethanol on a water bath by azeotropic removal of water by refluxing for 3-4 hours [66].

The hydrothermal reaction of nitroterephthalic acid, H_2NTPA or diphenic acid (H_2DPA) with 4, 4'-bipyridine and trimethyltin chloride in a molar ratio 1:1:2 at 140 °C for 3 days produced a one-dimensional chain polymer $[(Me_2Sn)_2(\mu_3\text{-NTPA})(\mu_3\text{-O})]_n$ or a two-dimensional corrugated sheet polymer $[(Me_2Sn)_4(\mu_3\text{-DPA})(\mu_4\text{-DPA})(\mu_3\text{-O})_2]_n$ respectively [67].

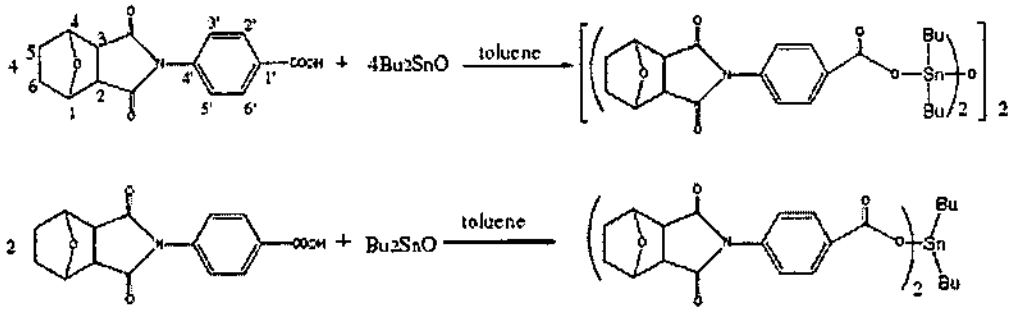
Di-*n*-butyltin oxide react with rhodanine–*N*-acetic acid in 1:1 and 1:2 molar ratios to form $\{[n\text{-}Bu_2Sn(O_2CC_6H_4NOS_2)]_2O\}_2$ (**1**), and $n\text{-}Bu_2Sn(O_2CC_6H_4NOS_2)_2$ (**2**)

respectively. Complex $[PhSn(O)O2CC_6H_4NOS_2)_6].3H_2O$ (**3**) is however produced through the dearylation reaction of diphenyltin oxide and rhodanine–*N*-acetic acid in 1:1 molar ratio [68] .The synthetic procedures are shown in the Scheme 3.1.



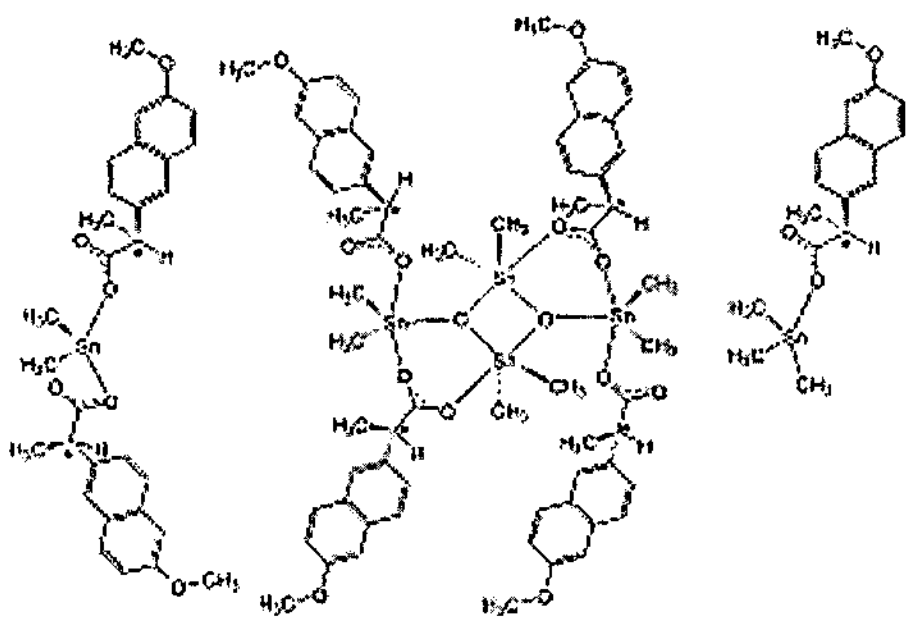
Scheme 3.1

The carboxylic acid 4'-(7-oxabicyclo[2,2,1]-5-heptane-2,3-dicarboximide)benzoic acid (A) reacts with di-*n*-butyltin oxide yielding two different compounds (Scheme 3.2) depending on molar ratio of acid/tin engaged in the reaction: bis[di-*n*-butyl(carboxylato)tin]oxide (**1**) for a 1:1 ratio and di-*n*-butyltin di(carboxylato) (**2**) for a 2:1 ratio [69].



Scheme 3.2

To prepare enantiomerically pure methyltin(IV) naproxenates, dimethyltin dichloride , dimethyltin oxide and trimethyltin chloride were allowed to react with (*S*) – naproxen or its sodium salt. The reactions gave the $Me_2Sn(nap)_2$ (**1**), {[$Me_2Sn(nap)_2]_2O_2$ (**2**) and $Me_3Sn(nap)$ (**3**) complexes (where nap = (*S*)-(+)-6-methoxy-α-methyl-2-naphthaleneaceto anion) [70] .



(1) (2) (3)

Fig. 3.2 Structure of methyltin(IV) naproxenates [70].

A number of distannoxanes have been isolated as the products either from the condensation of a diorganotin oxide with two molar equivalents of the carboxylic

acid, or from the metathetical reaction of a diorganotin dihalide with a metal carboxylate [21, 71].

3.1.2 Structure of organotin carboxylates

The structural investigations of organotin carboxylates are carried out by IR, NMR (^{1}H, ^{13}C, ^{119}Sn) and ^{119m}Sn Mössbauer spectroscopy and by X-ray Crystallography. The structure of organotin carboxylates have been studied extensively by Okawara and Wada [72]. The possibility of chelation through weak coordination of oxygen atoms of carboxylate groups to tin atoms was pointed out by Beattie and Gilson [73] against the postulation of ionic nature of bonding by Freeman [74].

A vast literature on the structure of organotin carboxylates were covered in the review written by Davies *et al.* [16] and on ^{119}Sn–NMR spectroscopy by P. J. Smith and A.P. Tupciauskas [75] and by B. Wrackmeyer [76].

Recently an excellent review by Chandrasakhar *et al.* [77] dealing with the structural diversity of organotin assemblies containing Sn-O bonds was published. The X-ray crystal structures of several organotin carboxylate have been elucidated. This aspect has been critically and quite exhaustively dealt in literatures [21, 71].

3.1.2.1 Structure of triorganotin(IV) carboxylates

Triorganotin carboxylates are known to exist in several structural forms, depending on the physical state and the nature of the substituents on the tin and the carbonyl group. These compounds can exist as monomeric compounds with four-coordinate Sn sites , as monomeric compounds with bidentate carboxylate groups producing a five-coordinate tin, or as polymeric compounds with bridging carboxylate groups that generally produces five-coordinate Sn sites [15].

Based on the studies of the X-ray crystal structures of several triorganotin carboxylate, the structures of these can be divided into two major structural types viz.; (a) discrete and (b) polymeric structures.

Steric effects associated with Sn- and/or ligand-based substituents have been found to be responsible for dictating the nature of structure in the solid state [78].

In the triorganotin carboxylates R_3SnO_2CR' having discrete structures, the tin is bound covalently to three carbons and one oxygen and is present in a distorted tetrahedral geometry [79-81].

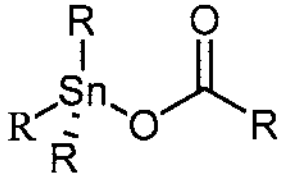


Fig. 3.3 Discrete structural form (no intramolecular coordination).

An X-ray crystal study on tricyclohexyltin acetate, $Cy_3SnOCOMe$ showed the presence of discrete molecules, with the tin atom occupying a distorted tetrahedral geometry.The compound was suggested to be a tetra-coordinated monomer probably due to steric hindrance arising from bulky organic groups [82].

Q. Xie and J. Zheng [83] in 1991 on the basis of IR, ^1H HMR and ^{13}C NMR studies have shown that compounds of the type $ROCH_2COOSnR'_3$ (R'=Ph, Substituted Ph) adopt a distorted tetrahedron containing four-coordinated Sn atom.

The crystal structure of trimesityltin(IV) benzoate, $(C_{27}H_{33})_3Sn(O_2CC_6H_5)$ is monomeric with tin atom in a distorted tetrahedral environment defined by a C_3O donor set as the carboxylate ligand coordinates in a monodentate mode [84].

Even in discrete form, participation of carbonyl oxygen in an intramolecular coordination would lead to approximate trigonal bipyramidal geometry around tin (Fig. 3.4).

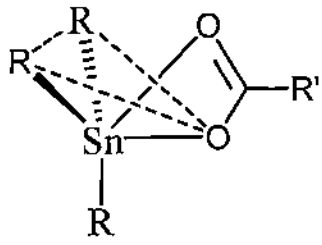


Fig. 3.4 Discrete structural form with intramolecular coordination.

The extent of intramolecular coordination in a complex depends also upon the presence of intramolecular hydrogen bonding. Thus among the $Ph_3SnO_2CC_6H_4$–2–NH_2, $Ph_3SnO_2CC_6H_4$–2–NMe_2 & $Ph_3SnO_2CC_6H_4$-4-NH_2, the anthranilic acid derivative in which the NH_2 group is intramolecularly hydrogen bonded to the C=O has the longest Sn-O distance[85].

The participation of the carbonyl group in intermolecular coordination would give rise to a polymeric associated structure (Fig.3.5) [24].

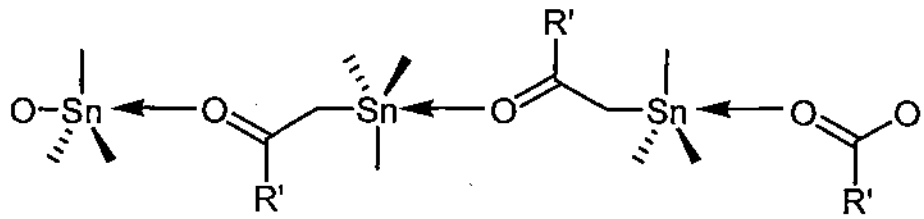


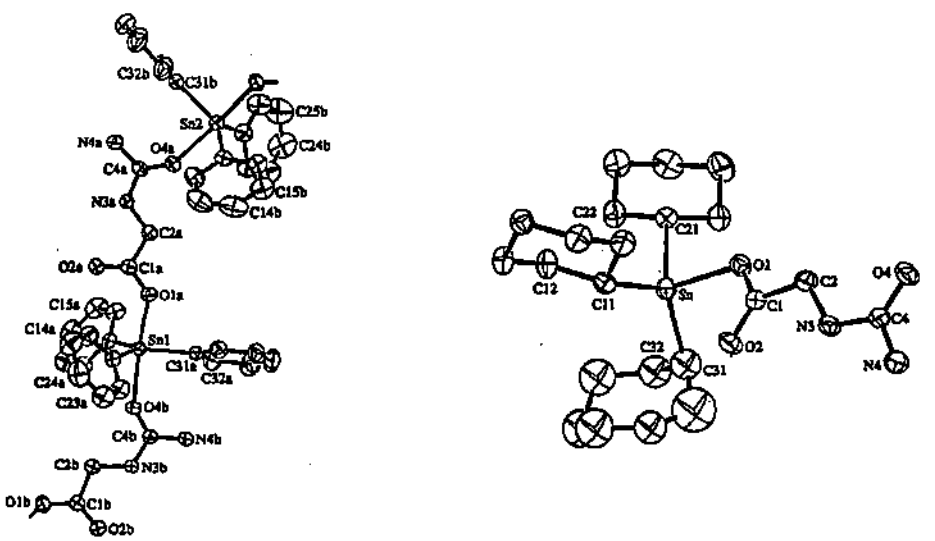
Fig. 3.5 Polymeric form of triorganotin(IV) carboxylates.

These chain polymers, involving bridging carboxylate groups are well documented in literature [86, 87].The coordination polyhedron around Sn is essentially a trigonal bipyramidal with the equatorial positions being occupied by the carbon substituents and the axial positions being occupied by the two oxygens. The Sn–O distances are non-equivalent and because of this variation of the bond distances in the triorganotin carboxylates the Sn is displaced from the equatorial plane towards the covalently bonded oxygen.

The preference for the chain structures seems to be the natural consequence of the principles of penta-coordination. However, the formation of chain structures for

$Ph_3SnO_2CC_6H_4$-2-Cl [88] and for $Ph_3SnO_2CCH_3$ [16] suggests that the factors such as pK_a of the acid and crystal packing may tilt the balance from one structure to another [89].

The structure of $[Ph_3Sn(O_2CCH_2N(H)C(O)NH_2]$ is polymeric in consequence of the bridging property of the carboxylate group. Each ligand coordinates to one Sn atom via one of the carboxylate 'O' atoms and to a symmetry-related Sn atom via a carbonyl group at the other end of the molecule (Fig. 3.6). The structure is distorted trigonal bipyramidal around the Sn atom, with a trans–R_3SnO_2 motif characteristic of triorganotin(IV) complexes. The structure of $[c\text{-}Hex_3Sn(O_2CCH_2N(H)C(O)NH_2]$, by contrast is monomeric with monodentate carboxylate group [90].



(a) (b)

Fig. 3.6 Structure of (a) $[Ph_3Sn(O_2CCH_2N(H)C(O)NH_2]$ and (b) $[c\text{-}Hex_3Sn(O_2CCH_2N(H)C(O)NH_2]$ [90].

$Ph_3Sn(IV)^+$ compounds of *p*-ethoxybenzoic acid and acetylsalicylic acid contain molecular units with Sn-O bonds and distorted tetrahedral tin centres. The phthalic acid derivative contains two tetra-coordinated tin atoms with a phthalic acid unit bridging them. The salicylaldehydato compound is polymeric with trigonal bipyramidal tin centres in which Ph group takes equatorial positions [91].

Khoo *et al.* studied the sarcosine $Ph_3Sn(IV)^+$ complexes with composition $[Ph_3Sn(OCOCH_2NH_2CH_3)_2]X$ ($X=Cl^-$, SCN^-). Sarcosine reacts in a zwitterionic form and behaves as a monodentate ligand via coordination through the carboxylate 'O'. All data support the trans–R_3SnO_2 (tbp) structure of the complexes [92].

The preparation and spectroscopic characterization of $[R_3Sn(O_2CCH_2SC_5H_4N\text{-}4)]$ (R=Ph, Bz, c-Hex and n-Bu) and $[R_3Sn(O_2CCH_2SC_4H_3N_2\text{–}2,6)]$ (R=Me, Ph, n-Bu) have been reported. The 2-pyrimidyl complexes have tbp Sn centres with trans–R_3SnO_3 geometry as confirmed by X-ray diffraction studies on $[Ph_3Sn(O_2CCH_2SC_4H_3N_2\text{–}2,6)]$. By contrast, 4–pyridyl complexes have tbp geometry in the solid state arising from the intermolecular Sn....N interactions and T_d structure in solution [93].

Triorganotin(IV) and diorganotin(IV) halides and pseudohalides form molecular adducts with zwitterions such as picolinic acid [94,95] and quinaldic acid [96]. With carboxylic acids, hydrated complexes are generally obtained. The acid in its Zwitterionic form binds to the $Ph_3Sn(IV)^+$ moiety and generates trigonal bipyramidal geometry around tin. Hydrogen bonding involving non-coordinated water molecules serves to bind the penta-coordinated units together in the form of a dimer. Such compounds display unusual structure [94-96].

V.G. Kumar Das and his coworkers [97] analyzed X-ray data for a number of polymeric triorganotin carboxylates which gave a repeat distance of 5.19 ± 0.21 Å for the carboxylate-bridged R_3SnO_2CR' unit that defines the crystal lattice. The repeat distance is sensitive to organic substituents on either the Sn or the carboxylate group.

Complexes with the formula R_3SnH_2Or (Or = Orotic acid, R= Me, n-Bu) were obtained with the $R_3Sn(IV)^+$ moieties, in which orotic acid (Or) behaves as a monoanionic bidentate bridging ligand and furnishes trigonal bipyramidal complexes [98].

An X-ray analysis of $[(c\text{-}C_6H_{11})_2NH_2]$ $[n\text{-}Bu_3Sn(O_2C)_2C_5H_3N)]$ compound shows that the structure is polymeric with neighbouring triorganotin centres being linked by dicarboxylate ligands [38]. Each carboxylate moiety is involved in coordination to a

Sn atom via one 'O' atom only which has the result that the Sn atoms are five-coordinate and exist in trigonal bipyramidal geometries with the 'O' atoms in axial positions. The pyridine 'N' atom is not involved in co-ordination to Sn.

The crystal structure of $[Me_3SnL]$, L=2',4'-difluoro- 4- hydroxyl-[1,1']-biphenyl-3-carboxylic acid, $C_{13}H_8O_3F_2$, indicates that the tin atom in the asymmetric unit exists in a trigonal bipyramidal geometry, with an orthorhombic crystal system [100].

The structural aspects of triorganotin carboxylates in the solid state and in the solution phase have been investigated by several workers by IR and far-IR spectroscopy [100,101]. The investigations showed that upon dilution of the associated triorganotin esters in organic solvents oligomeic and finally monomeric species containing tetrahedral tin atom and free ester carbonyl functionality is produced [100, 102].

The compound $[Sn(CH_3)_3(C_{15}H_9Cl_2O_2)]_n$ forms polymeric chain involving both O atoms of the carboxylate group.The coordination geometry around the Sn atom is distorted trigonal bipyramidal. The three methyl C atoms occupy the equatorial positions and two O atoms are at axial positions [103].

Several new triorganotin(IV) derivatives of L-homocysteic acid (LCAH) with formula $R_3Sn(LHCA)$ (R= Me, n-Bu, Ph) have been synthesized. Their solid state configurations were determined by IR and Mössbauer spectroscopy. The tin(IV) atom is five-coordinated in all the complexes, with the L-homocysteic acid behaving as a monoanionic bidentate ligand coordinating the tin(IV) through a chelating or bridging carboxylate group. The sulphonate $(SO_3)^-$ and NH_3^+ groups of L-homocysteic acid maintain their free acid configuration and hence do not participate to the coordination of the tin(IV) atom [104].

The crystal structure of *catena*-poly[[tri-n-butyltin]-μ-*N*-(1-naphthylmaleamato] is composed of polymeric chains wherein the metal centre exhibits a distorted trigonal bipyramidal geometry, with three n-Bu groups defining the trigonal plane and the axial positions being occupied by the carboxylate oxygen atoms of two different *N*-(1-naphthyl)maleamate ligands with inequivalent Sn-O distances. The *N*-(1-

naphthyl)maleamate fragment forms an essentially planar seven-membered ring involving an intramolecular N-H....O hydrogen bond [105].

The X-ray diffraction study of μ-oxalatobis(tricyclohexyltin) μ-(O_2CCO_2) [(c-$C_6H_{11})_3Sn]_2$ has revealed the presence of two symmetry – independent molecules, each of which contains a pair of tin atoms in a isomeric *cis* -, *trans* – C_3SnO_2 trigonal bipyramidal configuration arising from the quadridentate (chelating and bridging) behaviour of the oxalato ligand [41].

Some triorganotin carboxylates crystallize with a solvent molecule. These carboxylates show regular five-coordinate discrete structures [n-Bu_3Sn(*N*-phthaloylglycinate)OH_2] [39] is one such example. In all compounds of this type the tin is in trigonal bipyramidal geometry with the equatorial positions being taken up by the aryl or alkyl substituents on tin and the axial position being occupied by the oxygen of the solvent molecule and the covalently bonded oxygen of the Sn-O-C bond.

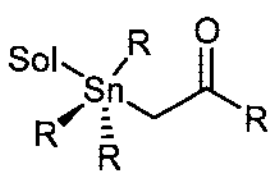


Fig. 3.7 Structure of triorganotin(IV) carboxylates crystallizing with a solvent molecule.

N.W. Alcock and S.M. Roe [49] established the structure of some phenyltin trichloroacetate complexes by X-ray crystallography. The complex $SnPh_3(O_2CCl_3)(MeOH)$ is a five -coordinated monomer. Two isomers of $\{\{[SnPh_2(O_2CCCl_3)]_2\ O\}_2$ are centrosymmetric dimers with all their carboxylate groups bridging and with half of them unidentate respectively. The complex $Sn_2Ph_8(O_2CCCl_3)_6.(OH_2)$ is a linear chain connected by hydroxy and acetate bridges. The hexatin complex $[SnPh(O_2CCCl_3)_3]_6$.$3C_6H_6$ has a drum structure.

3.1.2.2 Structure of diorganotin(IV) dicarboxylates

The dicarboxylates $R_2Sn(O_2CR')_2$ are monomeric and the Sn is hexa-coordinate in a skew-trapezoidal bipyramidal geometry resulting from a chelating anisobidentate coordination mode of the two dicarboxylate ligands[106-108]. The ^{119}Sn-NMR of the dicarboxylates show a single resonance [108].

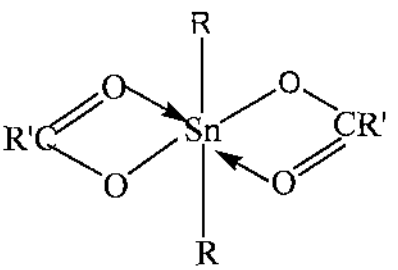


Fig. 3.8 Structure of diorganotin dicarboxylates.

For example, the crystal structure of $[n\text{-}Bu_2Sn(O_2CC_6H_4NOS_2)_2]$ is seen to be comprised of discrete molecules with tin atom hexa-coordinated [68].

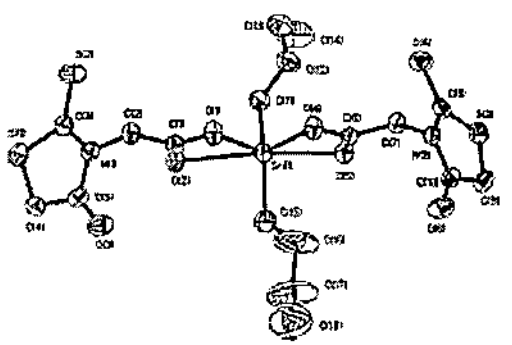


Fig. 3.9 Structure of $[n\text{-}Bu_2Sn(O_2CC_6H_4NOS_2)_2]$ [68].

The crystal structure of $[n\text{-}Bu_2Sn(5\text{-}Cl\text{-}2\text{-}OH\text{-}C_6H_3CO_2)_2]$ shows that in the monomeric species the hexa-coordinated tin atom exists in a skew-trapezoidal geometry in which the four {O} donor atoms, derived from two asymmetrically chelating carboxylate ligands, define the basal plane [109].

The di(n-butyl)tin(IV) bis(dihydroxybenzoate)s have skew-trapezoidal-bipyramidal or bicapped tetrahedral structures in the solid state[110] comparable with those of dimethyltin(IV) diacetate [111] and di(n-butyl)-bis(o-amino benzoate)tin(IV) [109].

Diphenic acid (A) forms diorganotin(IV) complexes, which are tetrahedral with two monodentate carboxylic groups. On the other land, soluble dinuclear triorganotin(IV) complexes (where the organo moieties are Me and Ph) contain symmetrically bound carboxylates, while the less soluble compound $(Cyh_3Sn)_2A$ has two asymmetrically bonded carboxylates. All have trigonal bipyramidal structures with $R_3Sn(IV)^+$ units remote from each other [45].

Orotic acid coordinates $R_2Sn(IV)^{2+}$ moieties to yield two different classes of derivatives with formulae $R_2SnHOr.nH_2O$ and $R_2Sn(H_2Or)_2.nH_2O$ (R=Me, n=0; R=Bu ,n=1) .In $R_2SnHOr.nH_2O$, the orotic acid behaves as a dianionic tridentate ligand [98].In $R_2Sn(H_2Or)_2.nH_2O$ two different Sn(IV) sites have been evidenced by Mössbauer spectroscopy in the solid state, and by ^1H and ^{13}C-NMR in DMSO-d_6 solution.

The diorganotin dicarboxylates also adopt polymeric structures (in the solid state) with intermolecularly bridging carboxylate groups and an octahedral *trans* $R_2Sn(O_2CR')$ tin atom geometry. For instance, the crystal structure of *catena*-poly[[di-n-butyltin(IV)]-μ-glutarato], $[Sn(C_4H_9)_2(C_5H_6O_4)]$, is composed of polymeric chains formed by the coordination of glutarate , through both ends to di-n-butyltin. The hexa-coordinated Sn atom is surrounded by four glutarate 'O' atoms forming an almost square base, with the n-butyl groups occupying the two axial positions. The geometry around the tin atom is a highly distorted octahedral, and may be best described as based on a skew-trapezoidal planar geometry. The symmetry-related glutarate ligands are asymmetrically coordinated to the Sn atoms with two unequal Sn-O distances [112].

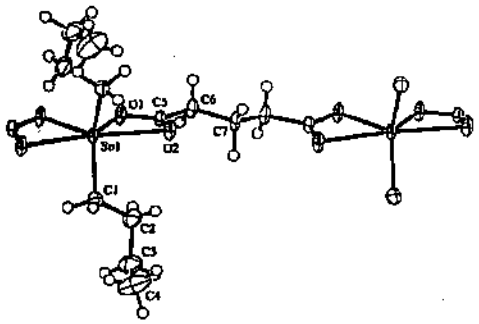


Fig. 3.10 Structure of $[Sn(C_4H_9)_2(C_5H_6O_4)]$ [112].

A crystal structure study of $[n\text{-}Bu_2Sn(O_2CCH_2SC_6H_5)_2]$ reveals the compound to be monomeric with the tin atom situated on a crystallographic two-fold axis in a skew-trapezoidal bipyramidal geometry. The carboxylate groups coordinate in an asymmetric mode forming both short Sn-O and long Sn-O bonds. The sulphur atoms do not participate in any significant interactions to the tin atom [113].

The X-ray diffraction study of the polynuclear compound $[Bu_2Sn(picolinate)_2]_n$ revealed that the central Sn atom is in a pentagonal bipyramidal environment with bond distances characteristic of organotin(IV) compounds. One of the picolinate moieties serves as bridge between Sn atoms by chelating to one Sn through one carboxylate O and the heterocyclic N atom, and binding monodentately through the other carboxylate O to the neighbouring Sn. There are hence two crystallographically distinct picolinate moieties in the structure, one bridging and the other terminal (chelating to the Sn through one carboxylate O and one N). The two butyl groups are located in axial positions. The ^{119}Sn NMR measurements in DMSO solution indicated that the polymeric structure of the complexes is not retained in the solution [114].

The crystal structure of $[t\text{-}Bu_2Sn(O_2CCH_3)(\mu\text{-}OH)]_2$ shows the presence of asymmetrically bridging hydroxyl groups leading to a planar Sn_2O_2 unit. Each Sn atom is also coordinated by an O atom of a monodentate carboxylate ligand and two C atoms of the t-Bu groups so that the environment around Sn is based on a trigonal bipyramid [62].

The crystal structure of the compound di-n-butylbis(2',4'-difluoro-4-hydroxybiphenyl-3-carboxylato-*O*,*O*')tin(IV), $[Sn(C_4H_9)_2(C_{13}H_7F_2O_3)_2]$, contains

discrete molecules in which the central Sn atoms are asymmetrically coordinated to two carboxylates and by two C atoms of two n-butyl groups. The geometry around Sn is highly distorted octahedral, that may be best described as one based on a skew-trapezoidal planar geometry. The hydroxyl groups and the carboxylate O atoms are hydrogen bonded, forming six-membered rings [115].

Several structures exhibiting similar geometry around Sn and an anisobidentate mode of coordination of the carboxylate ligand as stated above have been reported in literature [111,116-118].

The crystal structure of diphenyltin(IV) *N*-(2-hydroxy-5-ethylacetophenone) glycinate was investigated. The authors proposed trigonal bipyramidal geometry around the Sn atom with the ligand behaving as a dinegative tridentate one [119].

3.1.2.3 Structure of diorganodicarboxylato tetraorganodistannoxanes

There have been numerous crystallographic studies of the diorganodicarboxylato tetraorganodistannoxanes, of formula $\{[R_2Sn(O_2CR')]_2O\}_2$, and there are atleast five distinct types of structure known for them [21].

Structure type A, (Fig. 3.11) is by far the predominant structural form that involves a centrosymmetric structure built up around a four-membered cyclic Sn_2O_2 core in which the two endocyclic tin atoms are five-coordinate. Each of the two exocyclic five-coordinate tin atom is bound to one bridging oxygen atom of the four-membered ring, making these 'O' atoms tri-coordinate. The two independent carboxylate groups are characterized by two distinct ligating modes. One ligand is unidentate and is coordinated exclusively to the exocyclic Sn atoms. The other ligand is bidentate, one 'O' atom of the carboxylate group being coordinated to the exocyclic Sn atom and the other 'O' atom being coordinated to the endocyclic Sn atom. There are numerous examples of this common structural mode in literature [58, 60, 69,120-124].

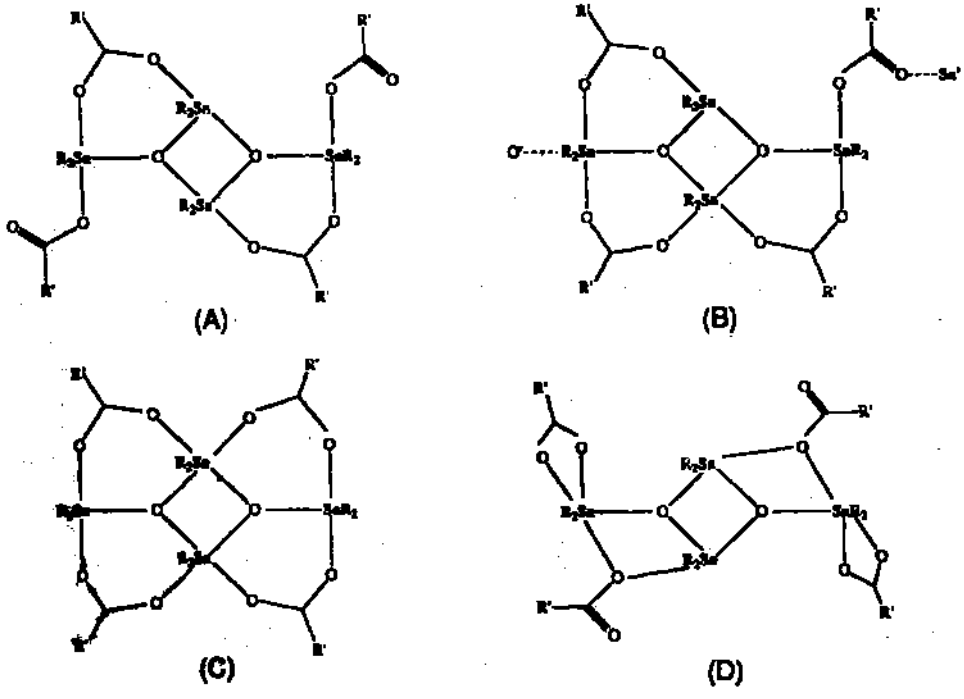


Fig. 3.11 Different types of dimeric structures of tetraorganodistannoxanes [49,108,120-124].

Variations on this basic structure are shown in B, C and D structural forms (Figure 3.11). In B three of the carboxylate ligands are bridging (e.g. R=Me, R'=Me [124]) and in C each of the four carboxylate ligands bridge a pair of Sn atoms (e.g. R=Me, R'=CCl_3 [49] and R=Me, R'= t-Bu [1]). A fourth structural type (D) is found for R=Me, R'=$C_6H_4NH_2$-*p* complex [108], in which two ligands are bridging and two ligands are chelating.

In type E, Sn_2O_2 core of the type A structure is retained, but the two bidentate, bridging carboxylate ligands of the type A now each utilize only one 'O' atom in bridging the two Sn centres. The structure of {[n-$Bu_2Sn(O_2CC_5H_4N$-2)]$_2O_2$} [2] is an example of type E. In this structure there are also interactions between the pyridyl 'N' atoms and the exocyclic Sn atom for two of the carboxylate ligands, so that these ligands may also be considered as chelating.

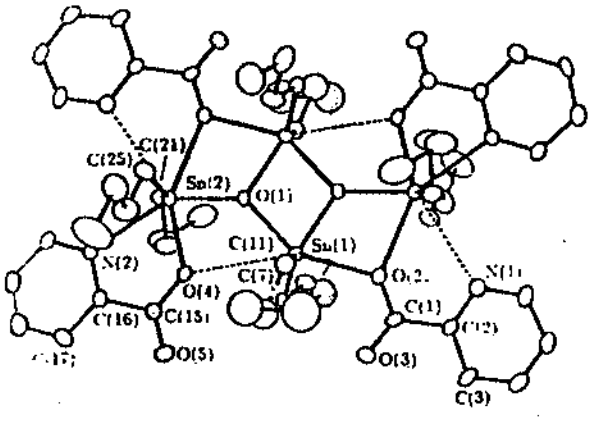


Fig. 3.12 Structure of $\{[n\text{-}Bu_2Sn(O_2CC_5H_4N\text{-}2)]_2O_2\}$ [2].

The crystal structure of $[Bu_2LSnOSnLBu_2]_2$ (where L= tolfenamic acid) has been determined by Demertzi and his coworkers [125]. Three distannoxane rings are present to the dimeric tetraorganodistannoxanes of planar ladder arrangement with distorted trigonal-bipyramidal geometry about the five-coordinated tin centers. The structure, which has two-fold symmetry, features a central Sn_2O_2 unit with two additional tin atoms linked at O. Pairs of tin atoms are bridged by bidentate carboxylate ligands and the external tin atoms have their coordination geometry completed by a monodentate carboxylate ligand. The tin atom geometries are similar and are based on trigonal bipyramidal arrangement [125].

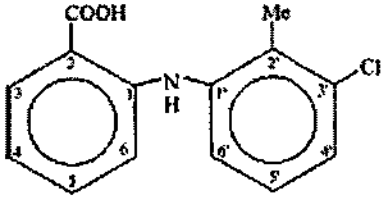


Fig. 3.13 Structure of tolfenamic acid [125].

3.1.3 Biological properties of organotin carboxylates

Organotin(IV) compounds have a range of pharmacological applications. They are used to a limited but significant extent as biocidal agents in agriculture and technology [126, 127]. The toxicology of tin compounds was reviewed in1959 [128] and 1964 [126].

One of the most important uses of organotin compounds is their ability to act as effective agrochemicals. For instance, triphenyltin compounds, including triphenyltin acetate, have received commercialization as agricultural fungicides [16,129-132]. Tributyltin, in the form of halides, oxides and acetates, are used extensively as wood preservatives [133]. Aquatic organisms such as fish, molluscs, crustaceans, algae are sensitive to tri-n-butyltin, and tricyclohexyltin compounds leading to the incorporation of these triorganotin moieties in anti-fouling paints for marine transport vessels [134], although there has been considerable environmental concern about the use of tributyltin compounds as anti-fouling paints [135]. However, the tributyltin compounds have not been shown to be neurotoxins, mutagens or carcinogens in humans [135].A full listing of reports which have evaluated organotin compounds in agriculture is to be found in a two-part review by Crowe [130,136].

The fungicidal activity of organotin complexes is strikingly dependent on the extent of alkylation of the Sn atom, being at a maximum in compounds with 3 Sn-C bonds [137] and also on the nature of the organic groups attached to Sn. In the case of tributyltin compounds, Bu_3SnX, the fungicidal activity is found to be largely independent on the nature of the group 'X' [138].

The application of multicriteria decision-making methods to the results of *in vitro* antifungal properties of organotin compounds of the type Ph_xSnX_z (n =2 or 3; X=$O_2CC_6H_4OH$, $O_2CC_6H_4OCOCH_3$, Cl or O_2CCH_3; z =1 or 2) and of free 2-hydroxybenzoic acid 2-acetoxybenzoic acids against *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, *Penicillium citrinum*, *Trichophyton rubrum and tricbophyton violaceum* have been described. [139]. Ranking information necessary to select one toxicant in preference to others and to assess the properties influencing the preference has been obtained. Patterns in the multivariate analyses suggest that cationic and anionic moieties of the toxicant play some role in their fungicidal activities. The triphenyltin compounds were generally more active than their diphenyltin analogues, the acetoxybenzoates were more active than the corresponding hydroxybenzoates, acetates or chlorides. Thus, triphenyltin acetoxybenzoate is upto 7.5 times as active as the corresponding acetate, which is commercially marketed a fungicide. The results of the analyses have been discussed in the light of the mechanism of antifungal activity of organotin compounds and the potential of

multivariate analysis techniques to facilitate the screening and ranking of antifungal agents.

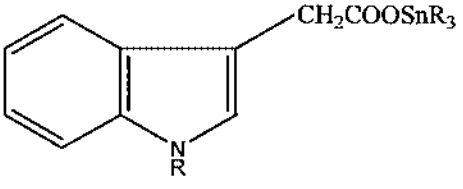
Fungitoxicity and phytotoxicity studies of $[R_3Sn(O_2CCH_2N(H)C(O)NH_2]$ (hydantoic acid) (R= Ph, c-Hex, n-Bu) indicated that the n-Bu derivative was the most active compound [90].

$Ph_3Sn(IV)^+$ compounds of *p*-ethoxybenzoic acid and acetyl salicylic acid have significant activity against a range of fungi [140].

The fungicidal activity of a number of ArSn(IV) compounds, $(p\text{-}ZC_6H_4)_3SnX$ [where X = OAC, OH or Z =F, Cl, CH_3, C_2H_5 or $(CH_3)_3C$] are reported. The results are compared with those on the Ph_3SnOAC and Ph_3SnOH archetypes. It was found that in most cases, para-substitution reduces the biocidal activity only slightly, but with p-OCH_3 the ArSn(IV) is completely ineffective. A model for the fungicidal action was proposed [141].

Q. Xie and coworkers reported the fungicidal activity of about 30 butyl tin carboxylates [142].

Molloy *et al.* [7] showed that triorganotin indolyl acetates of the type



(where R = Me, H, c-Hex) possesses fungicidal, bactericidal and insecticidal activity.

The triorganotin compounds, R_3SnX have been known for several years as having a specific action on mitochondrial oxidative phosphorylation; the activity is independent of the 'X' group but dependent on the R group [143]. Triorganotin (IV) compounds appear to inhibit the mitochondrial function in at least three ways : by (i) causing large-scale swelling at high concentrations, (ii) mediating Cl^-/OH^- exchange

across membranes, and (iii) inhibiting oxidative phosphorylation or ATP hydrolysis, like oligomycin [144]. The last process is usually assumed to be the most significant one, although binding of $Ph_3Sn(IV)^+$ to the cell wall was concluded to be responsible for the toxicity of *Ceratocystis ulmi* (*C. ulmi*)[145]. Dutch elm disease continues to devastate the diminishing population of American elm trees. The pathogenic fungus responsible for the disease is *C. ulmi*. The incorporation of the biologically active entities into a triorganotin (IV) system leads to the formation of potent biocides [146]. A number of $Ph_3Sn(IV)^+$ carboxylates were synthiszed and investigated spectroscopically. These complexes were found to be effective inhibitors of *C. ulmi* [147].

Tributyltin compounds are active against Gram-positive bacteria [136,148]. Their combination with a second chemical which combats Gram-negative bacteria produces a highly effective disinfectant which may be used on open areas posing a risk of infection, such as hospital floors and in sports pavilions. One such formulation (Incidin, Henkel) contains a mixture of tributyltin benzoate and formaldehyde [149].

Biological activity tests of the di-and tri-organotin carboxylates of 4-*p*-(chlorophenyl)-2-phenyl-5-thiazoleacetic acid (R=Me, Et, n-Bu, Ph, Bz) were carried out against various bacteria and fungi by the agar diffusion technique. All the complexes were screened for antibacterial and antifungal activity. The screening test shows that the n-Bu- and Ph- tin carboxylates are the most potent biocides against the tested bacteria. The activity of the other derivatives varies according to their R groups. However, they found that all of these compounds were active against *E. Coli* [27].

Organotin(IV) compounds are also a widely studied class of metal based antitumour drugs [132,150]. In recent years many tri- and di- organotin carboxylates have been tested for their *in vitro* activity against a large variety of tumour lines and have been found to be as effective as or better than traditional heavy metal anticancer drugs such as cisplatin [69,151,152].

In recent years, much work on organotin carboxylates containing other donor atoms (N, S) and functional groups have been reported [153-155]. Since the present work

deals with the interactions of organotin precursors with simple carboxylic acids (containing no other donor atoms except 'O'), the author has tried to confine this discussion around the organotin derivatives of very simple carboxylic acids.

3.2 Scope and Objective

The biocidal properties of organotin carboxylates are very rich [7, 156,157] and in addition these compounds show an interesting range of structural variations [21] leading to the proposal of some structure-activity relationships [14].These latter studies have shown that triorganotin carboxylates that have either isolated tetrahedral tin centres or *trans*-R_3SnO_2 tin geometries (arising from bridging carboxylate ligand) possess significantly greater activity than the compounds with the monomeric *cis*-R_3SnO_2 structural type [7,14,158].

The above led the author to study the structural behaviour and biocidal activity of a new series of organotin carboxylates, with varying R groups (alkyl or aryl). This chapter deals with the preparation, spectroscopic characterization and biological activity of the organotin(IV) carboxylates of cyclopropane carboxylic acid and 3-cyclohexyl propanoic acid and the X-ray crystal structure determination of dimethyltin(IV) derivative of cyclopropane carboxylic acid.

3.3 Experimental

3.3.1 Materials

Cyclopropane carboxylic acid (Lancaster, USA) and 3-cyclohexylpropanoic acid (Lancaster, USA) were used as received from commercial sources. Triphenyltin- (Fluka, Germany), tricyclohexyltin- (Aldrich, USA), tri-n-butyltin- (Merck,Germany), trimethyltin- (Merck, Germany) chlorides, dimethyltin- (Fluka, Germany), di-n-butyltin- (Merck,Germany) dichlorides were used after purification wherever necessary. Triphenyltin hydroxide was prepared by alkaline hydrolysis of the triphenyltin chloride. Tribenzyltin chloride and dibenzyltin dichloride were prepared using the method of Sisido *et al.* [159]. All the solvents used in the reactions were of AR grade and obtained from commercial sources (Merck, Germany). The solvents were dried using standard literature methods before use.

3.3.2 Measurements

The ^{1}H and ^{13}C NMR spectra were carried out in $CDCl_3$ solution using TMS as an internal standard on a Bruker DPX 300 spectrophotometer. The solution ^{119}Sn NMR spectra were measured in $CDCl_3$ solution at 149.05 MHz using a Jeol Eclipse Plus 400 spectrometer and were referenced against $SnMe_4$. IR spectra in the range 4000-400 cm^{-1} were obtained on an FTIR-8300 Shimadzu spectrophotometer with samples investigated as KBr discs. Thermogravimetric measurements was carried out from room temperature upto 800 °C, with a Mettler Toledo Star System operating in a pure nitrogen atmosphere in alumina crucible and at heating rate of 13 °C per minute using alumina as reference. Microanalysis were performed at RSIC, NEHU, Shillong, India and at IACS, Jadavpur, Kolkata. Tin was estimated gravimetrically as SnO_2 using standard procedure in our laboratory.

3.3.3 Synthetic procedures

The preparation of sodium salt of the ligand acids cyclopropane carboxylic acid (L^1H) and 3-cyclohexylpropanoic acid (L^2H) are described in section 3.3.3.1 and 3.3.3.2 respectively. The synthesis of organotin (IV) complexes of cyclopropane carboxylic acid (L^1H) and 3-cyclohexylpropanoic acid (L^2H) are described in section 3.3.3.3-3.3.3.16.Their characterization, analytical and spectroscopic data are given in section 3.4. All reactions were carried out under inert atmosphere of nitrogen.

3.3.3.1 Preparation of sodium salt of cyclopropane carboxylic acid (L^1H)

To a solution of cyclopropane carboxylic acid (2.5 g, 29.04 mmol) in methanol (40 ml) was added dropwise with continuous stirring 0.5 N methanolic NaOH (1.161 g, 59.2 ml, 29.02 mmol) in the presence of phenolphthalein as an indicator. The reaction system was stirred for half an hour. It was then evaporated to dryness leaving behind the sodium salt of cyclopropane carboxylic acid (L^1Na) as the product. The sodium salt thus prepared was recrystallized from methanol and then dried in an air oven at 105 °C for 48 hours.

L^1Na : Yield: 2.8 g, 76.5 %. M.p. : >245 °C

Elemental analysis (Calcd. for $C_4H_5O_2Na$) :

Calcd.: C, 44.31 ; H, 4.63 %.

Found: C, 44.39 ; H, 4.61 %.

IR (cm^{-1}) : $\nu(COO)_{asym}$, 1554; $\nu(COO)_{sym}$, 1414.

3.3.3.2 Preparation of sodium salt of 3-cyclohexylpropanoic acid (L^2H)

To a methanolic solution (35 ml) of 3-cyclohexylpropanoic acid (L^2H) (3 g, 19.23 mmol) was added dropwise with continuous stirring 0.5 N methanolic NaOH (0.769 g, 38.84 ml, 19.23 mmol) in the presence of phenolphthalein as an indicator. The reaction system was stirred for half an hour. It was then evaporated to dryness leaving behind the product of sodium salt of 3-cyclohexylpropanoic acid (L^2Na). The sodium salt thus prepared was recrystallized from methanol and then dried in an air oven at 105 °C for 48 hours.

L^2Na : Yield: 2.73 g, 72.4 % , M.p.: >245 °C .

Elemental analysis (Calcd. for $C_9H_{15}O_2Na$) :

Calcd.: C, 60.67 ; H, 8.42 %.

Found: C, 60.63 ; H, 8.41 %.

IR (cm^{-1}) : $\nu(COO)_{asym}$, 1570; $\nu(COO)_{sym}$, 1418.

3.3.3.3 Synthesis of tri-n-butyltin cyclopropylcarboxylate (1)

Tributyltin chloride (0.500 g, 1.536 mmol) in 30 ml of methanol was added to a hot methanol solution (30 ml) containing sodium salt of cyclopropane carboxylic acid (L^1-Na) (0.166 g, 1.536 mmol). The reaction mixture was heated under reflux for five hours and then the volatiles were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (b.p. 60-80 °C) in quantities of 2-3 ml for 6 times. The crude product obtained was recrystallized from the same solvent to yield crystals of the desired product.

3.3.3.4 Synthesis of triphenyltin cyclopropylcarboxylate (2)

The compound was prepared by reacting Ph_3SnCl (0.700 g, 1.82 mmol) and L^1Na (0.196 g, 1.82 mmol) in dry methanol (65 ml) under reflux conditions for 5 h. The reaction mixture was filtered while hot and the filterate was evaporated to dryness. The residue was extracted with hot petroleum ether (b.p. 60-80 °C). The crude product obtained was recrystallized from benzene to yield crystals of **2.**

3.3.3.5 Synthesis of tricyclohexyltin cyclopropylcarboxylate (3)

$(c\text{-}Hex)_3SnCl$ (0.630 g, 1.56 mmol) in 35 ml of methanol was added to a hot methanolic solution of L^1Na (0.168 g, 1.56 mmol).The reaction mixture was heated at reflux temperature for 5 h, and then the solvent was removed by distillation. The dry mass was extracted with hot petroleum ether (b.p. 60-80 °C) in quantities of 2-3 ml for 10 times. The crude product obtained was recrystallized from the same solvent to yield the desired product.

3.3.3.6 Synthesis of trimethyltin cyclopropylcarboxylate (4)

Trimethyl cyclopropyl carboxylate (**4**) was prepared by heating at reflux for 5h the methanolic solution (35 ml) of Me_3SnCl (0.300 g, 1.505 mmol) with L^1Na (0.163 g, 1.508 mmol).The reaction system was cooled to room temperature. The sodium chloride formed was filtered off and the filterate was evaporated to dryness on a water bath. The residue obtained was extracted with hot petroleum ether (b.p. 60-80 °C) (35 ml) and kept undisturbed. Shiny white crystals of **4** were obtained the next day.

3.3.3.7 Synthesis of tribenzyltin derivative of cyclopropyl carboxylate (5)

Tribenzylltin chloride (0.500g, 1.170 mmol) in 45 ml of methanol was added to a hot methanol solution (30 ml) containing sodium salt of cyclopropane carboxylic acid (L^1-Na) (0.126 g, 1.170 mmol). The reaction mixture was heated under reflux for five hours and then the volatiles were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (b.p. 60-80 °C) in quantities of 2-3 ml for 10 times. Shiny white crystals were obtained on cooling the petroleum ether solution.

3.3.3.8 Synthesis of dimethyltin(IV) derivative of cyclopropane carboxylic acid, $\{[Me_2Sn(cyclo\text{-}CH_2)_2CHCOO)]_2O\}_2$ *(6)*

The dimethyltin(IV) derivative of cyclopropane carboxylic acid (**6**) was obtained during an attempted synthesis of dimethyltin(IV) dicyclopropylcarboxylate. Me_2SnCl_2 (0.700g, 3.186mmol) in 40 ml of methanol was added to a hot methanol solution (45 ml) containing sodium salt of cyclopropane carboxylic acid, L^1Na (0.688g, 6.366 mmol). The reaction mixture was heated under reflux for six hours and then the solvents were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (60-80 °C) in portions of 2-3 ml for 7 times. The product was recrystallized from methanol to yield crystals of **6**.

3.3.3.9 Synthesis of di-n-butyltin(IV) derivative of cyclopropane carboxylic acid, $\{[n\text{-}Bu_2Sn(cyclo\text{-}CH_2)_2CHCOO)]_2O\}_2$ *(7)*

The di-n-butyltin(IV) derivative of cyclopropane carboxylic acid (**7**) was obtained in an attempt to synthesize the di-n-butyltin(IV) dicyclopropylcarboxylate. $n\text{-}Bu_2SnCl_2$ (0.800 g, 2.63 mmol) in 45 ml of methanol was added to a hot methanolic solution (30 ml) containing sodium salt of cyclopropane carboxylic acid, L^1Na (0.569g, 5.26 mmol). The reaction mixture was heated under reflux for six hours and then the solvents were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (60-80 °C) (40 ml). The product was recrystallized from methanol to yield crystals of **7**.

3.3.3.10 Synthesis of dibenzyltin(IV) dicyclopropyl carboxylate (8)

Bz_2SnCl_2 (0.500 g, 1.345 mmol) in 30 ml of methanol was added to a hot methanolic solution (25 ml) of L^1Na (0.291 g, 2.69 mmol).The reaction mixture was heated at reflux temperature for 6 h, and then the solvent was removed by distillation. The dry mass was extracted with hot petroleum ether (60-80 °C, 35 ml).The solution was concentrated and kept. White crystals of **8** were obtained the next day from the petroleum ether solution. The crystals were filtered and recrystallized from the same solvent.

3.3.3.11 Synthesis of tri-n-butyltin derivative of 3-cyclohexylpropanoic acid (9)

To a methanolic solution (35 ml) of sodium salt of 3-cyclohexylpropanoic acid (L^2Na) (0.273 g, 1.536 mmol) was added methanolic solution (30 ml) of tributyltin chloride (0.500g, 1.536 mmol). The reaction mixture was heated under reflux for five hours and then the volatiles were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (b.p.60-80°C, 40ml). The product obtained was recrystallized from the same solvent to yield shiny crystals of **9**.

3.3.3.12 Synthesis of triphenyltin derivative of 3-cyclohexylpropanoic acid (10)

Triphenytin hydoxide (0.500 g, 1.363 mmol) in 45 ml benzene was added to the solution of the 3-cyclohexylpropanoic acid (0.212 g, 1.363 mmol) in benzene. The reaction was performed under reflux for 4 hours with water being produced removed azeotropically using a Dean-Stark trap. The volatiles were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (60-80 °C) in quantities of 3-4 ml for 15 times. The product obtained was recrystallized from benzene to give **10**.

3.3.3.12 Synthesis of tricyclohexyltin derivative of 3-cyclohexylpropanoic acid (11)

$(c\text{-}Hex)_3SnCl$ (1 g, 2.48 mmol) in 40 ml of methanol was added to a hot methanolic solution of L^2Na (0.441 g, 2.48 mmol).The reaction mixture was heated at reflux temperature for 5 h, and then the solvent was removed by distillation. The dry mass was extracted with hot petroleum ether (b.p. 60-80 °C) in quantities of 2-3 ml for 10 times. The crude product obtained was recrystallized from the same solvent to yield the desired product.

3.3.3.13 Synthesis of trimethyltin derivative of 3-cyclohexylpropanoic acid (12)

The compound was prepared by reacting Me_3SnCl (0.300 g, 1.505 mmol) and L^2Na (0.268 g, 1.505 mmol) in dry methanol (40 ml) under reflux conditions for 5 h. The reaction mixture was filtered while hot and the filterate was evaporated to dryness.

The residue was extracted with hot petroleum ether (b.p. 60-80 °C). The crude product obtained was recrystallized from benzene to yield shiny white crystals of **12.**

3.3.3.14 Synthesis of dimethyltin(IV) derivative of 3-cyclohexylpropanoic acid, $\{[Me_2Sn(C_6H_{11}CH_2CH_2COO)]_2O\}_2$ *(13)*

The dimethyltin(IV) derivative of 3-cyclohexylpropanoic acid (**13**) was obtained during an attempt to synthesize the dimethyltin(IV) dicarboxylate of L^2H. Me_2SnCl_2 (0.500 g, 2.27 mmol) in 35 ml of methanol was added to a hot methanol solution (40 ml) containing L^2Na (0.810 g, 4.55 mmol). The reaction mixture was heated under reflux for six hours and then the solvents were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (60-80 °C, 50 ml). The product was recrystallized from methanol to yield shiny crystals of **13.**

3.3.3.15 Synthesis of di-n-butyltin(IV) dicarboxylate of 3-cyclohexylpropanoic acid (14)

n-Bu_2SnCl_2 (0.700 g, 2.303 mmol) in 45 ml of methanol was added to a hot methanolic solution (30 ml) containing L^2Na (0.820 g, 4.607 mmol). The reaction mixture was heated under reflux for six hours and then the solvents were removed by distillation. The dry mass was extracted thoroughly with hot petroleum ether (60-80 °C) (40 ml). The product obtained was a viscous liquid.

3.3.4 X-ray Crystallography

A suitable single crystal of the compound **6** was selected under a polarizing microscope and glued to a thin glass fiber with cyanoacrylate (super glue) adhesive. Single crystal structure determination by X- ray diffraction was performed with a Siemens smart CCD diffractometer equipped with a normal focus, 2.4 kW sealed tube X-ray source (MoKα radiation, λ = 0.71073 A^0) operating at 50 kV and 40mM. A hemisphere of intensity data was collected at room temperature at 1321 frames with ω scans (width of 0.300 and exposure time 20 s per frame) in the 2θ range 2.5-46.50. The structure was solved by direct methods using SHELXS-86[160], which readily

established the heavy atom positions (Sn) and facilitated the identification of the light atoms (O, C) from different Fourier maps. An empirical absorption correction based on symmetry equivalent reflections was applied using SADABS program [161]. All the hydrogen positions were initially observed in the Fourier maps, but for the final refinement the hydrogen atoms were placed geometrically and held in the riding mode. The last cycle refinement included atomic positions for all the atoms, anisotropic thermal parameters for all the non- hydrogen atoms and isotropic thermal parameters for all the hydrogen atoms. Seven carbon atoms (C5, C7, C15, C16, C19, C20 and C23) were refined only isotropically because of their poor thermal parameters. Full-matrix-least-squares structure refinement against F^2 was carried out using SHELXTL-PLUS package of program [162]. The details of final refinements are given in Table 3.1.

3.3.5 Biological Studies

The newly synthesized compounds were tested for their antifungal activity and antibacterial activity. The compounds were also tested for their phytotoxicity on healthy wheat seeds. Compounds which were highly phytotoxic would be of no use in the practical field of application.

3.3.5.1 Fungicidal activity

The biocidal activity of a few selected organotin carboxylates against four fungal pathogens (*Curvularia eragrostidis, Macrophomina phaseolina, Dreschlerea oryzae, Alternaria porri)* of four different crops were investigated. The fungal strains used in the study were gifts from the Plant Pathology Laboratory, Dept. of Botany, North Bengal University.

Table 3.1 Crystal data and structure refinement for the compound $\{[Me_2Sn(cyclo\text{-}CH_2)_2CHCOO)]_2O\}_2$ (**6**)

Identification code	sad
Empirical formula	$C_{24}H_{44}O_{10}Sn_4$
Formula weight	967.35
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	*P*-1
Unit cell dimensions	a = 10.18060(10) Å α=84.4540(10)°.
	b = 11.3774(2) Å β= 83.6480(10)°.
	c = 15.9447(3) Å γ = 74.23°.
Volume	1762.11(5) Å^3
Z	2
Density (calculated)	1.823 Mg/m^3
Absorption coefficient	2.845 mm^{-1}
F(000)	936
Crystal size	0.28 x 0.08 x 0.08 mm^3
Theta range for data collection	1.29 to 23.25°. -11<=h<=10, -12<=k<=12, -14<=l<=17.
Reflections collected	7328
Independent reflections	4923 [R(int) = 0.0245]
Absorption correction	SADABS
Max. and min. transmission	1.000000 and 0.437669
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4923 / 0 / 310
Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0391, wR2 = 0.1017
R indices (all data)	R1 = 0.0562, wR2 = 0.1112
Extinction coefficient	0.0009(2)
Largest diff. peak and hole	0.888 and -0.754 e.Å^{-3}

Materials and Methods

3.3.5.1.1 Fungal strains used for the study[a]

Species	Identification code	Host of origin
Curvularia eragrostidis	ITCC[b] No. 4150 2k	Tea *(Camellia sineusis)*
Macrophomina phaseolina	Identified by Dr. A. Saha, Dept. of Botany, N.B.U	Brinjal *(Solanum melongena)*
Dreschlerea oryzae	ITCC[b] No. 1849	Rice (*Oryzae sativa*)
Alternaria porri	Identified by Dr. A. Saha, Dept. of Botany, N.B.U	Niger (*Guizotia abyssinica*)

[a]Source of isolate: Plant Pathology Laboratory, Dept. of Botany, North Bengal University.

[b]ITCC- Indian Type Culture Collection, IARI, New Delhi.

3.3.5.1.2 Preparation of culture media

Fungi were grown on potato-dextrose-agar (PDA) medium at 28±1°C. The PDA medium was prepared as described below.

Materials required for preparing 100 ml PDA: 40 g potato (peeled), 2 g agar-agar (SRL), 2 g dextrose (Merck).

Method: 40 g of peeled potato was boiled in double distilled water and the volume was reduced to 100 ml. Then 2 g dextrose followed by 2g of agar-agar was added and the mixture was boiled just to dissolve the agar-agar and obtain a homogeneous solution. The solution was then autoclaved for 20 minutes. Now slants for culture of fungi were prepared with this media by pouring about 2 ml of this molten media in each test tubes, subsequently the test tubes were kept in a slanting condition till the media solidified. Then the media was impregnated with the spore and kept in the incubator at 28 ±1 °C. Average age of spores used for the study was 15 days.

3.3.5.1.3 Preparation of spore suspension

After average time period of 15 days, spore suspension was prepared by sterile double distilled water and the concentration was adjusted to 30-40 spores per field and used subsequently for experiments.

3.3.5.1.4 Study of the biocidal effects

The fungicidal activities were determined following spore germination bioassay as described by Rouxel *et al.* [163]. Purified eluents (10μl) were placed on two spots 3 cm apart on a clean, grease-free slide and the solvent was allowed to evaporate. One drop of spore suspension (0.02 ml per drop) prepared from 15-day-old cultures of the fungi was added to the treated spots. In this way, sets for various concentrations of the compounds were prepared. The slides were incubated at 27±1°C for 24 hours under humid conditions in Petri plates. Finally, after proper incubation period, one drop of a Cotton Blue-lactophenol mixture was added to each spot to fix the germinated spores. The number of spores germinated compared with the germinated spores of control (where no chemicals were used) was calculated using an average of 300 spores per treatment. The minimum inhibitory concentration required for complete inhibition was recorded in units of μg/ml.

3.3.5.2 Bactericidal activity

Some of the newly synthesized organotin(IV) carboxylates were screened for their antibacterial activity against *Pseudomonas fluorescens*, a fish-pathogenic, Gram-negative bacteria. The bacterial strain used in the study was kind gift from Dr. A. Saha, Plant Pathology Laboratory, Dept. of Botany, North Bengal University.

3.3.5.2.1 Preparation of culture media (Supplement nutrient agar)

Materials required for preparing 100 ml supplement nutrient agar: 1 g of beef extract (Himedia), 1 g of peptone (Himedia), 0.300 g of NaCl (SRL), 0.100 g of glucose (Merck), 2 g of agar powder (SRL).

Method: All the above except agar were boiled in double distilled water and the volume was reduced to 100 ml. Then the agar was added and the mixture boiled just to dissolve the agar. pH of the medium was adjusted to 7.4. The solution was autoclaved for 20 minutes.

3.3.5.2.2 Study of the biocidal effects

The bactericidal activities were determined using the agar well diffusion method [164]. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm apart. Two to eight hours old bacterial inoculums containing approximately 10^4 -10^6 colony forming units (CFU)/ml were spread on the surface of a nutrient agar with the help of a sterile cotton swab. Concentration of the test samples (1 mg/ml in methanol) was introduced into the respective wells. Other wells were supplemented with methanol serving here as control. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the diameter of the zones showing complete inhibition (mm). Each experiment was repeated in triplicate. All apparatus and materials used were sterilized where necessary using standard procedures.

3.3.5.3 Phtotoxicity studies

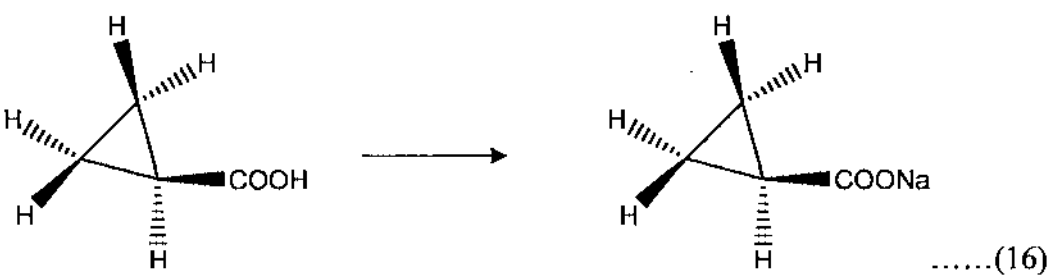
Phytotoxicities of these new organotin compounds were determined [165] on healthy wheat seeds (variety-Sonalika) purchased from Anup Seed Company, Bidhan Market, Siliguri, West Bengal. These healthy seeds were dipped in acetone-water suspensions of the compounds of different concentrations (25, 50, 100 μg/ml) for 1, 4 and 8 hours. The treated seeds were allowed to germinate sown over a mat of moist filter papers arranged in covered Petri plates. One hundred seeds were treated for each experiment. After two days, the germinated seeds (treated with compounds) were counted against the germinated seeds of the control (where no compounds were used) and those seeds, which had produced coleoptiles, were considered to have germinated. Each experiment was repeated in triplicate. All apparatus and materials used were sterilized where necessary using standard procedures.

3.4 Results and Discussion

In the previous section the synthetic recipe for the preparation of sodium salt of the ligand acids and their organotin(IV) complexes are described. A discussion of the synthetic methods adopted is carried out in this section in detail, regarding the yields obtained and the general physical characteristic of the compounds.

3.4.1 Synthesis of sodium salt of cyclopropane carboxylic acid (HL^1)

The sodium salt of cyclopropane carboxylic acid was prepared by titrating the acid with 0.5 M methanolic NaOH in the presence of phenolphthalein as an indicator.



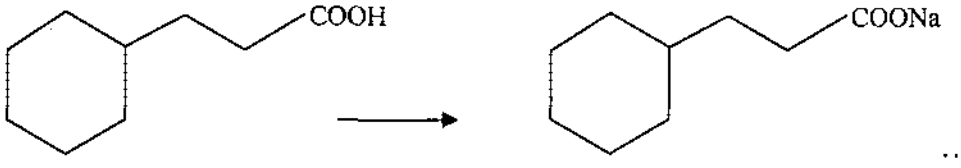
.....(16)

L^1H L^1Na

L^1Na was first obtained as a colourless liquid after titrating the acid with 0.5 M methanolic NaOH; upon concentration and cooling it slowly solidified to give an amorphous form of L^1Na. It was recrystallized from methanol and then dried in the oven at 105 °C for 48 hours. The yields were greater than 65%.The salt was found to be soluble in water, methanol, ethanol but insoluble in benzene, CCl_4 and CH_2Cl_2. L^1Na neither melted nor decomposed up to 245 °C in the melting point bath (Sulphuric acid bath).The sodium salt of the ligand was found to decompose after two to three days when kept in contact with the atmosphere. Hence, it was stored in a dessicator and the reactions of the salt carried out within 15 days of its preparation. The synthetic details and characterization data are described in section 3.3.3.

3.4.2 Syntheses of sodium salt of 3-cyclohexylpropanoic acid (HL^2)

Among all reported methods for the preparation of organotin carboxylates as discussed in section 3.1.1, the reactions of alkali metal salts with the organotin precursors is found to be one of the most straightforward and productive method.



.....(17)

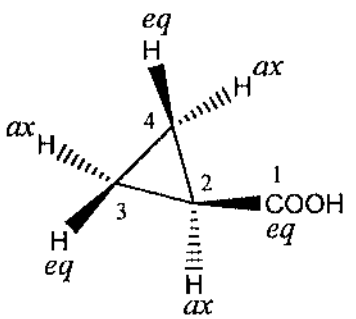
L^2H L^2Na

The ligand acid was titrated with 0.5 M methanolic NaOH. The reaction system was concentrated on a water bath, which upon cooling solidified to give L^2Na .The sodium salt of L^2H was obtained as an amorphous solid. It was recrystallized from methanol and then dried in the oven for 48 hours. Generally the yields were greater than 70%.The salt synthesized was soluble in water, methanol, ethanol and was insoluble in benzene, petroleum ether (60-80 °C) and carbon tetrachloride. The salt was found to slowly decompose when in contact with the aerial moisture and hence was stored in a dessicator. The reactions with the salt were carried out within 10-15 days of its synthesis. In the melting point bath the salt neither decomposed nor melted till 245°C. The synthetic details and characterization data are described in section 3.3.3.

3.4.3 Triorganotin(IV) and diorganotin(IV) complexes of cyclopropane carboxylic acid (L^1H)

The tri- and di- organotin (IV) complexes of cyclopropane carboxylic acid (L^1H) were prepared in moderate yields. The complexes were characterized by UV, IR, multinuclear (^1H, ^{13}C) NMR spectroscopy and elemental analyses. Thermogravimetric analysis were carried out for some selected compounds of L^1H. The numbering

scheme of the ligand and the abbreviations of the complexes are presented in the Scheme below.



(a) cyclopropane carboxylic acid (L^1H) (*ax*- axial, *eq* – equatorial)

1	Bu_3SnL^1
2	Ph_3SnL^1
3	$(c\text{-}Hex)_3SnL^1$
4	Me_3SnL^1
5	Bz_3SnL^1
6	$[Me_2Sn(L^1)_2]_2.[Me_2SnO]_2$
7	$[n\text{-}Bu_2Sn(L^1)_2]_2.[n\text{-}Bu_2SnO]_2$
8	$Bz_2Sn(L^1)_2$

Scheme 3.3

3.4.3.1 Triorganotin(IV) complexes of cyclopropane carboxylic acid, R_3SnL^1 (R=Ph, n-Bu, c-Hex, Me, Bz)

3.4.3.1.1 Synthesis of R_3SnL^1 (R=Ph, n-Bu, c-Hex, Me, Bz)

The triorganotin complexes were obtained in moderate to good yields by the reaction between the respective triorganotin chloride(R_3SnCl) and the sodium salt of the acid (L^1Na) in stoichiometric amounts in methanol.

$$R_3SnCl + L^1Na \longrightarrow R_3SnL^1 + NaCl \quad \text{.....(18)}$$

1: R= n-Bu; **2**: R= Ph; **3**: R= c-Hex; **4**: R= Me; **5**: R= Bz.

The triorganotin complexes can also be prepared by the reaction between R_3SnOH and the parent acid in benzene by the azeotropic removal of the water being produced during the reaction. But, the method using alkali metal salt of the ligand was preferred due to the ease of handling of the salt when compared to the acid. The reaction mixture was evaporated to dryness and then extracted in petroleum ether (b.p.60-80 °C) to remove NaCl produced during the reaction. The petroleum ether extract was concentrated to yield the crude product. The products were subsequently recrystallized from the appropriate solvents. The solubility of the triphenyltin analogue was poor in petroleum ether (b.p.60-80 °C) and a large amount of petroleum ether was required to extract the same. The synthetic details and analytical results are compiled in Table 3.2.

3.4.3.1.2 IR and UV spectra of R_3SnL^1 (R=Ph, n-Bu ,c-Hex, Me ,Bz)

Important IR bands for structural elucidation and their tentative assignments are presented in Table 3.3. The assignments of IR bands for all the complexes were done by comparing the IR spectra of the free acid, its sodium salt, and similar organotin compounds [16].The cyclopropane carboxylic acid display band at 1695 cm^{-1} which is assigned to the $\nu(OCO)_{asym}$ stretching vibration [166].The considerable shift of this vibration in the organotin (IV) complexes is owing to the coordination through the carbonyl oxygen atom [167]. Since the magnitude of the $\nu(OCO)_{asym}$ - $\nu(OCO)_{sym}$ (*i.e*, $\Delta\nu$) separation is of interest , therefore, the $\nu(OCO)_{sym}$ stretching frequencies[168-170] have also been identified for the compounds. The observed value of $\Delta\nu$, which are in the range 151-158 cm^{-1} indicate a bidentate bonding mode for the carboxylate moiety [27]. This suggests a penta-coordination [171] around the tin atom in the synthesized triorganotin(IV) carboxylates likely through intermolecular coordination [24]. In complex **3**, the observed value of $\Delta\nu$ (231 cm^{-1} respectively) indicates that the carboxylate moiety is behaving as a free organic ester type, in this case probably due to the bulky nature of the c-Hex groups around the tin atom [172-174]. The ν(Sn-C) stretching frequencies appear in the range of 440-511 cm^{-1} which is consistent with the literature data [12].

Table 3.2 The Physical and analytical data for **1-4**[a,b]

Complex	Crystallization Solvent	Yield (%)	M.p.(°C)	Elemental Composition[a] (%)		
				C	H	Sn
1	Petrolcum ether (b.p.60-80 °C)	92	93-94	51.19 (51.24)	8.50 (8.54)	31.58 (31.67
2	Benzene	85	136	60.64 (60.73)	4.84 (4.60)	27.28 (27.30)
3	Petroleum ether (b.p.60-80 °C)	80	139-142	58.29 (58.31)	8.44 (8.39)	26.14 (26.22)
4	Petroleum ether (b.p.60-80 °C)	84	124-126	33.60 (33.77)	5.60 (5.62)	47.34 (47.72)

[a]Calculated values in parentheses; [b]Reaction time was 5-6 h. All compounds are white.

Table 3.3 Characteristic IR absorption bands (cm^{-1}) for **1-4**[a]

Complex	$\nu(OCO)_{asym}$	$\nu(OCO)_{sym}$	$\Delta\nu(OCO)$	ν(Sn-C)
1	1566(s)	1415(m)	151	511(m), 457(w)
2	1571(m)	1413(m)	158	489(w), 451(s)
3	1635(m)	1404(m)	231	486(m), 442(w)
4	1569(m)	1418(m)	151	486(s), 440(w)

[a]s, strong; w, weak; m, medium.

The UV spectra of **1 - 4** were recorded in methanol (Table 3.4). The spectra of the complexes exhibited bands in the range of 210-213 nm, which may be due to the forbidden $n \rightarrow \pi^*$ transitions of the carboxylate group [175].

Table 3.4 UV spectral data for **1-4**

Complex	λ_{max} (nm)
1	210
2	211
3	213
4	Below 200

3.4.3.1.3 NMR spectra of R_3SnL^1 (R=Ph, n-Bu, c-Hex, Me, Bz) (1-5)

The ^1H NMR spectral data of the new triorganotin carboxylates (**1-5**) and the free acid have been recorded in $CDCl_3$ solution. The ^1H and ^{13}C NMR spectrum of **4** is presented in Fig. 3.14. The ^1H and ^{13}C NMR spectral data for the compounds (**1-4**) are reported in Table 3.5 ad 3.6 respectively.The observed resonances of protons have been assigned on the basis of their integration and multiplicity pattern. In the ^1H NMR spectra of L^1H, it is observed that the axial (H-3) and (H-4) protons in the cyclopropyl ring appear as multiplet at δ1.08-0.98 ppm and equatorial (H-3) and (H-4) protons appear as multiplet at δ0.96-0.82 ppm .The H-2 proton of the ligand (L^1H) appears as a septet at δ1.60 ppm. In the tri-n-Bu- and tri-c-Hex- organotin(IV) derivatives of L^1H the ligand protons overlap with the signal of the organic groups(n-Bu and c-Hex) attached to the tin atom, which makes the identification of the individual protons in the carboxylic acid ligand part difficult. The different R groups (Me, Ph, n-Bu, c-Hex) attached to the tin atom gave signals in the respective expected region [27, 99, 170,176].In the triphenyltin complex, the proton signals of the Ph groups appear as triplet and multiplet at δ 7.43 and 7.72-7.69 respectively. The $^3J(^{119}Sn-\ ^1H)$ for the triphenyltin complex is 63 Hz, which agree well with the data found for similar triphenyltin carboxylates [177-179].In the trimethyltin derivative of cyclopropane carboxylic acid, H-2 proton of the ligand appears at δ 1.56 as a septet. The $(H\text{-}3,4)^b_{axial}$ and $(H\text{-}3,4)^b_{equatorial}$ protons in **4** appear at δ 0.99-0.84 ppm and 0.83-0.70 ppm. The Sn-Me protons appear as a sharp singlet at δ 0.52. The $^2J(^{119}Sn-^1H)$ coupling constant = 58.8 Hz falls in the range of tetrahedral geometry in solution [180].

Table 3.5 ^{1}H NMR data (in ppm) for **1-4** [a,b,c]

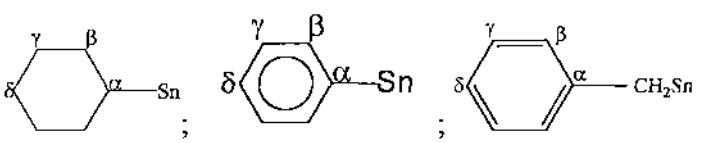
	1	2	3	4
(H-2)$^{b}_{axial}$	1.59 (s,1H)	1.69 (s,1H)	1.77-1.63 (m,1H)	1.56 (s,1H)
(H-3,4)$^{b}_{axial}$	1.07-0.88 (m,2H)	1.06-0.97 (m,2H)	1.02-0.85 (m,2H)	0.99-0.84 (m,2H)
(H-3,4)$^{b}_{equitorial}$	0.79-0.76 (m,2H)	0.93-0.82 (m,2H)	0.79-0.76 (m,2H)	0.83-0.70 (m,2H)
H–α	1.70-1.52 (m,6H)	-	1.45-1.31 (m,3H)	0.52 (m,9H) [58.8,56.4][e]
H–β	1.25-1.08 (m,6H)	7.72-7.69 (m,6H) [63 Hz][d]	1.91-1.81 (m,12H)	-
H–γ	1.49-1.29 (m,6H)	7.43 (t,9H)	1.77-1.63 (m,12H)	-
H–δ	0.90 (t,9H)	7.43 (t,9H)	1.45-1.31 (m,6H)	-

[a] Spectra recorded in $CDCl_3$, downfield to TMS, multiplicity is given as t, triplet; s, septet; m, multiplet.

[b] Refer to Scheme 3.3 for numbering scheme in the ligand skeleton.

[c] Numbering scheme for Sn-R skeleton as shown below:

$^{\alpha}CH_3$-Sn; $^{\delta}CH_3$-$^{\gamma}CH_2$-$^{\beta}CH_2$-$^{\alpha}CH_2$-Sn;



[d] $^{3}J(^{119}Sn-{}^{1}H)$ Hz.

[e] $^{2}J(^{119}Sn-CH_3)$ Hz, $^{2}J(^{117}Sn-CH_3)$ Hz.

The ^{13}C NMR spectral data reveals expected signals within the specified range [175]. The number of signals found in the spectra matches well with the number of magnetically non-equivalent carbon atoms. The R groups attached to the tin atom have their signals in different specific regions in correspondence with the literature [27, 99, 170, 176]. The assignment of the ^{13}C resonances of the tri-n-butyltin and

triphenyltin moieties follows from the $^{n}J(^{119/117}Sn - ^{13}C)$ coupling constants. In the triphenyltin complexes, the coupling constants $^{n}J(^{119/117}Sn - ^{13}C)$, especially the values of $^{1}J(^{119/117}Sn - ^{13}C)$ can be used to assign these compounds to two groups. Values of $^{1}J(^{119}Sn - ^{13}C)$ of 550-660 Hz are observed for the four-coordinate compounds and values of 750-850 Hz are observed for the five-coordinate compounds [169]. The triphenyltin complex of cyclopropane carboxylic acid **2**, exhibited $^{1}J(^{119}Sn-^{13}C) = 650$ Hz, falling in the range of four-coordinated triphenyltin(IV) species[178] in solution. In compound **4**, $^{1}J(^{119}Sn - ^{13}C)= 400$ Hz was observed which is in agreement with the previous literature report [181] and indicates a tetrahedral geometry around the Sn in solution.

Table 3.6 ^{13}C NMR data [a,b] (in ppm) of **1-4**

	Ligand skeleton			Sn-R skeleton			
	C-1	C-2	C-3	C-α	C-β	C-γ	C-δ
1	180.2	13.21	8.26	16.36 [360.0][d]	27.78 [28.3][e]	26.98 [66.7][f]	13.62
2	181.7	12.82	9.06	138.5	136.8 [47][e]	128.8 [62.2][f]	130.0 [13.5][g]
3	180.02	13.36	8.26	33.6	31.01 [14.2][e]	28.88 [63][f]	26.89 [59.2][g]
4	180.2	13.15	8.28	-2.43 [400.0 /382.8][d]	-	-	-

[a] Spectra recorded in $CDCl_3$, downfield to TMS; [b] For numbering scheme of the ligand, see Scheme 3.3; [c] For numbering scheme of Sn-R skeleton see footnotes of Table 3.5; [d] $^{1}J(^{119/117}Sn-^{13}C)$ in Hz; [e] $^{2}J(^{119}Sn-^{13}C)$ in Hz; [f] $^{3}J(^{119}Sn-^{13}C)$ in Hz. [g] $^{4}J(^{119}Sn-^{13}C)$ in Hz.

In order to gain further information about the possible coordination geometries in solution, a close examination of the $^{2}J(^{119}Sn-^{1}H)$ and $^{1}J(^{119}Sn-^{13}C)$ coupling constants was undertaken, as structural details, such as the determination of C-Sn-C bond angles, can be obtained by the use of literature methods [181, 182]. In the complex **1**, with the $^{1}J(^{119}Sn-^{13}C)$ value being 360.0 Hz and by the use of the Holecek and Lycka

equation [182], a C-Sn-C value of 112° was calculated , which corresponds to a tetrahedral geometry in $CDCl_3$ solution. Applying Lockhart's equation [181] the C-Sn-C angle for **4** was calculated as 111°, which confirms the tetrahedral geometry of tin in solution.

The ^{119}Sn chemical shifts of triorganotin(IV) complexes (**1-4**) in $CDCl_3$ solution are listed in Table 3.7.The spectrum of **1** is presented in Fig. 3.15. The chemical shift data are unambiguously characteristic for four-coordinate tin atoms in solution [79,170,183, 184].

Table 3.7 ^{119}Sn NMR data [a] (in ppm) of **1-4**

Complex	$\delta(^{119}Sn)$
1	104.68
2	-117.09
3	7.52
4	129.35

[a] Spectra recorded in $CDCl_3$ with Me_4Sn as an external reference.

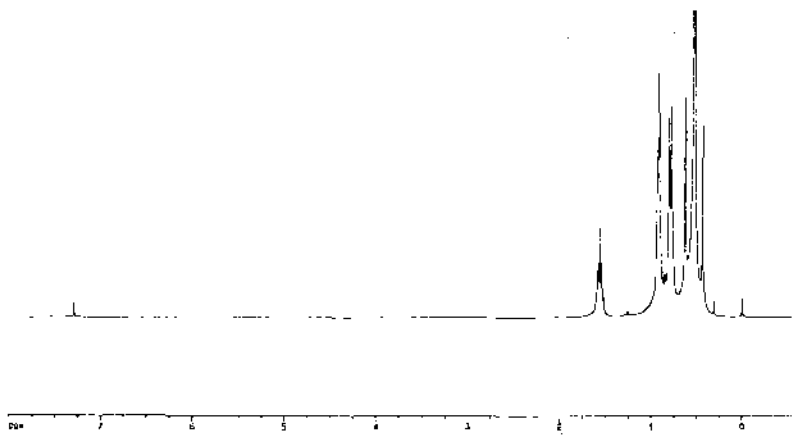
Inconclusive characterization of 5

The author was unable to characterize the complex **5**, with the help of NMR and IR spectroscopies. The compound is pure as indicated by its sharp melting point.

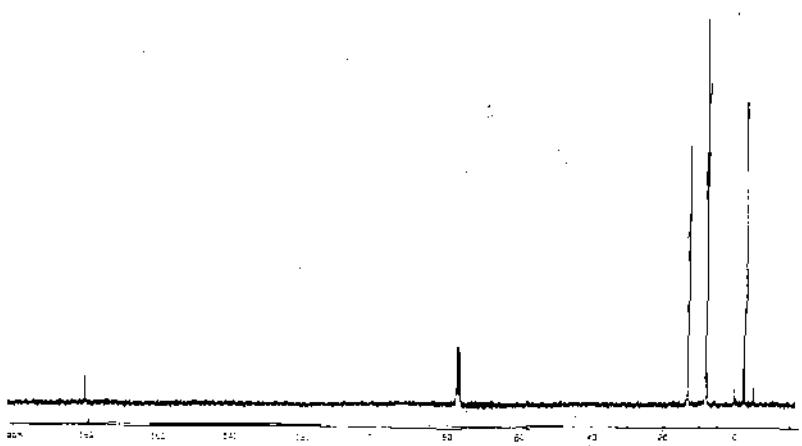
Yield: 65%, M.pt.: 116-117 °C, IR(cm^{-1}): $\nu(OCO)_{asym}$: 1570 cm^{-1}.

As the complex was unstable and decomposed within 2-3 days of its preparation on bench so the elemental analyses couldn't be done. The NMR though, revealed interesting features.

^1H NMR ($CDCl_3$, ppm): Ligand skeleton: H-2, 1.53-1.51; (H-3,4) $^b{}_{axial}$, 0.87-0.82; (H-3,4) $^b{}_{equitorial}$, 0.79-0.77; Sn-benzyl skeleton: aromatic protons, 7.34-6.74. In the ^1H NMR spectra of **5**, two types of tin-benzyl ($Sn-CH_2$) protons are identified one at δ 2.56 [$^2J(^{119}Sn-^1H)$ =72 Hz] and the other at δ 2.93 [$^2J(^{119}Sn-^1H)$ =90 Hz].The aromatic protons of the benzyl group and the presence of the ligand protons in the complex gave signals in the expected range indicating the binding of the ligand to the organotin precursor (Bz_3SnCl).



(a)



(b)

Fig. 3.14 (a) ^{1}H NMR spectrum of **4** (b) ^{13}C NMR spectrum of **4**.

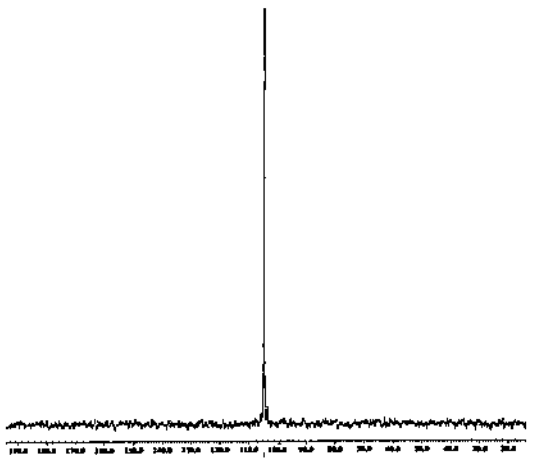


Fig. 3.15 ^{119}Sn NMR spectrum of **1**.

^{13}C NMR ($CDCl_3$, ppm) of **5** : Ligand skeleton: C-1, 182.4; C-2, 12.83; C-3, 8.80; Sn-benzyl skeleton: ring carbon atoms, 138.63, 135.89, 128.87, 128.55, 128.39, 128.33, 127.77, 124.34. Two Sn-CH_2 resonances were observed at δ 23.85 [$^1J(^{119}Sn\text{-}^{13}C)$ = 625.5 Hz] and δ 31.86 [$^1J(^{119}Sn\text{-}^{13}C)$ =367.5 Hz] in the ^{13}C NMR of **5**. Also, eight different phenyl carbons were seen in the ^{13}C NMR of **5**. Further studies and attempts to grow single crystals are in progress to establish the identity of the compound.

3.4.3.2 Diorganotin (IV) complexes of L^1H (R=Me, n-Bu, Bz)

3.4.3.2.1 Synthesis of diorganotin (IV) derivatives of L^1H (R=Me, n-Bu, Bz)

The dicarboxylato tetraorganodistannoxane derivatives (R=Me, n-Bu) of cyclopropane carboxylic acid were obtained during an attempted synthesis of diorganotin(IV) dicyclopropylcarboxylates. These were obtained in moderate yields by the reaction between the respective diorganotin dichloride(R_2SnCl_2) and the sodium salt of the ligand acid (L^1Na) in 1: 2 stoichiometric amounts in methanol. The attempt to synthesize diorganotin(IV) dicyclopropylcarboxylates (R=Me, n-Bu) using the reaction between R_2SnO (R=Me, n-Bu) and the ligand acid in benzene by

refluxing for 4 hours (water produced during the reaction being removed azeotropically) also gave the dicarboxylato tetraorganodistannoxanes (R=Me, n-Bu).

Dicarboxylato tetraorganostannoxanes are the hydrolysis products of diorganotin dicarboxylates [1,62,185] and the references of these compounds in literature are available [21]. This made the author to presume that the traces of moisture or alkali present as impurities might have caused the hydrolysis of the initially formed dicarboxylates as these compounds are very susceptible to hydrolysis [1,21, 62,124].

However, we could successfully isolate dibenzyltin dicyclopropylcarboxylate by the reaction between the dibenzyltin dichloride and the sodium salt of the ligand acid (L^1Na) in 1: 2 stoichiometric amounts in methanol.The analytical data for these complexes are presented in Table 3.8.

$$R_2SnCl_2 + 2\,L^1Na \longrightarrow [R_2Sn(L^2)_2]_2\,[R_2SnO]_2 + 2NaCl \quad .....(19)$$

6 : Me ; **7** : n-Bu

$$R_2SnO + 2\,L^1H \longrightarrow [R_2Sn(L^2)_2]_2\,[R_2SnO]_2 + H_2O \quad .....(20)$$

6 : Me ; **7** : n-Bu

$$R_2SnCl_2 + 2\,L^1Na \longrightarrow R_2Sn(L^2)_2 + 2NaCl \quad .....(21)$$

8 : Bz

Table 3.8 The Physical and analytical data for **6-8**[a,b]

Complex	Crystallization Solvent	Yield (%)	M.p. (°C)	Elemental Composition[a] (%)		
				C	H	Sn
6	Methanol	72	216-217	29.75 (29.79)	4.59 (4.55)	49.05 (49.10)
7	Petroleum ether (b.p.60-80°C)	77	130-132	44.19 (44.21)	7.05 (7.06)	36.40 (36.44)
8	Petroleum ether (b.p.60-80°C)	60	113-115	56.05 (56.08)	5.08 (5.09)	25.20 (25.21)

[a]Calculated values in parentheses.

[b]Reaction time was 5-6 h. All compounds are white.

3.4.3.2.2 IR spectra of diorganotin (IV) derivatives of L^1H (R=Me, n-Bu, Bz)(6- 8)

Important IR bands for structural elucidation and their tentative assignments are presented in Table 3.9. The assignments of IR bands for all the complexes were done by comparing the IR spectra of the free acid, its sodium salts, and similar organotin compounds [16,125]. In the dicarboxylato tetraorganodistannoxanes, two types of carboxylate stretching bands are identified in the same compound. In compound **6**, the difference Δ, [ν $(OCO)_{asym}$ - ν $(OCO)_{sym}$] between these frequencies is close to that found for monodentate (307 cm^{-1}) and bridging bidentate carboxylato groups (154 cm^{-1}) [125]. A strong band around 632 cm^{-1} can be assigned to the ν(Sn-O-Sn) mode [59, 66]. Similarly, in compound **7**, the difference [ν $(OCO)_{asym}$ - ν $(OCO)_{sym}$] corresponds to that found for monodentate (301 cm^{-1}) and bridging bidentate carboxylato groups (141 cm^{-1}) [185, 186]. In compound **8**, Δν(OCO) = 143 cm^{-1} indicates the presence of a bidentate carboxylato group [99].

Table 3.9 Characteristic IR absorption bands (cm^{-1}) for **6-8**[a]

Complex	$\nu(OCO)_{asym}$	$\nu(OCO)_{sym}$	Δν(OCO)	ν(Sn-C)	ν (Sn-O-Sn)
6	1560(m) 1616(m)	1406(m) 1309(m)	150 307	525(m) 503(m)	634(s)
7	1548(m) 1614(m)	1407(m) 1313(m)	141 301	532(m) 482(m)	632(s)
8	1604(m)	1461(s)	143	493(m) 455(m)	-

[a]s, strong; w, weak; m, medium.

3.4.3.2.3 NMR spectra of diorganotin(IV) derivatives of L^1H (R=Me, n-Bu, Bz)(6- 8)

The ^1H NMR and ^{13}C NMR spectral data of tetraorganodistannoxanes of cyclopropane carboxylic acid are presented in Table 3.10 and 3.11 respectively. The ^1H NMR and ^{13}C NMR spectrum of **7** is shown in Fig. 3.16. In the dimethyltin complex of L^1H the H-2 proton of the ligand appears as a multiplet at δ1.45-1.36 ppm. The (H-3) and (H-4) protons of the ligand appear along with the Sn-methyl

protons at δ1.01-0.52 ppm. Two Sn-methyl resonances (δ0.74 ppm, $^{2}J(^{119}Sn\text{-}^{1}H)$ 85 Hz, *exo*-cyclic and δ0.79 ppm, $^{2}J(^{119}Sn\text{-}^{1}H)$ 89 Hz, *endo*-cyclic) are observed as expected for tetraorganodistannoxanes [1,123,185,187].

In the ^{13}C NMR spectra, the diorganotin derivatives of the ligand acids displayed two sets of R-Sn resonances, as expected for the dicarboxylato tetraorganodistannoxanes [49], with high field resonances for the *exo*-cyclic R_2Sn carbon atoms and down field resonances for the *endo*-cyclic R_2Sn carbon atoms. In compound **6**, the Sn-Me resonances appeared at (δ5.94 ppm, $^{1}J(^{119/117}Sn\text{-}^{13}C)$ 753/720 Hz, *exo*-cyclic and δ8.65 ppm, $^{1}J(^{119/117}Sn\text{-}^{13}C)$ 800/763 Hz, *endo*-cyclic) as expected [1,123,185,187].

In the dibenzyltin derivative of $L^{1}H$ (**8**), methylene protons are observed as singlet (with tin satellites) at δ 2.95. The value of $^{2}J(^{119}Sn\text{-}^{1}H)$ is found to be 90 Hz [99]. This value is comparable with the value of dimethyltin chlorides confirming the tetrahedral environment around tin [188].In the dibutyltin complex of $L^{1}H$, the presence of two sets of ^{13}C, and in part ,^{1}H butyl resonances(due to non-equivalence of the *exo*- and *endo*-cyclic n-Bu_2Sn moieties), is in agreement with previous NMR data on dicarboxylato tetraorganodistannoxanes [99,185,187].

The C-Sn-C bond angles calculated for **6** from $^{1}J(^{119}Sn\text{-}^{13}C)$ values using Lockhart and Mander's equation [181] corresponds to 142.8° and 146.9° respectively and are nearer to the values obtained from the X-ray crystallographic study of **6** (142.6° and 147.9° respectively, see Table 3.13).

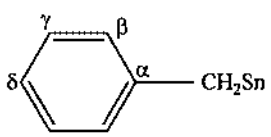
The ^{119}Sn NMR data for **6** and **7** in $CDCl_3$ are given in Table 3.12. The ^{119}Sn NMR spectra of **7** is shown in Fig. 3.17. The ^{119}Sn NMR spectra shows two well-separated high- and low- frequency ^{119}Sn resonances in accordance with the previous literature reports [117,121]. These data confirm the usual non-equivalence of the Me_2Sn and n-Bu_2Sn moieties in solution in these types of complexes reported earlier in literatures [60,189].

Table 3.10 ^{1}H NMR data (in ppm) for **6-8** [a,b,c]

Complex	Ligand skeleton	Sn-R
6	H-2 - 1.45-1.36 (s,2H) $(H\text{-}3,4)_{ax,eq}$ - 1.01-0.52 (m,8H)	H-α (12H): *exo*-cyclic 0.74 [85][d] *endo*-cyclic 0.79 [89][d]
7	H-2 - 1.71-1.57 (m,2H) $(H\text{-}3,4)_{eq}$ - 0.76(m, 8H) $(H\text{-}3,4)_{ax}$ 0.94-0.87	H-α- 1.71-1.57(m,8H) H-β,γ -1.45-1.28 (m,16H) H-δ - 0.92(t), 0.90(t) (12H)
8	H-2 - 1.44-1.45 (m,2H) $(H\text{-}3,4)_{ax,eq}$ - 0.82-0.78 (m,8H)	Sn-CH_2 - 2.95 (s, 4H) [90 Hz] H-α,β,γ,δ- 7.25-7.05 (m, 8H)

[a] Spectra recorded in $CDCl_3$,downfield to TMS, multiplicity is given as t, triplet; s, septet; m, multiplet; [b] For numbering scheme of the ligand see Scheme 3.3.

[c] Numbering scheme for Sn-R skeleton as shown below:



$^{\alpha}CH_3$-Sn; $^{\delta}CH_3$-$^{\gamma}CH_2$-$^{\beta}CH_2$-$^{\alpha}CH_2$-Sn;

[d] $^{2}J(^{119}Sn\text{-}H)$ Hz.

Table 3.11 ^{13}C NMR data (in ppm) for **6-8**[a,b,c]

	Ligand skeleton			δ(Sn-R)
	C-1	C-2	C-3	
6	181.2	14.3	8.08	5.94[753/720][d] 8.65[800/763][d]
7	180.6	14.4	7.99	α -28.67 β- 27.55[37.5][e], 27.30[n.o.][e] γ - 26.92[n.o.][f], 26.77[123.4][f] δ- 13.64
8	184.88	12.4	9.04	Sn-CH_2 – 31.94 [562.49][d] α-136.05, β- 128.3, γ-128.7, δ- 125.3

[a] Spectra recorded in $CDCl_3$,downfield to TMS.

[b] For numbering scheme of the ligands see Scheme 3.3.

[c] For numbering scheme of Sn-R skeleton see footnotes of Table 3.10.

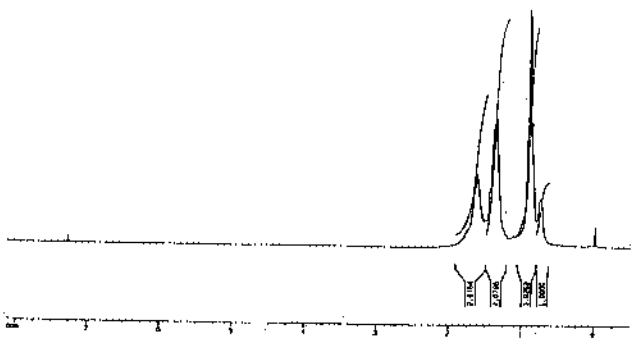
[d] $^{1}J(^{119/117}Sn\text{-}^{13}C)$ Hz ; [e] $^{2}J(^{119}Sn\text{-}^{13}C)$ in Hz; n.o. not observed.

[f] $^{3}J(^{119}Sn\text{-}^{13}C)$ in Hz; n.o. not observed.

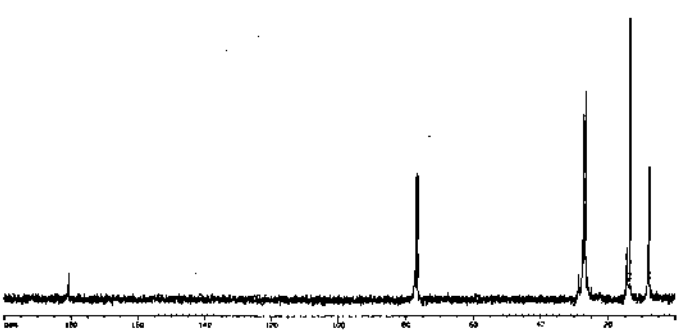
Table 3.12 ^{119}Sn NMR data (in ppm) for **6** and **7**[a]

	6	**7**
$\delta(^{119}Sn)_{exo}$	-179.1	-209.6
$\delta(^{119}Sn)_{endo}$	-190.8	-218.7

[a] Spectra recorded in $CDCl_3$ with Me_4Sn as an external reference.



(a)



(b)

Fig. 3.16 (a) ^{1}H NMR spectrum of **7** (b) ^{13}C NMR spectrum of **7**.

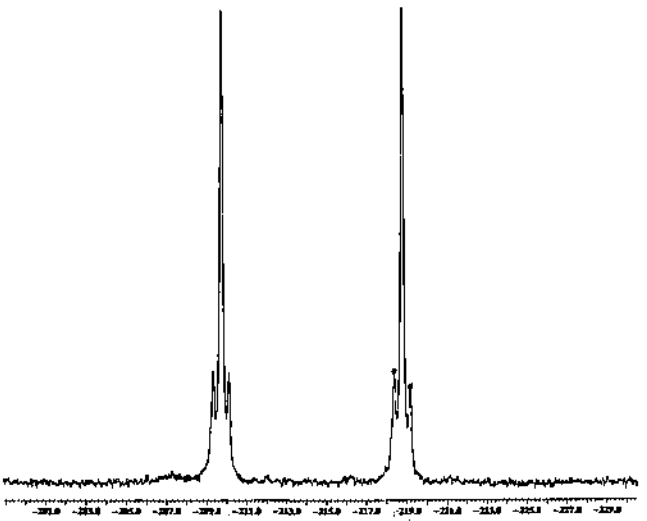


Fig. 3.17 ^{119}Sn NMR spectrum of **7**.

3.4.3.2.4 X-ray crystal analysis of 6

The author was able to successfully isolate suitable single crystals of **6** for X-ray crystallography. The selected geometric parameters of **6** are presented in Table 3.13. The atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) are presented in Table 3.14. The X-ray diffraction analysis of **6** reveals that the complex has a one-dimensional chain motif constructed from a secondary building unit of approximately rectangular Sn_2O_2 rings (Fig. 3.18). The rings are made up of a central planar $(Me_2Sn)_2O$ four-membered aggregates and two other peripheral (*exo*-cyclic) Me_2Sn units attached to two μ_3-oxygen atoms. The penta-coordinated Sn atoms have a bent C_2Sn skeleton C2-Sn1-C1 = 147.9(3) *exo*-cyclic and C7-Sn4-C8 = 144.8(4) *endo*-cyclic respectively. All the Sn atoms in the dimer are in five-coordinated environment. It is interesting to note that there are two different carboxylate ligands in the structure. One is bidentate bridging linking *endo*- and *exo*-cyclic Sn centres invoking two different Sn-O bond distances *e.g.* Sn4-O8 = 2.317(6) and Sn1-O3 = 2.224(6). The second carboxylate group bind the *exo*-cyclic Sn atom in a monodentate mode (free organic ester type) [1,123]. The pendant O atom, O9 is far removed from Sn1 atom which is reflected by the C9-O9 bond distance of 1.254(7)

indicative of the presence of substantial multiple bond character in it and is significantly shorter than the O2-C9 of 1.270(8).Slightly distorted axial angles of the trigonal bipyramidal geometry - O2-Sn1-O3 (*exo*-cyclic Sn) and O4-Sn4-O8 (*endo*-cyclic Sn) are 168.9(2) and 166.6(2) respectively. The distance between the two Sn atoms in the four membered ring is Sn3-Sn4 = 3.2761(7) which is smaller than the sum of the vander waals radii of Sn (II) (3.40 Å).This suggests that there exists possibly a weak metal-metal interaction in the ring. More over the non-covalent weak interactions via Sn1A-O10B; Sn2B- O9A; Sn1B-O10C; O9B-Sn2C etc allow the linear polymeric chain to propagate (Fig. 3.19). This work brings out the use of a carboxylic acid containing a strained ring as ligand for the synthesis of distannoxane not demonstrated earlier.

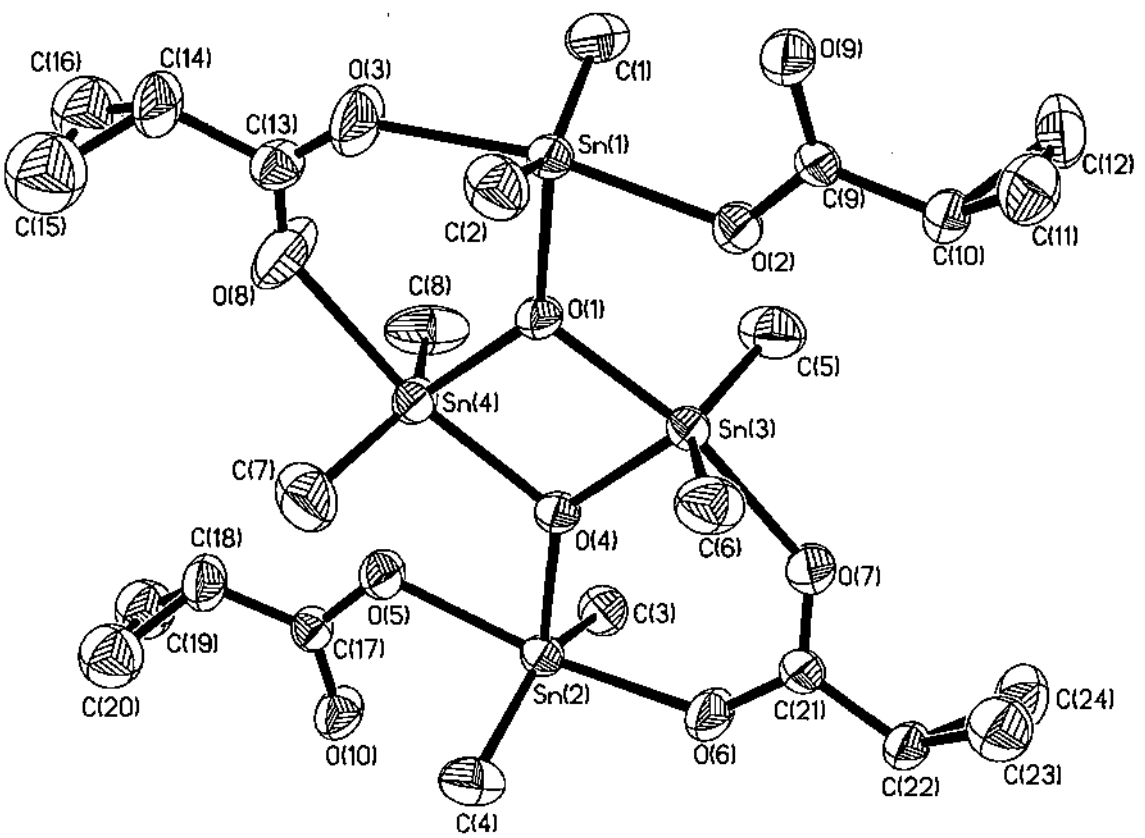


Fig. 3.18 ORTEP plot with atom labeling scheme of the molecular structure of $\{[Me_2Sn(cyclo\text{-}CH_2)_2CHCOO)]_2O\}_2$ **(6)**

Table 3.13 Selected geometric parameters – bond distances (Å) and angles (°).

Sn(1) - C(1)	2.090(7)	Sn(3) - O(1)	2.141(4)
Sn(1) - C(2)	2.083(7)	Sn(3) - O(7)	2.302(5)
Sn(1) - O(1)	2.032(4)	Sn(3) - O(4)	2.039(4)
Sn(1) - O(3)	2.224(6)	Sn(3) - Sn(4)	3.2761(7)
Sn(1) - O(2)	2.202(5)	O(2) - C(9)	1.270(8)
Sn(3) - C(5)	2.088(8)	C(9) - O(9)	1.254(7)
Sn(3) - C(6)	2.089(8)		
Sn(1) - O(10)	3.037	Sn(2) - O(9)	2.941
O(9) - Sn(2)	2.941	O(10) - Sn(1)	3.037

[Short non-hydrogen inter-molecular contacts contacts for inter-molecular clusters/or networks].

C(2)-Sn(1)-C(1)	147.9(3)	C(6)-Sn(3)-O(7)	87.0(3)
C(1)-Sn(1)-O(3)	89.5(3)	C(6)-Sn(3)-O(1)	99.9(3)
C(1)-Sn(1)-O(2)	94.3(3)	O(4)-Sn(3)-C(6)	106.7(3)
O(1)-Sn(1)-C(1)	106.7(3)	O(1)-Sn(3)-O(7)	164.4(2)
C(2)-Sn(1)-O(3)	87.9(3)	O(4)-Sn(3)-O(7)	88.2(2)
C(2)-Sn(1)-O(2)	94.3(3)	O(4)-Sn(3)-O(1)	76.5(2)
O(1)-Sn(1)-C(2)	105.3(3)	Sn(1)-O(1)-Sn(3)	121.7(2)
O(2)-Sn(1)-O(3)	168.9(2)	Sn(1)-O(1)-Sn(4)	135.1(2)
O(2)-Sn(1)-O(3)	91.0(2)	Sn(4)-O(1)-Sn(3)	103.2(2)
O(1)-Sn(1)-O(2)	77.9(2)	Sn(3)-O(4)-Sn(4)	103.5(2)
C(5)-Sn(3)-C(6)	142.6(4)	Sn(1)-Sn(4)-O(4)	76.7(2)
C(5)-Sn(3)-O(7)	83.0(3)		
C(5)-Sn(3)-O(1)	99.2(3)		
O(4)-Sn(3)-C(5)	108.8(3)		

Table 3.14 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for sad. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
Sn(1)	898(1)	2351(1)	7629(1)	50(1)
Sn(2)	2224(1)	-3632(1)	7259(1)	50(1)
Sn(3)	3021(1)	-555(1)	6894(1)	52(1)
Sn(4)	60(1)	-696(1)	7875(1)	59(1)
O(1)	1196(5)	528(4)	7532(3)	54(1)
O(2)	2960(5)	1835(4)	6958(3)	61(1)
O(3)	-1156(7)	2487(6)	8316(5)	122(3)
C(1)	-45(8)	3245(7)	6558(5)	77(2)
C(2)	1607(9)	2492(7)	8782(5)	79(2)
O(4)	1928(5)	-1790(4)	7304(3)	53(1)
O(5)	72(5)	-3023(4)	7792(3)	67(1)
O(6)	4408(6)	-3851(5)	6819(5)	97(2)
C(3)	1743(8)	-3812(7)	6048(4)	72(2)
C(4)	2902(9)	-4433(7)	8431(5)	81(3)
O(7)	4650(6)	-2110(5)	6255(4)	88(2)
C(5)	2631(9)	60(8)	5646(5)	89(3)
C(6)	4408(9)	-672(7)	7790(5)	85(3)
O(8)	-1703(8)	850(7)	8444(6)	160(4)
C(7)	316(10)	-1300(9)	9126(6)	103(3)
C(8)	-1196(10)	-515(8)	6889(7)	114(4)
C(9)	3606(7)	2655(6)	6823(4)	46(2)
O(9)	3049(5)	3726(4)	7028(3)	71(1)
O(10)	26(6)	-4935(5)	7917(4)	79(2)
C(10)	5028(7)	2309(7)	6450(5)	69(2)
C(11)	6038(8)	2901(8)	6693(6)	88(3)
C(12)	5560(9)	3191(8)	5870(5)	84(3)
C(13)	-1903(8)	1882(7)	8568(5)	61(2)
C(14)	-3215(9)	2424(9)	9083(6)	95(3)
C(15)	-3833(14)	1680(12)	9745(8)	150(5)

C(16)	-4478(12)	2058(10)	9023(7)	121(4)
C(17)	-527(7)	-3860(6)	8063(4)	50(2)
C(18)	-1886(9)	-3475(8)	8510(5)	84(3)
C(19)	-2879(11)	-4212(9)	8500(6)	102(3)
C(20)	-2241(11)	-4266(10)	9229(6)	109(3)
C(21)	5116(7)	-3213(6)	6428(4)	52(2)
C(22)	6555(7)	-3800(7)	6154(5)	69(2)
C(23)	7597(10)	-3140(9)	6181(5)	93(3)
C(24)	7235(9)	-3324(8)	5391(5)	89(3)

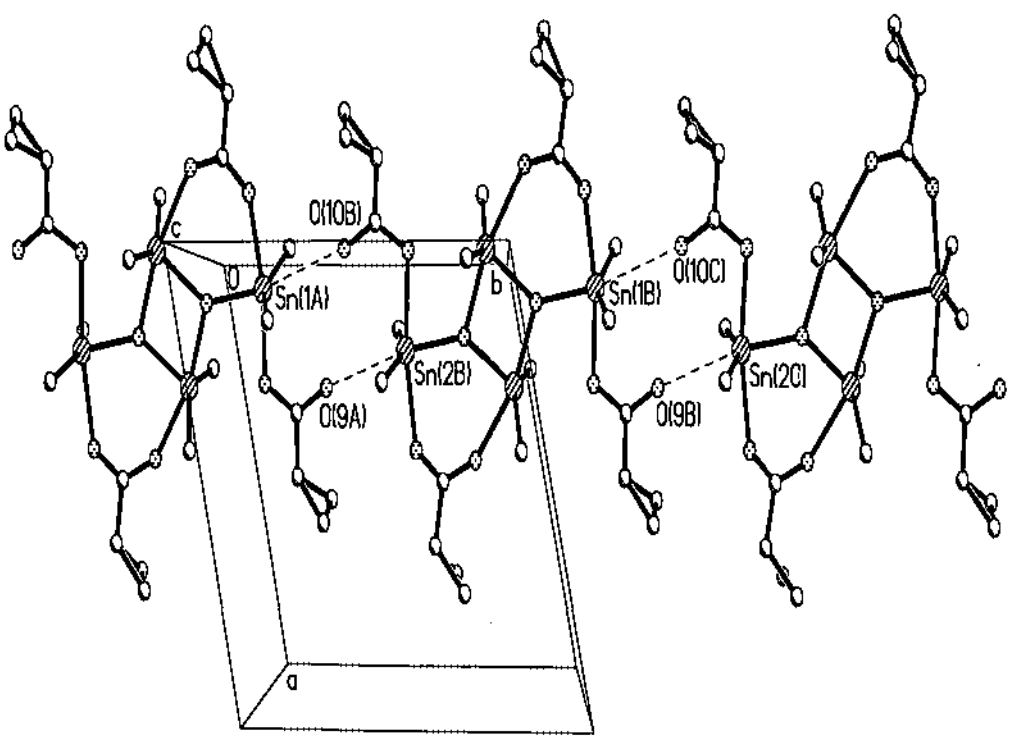
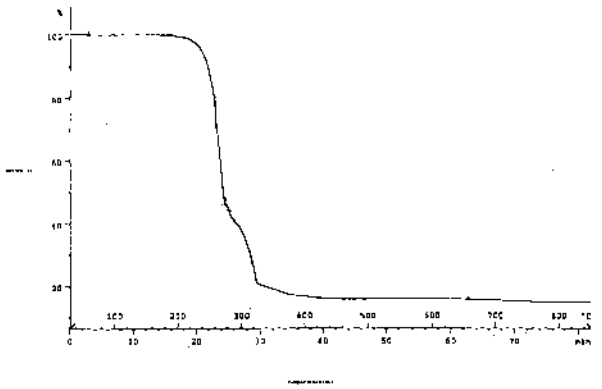


Fig. 3.19 Crystal packing in $\{[Me_2Sn(cyclo\text{-}CH_2)_2CHCOO)]_2O\}_2$ **(6)**.

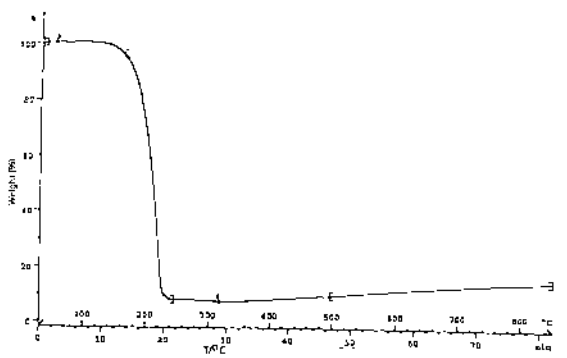
3.4.3.2.4. Thermogravimetric analysis

The thermogravimetric (TG) analysis of di- and tri- organotin(IV) derivatives of the ligand acids L^1H reveal that decomposition of the complexes occur as the temperature

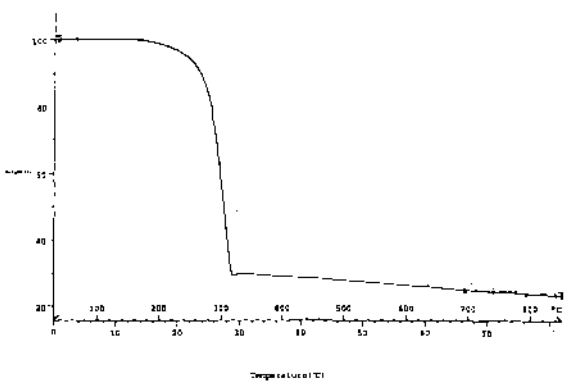
increases. The TG curves of the triorganotin(IV) and diorganotin(IV) complexes of L^1H are shown in Fig.3.20 and 3.21 respectively.



(a)



(b)



(c)

Fig. 3.20 (a) TG Curve of **1** (b) TG Curve of **2** (c) TG Curve of **3**.

The degradation pattern of the triorganotin complexes is different from those of the diorganotin complexes. In the case of the triorganotin complexes the ligand

decomposes in one step, while in the diorganotin complexes the ligand decomposes in two steps. Powder XRD analysis of the final product of **6** obtained at 800 °C shows this to be SnO_2 (mineral name-Cassiterite, JCPDS: 41-1445).

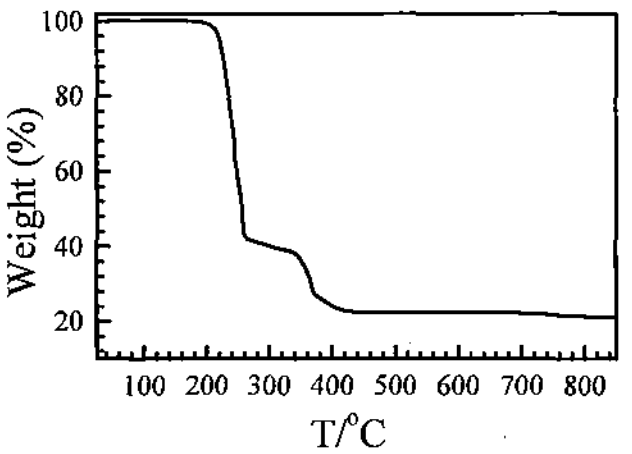
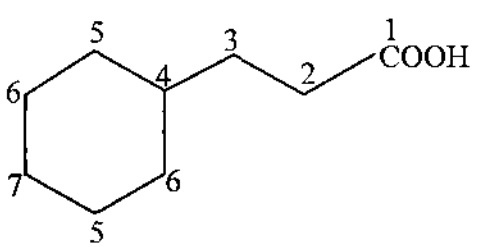


Fig. 3.21 TG Curve of **6**

3.4.4 Triorganotin(IV) and diorganotin(IV) complexes of 3-cyclohexylpropanoic acid(L^2H)

The tri- and di- organotin(IV) complexes of 3-cyclohexylpropanoic acid (L^2H) were obtained in moderate yields by heating at reflux the stoichiometric amount of L^2H or its sodium salt with the corresponding organotin hydroxide or chloride in benzene or methanol as solvents respectively . The complexes were characterized by IR, multinuclear (^1H, ^{13}C and ^{119}Sn) NMR spectroscopy and elemental analyses. Thermogravimetric analysis were carried out for some selected compounds of L^2H. The numbering scheme of the ligand and the abbreviations of the complexes are presented in the Scheme 3.4.



3-cyclohexylpropanoic acid (L^2H)

9	Bu_3SnL^2
10	Ph_3SnL^2
11	$(c\text{-}Hex)_3SnL^2$
12	Me_3SnL^2
13	$[Me_2Sn(L^2)_2]_2\text{-}[Me_2SnO]_2$
14	$n\text{-}Bu_2Sn(L^2)_2$

Scheme 3.4

3.4.4.1 Synthesis of triorganotin(IV) complexes of 3-cyclohexylpropanoic acid(L^2H), R_3SnL^2 (R=Ph, n-Bu, c-Hex, Me) (9-12)

The reaction between R_3SnOH and the parent acid in benzene by the azeotropic removal of the water produced during the reaction using a Dean-Stark apparatus produces the triorganotin(IV) carboxylates. But, the method using alkali metal salt of the ligand was preferred due to the ease of handling of the salt when compared to the acid. Only the triphenyltin complex of the acid (L^2H) was synthesized by the reaction of Ph_3SnOH and L^2H in benzene using a Dean-Stark trap. The aim was to compare the yields obtained via two different synthetic methodologies. In this case, it was found that **10** was obtained in much higher yields by the reaction of Ph_3SnOH and L^2H in benzene than by the method using alkali metal salt of the ligand and Ph_3SnCl.

$$Ph_3SnOH + L^2H \longrightarrow Ph_3SnL^2 + H_2O \quad \text{.....(22)}$$

10: Ph_3SnL^2

The other triorganotin(IV) complexes of 3-cyclohexylpropionic acid(L^2H), were obtained in moderate yields by the reaction of the respective triorganotin chloride(R_3SnCl) and the sodium salt of the ligand acid (L^2Na) in stoichiometric amounts in methanol.

$$R_3SnCl + L^2Na \longrightarrow R_3SnL^2 + NaCl \quad \text{.....(23)}$$

9: R=n-Bu; **11** :R=c-Hex; **12**: R=Me

The reaction mixture obtained by either of the above two methods was evaporated to dryness and then extracted in petroleum ether (b.p.60-80 °C).The petroleum ether extract was concentrated to yield the crude product. The products were subsequently recrystallized from the appropriate solvents. The solubility of the triphenyltin analogue was poor in petroleum ether(b.p.60-80 °C)and a large amount of petroleum ether was required to extract the same. The reaction conditions for each of the above mentioned complexes are listed in Table 3.15.

Table 3.15 Characterization and analytical data for **9-12**[a,b,c]

Complex	Crystallization Solvent	Yield (%)	M.p.(°C)	Elemental Composition[a](%)		
				C	H	Sn
9[b]	Petroleum ether (b.p.60-80°C)	88	96	56.14 (56.22)	9.30 (9.44)	26.61 (26.69)
10[c]	Benzene	73	111-112	63.46 (64.19)	5.35 (5.94)	23.42 (23.51)
11[b]	Petroleum ether (b.p.60-80°C)	67	168-170	61.72 (61.98)	9.10 (9.18)	22.59 (22.70)
12[b]	Petroleum ether (b.p.60-80°C)	79	130-131	45.35 (45.61)	6.61 (6.65)	37.47 (37.59)

[a]Calculated values in parentheses.

[b] Reflux in methanol ; reaction time was 5-6 h. All compounds are white.

[c] Reflux in benzene for 4 hours.

3.4.4.1.1 IR spectra of triorganotin (IV) derivatives of L^2H (R= n-Bu, Ph, c-Hex, Me) ***(9- 12)***

The IR spectra of all the compounds were scanned in the range 4000-250cm^{-1}. The coordinating mode of 3-cyclohexylpropionic acid towards organotin(IV) moieties can be inferred by comparing the IR spectra of the free acid, its sodium salt and the organotin compounds. Frequencies assigned to ν_{asym}(OCO) and ν_{sym}(OCO) have been

identified for all species and are reported together with bands tentatively assigned to ν(Sn-C) in Table 3.16.

For a bridging or chelating carboxylate group, $\Delta\nu \leq 150$ [190] as widely observed in the IR spectra of triorganotin carboxylates [191]. It is clear from the tabulated values that in all compounds (except the tri-c-Hex tin analogue) have Δν in the range 123-150 cm^{-1} indicating that these organotin carboxylates are carbonyl bridged polymers in the solid state [192]. The observed value of $\Delta\nu = 231$ cm^{-1} for the tricyclohexyl tin analogue [193] have been found to be comparable to those found for the mono-coordinated triorganotin carboxylates, indicating that the carboxylate group acts as a monodentate ligand [194, 195].The appearance of medium to weak intensity bands in the range 560-453 cm^{-1} due to ν(Sn-C) further confirms the formation of the complexes.

Table 3.16 Characteristic IR absorption bands (cm^{-1}) for **9-12**[a]

Complex	$\nu(OCO)_{asym}$	$\nu(OCO)_{sym}$	Δν(OCO)	ν(Sn-C)
7	1572(m)	1449(m)	123	560(w), 485(w)
8	1583(m)	1428(w)	155	554(w),454(w)
9	1614(m)	1384(w)	230	551(m),453(w)
10	1560(m)	1420(w)	140	547(m),455(m)

[a]s, strong; w, weak; m, medium.

3.4.4.1.2 NMR Spectra of ***9 – 12***

The ^1H NMR spectral data (Table 3.17) further support the composition of the new complexes suggested by IR spectral data. ^1H NMR spectra were recorded for the free ligand acid and its complexes in $CDCl_3$. The ^1H NMR spectrum of the ligand exhibits the chemical shifts for the ligand protons as follows: H-1, 11.40 (s, 1H); H-2, 2.35 (t, 2H); H-3, 1.57-1.49(m, 2H); H-4,5, 1.71-1.63 (m,5H); H-6, 1.32-1.06 (m,4H); H-7, 0.94-0.83 (m,2H). All the signals in the pure ligand were observed in the organotin(IV) complexes with slight shifts.

In the tri-n-Bu and tri-c-Hex derivatives the ligand protons overlap with the Sn-alkyl protons making the identification of individual protons difficult. All the CH_2 signals of the butyl groups are multiplets, therefore the determination of $^{n}J(^{119/117}Sn\text{-}^{1}H)$ coupling constants was not possible.

In the tri-Ph tin complex, **10**, the Sn-phenyl protons appear at 7.69 and 7.41 as multiplets. A coupling value $^{3}J(^{119}Sn\text{-}^{1}H)$ of 57 Hz was observed. Both the chemical and shifts and coupling constants for the triphenyltin complex, agree well with the data found for the other reported triphenyltin compounds [176,196].

In the trimethyltin complex of L^2H, the Sn-Me protons resonate at δ0.53. The percentage s-character of the tin-methyl orbital has been related to the $^{2}J(^{119}Sn\text{-}^{1}H)$ coupling constants[197]. For **12**, the $^{2}J(^{119}Sn\text{-}CH_3)$ coupling value was observed to be 57 Hz in agreement with the previous literature data[198,199]. This value of $^{2}J(^{119}Sn\text{-}CH_3)$ indicates that the tin atom has an approximately 25% s-character. In addition, a C-Sn-C bond angle of was calculated using the Lockhart's equation. Both these observations indicate that the methyl derivative is four-coordinated in solution.

^{13}C NMR data of the investigated compounds are given in Table 3.18. The number of signals found correspond with the presence of magnetically non-equivalent carbon atoms, which were assigned by comparison with other related organotin complexes [200, 201]. The ^{1}H and ^{13}C NMR spectrum of **12** is presented in Fig. 3.22. The carboxylate carbon shifts to a lower field in all the complexes, indicating participation of the carboxylic group in coordination to tin(IV) [201]. The $^{1}J(^{119}Sn\text{-}^{13}C)$ coupling constants have been used to infer the coordination number of the tin atom in these organotin compounds. As can be seen from Table 3.18, the $^{1}J(^{119}Sn\text{-}^{13}C)$ coupling constants range from 340.5 to 398.6 Hz for the alkyl compounds. These values are consistent with the values for similar compounds with a tetrahedral geometry [182,200,201] in solution.

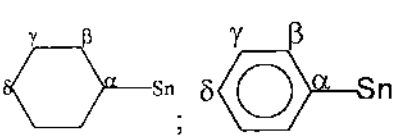
Table 3.17 ^{1}H NMR data (in ppm) for **9 - 12**[a,b,c]

	9	**10**	**11**	**12**
H-2	2.30 (t,2H)	2.41 (t,2H)	2.37-2.17 (m,2H)	2.29 (t,2H)
H-3	1.68-1.47 (m,2H)	1.63-1.50 (m,2H)	2.37-2.17 (m,2H)	1.54-1.46 (m,2H)
H-4	-	-	1.32-1.19 (m,H)	-
H-5	-	-	1.98-1.95 (m,H)	-
H-4,5	1.68-1.47 (m,5H)	1.63-1.50 (m,5H)	-	1.71-1.67 (m,5H)
H-6	1.39-1.16 (m,4H)	1.11-1.09 (m,4H)	1.42-1.19 (m,4H)	1.26-1.10 (m,4H)
H-7	0.98-0.83 (m,2H)	0.89-0.82 (m,2H)	0.94-0.87 (m,2H)	0.93-0.83 (m,2H)
H-α	1.68-1.47 (m,6H)	-	1.98-1.94 (m,3H)	0.53(t,9H) [57][e]
H-β	1.39-1.16 (m,6H)	7.69(m,6H) [57][d]	1.87-1.46 (m,12H)	-
H-γ	1.39-1.16 (m,6H)	7.41 (m,6H)	1.87-1.46 (m,12H)	-
H-δ	0.90 (t,9H)	7.41 (m,3H)	1.42-1.19 (m,6H)	-

[a] Spectra recorded in $CDCl_3$, downfield to TMS, multiplicity is given as t, triplet; m, multiplet.

[b] Refer to Scheme 3.4. for numbering scheme in the ligand skeleton.

[c] Numbering scheme for Sn-R skeleton as shown below:

$^{\alpha}CH_3$-Sn; $^{\delta}CH_3$-$^{\gamma}CH_2$-$^{\beta}CH_2$-$^{\alpha}CH_2$-Sn; 

.

[d] $^{3}J(^{119}Sn-^{1}H)$ in Hz.

[e] ^{2}J (^{119}Sn-CH_3) in Hz.

Table 3.18 ^{13}C NMR data [a,b] (in ppm) of **9 - 12**

	Ligand skeleton							Sn-R skeleton			
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-α	C-β	C-γ	C-δ
9	179.82	37.40	33.26	32.45	33.04	26.60	26.30	16.36 [357.7 /342.1][d]	27.84 [19.5][e]	27.02 [64.5][f]	13.63
10	181.27	37.33	33.06	31.71	32.94	26.51	26.21	138.45	136.85 [47.2][e]	128.83 [62.2][f]	130.03 [15][g]
11	184.40	37.37	32.56	28.52	29.45	26.55	26.30	32.99 [340.5][d]	29.76 [18.7][e]	28.85 [56.25][f]	26.48 [45][g]
12	179.8	37.40	33.08	32.39	32.97	26.54	26.23	-2.50 [398.62 /381.0][d]	-	-	-

[a] Spectra recorded in $CDCl_3$, downfield to TMS.

[b] For numbering scheme of the ligands see Scheme 3.4.

[c] For numbering scheme of Sn-R skeleton see footnotes of Table 3.17.

[d] $^1J(^{119/117}Sn-^{13}C)$ in Hz; [e] $^2J(^{119}Sn-^{13}C)$ in Hz; [f] $^3J(^{119}Sn-^{13}C)$ in Hz.

[g] $^4J(^{119}Sn-^{13}C)$ in Hz.

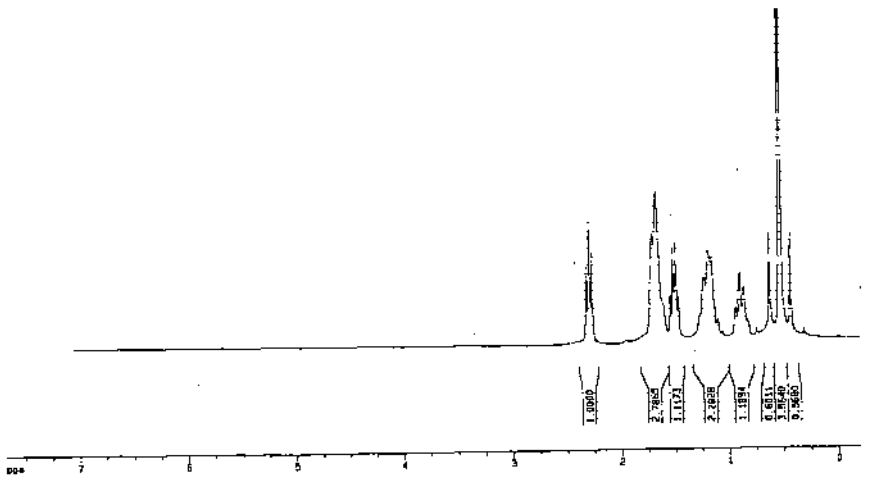
The ^{119}Sn NMR spectra of **9-12** were recorded in $CDCl_3$ solution with Me_4Sn as an external reference. The spectrum of **10** is shown in Fig. 3.23. The data for all the compounds are tabulated in Table 3.19. The chemical shifts obtained for the triorganotin(IV) derivatives lie in the range expected for a tetrahedral geometry [182, 201].

Table 3.19 ^{119}Sn NMR data [a] (in ppm) of **9-12**

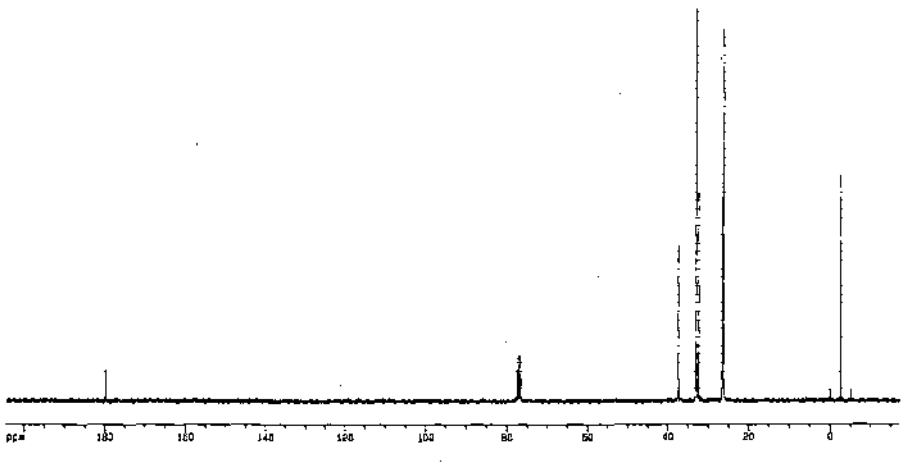
Complex	$\delta(^{119}Sn)$
9	103.73
10	-115.18
11	n.m.[b]
12	128.82

[a] Spectra recorded in $CDCl_3$ with Me_4Sn as an external reference.

[b] n.m. = not measured.



(a)



(b)

Fig. 3.22 (a) ^{1}H NMR spectrum of **12** (b) ^{13}C NMR spectrum of **12**.

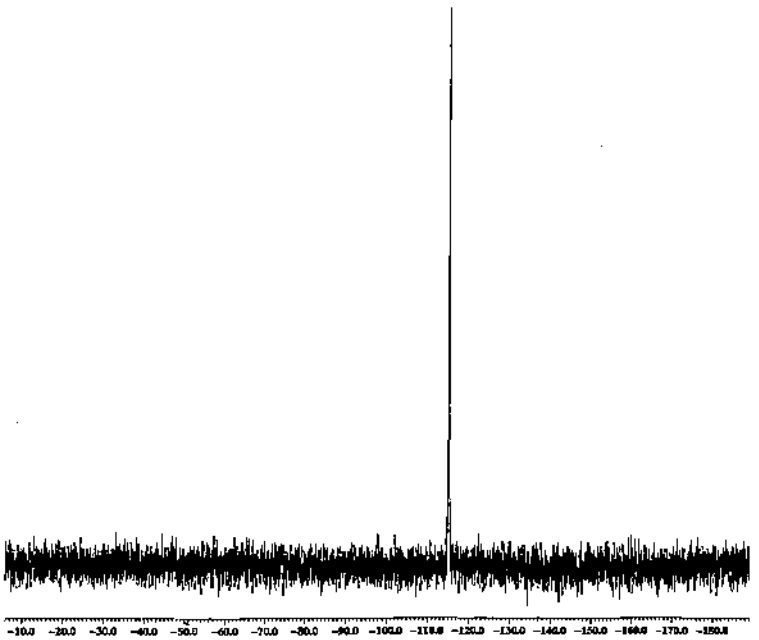


Fig. 3.23 ^{119}Sn NMR spectrum of **10.**

3.4.4.2 Diorganotin (IV) complexes of L^2H (R=Me and n-Bu)

3.4.4.2.1 Synthesis of diorganotin (IV) derivatives of L^2H (R=Me, n-Bu) (13,14)

The diorganotin derivatives of L^2H (R=Me, n-Bu) were obtained in moderate yields by the reaction between the respective diorganotin dichloride(R_2SnCl_2) and the sodium salt of the ligand acid (L^2Na) in 1: 2 stoichiometric amounts in methanol. As in the case of the diorganotin derivatives (R=Me, n-Bu) of cyclopropane carboxylic acid, the author was unable to isolate dimethyltin dicarboxylate of L^2H , instead, dicarboxylato tetraorganostannoxane was obtained as the product of the reaction of the Me_2SnCl_2 and the sodium salt of the ligand acid (L^2Na).The product is most probably obtained from the hydrolysis of the dimethyltin dicarboxylate by aerial

moisture or by traces of moisture present in the solvents used [1,21,62,124] .**14** was isolated as a dicarboxylate and is a viscous liquid. The analytical data for these complexes are presented in Table 3.20.

$R_2SnCl_2 + 2\,L^2Na \longrightarrow [R_2Sn(L^2)_2]_2\,[R_2SnO]_2 + 2NaCl$ ....(24)

13 : Me

$R_2SnCl_2 + 2\,L^2Na \longrightarrow R_2Sn(L^2)_2 + 2NaCl$ .....(25)

14 : n-Bu

Table 3.20 The Physical and analytical data for **13, 14**[a,b,c]

Complex	Crystallization Solvent	Yield (%)	Melting Point(°C)	Elemental Composition[a](%)		
				C	H	Sn
13	Petroleum ether (b.p.60-80°C)	72	102-104	42.19 (42.35)	6.72 (6.73)	37.98 (38.07)
14[c]	-	65	-	57.45 (57.49)	8.82 (8.84)	21.84 (21.87)

[a]Calculated values in parentheses.

[b]Reaction time was 5-6 h.

[c] viscous liquid

3.4.4.2.2 IR spectra of diorganotin (IV) derivatives of L^2H (R= Me, n-Bu) (13,14)

The assignments of IR bands for the complexes are made by comparison with the IR spectra of the free aids, its sodium salt and similar organotin compounds [16]. The IR spectral data for **13** & **14** are presented in Table 3.21.

In **13**, the magnitude of $\Delta[\nu\,(OCO)_{asym} - \nu\,(OCO)_{sym}]$, of 310 cm^{-1} and 146 cm^{-1} indicates the presence of two types of carboxylate moieties, functioning as monodentate and bidentate, respectively. This is usually observed for dicarboxylato tetraorganodistannoxanes[125,186]. In **14**, $\Delta\nu$= 145 cm^{-1} indicates that the carboxylate ligand is functioning as a bidentate one [66,185].

Table 3.21 Characteristic IR absorption bands (cm^{-1}) for **13,14**[a]

Complex	$\nu(OCO)_{asym}$	$\nu(OCO)_{sym}$	$\Delta\nu(OCO)$	ν(Sn-C)	ν (Sn-O-Sn)
13	1561(s) 1635(m)	1415(m) 1325(m)	146 310	551(m) 453(w)	626(s)
14	1558(m)	1413(w)	145	542(m) 451(w)	-

[a]s, strong; w, weak; m, medium.

*3.4.4.2.3. NMR spectra of diorganotin (IV) derivatives of L^2H (R= Me, n-Bu) (**13,14**)*

The ^1H and ^{13}C NMR spectral data of **13** & **14** are given in Table 3.22 and 3.23 respectively. The ^1H and ^{13}C NMR spectra of **14** is presented in Fig. 3.24. For R=Me, compound, two sets of methyl resonances are observed which show different $^2J(^{119}Sn\text{-}^1H)$ values, as expected for dicarboxylato tetraorganodistannoxanes [59]. The high field methyl resonance with smaller $^2J(^{119}Sn\text{-}^1H)$ value is assigned to *exo*-cyclic Me_2Sn group and the low field resonance, with higher $^2J(^{119}Sn\text{-}^1H)$ value is assigned to *endo*-cyclic Me_2Sn moiety [124].^{13}C NMR spectra of **13** also displayed two sets of Me-Sn resonances, as expected for dicarboxylato tetraorganodistannoxanes [59, 124].

^1H and ^{13}C NMR spectral data of **14** shows only one set of Sn-Bu resonances indicating that it is a dicarboxylate [99,201].

The ^{119}Sn NMR spectra of **13** displayed two well-separated resonances(Table 3.24), as is usually observed for dicarboxylato tetraorganodistannoxanes [117,121], and supporting the presence of dimeric structure in solution. The low field and high field shifts observed for distannoxanes are attributed to *exo*-cyclic and *endo*-cyclic tin atoms, respectively [1,185]. The ^{119}Sn NMR spectra of **13** is presented in Fig. 3.25.

Diorganotin dicarboxylates having a five-coordinate tin centre show tin chemical shifts in the range of -110 to -161 ppm [202].The ^{119}Sn NMR spectra of **14** show a sharp signal at -148.63 ppm which can therefore be assigned to a five-coordinate tin atom[169]. The ^{119}Sn NMR spectra of **14** is presented in Fig. 3.26.

Table 3.22 ^{1}H NMR data(in ppm) for ***13,14*** [a,b,c]

	Ligand skeleton	Sn-R
13	(H-2) , 2.18(t, 4H); H-3, 1.49-1.41(m,4H); H-4,5 1.71-1.67 (m,10H); H-6, 1.27-1.10 (m,8H); H-7, 0.96-0.82 (m,4H)	H-α(12H) : *exo*-cyclic 0.76 [84][d] *endo*-cyclic 0.78 [90][d]
14	(H-2) , 2.36(t, 4H); H-3, 1.41-1.32(m,4H); H-4,5, 1.72-1.48 (m,10H); H-6, 1.25-1.10 (m,8H); H-7, 0.93-0.83 (m,4H)	H-α, 1.72 – 1.48(m,4H) H-β, γ, 1.41 – 1.32 (m,8H) H-δ, 0.91 (t, 6H)

[a] Spectra recorded in $CDCl_3$,downfield to TMS, multiplicity is given as t, triplet; m, multiplet.

[b] For numbering scheme of the ligands see Scheme 3.4.

[c] Numbering scheme for Sn-R skeleton as shown below:

$^{\alpha}CH_3$-Sn; $^{\delta}CH_3$-$^{\gamma}CH_2$-$^{\beta}CH_2$-$^{\alpha}CH_2$-Sn

[d] $^{2}J(^{119}Sn\text{-}H)$ in Hz.

Table 3.23 ^{13}C NMR data (in ppm) for **13,14**[a,b,c]

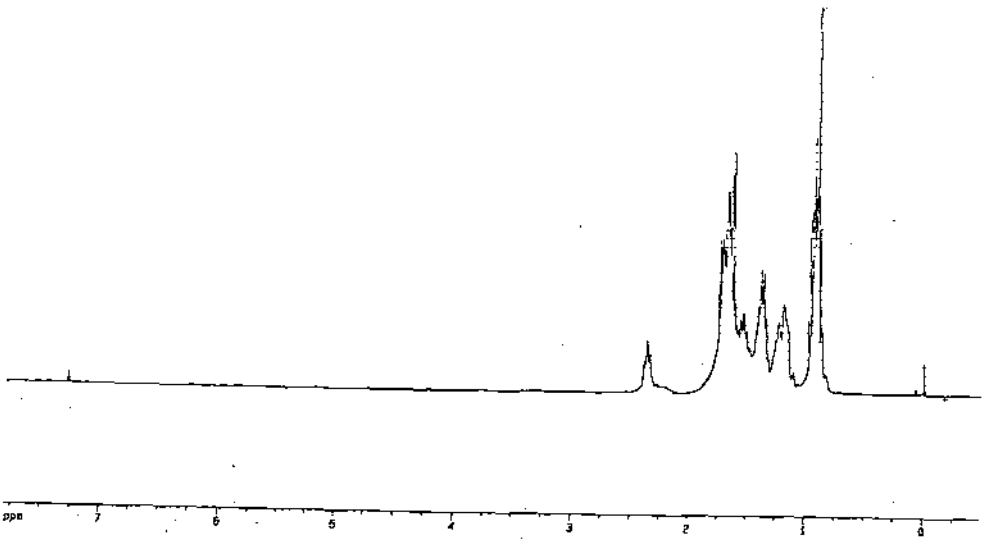
	Ligand skeleton							δ(Sn-R)
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	
13	180.61	37.37	33.79	30.04	30.09	26.53	26.25	8.75[807.69][d] 6.35[750.0][d]
14	184.55	37.28	32.88	27.19	31.71	26.57	26.23	α : 24.81, β :26.45, γ : 26.16, δ : 13.45

[a] Spectra recorded in $CDCl_3$,downfield to TMS.

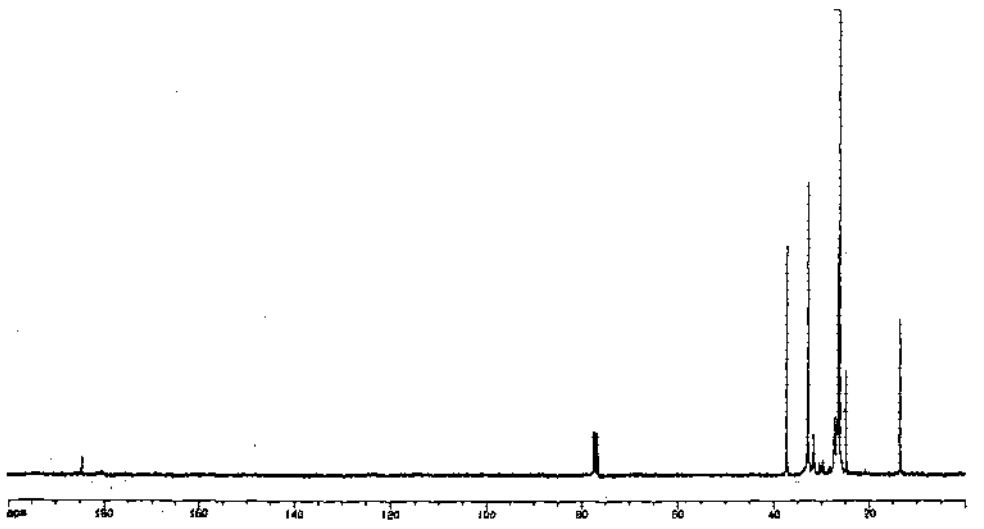
[b] For numbering scheme of the ligand see Scheme 3.4.

[c] For numbering scheme of Sn-R skeleton see footnotes of Table 3.22.

[d] $^{1}J\ (^{119/117}Sn\text{-}^{13}C)$ in Hz.



(a)



(b)

Fig. 3.24 (a) ^{1}H NMR spectrum of **14** (b) ^{13}C NMR spectrum of **14**.

Table 3.24 ^{119}Sn NMR data (in ppm) for **13** and **14**[a]

Complex	$\delta(^{119}Sn)$
13	$\delta(^{119}Sn)_{exo}$, -176.1; $\delta(^{119}Sn)_{endo}$, -186.9
14	-148.63

[a] Spectra recorded in $CDCl_3$ with Me_4Sn as an external reference.

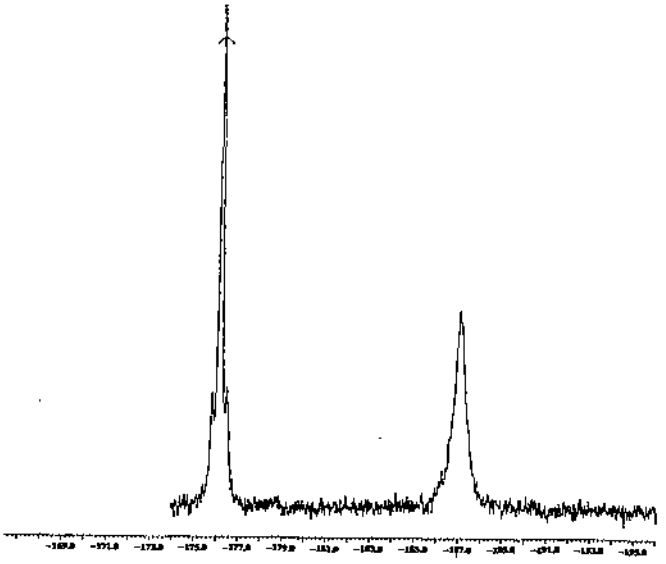


Fig. 3.25 ^{119}Sn NMR spectrum of **13**.

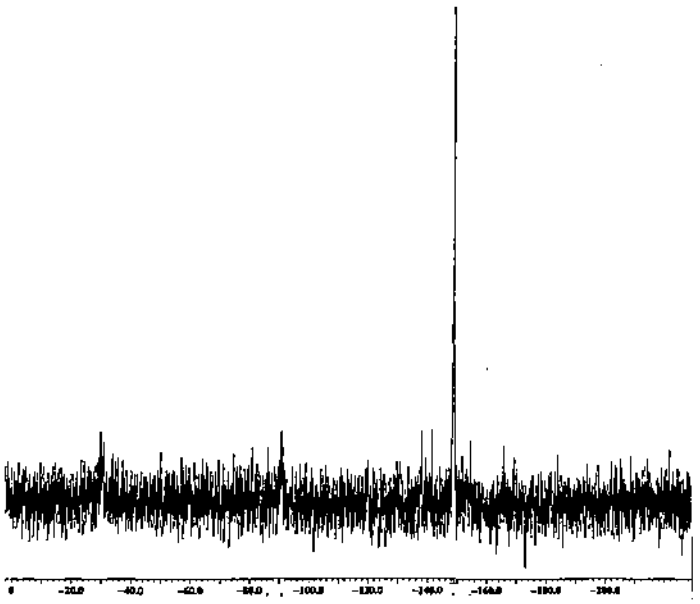
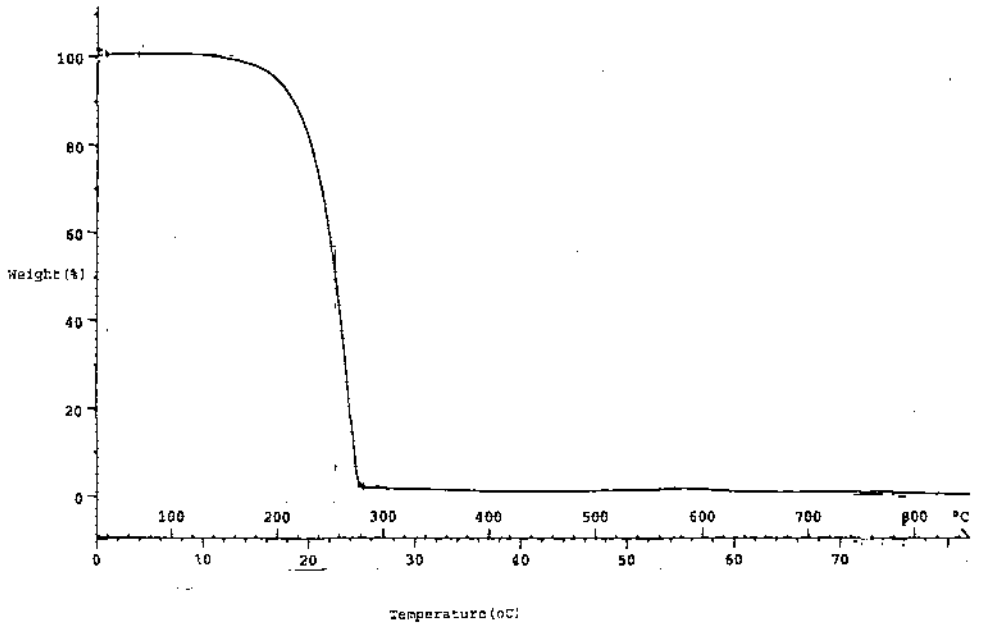


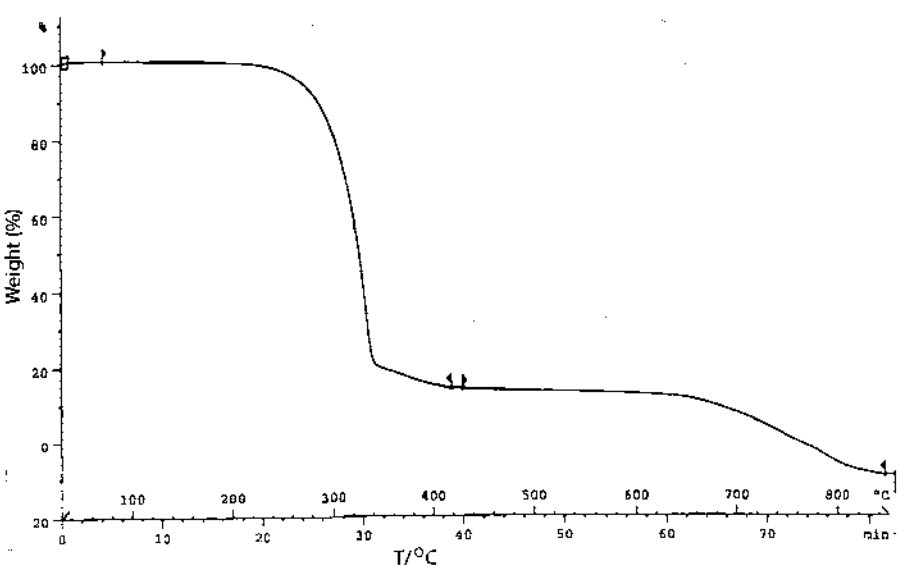
Fig. 3.26 ^{119}Sn NMR spectrum of **14**.

3.4.4.2.4 Thermogravimetric analysis of organotin(IV) carboxylates of 3-cyclohexylpropanoic acid

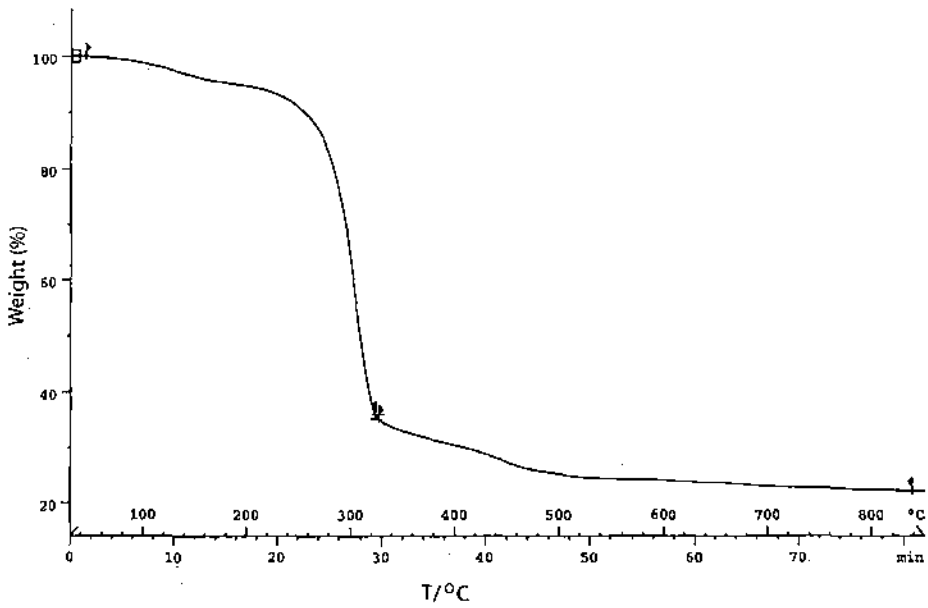
The thermogravimetric (TG) analysis of di- and tri- organotin(IV) derivatives of L^2H reveal that decomposition of the complexes occur as the temperature increases. The degradation pattern of the triorganotin complexes is different from those of the diorganotin complexes. The triorganotin complexes of L^2H (tri-c-Hex and tri-Ph) exhibit a two-step decomposition in a similar manner as that observed for the diorganotin derivatives. The tri-n-Bu derivative though, decomposed in a single step similar to that of the triorganotin derivatives of L^1H. The TG curve of triorganotin and diorganotin(IV) derivatives are presented in Fig. 3.27 and 3.28 respectively. Powder XRD analysis of the final product of **11** obtained at 800 °C show this to be a mixture of SnO_2 (JCPDS: 41-1445), SnO (JCPDS: 24-1342) and β-SnO (JCPDS: 07-0195).


Weight (%)
100
80
60
40
20
0
100
200
300
400
500
600
700
800
°C
0
10
20
30
40
50
60
70
Temperature (oC)

(a)


Weight (%)
100
80
60
40
20
0
100
200
300
400
500
600
700
800
°C
0
10
20
30
40
50
60
70
min
T/°C

(b)



(c)

Fig. 3.27 (a) TG curve of **9** (b) TG curve of **10** (c) TG curve of **11**.

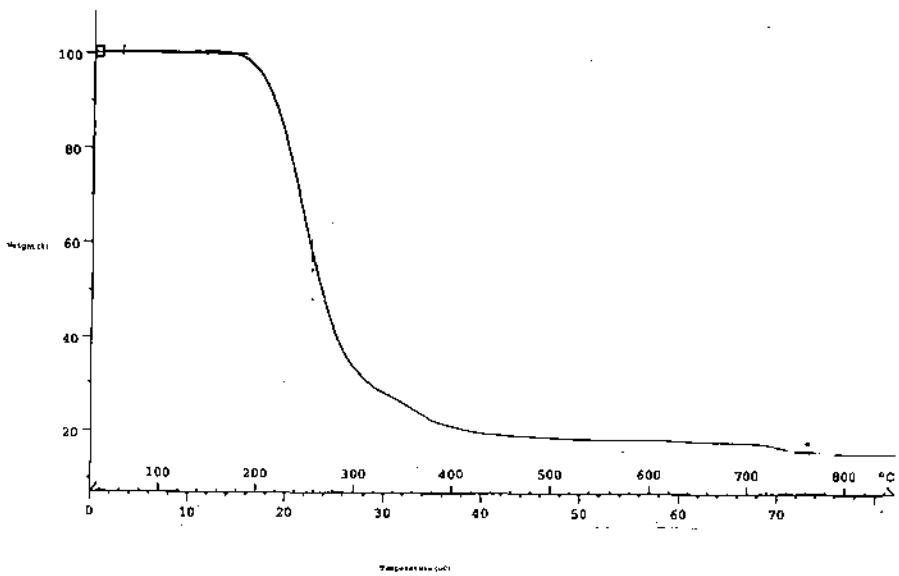


Fig. 3.28 TG curve of **13**.

3.4.5 Biocidal activity

The results of antifungal assay, antibacterial assay and phytotoxicity studies are presented in Table 3.25, 3.26 and 3.27 respectively.

3.4.5.1 Study of the antifungal activity of the organotin(IV) carboxylates

The newly synthesized tri- and diorganotin(IV) complexes of cyclopropane carboxylic acid and 3-cyclohexylpropanoic acid were tested for their antifunal activity by spore germination method as described by Rouxel *et al.* [163]. The data are given in Table 3.25.Most of the compounds showed moderate fungicidal activity. However, enhanced fungicidal activity was found to be associated with the tributyl and triphenyl tin carboxylates. It is well established that triorganotin compounds are significantly more biologically active than classes with either more or less hydrocarbons bonded to tin [158].Within the triorganotin carboxylates, the nature of the R group was found to play a pivotal role in the determination of the fungicidal activity of the complex. In this case, the tri-n-butyl carboxylates were found to be more active (over the range of fungi tested) than tri-phenyltin derivative which was found to be more active than the tri-cyclohexyltin complex [16, 158]. Apparently, the function of the ligand is to support the transfer of the active organotin moiety to the site of action where it was released by hydrolysis. The findings are in agreement with the literature reports which says that anionic groups in the organotin complexes play a secondary role in determining the degree of activity of R_3SnL compounds [6,12]. It was noticed that fairly high concentrations of diorganoin derivatives of L^1H and L^2H were required to inhibit the fungal growth when compared to the R_3SnL analogues. The dibutyltin derivative of L^1H is found to be the least effective among the compounds against the tested fungal strains.The biocidal activity of the triorganotin carboxylates relate to their structure by the fact that the species generating tetrahedral structure in solution are more active[158]. And as explained before, while discussing the NMR spectra of these complexes, all the triorganotin complexes adopted tetrahedral structure in solution.

3.4.5.2 Study of the antibacterial activity of the organotin(IV) carboxylates

The compounds were also screened for their antibacterial activity against *Pseudomonas fluorescens*, a fish-pathogenic, Gram-negative bacteria by following agar well diffusion method [164]. The inhibition zones appearing around each disc were measured and the sensitivity determined from the zone diameters appearing on the plates based on NCCLS charts. When the bacteria gave a zone with diameter less than 13 mm in the presence of an organotin, it was interpreted as resistant (R), when the zone had a diameter of 15-16 mm, the bacteria were considered to have intermediate sensitivity (I) and a clear zone with diameter of 17 mm or more indicated a high degree of sensitivity towards the compound (S).All the compound were tested at 1 mg/ml concentration level. The results are given in Table 3.26. The screening tests show that the tributyltin carboxylates **1** and **9** are the most potent candidates against *Pseudomonas fluorescens,* with decreasing activity for the other triorganotin complexes followed by the diorganotin derivatives [6,41].

3.4.5.3 Phytotoxicity Studies

Wheat seed (variety Sonalika) germination studies (Table 3.27) showed that the compounds have practically insignificant phytotoxicity at the concentrations levels tested. A comparison among the level of phytotoxicities among these compounds reveals that the tri-n-butyl compounds are more phytotoxic than the triphenyltin compounds followed by the other organotin derivatives of L^1H and L^2H. The difference may, however, be attributable to the triphenyltin moiety in **2** and tributyltin moiety in **1,** and is consistent with literature observation that triphenyltin derivatives are tolerated by plants to a greater degree compared to the tributyltin compounds [40].

Table 3.25 Effect of Organotin(IV) carboxylates on spore germination

Spore	Complex	MIC[a]
Curvularia eragrostidis	**1**	2.08
	2	22.40
	3	49.80
	6	50.00
	7	570.00
	9	3.15
	13	62.5
Alternaria porri	**1**	1.95
	2	2.24
	3	50.50
	6	60.00
	7	57.00
	9	2.95
	13	64
Dreschlerea oryzae	**1**	1.64
	2	2.29
	3	49.80
	6	56.00
	7	570.00
	9	3.00
	13	62.5
Macrophomina phaseolina	**1**	2.00
	2	2.45
	3	4.58
	6	52.00
	7	59.00
	9	3.15
	13	70.5

[a] Minimum Inhibitory Concentration in µg/ml

Table 3.26 Effect of different organotin compounds on bacterial growth[a,b]

Complex	Zone of Inhibition (in mm)
1	30
2	20
3	9
6	11
7	14
9	26
10	21
13	13

[a] The values represent mean of three experiments.

[b] Concentrations of compound used: 1 mg/ml.

Table 3.27 Effect of organotin(IV) derivatives of cyclopropane carboxylic acid and 3-cyclohexylpropionic acid on wheat seed germination

Complex	Concentration (μg/ml)	Percentage of germinated seeds[a] after treatment		
		Duration of treatment		
		1h	4 h	8h
1	100	90	90	85
	50	93	93	92
	25	95	95	94
2	100	97	97	97
	50	98	98	98
	25	99	98	98
3	100	97	96	96
	50	99	98	98
	25	99	99	99
6	100	97	97	97
	50	98	98	98
	25	98	98	98
7	100	97	97	97
	50	97	97	97
	25	98	98	98
9	100	91	91	87
	50	94	94	92
	25	95	95	94
13	100	92	92	95
	50	95	95	98
	25	96	96	98
Control	100	100	99	99
	50	99	99	99
	25	99	99	99

[a] With respect to the control.

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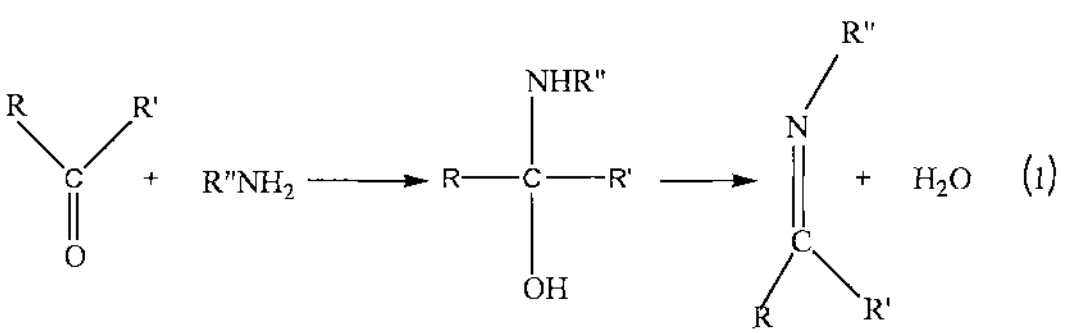
CHAPTER 4

SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION, FLUORESCENCE AND BIOCIDAL PROPERTIES OF SOME DIORGANOTIN(IV) COMPLEXES OF SALICYLALDEHYDE THIOSEMICARBAZONE AND RELATED LIGANDS

4.1 Introduction to organotin(IV) complexes of Schiff bases

The organotin complexes have been the subject of great interest for some time because of their versatile bonding modes [1,2] as well as their biomedical, commercial [3] and agricultural applications [4, 5, 6]. An important class of organotin(IV) complexes are those derived from Schiff bases. Over the recent decades, investigations on coordination of Schiff bases with organotin(IV) moieties have received considerable attention with respect to their potential applications in medicinal chemistry and biotechnology and their structural variety [7-13].These type of compounds have also found application in homogeneous catalysis [14]. Increasing attention has also been devoted to these classes of compounds in view of their special antitumour activities [13, 15-22]. Schiff bases in neutral and deprotonated forms react with organotin(IV) moieties and the complexes that are formed exhibit variable stoichiometry and different modes of coordination [23-25].

The condensation (Eq.1) of aliphatic or aromatic primary amines with aldehydes and ketones give products known as imines which contain a C=N bond. These compounds rapidly decompose or polymerize unless at least one among R, R' or R" is an aromatic organic group. The latter imines are called Schiff bases, since their synthesis was first reported by Schiff [26].



Aldehyde or Ketone | Primary amine | α-hydroxyamine | Schiff base

Dayagi and Degani [27] have reviewed the other methods of synthesis of the Schiff bases in the past.

4.1.1 Interactions of organotin(IV)$^{n+}$ with Schiff bases and their derivatives

The Schiff base complexes of organotin(IV) moieties have widely been investigated [28-33] and the subject was reviewed in 1984 [34].

Organotin(IV) Schiff base complexes of the type (L)SnR_2 [where R= CH_3, C_6H_5 or $CH_2CH_2CO_2CH_3$], (LH)$Sn(C_6H_5)_3$ and (L)$SnCl(CH_2CH_2CO_2CH_3)$ [where ligand, H_2L=2-*N*-salicylideneimino-2-methyl-1-propanol, derived from the condensation of salicylaldehyde and 2-amino-2-methyl-1-propanol] have been prepared and characterized on the basis of their elemental analyses, IR, ^1H, ^{13}C and ^{119}Sn NMR studies [35]. In these mononuclear complexes the Schiff base acts either as a dianionic tridentate or as a monobasic bidentate moiety by coordinating through an alkoxy group, an azomethine nitrogen and a phenoxide ion to tin. Sulphur dioxide inserts in the tin-methyl/-phenyl bond in the above Schiff base complexes to give tin-*O*-sulphinates of formulae (L)$RSn(SO_2R)$ and (LH)$(C_6H_5)_2Sn(SO_2C_6H_5)$. In a similar type of Sn-C bond cleavage reactions we have obtained di-μ_2-methoxo-bis[benzyl{5-chloro-2-oxido-benzaldehyde thiosemicarbazonato} tin(IV)] from the attempted recrystallization of an sample of $(PhCH_2)_2SnL$, where ligand LH_2 is *p*-chlorosalicylaldehyde thiosemicarbazone, from a methanol solution [36].

Equimolar reactions of Bu_2SnO with Schiff bases derived from amino acids led to the formation of a new series of dibutyltin(IV) complexes of general formula, Bu_2SnL (L=dianion of tridentate Schiff bases derived from the condensation of 2-hydroxy-1-naphthaldehyde or acetyl acetone with glycine, L-β-alanine, DL-valine, DL-4-aminobutyric acid, L-methionine, L-leucine and phenylglycine). The central Sn(IV) ions in all these complexes are penta-coordinated with a monodentate carboxylic group. The complexes have been tested against various bacteria and exhibited moderate activity. The cytotoxicities of these complexes were tested *in vitro* against several human tumour cell lines, namely, MCF-7, EVSA-T, WiDr, IGROV, M19 MEL, A498 and H226. The activities found experimentally were higher than those observed for cisplatin and carboplatin [37].

From the reactions of $SnCl_4$ with organotin(IV) chlorides ($RSnCl_3$, R_2SnCl_2 and R_3SnCl, where R = Bu, Me and Ph) with *N*-(2-hydroxybenzaldehyde)-1-amino-2-phenyleneimine, *N*-(2-hydroxyl-1-naphthaldehyde)-1-amino-2-phenyleneimine, *N*, *N'*-bis(2-hydroxybenzaldehyde)-1,2-phenylenediimine and *N*,*N'*-bis(2-hydroxy-1-naphthaldehyde)-1,2-phenylenediimine, a series of complexes have been synthesized and characterized, respectively, by microanalytical, IR, and ^1H NMR spectroscopic methods [38]. The Ph_2SnCl_2 reacted with *N*-(2-hydroxy-1-naphthaldehyde)-1-amino-2-phenyleneimine giving Ph_2Sn(NAPPDI) [where NAPPDI = deprotonated *N*, *N'*-bis(2-hydroxy-1-naphthaldehyde)-1,2-phenylenediimine], wherein the former Schiff base exhibited a facile intramolecular C=N bond cleavage and intermolecular C=N bond formation.

Diphenyltin(IV) complexes of *N*-(3,5-dibromosalicylidene)-α-amino acid, $Ph_2Sn[3,5\text{-}Br_2\text{-}2\text{-}OC_6H_2CH{=}NCH(R)COO]$ (where R=H, Me, *i*-Pr, Bz), and their 1:1 adducts with diphenyltin dichloride, $Ph_2Sn[3,5\text{-}Br_2\text{-}2\text{-}OC_6H_2CH{=}NCH(R)COO].Ph_2SnCl_2$, have been synthesized by Tian *et al.*[39].The crystal structure of $Ph_2Sn[3,5\text{-}Br_2\text{-}2\text{-}OC_6H_2CH{=}NCH(i\text{-}Pr)COO]$ shows a distorted trigonal bipyramidal geometry with axial locations occupied by a carboxylate-oxygen and a phenolic-oxygen atom of the ligand, and that of $Ph_2Sn[3,5\text{-}Br_2\text{-}2\text{-}OC_6H_2CH{=}NCH(i\text{-}Pr)COO].Ph_2SnCl_2$ reveals that the two tin atoms are joined via the carbonyl atom of the ligand to form a mixed organotin binuclear complex. Bioassay indicates that the compounds possess better cytotoxicity against three human tumour cell lines (HeLa, Col.o205 and MCF-7) than cisplatin and moderate antibacterial activity against two bacteria(*E.coli* and *S.aureus*).

Investigations on organotin(IV) amino acid and 2-amino-2-methyl-1-propanol Schiff base complexes were reported in literature [40,41].

Four tin(IV) complexes of tridentate dithiocarbazate Schiff bases have been synthesized and characterized by their elemental analyses, UV, ^1H NMR, Mössbauer spectroscopies and X-ray powder diffraction. The reactions of tin tetraacetate with the ligand LH_2 (Fig. 4.1) proceed smoothly but slowly with the elimination of acetic acid, which was removed azeotropically with toluene. Complexes having general formulae, $Sn(OCOCH_3)_2L$, where L= dianion of *S*-benzyl-*β*-*N*-(2-hydroxyphenyl)methylene and methyl dithiocarbazate (Fig. 4.1), are five-coordinated in distorted trigonal

bipyramidal geometry, whereas complexes of the type SnL_2 show hexa-coordination about the tin atom which is arranged in a distorted octahedral geometry with an orthorhombic lattice [42].

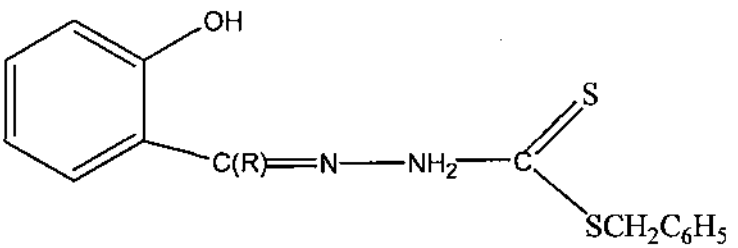


Fig.4.1 Structure of ligand LH_2 [42].

The schiff bases [H_2SBSaD], [H_2SBVD] and [H_2SBND], derived by the condensation of *S*-benzyldithiocarbazate and salicylaldehyde, 2-hydroxy-3-methoxybenzaldehyde and 2-hydroxy-1-naphthaldehyde respectively, react with diestertin dichlorides, R_2SnCl_2 [R= $-CH_2CH_2CO_2CH_3$, $-CH_2CH_2CO_2C_2H_5$ or $-CH_2CH_2CO_2C_4H_9$] in 1:1 molar ratio to yield complexes of the type R_2Sn(Schiff base), the base being tridentate [43]. The ^{13}C and ^{119}Sn NMR and the tin-carbon coupling constant data reveal the structures of the complexes to be octahedral with *trans* ester grouping, and bidentate ester linkages. The penta-coordinated complex, Me_2Sn(SBSaD) was prepared by the reaction of dimethyltin oxide with H_2SBSaD in equimolar proportions.

Diorganotin(IV)$^{2+}$ complexes with general formula R_2SnL (R= Ph, n-Bu, Me) were recently prepared by reacting R_2SnCl_2 and tetradentate Schiff bases (H_2L) containing N_2O_2 donor atoms in the presence of triethylamine (as base) in benzene. In the $Bu_2Sn(IV)^{2+}$ complexes formed with 3-methoxysalicylaldehyde derivatives, the Sn atom has a distorted octahedral structure, where the donor atoms of the Schiff base ligand occupy the four equatorial positions and the organo moieties are in *trans* axial positions [23].

Liu *et al.* [44] used the reaction of substituted benzoyl salicylahydrazone (Fig.4.2) (A= 2-phenyl, X=O, Y=H) with $[Cp(CO)_2Fe]_2SnCl_2$ and Ph_2SnCl_2 to synthesize complexes (Fig. 4.3 : B=$Fe(CO)_2Cp$ or Ph) and determined their molecular features.

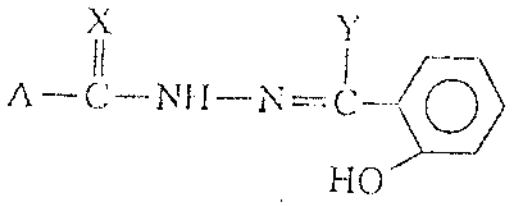


Fig. 4.2 Structure of substituted benzoyl salicylahydrazone.

In a similar work, the n-Bu_2[$(MeO)_3C_6H_2C(O)N_2CHC_6H_4O$]Sn complex (Fig. 4.3) was synthesized in the reaction of di-n-butyltin(IV) oxide with 3,4,5-trimethoxy-benzoyl salicylahydrazone (Fig. 4.2: A= 3,4,5-trimethoxyphenyl, X=O, Y=H) in dry benzene with azeotropic removal of water using a Dean-Stark trap [45].The complex was characterized by ^{1}H, ^{13}C and ^{119}Sn NMR and IR spectra. A single crystal X-ray diffraction study confirmed its molecular structure and revealed that 3,4,5-trimethoxy-benzoyl salicylahydrazone was a tridentate and approximately planar ligand. The tin atom had a distorted trigonal bipyramidal coordination (Fig.4.3: A= 3,4,5-trimethoxyphenyl , B= n-Bu).Two chain carbon atoms and the chelating nitrogen atom occupied the basal plane. The skeleton of two erect oxygen atoms and the tin atom was bent. In the complex, the ligand existed in the enol form.

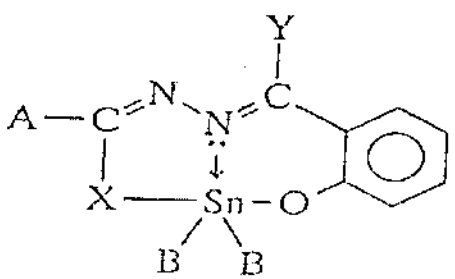


Fig.4.3 Structure of the organotin(IV) complex of substituted benzoyl salicylahydrazone.

2-Furanthiocarboxyhydrazide (Hfth), 4-hydroxyphenylthiocarboxyhydrazide (Hoth) and salicylaldehyde-2-furanthiocarboxyhydrazone (H_2L) form stable complexes of the compositions Ph_2SnCl_2·Hfth, $R_2Sn(LH)_2$ (where R = Ph or Bu and L = Hfth or Hoth), Ph_2SnCl_2·H_2L, $Ph_2Sn(HL)Cl$ and Bu_2SnL which have been characterized by elemental analysis and spectroscopic studies [46]. All the complexes were of octahedral geometry.

The ligating behaviour of di-2-pyridylketone-2-aminobenzoylhydrazone (HDPA), and phenyl(2-pyridyl)ketone 2-aminobenzoylhydrazone towards organotin derivatives was investigated [47]. The synthesis, IR and ^{119}Sn NMR spectroscopic characterization of the compounds were reported, together with the X-ray crystal structures of HDPA and $Sn(C_6H_5)_3Cl(OH_2)\cdot$HDPA, which were discussed and compared. The *in vitro* evaluation of antimicrobial properties revealed the strong activity of $Sn(C_6H_5)_2$(HDPA)Cl_2 and $Sn(C_6H_5)_3Cl(OH_2)\cdot$HDPA complexes. None of the compounds showed genotoxicity in the *Bacillus subtilis rec*-assay and in the *Salmonella*-microsome test.

Further results on organotin complexes with Schiff bases derived from hydrazones or substituted hydrazones were reported in [48-50].

Two compounds with the formula $[R_2Sn(OC_{10}H_6CH{=}NCH_2CH_2COO)]_2$ where R = CH_3 or n-C_4H_9, have been synthesized by Goh *et al.* [51]. The crystal structure of the dimethyltin compound is reported along with ^{1}H, ^{13}C and IR spectroscopic data for both compounds. The centrosymmetric dimethyltin complex exhibited octahedral coordination for each tin atom. The tridentate ligand chelate meridionally via the phenolate oxygen, the imino nitrogen and one carboxylate oxygen atom. Two further *trans* positions in the tin coordination sphere are taken up by the two methyl groups while the apical (sixth) position is filled by a shared carboxylate oxygen atom from the other organotin unit.

The reaction of 1-[3'-methoxyphenylimino)methyl]-2-naphthol with dimethyltin(IV) dichloride yielded an addition compound having 2:1 stoichiometry (ligand : organotin). The complex formed was characterized by elemental analysis, (^{1}H- and ^{13}C-) NMR, IR spectroscopy and X-ray analysis [52]. The coordination of the Schiff base to the metal occurred via the phenolic oxygen atom. This preferred mode of bonding was associated with the shift of the phenolic proton towards the azomethine atom resulting in a zwitter-ionic configuration for the ligand.

The crystal and molecular structure of the triphenyltin complex of 1-[4'-methylphen-ylimino)-methyl]-2-naphthol was reported. The complex adopted a five-coordinate trigonal bipyramidal geometry, with the phenyl groups taking up the equatorial positions around the tin atom. The ligand which existed in the form of a zwitter-ion

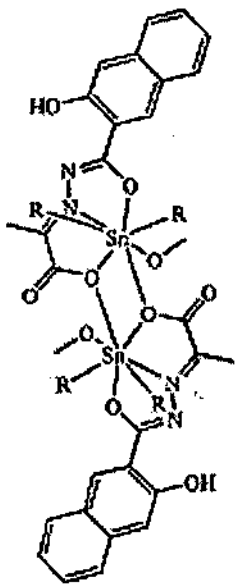
in the complex, binded to the tin via the phenolic oxygen atom. Free ligand cocrystallized with the complex in the ratio of one free ligand molecule to every two of the organotin complex units. The free ligand molecules pack in parallel strings in the crystal, between the organotin complex moieties, which are arranged as pairs of centrosymmetrically-related dimers [53].

Several Schiff bases derived from salicylaldehyde and aminopyridines were found to coordinate with Me_2SnCl_2 in 1:1 or 1:2 (tin:base) molar ratio in diethyl ether, depending on the nature of the Schiff base used, to form complexes of the general formula $Me_2SnCl_2.L$ or $Me_2SnCl_2.2L$ respectively [54].These Schiff bases coordinated with Ph_2SnCl_2 in similar manner, but if the reaction was carried out in chloroform or if the product formed was either dissolved in chloroform then colorless to pale yellow crystals were deposited. The latter were analyzed and found to be due to the ionic compounds $[H_2NpyN\text{-}H^+]_2[Ph_2SnCl_4]^{2-}$ which were formed as a result of an unusual cleavage of the C=N bond of the Schiff bases. The Schiff bases, their Me_2SnCl_2 complexes and the ionic compounds were analyzed physicochemically and spectroscopically. The crystal structures of two of the ionic compounds showed that the cation $[H_2NpyN\text{-}H^+]$ binds with the anion $[Ph_2SnCl_4]^{2-}$ via hydrogen bonds. The Schiff bases, their Me_2SnCl_2 complexes and the ionic compounds were screened against the three tumour cell lines, L_{929}, K_{562} and HeLa, and the results were compared with those of the anticancer drugs, cisplatin and carboplatin.

A series of organotin(IV) complexes with Schiff base ligand pyruvic acid-3-hydroxy-2-naphthoylhydrazone $[R_2SnLY]_2$, L=3-OH-$C_{10}H_6$-2-CON HN=C(CH_3) -COOH, R=n-C_4H_9, Y=CH_3OH(**1**), R=n-C_4H_9, Y= N (**2**), R=$PhCH_2$ (**3**), R=Ph, Y=CH_3OH(**4**), R=Me(**5**) and $[R_3SnLY]$, L=3-OH-C_{10}H6-2-CONHN=C(CH_3)-COOH, R= n-C_4H_9, Y=H_2O, (**6**), R= Ph (**7**), R= Me (**8**) were synthesized by the reaction of the Schiff base and trialkyltin in 1:1 stoichiometry [55]. By determination of the crystal structure of complex **1** it was noted that crystal containing two n-butyl and one oxygen atom from methanol coordinate to the tin atom. In the complexes **6-8** the Schiff base ligand coordinated to the Sn atom as a unidentate and the oxygen atom from the carboxylate participate to the coordination. Though strong bases were used in the reaction of complexes **1-5**

Fig.4.5 Structure of Schiff base salopH_2 [63].

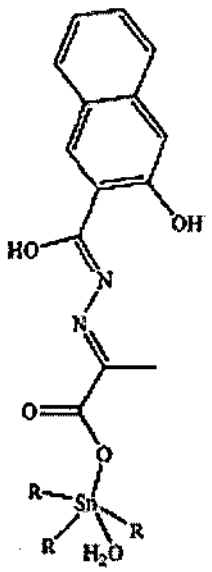
(Fig. 4.4) and mild base in the complexes **6-8** (Fig. 4.4), the enolization was observed in all complexes. The reaction were carried out in methanol at refluxing temperature, however, these complexes could also be prepared in methanol at room temperature, but the reaction time should be prolonged for 24 hours. Different substitutes on n-butyl didn't cause obvious variation in the yield of the reaction.



R= n-C_4H_9 (**1**)

R= Ph (**4**)

R= Me (**5**)



R= n-C_4H_9 (**6**)

R= Ph (**7**)

R= Me (**8**)

Fig. 4.4 Structure of organotin(IV) complexes of Schiff base ligand pyruvic acid 3-hydroxy-2-naphthoylhydrazone [55].

2- {[(2-Hydroxyhenyl)imino]methyl}phenol (salopH_2) (Fig. 4.5) is a typical potentially tridentate Schiff base ligand forming stable complexes with many transition and post- transition metal ions [56, 57]. Literature on metal-salopH_2 complexes of the group 14 elements is rather sparse [58, 59], only three tin (IV) complexes structurally characterized being reported, i.e. [$SnMe_2$(salop)] [60], [$SnPh_2$(salop)] [61] and [Sn(salop)]$_2$ [62].

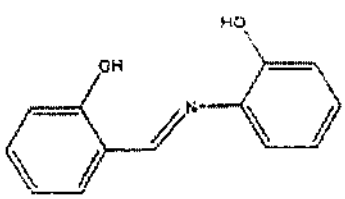
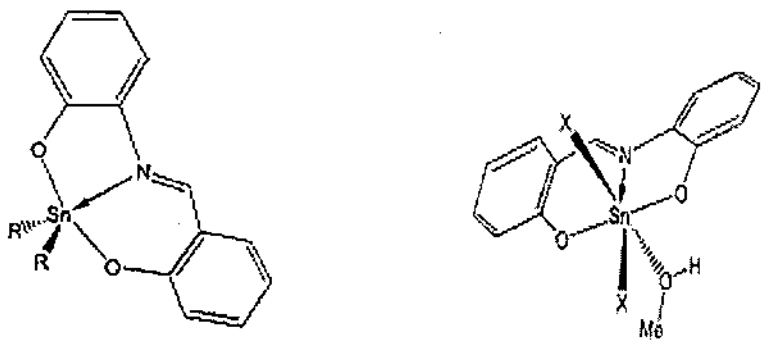


Fig.4.5 Structure of Schiff base salopH_2 [63].

From the reaction of SnR_2Cl_2 acceptors with an equimolar amount of 2- {[(2-hydroxyhenyl)imino]methyl}phenol ($salopH_2$) in methanol in the presence of bases (KOH, MeONa or NEt_3) the complexes [SnR_2(salop)] (R=Me, Ph, Vin, n-Bu and t-Bu) (Fig. 4.6 a) containing the donor in the dianionic tridentate form, have been obtained. The X-ray diffraction study of [$SnVin_2$(salop)] showed the metal to be five-coordinated in a distorted square pyramidal environment. The whole structure consisted of molecular units connected by intermolecular Sn-O interactions [63].



(a) (b)

Fig. 4.6 Structure proposed for (a) the diorganotin(IV) salop derivatives (b) mono- and dihalotin(IV) salop derivatives [63].

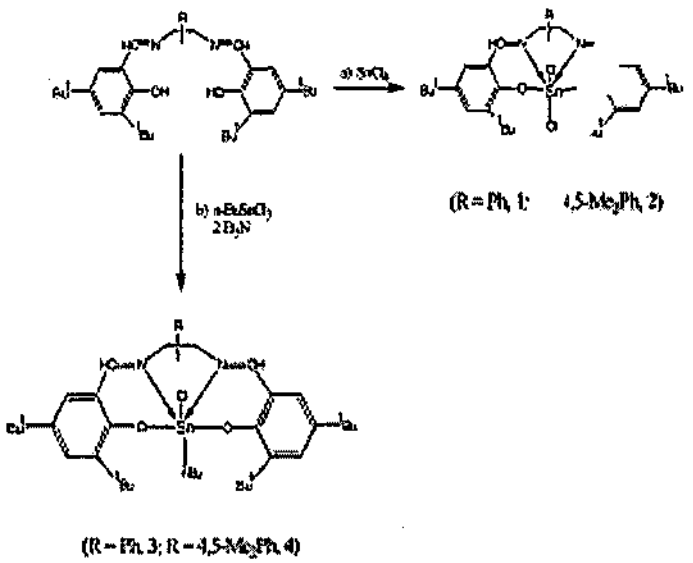
When $SnRX_3$ or SnX_4 acceptors were employed in the same reaction conditions, the complexes [SnX_2(salop)(S)] (X=Cl, Br,I ; R=Me, Ph, n-Bu; S=H_2O, MeOH) were obtained. Although these reactions seemed instantaneous when all reactants were mixed, refluxing for approximately 24 hours was carried out to ensure complete reaction. In the complexes [SnX_2 (salop)(CH_3OH)].CH_3OH (X= Cl or Br), the tin atom was found in a strongly distorted octahedral environment (Fig.4.6 b). All the [SnR_2(salop)] and [SnRX(salop)(solvent)] were fluxional in solution. On the other hand the reaction of SnX_4 with 2 mol of $salopH_2$ and 4 mol of base afforded the complex [Sn(salop)$_2$] in which all halide groups were substituted by two dianionic Schiff bases [63].

The synthesis and characterization of five organotin compounds containing the Schiff base ligands, LH_2 [L= Salophen(t-Bu), Salophen(t-Bu) = *N*, *N*'-phenylene-bis(3,5-di-*tert*-butylsalicylidenciminc) ; L= Salomphen(t-Bu), Salomphen(t-Bu) = *N*,*N*'-(4,5-dimethyl)phenylene-bis(3,5-di-*tert*-butylsalicylidenciminc)] and LH_3 [L= Phensal(t-Bu) [Phensal(t-Bu) = 3,5-di-*tert*-butylsalicylidenc(1-aminophenylene-

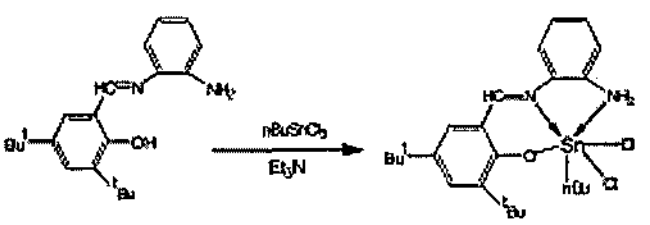
2-amine)] were described by Yearwood *et al.* [64]. The compounds of the ligand of the type LH_2 were prepared by combining $SnCl_4$ with LH_2 (compounds **1** and **2**) in the presence of triethylamine. Synthesis of compounds **1** and **2,** along with the compounds **3** and **4,** could also be achieved by combining n-$BuSnCl_3$ with LH_2 in presence of triethylamine (see Scheme 4.1). This lead to a mixture of L(n-Bu)SnCl and $LSnCl_2$. The formation of $LSnCl_2$ might be due to a disproportionation reaction (Eq.2) or a redistribution (Eq.3) occurring in solution.

$$2L(n\text{-}Bu)SnCl \longrightarrow LSnCl_2 + (n\text{-}Bu)_2SnL \quad \ldots\ldots\ldots (2)$$

$$L(n\text{-}Bu)SnCl + (n\text{-}Bu)SnCl_3 \longrightarrow LSnCl_2 + (n\text{-}Bu)_2SnCl_2 \quad \ldots\ldots\ldots (3)$$



(a)



(b)

Scheme 4.1 (a) General Syntheses of compounds **1** – **4** (b) General Syntheses of compound **5** [64].

The organotin complex **5** of the ligand LH_3 was prepared by the reaction of the tridentate ligand (LH_3) with n-$BuSnCl_3$ in the presence of Et_3N.

Several investigations have shown that the salicylaldimine complexes with X=H are effective ligands for both inorganic and organotin(IV) species. Replacement of X by a methoxy group radically altered the nature of the metal salicylaldimine complexes as ligands, transforming them from bidentate to extremely effective tetradentate ligands. Much more surprising, however, was the finding that the behaviour of the complexes as ligands was markedly and dramatically influenced by the nature of the bridging group B (Fig. 4.7 a). When the number of 'C' atoms linking the imine 'N' atoms was increased beyond three, the effectiveness of the metal salicylaldimines as ligands was greatly reduced. For example, practically no organotin(IV) Lewis acids react with the complex of *N*, *N*-bis(3-methoxysalicylidene)pentane-1,5-diamine [65,66].

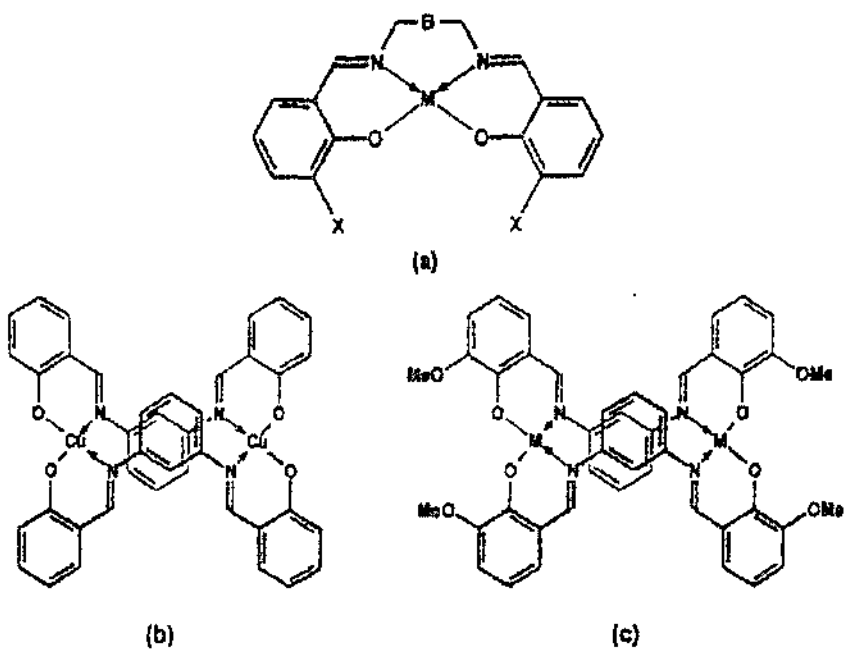
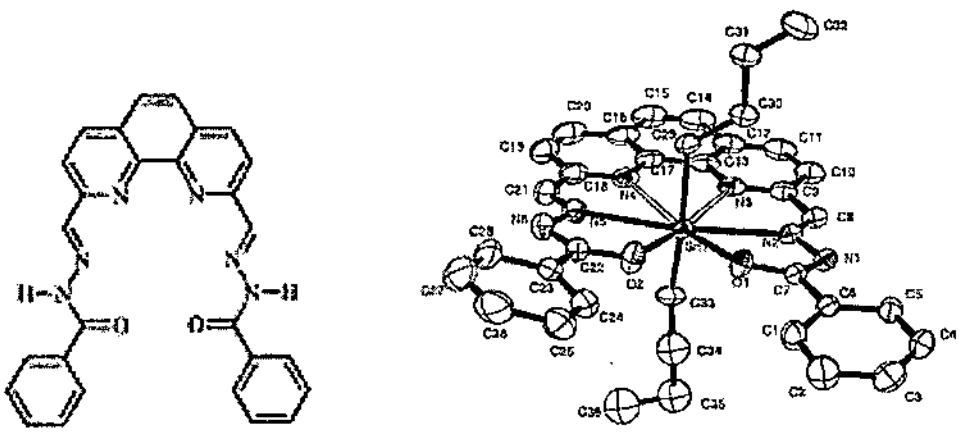


Fig. 4.7 Structures of metal salicylaldimine complexes [65, 66].

The dibutyltin complex of the Schiff base ligand 2, 9-diformylphenanthroline bis-acylhydrazone (H_2L) (Fig.4.8 a) was synthesized by refluxing the methanolic solution of the ligand with methanolic solution of dibutyltin diacetate for 2 hours, to give $[(C_4H_9)_2SnL]$ in good yield. The IR spectrum suggests a complete deprotonation

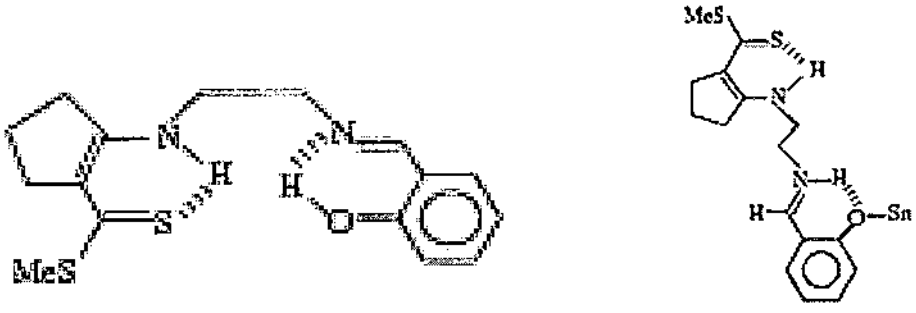
of the ligand and the coordination of the hydrazonic C=O groups, in fact the ν(N-H) and ν(C=O) bands disappear. These data are confirmed by the ^1H spectrum, where the N-H proton disappears and the aldehyde proton undergo an upfield shift in the complex. The crystal structure of $[(C_4H_9)_2SnL]$ (Fig. 4.8 b) confirmed that the ligand was deprotonated, in accord with the spectroscopic data. Based on the crystallographic data the authors have preferably described the coordination geometry around the metal in terms of a distorted hexagonal bipyramid with the ligand in the equatorial plane and the organic groups in the apical positions; it is noteworthy that this geometry is unusual, particularly for tin that results in eight-coordinated geometry [67].



(a) (b)

Fig.4.8 (a) Schiff base ligand 2,9-diformylphenanthroline bis-acylhydrazone (H_2L)
(b) Perspective view of the crystal structure of $[(C_4H_9)_2SnL]$ [67].

The synthesis and characterization of new organotin(IV) complexes containing a potentially tetradentate NN'OS Schiff base ligand, methyl 2-[2(salicylideneamino)-ethylamino]cyclopent-1-ene-1-dithiocarboxylate (H_2cdsalen) was reported recently by T. Sedaghat and S. Menati [68]. This is an interesting Schiff base forming stable complexes with transition metal ions in deprotonated form as both tetradentate and bidentate ligand [69, 70]. H_2cdsalen (Fig.4.9 a) is conformationally flexible and contains hard and soft donor atoms.

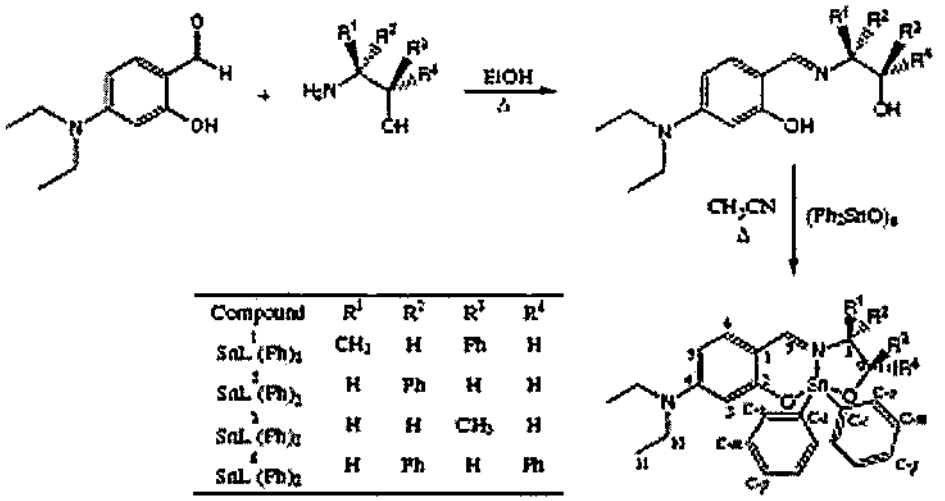


(a) (b)

Fig. 4.9 (a) Schiff base H_2cdsalen (b) Structure suggested for the coordination of Sn(IV) to H_2cdsalen [68].

The reactions in this study were performed by stirring SnR_2Cl_2 (where R=Me, Ph) with H_2cdsalen in benzene (or toluene) solution at room temperature and the new adducts [$SnMe_2Cl_2(H_2cdsalen)$] and [$SnPh_2Cl_2(H_2cdsalen)_2$] precipitated after 3 hours [68]. The new products were characterized by elemental analysis, IR, ^1H and ^{119}Sn NMR spectroscopies. Spectroscopic data suggested that in both complex the ligand was coordinated through oxygen. The phenolic hydrogen within the free ligand was transferred to the imine nitrogen atom due to the coordination of oxygen with tin after the complex formation (Fig.4.9 b).

Four new chiral organotin derivatives have been reported by Rivera *et al.* [71] with their crystal structures. They were synthesized by reaction of diphenyltin oxide and four different ligands obtained from the Schiff base condensation of 4-(diethylamino) salicylaldehyde and (1*R*, 2*S*) – (+) –norephedrine, (*R*) – (-) – phenylglycinol , (*R*) – (-) – 1-amino-2-propanol and (1*S*, 2*R*) – 2-amino-1,2-diphenylethanol. In the synthesis of the tin complex, equimolecular quantities of Schiff bases and diphenyltin oxide were reacted in acetonitrile for 3-6 h. The compounds were fully characterized by spectroscopic techniques.



Compound	R^1	R^2	R^3	R^4
$SnL^1(Ph)_3$	CH_3	H	Ph	H
$SnL^2(Ph)_3$	H	Ph	H	H
$SnL^3(Ph)_3$	H	H	CH_3	H
$SnL^4(Ph)_3$	H	Ph	H	Ph

Scheme 4.2 Synthesis of chiral organotin derivatives [71].

The organotin complexes, namely $[(Bu_2Sn)_2O(EtO)(L1)]_2$ (**1**), $[(Bu_2Sn)_2O(EtO)(L2)]_2$ (**2**), $[(Bu_2Sn)_2O(EtO)(L3)]_2$ (**3**) were obtained by the reactions of n-dibutyltin oxide with 0.5 equivalent of 4-phenylideneamino-3-methyl-1,2,4-triazole-5-thione (HL1) , 4-furfuralideneamino-3-methyl-1,2,4-triazole-5-thione (HL2) , 4-(2-thienylideneamino-3-methyl-1,2,4-triazole-5-thione (HL3) in a mixed solvent of benzene and ethanol (2:1) , under reflux for eight hours. Complexes **1-3** showed similar structures containing a Sn_4O_4 ladder skeleton in which each of the *exo* tin atoms was bonded to the N atom of a corresponding thione-form deprotonated ligand. The compound $[Ph_3Sn(L4)].0.5H_2O$ (**4**) was obtained by the reaction of Ph_3SnOH with an equivalent amount of HL4 in benzene. The reaction system was refluxed for eight hours. Complex 4 showed a mononuclear structure in which the Sn atom of triphenyltin group was coordinated by the S atom of a thiol-form $L4^-$ anion [72].

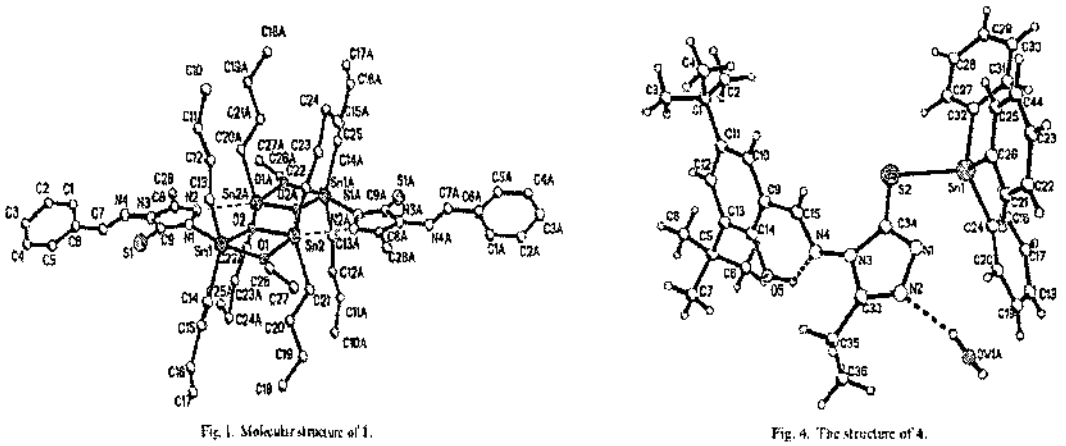


Fig. 4.10 (a) Molecular structure of **1** (b) Molecular structure of **4** [72].

The literature on organotin complexes of Schiff bases is vast and inexhaustive. The author has presented above a few selected examples to give a glimpse of the work done in the field of organotin Schiff bases. The organotin complexes of thiosemicarbazones are comparatively less studied than their transition metal analogues. At this point the author shall restrict her discussion on organotin(IV) complexes of Schiff bases derived from thiosemicarbazides, as they form one of the subject matter of the thesis.

4.1.2 Organotin(IV) complexes of thiosemicarbazones

Thiosemicarbazones and their metal complexes has been the subject of great interest of many researchers for a number of years. The statement is supported by the large number of papers and review articles [73-81]. Like majority of similar Schiff bases, thiosemicarbazones are obtained in good yield by the condensation of aqueous or alcoholic solutions of thiosemicarbazides with suitable aldehydes or ketones.

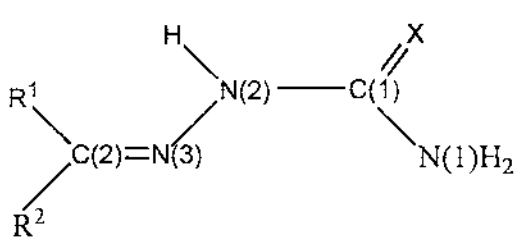


Fig.4.11 General formula of a thiosemicarbazone.

Thiosemicarbazones are versatile ligands in both neutral and anionic forms. They predominantly exist in thione form in the solid state but exist as an equilibrium mixture of thione and thiol forms in the solution state (Fig. 4.12).

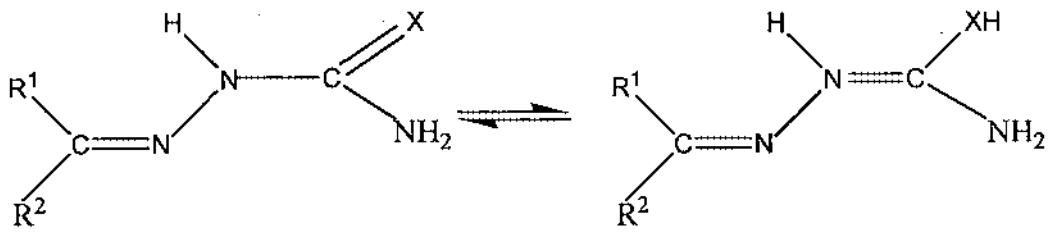


Fig.4.12 Thione-thiol tautomerism of thiosemicarbazones in solution.

These classes of compounds usually react with metallic cations giving complexes in which the thiosemicarbazones behave as chelating ligands. The coordination possibilities of thiosemicarbazones are increased if substituents R^1 and/or R^2 include additional donor atoms. In the canonical thiol form, there is an effective conjugation along the thiosemicarbazone skeleton resulting in an efficient electron delocalization along the thiosemicarbazone backbone. Presence of aromatic radicals bound to the azomethine carbon atom further enhances the delocalization of electron charge density [82].The coordination chemistry of thiosemicarbazones appeared to be very interesting from the point of view of both the number of metals forming the complexes with them and the diversity of the ligand systems themselves [83-85], i.e., their denticity, set of donor atoms, stabilization of various (less common) oxidation state of metals [86-89], reactions of coordinated ligands [85,90] etc.

S. Belwal and her coworkers [91] reported the synthesis of diorganotin(IV) derivatives of the type $R_2SnCl(TSCZ)$ and $R_2Sn(TSCZ)_2$ (where TSCZ is the anion of a thiosemicarbazone ligand, R=Ph or Me). The complexes were characterized by elemental analyses, molecular weight determinations and conductivity measurements. The mode of bonding was established on the basis of IR, ^1H, ^{13}C and ^{119}Sn NMR spectroscopic studies. Some of the complexes were also evaluated for their antimicrobial effects on different species of pathogenic fungi and bacteria *in vivo* as well as *in vitro*.

Three tin (IV) complexes of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone were prepared: $[Sn(L)Cl_3]$, $[n\text{-}BuSn(L)Cl_2]$ and $[(n\text{-}Bu)_2Sn(L)Cl]$, in which L stands for

the anionic ligand formed upon complexation with deprotonation and release of HCl. The complexes were characterized by a number of spectroscopic techniques. The crystal structure of $[(n\text{-}Bu)_2Sn(L)Cl]$ was determined. The molecules of this complex are associated by an intermolecular N4–H4---Cl bond. The Sn(IV) lies in the centre of a very distorted octahedron, formed by the carbon atoms of two n-Bu groups, one chloride and the anionic thiosemicarbazone coordinated through an N, N, S tridentate system [92].

2-Benzoylpyridine thiosemicarbazone (HL1), its *N*(4)- methyl (HL2) and *N*(4)-phenyl (HL3) derivatives with $SnCl_4$ and diphenyltin dichloride (Ph_2SnCl_2) gave $[Sn(L1)Cl_3]$ (**1**), $[Sn(L1)PhCl_2]$ (**2**), $[Sn(L2)Cl_3]$ (**3**), $[H_2L2]^+_2\,[Ph_2SnCl_4]^{2-}$(**4**) $[Sn(L3)PhCl_2]$ (**5**) and $[Sn(L3)Ph_2Cl]$ (6). IR, ^1H-, ^{13}C- and ^{119}Sn- NMR spectra of **1 – 3**, **5** and **6** are compatible with the presence of an anionic ligand attached to the metal through the N_{py}– N –S chelating system and formation of hexa-coordinated tin complexes. The crystal structures of **1 –3**, **5** and **6** showed that the geometry around the metal was a distorted octahedron. The crystal structure of **4** revealed the presence of *trans* $[Ph_2SnCl_4]^{2-}$ and $[H_2L2]^+_2$ [93].

The chelating behaviour of N, N, S-tridentate thiosemicarbazones derived from 2-formyl pyridine (HFPT) have been investigated and three different modes of coordination have been identified. 2-formyl pyridine thiosemicarbazone (HFPT) reacts with tin tetrahalides (X=Cl, Br, I) with abstraction of HX and the formation of hexa-coordinated species $[SnX_3(FPT)]$ (Fig. 4.13). In this complex the ligand acts as a mononegative N,N, S-tridentate ligand and coordinate to the metal through both nitrogen and the thiolate sulphur atoms [94]. A single crystal X-ray diffraction study of $[SnCl_3(FPT)]$ established *mer*-isomerism, the ligand coordinating through its N(3), S and pyridine 'N' atoms. The distorted octahedral coordination polyhedron of the tin atom is completed by three Cl atoms.

While in the corresponding dimethyltin(IV) complex $[Sn(CH_3)_2(FPT)Cl]$, the thiosemicarbazone anion acts as a bidentate ligand where the tin(IV) is coordinated to the azomethine nitrogen and deprotonated thiol sulphur while the pyridine nitrogen remains uncoordinated [95].

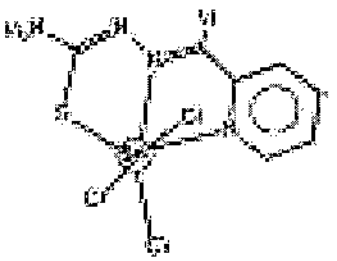


Fig. 4.13 Structure of $[SnCl_3(FPT)]$ [94].

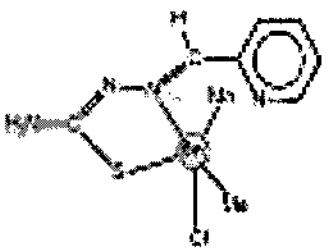


Fig. 4.14 Structure of $[Sn(CH_3)_2(FPT)Cl]$ [95].

The complex formation between organotin chlorides and 2-pyridinecarboxaldehyde thiosemicarbazone (PT) have been investigated. In only one case was a substitution reaction observed whereas in all other cases, 1:1 addition complexes were formed. The solid state configuration of the complexes was studied by ^{119m}Sn Mössbauer and far infrared spectroscopy. The chelating ligand (PT) functioned as a bidentate ligand towards diorganotin chlorides giving octahedral coordination geometry around the tin atom [96].

The synthesis, X-ray structure, behaviour in solution, and biological properties of the complex $[SnMe_2(PyTSC)(OAc)]$.HOAc (HPyTSC = pyridine-2-carbaldehydethiose -micarbazone) were reported. The complex was synthesized by refluxing a mixture of HPyTSC and $Sn_2Me_2(OAc)_2$ in dry methylene chloride [97]. The tin atom of this complex was coordinated to an N, N, S-tridentate PyTSC anion, to a monodentate acetate ion, and to the two methyl groups (in axial positions) in an approximately pentagonal bipyramidal environment with a vacant equatorial position. In this compound, the PyTSC ligand adopts Z- configuration and is planar. Although the

acetate anion was monodentate the non-coordinated 'O' atom probably played an important role in determining the geometry of the coordination polyhedron around the tin atom.

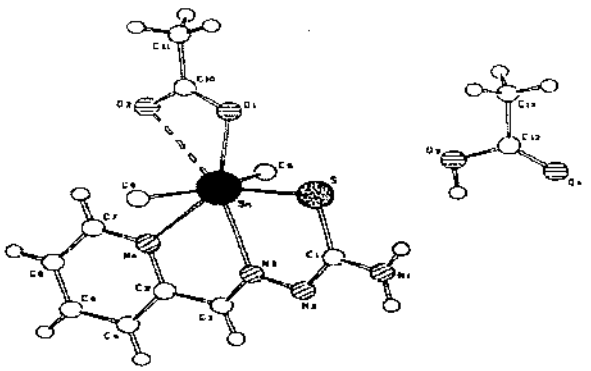


Fig. 4.15 Structure of $[SnMe_2(PyTSC)(OAc)].HOAc$ [97].

Investigations on the chelating properties of 2,6-diacetylpyridinebis(semicarbazone) (H_2DAPSC) and 2,6-diacetylpyridinebis(thiosemicarbazone) ($H_2DAPTSC$) have revealed that tin in these complexes attain a seven-coordinated geometry. Two tin complexes of H_2DAPSC and $H_2DAPTSC$ have been characterized. The planar pentadentate ligand 2,6-diacetylpyridinebis(semicarbazone), H_2DAPSC, was found to combine with $SnCl_3^-$ dissociated from $[Pt(SnCl_3)_5]^{3-}$ and formed a pentagonal bipyramidal complex of Sn(IV), $[SnCl_2(H_2DAPSC)]Cl_2{\cdot}2H_2O$ [98]. The complex was characterized by an X-ray crystal structure study. The cation, $[SnCl_2(H_2DAPSC)]^{2+}$ was a slightly distorted pentagonal bipyramid in which the H_2DAPSC ligand formed a pentagonal plane and two chloride ions occupied the axial positions. This is the first example of a metal oxidation taking place in the presence of H_2DAPSC and being stabilized by the ligand.

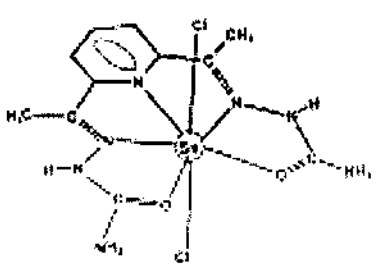


Fig. 4.16 Structure of $[SnCl_2(H_2DAPSC)]Cl_2{\cdot}2H_2O$ [98].

Two hepta-coordinated organotin complexes, [MeSnCl(HDAPTSC)]Cl·MeOH and [MeSnCl(H_2DAPSC)]Cl_2·$2H_2O$, have been prepared from the reaction between $MeSnCl_3$ and H_2DAPTSC or H_2DAPSC, respectively. Single crystal X-ray diffraction studies showed them to be approximately pentagonal bipyramidal (PBP), with the organic ligands lying in the equatorial plane. H_2DAPTSC and $SnCl_4$ formed a complex with the formula [ClSnCl(HDAPTSC)]Cl , which was presumed to have an analogous PBP structure. On the other hand, the complex obtained from H_2DAPSC and Me_2SnCl_2 was tentatively formulated as [(Me_2SnCl_2)$_2$(H_2DAPSC)] and ^{119}Sn Mössbauer spectroscopic evidence suggested an octahedral coordination for the two tin atoms [99].

The reaction of the title ligand (H_2DAPTSC) with SnR_2O (R=Me, Ph) in DMF afforded the complexes [SnR_2(DAPTSC)]. The phenyl derivative crystallized as [$SnPh_2$(DAPTSC)]·2DMF. The molecular complex was pentagonal bipyramidal with the five donor atoms of the ligand in the pentagonal plane and the two phenyl groups in the axial positions [100].

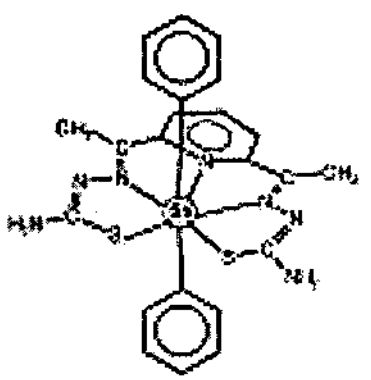


Fig. 4.17 Structure of [$SnPh_2$(DAPTSC)]·2DMF [100]

A comparative study based on the spectral properties (IR, Mössbauer and ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy) of the two complexes suggested a similar structure for [$SnMe_2$(DAPTSC)] [100].

[$SnPh_2$(HDAPTSC)]Cl was obtained by refluxing H_2DAPTSC.HCl and Ph_2SnCl_2 in methanol [101]. The Sn(IV) atom in this complex is hepta-coordinated and also had a pentagonal bipyramidal geometry, where only one of the H_2DAPTSC arms has undergone deprotonation. But, this does not significantly modify the bond lengths in

either of the thiosemicarbazone arms or in the coordination polyhedron, and the angles underwent only small changes.

S.W. Ng *et al.* [102] have prepared dibutyltin salicylaldehydethiosemicarbazonate [$SnBu_2$(STSC)] by melting together equimolar amounts of dibutyltin oxide and salicylaldehyde thiosemicarbazone. The ligand behaved as a (N, S, O)-tridentate ligand in Z- configuration and a *cis*-trigonal bipyramidal coordination polyhedron with the phenolic hydroxyl 'O' in one axial positions and the thiosemicarbazonate 'S' in the other.

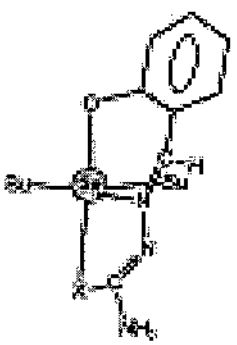
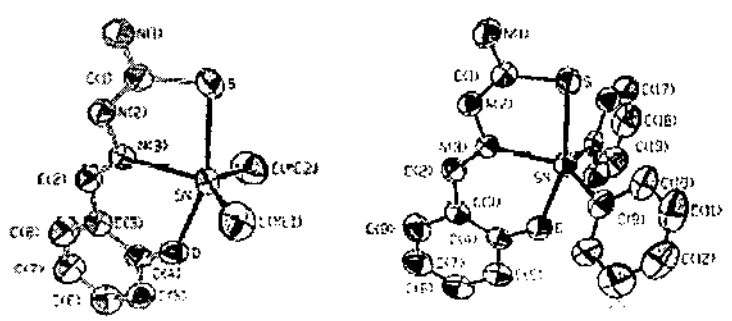


Fig.4.18 Structure of [Bu_2Sn(STSC)] [102].

Similar structures have been reported [103] for [$SnMe_2$(STSC)] and [$SnPh_2$(STSC)], the slight differences being due to the different organotin units. Both these compounds were obtained by refluxing $SnR_2(O)$ and salicylaldehyde thiosemicarbazone in benzene for five days and removing the resulting azeotropic benzene–water mixture by distillation in a Dean-Stark apparatus.



(a) (b)

Fig.4.19 Structure of (a) [Me_2Sn(STSC)] (b) [Ph_2Sn(STSC)] respectively with their atom numbering scheme [103].

The crystal structure of triphenyltin 1-amino-4-(2-hydroxyphenyl)-2, 3- diazapenta-(*E*)-1, (*E*)- 3- dienyl -1- thiolate was reported by Ng *et al.* [104]. The complex was obtained by slow evaporation of a solution of triphenyltin hydroxide and the thiosemicarbazone in 1 :1 molar ratio in ethanol. The tin atom was in a distorted tetrahedral environment, with the three carbon atoms of the phenyl groups and the thiosemicarbazone 'S' atom defining the tetrahedral polyhedron. In this compound, the *S*-coordinated thiosemicarbazonate group was twisted rather than planar. The phenolic proton in the thiosemicarbazonate and in the uncomplexed ligand was hydrogen -bonded to the N (3) atom.

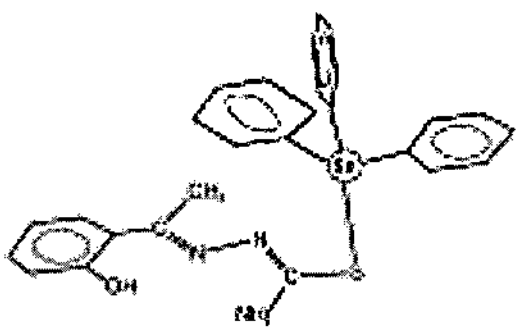


Fig. 4.20 Structure of triphenyltin 1-amino-4-(2-hydroxyphenyl)-2,3-diazapenta-(*E*)-1, (*E*)-3-dienyl-1-thiolate [104].

The reaction between Ph_2SnCl_2 and thiosemicarbazide using acetone-ethanol as solvent resulted in the formation of bis(acetone thiosemicarbazone-*S*) dichlorophenyltin(IV), $[SnPh_2Cl_2(ATSC)_2]$, acetone thiosemicarbazone (ATSC) having been derived *in situ* from the reaction of thiosemicarbazide and acetone [105]. The X-ray crystal structure of the bis(acetone thiosemicarbazone-*S*) dichlorophenyltin(IV) showed a distorted octahedron about tin atom which was coordinated to two phenyl, two chloride and two acetone thiosemicarbazone (ATSC) groups. Each of the ATSC ligand coordinated to the tin atom in a *trans* configuration and therefore behaved as a monodentate ligand bonding only through 'S' atom.

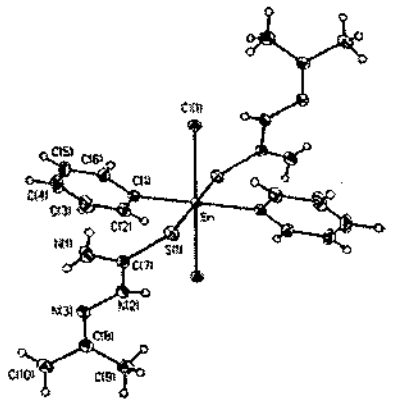


Fig.4.21 Structure of $[SnPh_2Cl_2(ATSC)_2]$ [105].

The reactivity of the polydentate ligands bis(2-acetylpyridine) carbonohydrazone (H_2APE) and 2-acetylpyridine semicarbazone (HAPS) as well as of their sulphur containing analogues bis(2-acetylpyridine) thiocarbonohydrazone (H_2APT) and 2-acetylpyridine thiosemicarbazone (HAPTS) was investigated towards organotin compounds [106]. An X-ray crystal structure determination carried out on $Ph_2Sn(HAPT)Cl.H_2O$ and $(n\text{-}Bu)_2Sn(APTS)(OAc)$ revealed that in both compounds the hydrazonic ligand was terdentate via sulphur atom and two nitrogen atoms. The tin atom was six-coordinated in $Ph_2Sn(HAPT)Cl.H_2O$ (Fig. 4.22) and seven-coordinated in the dibutyltin derivative $(n\text{-}Bu)_2Sn(APTS)(OAc)$. The similarities observed in the IR and ^1H NMR spectra were indicative of a similar behaviour of the ligand in all the complexes, thus suggesting a six-coordinated tin in the chloro derivatives and a seven-coordinated tin in the acetate ones. In $Ph_2Sn(HAPT)Cl.H_2O$, the hydrazone ligand was monodeprotonated and acted as a terdentate N_2S donor giving rise to two five-membered chelate rings, one of which (SnNCCN) was strictly planar, while the other (SnSCNN) showed a slight degree of puckering. The coordination sphere of the metal was completed to a highly distorted octahedral by a chlorine atom in the equatorial plane and two *trans*-positioned phenyl rings in the axial sites. The main distortion from the regular octahedral geometry came from the stereochemical constraint of HAPT. The water molecule was involved in an intermolecular O...Cl hydrogen bond [106].

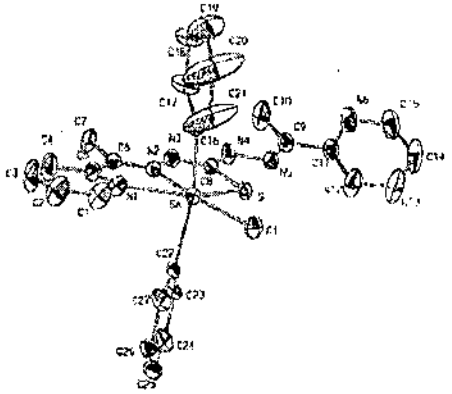
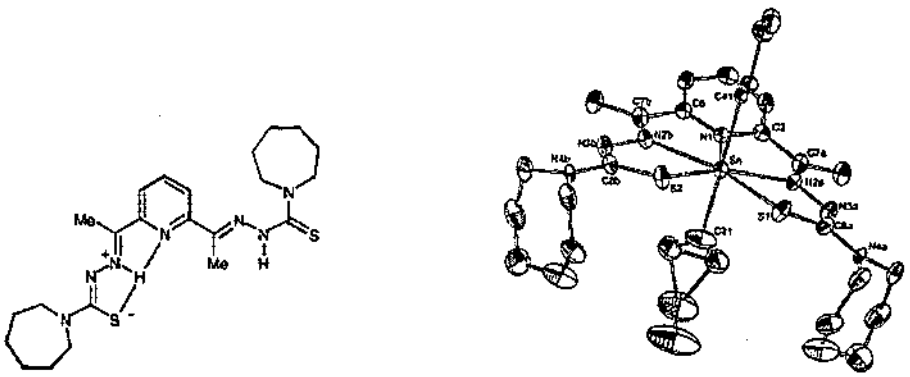


Fig. 4.22 Structure of $Ph_2Sn(HAPT)Cl.H_2O$ [106].

Treatment of 5-methoxy -5, 6- diphenyl -4, 5 – dihydro -2*H* - [1, 2, 4]triazine-3-thione (LH_2OCH_3) with compounds SnR_2X_2 (R = Me and Ph; X = Cl and NO_3) afforded, for the first time, metal derivatives of a cyclic thiosemicarbazone [107]. Treatment of LH_2OCH_3 with the appropriate diorganotin(IV) chloride in dichloromethane provided 1:1 complexes, but 1:2 derivatives were isolated when the nitrate salts in distilled water were used. The complexes were studied by mass spectrometry, IR and multinuclear (^1H, ^{13}C and ^{119}Sn) NMR in solution, and also by ^{119}Sn CP/MAS NMR spectroscopy and by X-ray diffraction in the solid state. In all the complexes, the thiosemicarbazone had been modified by formation of a new C=N bond. In addition, the ligand had lost a hydrogen atom, acting as an anion. The crystal structures of $[SnPh_2(C_{15}H_{10}N_3S)Cl]$ and $[SnMe_2(C_{15}H_{10}N_3S)_2]$ each consisted of discrete molecules with the tin atom bonded to the sulphur and amine nitrogen atoms to give a four-membered chelate ring with the [1,2,4]triazine modified. For phenyl derivative, the tin atom was in a trigonal bipyramidal environment with the phenyl rings in equatorial positions, and for the methyl derivative, it was in an octahedral arrangement, with the methyl groups in axial positions.

The synthesis and crystal structure of the $[Bu_2Sn(2,6Achexim)]$ was reported recently by G.F. de Sousa *et al.* The dianion of $H_2$2,6Achexim {where $H_2$2,6Achexim=2,6-diacetylpyridine bis(3-hexamethyleneiminylthiosemicarbazone) monohydrate} acted as a pentadentate ligand , 2, 6Achexim, in a planar conformation to a central tin(IV) ion. The tin(IV) was hepta-coordinated in a distorted pentagonal bipyramidal configuration , with five SNNNS donor atoms of 2,6Achexim in the pentagonal plane and the two n-butyl groups in the axial positions [108].



(a) (b)

Fig. 4.23 (a) $H_2$2,6 Achexim and (b) Structure of [Bu_2Sn(2,6Achexim)] [108].

4.1.3 Biological activity of thiosemicarbazones

Thiosemicarbazones are amongst the most important N, S donor ligands [74, 109] because of their highly interesting chemical, biological and medicinal properties [73, 74, 110].

One of the main reasons why the literature concerning thiosemicarbazones is rich and diverse is the higher biological activity of the same. Since the pioneering work of Domagk *et al.* [111] in 1946 on the antitubercular activity of *p*-acetamidobenzaldehyde thiosemicarbazone (trivial names Thiacetazone or Tibon) and *p*-methoxybenzaldehyde thiosemicarbazones, the number of papers concerning the pharmacological use of these compounds has dramatically expanded due to the wide spectrum of their biological activity found in recent years [76,112-115]. Some of the detected biological activities of thiosemicarbazones are antibacterial [116-122], antifungal [123,124], antimalarial [125], antiviral [126-129], antiamoebic [130], antitumour [131,132] and specially anti-HIV activity [133,134].Thiosemicarbazones have also been found to be active against influenza [135] and smallpox [136]. Genova *et al.* reported the toxic effects of bis(thiosemicarbazone) compounds and its Palladium (II) complexes on herpes simplex virus growth [137].It has been reported

by Gausman *et al.*[138] in 1953 that the activity of thiosemicarbazones is due to their property of forming chelates with metals.

In a recent study by Singh and his coworkers, they found two dimethyl silicon complexes of biologically active hetrocyclic thiosemicarbazones act as sterilizing agents by reducing the production of sperm in male mice, thus indicating their antifertility activity [79].

Many recent works report the antimicrobial (antibacterial and antifungal) activities of thiosemicarbazones[139-144].

It has been reported that the fungicidal activity of the thiosemicarbazones is due to their ability to chelate essential metals which the fungus needs for its metabolism [145,146]. On the basis of chelation theory the fungicidal activity of compounds containing an SH group adjacent to nitrogen have been well explained [147]. Also, metal complexes can act as antifungals by inhibiting enzymes, such as those involved in the biosynthesis of yeast cell walls [148].

S. Belwal *et al.* [91] synthesized diorganotin derivatives of the types $R_2SnCl(TSCZ)$ and $R_2Sn(TSCZ)_2$ (where TSCZ is the anion of a thiosemicarbazone ligand, R=Ph or Me) and evaluated their antimicrobial effects on different species of pathogenic fungi and bacteria *in vivo* as well as *in vitro*.

The antifungal activity of acetone thiosemicarbazone and its diphenyltin derivative was investigated by S.G.Teoh and his coworkers [105]. They found that the complex displayed marked fungitoxicity against the fungal strains tested and that the complex was more fungitoxic than acetone thiosemicarbazone and Ph_2SnCl_2.

Rebolledo *et al.* studied the antifungal activity of the 2-benzoylpyridine *N*-(4)-phenylthiosemicarbazone ligand and its tin(IV) complexes against *Candida albicans*. In this case, they found that the thiosemicarbazone proved to be more active than the tin(IV) complexes [92]. They proposed that the activity of thiosemicarbazone complexes depends upon two factors:

- Bulkiness of complexes: The bulkiness of complexes do not facilitate their permeation through the yeast cell membranes and hence decreases the activity.
- Lipophilicity of the complexes: Increase in lipophilicity leads to increased activity since the compounds can cross the cell membranes better.

Collins *et al.* have reported the correlation between structure and anti-mycobacterial activity in a series of 2-acetylpyridine thiosemicarbazones [149].

A study of novel pyrazoles and thiosemicarbazones by *Brown et al.* [150] have shown a definite correlation between compound structure and antibacterial activity. Those compounds having a lipophilic chain had greater antibacterial activity than compounds having less lipophilic structure such as the methoxy group. The hydrophilic core of the compound contributes to the movement of the compound into aqueous solution while the lipophilc characteristic enhances the ability to interact with the hydrophobic area of the membrane. Structural features that contributed to increased solubility and membrane interaction may greatly increase biological activity of compounds.

4.2 Scope and Objective

The Schiff bases obtained by the condensation of salicylaldehyde and substituted salicylaldehydes with thiosemicarbazide form a class of versatile O,N,S donor ligands. Many studies of these latter molecules as ligands have so far dealt with transition metal complexes of thiosemicarbazones of salicylaldehyde and substituted salicylaldehydes [81,151-153] whereby they stabilize unusual oxidation states and exhibit different coordination numbers in the complexes. Recently, an unusual coordination mode of salicylaldehyde thiosemicarbazone was observed in a group of $[M(PPh_3)_2(saltsc)_2]$ complexes, where R= Ru, Os and saltsc = anion of salicylaldehyde thiosemicarbazone [154,155]. Thiosemicarbazones and related ligands are reported to bind a metal ion as monoanionic bidentate ligand coordinating through N and S atoms forming a five-membered chelate ring [74,156]. This work was motivated by the desire to investigate the ligating behaviour of the versatile thiosemicarbazones towards the organotin(IV) moieties. Also, organotin compounds

are being used as agricultural biocides [157].Besides, the high fungicidal and bactericidal properties [158], various organotin compounds have been reported to possess antitumour activity with some derivatives being more active than cisplatin [159,160].The present work was also motivated by the desire to study the biocidal activity and cytotoxicty of these newly synthesized organotins. It is to be noted that during the progress of this work we became aware of reports of closely related studies [102,103,161] where some organotin(IV) complexes of semi- and thiosemicarbazones, along with the compounds (**1**) – (**3**) (Scheme 4.3) were described. These have been included herein to allow comparison of their biocidal properties with the corresponding Cl/Br-substituted ligands and because the compounds were synthesized via a different route, requiring shorter reaction times giving higher yields. Further, full details of their supramolecular structures are reported as well as a correlation of geometric parameters with those of the halide congeners.

4.3 Experimental

4.3.1 General comments

The solvents used in the reactions were of AR grade and were obtained from commercial sources (Merck, Germany). The solvents were dried using standard literature procedures. Petroleum ether and benzene were distilled from sodium whereas methanol was distilled after reacting it with magnesium. Proper health precautions were undertaken while working with benzene as a solvent.

4.3.2 Materials

Salicylaldehye (Fluka AG, Switzerland), 5-chlorosalicylaldehye (Lancaster, USA), 5-bromosalicylaldehyde (Lancaster, USA), thiosemicarbazide (Loba chemie, India), n-dibutyltinoxide (Alfa, USA), Me_2SnCl_2 (Fluka, Germany), Ph_2SnCl_2 (Aldrich, USA) and n-Bu_2SnCl_2 (Merck, Germany) were used as received from commercial sources. Bz_2SnCl_2 was prepared using the method of Sisido *et al.* [162]. Me_2SnO and Ph_2SnO were prepared by the alkaline hydrolysis of Me_2SnCl_2 and Ph_2SnCl_2 respectively in water/ether mixtures.

4.3.3 Measurements

IR spectra in the range 4000-250 cm $^{-1}$ were recorded on Pye-Unicam SP 300S spectrophotometer as Nujol mulls using CsI optics. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ and C_6D_6 using TMS as an internal standard on a Bruker DPX 300 spectrometer. The solution ^{119}Sn NMR spectra were measured in $CDCl_3$ solution at 149.05 MHz using a Jeol Eclipse Plus 400 spectrometer and were referenced against $SnMe_4$. Tin was estimated gravimetrically as SnO_2 using standard procedures. Microanalyses were performed at RSIC, NEHU, Shillong, India. The electronic spectra were recorded on a Shimadzu UV 240 spectrophotometer with methanol as the solvent. Fluorescence studies were carried out on Elico SL174 spectrofluorometer. Melting points were determined using sulphuric acid bath and are uncorrected.

4.3.4 Synthetic procedures

The methods employed for the preparation of Schiff bases of salicylaldehyde/substituted salicylaldehyde from thiosemicarbazide are described in Section *4.3.4.1 – 4.3.4.4.* The synthesis of organotin(IV) complexes of the thiosemicarbazones are described in Sections *4.3.4.5 – 4.3.4.18.* Their characterization, analytical and spectroscopic data are given in Section 4.4.

4.3.4.1 Preparation of salicylaldehyde thiosemicarbazone (L^1H)

To a hot 1:1 ethanol-water solution (100 ml) of thiosemicarbazide (2.238 g, 24.56 mmol) was added dropwise an ethanolic solution (25 ml) of salicylaldehyde (3 g, 24.56 mmol) with continuous stirring. The stirring was continued for one hour at room temperature. The resultant solution was concentrated on a water bath and kept overnight. The pale yellow crystals were obtained the next day. The crystals were filtered and then thoroughly washed with ethanol to yield L^1H. The product was dried in vacuo.

L^1H : Yield: 4.26 g, 81.3 %., M.P.: 230 °C (dec.).

Elemental analysis (Calcd. for $C_8H_9N_3OS$):

Calcd.: C, 49.23 ; H, 4.61; N, 21.54 %.

Found: C, 49.20; H, 4.65; N, 21.43 %.

IR (cm^{-1}) : $\nu(NH_2)_{asym}$ 3442 cm^{-1}, $\nu(NH_2)_{sym}$ 3317 cm^{-1}, ν(C=N) 1612 cm^{-1}, ν(C=S) 777 cm^{-1}.

4.3.4.2 Preparation of 5-bromosalicylaldehyde thiosemicarbazone (L^2H)

A hot ethanolic solution (50 ml) of 5-bromosalicylaldehyde (4 g, 19.89 mmol) was added to a hot 1:1 ethanol-water solution (75 ml) of thiosemicarbazide (1.813 g, 19.89 mmol) with continuous stirring. The stirring was continued for two hours at hot conditions. The resultant solution was concentrated on a water bath and kept overnight. The cream coloured flaky crude product was obtained the next day. The product was filtered and then recrystallized from ethanol to yield L^2H. The product was dried in vacuo.

L^2H : Yield: 4.6 g, 79 %, M.P.: > 245 °C (dec.).

Elemental analysis (Calcd. for C_8H_8NOSBr):

Calcd.: C, 35.05 ; H, 2.92; N, 15.33 %.

Found: C, 35.10 ; H, 2.93; N, 15.26 %.

IR (cm^{-1}) : $\nu(NH_2)_{asym}$ 3412 cm^{-1}, $\nu(NH_2)_{sym}$ 3236 cm^{-1}, ν(C=N) 1611cm^{-1}, ν(C=S) 776 cm^{-1}.

4.3.4.3 Preparation of 5-chlorosalicylaldehyde thiosemicarbazone (L^3H)

A hot 1:1 ethanol-water solution (75 ml) of thiosemicarbazide (1.45 g, 15.96 mmol) was added dropwise to a hot ethanolic solution (50 ml) of 5-chlorosalicylaldehyde (2.5 g, 15.96 mmol) with continuous stirring. The stirring was continued for two hours at hot conditions. The pale yellow crystals were obtained upon concentration of the resultant mixture. The crystals were filtered and then thoroughly washed with ethanol to yield L^3H. The product was dried in vacuo.

L^3H : Yield: 3 g, 75.9 %., M.P.: 235 °C (dec.).

Elemental analysis (Calcd. for C_8H_8NOSCl) :

Calcd.: C, 41.83 ; H, 3.48 ; N, 18.30 %.

Found: C, 41.79; H, 3.52 ; N, 18. 41 %.

IR (cm^{-1}) : $\nu(NH_2)_{asym}$ 3406 cm^{-1}, $\nu(NH_2)_{sym}$ 3234 cm^{-1}, ν(C=N) 1610 cm^{-1}, ν(C=S) 777 cm^{-1}.

4.3.4.4 Preparation of napthaldehyde thiosemicarbazone (L^4H)

Naphthaldehyde (4 g, 23.23 mmol) in 100 ml of ethanol was added dropwise with continuous stirring to a hot 1:1 ethanol-water solution (75 ml) of thiosemicarbazide (2.11 g, 23.23 mmol). The reaction mixture was stirred at hot conditions for three hours. The brown coloured product was obtained upon concentration of the resultant mixture. The product was filtered and then thoroughly washed with ethanol to yield L^4H. The product was then dried in vacuo.

L^3H : Yield: 4.82 g, 78.8 %. M.P.: >245 °C (dec.).

Elemental analysis (Calcd. for $C_{10}H_7NOS$):

Calcd.: C, 58.77 ; H, 4.48 ; N, 17.14 %.

Found: C, 58.62 ; H, 4.45 ; N, 17.02 %.

IR (cm^{-1}) : $\nu(NH_2)_{asym}$ 3448 cm^{-1}, $\nu(NH_2)_{sym}$ 3240 cm^{-1}, ν(C=N) 1610 cm^{-1}, ν(C=S) 775 cm^{-1}.

4.3.4.5 Synthesis of dimethyltin(IV) salicylaldehyde thiosemicarbazonate, Me_2SnL^1 (1)

To a solution (45 ml) of salicylaldehyde thiosemicarbazone (0.650 g, 3.33 mmol) in methanol was added dropwise 0.1 N methanolic NaOH (74 ml, 0.266 g, 6.65 mmol) under stirring. The reaction system was stirred for 2 h and then a methanolic solution (40 ml) of Me_2SnCl_2 (0.732 g, 3.33 mmol) was added. The reaction mixture which turned fluorescent yellow was refluxed for 8 h under inert conditions. The volatiles were removed and the dry mass extracted with hot petroleum ether (60-80°C, 75 ml).The crude product obtained was recrystallized from benzene to yield yellow crystals of the desired product.

4.3.4.6 Synthesis of dibutyltin(IV) salicylaldehyde thiosemicarbazonate, $n\text{-}Bu_2SnL^1$ (2)

To a solution (45 ml) of salicylaldehyde thiosemicarbazone (0.500 g, 2.564 mmol) in methanol was added dropwise 0.1 N methanolic NaOH (57 ml, 0.205 g, 5.128 mmol) under stirring. The reaction system was stirred for 2 h and then a methanolic solution

(35 ml) of n-Bu_2SnCl_2 (0.779 g, 2.564 mmol) was added. The reaction mixture which turned fluorescent yellow was refluxed for 8 h under inert conditions. The volatiles were removed and the dry mass extracted with hot petroleum ether (60-80°C, 50 ml). Yellow needle- shaped crystals of the desired product were obtained immediately.

4.3.4.7 Synthesis of diphenyltin(IV) salicylaldehyde thiosemicarbazonate, Ph_2SnL^1 (3)

To a solution (50 ml) of salicylaldehyde thiosemicarbazone (0.500 g, 2.564 mmol) in methanol was added dropwise 0.1 N methanolic NaOH (57 ml, 0.205 g, 5.128 mmol) under stirring. The reaction system was stirred for 2 h and then a methanolic solution of Ph_2SnCl_2 (0.881 g, 2.562 mmol) was added. The fluorescent yellow reaction mixture was refluxed for 8 h under inert nitrogen gas condition. The volatiles were removed and the dry mass extracted with hot petroleum ether (60-80°C, 100 ml). Slow cooling yielded yellow crystals of the desired product.

4.3.4.8 Synthesis of dimethyltin(IV) 5-bromosalicylaldehydethiosemicarbazonate $Me_2SnL^2.H_2O$ (4)

A mixture of Me_2SnO (0.359g, 2.18 mmol) and 5-bromosalicylaldehyde thiosemicarbazone (0.597g, 2.18 mmol) in benzene (100 ml) was refluxed under inert nitrogen atmosphere conditions for 10 h, the water produced being removed azeotropically. The volatiles were removed from the fluorescent yellow reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 50 ml). Yellow crystals of the desired product were obtained by cooling the solution.

4.3.4.9 Synthesis of dibutyltin(IV) 5-bromosalicylaldehyde thiosemicarbazonate n-Bu_2SnL^2 (5)

The compound **5** was prepared by refluxing a mixture of n-Bu_2SnO (0.500g, 2.01 mmol) and 5-bromosalicylaldehyde thiosemicarbazone (0.550g, 2.01 mmol) in benzene (100 ml) under inert conditions for 10 h, the water produced being removed

azeotropically. The volatiles were removed by distillation from the fluorescent yellow reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 45 ml) to give a viscous deep yellow colour liquid as the product. The product was then dried in vaccum pump to exclude traces of any solvent and then stored in a dessicator.

4.3.4.10 Synthesis of diphenyltin(IV) 5-bromosalicylaldehyde thiosemicarbazonate Ph_2SnL^2 (6)

A mixture of Ph_2SnO (0.630 g, 2.18 mmol) and 5-bromosalicylaldehyde thiosemicarbazone (0.597g, 2.18 mmol) was suspended in benzene (100 ml) and refluxed under inert conditions for 10 h, the water produced being removed azeotropically. The volatiles were removed from the fluorescent yellow reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 135 ml). Yellow crystals of the desired product were obtained by cooling the solution.

4.3.4.11 Synthesis of dimethyltin(IV) 5-chlorosalicylaldehydethiosemicarbazonate Me_2SnL^3 (7)

The compound 7 was synthesized by reacting 5-chlorosalicylaldehyde thiosemicarbazone (0.836g, 3.64 mmol) and Me_2SnO (0.600g, 3.64 mmol) in 125 ml anhydrous benzene in a 250 ml flask fitted with a Dean-Stark trap and water-cooled condenser. The reaction mixture was refluxed for 10 h, and filtered while hot. The filterate was collected and the volatiles were removed. The residue was extracted with hot petroleum ether (60-80°C, 80 ml). Yellow crystals of the desired product were obtained after two days from the petroleum ether extract of 7 kept at room temperature.

4.3.4.12 Synthesis of dibutyltin(IV) 5-chlorosalicylaldehydethiosemicarbazonate $n\text{-}Bu_2SnL^3$ (8)

A mixture of $n\text{-}Bu_2SnO$ (0.650g, 2.614 mmol) and 5-chlorosalicylaldehyde thiosemicarbazone (0.599 g, 2.614 mmol) in anhydrous benzene (100 ml) was

refluxed under inert conditions for 10 h, the water produced being removed azeotropically using a Dean-Stark trap. The volatiles were removed from the fluorescent yellow reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 50 ml). The product obtained was a deep yellow viscous liquid which was pumped for 8 hours in a vaccum pump to exclude traces of solvent and subsequently stored in a dessicator.

4.3.4.13 Synthesis of diphenyltin(IV) 5-chlorosalicylaldehydethiosemicarbazonate Ph_2SnL^3 (9)

A mixture of Ph_2SnO (0.700g, 2.42 mmol) and 5-chlorosalicylaldehyde thiosemicarbazone (0.556g, 2.42 mmol) in benzene (135 ml) was refluxed under inert conditions for 10 h, the water produced was removed azeotropically using a Dean-Stark trap. The volatiles were removed from the fluorescent yellow reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 150 ml). The petroleum ether solution was concentrated and left for crystallization at room temperature. Yellow crystals of the desired product were obtained after 2 days from the petroleum ether solution.

4.3.4.14 Synthesis of dimethyltin(IV) napthaldehydethiosemicarbazonate Me_2SnL^4 (10)

A mixture of Me_2SnO (0.650g, 3.94 mmol) and naphthaldehyde thiosemicarbazone (0.966 g, 3.94 mmol) was suspended in 135 ml anhydrous benzene and refluxed under inert conditions for 12 h, the water produced during the reaction was removed azeotropically using a Dean- Stark trap. The reaction mixture was filtered while hot. The volatiles were removed from the filterate to yield a dry mass. The dry mass was then extracted with hot petroleum ether (60-80 °C) in quantities of 4-5 ml for 20 times. The petroleum ether solution was concentrated and left for crystallization at room temperature. Reddish brown crystals of **10** were obtained after one day.

4.3.4.15 Synthesis of dibutyltin(IV) napthaldehydethiosemicarbazone, n-Bu_2SnL^4 (11)

A mixture of n-Bu_2SnO (0.600g, 2.41 mmol) and naphthaldehyde thiosemicarbazone (0.591g, 2.41 mmol) in benzene (150 ml) was refluxed under inert conditions for 12 h, the water produced being removed azeotropically. The volatiles were removed from the reaction mixture and the dry mass extracted with hot petroleum ether (60-80°C, 50 ml). A reddish brown coloured viscous liquid was obtained as the product. The product was dried in vacuo and then stored in a dessicator.

4.3.4.16 Synthesis of diphenyltin(IV) napthaldehydethiosemicarbazonate Ph_2SnL^4 (12)

The compound **12** was synthesized by reacting napthaldehydethiosemicarbazone (0.424g, 1.73 mmol) and Ph_2SnO (0.500g, 1.73 mmol) in 100 ml anhydrous benzene in a 250 ml flask fitted with a Dean-Stark trap and water-cooled condenser. The reaction mixture was heated under reflux for 12 h, and filtered while hot. The filterate was collected and the volatiles were removed. The residue was extracted with hot petroleum ether (60-80°C, 90 ml). Reddish brown crystals of the desired product were obtained after 48 h from the petroleum ether extract of **12** at room temperature.

4.3.4.17 Synthesis of dibenzyltin(IV) of salicylaldehyde thiosemicarbazonate, Bz_2SnL^1 (13)

To a solution of salicylaldehyde thiosemicarbazone (0.650 g, 3.33 mmol) in methanol was added dropwise 0.1 N methanolic NaOH (74 ml, 0.266 g, 6.65 mmol) under stirring. The reaction mixture was stirred for 2 h and then a methanolic solution (45 ml) of Bz_2SnCl_2 (0.732 g, 3.33 mmol) was added. The fluorescent yellow reaction mixture was refluxed for 6 h under inert conditions. The volatiles were removed and the dry mass extracted with hot petroleum ether (60-80°C, 75 ml). A yellow coloured solid product was obtained.

4.3.4.18 Synthesis of dibenzyltin(IV) derivative of 5-chlorosalicylaldehyde thiosemicarbazone, $[Sn(Bz)_2(C_8H_6ClN_3OS)_2(CH_3O)_2]$ (14)

A methanol solution (50 ml) of 5-chlorosalicylaldehyde thiosemicarbazone (0.500 g, 2.17 mmol) was stirred continuously in a 0.1 N methanolic NaOH solution (45.9 ml, 0.174g, 4.35 mmol) for 2 h. Bz_2SnCl_2 (0.809g, 2.17mmol) dissolved in 50 ml of methanol was then added to the reaction mixture which was refluxed for 6 h under an inert atmosphere. The volatiles were removed by distillation and the residue obtained was washed thoroughly with hot petroleum ether (b.p. 60-80°C) in quantities of 4-5 ml, extracted into benzene (50 ml) and filtered. The product obtained was then repeatedly recrystallized from methanol to give **14**.

4.3.5 Crystal structure determinations

4.3.5.1 Crystal structure determinations of 1, 3, 4, 6 and 9

Intensity data were measured for selected crystals of **1, 3, 4, 6** and **9** at 223 K on a Bruker AXS SMART CCD with graphite monochromatized Mo*K*α radiation (0.71069 Å) so that θ_{max} = 30.0/30.1°. Each structure was solved by heavy-atom methods [163] and refined [164] on F^2 with non-hydrogen atoms modelled with anisotropic displacement parameters, with hydrogen atoms in the riding model approximation and using a weighting scheme of the form $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + 2F_c^2)/3$). In the refinement of **6**, rather large residual electron density peaks within 1 Å of the bromide atoms were noted. This is ascribed to the rather poor quality of the crystals and the possibility of pseudo symmetry -- the unit cell parameters roughly approximate a hexagonal unit cell. Otherwise, the final difference maps were relatively featureless. The crystallographic data and refinement details are given in Table 4.1- 4.5. The numbering schemes are shown in Section 4.4 and were drawn with ORTEP [165]. Diagrams of the supramolecular structures were generated with the aid of the DIAMOND [166] programme.

4.3.5.2 Crystal structure determination of 14

Intensity data were measured for selected crystals of **14** at 173 K on a Rigaku AFC12K/SATURN724 diffractometer with graphite monochromatized Mo$K\alpha$ radiation so that $\theta_{max} = 27.6°$. The structure was solved by heavy-atom methods [163] and refined [164] on F^2 with non-hydrogen atoms modelled with anisotropic displacement parameters, with hydrogen atoms in the riding model approximation and using a weighting scheme of the form $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ where $P = (F_o^2 + 2F_c^2)/3$).Crystal data are given in Table 4.6. The numbering scheme is shown in Fig. 4.34 and was drawn with ORTEP [165]. Diagrams of the supramolecular structures were generated with the aid of the DIAMOND [166] programme.

4.3.6 Biological studies

4.3.6.1 Antibacterial activity

4.3.6.1.1 Bacterial strains and determination of antibacterial properties of organotin complexes

The organotin compounds studied were dissolved in 0.3 % DMSO-water. The solutions were always prepared fresh and the pH adjusted to 7.4. The bacterial strains used in the study were *Aeromonas hydrophila* strain 646 (MTCC, India, Gram-negative pathogenic), *Salmonella typhi* strain 737 (NICED, India, Gram-negative pathogenic), *Salmonella typhimurium* strain 3099 (NICED, India, Gram-negative pathogenic), *Salmonella flexnri* strain NK 2226 (NICED, India,Gram-negative pathogenic), *Escheria coli* strain 25922 (NICED, India, Gram-negative pathogenic), *Salmonella aureus* (kind gift from M. Saha, National Institute for Cholera and Enteric Diseases, Kolkata, India, Gram-negative pathogenic), *Bacillus subtilis* strain 6633 (ATCC, India, Gram-positive non-pathogenic) and *Lactobacillus rhamnosus* strain 1408 (ATCC, India, Gram-positive non-pathogenic). Bacteria were maintained in nutrient agar slant at 4°C and for experimental need they were grown in specific medium to log phase at optimal temperature.

The antibacterial properties of the organotins were evaluated by the disc-diffusion method [167]. Bacteria were grown to mid-log phase and spread on nutrient agar plates. Sterile filter discs containing different concentrations of the organotins in 20-40 µl were applied on the bacterial plates and incubated at optimal temperature for 24 h. The inhibition zones appearing around each disc were measured and the sensitivity determined from the zone diameters appearing on the plates based on NCCLS charts. When the bacteria gave a zone with diameter less than 13 mm in the presence of an organotin, it was interpreted as resistant (R), when the zone had a diameter of 15-16 mm, the bacteria were considered to have intermediate sensitivity (I) and a clear zone with diameter of 17 mm or more indicated a high degree of sensitivity towards the compound (S).

4.3.6.1.2 Role of 2 on bacterial disease

Aeromonas hydrophila is a known fish pathogen responsible for E.U.S (Epizootic Ulcerative Syndrome). 1 x 10^{10} bacteria were incubated with **2** overnight at 30 °C in BHI containing ampicillin (100 µg/ml). Following incubation the bacteria were washed repeatedly with sterile saline water (0.9%) and introduced by intramuscular route into healthy fish in 100 µl saline. Control fish were injected with untreated bacteria. The development of redness and ulcer formation were checked in both group of animals. Healthy fish were also injected with untreated bacteria (1 x 10^{10}/100 µl saline). 72 hours after **2** was locally injected at the site of infection, at 24 hours interval for three consecutive days, the development of disease phenotype was checked. Control fish were injected with 0.3% DMSO solution or saline [167].

4.3.6.2 Antifungal activity

The fungal strains used were gifts from The Department of Botany, University of North Bengal. The strains were *Curvularia eragrostidis* (a pathogen of tea, *Camellia sineusis*), *Alternaria porri* (a pathogen of niger, *Guizotia abyssinica*), *Dreschlerea oryzae* (a pathogen of rice, *Oryzae sativa)* and *Macrophomina phaseolina* (a pathogen of brinjal, *Solanum melongena*). These strains were grown on potato-dextrose-agar (PDA, HiMedia, India) medium at 28 ±1 °C.

The fungicidal activities were determined following spore germination bioassay as described by Rouxel *et al.* [168]. Purified eluents (10 µl) were placed on two spots 3 cm apart on a clean, grease-free slide and the solvent was allowed to evaporate. One drop of spore suspension (20 µl), prepared from 15 day-old cultures of the fungi, was added to the treated spots. The slides were incubated at 27±1 °C for 24 h under humid conditions in Petri plates. Finally, after proper incubation period, one drop of a Cotton Blue-Lactophenol mixture was added to each spot to fix the germinated spores. The number of spores germinated compared with the germinated spores of control (where no chemicals were used) was calculated using an average of 300 spores per treatment. The minimum inhibitory concentration required for complete inhibition was recorded in units of µg/ml.

4.3.6.3 Phytotoxic effects

Oryzae sativa (IR-8, ICAR, India), *Lens culinaris,* and *Cicer aurantinum* were collected from the University Agricultural Research Institute, Visva-Bharati, and the phytotoxic effects of different organotins determined [169]. Briefly, seeds of different species were incubated with different concentration of organotins for different time periods. Following incubation the seeds were washed with distilled water and incubated in aerated moist chambers for 96 h at 28 °C. The percentage of seed germination was calculated and compared with the results obtained with seeds dipped in DMSO-water as well as with those incubated in water only.

4.3.7 Crystallographic data and refinement details for **1**, **3**, **4**, **6**, **9**, & **14**

Table 4.1 Crystallographic data and refinement details for $[Me_2SnL^1]$ (**1**)

	1
Formula	$C_{10}H_{13}N_3OSSn$
Formula weight	341.98
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	9.4175(6)
b (Å)	13.4230(9)
c (Å)	10.5187(7)
α (°)	90
β (°)	100.266(1)
γ (°)	90
V (Å^3)	1308.39(15)
Z	4
D_c (g cm^{-3})	1.736
μ (Mo$K\alpha$, mm^{-1})	2.096
Measured data	10789
Unique data	3792
Observed data	
[$I \geq 2.0\sigma(I)$]	3291
R, obs. data; all data	0.030; 0.036
a; b in weighting scheme	0.038; 0.431
R_w, obs. data; all data	0.075; 0.079
Largest residual (e Å^{-3})	0.85
CCDC deposition no.	638421

Table 4.2 Crystallographic data and refinement details for $[Ph_2SnL^1]$ (**3**)

	3
Formula	$C_{20}H_{17}N_3OSSn$
Formula weight	466.12
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	15.5284(8)
b (Å)	10.0604(5)
c (Å)	13.3743(7)
α (°)	90
β (°)	113.673(2)
γ (°)	90
V (Å^3)	1913.54(17)
Z	4
D_c (g cm^{-3})	1.618
μ (Mo$K\alpha$, mm^{-1})	1.458
Measured data	15651
Unique data	5538
Observed data	
$[I \geq 2.0\sigma(I)]$	4188
R, obs. data; all data	0.035; 0.052
a; b in weighting scheme	0.040; 0
R_w, obs. data; all data	0.080; 0.087
Largest residual (e Å^{-3})	0.86
CCDC deposition no.	638422

Table 4.3 Crystallographic data and refinement details for $[Me_2SnL^2].H_2O$ (**4**)

	4
Formula	$C_{10}H_{14}BrN_3O_2SSn$
Formula weight	438.90
Crystal system	monoclinic
Space group	*C*2/*c*
a (Å)	15.5788(8)
b (Å)	13.6076(7)
c (Å)	13.9124(7)
α (°)	90
β (°)	93.936(2)
γ (°)	90
V (Å^3)	2942.3(3)
Z	8
D_c (g cm^{-3})	1.982
μ (Mo*K*α, mm^{-1})	4.592
Measured data	12167
Unique data	4300
Observed data	
[$I \geq 2.0\sigma(I)$]	3384
R, obs. data; all data	0.038; 0.054
a; *b* in weighting scheme	0.035; 0
R_w, obs. data; all data	0.080; 0.085
Largest residual (e Å^{-3})	1.13
CCDC deposition no.	638423

Table 4.4 Crystallographic data and refinement details for $[Ph_2SnL^2]$ (**6**)

	6
Formula	$C_{20}H_{16}BrN_3OSSn$
Formula weight	545.02
Crystal system	triclinic
Space group	*P*-1
a (Å)	12.7793(5)
b (Å)	12.8645(5)
c (Å)	13.5952(5)
α (°)	93.877(2)
β (°)	93.640(2)
γ (°)	118.031(2)
V (Å^3)	1956.79(13)
Z	4
D_c (g cm^{-3})	1.850
μ (Mo*K*α, mm^{-1})	3.470
Measured data	16439
Unique data	11161
Observed data	
[$I \geq 2.0\sigma(I)$]	8228
R, obs. data; all data	0.053; 0.075
a; *b* in weighting scheme	0.077; 0.429
R_w, obs. data; all data	0.131; 0.142
Largest residual (e Å^{-3})	4.78
CCDC deposition no.	638424

Table 4.5 Crystallographic data and refinement details for $[Ph_2SnL^3]$ (**9**)

	9
Formula	$C_{20}H_{16}ClN_3OSSn$
Formula weight	500.56
Crystal system	triclinic
Space group	*P*-1
a (Å)	8.8596(6)
b (Å)	9.9809(7)
c (Å)	12.7142(8)
α (°)	111.759(1)
β (°)	109.741(1)
γ (°)	91.927(1)
V (Å^3)	966.44(11)
Z	2
D_c (g cm^{-3})	1.720
μ (Mo*K*α, mm^{-1})	1.583
Measured data	8204
Unique data	5504
Observed data	
[$I \geq 2.0\sigma(I)$]	4898
R, obs. data; all data	0.045; 0.051
a; *b* in weighting scheme	0.055; 0.497
R_w, obs. data; all data	0.103; 0.107
Largest residual (e Å^{-3})	1.45
CCDC deposition no.	638425

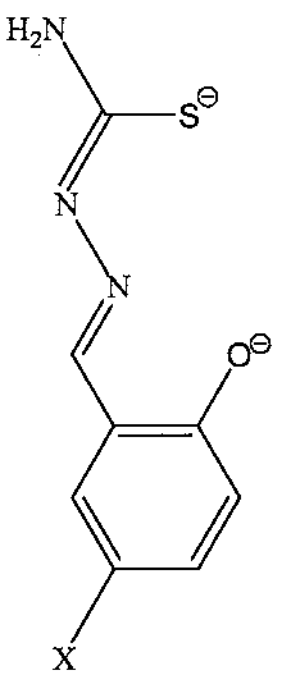
Table 4.6 Crystallographic data and refinement details for **14**

	14
Formula	$[Sn_2(C_7H_7)_2(C_8H_6ClN_3OS)_2.(CH_3O)_2]$
Formula weight	937.04
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	11.617(7)
b (Å)	13.484(4)
c (Å)	12.430(4)
β (°)	117.367(5)
V (Å^3)	1729.1(13)
Z	2
D_c (g cm^{-3})	1.800
μ (Mo$K\alpha$, mm^{-1})	1.77
Measured data	44284
Unique data	3906
Observed data	
[$I \geq 2.0\sigma(I)$]	3887
R, obs. data; θ_{max}	0.051; 27.6°
a; b in weighting scheme	0.0396; 5.0883
R_w, obs. data; all data	0.050; 0.117
Largest residual (e Å^{-3})	0.99

4.4 Results and Discussion

4.4.1 Synthesis of Schiff base of salicylaldehyde, substituted salicylaldehyde and naphthaldehyde from thiosemicarbazide

The ligands used here are Schiff bases derived either from salicylaldehyde or substituted salicylaldehyde (5-bromosalicylaldehyde, 5-chlorosalicylaldehyde) or naphthaldehyde with thiosemicarbazide. The thiosemicarbazones were obtained in good yield (> 75%) by reacting equimolar amounts of thiosemicarbazides and respective salicylaldehyde/ substituted salicylaldehydes/ naphthaldehyde in 1:1 ethanol-water mixture [155]. The products were recrystallized from ethanol. The formulae of the ligands and the abbreviations of the complexes are presented in Scheme 4.3.



L^1: X =H ; L^2: X = Br ; L^3: X = Cl ; L^4: X = C_6H_4 .

1: Me_2SnL^1; **2**: n-Bu_2SnL^1; **3**: Ph_2SnL^1; **4**: $Me_2SnL^2.H_2O$; **5**: n-Bu_2SnL^2;
6: Ph_2SnL^2, **7**: Me_2SnL^3; **8**: n-Bu_2SnL^3; **9**: Ph_2SnL^3 ; **10**: Me_2SnL^4;
11: n-Bu_2SnL^4;**12**: Ph_2SnL^4.

Scheme 4.3

The Schiff bases synthesized are soluble in ethanol, methanol but insoluble in petroleum ether (b.p. 60-80 °C), benzene and carbon tetrachloride. They are all high and sharp melting compounds. The synthetic details and characterization data for $L^1H - L^4H$ are described in section 4.3.

4.4.2 Synthesis of diorganotin(IV) complexes of salicylaldehyde/ substituted salicylaldehyde/naphthaldehyde thiosemicarbazones

In this section the synthesis, characterization and crystal structures of new organotin derivatives of thiosemicarbazones are presented. Two different methods for the synthesis were adopted for the diorganotin(IV) complexes of the Schiff bases reported here. The objective was to compare the yields obtained by following two different synthetic routes. The synthetic conveniences, though, primarily led to the choice of a suitable procedure and have been described in detail in section 4.3.

4.4.2.1 Synthesis of diorganotin(IV) complexes of salicylaldehyde thiosemicarbazo - ne (L^1HH')

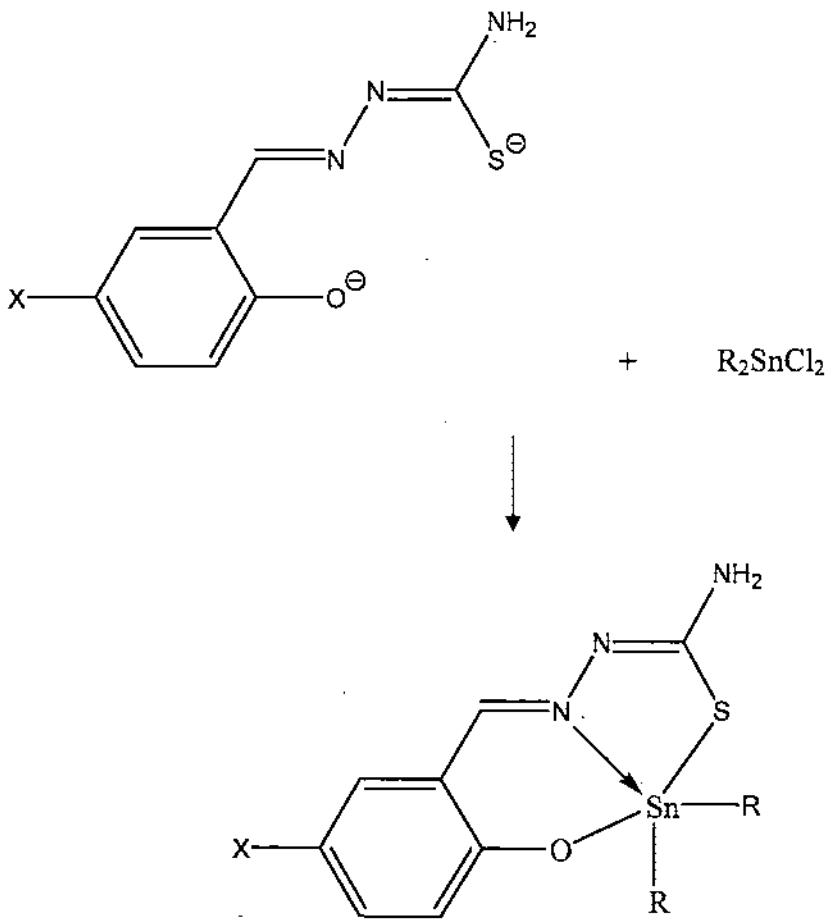
The diorganotin(IV) derivatives of salicylaldehyde thiosemicarbazone (R=Me, n-Bu, Ph) were obtained in moderate yields by the equimolar reaction of diorganotin(IV) dichlorides with the sodium salt of the ligand in methanol as solvent at reflux temperature (Scheme 4.4). The sodium salt of the ligand was generated *in situ* by the addition of methanolic solution of NaOH to the hot methanolic solution of salicylaldehyde thiosemicarbazone.

$$L^1HH' + 2NaOH \longrightarrow L^1Na_2 + 2H_2O \quad \ldots\ldots\ldots (4)$$

$$L^1Na_2 + R_2SnCl_2 \longrightarrow R_2SnL^1 + 2NaCl \quad \ldots\ldots\ldots (5)$$

The reactions were completed in 8 hours time. The reaction mixture was evaporated to dryness and then subsequently extracted with hot petroleum ether (b.p. 60- 80 °C) in quantities of 2-3 ml for 10 –15 times. A comparatively large amount of petroleum ether (100 ml) was needed to extract the diphenyltin analogue as the solubility was found to be poor in petroleum ether (b.p. 60- 80 °C).The synthetic methodology is

described in Scheme 4.4. The exact synthetic details for the above complexes along with their characterization data are listed in Table 4.7.



1: R= Me ; **2**: R= n-Bu ; **3**: R= Ph.

Scheme 4.4

The dibenzyltin(IV) complexes of salicylaldehyde thiosemicarbazones were synthesized analogously. These complexes are discussed separately in Section 4.4.4.

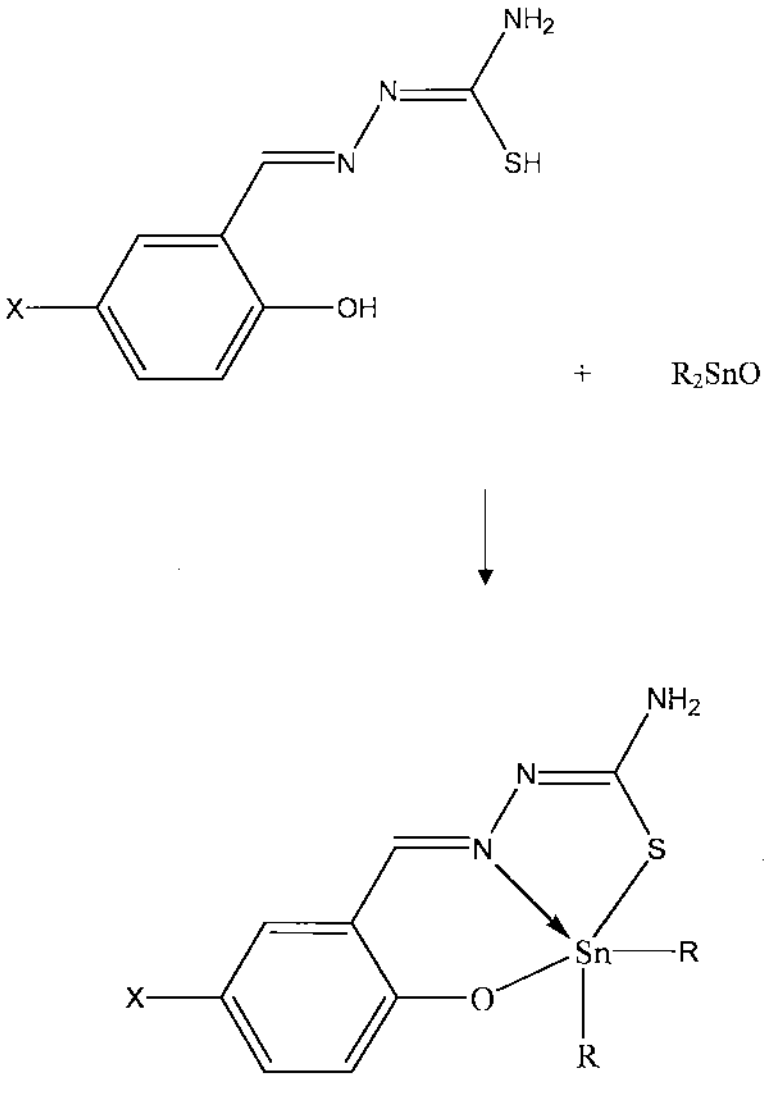
4.4.2.2 Synthesis of diorganotin(IV) complexes of substituted salicylaldehyde/ naphthaldehyde thiosemicarbazones (L^2HH'- L^4HH')

The diorganotin(IV) complexes of substituted salicylaldehyde/ naphthaldehyde thiosemicarbazones were synthesized by the reaction of the diorganotin(IV) oxides

with the respective ligand in 1:1 molar ratio in benzene as the solvent at reflux temperature. Since the Schiff bases were insoluble in benzene, the reaction mixture turned out to be heterogeneous and greater reaction times were usually required for the completion of the reaction. The water produced during the reaction was removed using a Dean-Stark trap to facilitate faster completion of the reactions. The compounds were obtained in moderate to good yields. The reaction system in all cases were evaporated to dryness and then extracted with hot petroleum ether (b.p.60-80 °C). The solubility for the diphenyltin analogues was generally poor when compared to the other complexes. Therefore, large quantities of petroleum ether (b.p. 60-80 °C) was required to extract the diphenyltin(IV) complexes, however the other diorganotin(IV) complexes were extracted readily using petroleum ether. The compound **4** was isolated as a monohydrate. The compounds are relatively stable in moist air and can be recrystallized from suitable organic solvents. The synthetic methodology is described in Scheme 4.5. Synthetic details along with the physical data are summarized in Table 4.7. All the complexes are soluble in chloroform, methanol, acetone, n-hexane and benzene.

$$LH_2 + R_2SnO \longrightarrow R_2SnL + H_2O \quad \text{..... (6)}$$

4 : R= Me, L= L^2; **5** : R= n-Bu, L= L^2; **6** : R= Ph, L= L^2
7 : R= Me, L= L^3; **8** : R= n-Bu, L= L^3; **9** : R= Ph, L= L^3
10 : R= Me, L= L^4; **11** : R= n-Bu, L= L^4; **12** : R= Ph, L= L^4



Scheme 4.5

Table 4.7 Characterization and analytical data for the diorganotin(IV) complexes[a]

Complex	Reaction time (h)	Crystallization solvent	Colour	Yield (%)	M.p. (°C)	Elemental composition: Found (Calc.) (%)			
						C	H	N	Sn
1	8[b]	Benzene	Yellow	85	152	34.59 (35.12)	3.78 (3.80)	12.27 (12.29)	34.60 (34.73)
2	8[b]	Petroleum ether[d]	Yellow	80	93-94	45.01 (45.10)	5.85 (5.87)	9.79 (9.87)	27.69 (27.88)
3	8[b]	Petroleum ether[d]	Yellow	70	131	51.45 (51.53)	3.61 (3.65)	9.00 (9.02)	25.40 (25.49)
4	10[c]	Petroleum ether[d]	Yellow	75	111-113	27.29 (27.36)	3.12 (3.19)	9.55 (9.57)	26.99 (27.06)
5	10[c]	Petroleum ether[d]	Yellow	69	-	37.98 (38.04)	4.73 (4.75)	8.30 (8.32)	23.49 (23.52)
6	10[c]	Petroleum ether[d]	Yellow	67	161-163	44.01 (44.06)	2.91 (2.93)	7.68 (7.71)	21.65 (21.79)
7	10[c]	Petroleum ether[d]	Yellow	45	105-106	31.88 (31.90)	3.18 (3.19)	11.15 (11.16)	31.48 (31.55)
8	10[c]	Petroleum ether[d]	Yellow	65	-	41.05 (41.72)	5.18 (5.21)	9.10 (9.13)	25.69 (25.79)
9	10[c]	Petroleum ether[d]	Yellow	48	169-171	47.90 (47.98)	3.18 (3.20)	8.38 (8.39)	23.61 (23.73)
10	12[c]	Petroleum ether[d]	Reddish brown	49	165-167	42.81 (42.89)	3.84 (3.82)	10.70 (10.72)	30.27 (30.30)
11	12[c]	Petroleum ether[d]	Reddish brown	56	-	50.43 (50.45)	5.65 (5.67)	8.82 (8.83)	24.90 (24.95)
12	12[c]	Petroleum ether[d]	Reddish brown	42	194-195	55.85 (55.84)	3.67 (3.68)	8.09 (8.14)	23.02 (23.01)

[a]Sticky liquid.

[b] Method: reflux in methanol ; [c] Method: reflux in benzene.

[d] Petroleum ether (b.p. 60-80 °C).

4.4.3 Spectroscopic characterization and X-ray crystallography of diorganotin(IV) complexes

4.4.3.1 Spectroscopic characterization and X-ray structure determination of diorganotin(IV) complexes, R_2SnL ($L=L^1$ to L^4; R=Me, n-Bu, Ph)

The complexes were characterized by UV, IR, NMR (^1H, ^{13}C and ^{119} Sn) and elemental analyses. In general, the X-ray crystallographic data of the complexes supports the observed spectral data. Fluoresence spectra of some complexes of distinctly different types to study the fluorescence properties of these newly synthesised compounds were also recorded.

4.4.3.1.1 IR Spectra

Selected IR bands and their assignments for the diorganotin complexes have been presented in Table 4.8. The infrared spectral data together with the stoichiometric composition of these organotin(IV) complexes suggested that the salicylaldehyde thiosemicarbazones and the naphthaldehyde thiosemicarbazone act as dinegative O,N,S tridentate ligands, with the central tin (IV) coordinated to the deprotonated phenolic 'O', azomethine 'N' and the deprotonated thiocarbonyl/thiol 'S' atom. This mode of chelation was confirmed by X-ray crystallographic structure of the organotin(IV) complexes of salicylaldehyde thiosemicarbazones in this study. The $\nu(NH_2)$, $\nu(C{=}N{-}N{=}C)$ and $\nu(Sn{-}C)$ bands were identified based on literatures values [170,171]. The $\nu(NH_2)_{asym}$ and $\nu(NH_2)_{sym}$ stretching vibrations of the ligands appear in the range 3234-3442 cm^{-1}. These bands did not shift significantly upon complex formation in the diphenyltin derivatives of the ligands indicating that the amino nitrogen atom is not involved in coordination with tin. In the dimethyltin and dibutyltin derivatives of these ligands, the $\nu(NH_2)_{asym}$ and $\nu(NH_2)_{sym}$ stretching vibrations are shifted to smaller wave numbers than in the free ligand spectrum. These shifts are probably due to the hydrogen bond in which the NH_2 group is involved being stronger than in the phenyl derivatives [13,103].The $\nu(C{=}S)$ vibration in free salicylaldehyde thiosemicarbazones and naphthaldehyde thiosemicarbazone occurring

around 777 cm^{-1} was shifted towards lower frequency to 740 ±10 cm^{-1} in complexes suggesting coordination of thiocarbonyl 'S' to the metal ion. The spectra showed medium to strong absorptions within the range of 1600-1651 cm^{-1} due to ν(C=N–N=C) [171]. The $\nu(Sn–C)_{asym}$ and $\nu(Sn–C)_{sym}$ bands appear at 520-540 cm^{-1} and 460-480 cm^{-1} respectively. In the spectrum of **4**, a broad band in the range 3290-3410 cm^{-1} was observed which indicated the presence of both OH stretching vibrations and the NH_2 stretching vibrations, consistent with **4** crystallizing as a hydrate [13]. The new bands which appeared at 340-350 cm^{-1} have been assigned to ν(Sn-S) stretching bands.

Table 4.8 IR spectral data (cm^{-1}) for **1-12**[a]

Complex	$\nu(NH_2)_{asym}$	$\nu(NH_2)_{sym}$	ν(C=N-N=C)	ν(Sn-C)	ν(Sn-S)
1	3300(w)	3124(w)	1651(s)	536(m),478(w)	340(m)
2	3307(w)	3151(w)	1645(m)	532(w), 461(s)	342(m)
3	3446(w)	3340(w)	1604(m)	530(w),475(w)	342(m)
4	3290-3410(b,w)	-	1633(m)	521(w),475(w)	347(m)
5	3302(w)	3158(m)	1620(m)	525(w).470(w)	345(m)
6	3452(w)	3292(w)	1622(m)	535(w),480(w)	342(m)
7	3433(m)	3280(w)	1606(m)	520(w),475(w)	338(m)
8	3300(s)	3168(s)	1600(s)	538(w),480(w)	350(m)
9	3452(w)	3292(w)	1624(m)	540(w),485(w)	345(m)
10	3374(w)	3200(w)	1634(s)	535(m),474(m)	341(m)
11	3380(w)	3290(w)	1600(s)	539(w),480(m)	349(m)
12	3443(w)	3238(m)	1609(s)	541(w),486(w)	346(m)

[a] s, strong; m, medium; w, weak; b, broad.

4.4.3.1.2 NMR Spectra

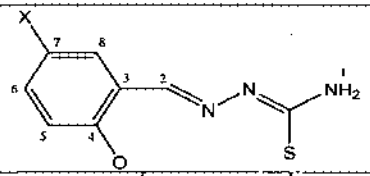
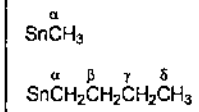
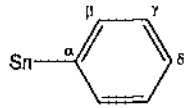
The ^1H NMR data for the diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones are presented in Table 4.9 while the ^1H NMR data for the

diorganotin(IV) complexes of naphthaldehyde thiosemicarbazones are presented in Table 4.10 respectively. The observed resonances were assigned on the basis of their integration and multiplicity patterns. The ligand and tin-bound organic group protons gave signals in the expected ranges [103,172,173].

The spectrum of the diphenyltin compounds **3, 6** and **9** show complex patterns for the aromatic protons (both ligand and Sn-Ph). In compound **3,** the C–H and aromatic protons appeared as complex multiplets in the range 8.40-6.50 ppm. In **3**, the C–H proton of CH=N has been identified at 8.24 ppm. Spin-spin coupling between the tin nucleus and the azomethine-proton, ^{3}J (SnN=CH), were detected in all spectra thereby confirming the presence of nitrogen-tin coordination. In addition, the values of the coupling constants for ^{3}J(SnN=CH), i.e. 33-45 Hz, ^{2}J($SnCH_3$), i.e. 69-74 Hz, are within the ranges reported for penta-coordinated organotin(IV) complexes with ONO and ONS tridentate Schiff bases [174].

Solution ^{13}C NMR data of the diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones are presented in Table 4.11 while the ^{13}C NMR data for the diorganotin(IV) complexes of naphthaldehyde thiosemicarbazone presented in Table 4.12 respectively. The number of ^{13}C signals found corresponded with the number of magnetically non-equivalent carbon atoms in the complexes. Contrary to the literature [103,161] the author was inclined to propose C-2 signal (attached to a phenyl group and a =N-N= moiety) to be the most deshielded carbon atom followed by C-1 (attached to two N atoms and a –S-Sn moiety) and then the C-4 carbon of the phenyl ring of the ligand. In author's opinion, the satellites attached here with the C-4 carbon atom should be associated with $^{2}J(^{119}Sn–O-^{13}C)$ [175] rather than the $^{2}J(^{119}Sn –N-^{13}C)$ as proposed by Casas and his coworkers [103].The dimethyltin complexes **1, 4, 7, 10** exhibited $^{1}J(^{119}Sn-^{13}C)$ coupling values in the range 592-596 Hz. The $^{1}J(^{119}Sn-^{13}C)$ coupling values in all the complexes were indicative of penta-coordination around the tin atom [176] and were in accordance with the X-ray crystal structures [13] and previous literature reports [103,161]. The di-*n*-butyltin(IV) complexes exhibited $^{1}J(^{119}Sn-^{13}C)$ coupling values in the range 557-564 Hz.

Table 4.9 ^{1}H NMR chemical shifts (ppm) and coupling data (Hz) for **1-9**[a]

										
	H-1	**H-2**	**H-5**	**H-6**	**H-7**	**H-8**	**H-α**	**H-β**	**H-γ**	**H-δ**
1	5.10 (s, 2H)	8.49 (s, 1H) [40][c]	6.78-6.76 (d, 1H)	7.29 (m, 1H)	6.72 (t, 1H)	7.12-7.09 (d, 1H)	0.87 (s, 6H) [72][d]	-	-	-
2	4.97 (s, 2H)	8.48 (s, 1H) [37.5][c]	6.78-6.75 (d, 1H)	7.29 (m, 1H)	6.69 (t, 1H)	7.10-7.08 (d, 1H)	1.82-1.61 (m, 4H)	1.55-1.42 (m, 4H)	1.34 (m, 4H)	0.87 (t, 6H)
3	4.47 (s, 2H)	8.24 (s, 1H)	6.63-6.61 (d, 1H)	7.23 (m, 1H)	6.52 (m, 1H)	7.28 (d, 1H)	-	8.27 (m, 4H)	7.23 (m, 4H)	7.23 (m, 2H)
4	5.02 (s, 2H)	8.40 (s, 1H) [39][c]	6.68-6.65 (d, 1H)	7.35-7.31 (d, 1H)	-	7.21-7.20 (s, 1H)	0.87 (s, 6H) [73/70][d]	-	-	-
5	5.18 (s, 2H)	8.37 (s, 1H) [39][c]	6.67-6.64 (d, 1H)	7.30 (d, 1H)	-	7.18-7.17 (s, 1H)	1.69-1.57 (m, 4H)	1.55-1.49 (m, 4H)	1.42-1.25 (m, 4H)	0.87 (t, 6H)
6	4.33 (s, 2H)	7.96 (s, 1H) [n.d.][b]	6.66-6.65 (d, 1H)	6.83-6.80 (d, 1H)	-	7.31-7.17 (s, 1H)	-	8.33-8.03 (m, 4H)	7.31-7.17 (m, 4H)	7.31-7.17 (m, 2H)
7	5.14 (s, 2H)	8.39 (s, 1H) [38][c]	6.72-6.70 (d, 1H)	7.26-7.19 (d, 1H)	-	7.07-7.06 (s, 1H)	0.87 (s, 6H) [74/71][d]	-	-	-
8	5.00 (s, 2H)	8.39 (s, 1H) [34][c]	6.72-6.69 (d, 1H)	7.22-7.18 (d, 1H)	-	7.05-7.04 (s, 1H)	1.69-1.59 (m, 4H)	1.55-1.44 (m, 4H)	1.42-1.26 (m, 4H)	0.87 (t, 6H)
9	5.10 (s, 2H)	8.41 (s, 1H) [44][c]	7.05-6.97 (d, 1H)	7.05-6.97 (d, 1H)	-	7.44-7.24 (s, 1H)	-	8.01-7.65 (m, 4H)	7.44-7.24 (m, 4H)	7.44-7.24 (m, 2H)

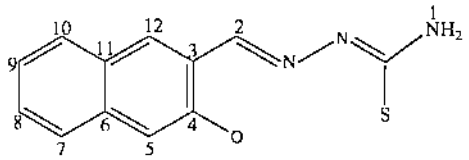
[a] Spectra recorded in $CDCl_3$ except for compounds **3** and **6** which were measured in C_6D_6, downfield to TMS; Multiplicity is given as s, singlet;d, doublet; t, triplet; m, multiplet; [b] n.d. = not detected; [c] $^{3}J(^{119}Sn - H)$ Hz; [d] $^{2}J(^{119/117}Sn - CH_3)$ Hz.

Table 4.10 ^{1}H NMR chemical shifts (ppm) and coupling data (Hz) for **10-12**[a]

	10	11	12
H-1	5.03(s, 2H)	5.07	5.02(s, 2H)
H-2	9.35(s, 1H) [42][d]	9.38(s, 1H) [44][d]	9.41(s, 1H) [48][d]
H-5	6.96-6.93(d,1H)	6.96-6.94(d, 1H)	7.28-7.20(m,1H)
H-7	7.31-7.25(m,1H)	7.28-7.21(m,1H)	7.28-7.20(m,1H)
H-8,9	7.75-7.67(m,2H)	7.73-7.65(m,2H)	7.80-7.65(m,2H)
H-10	7.50-7.44(m, 1H)	7.50-7.42(m, 1H)	7.45-7.35(m,1H)
H-12	7.91-7.88(d, 1H)	7.89-7.86(d,1H)	7.88-7.85(d,1H)
H-α	0.89(s,6H) [73.5/70.5]	1.80-1.62(m, 4H)	-
H-β	-	1.55-1.46(m, 4H)	7.94-7.91(m,4H)
H-γ	-	1.42-1.32(m,4H)	7.45-7.35(m,4H)
H-δ	-	0.89(t, 6H)	7.45-7.35(m,2H)

[a] Spectra recorded in $CDCl_3$, downfield to TMS; Multiplicity is given as s, singlet; d, doublet; m, multiplet, t; triplet.

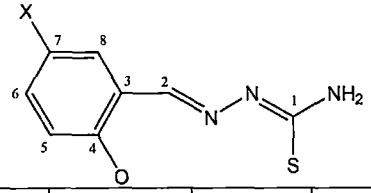
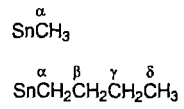
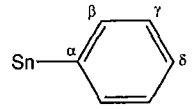
[b] Refer to the Fig. shown below for the numbering scheme in the ligand



[c] Refer to Table 4.9 for numbering scheme in the Sn-R skeleton

[d] $^{3}J(^{119}\text{Sn-H})$ Hz ; [e] $^{2}J(^{119/117}\text{Sn-CH}_3)$ Hz.

Table 4.11 ^{13}C NMR chemical shifts (ppm) and coupling data (Hz) for **1-9**[a]

												
	C-1	**C-2**	**C-3**	**C-4**	**C-5**	**C-6**	**C-7**	**C-8**	**C-α**	**C-β**	**C-γ**	**C-δ**
1	165.85	167.94	121.39	160.62 [20.17][g]	116.77	133.55	117.16	134.6	5.94 [595.90][b]	-	-	-
2	166.62	168.18	121.41	160.86 [16.80][g]	116.69	133.61	116.77	133.66	25.86 [562.50][b]	27.41 [30.80][c]	26.46 [90.0][d]	13.58
3	166.21	166.72	121.70	161.03 [20.4][g]	116.83	133.83	117.43	134.97	142.49 [865.3]	135.78 [56.32]	128.65 [82.35][d]	129.98 [16.72][e]
4	164.98	168.45	123.47	159.21 [20.12][g]	108.19	134.88	118.39	137.07	5.98 [593.10][b]	-	-	-
5	165.28	168.79	123.19	158.83 [16.82][g]	107.69	134.74	118.37	136.82	25.84 [557.60][b]	27.30 [30.75][c]	26.35 [64.50][d]	13.53
6	165.48	166.81	123.61	159.26 [18.6][g]	108.41	135.04	118.36	136.09	142.08 [843.75][b]	135.71 [57][c]	128.74 [82.5][d]	130.1 [16.87][e]
7	164.33	168.50	122.93	159.01 [20.25][g]	117.55	131.73	121.39	134.25	5.98 [592.90][b]	-	-	-
8	164.91	168.79	122.39	158.93 [16.88][g]	117.60	131.67	120.93	134.15	25.82 [558.1][b]	27.31 [30.63][c]	26.37 [81.0][d]	13.5
9	165.13	166.83	123.23	159.52 [20.25][g]	117.62	131.99	121.08	134.59	142.14 [807.69][b]	135.73 [56.4][c]	128.75 [82.65][d]	130.14 [16.57][e]

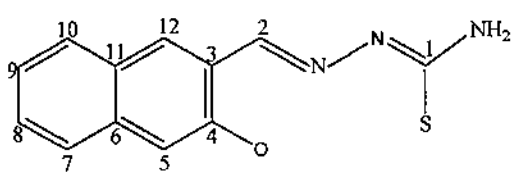
[a] Spectra recorded in $CDCl_3$ solution, downfield to TMS; [b] $^1J(^{119}Sn - ^{13}C)$ in Hz; [c] $^2J(^{119}Sn - ^{13}C)$ in Hz; [d] $^3J(^{119}Sn - ^{13}C)$ in Hz; [e] $^4J(^{119}Sn - ^{13}C)$ in Hz; [g] $^2J(^{119}Sn\text{-}O\text{-}^{13}C)$ in Hz.

Table 4.12 ^{13}C NMR chemical shifts (ppm) and coupling data (Hz) for **10-12**[a]

	10	**11**	**12**
C-1	166.63	166.61	164.77
C-2	168.02	168.10	168.88
C-3	123.07	123.12	123.18
C-4	156.62	156.84	156.92
C-5	107.35	107.30	107.54
C-6	133.47	133.35	133.52
C-7	124.03	124.09	124.14
C-8	127.94	127.09	128.03
C-9	127.25	127.31	127.39
C-10	129.08	129.10	129.15
C-11	119.36	119.32	119.28
C-12	136.17	136.25	136.68
C-α	5.35 [593.75][d]	25.83 [563]	141.96 [865.38][d]
C-β	-	27.42 [31]	135.85 [56.25][e]
C-γ	-	26.46 [89]	128.74 [81.75][f]
C-δ	-	13.54	130.08 [16.5][g]

[a] Spectra recorded in $CDCl_3$ solution, downfield to TMS.

[b] Refer to the Fig. shown below for the numbering scheme in the ligand



[c] Refer to Table 4.11 for numbering scheme in the Sn-R skeleton.
[d] $^1J(^{119}Sn - ^{13}C)$ in Hz.
[e] $^2J(^{119}Sn - ^{13}C)$ in Hz.
[f] $^3J(^{119}Sn - ^{13}C)$ in Hz.
[g] $^4J(^{119}Sn - ^{13}C)$ in Hz.

Important information relating to the structure of coordination polyhedron of dimethyltin and di-*n*-butyltin(IV) complexes are obtained from the values of coupling

constants $^{1}J(^{119}Sn-^{13}C)$ because they are directly linked to the size of the C-Sn-C angle (θ) according to the literature reports [177,178]. For **1**, using Lockhart-Manders' equation [177] a C-Sn-C angle of 129.02° was calculated (Table 4.13) which is in reasonable agreement with the angle observed in the solid state by X-ray study.

Table 4.13 C-Sn-C angles (°) calculated from NMR parameters

Complex	$^{1}J(^{119}Sn-^{13}C)$	C-Sn-C angles (°)
1	595.9	129.02
2	562.5	131.38
4	593.1	128.78
5	557.6	130.93
7	592.9	128.76
8	558.1	130.97
10	593.7	128.83

[a] C-Sn-C angles (°) calculated from $^{1}J(^{119}Sn-^{13}C)$.

The ^{119}Sn NMR data of **1-9** were recorded in $CDCl_3$ solution (Table 4.14). All of the spectrum displayed a sharp singlet. The number of signals observed and the value of chemical shifts $\delta(^{119}Sn)$ confirm the chemical composition of the investigated complexes. The observed ^{119}Sn shifts are indicative of penta-coordination [103, 176-178] around the tin atom in these complexes. A five-coordinated di-*n*-butyltin(IV) compound according to previous reports [178-180] can be characterized by chemical shifts $\delta(^{119}Sn)$ between -90 to -190 ppm .The chemical shift $\delta(^{119}Sn)$ values of -120.2 ppm and -116.4 ppm for **2** and **5** respectively are thus, indicative of five-coordinated di-*n*-butyltin(IV) compounds. In the diphenyltin derivatives (**3**, **6** and **9**), the ^{119}Sn signal lies as usual [181] at lower frequencies than the respective dimethyltin derivatives.

Table 4.14 ^{119}Sn NMR chemical shifts (ppm) for **1-9**[a]

Complex	^{119}Sn
1	–102.5
2	-120.2
3	–232.4
4	–98.0
5	-116.4
6	–229.4
7	-98.1
8	n.m.[b]
9	–229.3

[a] Spectra recorded in $CDCl_3$ solution.

[b] n.m. = not measured.

4.4.3.1.3 Electronic Spectra

Visible spectra of selected compounds are recorded in Table 4.15. As expected in the visible region the electronic spectra showed one broad absorption of medium intensity.

4.4.3.1.4 Study of Fluorescence properties

Fluorescent spectra of selected compounds are recorded in Table 4.16. The yellow colour is due to the n-π* transition of the thiosemicarbazide chromophore. Interestingly, the compounds are fluorescent under ordinary conditions of visible light. At this time it is difficult to conclusively indicate what the origin of this property is. However, in future, detailed studies would be undertaken.

Table 4.15 Electronic absorption spectra of organotin(IV) compounds recorded in methanol solution

Complex	λ_{max} (nm)
1	392
2	393
3	390
4	405
5	407
6	403
7	397
9	398
10	409
11	410
12	412

Table 4.16 Fluorescence data of selected compounds recorded in methanol solution

	Excitation (nm)	Emission (nm)
1	451.4	489.5
2	357.0, 451.4	491.3
3	308.0, 357.0, 445.9	487.7
4	373.3, 455.0	494.7
6	318.2, 366.1, 455.0	498.6
7	373.2, 459.6	490.3
9	311.6, 366.1, 453.2	493.1

4.4.3.1.5 X-ray Crystal Structures

This section deals with the X-ray crystallographic studies of diorganotin(IV) complexes of the type R_2SnL (R=Me and Ph) where L is the dianion derived from salicylaldehyde/ substituted salicylaldehyde thiosemicarbazones (L^1HH'-L^3HH'). In the present study efforts were undertaken to obtain single crystals for the X-ray analysis of the diorganotin derivatives of the ligands described above in Scheme 4.3. Compounds **1**, **3**, **4**, **6** and **9** provided single crystals suitable for the X-ray crystal structure determination .The crystal structures of all these complexes are described below.

It should be noted that during the progress of this work the author became aware of a few reports of closely related studies [102,103,161] where some organotin(IV) complexes of semi- and thiosemicarbazones, along with the compounds **1-3** (Scheme 4.3), were described as well as their molecular structures [102,103]. The author has included her data on the same compounds herein to allow comparison of their biocidal properties with the corresponding Cl/Br-substituted ligands. Further, those compounds were synthesized via a different route as reported here, requiring shorter reaction times and giving higher yields. In addition, full details of their supramolecular structures (which were not reported earlier in [102,103]) are reported as well as a correlation of geometric parameters with those of halide congeners.

4.4.3.1.5.1 Crystal structure of [Me_2SnL^1] (1)

The author could successfully isolate X-ray quality single crystal of **1** from the benzene solution of the compound. The molecular structure of **1** along with the crystallographic numbering scheme is given in Fig. 4.24. The crystal data and structural refinement parameters are presented in section 4.3 (Table 4.1).The selected bond lengths and bond angles are given in Table 4.17. The compound **1** crystallizes into a monoclinic lattice with $P2_1/n$ space group. The structure of **1** features a five-coordinate tin atom coordinated by the S1, O1 and N3 atoms of the tridentate ligand as well as two methyl groups.

The overall coordination geometry is based on a trigonal bipyramid with the S1 and O1 defining the axial positions. Distortions from the ideal geometry may be traced to the restraints imposed by the chelate rings. An examination of the geometric parameters indicates that the structure conforms to the generic structure shown in Scheme 4.3, with no evidence of tautomerism. The molecular geometries of the remaining structures of **3**, **4**, **6** and **9** are in essential agreement with that just described and are in agreement with previous literature reports of **1** and **3** [103], but have been determined to a higher level of precision.

Table 4.17 Selected bond distances (Å) and angles (°) for $[Me_2SnL^1]$ **(1)**

	1
Sn–S1	2.540(1)
Sn–O1	2.105(2)
Sn–N3	2.196(2)
C1–S1	1.729(2)
C1–N1	1.334(3)
C1–N2	1.315(3)
N2–N3	1.388(3)
S1–Sn–O1	158.44(5)
S1–Sn–N3	77.01(5)
O1–Sn–N3	81.74(7)
C9–Sn–C10	127.3(1)
C9–Sn–C15	-

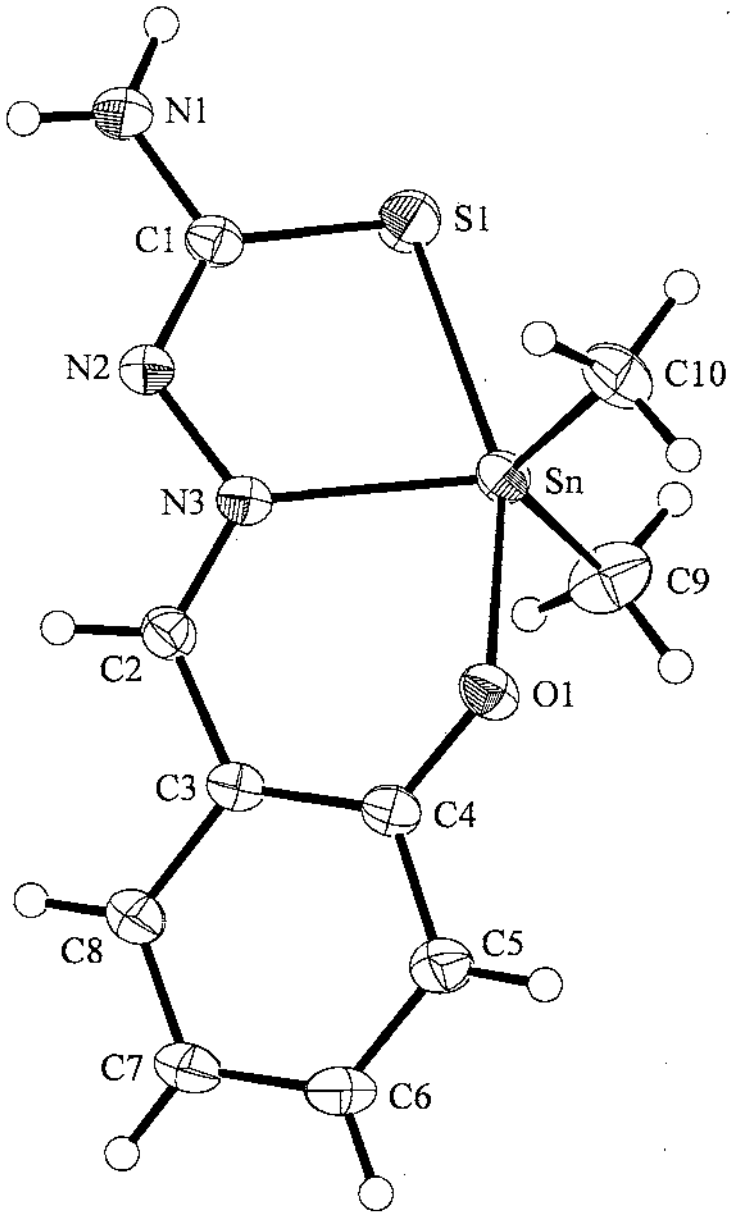
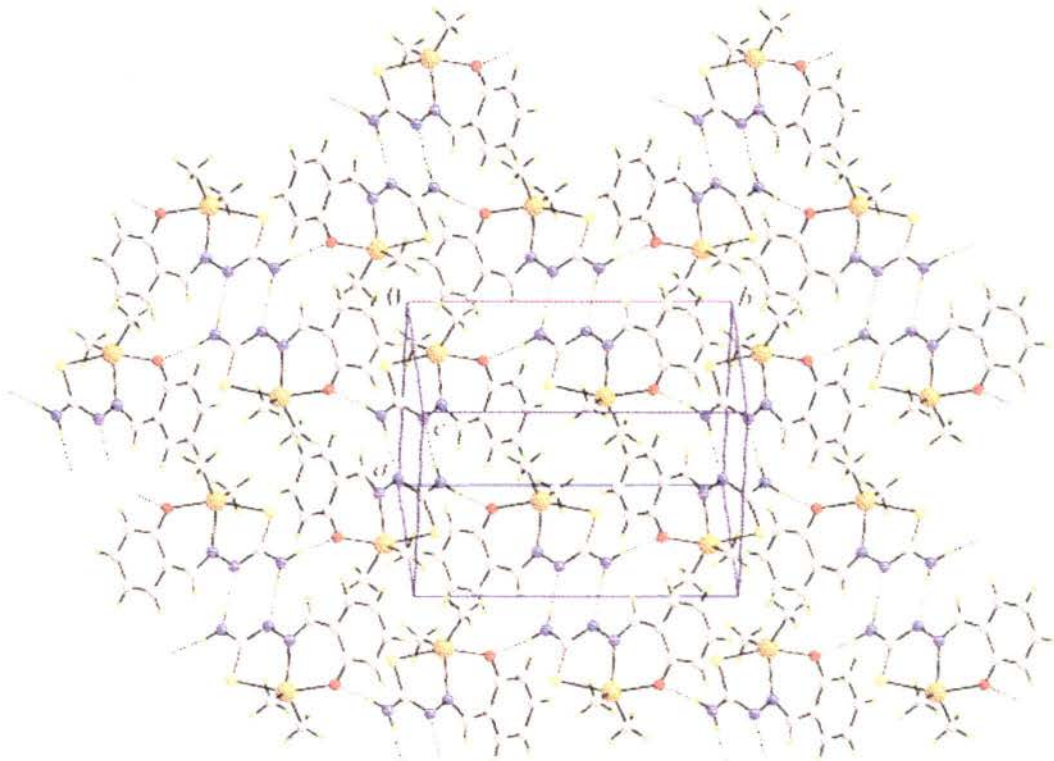


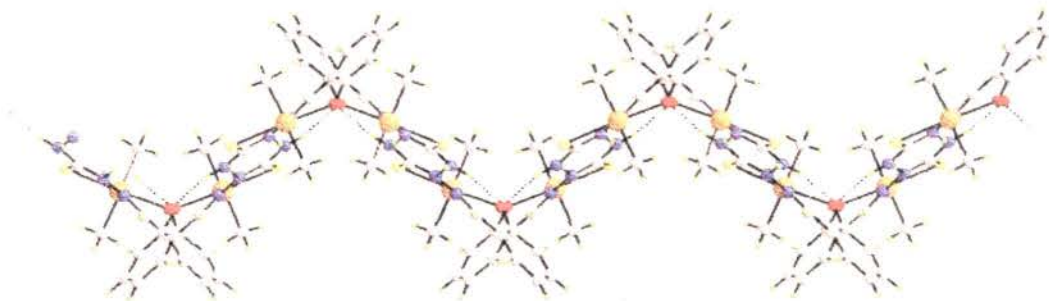
Fig.4.24 Molecular structure and crystallographic numbering scheme for $[Me_2SnL^1]$ (**1**).

In the crystal structure of $[Me_2SnL^1]$ (**1**), N–H...O hydrogen bonding interactions lead to a chain along the *b*-axis and these were connected to neighbouring chains by N–H...N hydrogen bonds via eight-membered $\{N–C–N–H\}_2$ synthons to form a 2D array that had a zig-zag topology as highlighted in Fig. 4.25. The geometric parameters defining these interactions and those found in the remaining structures are listed in Table 4.22.

(a)



(a)



(b)

Fig. 4.25 Crystal packing in $[Me_2SnL^1]$ (**1**): (a) unit cell contents showing hydrogen bonding as dashed lines and (b) the zig- zag topology for the two-dimensional array.

4.4.3.1.5.2 Crystal structure of [Ph_2SnL^1] (3)

The author could successfully isolate X-ray quality single crystal of **3** from the petroleum ether (b.p. 60-80 °C) solution of the compound. The compound **3** crystallizes into a monoclinic lattice with $P2_1/c$ space group. The molecular structure of **3** along with the crystallographic numbering scheme is given in Fig. 4.26. The crystal data and structural refinement parameters are presented in section 4.3 (Table 4.2).The selected bond lengths and bond angles are given in Table 4.18.

The structure of **3** also features a five-coordinate tin atom surrounded by S1, O1 and N3 atoms of the tridentate ligand as well as two phenyl groups. As stated above, the molecular geometry of **3** is in essential agreement with previous literature report of the molecular structure of **3** [103], but has been determined to a higher degree of precision.

Table 4.18 Selected bond distances (Å) and angles (°) for [Ph_2SnL^1] **(3)**

	3
Sn–S1	2.546(1)
Sn–O1	2.067(2)
Sn–N3	2.191(2)
C1–S1	1.738(3)
C1–N1	1.349(3)
C1–N2	1.298(3)
N2–N3	1.387(3)
S1–Sn–O1	161.31(6)
S1–Sn–N3	77.94(5)
O1–Sn–N3	84.22(7)
C9–Sn–C10	-
C9–Sn–C15	127.24(9)

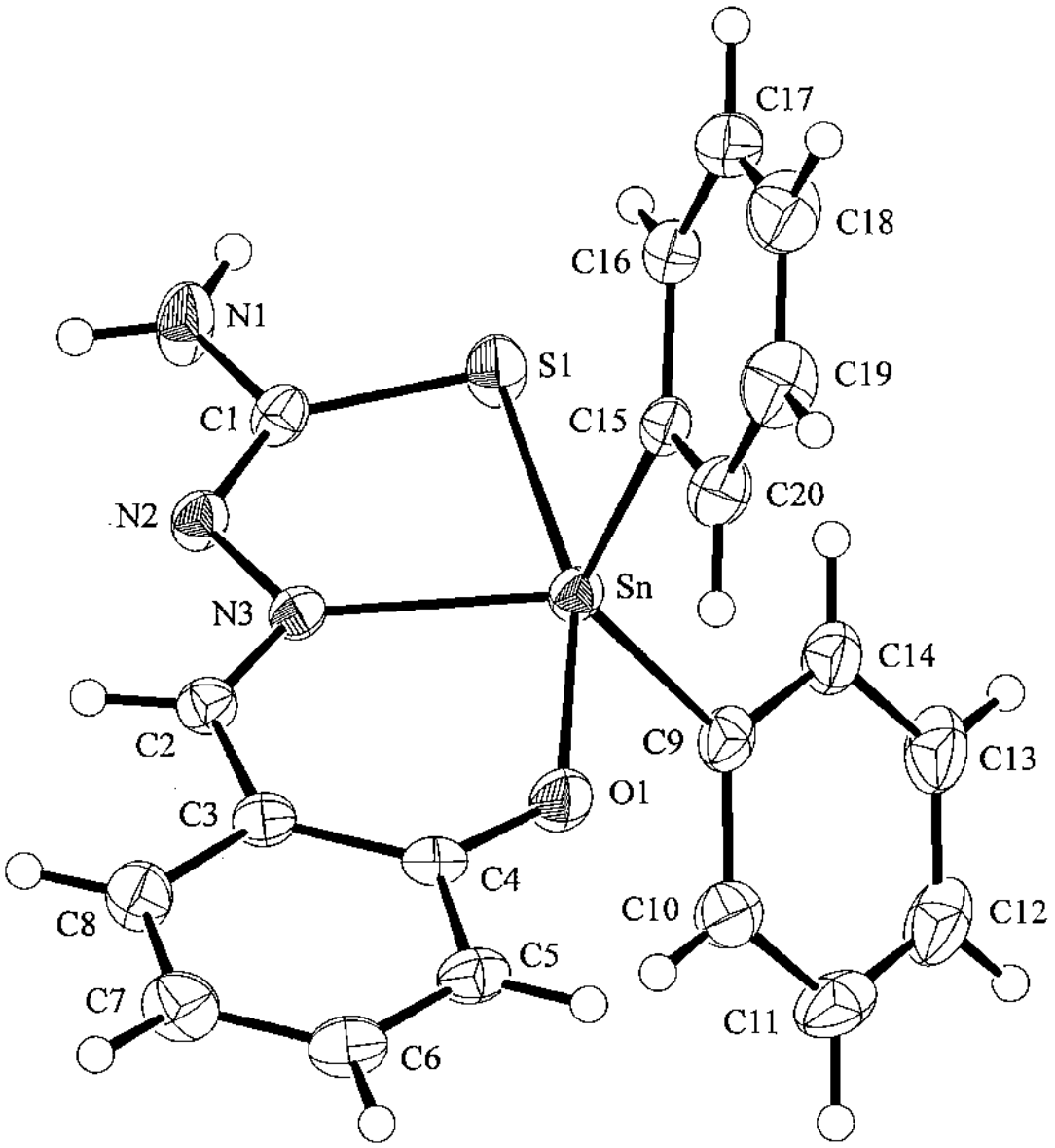


Fig. 4.26 Molecular structure and crystallographic numbering scheme for $[Ph_2SnL^1]$ (**3**).

The presence of tin-bound phenyl rings in $[Ph_2SnL^1]$ (**3**) had a profound influence upon the supramolecular aggregation pattern as the oxygen atom now formed an intramolecular C–H...O interaction that precluded its further association in the crystal structure. The global crystal packing may be described as being comprised of double layers of molecules that are connected via $\{S–C–N–H\}_2$ synthons as shown in

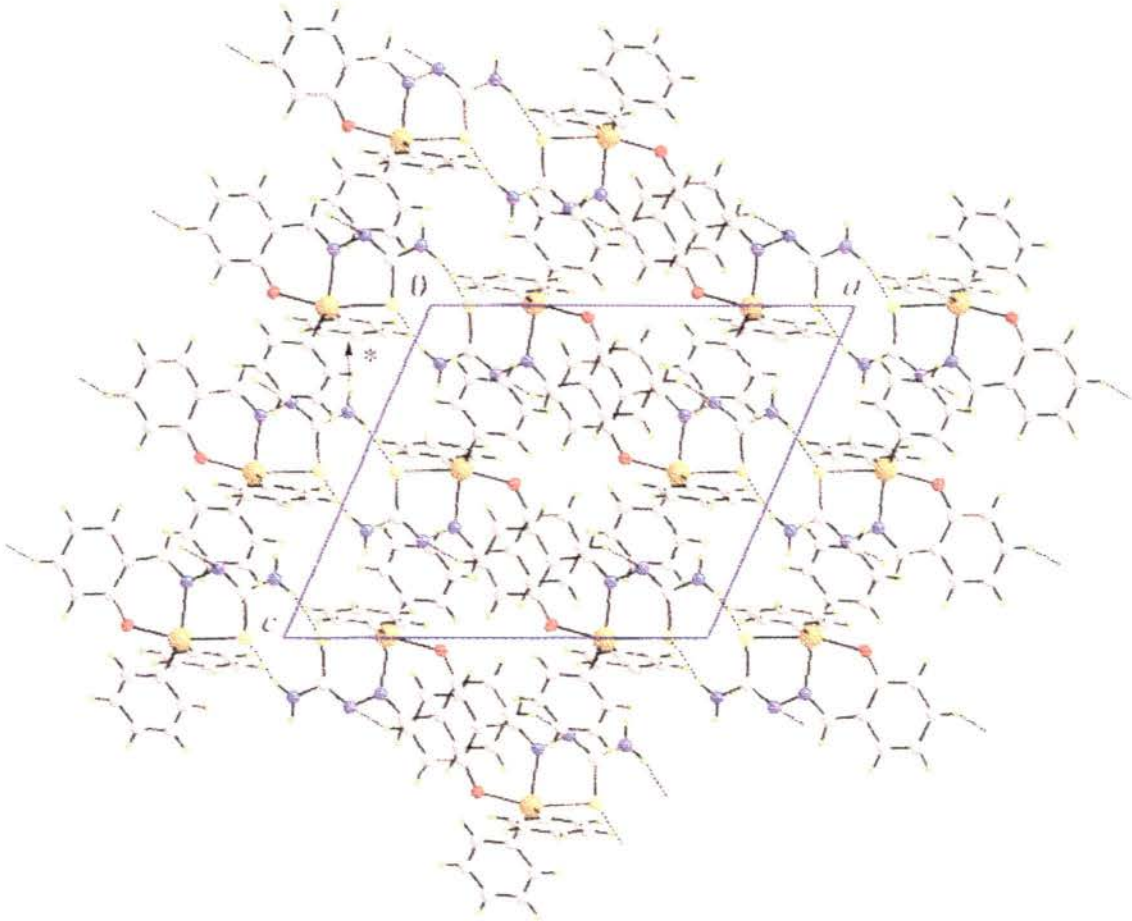


Fig. 4.27 View of the unit cell content of $[Ph_2SnL^1]$ (**3**) along the *b*-axis.

Fig. 4.27. The remaining N–H atom participates in N–H...π interactions with tin-bound phenyl groups: an example is marked with an asterisk in Figure 4.27. Finally, the imine-N2 atom participates in a C–H...N interaction and thereby contributes to the stability of the aforementioned double layer.

4.4.3.1.5.3 Crystal structure of $[Me_2SnL^2].H_2O$ (4)

Single crystals suitable for X-ray diffraction of the compound $[Me_2SnL^2].H_2O$ were grown by slow evaporation of the petroleum ether (b.p. 60-80 °C) solution of the compound. The structure of the molecule with atom numbering scheme is given in Fig. 4.28. The structural refinement parameters are described in section 4.3 and the selected bond distances and bond angles are given in Table 4.19. The compound **4** crystallizes into a monoclinic lattice with *C*2/c space group. The structure of $[Me_2SnL^2]$ (**4**) was isolated as a monohydrate and the water molecule plays a pivotal role in the crystal packing.

Table 4.19 Selected bond distances (Å) and angles (°) for $[Me_2SnL^2].H_2O$ (**4**)

	4
Sn–S1	2.510(1)
Sn–O1	2.103(2)
Sn–N3	2.250(3)
C1–S1	1.731(4)
C1–N1	1.339(4)
C1–N2	1.311(4)
N2–N3	1.382(3)
S1–Sn–O1	147.91(7)
S1–Sn–N3	76.92(7)
O1–Sn–N3	80.98(9)
C9–Sn–C10	118.5(2)
C9–Sn–C15	-

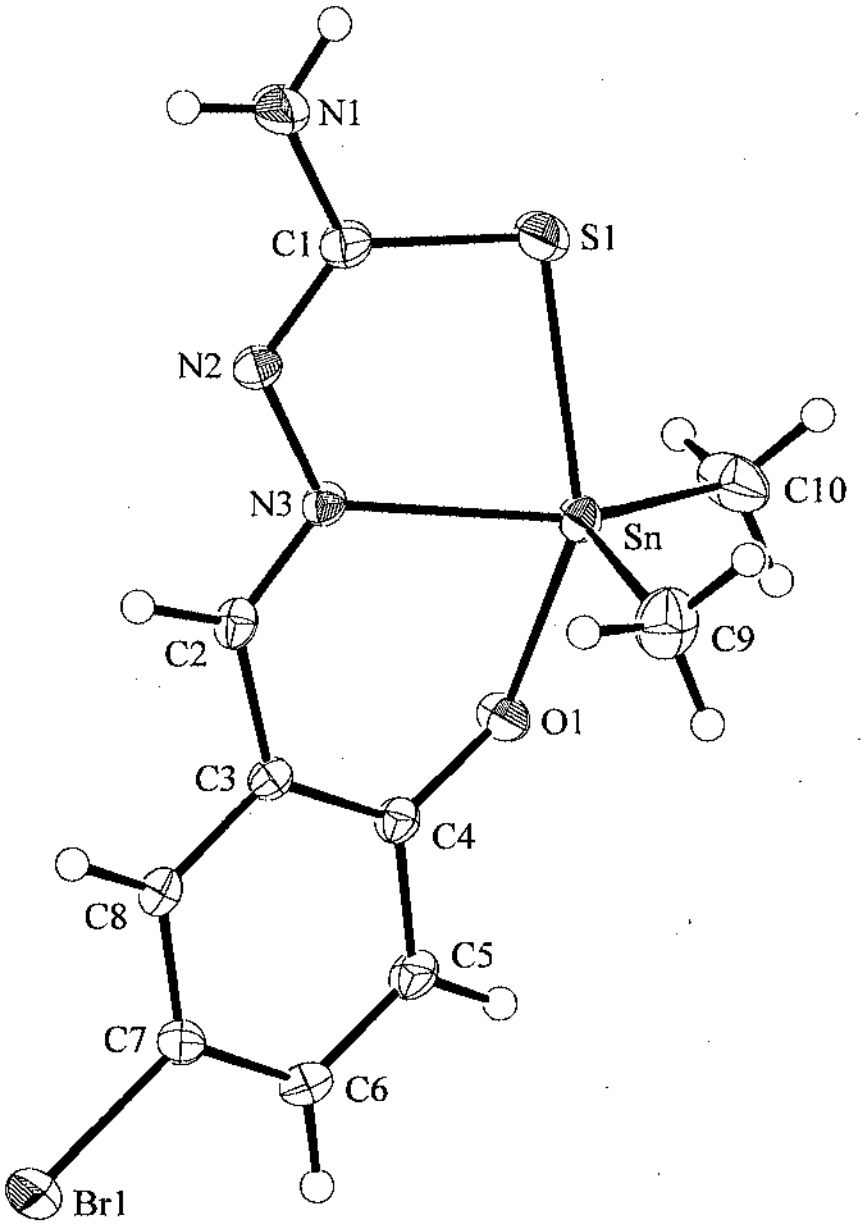


Fig. 4.28 Molecular structure and crystallographic numbering scheme for $[Me_2SnL^2].H_2O$ (**4**). Water molecule of crystallization is omitted.

Centrosymmetric molecules of **4** associate via the eight-membered $\{N–C–N–H\}_2$ synthon seen in compound **1**. These dimers are then linked into chains via a N1–H1b...O2–H1w...O1 sequence of hydrogen bonds and these chains are finally linked via weaker O–H...O hydrogen bonds involving the water molecules exclusively. As seen from the view in Figure 4.29, this arrangement resulted in the formation of narrow channels aligned along the *c*-axis.

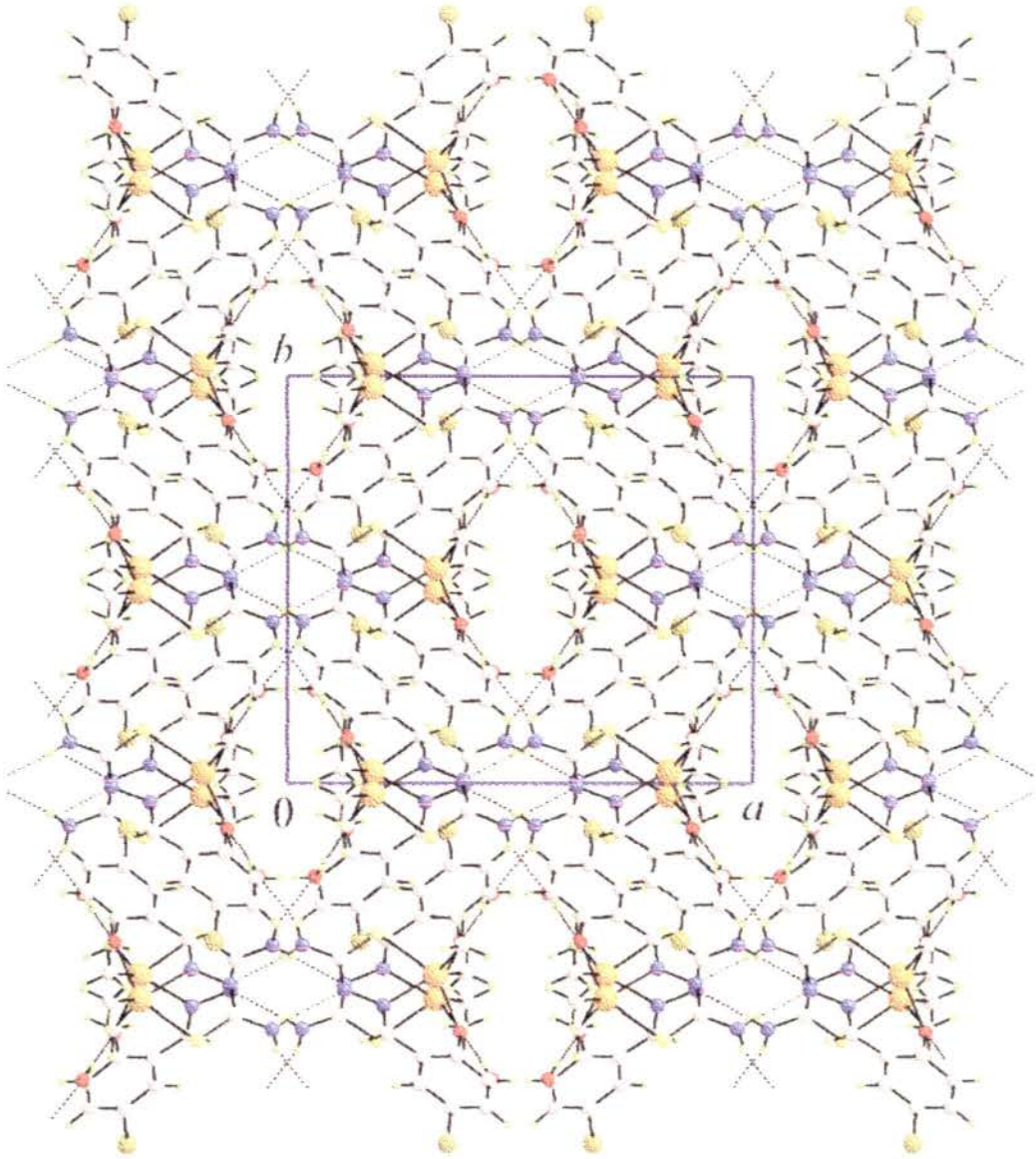


Fig. 4.29 View of the unit cell content of $[Me_2SnL^2].H_2O$ (**4**) along the *c*-axis.

4.4.3.1.5.4 Crystal structure of $[Ph_2SnL^2]$ 6 and $[Ph_2SnL^3]$ 9

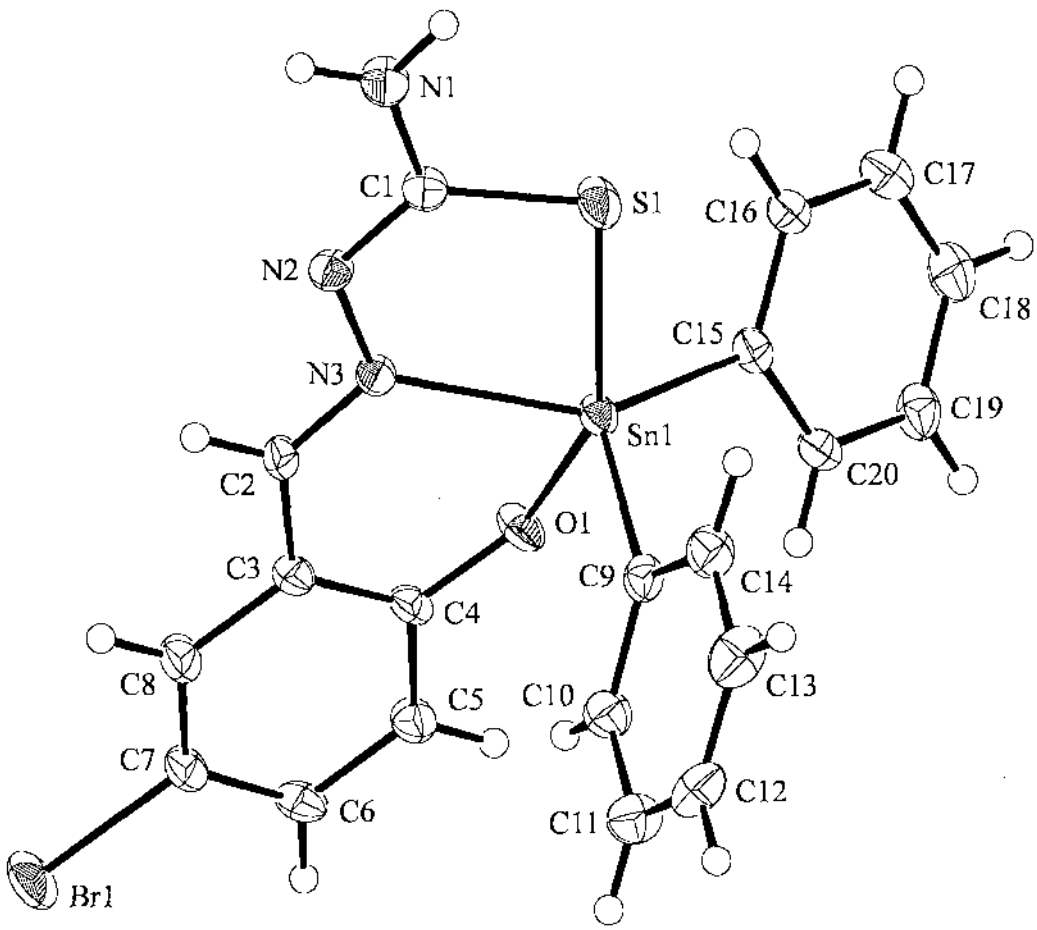
Suitable X-ray quality single crystals of diphenyl tin derivatives of 5-bromosalicylaldehyde thiosemicarbazone $[Ph_2SnL^2]$ **6** and 5-chlorosalicylaldehyde thiosemicarbazone $[Ph_2SnL^3]$ **9**, were obtained from petroleum ether (b.p. 60-80 °C) solution of **6** and **9** respectively, by slow evaporation of the solvent at room temperature. The molecular structure of **6** and **9** along with their crystallographic numbering scheme are given in Fig. 4.30 and Fig.4.32 respectively. The crystal data and structural refinement parameters of **6** and **9** are presented in Table 4.4 and 4.5 respectively (section 4.3). The selected bond lengths and bond angles of **6** and **9** are given in Table 4.20 and 4.21 respectively. Both the complexes crystallize into triclinic lattice with *P*-1 space group.

Table 4.20 Selected bond distances (Å) and angles (°) for $[Ph_2SnL^2]$ **(6)**

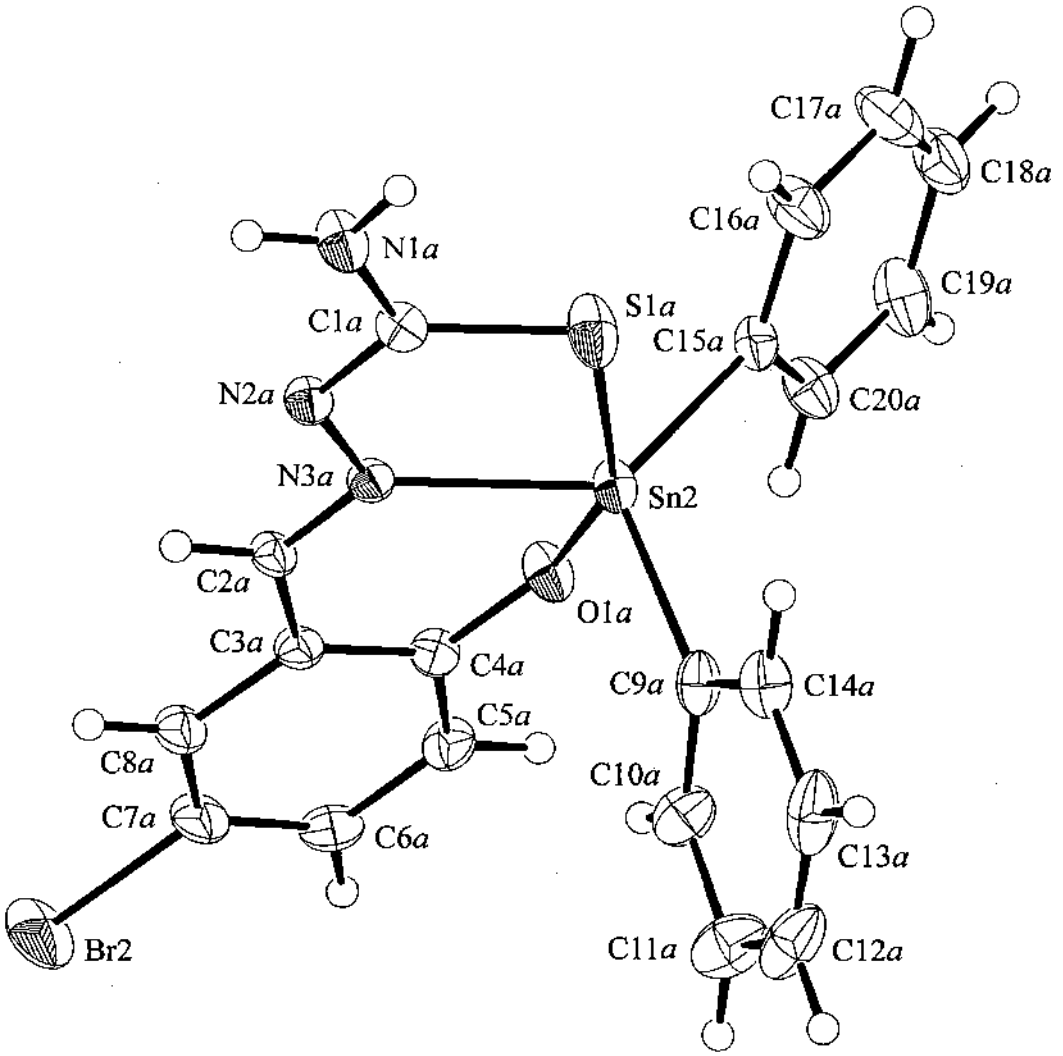
	6 (a, b)
Sn–S1	2.494(1), 2.510(1)
Sn–O1	2.061(3), 2.071(3)
Sn–N3	2.265(3), 2.250(3)
C1–S1	1.740(4), 1.740(5)
C1–N1	1.350(5), 1.335(6)
C1–N2	1.313(5), 1.320(5)
N2–N3	1.388(5), 1.381(5)
S1–Sn–O1	150.1(1), 155.3(1)
S1–Sn–N3	77.11(9), 77.22(9)
O1–Sn–N3	80.8(1), 81.4(1)
C9–Sn–C10	-

Two independent molecules comprise the crystallographic asymmetric unit of **6** that differ from each other only in terms of minor conformational changes and the way they interact in the crystal structure (see below). The availability of a series of structures allows for the discernment of a number of trends in geometric parameters. From Table 4.20, it is evident that the inclusion of a halide substituent, i.e. chloride or

bromide, at the C7 position results in significant stronger Sn-S bonds with concomitant weakening of the Sn-N3 bonds and greater deviation of the axial angle from 180°. A systematic variation in the Sn-O1 bond is also apparent in that this bond is shorter in the dimethyltin derivatives compared with the diphenyltin species. The presence of hydrogen bond donors and acceptors in each of the structures lead to a variety of supramolecular arrays and these are discussed in turn below.



(a)



(b)

Fig. 4.30 Molecular structure and crystallographic numbering scheme for the two independent molecules comprising the asymmetric unit of $[Ph_2SnL^2]$ (**6**).

Eight-membered $\{N–C–N–H\}_2$ synthons are the dominant intermolecular interactions found in the crystal structure of $[Ph_2SnL^2]$ (**6**) and these occur between the two independent molecules comprising the asymmetric unit; these interactions are emphasized in Fig. 4.31. Each of the remaining amine-H atoms is involved in an N–H...π interaction but rather than interacting with a ring system, each was orientated towards the C19–C20 bond of the other molecule comprising the dimer. Again, the oxygen atoms are shielded from forming intermolecular interactions owing

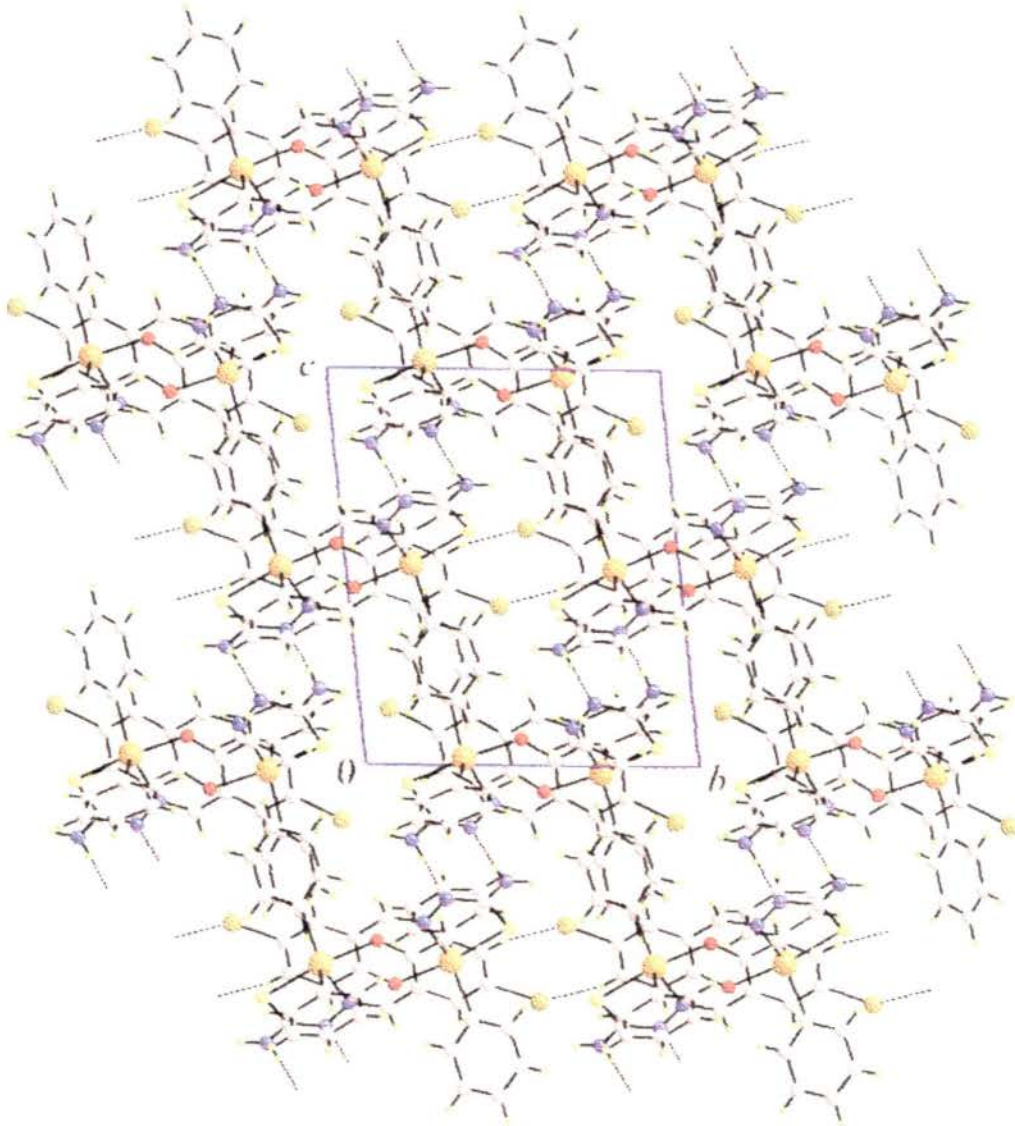


Fig. 4.31 View of the unit cell content of $[Ph_2SnL^2]$ (**6**) down the *a*-axis.

to the presence of intramolecular C–H...O interactions. The remaining interactions of note are of the type C–H...Br, with the closest of these involving each independent bromide atom listed in Table 4.22; those involving the Br2 atom are shown in Fig. 4.31. Finally, C–H...π contacts involving phenyl rings is noted.

Although not isomorphous, the crystal packing found in $[Ph_2SnL^3]$ (**9**) is similar to that just described for **6**. Hence, the $\{N–C–N–H\}_2$ synthon is present and these are connected to neighbouring molecules via N1–H1b...πC19–C20 interactions. In this way, chains are formed which are linked via C–H...Cl interactions. Two rows of chloride atoms align along the *a*-axis and interdigitate with each other, forming two C–H...Cl contacts with molecules of the opposite row and resulting in the formation of a double zig-zag ribbon.

Table 4.21 Selected bond distances (Å) and angles (°) for $[Ph_2SnL^3]$ (**9**)

	170 A
Sn–S1	2.500(1)
Sn–O1	2.065(2)
Sn–N3	2.250(3)
C1–S1	1.732(4)
C1–N1	1.340(4)
C1–N2	1.312(4)
N2–N3	1.394(3)
S1–Sn–O1	152.28(8)
S1–Sn–N3	77.40(7)
O1–Sn–N3	80.92(9)
C9–Sn–C10	-
C9–Sn–C15	118.7(1)

The geometric parameters defining intermolecular interactions operating in the crystal structure of **6** and **9** are presented in Table 4.22.

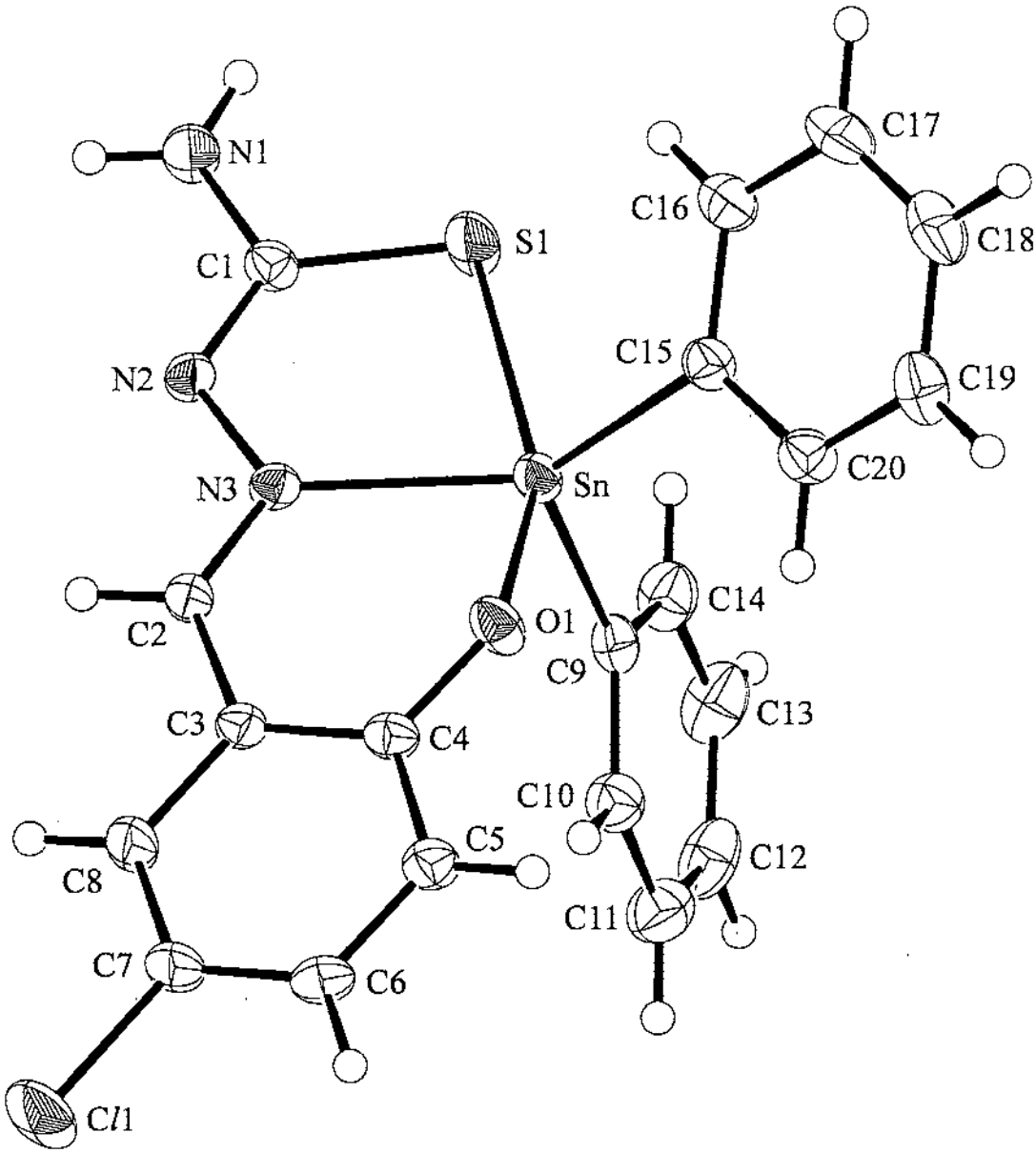


Fig. 4.32 Molecular structure and crystallographic numbering scheme for [Ph_2SnL^3] (**9**).

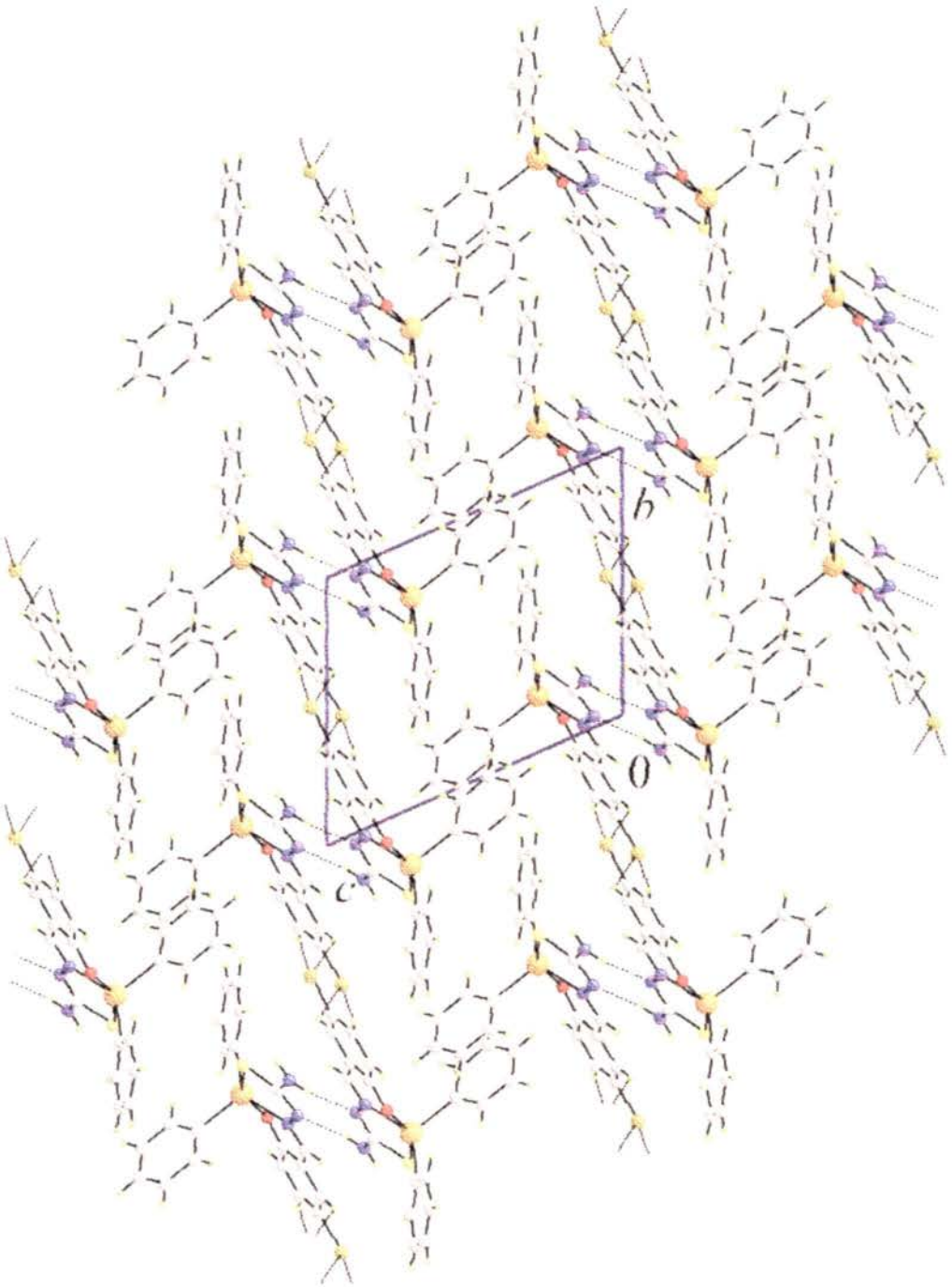


Fig. 4.33 View of the unit cell content of $[Ph_2SnL^3]$ (**9**) down the *a*-axis.

Table 4.22 Summary of intermolecular interactions (A–H...B; Å, °) operating in the crystal structures of $[Me_2SnL^1]$ (**1**), $[Ph_2SnL^1]$ (**3**), $[Me_2SnL^2].H_2O$ (**4**), $[Ph_2SnL^2]$ (**6**) and $[Ph_2SnL^3]$ (**9**)

	A	H	B	H...B	A...B	A–H...B	Symmetry operation
1	N1	H1b	O1	2.03	2.866(3)	162	½–*x*, –½+*y*,
	N1	H1a	N2	2.11	2.982(3)	176	1–*x*, –*y*, 1–*z*
3	N1	H1b	S1	2.77	3.507(3)	143	–*x*,–*y*,–*z*
	N1	H1a	Cg(C15–C20)[a]	2.59	3.445(3)	167	*x*, ½–*y*, ½+*z*
	C6	H6	N2	2.55	3.345(4)	143	1–*x*, ½+*y*, ½–*z*
4	N1	H1a	N2	2.23	3.102(4)	177	1–*x*, –*y*, –*z*
	N1	H1b	O2	2.18	2.979(4)	152	½+*x*, ½+*y*, *z*
	O2	H1w	O1	1.97	2.805(4)	177	*x*, *y*, *z*
	O2	H2w	O2	2.51	2.809(4)	102	–*x*, *y*, ½–*z*
6	N1	H1a	N2a	2.24	3.099(6)	168	–1–*x*, –*y*, –*z*
	N1a	H1a	N2	2.29	3.161(6)	174	–1–*x*, –*y*, –*z*
	C8	H8	Br1	3.03	3.628(5)	123	–*x*, 1–*y*, –*z*
	C6	H6	Br2	2.95	3.858(4)	163	–*x*, 1–*y*, 1–*z*
	C17	H17	Cg(C3a–C8a)[a]	2.88	3.576(7)	132	*x*, *y*, *z*
9	N1	H1a	N2	2.25	3.112(5)	173	1–*x*, –*y*, –*z*
	C8	H8	Cl	2.93	3.618(5)	131	–*x* 1–*y*, –*z*
	C6	H6	Cl	2.95	3.883(4)	169	1–*x* 1–*y*, –*z*

[a] Cg = centroid of indicated aromatic ring

4.4.4 Synthesis, spectroscopic characterization and X-ray crystallography of dibenzyltin(IV) derivatives of salicylaldehyde thiosemicarbazones

4.4.4.1 Synthesis and spectroscopic characterization of dibenzyltin(IV) derivatives of salicylaldehyde thiosemicarbazones *($L=L^1$ and L^3)*

The dibenzyltin derivatives (**13** and **14**) of salicylaldehyde thiosemicarbazones ($L = L^1$ and L^3) were obtained in 30-40% yields by the reaction of sodium salt of the respective salicylaldehyde thiosemicarbazone ligands with Bz_2SnCl_2.The products obtained were poorly soluble in the common organic solvents. This led to the technical difficulty of recording the NMR spectra of these compounds. The ^1H NMR spectral data were recorded and these provided some information about the chemical shifts of the different protons present indicating the binding of the ligand to the dibenzyltin moieties. Due to very poor signal-to-noise ratio in the ^{13}C NMR spectra of these complexes no substantial information could be obtained from these. IR spectra were recorded for these compounds.

4.4.4.1.1 Dibenzyltin(IV) salicylaldehyde thiosemicarbazonate (13)

Yellow crystals of **13** were isolated from benzene and dried in vacuo. Yield : 35%, M.p. 118-120 °C, IR (cm^{-1}): $\nu(NH_2)_{asym}$, 3400-3280 (b,w); $\nu(NH_2)_{sym}$, 3162 (w); ν(C=N-N=C), 1650 (m); $\nu(C=N)_{thio}$, 1600 (s); ν(C-O), 1209 (m); ν(C-S), 1035(m); ν(S-C-N), 761 (w). ^1H NMR: Ligand skeleton (see Table 4.9 for numbering scheme in the ligand skeleton): H-1, 5.17 (s, 2H); H-2 , 8.46 (s, 1H); H-5, 6.85-6.77 (d, 1H); H-6, 7.25 (m, 1H); H-7, 6.56 (m, 1H); H-8, 7.14-7.08 (d, 1H); Sn-benzyl skeleton: Sn-CH_2 , 2.17 (s, 4H); Ring protons, 7.25 (m, 10H).

4.4.4.1.2 Dibenzyltin(IV) derivative of 5-chlorosalicylaldehyde thiosemicarbazone Bz_2SnL^1 (14)

Yellow prism-shaped crystals of **14** were obtained from repeated recrystallization from methanol solution [36]. Yield: 30%, M.p. 144-146 °C, IR(cm^{-1}): $\nu(NH_2)_{sym}$,

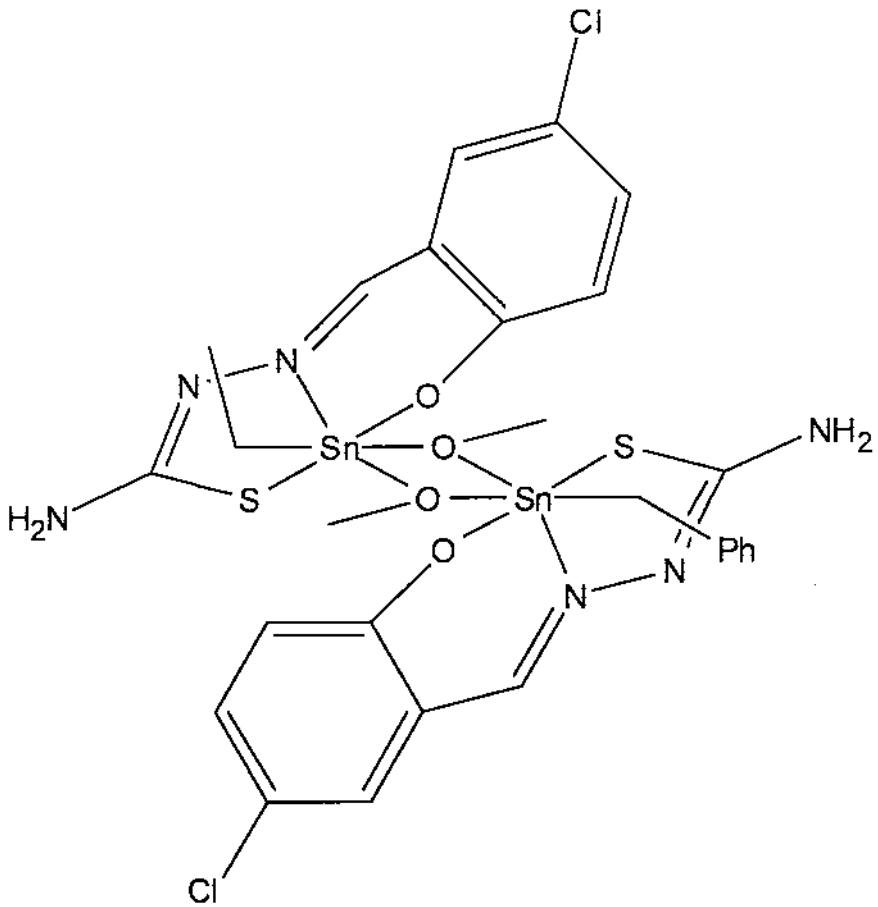
3285(m); ν(C=N-N=C), 1619 (s); $\nu(C=N)_{thio}$, 1596 (s); ν(C-O), 1184 (m); ν(C-S), 996 (w); ν(C-S-N), 754 (w).). ^{1}H NMR: Ligand skeleton (see Table 4.9 for numbering scheme in the ligand skeleton): H-1, 5.10 (s,2H); H-2 , 8.45 (s,1H); H-5,6, 7.05-6.75 (m, 2H) H-8, 7.21 (s,1H); Sn-benzyl skeleton: Sn-CH_2 , 1.63 (s, 4H), Sn-OCH_3 (see Fig. 4.34), 3.48 (s, 6H); Ring protons, 7.30 (m, 8H).

Both the NMR and TGA analysis indicates the presence of OMe group in **14.14** was obtained as a result of debenzylation of an authenticated sample of $(PhCH_2)_2SnL^3$, where L^3H_2 is *p*-chlorosalicylaldehyde thiosemicarbazone, from a methanol solution. Debenzylation reactions are well documented in literature [182-184].It should be noted that in all the debenzylation reactions the final product still contains one benzyl group on tin [182], as is observed in this case too.Heterolytic cleavage of a Sn-C bond has been reported to occur with basic nucleophilic agents [185]. Sometimes, solvent may be the strongest nucleophile present [186]. In presence of polar nucleophilic solvents such as methanol or acetic acid the nucleophilic assistance is rendered by coordination of the solvent to the tin atom thereby increasing the polarity of Sn-C bonds [187] and hence facilitating debenzylation.

The debenzylation reaction observed in this case is remarkably facile taking place even during recrystallization. This is presumably mediated by traces of water in the solvents [188] or may be due to methanol which is rendering nucleophilc assistance at tin.

*4.4.4.2 Crystal Structure of di-μ_2-methoxo-bis[benzyl{5-chloro-2-oxido-benzaldehyde -thiosemicarbazonato}tin(IV)] [$Sn(Bz)_2(C_8H_6ClN_3OS)_2(CH_3O)_2$] **(14)***

Di-μ_2-methoxo-bis[benzyl{5-chloro-2-oxido-benzaldehydethiosemicarbazonato} tin(IV)] was isolated as yellow prisms from the attempted recrystallization of an authenticated sample of $(PhCH_2)_2SnL^3$ where L^3H_2 is *p*-chlorosalicylaldehyde thiosemicarbazone, from a methanol solution.



(14)

The crystal structure analysis showed a centrosymmetric molecule (Fig. 4.34) in which two $(PhCH_2)Sn$ entities were symmetrically bridged by two methoxide ligands (Table 4.23). The distorted octahedral coordination geometry for tin was completed by N-, O- and S-donor atoms derived from the dinegative and tridentate L^{2-} ligand. Distortions from ideal geometry may be traced to the strain found in the centrosymmetric Sn_2O_2 core and chelate rings [36].

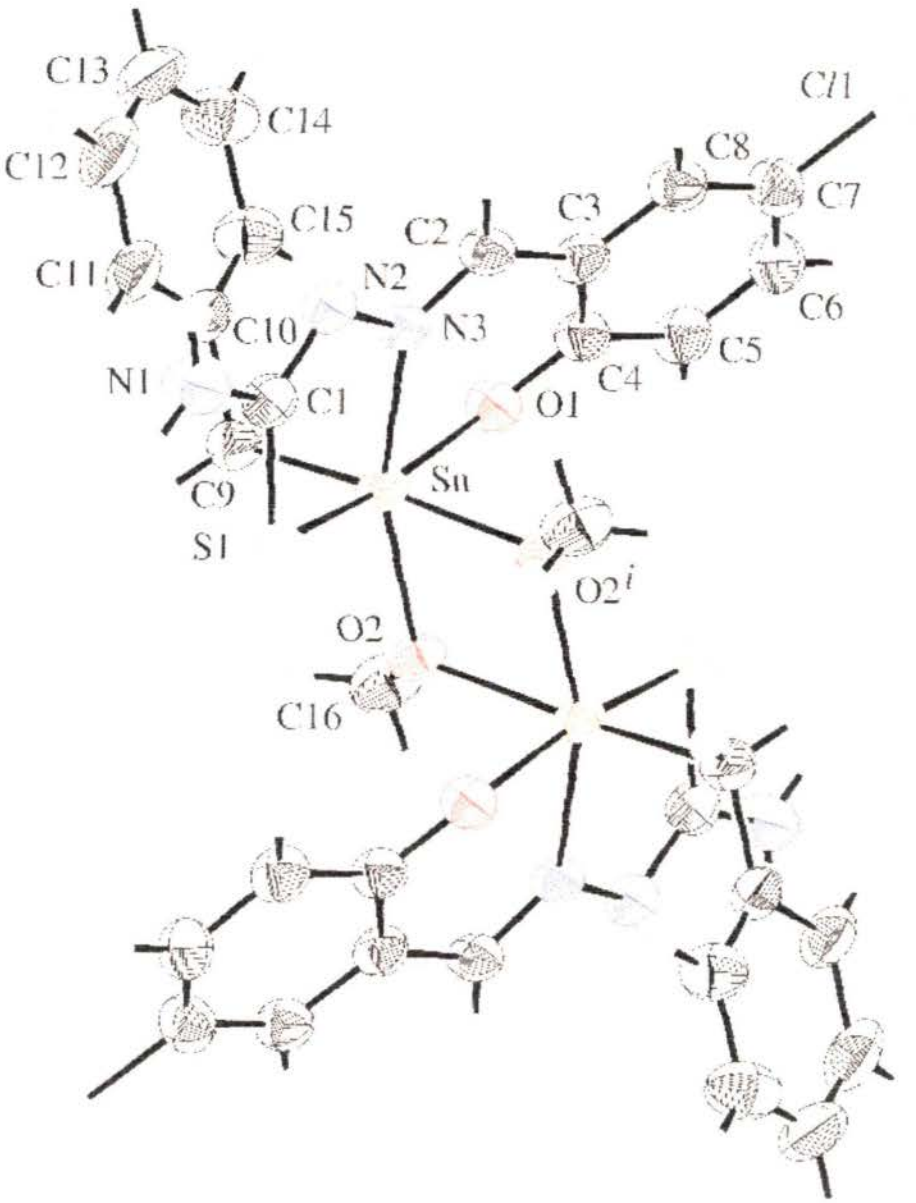


Fig.4.34 The molecular structure and atom-labelling scheme for **14**, showing 50% probability displacement ellipsoids [Symmetry code : (i) x , y , z].

Table 4.23 Selected geometric parameters (Å, ^{0}) of **14**

Sn-S1	2.1915(16)	O1-C1	1.326(6)
Sn-N3	2.221(4)	O2-C16	1.430(6)
Sn-O1	2.015(3)	N1-C1	1.343(6)
Sn-O2	2.108(3)	N2-N3	1.388(5)
Sn-O9	2.168(5)	N2-C1	1.317(6)
Sn-O2	2.161(3)	N3-C2	1.289(6)
S1-C1	1.753(5)		
S1-Sn-O1	162.51(9)	O2-Sn-O2	72.16(13)
S1-Sn-O2	99.97(10)	O9-Sn-O2	167.90(16)
S1-Sn-N3	78.35(10)	O9-Sn-N3	103.09(16)
S1-Sn-O9	99.11(15)	N3-Sn-O2	86.36(13)
S1-Sn-O2	89.82(10)	Sn-S1-C1	94.97(18)
O1-Sn-O2	93.59(13)	Sn-O1-C1	126.4(3)
O1-Sn-N3	85.00(13)	Sn-O2-C16	118.9(3)
O1-Sn-C9	89.49(17)	Sn-O2-C16	123.0(3)
O1-Sn-O2	83.75(14)	Sn-O2-Sn	107.54(13)
O2-Sn-N3	158.79(14)	Sn-N3-N2	119.9(3)
O2-Sn-O9	98.05(15)	Sn-N3-C2	124.3(3)

Symmetry code : (i)) $-x, -y, -z$.

Molecules were held in a three-dimensional array by a combination of N–H….N, N–H….π and C–H….π interactions. The hydrogen bonding between N1….H1*A* and N2^{ii} [symmetry code : (ii) $1-x, -y, 1-z$] lead to the formation of chain along [101] (see Fig. 4.35).The parameters associated with these interactions were N1–H1*A*….N2^{ii} – 2.26 Å and N1….N2^{ii} – 3.126 (6) Å with an angle of 169^{o} at H1*A*. While not involved in a conventional hydrogen bonding interaction , the amine

atom H1*B* formed an N-H....π interaction with the ring centroid of the aromatic proton of a tin-bound benzyl residue so that the N1–H1*B*.....ring centroid (C10-C15)^{iii} distance was 2.81 Å with an angle of 176° at H1*B* [symmetry code : (iii) $1-x$, $-1/2+y$, $1/2-z$] : some of these intearactions are highlighted with an '(a)' in Fig. 4.36. The methoxide –bound methyl - H atoms formed C–H....π interactions with the six-membered aromatic ring (C3-C8)^{iv} so that the H....ring centroid distance was 2.66 Å and the angle at H was 1.22° [symmetry code : (iv) x, $1/2-y$, $-1/2+z$], shown as '(b)' in Fig.4.36.

4.5 Biological Properties of diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones

4.5.1 Antibacterial activity

The antibacterial properties of the diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones were evaluated and results are summarized in Table 4.24. It was observed that all the test compounds inhibited bacterial growth to varying extent.

Compound **1** was found to be least potent among the four compounds tested. With the exception of *S. aureus* it had no effect on the different Gram-negative bacteria chosen for the study. However, it inhibited the growth of Gram-positive bacteria *B. subtilis* and *L. rhamnosus* when tested at high concentrations. It was found to be most sensitive to *S. aureus* (ED_{50} = 22.48 μg/ml).

It is evident from Table 4.24, that the dibutyltin compound **2** exhibited very powerful antibacterial properties. Different doses of the compound when used against both Gram-positive and Gram-negative bacteria could effectively kill these organisms. Even when present at low concentrations it brought about 50% inhibition of bacterial growth. It was noted that **2** was more potent against Gram-positive bacteria than Gram-negative bacteria. The compound **2** had a very low ED_{50} dose against *L. rhamnosus* and S. *aureus*. Interestingly, this compound had no effect on *B. Subtilis*. It would be interesting to study why **2** is ineffective against this bacterium [13].

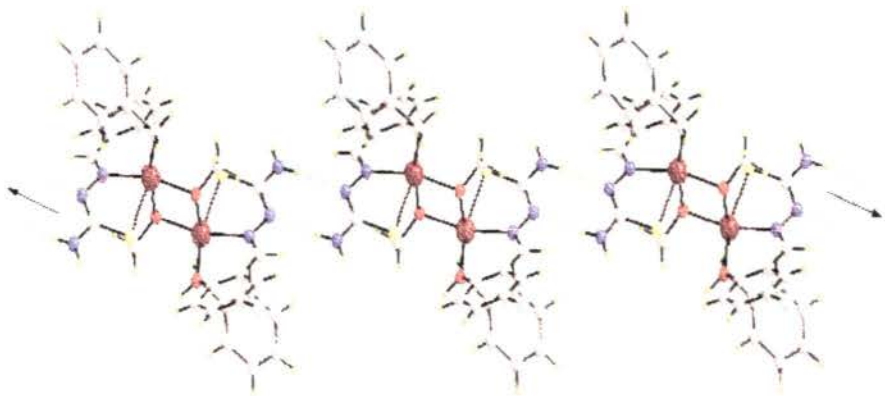


Fig. 4.35 Chains mediated by N–H....H hydrogen bonding interactions, shown as golden dashed lines, in (**14**) (Crystal Impact, 2006). Colour code: Sn (brown), Cl (cyan), S (yellow) O (red), N (blue), C (grey) and H (green).

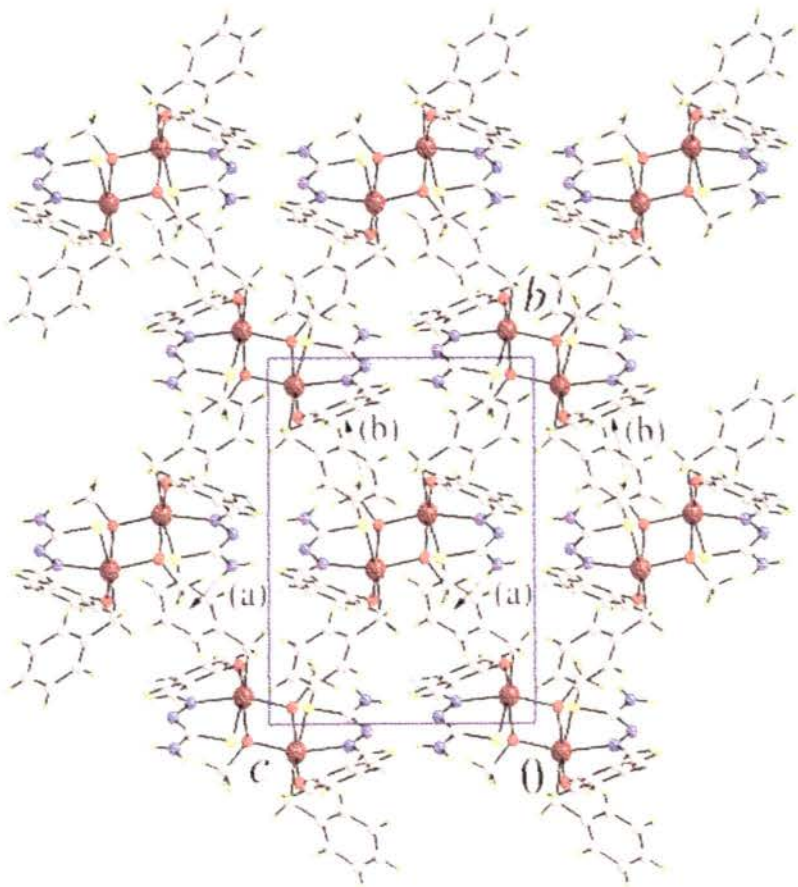


Fig. 4.36 The packing of (**14**), viewed down the *a* axis (Crystal Impact, 2006). Colour code as in Fig. 4.35.

On calculating the effect of **4** on bacterial growth it was noted that the compound was active only against gram negative bacteria like *S. typhi*, *A. hydrophila* and *E. coli*. The compound had no effect on *S. flexnri* and *S. typhimurium* as well as on any of the gram positive bacteria used in this study except *S. aureus*.

The compounds **3** and **6** appeared to have an almost similar antibacterial profile.

Table 4.24 Effect of different organotin compounds on bacterial growth[a] [ED_{50}=Effective Dose ($\mu g\ ml^{-1}$)]

	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**
1	n.e.	n.e.	n.e.	n.e.	n.e.	32.58	22.28	45.00
2	7.3	3.4	n.e.	n.e.	38.01	n.e.	3.2	2.05
3	5.50	20.12	26.38	40.53	30.28	6.50	n.e.	2.02
4	28.88	35.55	17.07	13.35	37.20	40.00	n.e.	6.05
6	12.50	26.40	32.40	32.96	17.52	40.70	n.e.	23.10

[a] The doses mentioned represent the minimum effective dose needed to inhibit 50% growth of bacteria. MIC values above 50 $\mu g\ ml^{-1}$ were not considered significant.

n.e. = no effect. The values represent mean of three experiments.

[b] **a**, *A. hydrophila*; **b**, *S. typhi*; **c**, *S. typhimurium*; **d** ,*S. flexnri*; **e**, *E. coli*; **f**, *B. subtilis*; **g**, *S. aureus*; **h**, *L. rhamnosus*.

4.5.2 Effect of n-Bu_2SnL^1 (2) on bacterial disease

Since it was observed that **2** could effectively control the growth of different gram negative bacteria, an attempt was made to see whether the compound could control the progression of a disease caused by any of the pathogenic bacteria used in the study. *Aeromonas hydrophila*, a Gram-negative bacterium, is one of the etiologic agents responsible for EUS (Epizootic Ulcerative Syndrome) in fish. *A. hydrophila* were incubated with **2** for 6-8 hours and then injected into fish via intra-muscular route. Control fish were injected with untreated *A. hydrophila.* It was found that **2** treated bacteria failed to produce the redness and lesion characteristic of EUS, but the control fish exhibited all the characteristic features of EUS.

It was observed that, when **2** was injected locally into preformed bacterial lesions it effectively prevented the spread of this disease in infected fish. It was also noted that if **2** was dissolved in the tank it significantly reduced the bacterial load in water.

EUS is a fish disease affecting different parts of the globe. With the advent of multi-drug resistant strains it has become difficult to control the spread of this disease. Organotin compounds as mentioned before have been reported to have potent bactericidal properties [91].The experimental results obtained from this study also confirm the previous reports of high bactericidal activity of organotin compounds. Moreover, the compound **2** was effective even at very low concentrations.

4.5.3 Antifungal activity

The antifungal activity of the diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones were investigated and the results are summarized in Table 4.25.When the antifungal properties of the compounds were evaluated it was observed that compound **4** was effective against all the four fungi selected in the study with the minimum MIC values obtained for *A. porri* and *M. phaseolina* (MIC 1.78 μg ml^{-1}). Compound **6** was effective against all the pathogenic fungi except *D. oryzae*, while **1** was effective against *A. porri* and *M. phaseolina* (MIC 3.76 μg ml^{-1}) and **3** was

effective only against *A. porri* (MIC 4.4 μg ml^{-1}). The study indicated that the alkyltin derivatives are more active than the aryltin compounds for both bacteria and fungi in accord with the literature conclusions [187].

It is not possible from this study to determine the structure activity relationship between the anti-microbial activity and structure of organotins used or suggest any specific mode of action of the organotins on the bacteria or fungi selected. However, earlier studies have suggested that charged metabolites of the organotins could play a role in their anti-microbial activities [189]. Moreover, the chelating potential of organotins could also be responsible for the enhanced anti-microbial activity observed [190,191]. The variation in the anti-microbial properties against different organisms observed probably depends on the impermeability of the cell or differences in ribosomes to the organotins used [192]. Also, the activity of any compound is a complex combination of steric, electronic and pharmacokinetic factors. A possible explanation for the toxicity of the complexes can be explained in the light of the chelation theory [193] which suggests that chelation reduces considerably the charge of the metal ion mainly because of the partial sharing of its positive charge with the donor groups and possible π-electron delocalization over the whole chelate ring. This increases the lipophilic character of the metal chelate which favours its permeation through lipid layers of fungus membranes. Furthermore, the mode of action of the compound may involve the formation of a hydrogen bond through the –N=C group of the chelate or the ligand with the active centres of the fungal cell constituents resulting in interference with the normal cell process. Further studies with bacteria and fungi are in progress to determine the mode of action of these compounds.

4.5.4 Phytotoxic Properties

The phytotoxic effects of selected organotin compounds were studied on three economically important crops namely *Oryzae sativa* (IR-8), *Lens culinaris,* and *Cicer aurantinum* (Table 4.26). It is evident from Table 4.26, that none of the compounds used in the study had any phytotoxic effect on seed germination.They did not affect the seed germination potency of *Oryzae sativa* , *Lens culinaris,* and *Cicer aurantinum.*

Table 4.25 Fungicidal activity of selected compounds against different fungi species - effects on spore germination[a]

Spore	Complex	Minimum Inhibitory concentration [MIC] (μg/ml)
Curvularia eragrostidis	**1**	37.6
	2	6.4
	3	440
	4	17.8
	6	18.4
	7	25
	9	20
Alternaria porri	**1**	3.76
	2	0.64
	3	4.4
	4	1.78
	6	1.84
	7	2.5
	9	2
Dreschlerea oryzae	**1**	376
	2	64
	3	440
	4	17.8
	6	184
	7	25
	9	200
Macrophomina phaseolina	**1**	3.76
	2	6.9
	3	44
	4	1.78
	6	18.4
	7	2.5
	9	20

[a] The reported values represent the mean determined from three experiments. MIC values above 30 μg ml^{-1} were not considered significant.

Table 4.26 Phytotxic effect (µg/ml) of selected organotin compounds[a,b,c]

Compound	Concentration (µg/ml)	Percentage germination following treatment with organotin compounds								
		Duration of treatment (**hrs**)								
		1			4			12		
		a	**b**	**c**	**a**	**b**	**c**	**a**	**b**	**c**
1	100	92	82	96	92	82	94	93	80	93
	50	95	83	95	94	85	94	94	80	92
	25	92	81	95	92	80	95	95	81	91
2	100	91	84	95	93	86	93	93	81	94
	50	93	85	96	94	86	94	95	83	94
	25	95	83	94	97	88	96	95	84	95
3	100	94	86	96	94	87	95	95	85	96
	50	94	88	94	95	87	96	95	85	98
	25	96	83	96	96	81	95	96	84	97
4	100	96	80	94	96	81	95	96	80	95
	50	94	82	93	94	81	93	94	83	93
	25	95	80	92	94	80	92	94	79	92
6	100	94	90	97	93	91	95	91	90	95
	50	93	92	96	94	90	94	93	91	94
	25	92	90	97	92	90	95	90	91	96
Control [d]		96	81	98	94	80	97	95	80	96

[a] The phytotoxicity of the compounds was checked by seed germination assays. Seeds were incubated with different concentrations of the compounds for 1, 4 and 12 h, washed to remove the excess unbound compounds and the percentage germination checked following incubation for 72 h. Control seeds exhibited 95-100 % germination efficacy. Values represent mean of three experiments.

[b] **a** *Cicer aurantinum*; **b** *Lens culinaris*; **c** *Oryzae sativa.*

[c] The control seeds were incubated in DMSO/water for the indicated time period.

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CHAPTER 5

CYTOTOXIC ACTIVITY OF DIORGANOTIN(IV) COMPLEXES OF SALICYLALDEHYDE THIOSEMICARBAZONES

5.1 Introduction

The relationship between metal ions and cancer are both intriguing and controversial. Since its discovery by Furst in 1963 [1], metal chelates continue to play an important role in the cure and cause of malignancy. In addition to this, the discovery of the antitumour activities of titanocene dichloride [2-4] and certain diorganotin derivatives [5-7] stimulated much interest in the research of organometallic compounds as antitumour agents.

5.1.1 Antitumour activity of organotin(IV) complexes

Although the first organotin(IV) compound was tested for its antitumour activity [8] in 1929, no systematic study was undertaken afterwards and as a result only 1509 organotin compounds had been tested in various tumour systems by the end of 1981[9]. Organotin compounds with coordination number greater than four are significant for their biological activity [10] and interesting structures. Along with this their potent antitumour activity has led many researchers to investigate them as effective antitumour agents [11- 26]. A large body of literature is now available.

Brown firstly reported [27] the restraint effect of triphenyltin acetate for the growth of anticancer cells. It has been demonstrated that certain triphenyltin benzoates exhibit exceptionally high *in vitro* activity [28] against MCF-7 and WiDr cell lines. Some novel triphenyltin carboxylates [29] also revealed interesting low ID values compared to the clinically established antitumour drugs.

Di-n-butyltin, di-t-butyltin and diphenyltin 2, 6-pyridine dicarboxylates [30-32] were found to be more active than cisplatin against MCF-7, a mammary tumour, and WiDr, a colon carcinoma. The anhydrous bis(dicylohexylammonium)bis(2,6-pyridine dicarboxylato) dibutylstannate is reported to display higher *in vitro* antitumour activity than those of carboplatin and cisplatin [33].

Bis{3-methoxysalicylato[di(n-butyl)]tin(IV)}oxide, obtained by the condensation of Bu_2SnO and 3-methoxysalicylic acid , exhibited higher antitumour activities *in vitro*

against two tumour cell lines , MCF-7 and WiDr than those of the 5-Me and 4-MeO analogues [34].

Gielen *et al.* synthesized and screened [35] a series of organotin compounds against MCF-7 and WiDr cell lines and found that the complexes exhibited very promising antitumour activities. Di-n-butyltin bis(2,5-dihydroxybenzoate) was found to be as active as cisplatin *in vitro* against murine Colon 26 carcinoma.

Saxena and Tandon [36] screened a series of di-n-butyltin complexes of Schiff bases derived from S-substituted dithiocarbazates and p-fluoroaniline for their activity against P-388 lymphoyte leukaemia and suggested that the presence of highly electronegative groups can greatly enhance the activity.

The dibutyltin complexes of the general formula Bu_2SnL (where L= dianion of tridentate Schiff bases derived from the condensation of 2-hydroxy-1-naphthaldehyde or acetyl acetone with Gly, L- β-Ala, DL- Val, DL- 4-aminobutyric acid, L-Met, L-Leu and PhGly) have exhibited higher antitumour activities than those observed for cisplatin and carboplatin [37].

Barbieri *et al.* [38] reported the antitumour activity of diorganotin(IV) complexes with adenine (R_2SnAd_2) and glcylglycine (R_2SnGly-Gly) against the P-388 lymphocyte leukaemia in mice. The compounds (R_2SnGly-Gly) were active against leukaemia in very small doses. They suggested the antileukaemic activity of R_2SnGly-Gly depends upon the peculiar structure and bonding of the solids.

Ruisi *et al.* have tried to interpret the action of R_2Sn(IV) glycylglycinates (R= Me, n-Bu, n-Oct and Ph) on a molecular basis. Of the various tumours studied the Bu_2Sn(Gly-Gly) was only active against P-388 leukaemia. On the basis of solution studies using various spectroscopic techniques, it is likely that solvated species in aqueous solution or a mixture of water and organic solvent and unsolvated species (mainly organic solvent) are present in equilibrium and contribute to passage of alkyltin complexes across the cell membrane which in turn produces the biological activity [39].

A series of organotin dipeptide compounds and a number of diorganotin halides and pseudohalides [$SnR_2X_2L_2$] (L= amino ligand e.g., py, bpy, phen, en) have displayed modest antitumour activity [40]. Many di-n-butyl, tri-n-butyl and triphenyltin complexes with hydroxyarylcarboxylic, ketocarboxylic, fluoroarylcarboxylic acids and many other oxygen and nitrogen containing derivatives of carboxylic acids display high antitumour activities [41- 45].

Cardarelli *et al.* investigated the antitumour activity of a number of organotin compounds, namely, tri-butyltin fluoride, dibutyltin dichloride.2-2'-bipyridyl, 1,10-phenanthroline.dibutyltin complex and dibutyltin histidine by administering these to cancerous mice in drinking water and found that the tumour growth rates were significantly reduced [46]. Studies on the tin content in various body organs led Cardarelli *et al.* [47] to hypothesize that soluble organotin compounds of various types introduced into the body are concentrated in the thymus gland. The tin in the thymus is then processed into one or more biochemical that acts as anticarcinogens. The isolation and evaluation of thymic extracts reasonably pointed to the unknown tin-bearing antioncogenic biochemicals of steroid nature. On the basis of their hypothesis, Cardarelli *et al.* [48] patented several organotin compounds of steroids which exhibited marked antitumour activity.

The synthesis and *in vitro* screening of even more water soluble organotin compounds, containing a polyoxaalkyl moiety linked to tin either by a carbon-tin or by a carbon-oxygen bond is one of the latest development by Gielen and his coworkers [49, 50].

The compounds $Ph_2Sn(OH)Cl$, $(Et_2SnO)_n$ and $ClMe_2SnOSnMe_2Cl$ as well as their octahedral adducts $R_2SnX_2L_2$ (where R is alkyl or aryl, X is halide or thiocyanate and L_2 are nitrogen atoms of the bidentate ligands 1,10-phenanthroline, 2-2'-bipyridyl and 2-aminomethylpyridine) have been determined to be active against P-388 lymphocytic leukaemia in mice [51].The mechanism of antitumour action of these drugs proposed was the preferred transportation of the complex species into the tumour cells, which would be attacked by hydrolyzed $R_2Sn(IV)^{2+}$ moieties.

Three main factors which have an important role in determining the structure-activity relationship for organotin(IV) derivatives $(L)_xR_nSnX_{4-n}$ are:

- the nature of the organic group R
- the nature of halide or pseudohalide X
- the nature of donor ligand

Examination of the structures of Sn(IV) compounds containing a N-donor atom and tested for antitumour activity revealed that in the active tin complexes the average Sn-N bond lengths were greater than 239 pm, whereas inactive complexes had Sn-N bond lengths < 239 pm, which implied that predissociation of the ligand might be an important step in the mode of action of these complexes , while the coordinated ligand may favour transport of the active species to the site of action in the cells, where they are released by hydrolysis [52].

Also, a comparison of the structures of the active and inactive compounds suggest [53] that in all the active compounds there is

- The availability of coordination positions at Sn
- The occurrence of relatively stable ligand-Sn bonds, Sn-N and Sn-S
- Low hydrophilic decomposition of these bonds

With regard to the data published on all the Sn(IV) derivatives , it can be concluded that $R_2Sn(IV)^{2+}$ compounds generally exhibit higher antitumour activity than those of the corresponding mono-, tri- and tetra- organotin(IV) or the inorganic Sn(IV) derivatives, and within the diorganotin series , the highest activity is exerted by the $Et_2Sn(IV)^{2+}$ and $Ph_2Sn(IV)^{2+}$ complexes. Also, it has been established that the $R_2Sn(IV)^{2+}$ compounds which exhibit maximum antitumour activity combined with low mammalian toxicity are adducts of the type $R_2SnX_2L_2$ (X=halogen, pseudohalogen, L= O- or N- donor ligand) [52].

In aqueous solution, most of the organotin complexes undergo dissociation, aquation and hydrolysis reactions. For diorganotin complexes, mono-, di- and poly-nuclear dialkyltin(IV) species co-exist in the aqueous solution, depending on pH. Moreover dialkyl dihydroxo tin(IV) species prefer to be five- or six- coordinated by binding weakly to one or two water molecules [54]. R_2Sn bond seems rather stable in aqueous solution, but the triorganotins will release one alkyl group to give active R_2Sn species,

the half-life of this process has been shown to be between 3 and 6 days [55]. The $R_2Sn(IV)^{2+}$ has been suggested as the active species for the organotin anticancer agents [56].

Atassi assumed that water-soluble organotin(IV) compounds are probably more active than complexes soluble only in organic solvents. More recent results on the antitumour activity of the organotin complexes on the tumour cell lines seem to point to a necessary balance between solubility and lipophilicity in order to optimize their efficacy [57-59].Attempts to improve the bioavailability of the organotin(IV) cations by the formation of water soluble complexes [60] or by their inclusion into β-cyclodextrin [61] have also been reported.

DNA is believed to be the main cellular target for most of the metal anticancer agents. The anticancer nature is the coordination of metal ions with DNA molecules, causing DNA damage in cancer cells, blocking the division of the cancer cells and resulting in cell death. The aqueous interactions of solvated di- and tri- organotin(IV) species $R_2Sn(IV)$ and $R_3Sn(IV)$ (R=Me, Et, n-Bu, n-Oct, Ph in ethanol solution) with native DNA(calf thymus) have been investigated by ^{119}Sn Mössbauer spectroscopy at pH between 5 and 7.4 [62-65] . The addition of ethanolic organotins [$R_2SnCl_2(EtOH)_2$ or $R_3SnCl(EtOH)$] to DNA yielded solid products, the ^{119}Sn Mössbauer spectra suggested that the tin was coordinated by the phosphodiester groups of the nucleotides. While the water soluble hydrolyzed dimethyltin(IV) species did not show any interaction with native DNA [62, 65].

Yang *et al.* [66] studied the binding modes of $(CH_3)_2SnCl_2$, $(C_2H_5)_2SnCl_2$, $(C_2H_5)_2SnCl_2$(phen) with DNA and nucleotides in aqueous solution by using modern techniques. The results show that all the above compounds exhibit high affinity to the phosphate group of the nucleotides. The interactions of $(CH_3)_2SnCl_2$ and $(C_2H_5)_2SnCl_2$ with calf thymus DNA suggested that organotins(aqueous) binded to DNA via only the phosphate group. In addition, the relationship between DNA binding property of metal complex and their anticancer activity was discussed in the review and a hypothesis named 'Two-Pole Complementary Principle' was also put forward and some criterias were suggested as well.

5.1.2 Antitumour activity of thiosemicarbazones

Thiosemicarbazones constitute an important class of N, S donor ligands because of their highly interesting chemical, biological and medicinal properties [67].The studies developed during the last 35 years have yielded several conclusions. The biologically active thiosemicarbazone molecules are planar and contain pyridine rings or derivatives giving rise to N, N, S tridentate systems [68]. A plethora of references of metal complexes of thiosemicarbazones having potential antitumour activity are available [69-77].

It has been repeatedly shown [78] that compared to the ligands, thiosemicarbazone-based metal complexes (for e.g. Cu and Zn) are more efficient inhibitors of cancer cell growth.

French and Freelander [79] reported that glyoxal bis(thiosemicarbazone) and several related compounds exhibited antitumour activity against S-180 in mice when the drugs were included in their diet. Soon, thereafter they published [80] their results of screening of a large series of α-ketoaldehyde bis(thiosemicarbazones) and stated that four of about 50 compounds had significant activity against S-180.Among these with highest activity were 2-keto-3-ethoxybutyraldehyde bis(thiosemicarbazone) (KTS) and 2-Keto-3-ethoxybutyraldehyde bis(N^4-methylthiosemicarbazone) (KTSM).

Later, the studies with KTS, KTSM and several related compounds by Petering *et al.* [81] indicate that these have interesting biochemical and pharmacological activity and that KTS, especially has excellent broad spectrum antitumour activity against a number of transplanted rodent tumours both *in vivo* and *in vitro*. Dose-response relationships have been established for its toxicity, tumour-inhibitory activity, and capability of causing regressions. It was proposed that much of the toxicity which was found with KTS is related in some way with its capacity to bind trace metals, especially cupric and zinc ions. It was also suggested that both the toxicity and the antitumour activity of KTS is greatly affected by the nutritional intake of animals which received the drug [82, 83].

French and Blanz prepared [84] many thiosemicarbazone derivatives and found that all the tumour inhibitors potentially act as N, N, S type donor ligands. This has been attributed to their ability to chelate and form metal complexes [85, 86]. Thelander and Grasland [87] made a detailed study on the effects of 1-formayl isoquinoline thiosemicarbazone (IQ-1) with the mammalian ribonucleotide reductase to understand the environment of active siteand the reaction mechanism of the enzyme. This drug IQ-1 belongs to the group of α-*N*-heterocyclic carboxaldehyde thiosemicarbazones and act as strong metal chelating agent with affinity for Fe [88].

Thomas and Parmeswaran [89] studied the antitumour activities of Mn^{2+}, Co^{2+}, Ni^{2+} and Cu^{2+} chelates of anthracene-9-carboxaldehyde thiosemicarbazone. Murthy and Dharmaraja [90] reported the cytotoxic activity of phenylglyoxal bis(thiosemicarbazo -ne) against *Ehrlich ascites* carcinoma cells.

Miller *et al.* [91] studied the multiple mechanisms for cytotoxicity induced by Cu(II) complexes of 2-acetylpyrazine-*N*-substituted thiosemicarbazones. The purpose of the study was to evaluate the mechanism by which 2-acetylpyrazine-N^4-substituted thiosemicarbazone copper(II) complexes mediated their cytotoxicity. These compounds were shown to be cytotoxic to a variety of human and rodent tumours in cell ,culture and are potent cytocidal agents as determined by dilute agar colony assays. They demonstrated the ability to inhibit several enzymes *in vitro* including DNA topoisomerase II activity. The data presented that cytotoxicity may be mediated by the cumulative effect of several enzymes being inhibited by the agents.

Copper(II) complexes of 2-acetylpyridine thiosemicarbazones possess strong antineoplastic activity against a number of transplantable tumours, spontaneous murine tumours and human tumours. The mechanism of their antitumour action was thought to involve either inhibition of the enzyme ribonucleotide reductase, an obligatory enzyme in DNA synthesis [92-94] or creation of lesions in DNA strands [95].

Patole *et al.* [96] have shown that among the iron and platinum complexes of salicylaldehyde semi-/thiosemicarbazones the latter inhibits the growth of C6 glioma cells *in vitro* with an IC_{50} value of 45 μM. Their findings suggest that the platinum

compounds of salicylaldehyde thiosemicarbazone are potential candidates for the treatment of malignant gliomas. Patole *et al.* [97] have also synthesized copper complexes of salicylaldehyde semi-/thiosemicarbazones . The parent ligands are almost inactive against the rapidly dividing human breast cancer cell line MCF-7 while the copper conjugates of semicarbazone ligand are found to be potent antiproliferative agents due to their facile Cu^{2+}/Cu^{+} redox couple and can generate considerable intracellular oxidative stress.

The biological activity of organotin (IV) complexes with pyridoxal thiosemicarbazone (PLTSC) [SnR_2(PLTSC-2H)] (R=Me, Et, n-Bu, Ph) were also evaluated [98] . With the exception of the Me complex, the other three suppressed friend erythroleukaemia cells (FLC) proliferation with the lowest thresholds for the latter two compounds.

Casas *et al.* reported that [$SnMe_2$(PyTSC)(OAc)].HOAc, [$SnMe_2$(DAPTSC)], [$SnPh_2$(DAPTSC)].2DMF where H_2DAPTSC= 2,6-diacetylpyridinebis(thiosemicarba -zone) all suppress proliferation of FLC . DMSO-induced differentiation of FLC was slightly suppressed by [$SnMe_2$(DAPTSC)] and was unaffected by [$SnPh_2$(DAPTSC)]. 2DMF and [$SnMe_2$(PyTSC)(OAc)].HOAc [99].

S.-G. Teoh and coworkers reported that bis(acetonethiosemicarbazone-*S*)dichloro diphenyltin(IV), $SnPh_2Cl_2(atsc)_2$ exhibited significant cytotoxicity against human colon adenocarcinoma, breast adenocarcinoma, hepatocellular carcinoma and acute lymphoblastic leukaemia [100].

From the foregoing description of the antitumour properties of organotin(IV) complexes and thiosemicarbazones, it is clear that such complexes are likely to find applications in medicine.

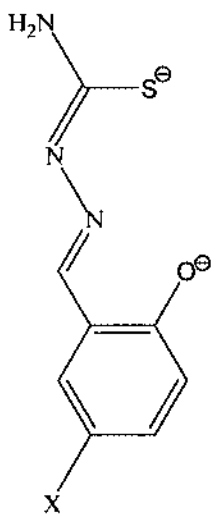
5.2 Scope and Objective

The antitumour activity of transition metal complexes of thiosemicarbazones are well explored. But, little work has been done on the antitumour activity of organotin(IV) complexes of thiosemicarbazones. This motivated the author to study the antitumour activity of the organotin(IV) complexes of salicylaldehyde thiosemicarbazones in search of better candidates with higher cytotoxicities . The present chapter reports the

investigations of a few organotin(IV) complexes of salicylaldehyde thiosemicarbazone and 5-bromosalicylaldehyde thiosemicarbazone against various tumour cell lines.

5.3 Synthesis and characterization of diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones

The salicylaldehyde thiosemicarbazones used for synthesizing the diorganotin(IV) complexes are described in Chapter 4 (see Section 4.3).The synthetic and characterization details for diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones [101] are described in Chapter 4 (see Section 4.3 and 4.4). The formulae of the ligands and the abbreviations of the complexes used for the present study are presented in Scheme 5.1.



L^1: X = H ; L^2: X = Br

1: Me_2SnL^1; **2**: n-Bu_2SnL^1; **3**: Ph_2SnL^1; **4**: $Me_2SnL^2.H_2O$; **6**: Ph_2SnL^2

Scheme 5.1

5.4 Experimental protocol

5.4.1 In vitro screening of cytotoxicity of the selected diorganotin(IV) derivatives of salicylaldehyde thiosemicarbazones against human cancer cell lines

The cytotoxicities of some selected diorganotin(IV) complexes of salicylaldehyde thiosemicarbazones (see Scheme 5.1) were evaluated against the different human

cancer cell lines mentioned below. The human cancer cell lines were maintained in DMEM (Gibco) containing 10% FBS supplemented with 1% penicillin-streptomycin solution. Tissue culture plates (96 well) were seeded with cancer cell suspensions at a final concentration of 1 x 10^5 cell per well and incubated at 37 °C for 24 h to allow the cells to adhere to the culture wells. The organotin compounds were added to the cells at final concentrations of 10, 20, 40 and 80 µg/ml respectively and incubated further for 48 h. Following incubation, the cells were fixed by adding 50 µl of 50% TCA for 60 min at 4 °C. The fixed cells were washed, air dried and 50 µl of 0.4 % Sulforhodamine B (SRB, Sigma) dye added to each well and incubated for 20 mins. Following incubation, the cells were washed with 1% acetic acid solution and air dried. 10 mM Tris-base (100 µl unbuffered) was added to each well and colour development recorded at 540 nm and subtracted from the background measurement at 690 nm [102]. Adriamycin (Sigma) was used as positive control in the assay.

Human cancer cell lines used for the experiment

S.No.	Human cancer cell lines	Cancer type	Tissue of Origin
1	Colo205 (TATA)	Colon cancer	Colon
2	Hop62 (TATA)	Lung cancer	Lung
3	MCF7 (TATA)	Breast cancer	Breast
4	PC3 (TATA)	Prostate cancer	Prostate
5	SiHa (TATA)	Cervical cancer	Cervix
6	ZR-75-1(TATA)	Breast cancer	Breast
7	A-2780 (TATA)	Ovarian cancer	Ovary
8	DWD (TATA)	Oral cancer	Throat
9	K562 (TATA)	Leukaemia	Leukaemia
10	DU145 (TATA)	Prostate cancer	Prostate

5.4.2 Effect of n-Bu_2SnL^1 (2) on mouse cancer cell line

5.4.2.1 Animal care and maintenance of cell lines

The experiments were performed at Immunobiology Laboratory, School of Life Sciences, Visva-Bharati University, Santiniketan, West Bengal under the supervision of Dr. Shibnath Mazumder. Close colony bred male Swiss albino mice (6-8 weeks of

age weighing around 22±2 gm) were obtained from the departmental vivarium. Animals were kept in cages and fed on commercial mouse food pellets and tap water *ad libitum*. EAC and SAR-180 cell lines were obtained from CNCRI, India, and used for the screening of test compound. Tumour cells were maintained in the ascetic fluid of the mice by serial transplantation.

5.4.2.2 *Effect of* n-Bu_2SnL^1 (**2**) *on mouse cancer cell lines EAC and SAR-180: An In vitro study*

Antitumour property of the compound **2** was evaluated as described here in. The mouse tumour cell lines EAC and SAR-180 were pulled by sterile hypodermic needle, suspended in culture medium, RPMI-1640 containing 10% Fetal Bovine Serum (FBS) supplemented with 1% Penicillin-Streptomycin (Gibco). The cell viability was checked and plated in 24 well culture plate (Nunc) @ $1x10^6$ cells ml^{-1}. Different concentration of solutions of compound **2** were prepared freshly and added in to the different wells of culture plate containing normal human peripheral blood mononuclear cells (PBMC) or tumour cell lines EAC and SAR-180. Normal and tumour cells were incubated in CO_2 incubator at 37 °C in presence of 5% CO_2 for different hours (8 h, 24 h, 48 h and 72 h). After incubation viability of cells from each group were checked by Trypan blue dye exclusion test (0.4 % Trypan blue) and the results were converted in to percentage cellular viability for each test groups.

$$\text{Percentage cell viability} = \frac{\text{Mean O.D. at 490 nm of treated cells}}{\text{Mean O.D. at 490 nm of control cells}} \times 100$$

5.5 Results and Discussion

5.5.1 Cytotoxicity of selected organotin compounds against cell lines by Sulforhodamine B (SRB) assay

The cytotoxic effect of organotin compounds were examined against several human cancer cell lines *in vitro* by Sulforhodamine B (SRB) assay. The cytotoxicity scores of organotin compounds against various cell lines by SRB assay are presented in Table 5.1 - 5.10.

Table 5.1 *In vitro* screening of anticancer activity against Colo205 human colon cancer cell line

Cell line: Colo205 human colon cancer cell line

Colo205 human colon cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	32.9	84.8	95.6	90.9
2	57	82.2	93.7	96.2
3	93.9	94.8	92.7	84.3
4	88.3	91	87.1	94.6
6	69.5	93.2	94.7	95.2
ADR	65.9	68.3	70.6	69.3

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 was considered to be positive action.

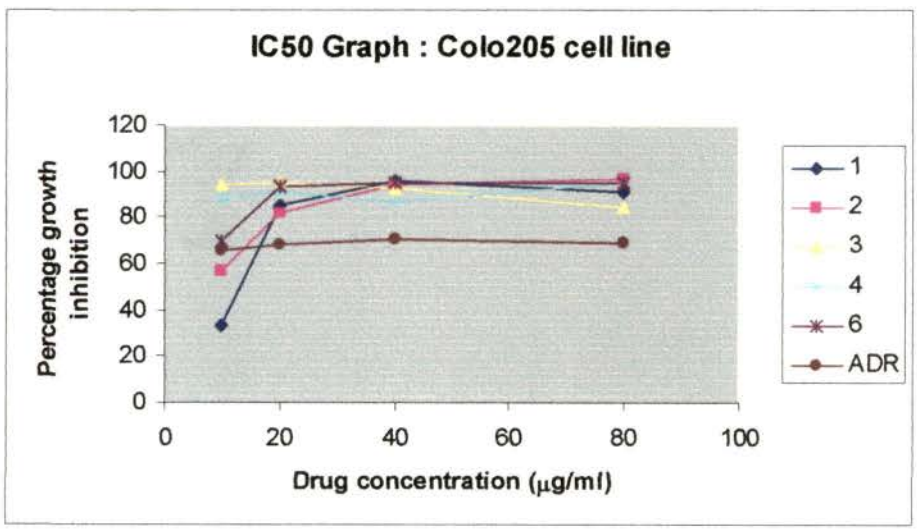


Fig. 5.1 IC50 graph: Colo205 cell line.

Compound **3** was found to be most active against Colo205 human colon cancer cell line at the concentration of 10 μg/ml.

Table 5.2 *In vitro* screening of anticancer activity against Hop62 human lung cancer cell line

Cell line: Hop62 human lung cancer cell line

Hop62 human lung cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	43.1	63.1	76.5	86.5
2	51.3	85.8	82	87.6
3	83	88.2	90.3	93.7
4	45.9	60.1	70.9	80.4
6	41.7	80.2	62.6	83.6
ADR	77.43	83.07	82.03	87.53

[a] All the observations are average of triplicate readings.

[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

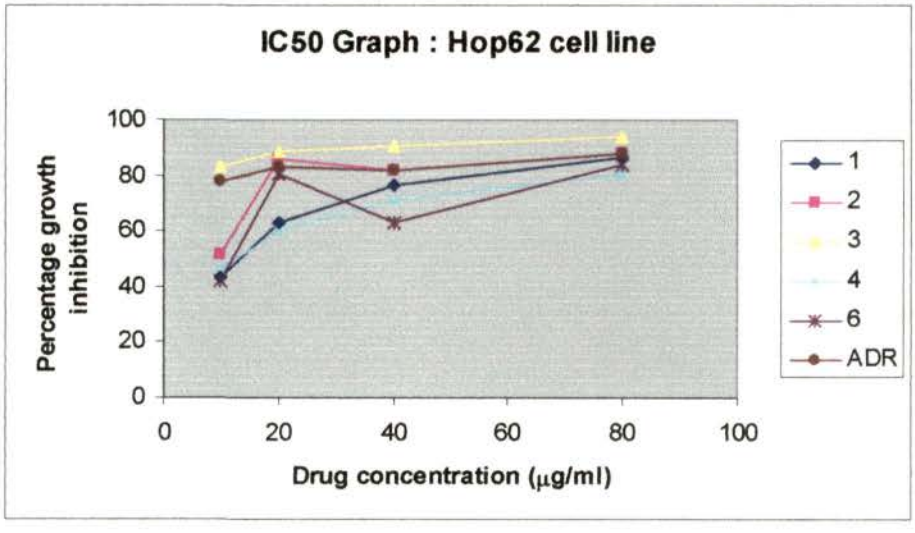


Fig. 5.2 IC50 graph: Hop62 cell line.

Compound **3** was found to be most active amongst the compounds tested inducing 83% growth inhibition of the Hop62 human lung cancer cell line at the concentration of 10 μg/ml. The activity of **3** was more than Adriamycin(ADR) which induced 77.4% growth inhibition at 10 μg/ml. Compound **2** followed by compound **6** also exhibited significant activity but at higher concentration level (20 μg/ml).

Table 5.3 *In vitro* screening of anticancer activity against MCF-7 human breast cancer cell line

Cell line: MCF-7 human breast cancer cell line

MCF-7 human breast cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	74	75.1	75.1	75.8
2	83	82.9	81.7	81.2
3	82.2	84.4	83	81.5
4	53.8	57.8	70.4	75.4
6	76.1	82.9	84.8	81.6
ADR	82.9	83.13	83.8	85.2

[a] All the observations are average of triplicate readings.

[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

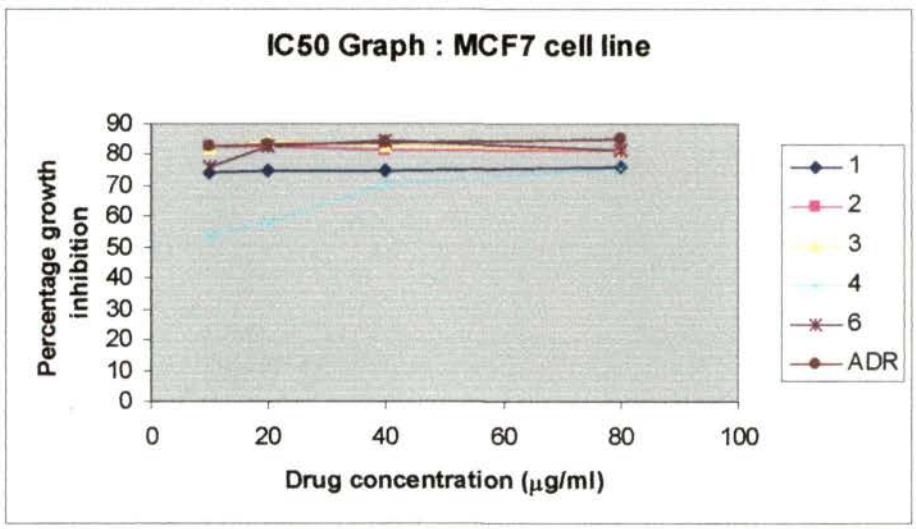


Fig. 5.3 IC50 graph: MCF7 cell line.

Compounds **2**, **3** and Adriamycin (ADR) exhibited similar percentage growth inhibitions of 83%, 82.2% and 82.9% respectively at the concentration of 10 μg/ml against MCF-7 human breast cancer cell line.

Table 5.4 *In vitro* screening of anticancer activity against PC3 human prostate cancer cell line

Cell line: PC3 human prostate cancer cell line

PC3 human prostate cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	37.6	72.4	83.3	89.2
2	72.1	84	88.8	90
3	86.4	87.7	92.6	91.7
4	13.8	23	47.3	57.1
6	85	88.5	83.9	85.2
ADR	71.9	72.8	75.87	81.77

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

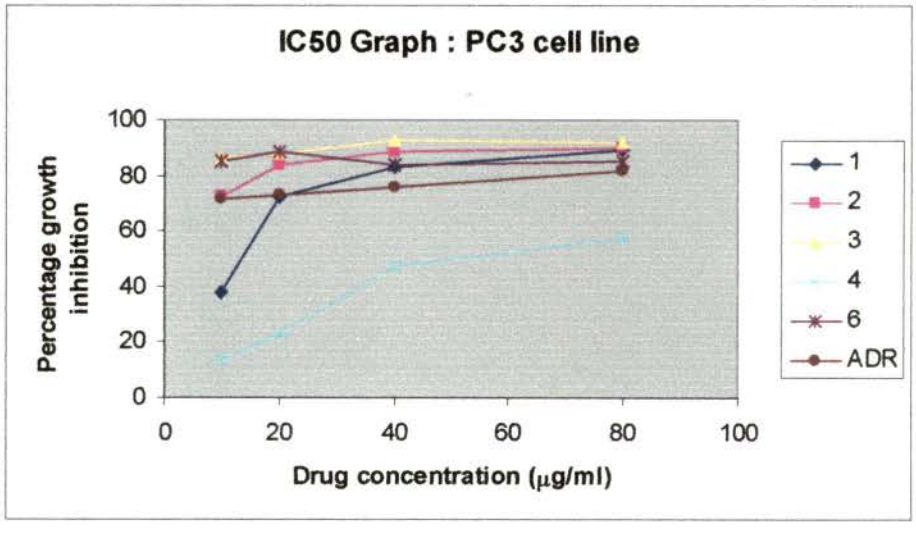


Fig. 5.4 IC50 graph: PC3 cell line.

At the concentration of 10 μg/ml compound **3** was found to be most active against PC3 human prostate cancer cell line followed by compound **6** and **2** respectively. All the three compounds (**3**, **6** and **2**) exhibited greater activity than ADR. Compound **4** was found to be least potent among all the compounds tested.

Table 5.5 *In vitro* screening of anticancer activity against SiHa human cervix cancer cell line

Cell line: SiHa human cervix cancer cell line

SiHa human cervix cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	28.6	66	70.3	74.3
2	79.2	83	81.3	82.5
3	79.4	81.2	85.3	89.2
4	0	45.9	59.1	77.8
6	84.9	87.9	90.2	88.7
ADR	88.9	93.5	96.4	94.9

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

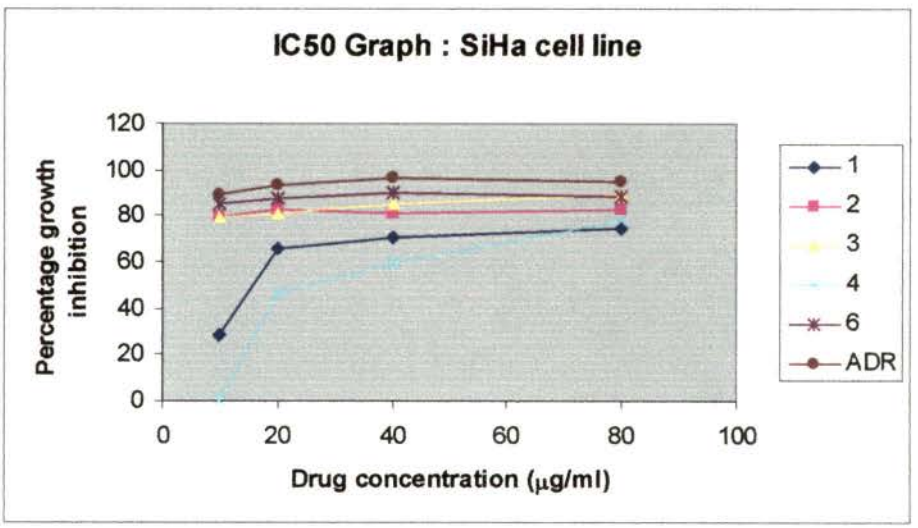


Fig. 5.5 IC50 graph: SiHa cell line.

In this case, compound **6** exhibited 84.9% growth inhibition at 10 μg/ml and was found to be the most active amongst organotin(IV) complexes tested. Compounds **2** and **3** exhibited almost same percentage growth inhibition at 10 μg/ml but compound **3** was more active at higher concentrations levels than **2**. ADR was found to be most active amongst all the compounds tested.

Table 5.6 *In vitro* screening of anticancer activity against Zr-75-1 human breast cancer cell line

Cell line: Zr-75-1 human breast cancer cell line

Zr-75-1 human breast cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	27.6	57.6	85.9	90.6
2	60.2	93.9	94.6	92.1
3	16	95.9	96.1	95.7
4	1.8	40.5	47.2	86.2
6	46.8	88.7	91.7	87.4
ADR	72.7	76.27	80.8	86.6

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

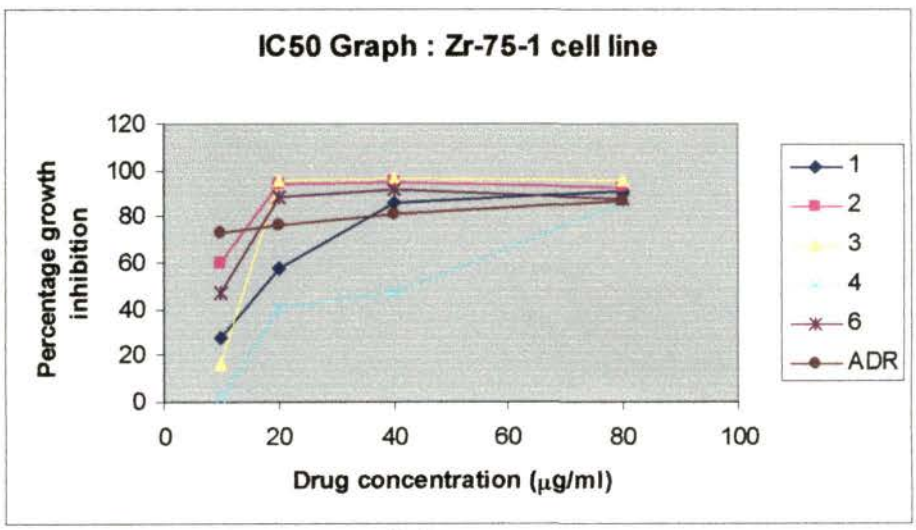


Fig. 5.6 IC50 graph: ZR-75-1 cell line.

At the concentration of 10 μg/ml ADR was most active (72.7% inhibition) followed by **2** which exhibited 60.2% growth inhibition of Zr-75-1 human breast cancer cell line. Other compounds were inactive at the concentration of 10 μg/ml.

Table 5.7 *In vitro* screening of anticancer activity against A2780 ovarian cancer cell line

Cell line: A2780 ovarian cancer cell line

A2780 ovarian cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	86.6	88.8	86.1	80.8
2	88.9	90.1	87	80.7
3	90	91.8	88	81.2
4	73	84.6	87.5	77.6
6	94.7	86	87.9	77.2
ADR	98.6	98.8	98.7	95.2

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

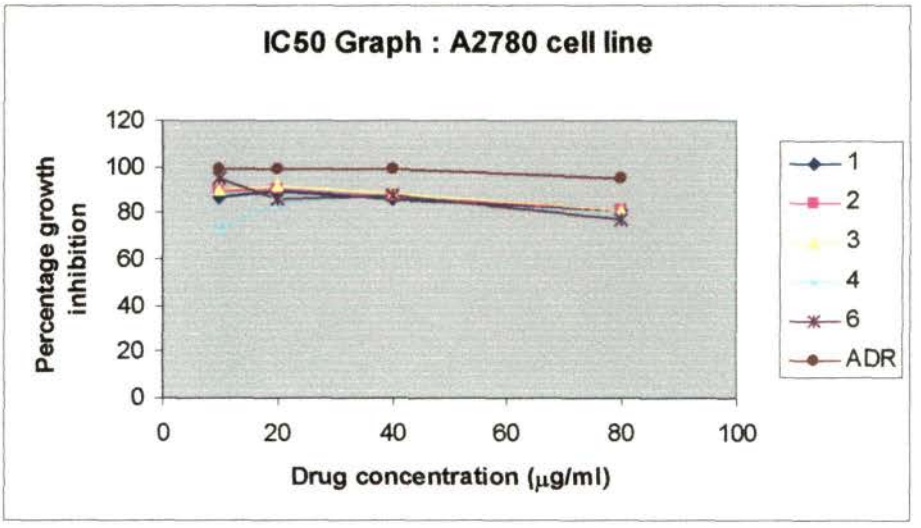


Fig. 5.7 IC50 graph: A2780 cell line.

At 10 μg/ml, ADR was found to be most active amongst the compounds tested against A2780 ovarian cancer cell line followed by **6**, **3**, **2**, **1** and **4** respectively.

Table 5.8 *In vitro* screening of anticancer activity against DWD human oral cancer cell line

Cell line: DWD human oral cancer cell line

Compound	DWD human oral cancer cell line			
	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	82.3	79.4	76.1	78.7
2	64	87.7	79.9	84.8
3	83.8	87.4	90.8	92.5
4	0	49.6	52.9	55.3
6	0.6	26.2	51.7	27.6
ADR	94.7	94.7	92.4	92.8

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

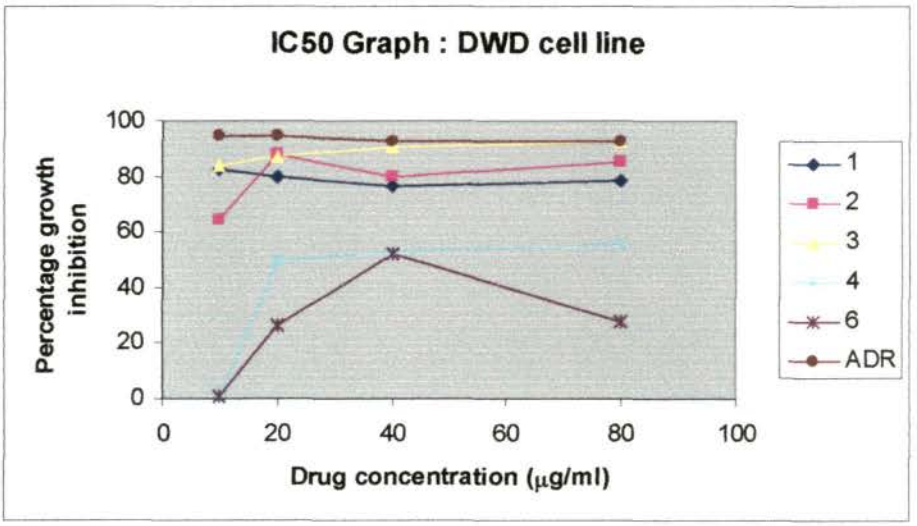


Fig. 5.8 IC50 graph: DWD cell line.

ADR was found to be most active against DWD human oral cancer cell line followed by **3**, **1** and **2** respectively.

Table 5.9 *In vitro* screening of anticancer activity against K562 human leukaemia cell line

Cell line: K562 human leukaemia cell line

K562 human leukaemia cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	35.2	28.1	40.6	40.3
2	40.5	44.7	40.3	39.7
3	60.3	61.2	62	58.1
4	13.2	11.2	21.4	43.1
6	4.1	39.1	34.4	40.5
ADR	82.1	85.6	87.2	92.5

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

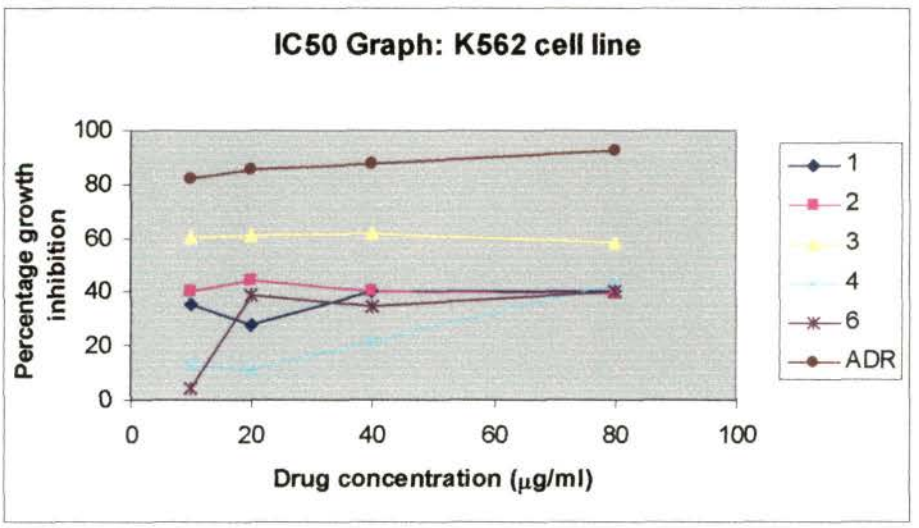


Fig. 5.9 IC50 graph: K562 cell line.

None of the organotins exhibited significant activity against K562 human leukaemia cell line except **3** which displayed 60.3% growth inhibition at the concentration of 10 μg/ml.

Table 5.10 *In vitro* screening of anticancer activity against DU145 human prostate cancer cell line

Cell line: DU145 human prostate cancer cell line

DU145 human prostate cancer cell line				
Compound	Percentage growth inhibition compared to Control [a,b]			
	Average value of 3 experiments Drug concentration (μg/ml)			
	10	20	40	80
1	24.4	65.6	77.6	82.9
2	35.6	74.4	78.9	86.1
3	79.2	87.9	89.1	88
4	52.3	74.5	85.1	87.4
6	41.8	80	85.5	85.1
ADR	70.7	73.5	73.8	78.3

[a] All the observations are average of triplicate readings.
[b] Percentage growth inhibition ≥ 50 is considered to be positive action.

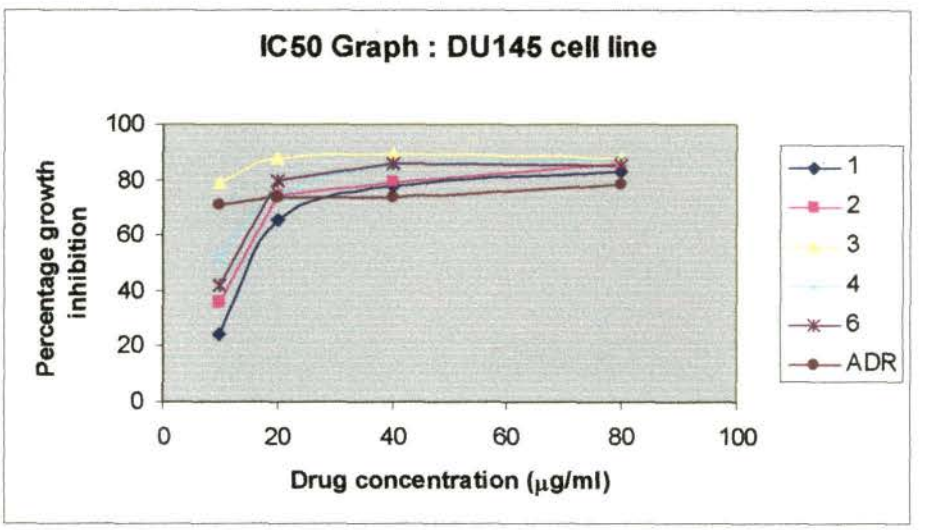


Fig. 5.10 IC50 graph: DU145 cell line.

Compound **3** was found to be most active against DU145 human prostate cancer cell line followed by ADR and **4** respectively at the concentration of 10 μg/ml. At the concentration of 20 μg/ml, the activity observed was **3** > **6** > **2**> **ADR** >**1**.

Summing up all the results obtained (represented above) indicates that amongst the different organotins selected for the study, compound **3** was found to possess the highest potency against most of the cell lines studied followed by compound **2** and **6** respectively. Compound **4** appeared to be the least potent, only inducing significant cell death against Colo205 (88.3%) [101].

It is interesting to note that, in contrast to the earlier reports on hexa-coordinated complexes [103], this study reports phenyl derivatives to be more active than the butyl derivatives.The reason behind the wide spectrum of cytotoxicity observed for the organotins in this study is not known at present. The results further suggest that the compounds are not equally effective against all the cell lines selected for the study. This difference in the degree of selectivity could, presumably, be either due to differential binding potential of the compounds or metabolic activities of the cell lines which helps in overcoming the cytotoxic effects of the organotins. Organotins offer the potential of reduced cytotoxicity, non-cross resistance and a different spectrum of activity compared to conventional chemotherapeutic agents such as platinum-containing compounds [104-106]. The organotins selected for this study appear attractive anticancer candidates because of the low doses required that minimize the chances of toxic side effects. From the available literature and our own observations it appears that the oragnotins described herein exert their cytotoxic effect at much lower doses compared to cisplatin [107-109] in the evaluated cell lines and adriamycin, which was used as positive control in this study. We now plan to extend the experiments at further lower concentrations under comparable conditions with standard controls.

The exact mechanism of action of organotins on controlling tumour growth is not well known [110]. It has been reported that organotins induce tumour cell death in a dose dependent manner [111-113]. At higher concentrations, these compounds induce degenerative changes indicative of necrosis accompanied by random DNA breakdown.

Electron microscopic studies revealed organotin-induced cytotoxicity to be associated with cell shrinkage, chromatin condensation, fragmentation of DNA, and development of apoptotic bodies [114].

It has been suggested that organotins, like other DNA binding drugs, induce cellular stress which activates the tumour suppressor p53 leading to apoptotic death [114]. The involvement of zinc and calcium dependent endonucleases has also been suggested in cytotoxicity induced by organotins [115]. The ongoing effort aims to determine the mode of action of these compounds on the sensitive cancer cell lines.

5.5.2 In vitro screening of n-Bu_2SnL^1 (2) for antitumour property against mouse tumour cell lines

The most potent organotin compound was selected from the antibacterial and antifungal [101] studies [see Chapter 4] for the *in vitro* evaluation of antitumour properties. Two mouse tumour cell lines (EAC and SAR-180) were chosen as the model cell line. The study revealed that the compound could kill the tumour cells even at lower dose like 1μg ml^{-1} = 3.36 μM. There was drastic decline in the cellular viability after 24 h of incubation with lower doses of compound **2** such as 3.36 μM and 7.34 μM. After 72 h of incubation with 3.36 μM of compound **2** the viability went down to around 2% in SAR-180 and 75% in EAC cells where-as the negative control and DMSO control for SAR-180 was 70% and for EAC was around 84%.

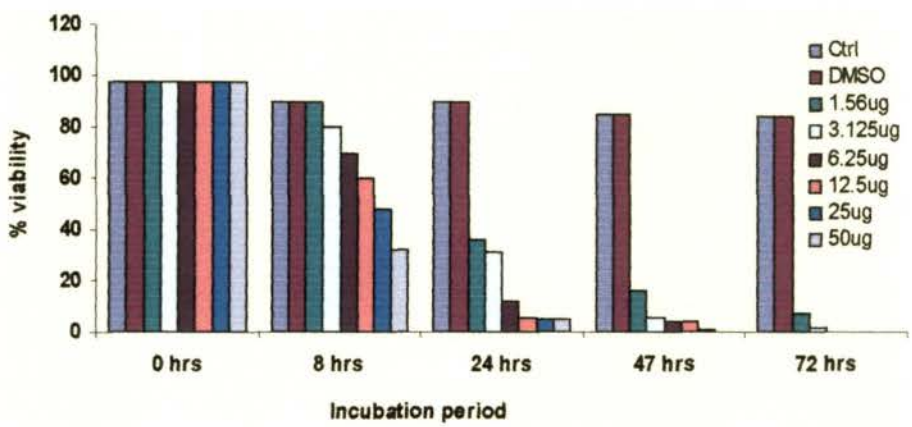


Fig. 5.11 Histogram representing the effect of n-Bu_2SnL^1 (**2**) on the survivability of SAR-180 *in vitro*.

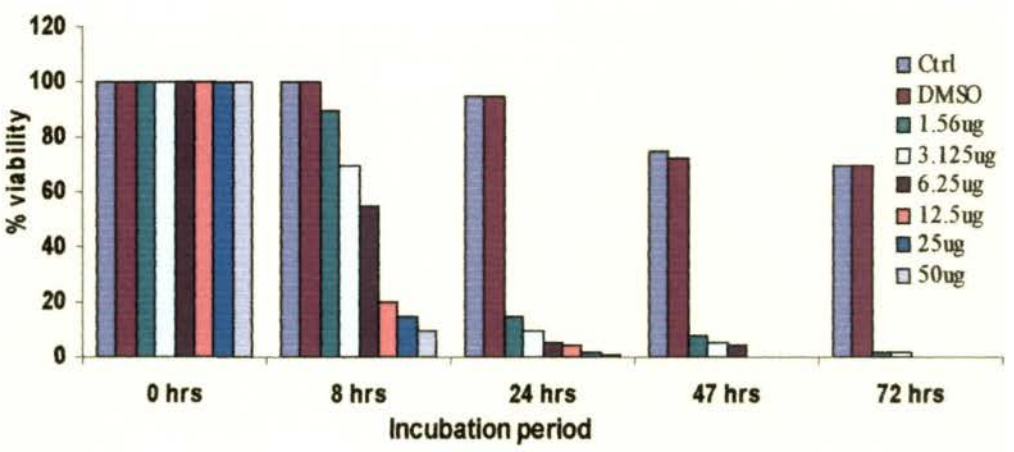


Fig. 5.12 Histogram representing the effect of n-Bu_2SnL^1 (**2**) on the survivability of EAC *in vitro*.

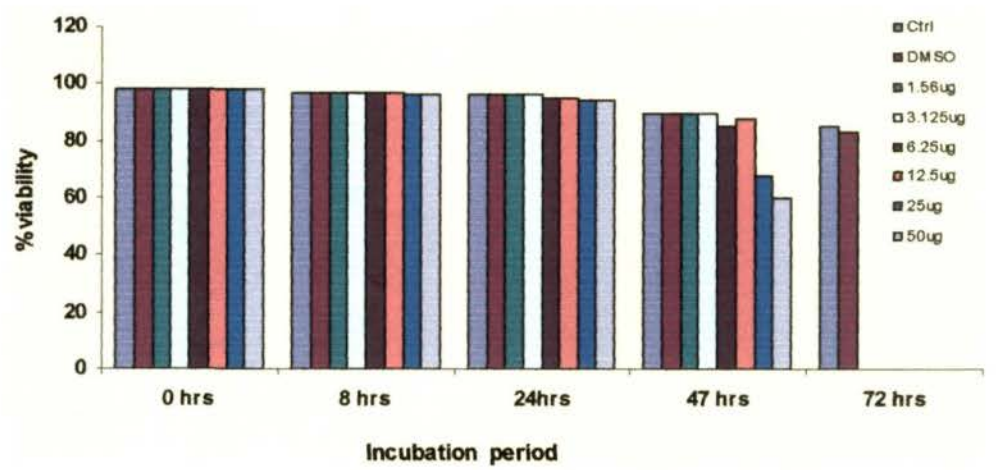


Fig. 5.13 Histogram representing the effect of n-Bu_2SnL^1 (**2**) on the survivability of peripheral blood mononuclear cells (PBMC).

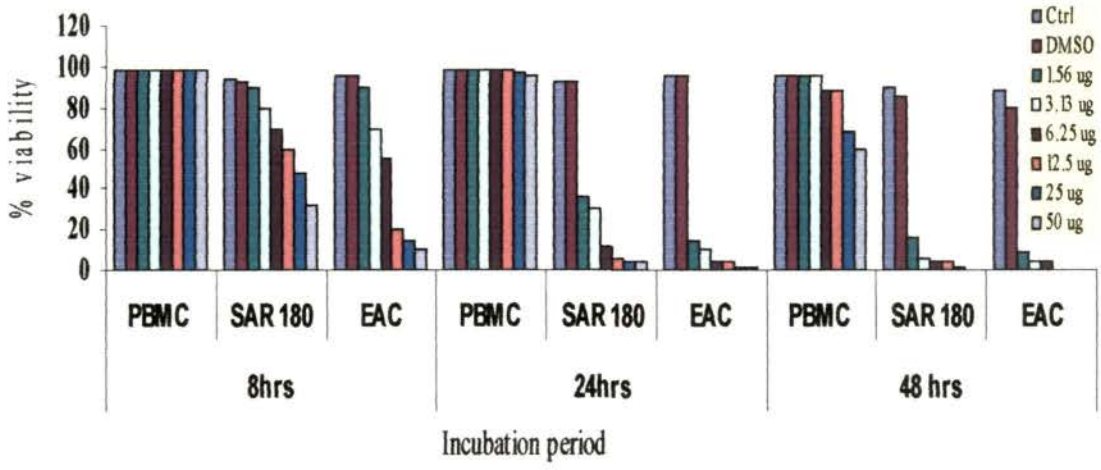


Fig. 5.14 Histogram representing effect of n-Bu_2SnL^1 (**2**) on the viability (Trypan blue dye exclusion test) of three different cell types i.e. peripheral blood mononuclear cells (PBMC), SAR-180 and EAC.

5.5.3 In vitro screening of n-Bu_2SnL^1 (2) for antitumour property against human cancer cell lines

The compound **2** was also tested for its antitumour activity against SW 480 (NIH, India) (a colon adinocarcinoma), HCT 116 (NIH, India) (a colon adinocarcinoma), RKO (NIH, India) (a colorectal cancer), HEK 293 (NIH, India) (a kidney cancer) along with the other cancer cell lines tested as discussed above (see section 5.5.1). The results of this study are represented in Fig. 5.15-5.17. The inhibitory effect of **2** on different human cancer cell lines was compared (Fig. 5.18). Adriamycin (ADR) was used as positive control in the study. The results show that the at the concentration of 10 μg/ml, **2** was most effective against A2780 followed by MCF-7, SiHa, PC3, ZR-75-1, Colo205 and Hop62 human cancer cell lines respectively

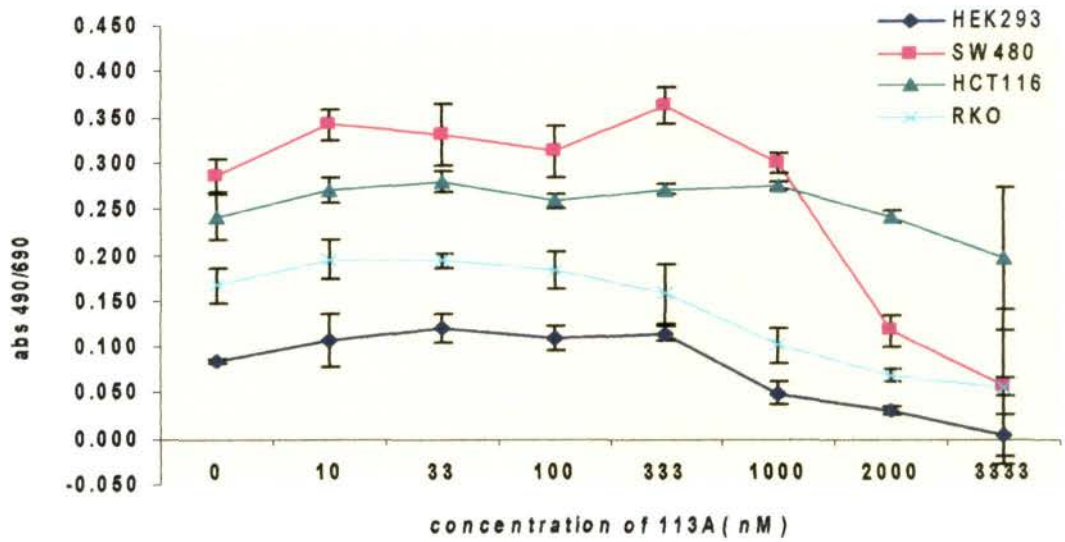


Fig. 5.15 Effect of **2** on cell growth of different human cancer cell line (HEK293, SW480, HCT116, RKO). Cells incubated with **2** for 24 hours. After 24 hours MTT assay was done and O.D. values measured.

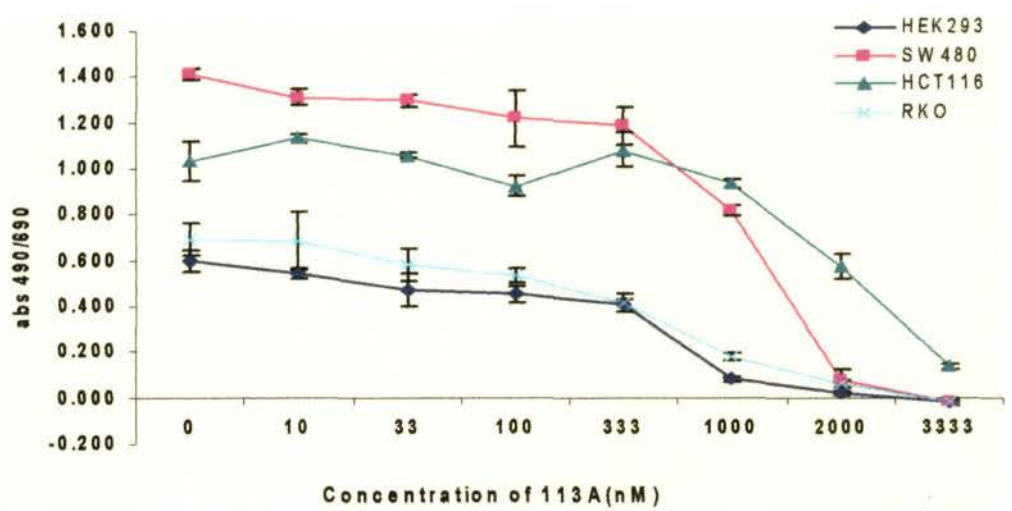


Fig. 5.16 Effect of **2** on cell growth of different human cancer cell line (HEK293, SW480, HCT116, RKO). Cells incubated with **2** for 48 hours. After 48 hours MTT assay was done and O.D. values measured.

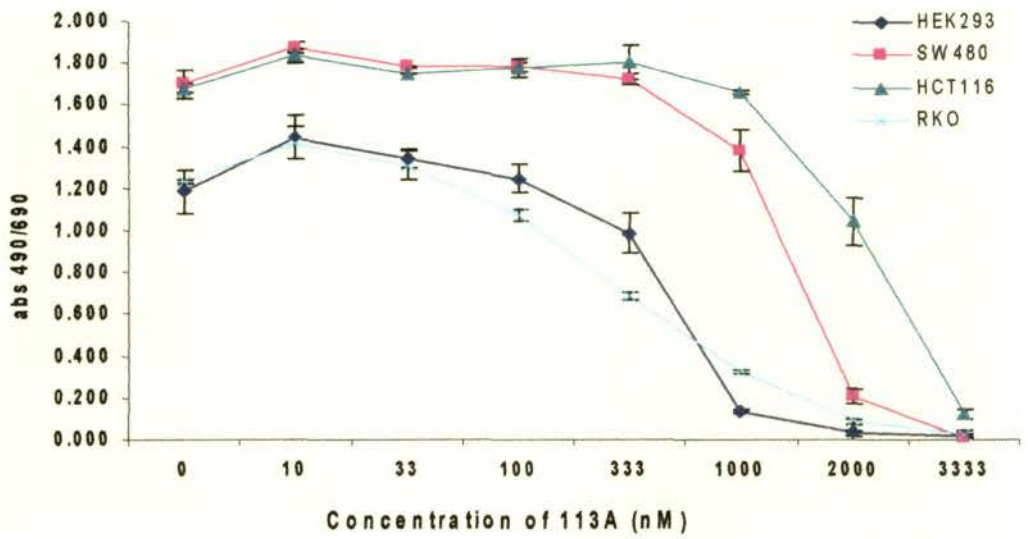


Fig. 5.17 Effect of **2** on cell growth of different human cancer cell line (HEK 293, SW480, HCT116, RKO). Cells incubated with **2** for 72 hours. After 72hours MTT assay was done and O.D. values measured.

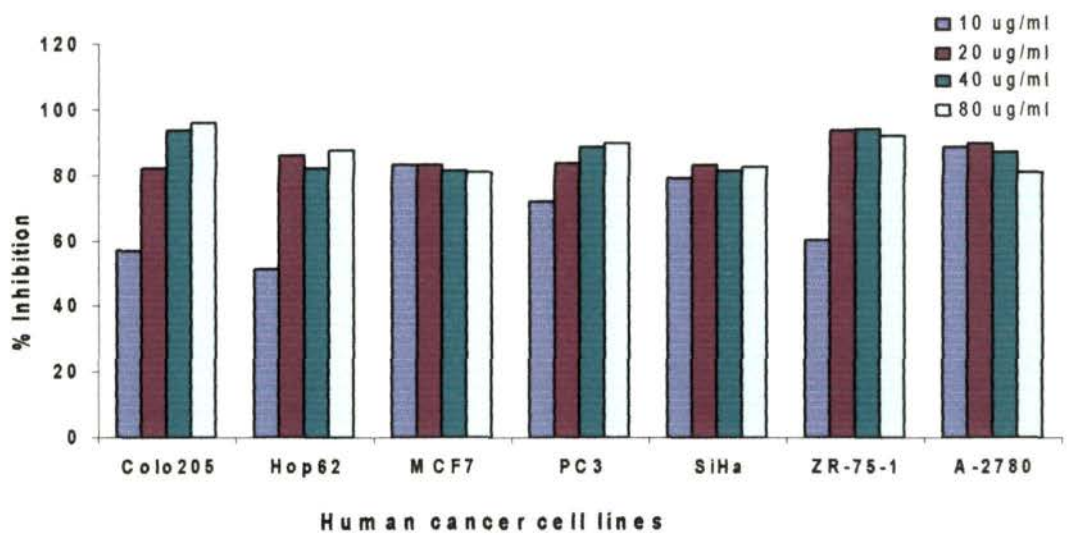


Fig. 5.18 Inhibitory effect of **2** on different human cancer cell lines. Adriamycin (ADR) has been used as positive control.

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LIST OF PUBLICATIONS

1. Synthesis, spectroscopic characterization and biocidal activity of some diorganotin(IV) complexes of salicylaldehydethiosemicarbazones and related ligands. Molecular and supramolecular structures of [$R_2Sn(OArCH{=}N\text{-}N{=}CSNH_2)$] where R=Me, Ph and Ar=-C_6H_4, -C_6H_3(5-Br) and [Me_2Sn {OC_6H_3 (5-Br) $CH{=}N\text{-}N{=}CSNH_2$}OH_2], M. Sen Sarma, S. Mazumder, D. Ghosh, A. Roy, A. Duthie, E.R.T. Tiekink, Appl. Organomet. Chem. (2007), DOI: 10.1002/aoc.1301.

2. Di-μ_2-methoxo-bis[benzyl(5-chloro-2-oxidobenzaldehydethiosemicarbazonato tin (IV)], M. Sen Sarma, C.A. Ellis, N. Moitra, A. Roy, E.R.T. Tiekink, Acta Cryst. **E62** (2006) m2067.

3. Organotin (IV) carboxylates of cyclopropane carboxylic acid and 3-cyclohexylpropanoic acid: their synthesis, characterization and biological activity. The crystal structure of dimeric 1,1,3,3- tetramethyl-1,3-dicyclopropylcarboxylatodistannoxane, M. Sen Sarma, A. Roy, A. Saha, Appl. Organomet. Chem. submitted.

4. Patent: The University of North Bengal and Visva Bharati have filed a patent application No.0353/KOL/2006 dt.19/4/2006 on ANTICANCER DRUGS HAVING BIOCIDAL ACTIVITY. Ms. Sen Sarma was one of the investigators.