Chapter 1

Organotin Chemistry

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1.1 General Introduction

Organotins are compounds which have at least one organic substituent linked directly to the tin atom *via* the carbon atom of the organic substituent. Organotin(II) and organotin(IV) compounds are known since tin has two stable oxidation states, that is +II and +IV. However, organotin(II) compounds are not very stable and tends to polymerize rapidly (Neumnn, 1970). The organotin(II) compounds are also easily oxidized to organotin(IV) which is more stable. Bis(cyclopentadienyl)tin(II) is the only known stable organotin(II) derivatives. The tin atom of this organotin(II) compound is sp^2 hybridized, with two of the hybrid orbitals involved in bonding with cyclopentadienyl ligands and the third containing the unshared pair of electrons as illustrated in Fig1.1.

Figure 1.1 Bis(cyclopentadienyl)tin(II)

Most known tin compounds are derivatives of organotin(IV) due to its stability. In organotin(IV) compounds, sp^3 hybridization of the valence orbital give rise to tetrahedral oriented bonds. The four principal classes of organotin(IV) compounds are mono-, di-, tri-, and tetraorganotins, which are represented by R_nSnX_{4-n} (n=1-4), where R is any organic group and X is anionic residue . Organotin(IV) compounds with electronegative groups such as organotin halides or pseudohalides are prone to use its empty 5d orbital to expand its coordination number beyond four. Hence, formation of 5-coordinate trigonal bipyramidal sp^3d or six-coordinate octahedral sp^3d^2 coordination geometries are commonly

observed in organotin(IV) complexes. In the case tetraorganotin compounds where there is absence of any electronegative groups, evidence for higher coordination in such compounds are also known, especially if the tetraorganotin contained organic groups with donor substituents such as 3-(2-pyridyl)-2-thiophene. These types of higher than four coordination compounds are reported in bis[3-(2-pyridyl)-2-thienyl-C,N]diphenyltin(IV) where the intramolecular coordination of the donor nitrogen atoms to the tin atom resulted in two additional coordination bonds in the tetraorganotin compounds (Kumar Das *et al*., 1987).

1.2 Synthetic methods

1.2.1 Synthesis of tetraorganotins

1. Grignard method (Polis, 1885)

Tetraalkyls, tetraaryls, tetravinyl and tetraethyltin compounds are prepared in coordinating solvents such as diethyl ether (Et_2O) or tetrahydrofuran (THF).

$$SnCl_4 + 4\ RMgCl \xrightarrow{THF} R_4Sn + 4\ MgCl_2$$

Mixed tetraorganotins may be prepared by reacting Grignard reagent with a diorganotin halide or triorganotin halide.

$$R'_3SnCl + RMgCl \xrightarrow{THF} RR'_3Sn + MgCl_2$$

[R, R' = aryl, alkyl or cycloalkyl]

2. Wurtz method

The reaction of alkyl halide with alkali metal such as sodium, followed by the addition of stannic chloride also yield the tetraorganotin.

$$SnCl_4 + 4\ RCl + 8\ Na \xrightarrow{Pentane} R_4Sn + 8\ NaCl$$

[R= alkyl or aryl]

3. Aluminium alkyl method

Organoaluminium compounds can be reacted with stannic chloride to produce tetraorganotin. The reactions are carried out in the absence of solvents. The addition of a complexing agent such as ether is required for high efficiency.

$$3\ SnCl_4 + 4\ R_3Al \xrightarrow{R_2O} 3\ R_4Sn + 4\ AlCl_3$$

[R= alkyl or aryl]

1.2.2 Synthesis of tri-, di- and monoorganotins

The first organotin derivative which was isolated some 130 years ago was diethyltin diiodide by Frankland (Colin, 1996). This organotin compound was synthesized by direct synthesis method.

The direct synthesis method was later extended to preparation of other organotin halides which involves the direct alkylation of metallic tin or tin halides by alkyl halides, in the presence of suitable catalyst (Murphy *et al.*, 1980;).

$$Sn + 2\ RX \xrightarrow{\text{catalyst}} R_2SnX_2$$

[R= alkyl or aryl]

The direct synthesis may be carried out in the absence of a catalyst. The reaction of benzyl chloride with tin powder is one such example, and the toluene or water used as the solvent gave good yield of dibenzyltin chloride (Sisido *et al.*, 1961) and tribenzyltin chloride (Sisido *et al.*, 1967), respectively.

$$2\ BzCl + Sn \xrightarrow{PhMe} Bz_2SnCl_2$$

$$3\ BzCl + 2\ Sn \xrightarrow{H_2O} Bz_3SnCl + SnCl_2$$

$$3\ Bz_2SnCl_2 + Sn \xrightarrow{H_2O} 2\ Bz_3SnCl + 2\ SnCl_2$$

Tin powder can also react with dry gaseous hydrogen chloride and an α,β-unsaturated carbonyl compound, to afford the substituted dialkyltin dihalide.

$$Sn + 2\ HCl + 2\ CH_2{=}CHCO_2R \longrightarrow (ROCOCH_2)_2SnCl_2$$

[R= alkyl or aryl]

The conventional method of preparing tri-, di- and monoorganotins is by the comproportionation reaction of tetraorganotins using different stoichiometric amounts of stannic chloride (Kocheshkov, 1926).

$$3\ R_4Sn + SnX_4 \longrightarrow 4\ R_3SnX$$

$$R_4Sn + SnX_4 \longrightarrow 2\ R_2SnX_2$$

$$R_4Sn + 3\ SnX_4 \longrightarrow 4\ RSnX_3$$

[R= alkyl or aryl]

The organotin halides particularly triorganotin halides, R_3SnX and diorganotin halides, R_2SnX_2 can be easily converted to organotin hydroxides and oxides by base hydrolysis using sodium hydroxide or ammonium hydroxide.

$$R_3SnX + OH^- \longrightarrow R_3SnOH + X^-$$

$$R_2SnX_2 + OH^- \longrightarrow R_2SnO + 2X^-$$

$$RSnX_3 + 3OH^- \longrightarrow RSnOOH + 3X^- + H_2O$$

[R= alkyl or aryl]

The trialkyltin oxides are distillable liquids or low melting solids which are readily soluble in organic solvents. Diorganotin and monoorganotin oxides are polymeric solids which are insoluble in all solvents except by reaction. Although exact structures for these oxides have not been determined due to their intractability, they are known to consist an extensive network of Sn-O-Sn bonds.

Triorganotin hydroxides in the liquid phase are in equilibrium with the oxides and water. The hydrolysis of the triorganotin halides which involve various intermediate hydrolysis products are shown as below:

$$R_3SnX \longrightarrow R_3SnOH \rightleftharpoons R_3SnOSnR_3 + H_2O$$

[R = alkyl or aryl]

On the other hand, triorganotin oxide can be used as starting material to synthesize other organotin with different functional group.

$$R_3SnOSnR_3 + 2HX \longrightarrow 2\ R_3SnX + H_2O$$

[R = alkyl or aryl]

Some of the triorganotin hydroxides and oxides with melting points or boiling points are quoted in the **Table 1.1** (Wilkinson *et al.*, 1982).

Table 1.1 Melting point or boiling point of triorganotin hydroxides and oxides

Compound	**M.P. (^oC) or B.P. (^oC/mmHg)**
Me_3SnOH	117 -118
Bu_3SnOH	48 -50
Ph_3SnOH	120
Cyh_3SnOH	198
Bz_3SnOH	122 -124
$Bu_3SnOSnBu_3$	154 -158/0.25
$Ph_3SnOSnPh_3$	117 -118

Organotin oxides react with inorganic and organic acids, alcohols, and mercaptans with ligands exchange. These reactions are equilibrium reactions which are driven to completion by removal of water, often by azeotropic distillation with toluene.

$$(R_3Sn)_2O + 2R'OH \rightleftharpoons 2R_3SnOR' + H_2O$$

$$R_2SnO + 2CH_3COOH \rightleftharpoons R_2Sn(OOCCH_3)_2 + H_2O$$

$$RSnOOH + 3HCl \rightleftharpoons RSnCl + 2H_2O$$

[R = alkyl or aryl]

The intermediates may be isolated from either the forward or reverse reactions by using anhydrides with the diorganotin and monoorganotin. The reaction of an organotin halide with the sodium salt of the carboxylic acid gave organotin-oxygen compounds as below:

$$R_2SnX_2 + R'COONa \rightleftharpoons R_2Sn(OOCR')_2 + 2NaX$$

[R, R' = alkyl or aryl]

Organotin oxides can also undergo insertion reactions with unsaturated compounds such as CO_2, SO_2, cyanides, and isocyanates.

$$[R_3Sn]_2O + CO_2 \longrightarrow R_3SnOCOOSnR_3$$

[R = alkyl or aryl]

Organotin sulphates, phosphates, nitrates, and metallostannoxanes are also known and prepared similarly. Organotin carboxylates and alkoxides may be used in exchange reactions to form other metal alkoxides. These two compounds can be used as intermediates for acylation and alkylation of hydroxy groups.

On the other hand, tin mercaptides, $R_xSn(SR)_{4-x}$ are much less susceptible to hydrolysis than tin alkoxides or carboxylates. They are readily prepared from an organotin oxide and mercaptans.

$$R_2SnO + 2R'SH \longrightarrow R_2Sn(SR')_2 + H_2O$$

[R = alkyl or aryl]

In addition, organotin mercaptides may be prepared from a stoichiometric amount of organotin halides, mercaptans and aqueous NaOH or in non-aqueous solution in presence of an amine to remove the HCl by-product.

$$R_2SnCl_2 + 2NaOH + 2R'SH \longrightarrow R_2Sn(SR')_2 + 2NaCl + H_2O$$

[R, R' = alkyl or aryl]

The tin-sulphur bond of tin mercaptides can be easily cleaved by halogens. The organotin sulfides, [$(R_3Sn)_2S$ and R_2SnS], which are similar to the tin mercaptides may be prepared from H_2S or a metal sulfide. Diorganotin sulfides are usually cyclic trimers with six-membered Sn-S-ring while monoorganotin sulfides, $R_2Sn_2S_3$, are oligomeric.

Alternatively, organotin monothio- or dithiocarbamates are the group of organotin compounds containing the Sn-S-C(S)- fragment. These compounds are prepared from tri- or diorganotin halides as shown below:

$$R_3SnCl + R'_2NC(S)S^-Na^+ \longrightarrow R_3SnSC(S)NR'_2 + NaCl$$

$$R_2SnCl_2 + 2R'_2NC(O)S^-Na^+ \longrightarrow R_2Sn[SC(O)NR'_2]_2 + 2NaCl$$

[R = alkyl or aryl]

1.3 Introduction of organotin carboxylates

1.3.1 Synthesis of organotin carboxylates

Organotin carboxylates are generally prepared by the reaction of organotin oxide or hydroxide with carboxylic acids. High yield of the products can be achieved by the azeotropic reflux of the reactants in boiling toluene using a Dean and Stark separator. These reactions are reversible reactions which can be driven to completion by the removal of water.

$$R_3SnOSnR + 2\ R'CO_2H \xrightarrow{PhMe} 2\ R_3SnOCOR' + H_2O$$

$$R_3SnOH + R'CO_2H \xrightarrow{PhMe} R_3SnOCOR' + H_2O$$

$$R_2SnO + 2\ R'CO_2H \xrightarrow{PhMe} R_2Sn(OCOR')_2 + H_2O$$

$$RSn(O)OH + 3\ R'CO_2H \xrightarrow{PhMe} RSn(O)(OCOR')_3 + H_2O$$

[R, R' = aryl, alkyl or cycloalkyl]

Organotin carboxylates can also be prepared by the reaction of organotin chlorides with metal carboxylates such as silver acetate and silver cinnamate in a suitable solvent.

$$R_nSnCl_{4-n} + (n\text{-}4)MOCOR' \longrightarrow R_nSn(OCOR')_{4-n} + (4\text{-}n)MCl$$

[M = Ag, Na, K; R, R' = aryl, alkyl or cycloalkyl]

Trimethyltin chloride has been reported to react with carboxylic acids at elevated temperature to form diorganochlorotin carboxylates. Similar product can also be obtained by reacting triorganotin carboxylate with diorganotin dichloride in chloroform.

$$R_3SnCl + R'CO_2H \longrightarrow R_2Sn(OCOR')Cl + RH$$

$$R_2SnCl_2 + R'_3SnOCOR'' \longrightarrow R_2Sn(OCOR'')Cl + R'_3SnCl$$

[R, R', R'' = aryl, alkyl or cycloalkyl]

Organotin carboxylates can also be prepared by the cleavage of one or more organic groups of the tetraorganotin compounds by carboxylic acids or mercury(I) carboxylate (Peruzzo *et al.*, 1972).

$$R_4Sn + n\ R'CO_2H \longrightarrow R_{4-n}Sn(OCOR')_n + n\ RH$$

$$2\ Me_4Sn + Hg_2(OCOMe)_2 \longrightarrow 2\ Me_3SnOCOMe + 2\ Hg + C_2H_6$$

[R, R' = aryl, alkyl or cycloalkyl]

There was also a report on the preparation of triphenyltin acetate by reacting organotin hydrides with carboxylic acid (Sawyer *et al.*, 1962).

$$Ph_3SnH + EtCO_2H \xrightarrow{Et_2O,60\ ^oC,\ 3\ hrs} Ph_3SnOCOEt + H_2$$

1.3.2 Coordination chemistry of organotin carboxylates

The chemistry of the organotin carboxylates has been previously reviewed by Okawara and Ohara (Okawara *et al.*, 1971). A large number of organotin carboxylates has been studied with respect to their solid and solution state structures as well as their biological properties (Molloy *et al.*, 1984; Molloy *et al.*, 1986; Molloy *et al.*, 1987). It was found that the anionic carboxylate groups can coordinate either inter or intramolecularly to the tin atom, giving rise to different structural motifs if it contains donor atoms. Thus, the structural chemistry of organotin carboxylates revealed that a wide variety of structures, including monomeric, oligomeric and polymeric have been discovered (Tiekink, 1991;

Tiekink, 1994; Szorcsik *et al.*, 2002; Sadiq-ur-Rehman *et al.*, 2005). Three types of idealized structures have been reported as shown in **Fig 1.2**.

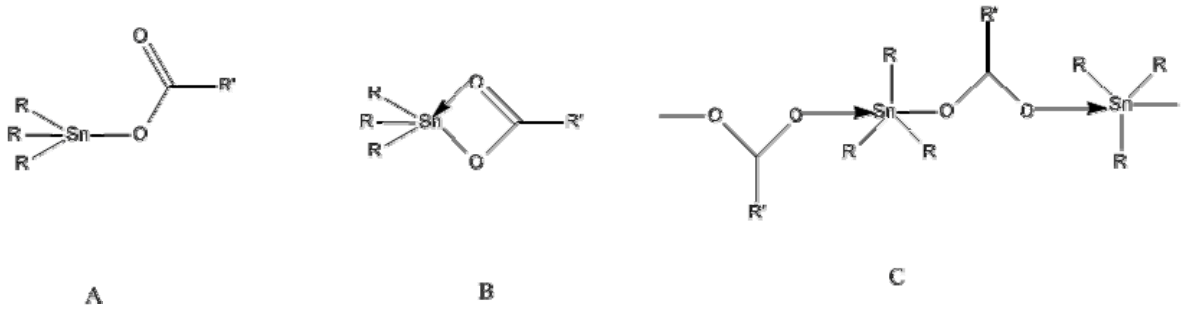

Figure 1.2 The idealized structures of triorganotin carboxylates, $R_3Sn(O_2CR')$

Structure **A** shows a four coordinate tin atom with a monodentate carboxylate ligand with a tetrahedral tin geometry. There is no interaction between the tin atom and carbonyl oxygen atom. Structure **B** gives a five coordinate tin atom with a bidentate chelating carboxylate ligand. Both structures **A** and **B** are monomeric species. The bond distance between the tin atom and the carbonyl O in structure **A** will be longer than that in structure **B** (Tiekink, 1991). The increase in C-O bond distances of the carbonyl group also provide indication of the presence of intramolecular Sn-O interaction in compound B. Structure **C** forms a polymeric species with five coordinate geometry at tin. The bidentate carboxylic ligand acts as bridging group and forms a distorted trigonal bypyramidal tin structure (Willem *et al.*, 1998).

The structural preference of organotin carboxylates depends mainly on steric and electronic factors. Organotin carboxylates with bulky R group will favor the monomeric structures. An X-ray diffractometric study on tricyclohexyltin ethanoate showed that the structure consists of discrete molecules with the tin atom occupying a distorted tetrahedral geometry (Alcock *et al.*, 1968). On the other hand, the R group which is sterically less

demanding such as in trimethyltin acetate (Chih *et al.*, 1973) will favor the polymeric structure. The presence of electron-withdrawing groups on the carboxylate fragment will enhance the acceptor characteristic of tin and the organotin carboxylate would be expected to favor a five coordination tin species when a donor ligand is added to the reaction.

1.3.3 Triorganotin *p*-substituted cinnamates

trans-Cinnamic acid has been found as part of the structural unit in anti-oxidant compounds in some drugs and balsams (Dewick, 1998). Cinnamic acid and its substituted derivatives are also found in plants and fruits such as cinnamon. The cinnamic acid and its derivatives are important in the synthesis of cumarinic derivatives and were found to be anti-bacterials (Tonari *et al.*, 2002) and anti-fungals (Cheng *et al.*, 2008). Organotin compounds are also known for their biological properties such as anti-tumor and anti-cancer activities (Barbieri *et al.*, 2002). Hence, the interest in triorganotin cinnamate will be focused mainly on whether such compounds provide enhanced biological activity as compared to the starting compounds.

A series of tributyltin *p*-substituted cinnamates has been synthesized and polymerised with styrene for the use as wood preservatives. In addition, some of the alkenoates was also synthesized and tested for their wood preservation activity (Siah, 1993).

1.3.4 Triorganotin diorganodithiocarbamyl acetates

The dithiocarbamato ligand and its derivatives have been extensively studied due to their potential biological activities (Giacobbe, 1977). A number of triorganotin dithiocarbamates has been synthesized previously and was found to have wide application in analytical chemistry due to their strong metal-binding properties (Thorn *et al.*, 1962). Some of the organotin dithiocarbamates, such as triphenyltin dimethyldithiocarbamate and triphenyltin diisopropyldithiocarbamate (Kumar Das *et al.*, 1984) was found to possess fungicidal activity.

The investigation of the biological activities of organotin dithiocarbamates was later extended to the preparation of compounds which has a methylenecarboxy -CH_2CO_2- fragment between the organotin and dithiocarbomato groups. Triorganotin esters which have been reported include trimetyl-, tributyl-, triphenyl- and tricyclohexyltin dithiocarbamylacetate (Ng *et al.*, 1991). The biological study of such triorganotin ester derivatives was found to have improved biological properties (Kumar Das *et al.*, 1987; Kuthubutheen *et al.*, 1989).

1.3.5 Bromination reactions of triorganotin carboxylates

Brominated organic compounds are important precursors in the preparation of many organometallic reagents, and in the transition-metal-mediated coupling reaction. Brominated organic compounds often exert enhanced bioactive properties, such as antitumor, antibacterial, antifungal, antiviral, and antioxidant activities. Bromine can be introduced into organometallic compounds by using brominating agents such as bromine, *N*-bromosuccinimide, ammonium tribromide, pyridinium tribromide and others.

Oxidative bromination by using combination of hydrobromic acid with hydrogen peroxide or tert-butylhydroperoxide (TBHP) (Barhate *et al.*, 1999) gave 1,2-dibromoalkanes which involves the formation of a cyclic " bromonium" ion intermediate on which unoxidised bromide ion attacks from the reverse side (Pincock *et al.*, 1970).

Bromination of (*E*)-PhCH=CHCOOCH$_3$ in 75% aqueous alcohol containing sodium bromide, sodium ethoxide and sodium perchlorate gives the product erytro-PhCHRCHBrCOOH (R=OH, Br). The reaction involves a weakly bridged bromium ion intermediate with some charge on the benzylic C atom (Susan *et al.*, 1979).

N-bromosuccinimide (NBS) is one of the most popular brominating agents due to its ease of handling, low cost and the byproduct, succinimide, can be easily recovered and converted back into NBS. Generally, the radical bromination of allylic and benzylic substrates takes place in CCl_4, while the nuclear brominations of activated aromatic systems are favoured in polar solvent (Pavlinac *et al.*, 2009). NBS is mainly used in bromination and oxidation of saturated and unsaturated organic compounds in protic solvent. The formation of 2-bromo-3-methoxy-3-phenylpropionic acid by using NBS in aqueous methanol has been reported (Karunakaran *et al.*, 1990).

Bromination, especially of aromatic substrates, is usually carried out by elemental bromine (Fuson *et al.*, 1962). The organic ammonium tribromides (OATB) including pyridine hydrobromide perbromide are preferred owing to the hazards associated with bromine. The advantages of OATB are that they are crystalline, easy to handle and maintain the desired stoichiometry (Mihir *et al.*, 1998). Although the preparation involve elemental bromine or hydrobromic acid would cause an environmental concern, the demand of brominating agents are important as synthetic intermediates and as antifungal, antibacterial, antitumor, antineoplastic and antiviral compounds (Butler *et al.*, 1993).

Tretrabutylammonium tribromide allows easy double bond bromination under mild reaction conditions (Mihir *et al.*, 1998).

4-dimethylaminopyridinium bromide perbromide which is an orange solid, has been prepared by treating 4-dimethylaminopyridine with hydrogen bromide and bromine. This reagent has been reported to brominate the α position of the ketone, as well as regioselective bromination of a 1,4-dihydropyridine derivative. This brominating agent has been used in the preparation of a number of organotin compounds as well as transition metal compounds such as the preparation of bis(4-dimethylaminopyridinium) dibromidodichloridodimethylstannate(IV) (Lo *et al.*, 2008) and bis,4-dimethylamino-pyridinium tetrabromidocobaltate (Lo *et al.*, 2009).

1.4 Structural techniques

A number of instrumental techniques have been used to investigate the structural features of organotin compounds. These techniques include infrared spectroscopy, ^{1}H and ^{13}C and ^{119}Sn nuclear magnetic resonance spectroscopy and X-ray crystallography.

1.4.1 Infrared Spectroscopy

The infrared spectroscopic technique has been widely used to provide useful information on the various substituents in organotin compounds. The stretching frequencies of the functional groups such as Sn-O, Sn-C, COO, C-Br, -CN, and C-S can be determined by this technique.

The stretching vibrations involving tin are quoted in the range of 200 -900 cm^{-1}. The stretching frequencies of the Sn-O, along with the carbonyl stretching frequency in the organotin carboxylate can be used to analyze the coordinative nature of the carboxylate group. However, the stretching frequencies of the Sn-O fall in a wide range and are depending on the environment of the Sn-O group in the molecule. On the other hand, the $\nu_{as(Sn-C)}$ and $\nu_{s(Sn-C)}$ are found in the range of 500 -600 cm^{-1} and 470 -530 cm^{-1} respectively. The Sn-C stretching frequencies are not particularly sensitive to the changes in the coordination number at the Sn atom (Ng, M. P., 1993).

The stretching frequencies of carbonyl group of the parent acid which is located around 1700 cm^{-1} (Ng *et al.*, 1991) and the shifting of the carbonyl group of the derived organotin esters to a lower region of the stretching frequencies shows the reaction have occurred. The asymmetric stretches of the carbonyl group appear in the range of 1500 - 1650 cm^{-1} and the symmetric stretches of the carbonyl group fall in the range of 1300 -1460

cm^{-1} (Nyquist, 2001). In addition, the difference of <150 cm^{-1} between the asymmetric and the symmetric stretching frequencies of C=O, suggests that the carboxylato group is engaged in strong bridging interactions. When the difference is exceeding 200 cm^{-1} the organotin carboxylates is non-bridged carboxylates and is indicative of negligible or weak bridging interaction, such as in tricyclohexyltin carboxylates (Ng *et al.,* 1991).

The C=S group is less polar than the C=O group and has a considerably weaker bond. In consequence, the IR band is not intense and falls at lower frequencies (Silverstein *et al.*, 1998). When the C=S group is linked to carbon, oxygen and sulphur atoms, the band can be located in the region 1030 -1270 cm^{-1} but when the C=S group is bonded to a nitrogen atom, the C=S group will be found in a wider range of 820 -1425 cm^{-1} (Shankaranarayana *et al.*, 1965).

The stretching vibration band of C-N which is coupled to C-S in triorganotin diorganodithiocarbamylacetates (Ng *et al*., 1991) appear in the region of 1020-1250 cm^{-1}, whereas the bending vibration of N-H is seldom detectable in the spectra of aliphatic secondary amines but detectable for the secondary aromatic amines which absorbs near 1515 cm^{-1} (Silverstein *et al.*, 1998). The nitro group can be detected in the region of 1600 - 1530 cm^{-1} for the asymmetric stretch and 1390 -1300 cm^{-1} for the symmetric stretch. The $\nu_{(C-N)}$ stretch in aromatic ring was found in the region of 850 - 800 cm^{-1} (Silverstein *et al.*, 1998).

The aliphatic C-Br bands fall mostly within the range of 515 -690 cm^{-1}. The $\nu_{(C-Cl)}$ peak for aryl chloride is located in the region of 1180 -1000 cm^{-1}. The actual position within this region depends on the substitution pattern (Silverstein *et al.*, 1998).

1.4.2 Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance is basically another type of absorption spectrometry, akin to infrared spectrometry. It is a property that magnetic nuclei have in a magnetic field and applied electromagnetic (EM) pulse or pulses, which cause the nuclei to absorb energy from the EM pulse and radiate this energy back out. The stable nuclides, such as ^{1}H, ^{13}C, ^{117}Sn and ^{119}Sn, that contain an odd number of protons and/or of neutrons (refer to different type of isotope) have an intrinsic magnetic moment and angular momentum, in other words a spin of ½.

The chemical shift, δ (in ppm relative to tetramethylsilane for ^{1}H and $CDCl_3$ for ^{13}C) is used to determine the structural formula of the organotin carboxylates. In the case of organotin compounds, the electronic effects of the SnR_3 groups, with different alkyl, cycloalkyl, aryl or heteroaryl ring, will show changes to the ground state electron density due to the nature and the position of the substituents. The carbonyl carbon of organotin carboxylates can be easily determined by its ^{13}C NMR chemical shift. Similarly, the chemical shifts for C=C and C-halogen can be identified by their ^{13}C NMR chemical shifts.

^{119}Sn Chemical shifts $\delta(^{119}Sn)$ of organotin compounds which are quoted relative to tetrametyltin, with down field shifts from the reference compound having a positive sign cover a range of over 600 ppm (Smith *et al.*, 1978; Harris *et al.*, 1978). As the electron-releasing power of the alkyl group increases, the tin atom becomes more shielded and the chemical shifts, $\delta(^{119}Sn)$ moves to a higher field. Replacement of alkyl groups in R_nSnX_{4-n} by unsaturated substituents, such as aryl or allyl groups, causes the ^{119}Sn chemical shift to move to a higher field (Kennedy *et al.*, 1974). Besides, by the addition of a complexing agent to a solution of the organotin compound in a non-coordinating solvent will cause an increase in coordination number of the tin atom in the organotin from four to five, six or

even seven and produces a large upfield shift of $\delta(^{119}Sn)$ (Hulme *et al.*, 1863). In addition, organotin compounds can undergo autoassociate in the solid state and in the solution. The coordination number of the tin atom increases on association can be observed by using ^{119}Sn NMR spectroscopy (Pommier *et al.*, 1968). The effect of R groups on $\delta(^{119}Sn)$ of organotin chlorides R_nSnCl_{4-n} are stated in **Table 1.2** (Wilkinson *et al.*, 1982)

Table 1.2 The effect of R groups on $\delta(^{119}Sn)$ of organotin chlorides R_nSnCl_{4-n}

R	$RSnCl_3$	R_2SnCl_2	R_3SnCl
Me	+20	+141	+164
Et	+6.5	+126	+155
Bu	+6.0	+122	+141
Ph	-63	-32	-48

The spin-spin coupling constant, *J* (Hz), involving tin and carbon ^1J (^{119}Sn-^{13}C), and involve tin and hydrogen ^2J (^{119}Sn-^{13}C -^1H) have been measured for a large number of organotin compounds. The coupling constant of ^{119}Sn-^{13}C for the four coordinated tributyltin compounds fall in a narrow range which is 330-390 Hz and the five coordinated tributyltin compounds in the range of 440-540 Hz (Willem *et al.*, 1996). The ^1J (^{119}Sn-^{13}C) of four coordinated tricyclohexyltin system is around 340 Hz (Danish *et al.*, 1995). The coupling constant value for four coordinated triphenyltin carboxylates is in the range 550-650 Hz while that for five coordinated triphenyltin system is in the range of 750-850 Hz (Willem *et al.*, 1996). The coupling constant ^1J (^{119}Sn-^{13}C) of tribenzyltin carboxylate at

300K in $CDCl_3$ approaches the value around 315 Hz. The lower value of ^1J (^{119}Sn-^{13}C) is attributed to pseudotetrahedral molecules of the simple complex Bz_3SnX and cis-trigonal bipyramid chelates as a result of lower s-electron contribution to the Sn-C bond (Lyčka *et al.*, 1987). The spin-spin coupling constants involving ^{119}Sn and other nuclei have been measured and quoted in **Table 1.3** (Wilkinson *et al.*, 1982)

Table 1.3 Spin-spin Coupling constant between ^{119}Sn and various nuclei in alkyltin compounds R_nSnX_{4-n} in non-coordinating solvents

Compound	**Coordination**	**^nJ(^{119}Sn-X) (Hz)**	**X**	**n**
R_4Sn	4	300 -340	^{13}C	1
R_4Sn	4	10 -25	^{13}C	2
R_3SnX	4	330 -390	^{13}C	1
R_3SnX	5	450 -480	^{13}C	1
R_2SnX_2	4	370 -480	^{13}C	1
R_2SnX_2	6	900 -970	^{13}C	1
R_3SnSnR_3	4	700 -4500	^{119}Sn	1

1.4.3 X-ray crystallography

The molecular structure of an organotin compound can be analyzed by X-ray crystallographic analysis on a single crystal. X-ray crystallographic analysis is a technique in which the pattern produced by the diffraction of X-rays through the closely spaced lattice of atoms in a crystal is recorded and then analyzed to reveal the nature of that lattice. This generally leads to an understanding of the material and molecular structure of a substance. The spacing in the crystal lattice can be determined using Bragg's law. The electrons that surround the atoms, rather than the atomic nuclei themselves, are the entities which physically interact with the incoming X-ray photons. This technique is widely used in chemistry to determine the structures of an immense variety of molecules, including inorganic compounds. X-ray diffraction is commonly carried out using single crystals of a material, but if these are not available, microcrystalline powdered samples may also be used, although this requires different equipment, gives less information, and is much less straightforward.

In inorganic and organotinmetallic chemistry, X-ray crystallography is widely used to determine lattice structures as well as chemical formulas, bond lengths and angles. The primary methods used in inorganic structures are powder diffraction and single-crystal diffraction. Many complicated inorganic and organometallic systems have been analyzed using single crystal methods, such as fullerenes, metalloporphyrins, and many other complicated compounds. The major limitation to the quality of single-crystal data is crystal quality. Inorganic single-crystal X-ray crystallography is commonly known as small molecule crystallography, as opposed to macromolecular crystallography.

When a crystal is subjected to X-rays, diffraction intensity data is collected resulting in a diffraction pattern. A typical small molecule crystal (>350 atoms) may have 1800

exposures to generate the diffraction pattern. Pattern location and intensity are used to determine size and composition of the molecule respectively. The phase relations of the diffracted beams are resolved mathematically before a model structure is deduced (referred to as the "Phase Problem"). Using computer software, structure parameters are systematically adjusted to give the best fit between observed intensities and calculations from the model structure. The final determination yields atom identities and positions in the unit cell and bond lengths and angles derived from the atom positions.

1.5 Application of organotin compounds

Organotin compounds have the widest range of uses of all main-group organometallic compounds. The increase in the industrial use is due to the technical application, toxicological and environment properties. The tetraorganotin have no significant commercial outlets but are important in manufacture of R_nSnX_{4-n}. Mono-, di- and triorganotin compounds contribute in the large scale application. Application of organotin compounds can be classified into two main fields, which is biological application and non-biocide application.

R_3SnX compounds are mainly used in biological application. The triorganotin compounds are used in agriculture as pesticides, insecticides, fungicides and acaricides (Evans, 1970). Tributytin oxide is used to preserve cellulose, wood and stonework to prevent fungal attack (Crowe *et al.*, 1978). Recent work has raised the possibility that certain dialkyltin compounds may have a role to play in cancer chemotheraphy (Crowe *et al.*, 1980). Tricyclohexyltin hydroxide is a systemic acaricide used in several countries to control phytophagous mites on apple, pear trees, grapes and other crops. This compound undergoes photodegradation in nature (Kumpulainen *et al*., 1977). Triphenyltin acetate can be used as rodent repellents.

Non-biocidal uses of organotin compounds are mainly found in R_2SnX_2 and $RSnX_3$. Mono- and dialkyltin compounds are mainly used in the stabilisation of rigid PVC against degradation by heat and exposure to the sunlight (Lanigan, 1978). Dimethyltin dichloride is used as a precursor for forming thin surface films of SnO_2 on glass (Evans, 1974) at the temperature of 500-600 ^oC. Dibutyltin compounds are used as homogenous catalysts in the manufacture of polyurethane foam (Karpel, 1980) and as cross-linking agents in room temperature vulcanizing silicones (Knoll, 1968). Certain monobutyltin compounds are used

as catalyst in the transesterification of oil. Some monobutyl- and monooctyltin compounds are used as water repellent chemicals.

1.6 Objective

The objectives of this project are

(i) to synthesize a series of triorganotin compounds bearing a substituted cinnamates or a thiocarbamato substituent. Cinnamic acid derivatives are widely used as a component in some anti-oxidant compounds, drugs and balsams. Cinnamic acid and its derivatives are also known to possess anti-bacterial, anti-fungal properties. The thiocarbamato substituents are known to exhibit biological properties, particularly antifungal properties, while the presence of halogen functional group in the compounds will improve the solubility of the resulting products.

(ii) to introduce hydrophilic functional group in the triorganotin carboxylates prepared so that the resulting compounds will improve their solubility in water, a factor which governs the biological properties of these compounds. The derivatization will be carried out by using brominating agents such as bromine, 4-dimethylaminopyridinium tribromide and *N*-bromosuccinimide.

(iii) to determine the structures of the triorganotin carboxyaltes and their bromination products by various spectroscopic techniques such as IR, NMR , elemental as well as by X-ray diffraction.

(iv) to determine the biological activities of selected triorganotin carboxylates and their bromination products.

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Chapter 2

Experimental Section

2. Experimental Section

2.1 General

The following commercial chemicals of reagent-grade quality were used in the synthesis: tricyclohexyltin chloride, tin powder, benzyl chloride, *p*-benzyl chloride, cyclopentyl bromide, sodium hydroxide, triphenyltin chloride, magnesium turnings and magnesium sulphate.

Triphenyltin hydroxide was purchased from Tokyo Kasei. Tricyclohexyltin hydroxide was converted from tricyclohexyltin chloride. Morpholine, chloroacetic acid, concentrated hydrochloric acid, sodium chloroacetate, anhydrous sodium sulphate and carbon disulphide were purchased from Merck.

Cinnamic acid, *p*-methylbenzaldehyde, *p*-methoxybenzaldehyde, *p*-chlorobenzaldehyde, *p*-nitrobenzaldehyde and malonic acid were purchased from Merck. Bromine, 4,4-dimethylaminopyridinium tribromide, pyridine tribromide, dibromotriphenylphosphine and *N*-bromosuccinamide were purchased from Sigma Aldrich.

The solvent used in the reaction such as tetrahydrofurane, toluene, acetone, ethanol, hexane, dichloromethane, chloroform, pyridine, piperidine were distilled before use.

The melting points of the organotin carboxylates were measured on an Electrothermal digital melting point apparatus and were uncorrected. The elemental analysis of the carboxylic acids and organotin carboxylates were carried out on a Perkin Elmer EA 2400 CHN Elemental Analyser. The compounds were characterized by using Perkin Elmer Spectrum RX1 spectrophotometer. The samples were prepared as nujol mulls in between KBr cells and the infrared spectroscopic analysis were recorded in the region of

600 -4000 cm^{-1}. The ^{1}H and ^{13}C NMR spectra were carried out on a JEOL JNM-ECA-400 FT-NMR spectrometer operating at 600 MHz for ^{1}H and 150 MHz for ^{13}C at ambient temperature. The carboxylic acids were dissolved in $CDCl_3$ with a few drops of deuterated DMSO, where as the triorganotin carboxylates were prepared dissolved in $CDCl_3$ as solvent. The chemical shifts of ^{1}H and ^{13}C were quoted relatively to both tetramethylsilane and $CDCl_3$. The X-ray crystallographic intensity data were measured by using Mo-Kα radiation (graphite-crystal monochromator, λ= 0.71069 Å). The data were collected at either 100 K or 300 K by using a (Bruker SMART APEX2 CCD diffractometer). The crystal structures were solved by using the *SHELXL-97* diagram (Sheldrick, 1997). The supplementary data including observed and calculated structure factors for selected compounds are available from the author. The cytotoxicity activity (MTT assay) was carried out on ThermoLabsystems, OpsysMR microplate spectrometer.

2.2 Synthesis of triorganotin

2.2.1 Conversion of tricyclohexyltin chloride to tricyclohexyltin hydroxide

Tricyclohexyltin hydroxide is prepared by dissolving 10 g of tricyclohexyltin chloride in 100 mL of acetone. 5 M of sodium hydroxide was added into the tricyclohexyltin chloride solution with vigorous stirring until white precipitate was formed. The solid was filtered and washed with water, dried under vacuum suction. Recrystallisation of the crude solid from chloroform gave product with m. p. 195 -198 ^{o}C yielded, 8.9 g (89%).

2.2.2 Preparation of tribenzyltin chloride

To 20.0 g (0.1798 mol) of tin powder in 200 mL of boiling water with efficient stirring was added 21.3 g (0.1798 mol) of benzyl chloride by using a dropping funnel. Refluxing and vigorous stirring were continued for 3 hrs. After cooling, solid mass containing the product and unreacted tin powder was filtered and dried in the air. When this was extracted with acetone for 6 hrs in a Soxhlet apparatus, 4.5 g (0.0150 mol) of metallic tin was recovered. Evaporation of the acetone solution under vacuum gave 22.3 g (93%, calculated base on benzyl chloride) of white crystal which was recrystallized by using ethyl acetate to give 19.5 g (87%) of colorless crystal, m. p. 140 -144 ^{o}C.

2.2.3 Conversion of tribenzyltin chloride to tribenzyltin hydroxide

Tribenzyltin hydroxide is prepared by dissolving 10 g of tribenzyltin chloride in 100 mL of acetone. 5 M of sodium hydroxide was added into the vigorous stirred tribenzyltin chloride solution until white precipitate was formed. 6.2 g (62%) of solid mass was filtered and washed with water. It was dried under vacuum suction. Recrystallization of the solid by using chloroform gave 5.1 g (82%) of product with m. p. 118 -119 ^{o}C.

2.2.4 Preparation of tris(*p*-chlorobenzyltin) chloride

To 20.0 g (0.1798 mol) of tin powder in 200 mL of boiling water was added 21.3 g (0.1798 mol) of *p*-chlorobenzyl chloride by using a dropping funnel with vigorous stirring of the reaction mixture. The reaction mixture turned into a pasty mass at the end of the addition. Chloroform was then used to extract the product. The bottom chloroform layer which contained the desired product and unreacted tin powder was filtered. The evaporation of the chloroform solution and recrystallized by using chloroform gave 10.5 g (87%) of colorless crystal, m. p. 114 -116 ^{o}C.

2.2.5 Conversion of tris(*p*-chlorobenzyltin) chloride to tris(*p*-chlorobenzyltin) hydroxide

Tris(*p*-chlorobenzyltin) hydroxide was prepared by dissolving 5 g of tris(*p*-chlorobenzyltin) chloride in 100 mL on acetone. 5 M of sodium hydroxide was added with vigorous stirring of tris(*p*-chlorobenzyltin) chloride solution until a white precipitate was

formed. 2.5 g (50%) of solid was filtered and washed with water. It was dried under vacuum suction.

2.2.6 Preparation of cyclopentyltriphenyltin

Cyclopentyl bromide (54.3 mL, 0.5 mol) in dry tetrahydrofuran was added drop wise to a suspension of magnesium (12.2 g, 0.5 mol) in dry tetrahydrofuran (200 mL). The reaction was initiated by the addition of a small amount of iodine crystals, accompanied by heating. Once the reaction commenced, the heat source was removed and the remaining cyclopentyl bromide solution was added dropwise. After the vigorous reaction had stopped, the mixture was refluxed with continuous stirring for 2 hrs to ensure the complete of reaction. Triphenyltin chloride (192.7 g, 0.5 mol) dissolved in dry toluene was added drop wise to the Grignard reagent at low temperature. The mixture was then refluxed for another 3 hrs. The mixture was hydrolyzed with 10% ammonium chloride solution at room temperature, and the organic layer was separated. The aqueous layer was extracted with toluene, and the combined toluene-THF extracts was then washed with distilled water and dried over calcium chloride. The dried toluene-THF extract was then concentrated under reduced pressure to a small volume. White solid were formed upon slow evaporation of concentrated mixture. The product was recrystallized from ethanol, m. p. 108 -110 ^{o}C.

2.2.7 Preparation of cyclopentyldiphenyltin hydroxide

Cyclopentyltriphenyltin (50.0 g, 0.1 mol) and iodine (25.4 g, 0.1 mol) were dissolved in 500 mL of DMF and stirred for 7 days at room temperature until all the tetraorganotin was converted to the triorganotin. Thin layer chromatographic analysis was used to monitor the progress of the reaction. The triorganotin iodide obtained was converted *in situ* to the hydroxide by the addition of acetone to facilitate the mixing of DMF with the aqueous phase, followed by 10% ammonia solution (equivalent volume to acetone). The mixtures were stirred at room temperature for two hrs and distilled water and then air-dried. It was next dissolved in chloroform, and the filtered chloroform solution dried over magnesium sulphate and concentrated to give a white solid product, m. p. 109 - 112 ^{o}C.

2.3 Preparation of carboxylic acid

2.3.1 Preparation of *p*-nitrocinnamic acid

p-nitrobenzaldehyde (0.15 g, 0.001 mol) and malonic acid (0.2 g, 0.002 mol) was heated in 100 mL of pyridine in the presence of a catalytic amount of piperidine. Refluxing and stirring were continued for 2 hrs until no evolution of carbon dioxide gas. The solution was then cooled and poured into water containing hydrochloric acid to neutralize the pyridine. The precipitated acid was filtered off under suction and washed with water. Recrystallization from ethanol gave product with m. p. 289 ^{o}C.

p-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxycinnamic acid (m. p. 170 - 173 ^{o}C), *p*-chlorocinnamic acid (m. p. 248 -250 ^{o}C) were prepared using similar method.

2.3.2 Preparation of 2,3-dibromo-3-phenylpropionic acid

Excess bromine (0.28 mL) was dissolved in dichloromethane and was added drop wise into cinnamic acid (0.74 g, 0.005 mol) in absolute ethanol 100 mL within 30 mins. Light brown solution was obtained. Sodium sulphite solution was added to remove excess bromine. The resulting solution was then extracted by using petroleum ether to obtain the product which was recrystallized from ethanol to give a white solid with m. p. 198 ^{o}C.

2.3.3 Preparation of 2,3-dibromo-3-(*p*-methylphenyl)propionic acid

Excess bromine (0.28 mL) was dissolved in dichloromethane and was added drop wise into *p*-methylcinnamic acid (0.81 g, 0.005 mol) in absolute ethanol within 30 mins. Pale brown solution was obtained. Sodium sulphite solution was added to remove excess bromine. The resulting solution was then extracted by using petroleum ether is used to extract the product. Recrystallization by using ethanol gave white solid with m. p. 144 -145 ^{o}C.

2.3.4 Preparation of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid

N-bromosuccinimide (0.17 g, 0.001 mol) and *p*-methoxycinnamic acid (0.17 g, 0.001 mol) was reflux in methanol for 1 hr. Evaporation of solvent gave a white solid with m. p. 154 -156 ^{o}C.

2.3.5 Preparation of *N*-piperidinyldithiocarbamylacetic acid

To a stirred solution of piperidine (10.0 mL, 0.1 mol) was added dropwise first carbon disulphide (6.0 mL, 0.01 mol) and then sodium hydroxide (4.0 g, 0.01 mol) in water (25 mL). The temperature of the reaction vessel was kept at 10 -15 ^{o}C by an ice water bath. The reaction mixture was stirred at room temperature (30 ^{o}C) for 2 hrs. Sodium chloroacetate (11.1 g, 0.1 mol) in water (25 mL) was then added to the stirred reaction mixture and stirring was continued for a further half hr. Addition of 20 % hydrochloric acid to the cooled mixture afforded a white solid, m. p. 148 -150 ^{o}C.

N,*N*-dimethyldithiocarbamylacetic acid (m. p. 134 - 137 ^{o}C), *N*,*N*-diethyl-dithiocarbamylacetic acid (m. p. 79 - 81 ^{o}C), *N*-methyl-*N*-butyl dithiocarbamyl acetic acid (m. p. 82 -84 ^{o}C), *N*-morpholinyldithiocarbamylacetic acid (m. p. 167 -170 ^{o}C) and *N*,*N*-diisopropyldithiocarbamylacetic acid (m. p. 122 -124 ^{o}C) were similarly prepared.

2.4 Preparation of triorganotin *p*-substituted cinnamates

2.4.1 Preparation of tributyltin *p*-substituted cinnamate

Bis(tributyltin) oxide (0.59 g, 0.001 mol) and cinnamic acid (0.28 g, 0.002 mol) in 100 mL of ethanol were refluxed in a Dean and Stark apparatus. A white solid was obtained upon evaporation of solvent. Recrystallization from hot hexane gave white crystals with m. p.74 -76^{o}C

Tributyltin *p*-methylcinnamate (m. p. 72 -74 ^{o}C), tributyltin *p*-methoxycinnamate (m. p. 60 -63 ^{o}C), tributyltin *p*-chlorocinnamate (m. p. 80 -82 ^{o}C) and tributyltin *p*-nitro-cinnamate (m. p. 75 -77 ^{o}C) were prepared using similar method.

2.4.2 Preparation of tricyclohexyltin *p*-substituted cinnamate

Tricyclohexyltin hydroxide (0.38 g, 0.001 mol) and cinnamic acid (0.14 g, 0.001 mol) were refluxed in a 1:1 mixture of ethanol and chloroform. A white solid was obtained upon evaporation of the solvent. Recrystallization from hot chloroform gave white crystals with m. p. 83 -86 ^{o}C.

Tricyclohexyltin *p*-methylcinnamate (m. p. 98 -100 ^{o}C), tricyclohexyltin *p*-methoxycinnamate (m. p. 93 -95 ^{o}C), tricyclohexyltin *p*-chlorocinnamate (m. p. 160 -163 ^{o}C) and tricyclohexyltin *p*-nitrocinnamate (m. p. 281-282 ^{o}C) were prepared using similar method.

2.4.3 Preparation of tribenzyltin *p*-substituted cinnamate

Tribenzyltin hydroxide (0.38 g, 0.001 mol) and cinnamic acid (0.14 g, 0.001 mol) were refluxed in 1:1 mixture of ethanol and chloroform for 1 hr. A white crystalline product was obtained upon evaporation of the solvent. Recrystallization from hot chloroform gave white crystals with m. p. 116 -118 ^{o}C.

Tribenzyltin *p*-methylcinnamate (m. p. 128 -130^{o}C), tribenzyltin *p*-methoxy-cinnamate (m. p. 121-124 ^{o}C), tribenzyltin *p*-chlorocinnamate (m. p. 138 -139 ^{o}C) and tribenzyltin *p*-nitrocinnamate (m. p. 165 -166 ^{o}C) were prepared using similar method.

2.4.4 Attempted preparation of tris(*p*-chlorobenzyltin) cinnamate

Tris(*p*-chlorobenzyltin) chloride was used to react with equimolar of cinnamics acid in ethanol and chloroform (1:1 ratio). However, the starting materials were recovered after worked up of the reaction mixture.

2.4.5 Attempted reaction of mixed organotin hydroxide and cinnamic acid

Cyclopentyldiphenyltin hydroxide (0.35 g, 0.001 mol) in hot toluene was added into cinnamic acid (0.15 g, 0.001 mol) in hot ethanol. The mixture was reflux for 3 hrs. The solvent was evaporated to give a white precipitate with m. p. 110 ^{o}C and m. p. 132-134 ^{o}C.

2.5 Preparation of triorganotin substituted propionate

2.5.1 Preparation of tributyltin 2,3-dibromo-3-phenylpropionate

2,3-dibromo-3-phenylpropionic acid (0.61 g, 0.002 mol) and tributyltin oxide (1.00 mL, 0.002 mol) was refluxed for 1hr in a mixture of ethanol and chloroform in 1:1 ratio. The resulting mixture was filtered while hot and removal of the solvent gave a white solid with m. p. 114 -116 ^{o}C.

Tributyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate (m. p. 105 -107 ^{o}C) and tributyltin 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionate (m. p. 93 -95 ^{o}C) were prepared using similar method.

2.5.2 Preparation of tricyclohexyltin 2,3-dibromo-3-phenylpropionate

2,3-dibromo-3-phenylpropionic acid (0.61 g, 0.002 mol) and tricyclohexyltin hydroxide (0.76 g, 0.002 mol) was refluxed for 1hr in a mixture of ethanol and chloroform in 1:1 ratio. The resulting mixture was filtered while hot and removal of the solvent gave a white solid with m. p. 126 -128 ^{o}C.

Tricyclohexyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate (m. p. 119 -121 ^{o}C) and tricyclohexyltin 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionate (m. p. 93 -96 ^{o}C) were prepared using similar method.

2.5.3 Preparation of tribenzyltin 2,3-dibromo-3-phenylpropionate

2,3-dibromo-3-phenylpropionic acid (0.61 g, 0.002 mol) and tribenzyltin hydroxide (0.76 g, 0.002 mol) was refluxed for 1hr in a mixture of ethanol and chloroform in 1:1 ratio. The resulting mixture was filtered while hot and removal of the solvent gave a white solid with m. p. 165 -168 ^{o}C.

Tribenzyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate (m. p. 145 -148 ^{o}C) and tribenzyltin 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionate (m. p. 120 -123 ^{o}C) were prepared using similar method.

2.6 Preparation of triorganotin diorganodithiocarbamylacetate

2.6.1 Preparation of tricyclohexyltin *N*-piperidinyldithiocarbamylacetate

Tricyclohexyltin hydroxide (0.38 g, 0.001 mol) and *N*-piperidinyldithiocarbamylacetic acid (0.23 g, 0.001 mol) were refluxed in a mixture of ethanol and chloroform in 1:1 ratio for 1 hr. The resulting mixture was filtered while hot and removal of the solvent gave a white solid with m. p. 123 -125 ^{o}C.

Tricyclohexyltin *N*,*N*-dimethyldithiocarbamylacetate (m. p. 68 -70 ^{o}C), tricyclohexyltin *N*,*N*-diethyldithiocarbamylacetate (m. p. 73 -75 ^{o}C), tricyclohexyltin *N*-methyl-*N*-butyldithiocarbamylacetate (m. p. 67 -68 ^{o}C), tricyclohexyltin *N*,*N*-diisopropyldithiocarbamylacetate (m. p. 61 -63 ^{o}C), tricyclohexyltin *N*-piperidinyldithiocarbamylacetate (m. p. 83 -84 ^{o}C) and tricyclohexyltin *N*-morpholinyldithiocarbamylacetate (m. p. 103 -108 ^{o}C) were similarly prepared.

2.6.2 Attempted lithiation of *N*-morpholinyldithiocarbamylacetic acid followed by addition of triphenyltin chloride

20 mL of 2 M lithium diisopropylamide in a mixture of THF/heptanes/ethylbenzene was introduced by using a syringe into *N*-morpholinyl dithiocarbamylacetic acid (0.02 g, 0.01 mol) in 15 mL of dried THF under nitrogen atmosphere at -20 ^{o}C. The mixture was allowed to stir for 1 hr and warm to room temperature and was then heated quickly to 50 ^{o}C for 30 mins. The mixture was cooled to 0 ^{o}C and triphenyltin chloride (1.67 g, 0.005 mol) dissolved in dry toluene was added rapidly. The mixture was stirred for 3 hrs and then

filtered. The solvent was evaporated to give a solid paste. Various solvents were used to purify the solid mass, but were unsuccessful.

2.7 Bromination of triorganotin carboxylate with brominating agents

2.7.1 Bromination reaction of tributyltin cinnamate with bromine at room temperature

Excess bromine (0.05 mL) in chloroform was added dropwise to tributyltin cinnamate (0.43 g, 0.001 mol) in 100 mL of ethanol. After stirring for 30 mins, the brown solution turned to orange colour. Sodium sulphite was added to remove the excess bromine. The product was extracted by petroleum ether. Upon evaporation of the petroleum ether fraction, a dark solid was obtained but was unable to identify.

2.7.2 Bromination reaction of tributyltin cinnamate with 4-dimethyl-aminopyridinium tribromide at room temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) dissolved in ethanol was added to tributyltin cinnamate (0.43 g, 0.001 mol) in 100 mL of ethanol. After 1 hr of vigorous stirring, the dark yellow solution was filtered and evaporation of solvent gave a white crystalline solid which was later identified as cinnamic acid with m. p. 132 -135 ^{o}C.

Similar bromination reactions were carried out for tributyltin *p*-methylcinnammate, tributyltin *p*-methoxycinnamate, tributyltin *p*-nitrocinnamate and tributyltin *p*-chlorocinnamate using equamolar of 4-dimethylaminopyridinium tribromide. The products obtained were also identified as *p*-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxycinnamic acid (m. p. 173 -174 ^{o}C), *p*-nitrocinnamic acid (m. p. 289 -290 ^{o}C) and *p*-chlorocinnamic acid (m. p. 248 -250 ^{o}C), respectively.

2.7.3 Bromination reaction of tributyltin cinnamate with pyridinium tribromide at room temperature

Pyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added into tributyltin cinnamate (0.43 g, 1 mmol) in 100 mL ethanol. Once the electrophile was added, the orange solution changed instantly to a yellow solution. Evaporation of solvent gave a white crystalline solid was identifical as cinnamic acid with m. p. 132-135 ^{o}C.

Similar bromination reactions were carried out for tributyltin *p*-methylcinnammate, tributyltin *p*-methoxycinnamate, tributyltin *p*-nitrocinnamate and tributyltin *p*-chloro-cinnamate using equamolar of pyridinium tribromide. The products obtained were also identified as *p*-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxycinnamic acid (m. p. 173 -174 ^{o}C), *p*-nitrocinnamic acid (m. p. 289 -290 ^{o}C) and *p*-chlorocinnamic acid (m. p. 248 -250 ^{o}C), respectively.

2.7.4 Bromination reaction of tributyltin cinnamate with dibromo-triphenylphosphine at room temperature

0.42 g (0.001 mol) of dibromotriphenylphosphine was weighed in a stoppered round bottom flask. To it was added 0.43 g (0.001 mol) of tributyltin cinnamate in 100 mL of ethanol. The red solution turned colorless instantly. Evaporation of the reaction mixture also found to recover the starting materials.

2.7.5 Bromination reaction of tributyltin cinnamate with 4-dimethyl-aminopyridinium tribromide at refluxing temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tributyltin cinnamate (0.43 g, 0.001 mol) which in 100 mL of ethanol. After refluxing for 3 hrs, a yellow solution was obtained. Evaporation of the yellow solution gave a white solid which was 2,3-dibromo-3-phenylpropionic acid with m. p. 195 -198 ^{o}C

2.7.6 Bromination reaction of tributyltin *p*-methylcinnamate with 4-dimethyl-aminopyridinium tribromide at refluxing temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tributyltin *p*-methylcinnamate (0.45 g, 0.001mol) in 100 mL of ethanol. After refluxing for 3 hrs, a yellow solution was obtained. Evaporation of the yellow solution gave a white solid which was found to be 2,3-dibromo-3-(*p*-methylphenyl)propionic acid with m. p. 144 -145 ^{o}C .

2.7.7 Bromination reaction of tributyltin *p*-methoxycinnamate with 4-dimethyl-aminopyridinium tribromide at refluxing temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in methanol to form dark yellow solution was added into tributyltin *p*-methoxycinnamate (0.46 g, 0.001 mol) which is dissolved in 100mL methanol. After refluxing for 3 hrs, a dark yellow solution was changed to yellow solution was obtained. Evaporation of the solvent gave a white

crystalline solid with m. p. 154 -156 ^{o}C which was found to be 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid.

2.7.8 Bromination reaction of tricyclohexyltin cinnamate with bromine at room temperature

Excess bromine (0.05 mL) in chloroform was added dropwise to tricyclohexyltin cinnamate (0.43 g, 0.001 mol) in 100 mL ethanol. After stirring for 30 mins, the brown solution turned to orange colour. Sodium sulphite was added to remove the excess bromine. Chloroform was used to extract the product. Upon evaporation of the solvent gave cinnamic acid with m. p. 132 -133 ^{o}C and tricyclohexyltin bromide with m. p. 198 ^{o}C.

Similar bromination reactions were carried out for tricyclohexyltin *p*-methylcinnammate, tricyclohexyltin *p*-methoxycinnamate, tricyclohexyltin *p*-nitro-cinnamate and tricyclohexyltin *p*-chlorocinnamate using equamolar of bromine. The products obtained were also identified as *p*-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxycinnamic acid (m. p. 173 -174 ^{o}C), *p*-nitrocinnamic acid (m. p. 289 -290 ^{o}C) and *p*-chlorocinnamic acid (m. p. 248 -250 ^{o}C), respectively.

2.7.9 Bromination reaction of tricyclohexyltin cinnamate with 4-dimethyl-aminopyridinium tribromide at room temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol were added to tricyclohexyltin cinnamate (0.51 g, 0.001 mol) in 100 mL ethanol and chloroform in 1:1

ratio. After 1 hr of vigorous stirring, an orange solution was obtained unchanged. Evaporation of the solvent gave a white crystalline solid which was found to be a mixture of cinnamic acid with m. p. 132 -135 ^{o}C and tricyclohexltin oxide with m. p. greater than 300˚C.

Similar bromination reactions were carried out for tricyclohexyltin *p*-methylcinnammate, tricyclohexyltin *p*-methoxycinnamate, and tricyclohexyltin *p*-nitrocinnamate using equamolar of 4-dimethylaminopyridinium tribromide. The products obtained were also identified as *p*-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxy-cinnamic acid (m. p. 173 -174 ^{o}C), *p*-nitrocinnamic acid (m. p. 289 -290 ^{o}C) and *p*-chloro-cinnamic acid (m. p. 248 -250 ^{o}C), respectively tricyclohexyltin *p*-chlorocinnamate did not react and the starting compound was recovered.

2.7.10 Bromination reaction of tricyclohexyltin cinnamate with pyridinium tribromide at room temperature

Pyridinium tribromide (0.36 g, 0.001 mol) in ethanol added to triyclohexyltin cinnamate (0.51 g, 0.001 mol) in a mixture of ethanol and chloroform in 1:1 ratio. After the addition, a yellow solution was obtained. Evaporation of the solvent gave a white crystalline solid which was cinnamic acid with m. p. 132 -135 ^{o}C and tricyclohexltin oxide with m. p. greater than 300 ^{o}C.

Reaction with or without reflux gave the same products as mention in **2.7.9**.

2.7.11 Bromination reaction of tricyclohexyltin cinnamate with dibromotriphenylphosphine at room temperature

0.42 g (0.001 mol) of dibromotriphenylphosphine was weighed in a stoppered round bottom flask. To it was added 0.43 g (0.001 mol) of tributyltin cinnamate in 100 mL of ethanol. The red solution turned colorless instantly. Evaporation of the reaction mixture also found to recover the starting materials.

2.7.12 Bromination reaction of tricyclohexyltin cinnamate with brominating agents at refluxing temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tricyclohexyltin cinnamate (0.51 g, 1mmol) in a mixture of ethanol and chloroform in 1:1 ratio. After refluxing for 3 hrs, an orange solution was obtained unchanged. Evaporation of the solvent gave a white crystalline solid was identical as a mixture of cinnamic acid with m. p. 132 -135 ^{o}C and tricyclohexltin oxide with m. p. greater than 300 ^{o}C.

The reaction with pyridinium tribromide with gave the same products as mention in **2.7.9**.

2.7.13 Bromination reaction of tribenzyltin cinnamate with bromine at room temperature

Excess bromine (0.05 mL) in chloroform was added dropwise to tribenzyltin cinnamate (0.42 g, 0.001 mol) in 100 mL ethanol. After stirring for 30 mins, the brown

solution turned to orange colour. Sodium sulphite was added to remove the excess bromine. The product was extracted by using chloroform upon evaporation of the chloroform, cinnamic acid with 132 -133 ^{o}C and tribenzyltin bromide were obtained.

Similar bromination reactions were carried out for tribenzyltin *p*-methylcinnammate, tribenzyltin *p*-methoxycinnamate, tribenzyltin *p*-nitrocinnamate and tricyclohexyltin *p*-chlorocinnamate using equamolar of bromine. The products obtained were also identified as *p*-methylcinnamic acid (m. p. 196 -198 ^{o}C), *p*-methoxycinnamic acid (m. p. 173 -174 ^{o}C), *p*-nitrocinnamic acid (m. p. 290 ^{o}C) and *p*-chlorocinnamic acid (m. p. 248 -250 ^{o}C), respectively.

2.7.14 Bromination reaction of tribenzyltin cinnamate with 4-dimethyl-aminopyridinium tribromide at room temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tritribenzyltin cinnamate (0.49 g, 0.001 mol) in 100 mL of a mixture of ethanol and chloroform in 1:1 ratio. After 1 hr of vigorous stirring, orange solution was obtained. Evaporation of the solvent gave a white crystalline solid which was identified as a mixture of cinnamic acid with m. p. 132 -135 ^{o}C and tribenzyltin oxide with m. p. greater than 300˚C.

Similar bromination reactions were carried out for tricyclohexyltin *p*-methyl-cinnammate, tricyclohexyltin *p*-methoxycinnamate, and tricyclohexyltin *p*-nitrocinnamate using equamolar of pyridinium tribromide and dibromotriphenylphosphine. The products obtained were found to be similar as section **2.7.9**.

2.7.15 Bromination reaction of tribenzyltin cinnamate with 4-dimethyl-aminopyridinium tribromide at refluxing temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tribenzyltin cinnamate (0.49 g, 0.001 mol) in a mixture of ethanol and chloroform in 1:1 ratio. After refluxing for 3 hrs, an orange solution was obtained. Evaporation of solvent gave 2,3-dibromo-3-phenylpropionic acid with m. p. 198 ^{o}C and tricyclohexltin oxide with m. p. greater than 300 ^{o}C.

Similar bromination reactions were carried out for tribenzyltin *p*-methylcinnammate, and tribenzyltin *p*-methoxycinnamate at refluxing temperature. The products obtained were also identified as 2,3-dibromo-3-(*p*-methylphenyl)propionic acid with m. p. 144 -145 ^{o}C and 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid with m. p. 154 -156 ^{o}C. However, the reactions of tribenzyltin *p*-nitrocinnamate and tribenzyltin *p*-chlorocinnamate lead to the recovery of starting material. The bromination reaction by using pyridinium tribromide gave the similar products. Starting materials were obtained by using dibromotriphenylphosphine.

2.7.16 Bromination reaction of tricyclohexltin dimethyldithiocarbamylacetate with 4-dimethylaminopyridinium tribromide at room temperature

4-dimethylaminopyridinium tribromide (0.36 g, 0.001 mol) in ethanol was added to tricyclohexyltin dimethyldithiocarbamylacetate (0.49 g, 0.001 mol) in 100 mL in a mixture of ethanol and chloroform in 1:1 ratio. After 30mins of vigorous stirring, an orange solution was obtained. Evaporation of the solvent gave a white crystalline solid which was identified

as a mixture of dimethyldithiocarbamylacetic acid with m. p. 134 -137 ^{o}C and tricyclohexyltin oxide with m. p. greater than 300˚C.

Similar bromination reactions were repeated by using 4-dimethylaminopyridinium tribromide and pyridinium tribromide. *N*,*N*-dimethyldithiocarbamylacetic acid (m. p. 134 -137 ^{o}C), *N*,*N*-diethyldithiocarbamylacetic acid (m. p. 79 -81 ^{o}C), *N*-methyl-*N*-butyldithiocarbamylacetic acid (m. p. 82 -84 ^{o}C), *N*-piperidinyldithiocarbamylacetic acid (m. p. 122 -124 ^{o}C), *N*-morpholinyldithiocarbamylacetic acid (m. p. 167 -170 ^{o}C) and *N*,*N*-diisopropyldithiocarbamylacetic acid (m. p. 122 -124 ^{o}C) were obtained.

2.8 Procedure for determining *in vitro* cytotoxic activity (MTT assay)

The cytotoxicity was evaluated by means of tetrazolium salts reduction test (MTT) (Mosmann, 1983). The cytotoxicity of the triorganotin carboxylates was tested on the HL-60 human promyelocytic leukemia cell line. The HL-60 tumour cells were obtained from American type culture Collection and cultured in RPMI1640 medium supplemented with 1% v/v glutamine and 10% fetal calf serum (FCS) (Gibco). The cells were cultured under the condition of 5% CO_2, 95% air and 100% humidity.

The stock solution (1 mg/mL) of the selected compounds, namely tributyltin *p*-nitrocinnamate **(C4),** tricyclohexyltin cinnamate**,** tricyclohexyltin *p*-methylcinnamate**,** tricyclohexyltin *p*-methoxycinnamate**,** tricyclohexyltin *p*-nitrocinnamate**,** tricyclohexyltin *p*-chlorocinnamate, tribenzyltin *p*-nitrocinnamate**,** tricyclohexyltin 2,3-dibromo-3-phenylpropionate, tricyclohexyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate and tricyclohexyltin 2-methoxy-3-bromo-3-(*p*-methoxyphenyl)propionate, were prepared in dimethylsulphoxide (DMSO). The stock solutions were diluted in phenol red free cultured medium, which did not exert any inhibitory effect on proliferation, before use. 10000 cells were added to each well of 96 well plates and incubated overnight with the tested compounds in triplicate. The condition of the incubation of the samples was set at 37 ^{o}C in 5% CO_2. After 24 hrs, the cultured medium was removed and replaced by fresh medium for the cells to proliferate. The test was continued with another overnight incubation at 37 ^{o}C. Each well was loaded with 10 µl of 0.5 mg/mL solution of 3-[4,5-dimethylthiozol-2-yl]-2,5-diphenyltetrasoliumbromide (MTT) which was dissolved in phosphate buffer saline (PBS), followed by another 4 hrs of incubation at 37 ^{o}C. Before screening the inhibition of the cells growth, 70 µl of the supernatant were removed and 100 µl DMSO were added to

dissolve the formazan crystal. Absorbance at 570 nm for the inhibition of the proliferation of the cells by the triorganotin carboxylates was detected by a microplate spectrometer.

The results of the percentage of the cells survived againts the control were plotted. The mean of the triplicate data was calculated and compared. The standard deviation of the percentage of the viability also stated. *Cisplatin* was used as the reference and included in the experiment.

References:

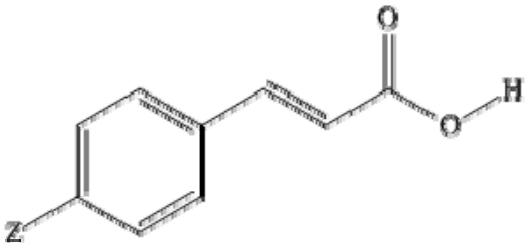
Mosmann, T., (1983) *J. Immunological Methods*, **65**, 55.

Sheldrick, G.M., (1997) *SHELXS97* and *SHELXL97*, University of Göttinge, German.

Chapter 3

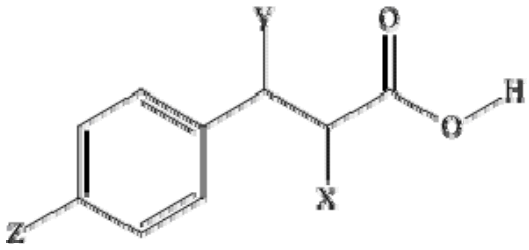
Result & Discussion

3.1 General



Z = H, CH_3, OCH_3, NO_2, Cl

Figure 3.1 *p*-Substituted cinnamic acid



Z= H, CH_3; Y =Br; X =Br;

Z= OCH_3; Y =Br; X = OCH_3

Figure 3.2 Substituted 3-phenylpropionic acid

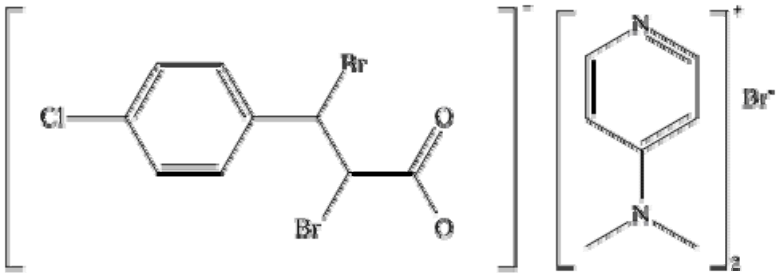


Figure 3.3 Bis[4-dimethylaminopyridinium]-2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide

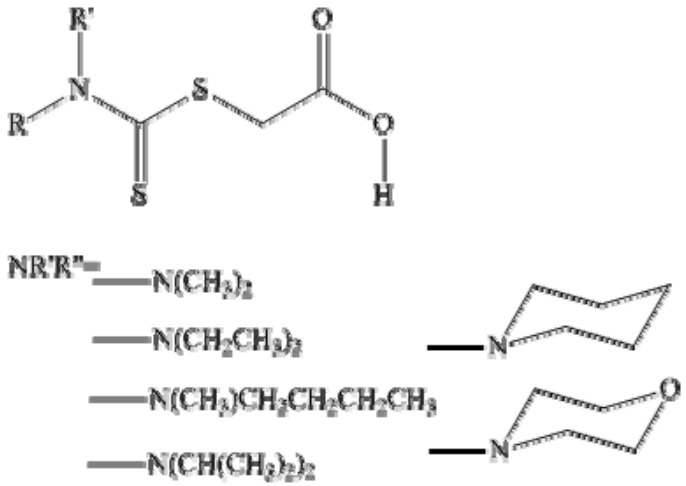
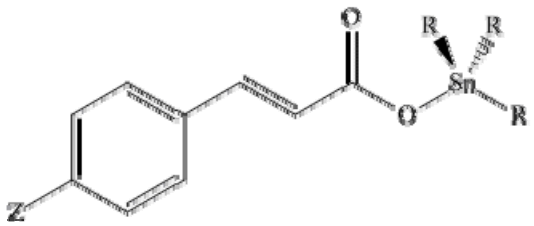


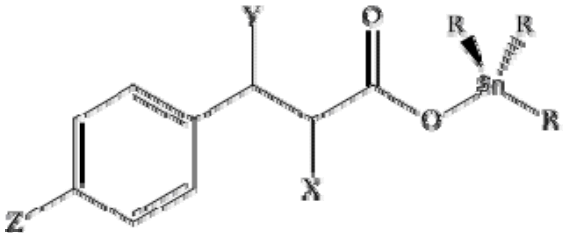
Figure 3.4 Diorganodithiocarbamylacetatic acid



R= Bu, Cyh, Bz

Z = H, CH_3, OCH_3, NO_2, Cl

Figure 3.5 Triorganotin *p*-substituted cinnamate



R= Bu, Cyh, Bz

Z= H, CH_3; Y =Br; X =Br; Z= OCH_3; Y =Br; X = OCH_3

Figure 3.6 Triorganotin substituted 3-phenylpropionate

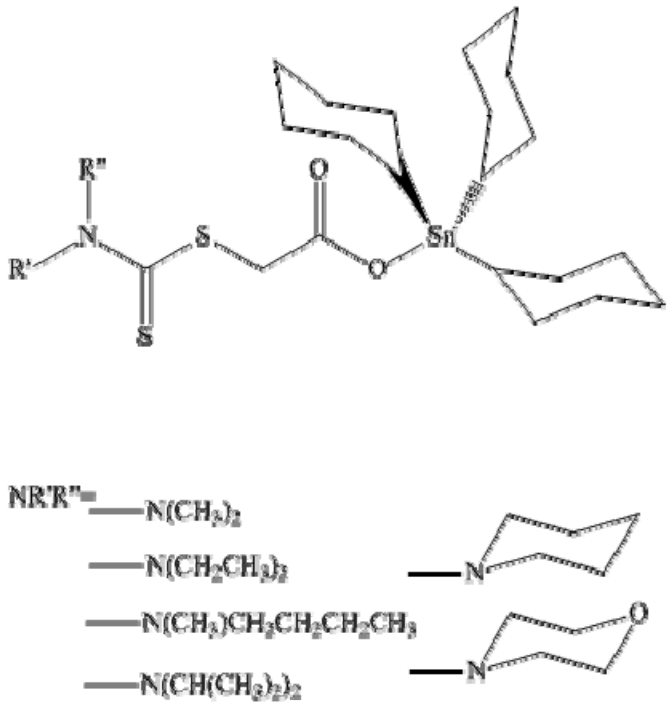


Figure 3.7 Tricyclohexyltin diorganodithiocarbamylacetate

3.2 Synthesis

3.2.1 Synthesis and reaction of substituted cinnamic acid

The Doebner condensation of *p*-substituted aldehydes with malonic acid in pyridine in the presence of catalytic amount of piperidine gave cinnamic acid and *p*-substituted cinnamic acids with the general formula, Z C_oH_4CH=CH COOH. The reaction is shown in **Figure 3.8**.

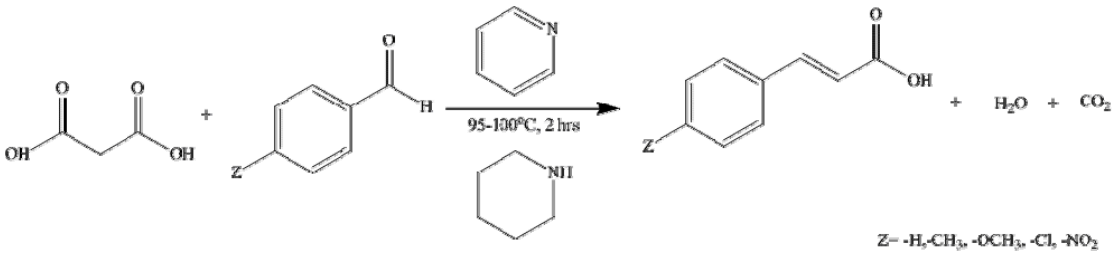


Figure 3.8 Synthesis of *p*-substituted cinnamic acids

The reaction of bis(tributyltin)oxide with cinnamic acid and *p*-substituted cinnamic acids in toluene by using Dean and Stark apparatus gave cinnamate salt with the general formula, $Bu_3SnOCCOCH$=CHC_6H_4Z (Z = H, CH_3, OCH_3, Cl, NO_2) as shown in **Figure 3.9**.

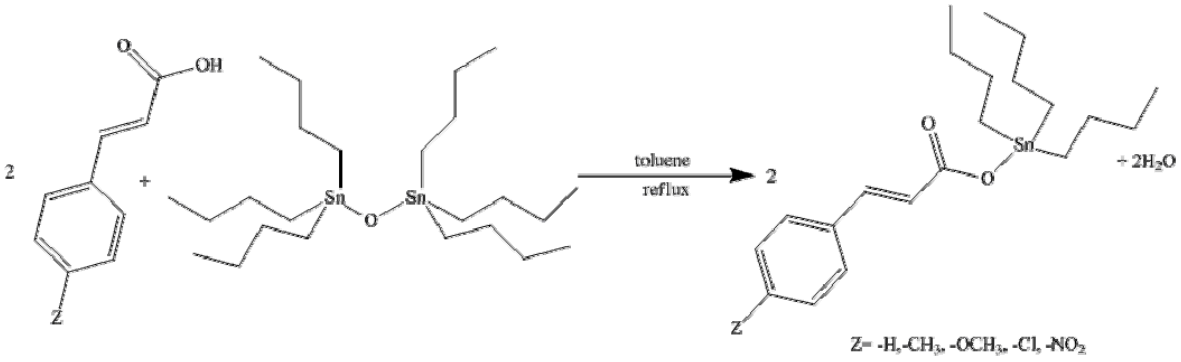


Figure 3.9 Synthesis of tributyltin *p*-substituted cinnamates

The tributyltin *p*-substituted cinnamate are all white solids with melting points below 100^{o}C (**Table 3.1**). The chemical formula of the products are supported by their elemental analytical results as given in **Table 3.1**. Further characterization of the tributyltin carboxylates was carried out by using various spectroscopic techniques such as IR, NMR and X-ray crystallography which will be discussed in the later section. The tributyltin cinnamates were then reacted with brominating agent such as, bromine and 4-dimethylaminopyridinium tribromide, in a mixture of 1:1 ethanol and chloroform at room temperature for 2 hrs or refluxed for 30 mins. The reactions of tributyltin cinnamate, tributyltin *p*-methylcinnamate and tributyltin *p*-methoxycinnamate with these two brominating agents resulted in the cleavage of tributyltin cinnamates, yielded the brominated cinnamic acid with the general formula, HOCOCH(Br)CH(Br)C_6H_4Z-*p* (Z = H, CH_3, OCH_3,) and tributyltin bromide. The above brominated products were obtained after recrystalization from ethanol. However, if methanol was used to recrystalise the product, *p*-$CH_3OC_6H_4CH(Br)CH(OCH_3)COOH$ was found to be the major product. In the case of tributyltin 4-chlorocinnamate and tributyltin *p*-nitrocinnamate, the bromination reaction using bromine gave the unbrominated cinnamic acid HOCOCH=CHC_6H_4Z-*p* (Z = Cl, NO_2) and tributyltin bromide. It was therefore shown that the bromination of tributyltin *p*-substituted cinnamates did not produce the brominated tributyltin cinnamates as anticipated. A summary of the bromination of tributyltin cinnamates is given in the **Figure 3.10**:

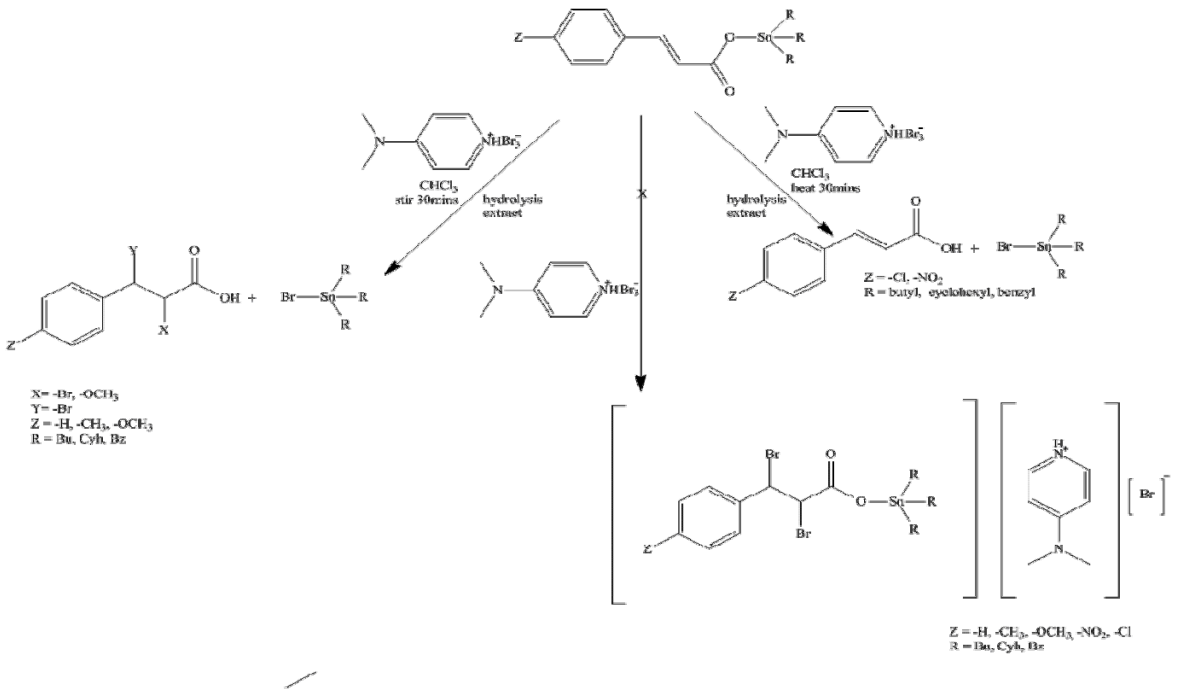


Figure 3.10 Bromination of tributyltin *p*-substituted cinnamates

Another brominating agent used in the study was 4-dimethylaminopyridinium tribromide. In this case the bromination reaction of tributyltin *p*-chlorocinnamate in chloroform and absolute ethanol resulted in the cleavage of the tributyltin *p*-chlorocinnamate and produced an ionic compound which was identified as bis(4-dimethylaminopyridinium)-2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide by its X-ray crystal structure discussed later. The reaction is shown in the **Figure 3.11**.

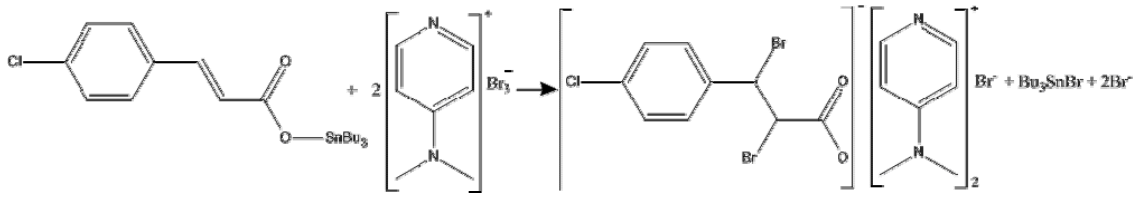


Figure 3.11 Synthesis of bis(4-dimethylaminopyridinium)-2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide

The reaction of other triorganotin hydroxide such as tricyclohexyltin hydroxide and tribenzyltin hydroxide with substituted cinnamic acid such as cinnamic acid, *p*-methylcinnamic acid, *p*-methoxycinnamic acid, *p*-chlorocinnamic acid and *p*-nitrocinnamic acid gave triorganotin cinnamate with the general formula, $R_3SnOCOCH=CHC_6H_4Z$-*p* (R = Cyh, Bz; Z = H, CH_3, OCH_3, Cl, NO_2), is shown in **Figure 3.12** .

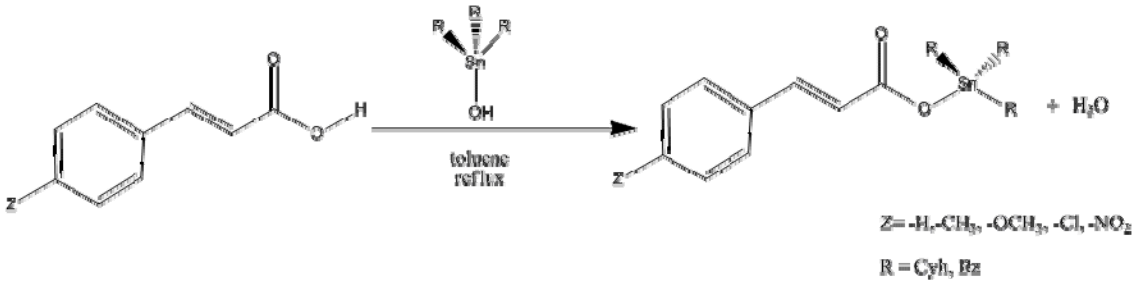


Figure 3.12 Synthesis of tribenzyltin *p*-substituted cinnamates

The melting point and the elemental analytical data of both tricyclohexyltin- and tribenzyltin carboxylates are given in **Table 3.1** as well.

The bromination of the resulting triorganotin cinnamates with bromine and 4-dimethylaminopyridinium tribromide also gave similar products as the tributyltin cinnamates analogues.

Due to the failure of preparing brominated triorganotin cinnamates by the reaction of 4-dimethylaminopyridinium tribromide and triorganotin cinnamates, a different approach to produce such compounds was attempted. The *p*-substituted cinnamic acid was first brominated by using brominating agents such as bromine and 4-dimethylaminopyridinium tribromide. Both bromination processes gave brominated substituted 3-phenylpropionic acid with the general formula of $HOCOCH(X)CH(Y)-C_6H_4Z$-*p* (X= Br, OCH_3; Y=Br; Z = H, CH_3, OCH_3). The brominated cinnamic acid was

subsequently reacted with triorganotin hydroxide to produce brominated triorganotin *p*-substituted cinnamates with the general formula of $R_3SnOCOCH(X)CH(Y)C_6H_4Z$-*p* (R= Cyh, Bz; X= Br, OCH_3; Y=Br; Z = H, CH_3, OCH_3). The summary of the reaction is given in the **Figure 3.13** below:

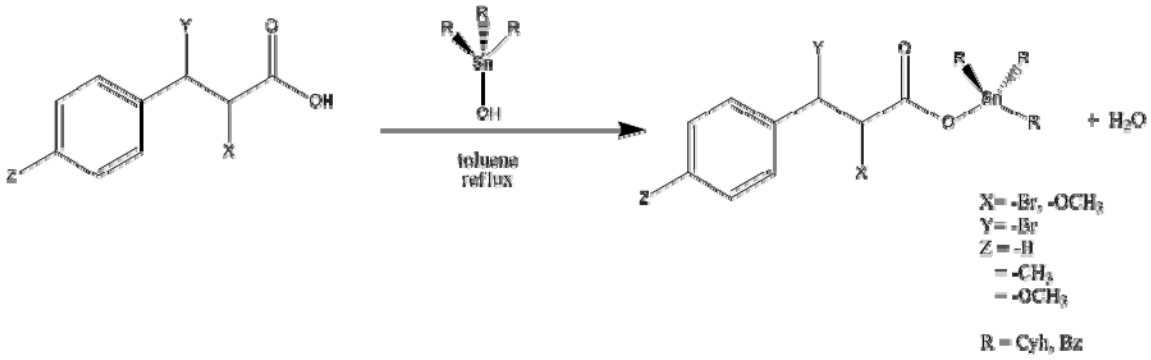


Figure 3.13 Synthesis of brominated triorganotin *p*-substituted cinnamates

The products prepared are stable with melting point above 100 ^oC and the elemental analysis carried out and given in **Table 3.1**.

3.2.2 Synthesis of diorganodithiocarbamylacetic acids and their reactions with triorganotin chloride.

Diorganodithiocarbamylacetic acids such as dimethyldithiocarbamylacetic acid, diethyldithiocarbamylacetic acid, methylbutyldithiocarbamylacetic acid, diisopropyl-carbamylacetic acid, morpholinylcarbamylacetic acid and piperidinylcarbamylacetic acid were synthesized by the reactions of secondary amine such as dimethylamine, diethylamine, methyl-butylamine, diisopropylamine, morpholinylamine and piperidinylamine, with carbon disulfide in the presence of sodium hydroxide, followed by the addition of sodium chloroacetate and hydrolysed by dilute hydrochloric acid as shown in **Figure 3.14** below:

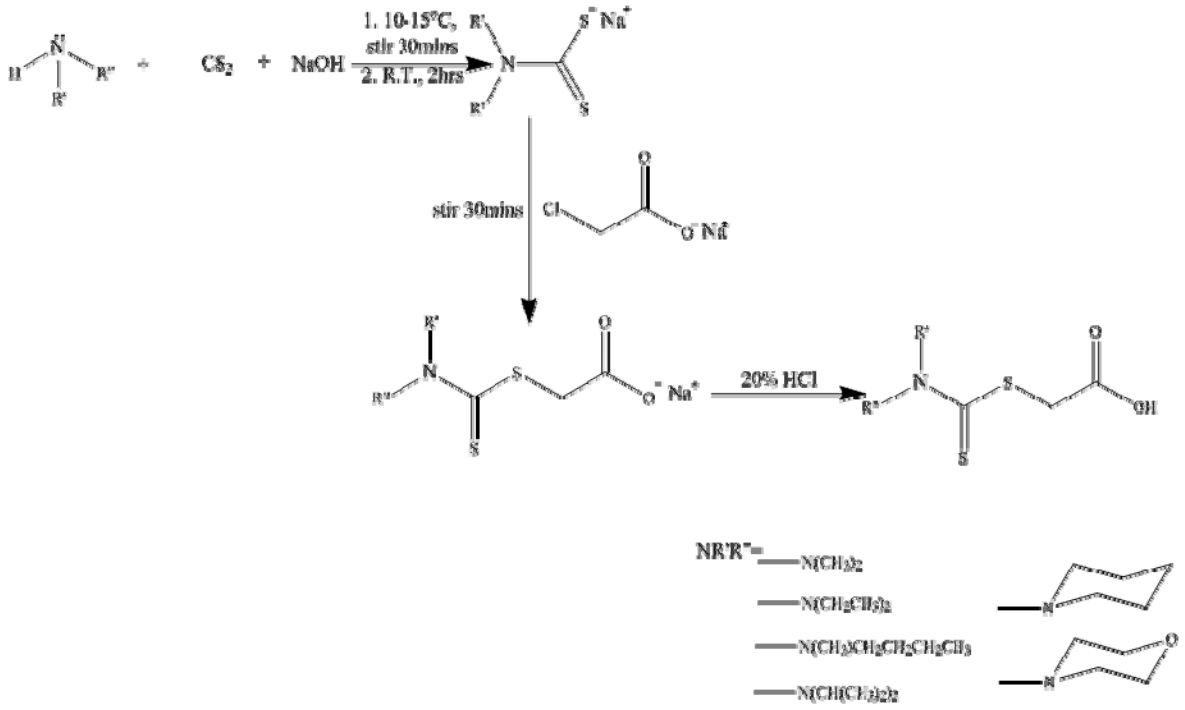


Figure 3.14 Synthesis of diorganodithiocarbamylacetate

Tricyclohexyltin diorganodithiocarbamylacetates were prepared by using tricyclohexyltin hydroxide, which was prepared from the base hydrolysis of tricyclohexyltin chloride by using sodium hydroxide in chloroform, and diorganodithiocarbamylacetic acid under reflux for 1 hr in toluene. The summary of the reaction is given in **Figure 3.15**.

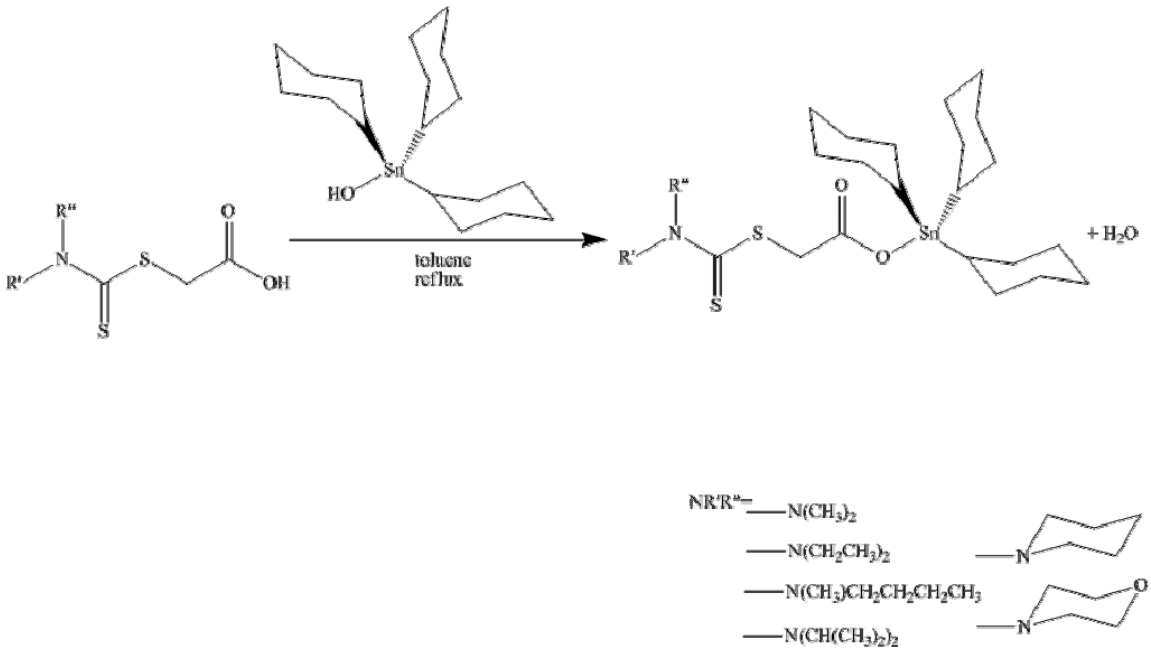


Figure 3.15 Synthesis of tricyclohexyltin diorganodithiocarbamylacetates

Tricyclohexyltin diorganodithiocarbamylacetates were subsequently reacted with bromine and 4-dimethylaminopyridinium tribromide in dichloromethane at room temperature. The resulting product was found to be diorganodithiocarbamylacetic acid and tricyclohexyltin bromide based on their melting points which is listed in **Table 3.1** as well as their elemental analysis. The summary of the reaction is shown in **Figure 3.16**.

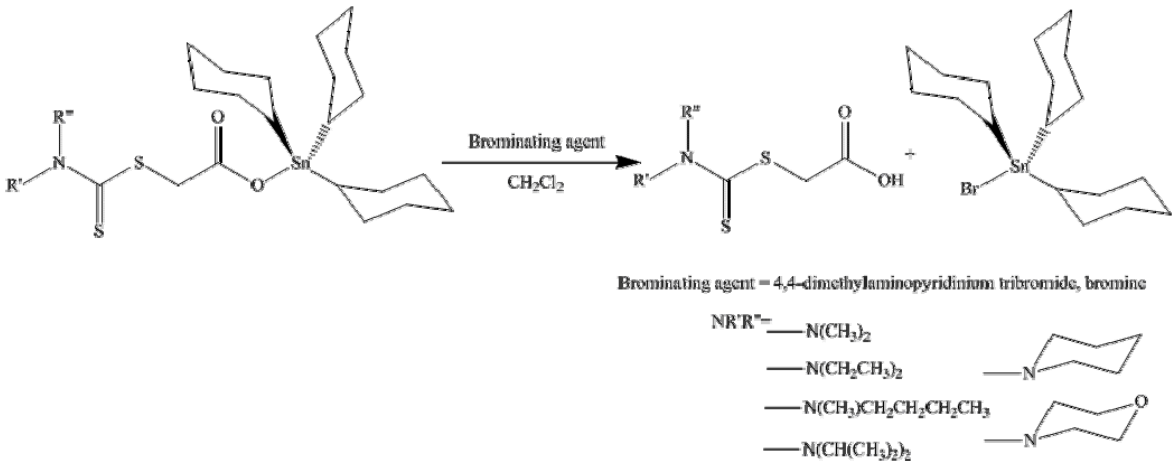


Figure 3.16 Bromination of tricyclohexyltin diorganodithiocarbamylacetates

The lithiation of triorganotin diorgaodithiocarbamylacetate by using lithium diisopropylamide, gave hexaorganoditin or tetraorganotin as the major product and the recovery of the diorganodithiocarbamylacetic acid.

An attempt to introduce a triorganotin group at the α-position of the diorganodithiocarbamylacetic acids by lithiation with lithium diisopropylamide followed by the addition of triorganotin chloride such as triphenyltin chloride and tricyclohexyltin chloride (**Figure 3.17**) failed as the major products obtained were hexaorganoditin and lithium chloride. A probable explanation in that the lithiation of the diorganodithiocarbamylacetic acid failed to proceed as expected and as a result the LDA reacted with the triorganotin chloride to afford the hexaorganoditin as the major products.

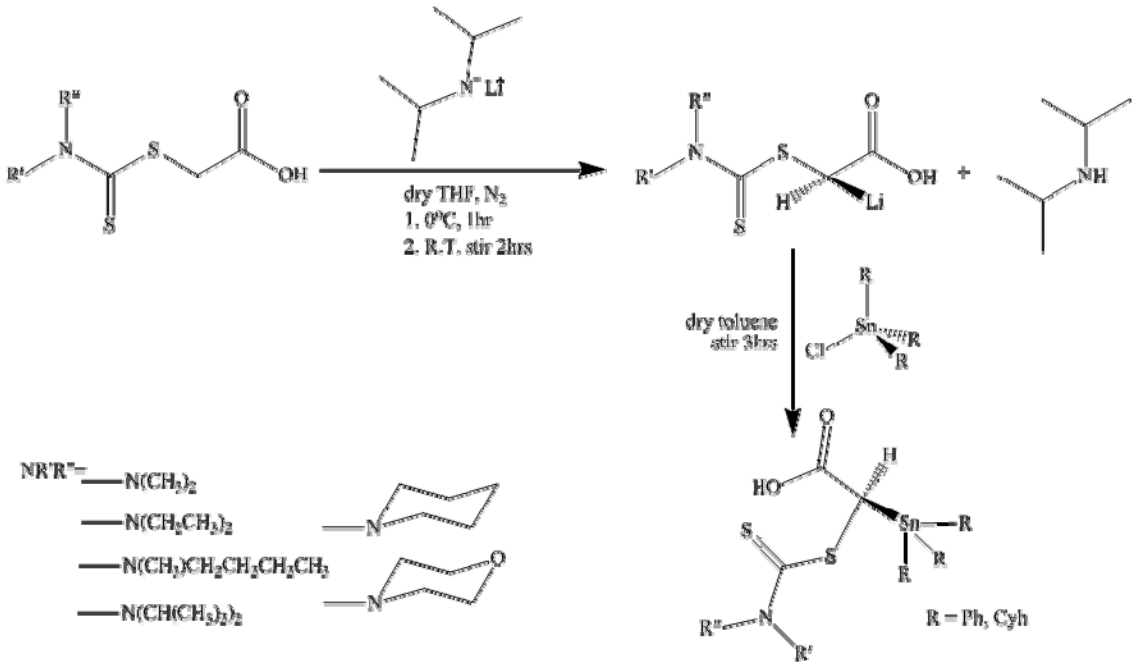


Figure 3.17 Synthesis of triorganotin diorganodithiocarbamylacetic acid by using LDA

The reaction was repeated by replacing lithium diisopropylamide with sodium ethanoate and butyl lithium. Similar products as above were obtained. The lithiation of diorganodithiocarbamylacetic acid were also attempted by changing the reactants ratio to 1:2, but again the desired products are not obtained. The use of glycocidic acid to protect the carboxylic acid before lithiation also failed to obtain the desired compound.

Other modification of reaction condition such by changing the lithiation temperature, duration of lithiation also failed to obtain the products.

In another modified method, the triorganotin chloride was first lithiated by the lithiation agents followed by the addition of the diorganodithiocarbamylacetic acid. The resulting product obtained was found to be hexaorganoditin indicating the lithiated triorganotin moiety did not react with the acid. Similar result was also obtained when the lithiating agent was replaced by sodium ethoxide.

Attempts to introduce an organotin fragment into the alpha position of carboxylic acids such as acetic acid, phenylacetic acid and propionic acid by lithiation with LDA also failed to produce any of the desired products, even after changing the various reaction conditions such as temperature, solvents, the duration of reaction and lithiation agents.

Table 3.1 Melting point and elemental analysis

Code	Compound	m. p.	%C		%H		%N		%S	
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
A1	cinnamic acid	132-135ºC	73.34	72.97	5.52	5.44	-	-	-	-
A2	*p*-methylcinnamic acid	196-198ºC	74.28	74.07	6.28	6.21	-	-	-	-
A3	*p*-methoxycinnamic acid	173-175ºC	67.68	67.42	5.77	5.65	-	-	-	-
A4	*p*-nitrocinnamic acid	289-290 ºC	56.09	55.98	3.44	3.65	7.07	7.25	-	-
A5	*p*-chlorocinnamic acid	248-250ºC	59.99	59.21	3.42	3.86	-	-	-	-
A6	2,3-dibromo-3-phenylpropionic acid	195-198 ºC	36.02	35.10	2.51	2.62	-	-	-	-
A7	2,3-dibromo-3-(*p*-methylphenyl)propionic acid	178-180ºC	37.92	37.30	3.54	3.13	-	-	-	-
A8	2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid	142-144ºC	46.52	45.54	3.90	4.86	-	-	-	-
A9	bis(4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl) propionate bromide (EtOH)	157-159ºC	34.01	33.20	4.51	3.93	4.98	4.55	-	-
A10	dimethyldithiocarbamylacetic acid	134-137ºC	33.02	33.51	5.66	5.06	6.83	7.81	35.38	35.78
A11	diethyldithiocarbamylacetic acid	79-81ºC	41.29	40.56	6.47	6.32	5.23	6.75	29.81	30.94

Table 3.1 Continued

Code	Compound	m. p.	%C		%H		%N		%S	
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
A12	*N*-methyl-*N*-buthyldithiocarbamylacetic acid	82-84^{o}C	42.48	43.42	6.03	6.83	6.01	6.33	28.32	28.98
A13	*N*,*N*-diisopropyldithiocarbamylacetic acid	122-124^{o}C	46.39	45.94	7.46	7.28	5.64	5.95	28.46	27.25
A14	*N*-piperidinyldithiocarbamylacetic acid	148-150^{o}C	43.22	43.82	5.15	5.97	5.98	6.38	28.44	29.24
A15	*N*-morpholinyldithiocarbamylacetic acid	169-170^{o}C	36.50	38.00	4.80	5.01	5.52	6.33	28.58	28.98
C1	tributyltin cinnamate	74-76^{o}C	58.01	57.70	7.91	7.83	-	-	-	-
C2	tributyltin *p*-methylcinnamate	72-74^{o}C	60.22	58.57	8.01	8.04	-	-	-	-
C3	tributyltin *p*-methoxycinnamate	60-63^{o}C	57.27	56.56	7.95	7.76	-	-	-	-
C4	tributyltin *p*-nitrocinnamate	75-77^{o}C	53.10	52.31	7.10	6.89	2.98	2.90	-	-
C5	tributyltin *p*-chlorocinnamate	80-82^{o}C	54.05	53.48	7.22	7.05	-	-	-	-
C6	tricyclohexyltin cinnamate	83-86^{o}C	63.66	62.94	6.53	7.82	-	-	-	-

Table 3.1 Continued

Code	Compound	m. p.	%C		%H		%N		%S	
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
C7	tricyclohexyltin *p*-methylcinnamate	98-100ºC	63.36	63.90	6.80	7.46	-	-	-	-
C8	tricyclohexyltin *p*-methoxycinnamate	93-95ºC	61.87	52.20	6.86	6.49	-	-	-	-
C9	tricyclohexyltin *p*-nitrocinnamate	281-282ºC	58.14	57.88	7.00	7.01	2.10	2.50	-	-
C10	tricyclohexyltin *p*-chlorocinnamate	160-163ºC	58.20	58.99	6.86	7.14	-	-	-	-
C11	tribenzyltin cinnamate ($7H_2O$)	116-118ºC	53.90	54.16	6.62	6.36	-	-	-	-
C12	tribenzyltin *p*-methylcinnamate ($5H_2O$)	128-130ºC	57.24	57.88	6.57	6.26	-	-	-	-
C13	tribenzyltin *p*-methoxycinnamate ($8H_2O$)	121-124ºC	51.68	52.20	6.04	6.49	-	-	-	-
C14	tribenzyltin *p*-nitrocinnamate ($2H_2O$)	165-166ºC	56.68	56.46	4.32	5.21	2.10	2.19	-	-
C15	tribenzyltin *p*-chlorocinnamate	138-139ºC	44.85	62.81	3.48	4.74	-	-	-	-
P1	tributyltin 2,3-dibromo-3-phenylpropionate (H_2O)	114-116ºC	41.34	41.01	6.23	5.93	-	-	-	-

Table 3.1 Continued

Code	Compound	m. p.	%C		%H		%N		%S	
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
P2	tributyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate	105-107ºC	42.65	43.25	5.49	5.78	-	-	-	-
P3	tributyltin 2-methoxy-3-bromo-3-(*p*-methoxyphenyl)propionate	93-95ºC	41.87	42.14	5.84	6.23	-	-	-	-
P4	tricyclohexyltin 2,3-dibromo-3-phenylpropionate $(2H_2O)$	126-128ºC	45.37	45.61	5.58	6.14	-	-	-	-
P5	tricyclohexyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate	119-121ºC	51.24	48.80	5.22	6.14	-	-	-	-
P6	tricyclohexyltin 2-methoxy-3-bromo-3-(*p*-methoxyphenyl)propionate	93-96ºC	52.83	53.08	6.82	6.91	-	-	-	-
P7	tribenzyltin 2,3-dibromo-3-phenylpropionate $(OC(CH_3)_2)$	165-168ºC	52.87	52.35	3.58	4.52	-	-	-	-
P8	tribenzyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate	145-148ºC	51.98	52.22	3.82	4.24	-	-	-	-
P9	tribenzyltin 2-methoxy-3-bromo-3-(*p*-methoxyphenyl)propionate	120-123ºC	55.94	56.51	5.37	4.89	-	-	-	-
D1	tricyclohexyltin dimethyldithiocarbamylacetate	68-70ºC	52.11	50.84	6.40	7.04	2.23	2.58	11.51	11.80
D2	tricyclohexyltin diethyldithiocarbamylacetate	73-75ºC	52.04	52.55	6.98	7.40	2.18	2.45	10.99	11.22

Table 3.1 Continued

Code	Compound	m. p.	%C		%H		%N		%S	
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
D3	tricyclohexyltin *N*-methyl-*N*-butyl-dithiocarbamylacetate	67-68ºC	54.66	54.10	7.14	7.73	2.16	2.34	10.99	10.70
D4	tricyclohexyltin *N*,*N*-diisopropyl-dithiocarbamylacetate	61-63ºC	51.39	53.34	6.83	7.57	2.11	2.39	10.87	10.95
D5	tricyclohexyltin *N*-piperidinyl-dithiocarbamylacetate	83-84ºC	54.20	53.53	6.7	7.25	2.36	2.40	11.53	10.99
D6	tricyclohexyltin *N*- morpholinyl-dithiocarbamylacetate	103-108ºC	51.52	51.30	6.56	6.88	2.46	2.39	12.99	10.95

3.3 Infrared spectral data

Infrared spectroscopy provides information on the stretching vibrations of the various functional groups present in a compound. The functional groups of organotin compounds which are sensitive to infrared spectroscopy are mainly found in the organic anionic groups which bonded directly to the tin atom. Hence, the stretching frequencies such as $\nu_{(NH)}$, $\nu_{(NO)}$, $\nu_{(COO)}$, $\nu_{(CS)}$,$\nu_{(C-Br)}$, $\nu_{(Sn-C)}$ and $\nu_{(Sn-O)}$ are often quoted in the infrared spectra of organotin compounds.

The infrared stretching frequencies of the triorganotin carboxylates are tabulated in **Tables 3.3** and **3.4**. Two absorption peaks in the regions of 1710 -1680 cm^{-1} and 1460 -1300 cm^{-1}, respectively are found in all the substituted cinnamic acid and 2,3-dibromo-3-phenylpropionic acid which are attributed to the $\nu_{as(COO)}$ and $\nu_{s(COO)}$ of the respective carboxylic acid. In the case of substituted cinnamic acids, a weak absorption peak in the region of 1595 -1635 cm^{-1} is indicative of the presence of C=C is these carboxylic acids. However, the products from the bromination of the cinnamic acids showed the disappearance of C=C absorption, indicating electrophilic addition had occurred to the cinnamic acids and the products are 2,3-dibromo-3-phenylpropionic acid. The presence of a peak in the region of 650 -510 cm^{-1} is due to the stretching vibration of C-Br .

Similarly, the $\nu_{as(COO)}$ and $\nu_{s(COO)}$ for the diorganodithiocarbamic acid are found in the region of 1700 -1650 cm^{-1} and 1460 -1300 cm^{-1}, respectively. The $\nu_{(C=S)}$ peak is found in the region between 1200 -1050 cm^{-1} which is broad and with a medium absorption in the region of 3250 -2990 cm^{-1}

The formation of triorganotin cinnamate and triorganotin propionate was evidenced from the disappearance of the -OH stretching frequencies in the IR spectra of

these compounds. The $\nu_{as(COO)}$ peak for triorganotin cinnamate and triorganotin propionate falls in the region of 1710 -1640 cm^{-1}, whereas the $\nu_{s(COO)}$ peak is found in the region of 1460 -1300 cm^{-1}. The difference of the stretching frequencies, $\nu_{as(COO)}$ and $\nu_{s(COO)}$ for tricyclohexyltin carboxylates is found to be in the range of 200 -232 cm^{-1}. This indicates that the tricyclohexyltin carboxylates are probably 4-coordinated tetrahedral molecules where the carboxylate group acts as a monodentate ligand. On the other hand, the tribenzyltin carboxylates are likely to be polymeric structures with carboxylate bridges. This is due to the fact that the difference between the stretching frequencies, $\nu_{as(COO)}$ and $\nu_{s(COO)}$ of the tribenzyltin carboxylates is in the range of 150 - 185 cm^{-1}, which is smaller than 200 cm^{-1}. Similarly, the difference of the stretching frequencies, $\nu_{as(COO)}$ and $\nu_{s(COO)}$ is in the range of 180 -200 cm^{-1}. The smaller difference in the stretching frequencies indicated the coordination of the carbonyl oxygen of the carboxylates with the adjacent tin fragment (Ng *et al.,* 1991).

The NO_2 stretching frequencies of *p*-nitrocinnamic acid and triorganotin *p*-nitrocinnamate were detected in the region of 1600 -1530 cm^{-1} for the asymmetric stretch and 1390 -1300 cm^{-1} for the symmetric stretch. The $\nu_{(C-N)}$ stretch in these compounds was found in the region of 850 -800 cm^{-1}. For *p*-chlorocinnamic acid and triorganotin *p*-chlorocinnamate, the $\nu_{(C-Cl)}$ peak for aryl chloride are located in the region of 1180-1000 cm^{-1}.

In general, the Sn-C and Sn-O stretching frequencies were found in the region of 590 -450 cm^{-1} and 480 -420 cm^{-1}, respectively.

In the case of brominated triorganotin substituted 3-phenylpropionate compounds, the stretching frequencies of the C-Br are found to be in the same region as the stretching frequencies of 2,3-dibromo-3-phenylpropionic acid.

Table 3.2 Selected infrared spectroscopic data for carboxylic acids

Code	Compounds	$\nu_{as(COO)}$ / (cm^{-1})	$\nu_{s(COO)}$ / (cm^{-1})	$\delta\nu$/ (cm^{-1})	Others
A1	$C_6H_5CH=CHCO_2H$	1681.6	1452.1	229.5	$1626.8_{(C=C)}$
A2	*p*-$CH_3C_6H_4CH=CHCO_2H$	1681.7	1455.0	226.7	$1621.8_{(C=C)}$
A3	*p*-$CH_3OC_6H_4CH=CHCO_2H$	1681.8	1455.0	226.8	$1622.0_{(C=C)}$, $1253.5\nu_{as(CO)}$, $1027.6\nu_{s(CO)}$
A4	*p*-$NO_2C_6H_4CH=CHCO_2H$	1681.2	1426.3	254.9	$1630.3_{(C=C)}$,$1536.9\nu_{as(NO2)}$,$1352.1\nu_{s(NO2)}$
A5	*p*-$ClC_6H_4CH=CHCO_2H$	1678.3	1453.2	225.1	$1626.1_{(C=C)}$,$820.7_{(C-Cl)}$
A6	$C_6H_5CH(Br)CH(Br)CO_2H$	1705.9	1455.9	250.0	$559.7_{(C-Br)}$
A7	*p*-$CH_3C_6H_4CH(Br)CH(Br)CO_2H$	1701.7	1458.6	243.1	$576.9_{(C-Br)}$
A8	*p*-$CH_3OC_6H_4CH(Br)CH(OCH_3)CO_2H$	1706.3	1464.3	242.0	$560.1_{(C-Br)}$,$1253.7\ \nu_{as(CO)}$, $1034.3\nu_{s(CO)}$
A9	[*p*-$ClC_6H_4CH(Br)CH(Br)COO^-$] $[(CH_3)_2NC_5H_4NH]^+Br^-$	1700.4	1462.3	238.1	$821.8_{(C-Cl),}$ $543.4_{(C-Br)}$

Table 3.2 continued

A10	$(CH_3)_2NCS_2CH_2CO_2H$	1697.1	1458.9	238.2
A11	$(CH_3CH_2)_2NCS_2CH_2CO_2H$	1712.4	1459.0	253.4
A12	$CH_3CH_2CH_2CH_2(CH_3)\ NCS_2CH_2CO_2H$	1701.5	1459.1	242.4
A13	$((CH_3)_2C)_2NCS_2CH_2CO_2H$	1695.8	1456.2	239.6
A14	 $CS_2CH_2CO_2H$	1700.6	1456.0	244.6
A15	 $CS_2CH_2CO_2H$	1697.0	1435.9	261.1

Table 3.3 Selected infrared spectroscopic data for triorganotin *p*-substituted cinnamates

Code	Compounds	$\nu_{as(COO)}$/ (cm^{-1})	$\nu_{s(COO)}$ / (cm^{-1})	$\delta\nu$/ (cm^{-1})	Others
C1	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH{=}CHC_6H_5$	1641.4	1451.8	189.6	$1608.2_{(C=C)}$
C2	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH{=}CHC_6H_4(CH_3\text{-}p)$	1641.5	1443.5	198.0	$1612.5_{(C=C)}$
C3	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH{=}CHC_6H_4(OCH_3\text{-}p)$	1634.8	1455.0	179.8	$1605.8_{(C=C)}$,1247.6$\nu_{as(CO)}$, 1038.5$\nu_{s(CO)}$
C4	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH{=}CHC_6H_4(NO_2\text{-}p)$	1641.0	1455.2	185.8	$1600.8_{(C=C)}$,1553.5$\nu_{as(NO2)}$, 1342.0$\nu_{s(NO2)}$
C5	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH{=}CHC_6H_4(Cl\text{-}p)$	1640.6	1453.2	187.4	$1605.2_{(C=C)}$,$823.9_{(C\text{-}Cl)}$
C6	$(C_6H_{11})_3SnO_2CCH{=}CHC_6H_5$	1651.4	1448.0	203.0	$1625.3_{(C=C)}$
C7	$(C_6H_{11})_3SnO_2CCH{=}CHC_6H_4(CH_3\text{-}p)$	1649.0	1449.0	200.0	$1618.2_{(C=C)}$
C8	$(C_6H_{11})_3SnO_2CCH{=}CHC_6H_4(OCH_3\text{-}p)$	1648.8	1448.5	200.3	$1613.2_{(C=C)}$,1248.2 $\nu_{as(CO)}$, 1038.1$\nu_{s(CO)}$
C9	$(C_6H_{11})_3$ $SnO_2CCH{=}CHC_6H_4(NO_2\text{-}p)$	1687.8	1447.1	230.7	$1629.9_{(C=C)}$,1520.8 $\nu_{as(NO2)}$,1349.7$\nu_{s(NO2)}$
C10	$(C_6H_{11})_3$ SnOvCCH=$CHC_6H_4(Cl\text{-}p)$	1714.4	1491.2	223.2	$1604.5_{(C=C)}$,$820.0_{(C\text{-}Cl)}$
C11	$(C_6H_5CH_2)_3SnO_2CCH{=}CHC_6H_5$	1635.8	1450.3	185.5	$1597.9_{(C=C)}$
C12	$(C_6H_5CH_2)_3SnO_2CCH{=}CHC_6H_4(CH_3\text{-}p)$	1636.3	1451.3	185.0	$1597.7_{(C=C)}$
C13	$(C_6H_5CH_2)_3SnO_2CCH{=}CHC_6H_4(OCH_3\text{-}p)$	1638.2	1455.4	182.8	$1594.7_{C=C)}$,1248.2 $\nu_{as(CO)}$, 1033.4$\nu_{s(CO)}$
C14	$(C_6H_5CH_2)_3$ $SnO_2CCH{=}CHC_6H_4(NO_2\text{-}p)$	1639.9	1452.3	187.6	$1597.7_{(C=C)}$,1548.2$\nu_{as(NO2)}$, 1343.5$\nu_{s(NO2)}$
C15	$(C_6H_5CH_2)_3$ $SnO_2CCH{=}CHC_6H_4(Cl\text{-}p)$	1635.7	1453.2	182.5	$1597.0_{(C=C)}$,$823.6_{(C\text{-}Cl)}$

Table 3.4 Selected infrared spectroscopic data for triorganotin substituted 3-phenylpropionates

Code	Compounds	$\nu_{as(COO)}$/ (cm^{-1})	$\nu_{s(COO)}$ / (cm^{-1})	$\delta\nu$/ (cm^{-1})	Others
P1	$(CH_3CH_2CH_2CH_2)_3SnO_2CCH(Br)CH(Br)C_6H_5$	1639.7	1453.0	186.2	$566.8_{(C-Br)}$
P2	$(CH_3CH_2CH_2CH_2)_3SnO_2C$ $CH(Br)CH(Br)C_6H_4(CH_3$-*p*$)$	1640.7	1458.5	182.2	$556.8_{(C-Br)}$
P3	$(CH_3CH_2CH_2CH_2)_3SnO_2C$ $CH(Br)CH(OCH_3)C_6H_4(OCH_3$-*p*$)$	1639.2	1456.8	182.4	$568.6_{(C-Br),}$1253.5 $\nu_{as(CO)}$, 1027.6$\nu_{s(CO)}$
P4	$(C_6H_{11})_3SnO_2CCH(Br)CH(Br)C_6H_5$	1660.3	1456.1	204.2	$560.7_{(C-Br)}$
P5	$(C_6H_{11})_3SnO_2CCH(Br)CH(Br)C_6H_4(CH_3$-*p*$)$	1659.7	1458.5	201.2	$556.8_{(C-Br)}$
P6	$(C_6H_{11})_3SnO_2CCH(Br)CH(OCH_3)C_6H_4(OCH_3$-*p*$)$	1661.3	1458.0	203.3	$577.3_{(C-Br),}$1253.5 $\nu_{as(CO)}$, 1027.6$\nu_{s(CO)}$
P7	$(C_6H_5CH_2)_3SnO_2CCH(Br)CH(Br)C_6H_5$	1614.8	1455.0	159.8	$565.9_{(C-Br)}$
P8	$(C_6H_5CH_2)_3SnO_2CCH(Br)CH(Br)C_6H_4(CH_3$-*p*$)$	1616.8	1456.7	160.6	$568.5_{(C-Br)}$
P9	$(C_6H_5CH_2)_3SnO_2CCH(Br)CH(OCH_3)C_6H_4(OCH_3$-*p*$)$	1620.3	1459.3	161.0	$570.1_{(C-Br),}$1253.5 $\nu_{as(CO)}$, 1027.6$\nu_{s(CO)}$

Table 3.5 Selected infrared spectroscopic data for tricyclohexyltin diorganodithiocarbamylacetates

Code	Compounds	$\nu_{as(COO)}$/ (cm^{-1})	$\nu_{s(COO)}$ / (cm^{-1})	$\delta\nu$/ (cm^{-1})	Others
D1	$(C_6H_{11})_3SnO_2CH_2CS_2N(CH_3)_2$	1661.7	1456.8	204.9	
D2	$(C_6H_{11})_3SnO_2CH_2CS_2N(CH_3CH_2)_2$	1661.2	1456.1	205.1	
D3	$(C_6H_{11})_3SnO_2CH_2CS_2N(CH_3)CH_2CH_2CH_2CH_3$	1660.8	1458.2	202.6	
D4	$(C_6H_{11})_3SnO_2CH_2CS_2N(C(CH_3)_2)_2$	1662.3	1458.8	203.5	
D5	$(C_6H_{11})_3SnO_2CH_2CS_2$ 	1673.8	1456.0	217.8	
D6	$(C_6H_{11})_3SnO_2CH_2CS_2$ 	1670.2	1455.9	214.3	1243.2 $\nu_{as(CO)}$, 1029.3$\nu_{s(CO)}$

3.4 ^{1}H and ^{13}C NMR spectral data

^{1}H NMR spectra data are useful for the identification of organic groups such as butyl, cyclohexyl and benzyl in organotin compounds. The ^{1}H NMR chemical shifts for the carboxylic acids and their triorganotin derivatives are recorded and listed in **Tables 3.6 -3.9**. The proton chemical shifts of the butyl groups in tributyltin *p*-substituted cinnamates are located as multiplets in the region of 0.8 -1.8 ppm. For the tricyclcohexyltin *p*-substituted cinnamates and tricyclohexyltin substituted 3-phenylpropionates, the ^{1}H NMR chemical shifts of the cyclohexyl protons fall in the region between 1.2 and 2.9 ppm. In the case of tribenzyltin *p*-substituted cinnamates and tribenzyltin substituted 3-phenylpropionates, the benzyl protons are found in the region between 6.8 -7.2 ppm and are overlapped with those of the phenyl protons. The chemical shift of the methylene proton (-CH_2-) from the benzyl group is located in the region of 1.5 -1.8 ppm. In the case of substituted cinnamic acids and their triorganotin derivatives, ^{1}H NMR chemical shift of the -CH=CH- protons are located as doublets in the region of 6.7 -6.8 ppm and 7.7 -7.9 ppm, respectively. In some cases, assignments of the benzyl and methlene protons will be difficult due to the overlapping of these proton chemical shifts. The chemical shifts of -CH(Br)CH(Br)- protons fall in the region of 4.6 -4.8 and 5.2 -5.4 ppm, respectively as doublets. The singlet for the OCH_3 group appeared at around 5.0 ppm for triorganotin *p*-methoxycinnamate and triorganotin 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionates. A singlet at around 4.7 ppm belongs to the methyl protons of triorganotin *p*-methylcinnamate and triorganotin 2,3-dibromo-3-(*p*-methylphenyl)propionate.

For the tricyclohexyltin diorganodithiocarbamylacetate, the proton chemical shift of cyclohexyl groups are located in the region of 1.2 -2.9 ppm. The proton chemical shifts of the methylene, -CH_2- (Tushar *et al.*, 2006), alkyl and aryl protons

which are present in these types of triorganotin carboxylates are located in the expected regions as listed in the **Tables 3.7 and 3.8**.

In contrast to ^{1}H NMR spectral data, the ^{13}C NMR spectra data provide information about the type and the number of carbon nuclei in the organotin compounds. The ^{13}C NMR chemical shift data were only recorded for those organotin complexes which are soluble in $CDCl_3$ and are tabulated in **Table 3.10, 3.11, 3.12** and **3.13**. The butyl carbons are assigned and found in the region of 13.5 -28.0 ppm. Whereas, the chemical shifts of cyclohexyl carbons of the cyclohexyltin compounds were located in the region of 25.0 -34.0 ppm, which is similar to the literature review (Muhammad D. *et al.*, 1995). In the case of trialkyltin compounds such as tributyltin compounds, the coupling constant, ^{1}J *(*^{119}*Sn-*^{13}*C)* values between the *alpha*-carbon of the butyl group and the tin atom was measured to be around 354.6 Hz and 333.0 Hz. These coupling constant values are indicative of four coordinated tin structure. Similar range of coupling constant values are also found in the tetrahedral tricyclohexyltin compounds such as tricyclohexyltin hydroxide where the ^{1}J value is reported as 352.7 Hz (Ng *et al.*, 1991; Muhammad D. *et al.*, 1995).

The ^{13}C NMR chemical shifts of the carbonyl carbons for the carboxylic acids and the triorganotin carboxylates were found at the downfield region of around 171.0 - 172.8 ppm. Similarly, the chemical shifts for the (-CH=CH-) group in triorganotin cinnamates were found in the region of 118.0 -120.5 ppm and 142.0 -144.0 ppm (Muhammad D. *et al.*, 1995). On the other hand, the chemical shift of –C(Br)H-C(Br)H- were located at 48.9 and 52.4 ppm, respectively.

Table 3.6 ^{1}H NMR data for carboxylic acids

Compounds	δ^{1}H (ppm)
A1	7.14-7.30 (m, Ph-H), 7.61 (d, C=C-H), 6.41 (d, C=C-H)
A2	7.01-7.18 (m, Ph-H), 7.60 (d, C=C-H), 6.38 (d, C=C-H), 2.35 (s, -CH_3)
A3	6.10-7.20 (m, Ph-H), 7.61 (d, C=C-H), 6.40 (d, C=C-H), 3.73 (s, -OCH_3)
A4	7.50-8.15 (m, Ph-H), 7.75 (d, C=C-H), 6.70 (d, C=C-H)
A5	7.20-7.25 (m, Ph-H), 7.61 (d, C=C-H), 6.39 (d, C=C-H)
A6	6.95-7.05 (m, Ph-H), 5.50 (d, -C(Br)H), 5.10 (d, -C(Br)H)
A7	7.10-7.15 (m, Ph-H), 5.45 (d, -C(Br)H), 5.10 (d, -C(Br)H), 2.34 (s, -CH_3)
A8	6.90-7.20 (m, Ph-H), 5.37 (s, -C(Br)H), 3.85 (Ar-OCH_3), 3.32 (s, -OCH_3)
A9	6.90-8.20 (m, Ph-H), 5.50 (d, -C(Br)H), 5.20 (d, -C(Br)H), 2.70 (s, -NCH_3)

Table 3.6 continued

Compounds	δ^1H (ppm)
A10	4.02 (s, -CH_2CO_2-), 3.04 (s, -CH_3)
A11	3.96 (s, -CH_2CO_2-), 3.84-3.87 (q, -CH_2-), 1.16-1.20 (t, -CH_3)
A12	4.02 (s, -CH_2CO_2-), 3.20 (s, -N-CH_3), 2.50-2.56 (t, -N-CH_2-), 1.29-1.37 (m, -CH_2-), 0.89 (s, -CH_3)
A13	4.01 (s, -CH_2CO_2-), 2.96-3.02 (m, -NCH-), 1.10-1.12 (d, -CH_3)
A14	3.98 (s, -CH_2CO_2-), 3.58-3.62 (t, -NCH_2-), 1.46-1.52 (m, -CH_2-)
A15	2.32 (s, -CH_2CO_2-), 3.50-3.54 (t, -OCH_2-), 2.89-2.93 (m, -NCH_2-)

Table 3.7 ^{1}H NMR data for triorganotin *p*-substituted cinnamates

Compounds	δ^{1}H (ppm)
C1	7.25-7.53 (m, Ph-H), 7.44-7.48 (d, C=C-H), 6.44-6.48 (d, C=C-H), 0.90-1.72 (m, Bu-H)
C2	7.12-7.58 (m, Ph-H), 7.44-7.50 (d, C=C-H), 6.44-6.48 (d, C=C-H), 2.36 (s, -CH_3), 0.92-1.68 (m, Bu-H)
C3	6.94-7.62 (m, Ph-H), 7.46-7.50 (d, C=C-H), 6.30-6.34 (d, C=C-H), 3.84 (s, -OCH_3), 0.92-1.72 (m, Bu-H)
C4	7.88-8.26 (m, Ph-H), 7.44-7.48 (d, C=C-H), 6.36-6.40 (d, C=C-H), 0.90-1.68 (m, Bu-H)
C5	7.23-7.55 (m, Ph-H), 7.42-7.48 (d, C=C-H), 6.54-6.58 (d, C=C-H), 0.90-1.68 (m, Bu-H
C6	7.25-7.51 (m, Ph-H), 7.44-7.48 (d, C=C-H), 6.42-6.46 (d, C=C-H), 1.23-1.99 (m, Cyh-H)
C7	7.12-7.41 (m, Ph-H), 7.46-7.50 (d, C=C-H), 6.40-6.46 (d, C=C-H), 2.38 (s, -CH_3), 1.23-2.88 (m, Cyh-H)
C8	6.96-7.62 (m, Ph-H), 7.45-7.48 (d, C=C-H), 6.40-6.44 (d, C=C-H), 3.82 (s, -OCH_3) 1.33-1.97 (m, Cyh-H)
C9	7.26-7.58 (m, Ph-H), 7.46-7.50 (d, C=C-H), 6.58-6.62 (d, C=C-H), 1.39-2.25 (m, Cyh-H)
C10	7.23-7.55 (m, Ph-H), 7.54-7.58 (d, C=C-H), 6.62-6.68 (d, C=C-H), 1.35-2.11 (m, Cyh-H)

Table 3.7 continued

Compounds	δ^1H (ppm)
C11	6.68-7.35 (m, Ph-H), 7.46-7.50 (d, C=C-H), 6.34-6.38 (d,C=C-H), 2.62 (s, Bz-CH_2-)
C12	6.70-7.35 (m, Ph-H), 7.46-7.50 (d, C=C-H), 6.34-6.38 (d, C=C-H), 2.40 (s, -CH_3), 2.62 (s, Bz-CH_2-)
C13	6.79-7.38 (m, Ph-H), 7.48-7.50 (d, C=C-H), 6.34-6.38 (d, C=C-H), 3.84 (s, -O-CH_3), 2.66 (s, Bz-CH_2-)
C14	6.60-8.26 (m, Ph-H), 7.58-7.62 (d, C=C-H), 6.56-6.60 (d, C=C-H), 2.68 (s, Bz-CH_2-)
C15	6.78-7.48 (m, Ph-H), 7.48-7.50 (d, C=C-H), 6.90-6.94 (d, C=C-H), 2.62 (s, Bz-CH_2-)

Table 3.8 ^{1}H NMR data for triorganoltin substituted 3-phenylpropionates

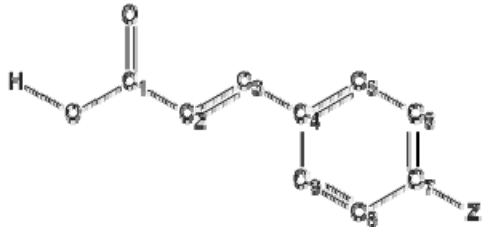
Compounds	δ^{1}H (ppm)
P1	7.28-7.38 (m, Ph-H), 5.32-5.36 (d, -CBr–H), 4.78-4.84 (d, -CBr–H), 0.98-2.02 (m, Bu-H)
P2	7.26-7.34 (m, Ph-H), 5.34-5.36 (d, -C(Br)H), 4.80-4.84 (d, -C(Br)H), 2.44 (s, -CH_3), 0.96-1.98 (m, Bu-H)
P3	6.75-7.32 (m, Ph-H), 4.45-4.49 (d, -CBr–H), 4.21-4.26 (d, -CH-), 3.82 (s, Ar-O-CH_3), 3.18 (s, -O-CH_3), 0.98-1.90 (m, Bu-H)
P4	7.32-7.41 (m, Ph-H), 5.32-5.35 (d, -CBr–H), 4.82-4.85 (d, -CBr–H), 1.31-2.02 (m, Cyh-H)
P5	7.28-7.35 (m, Ph-H), 5.34-5.38 (d, -C(Br)H), 4.80-4.84 (d, -C(Br)H), 2.46 (s, -CH_3), 1.30-1.98 (m, Cyh-H)
P6	6.85-7.29 (m, Ph-H), 4.43-4.47 (d, -CBr–H), 4.19-4.22 (d, -CH-), 3.78 (s, Ar-O-CH_3), 3.15 (s, -O-CH_3), 1.30-1.90 (m, Cyh-H)
P7	7.25-7.35 (m, Ph-H), 5.34-5.38 (d, -C(Br)H), 4.82-4.85 (d, -CBr–H), 2.67 (s, Bz-CH_2-)
P8	7.10-7.30 (m, Ph-H), 5.38-5.41 (d, -C(Br)H), 4.80-4.82 (d, -C(Br)H), 2.46 (s, -CH_3), 2.67 (s, Bz-CH_2-)
P9	6.79-7.32 (m, Ph-H), 4.49-4.51 (s, -CBr –H), 4.27-4.29 (d, -CH-), 3.84 (s, Ar-O-CH_3), 3.20 (s, -O-CH_3), 2.67 (s, Bz-CH_2-)

Table 3.9 ^{1}H NMR data for tricyclohexyltin diorganodithiocarbamylacetates

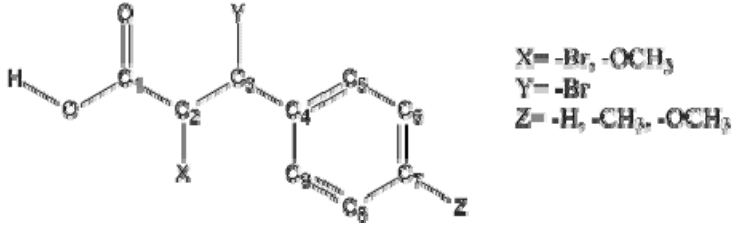
Compounds	δ^{1}H (ppm)
D1	3.98 (s, -CH_2CO_2-), 3.10 (s, -CH_3), 1.00-1.98 (m, Cyh-H)
D2	3.96 (s, -CH_2CO_2-), 3.82-3.84 (q, -CH_2-), 0.98-2.00 (m, Cyh-H)
D3	4.02 (s, -CH_2CO_2-), 3.24 (s, -N-CH_3), 2.52-2.58 (t, -N-CH_2-), 1.02-2.02 (m, Cyh-H)
D4	4.01 (s, -CH_2CO_2-), 2.96-3.02 (m, -NCH-), 0.98 -2.02 (m, Cyh-H)
D5	3.98 (s, -CH_2CO_2-), 3.56-3.62 (t, -NCH_2-), 1.04-1.98 (m, Cyh-H)
D6	2.38 (s, -CH_2CO_2-), 3.48-3.54 (t, -OCH_2-), 2.89-3.00 (m, -NCH_2-), 1.12-2.04 (m, Cyh-H)

Table 3.10 ^{13}C NMR Chemical shift data for carboxylic acids

Compounds	δ (^{13}C) / ppm										
	C1	C2	C3	C4	C5	C6	C7	C8	C9	X	Z
A1	172.5	116.8	143.2	135.5	129.2	128.9	127.1	128.9	129.2		
A2	172.2	118.8	143.7	132.4	139.8	129.5	127.9	129.5	129.8		21.6
A3	172.2	118.2	143.8	127.6	129.8	114.5	160.2	114.5	129.8		55.2
A4	172.0	119.8	142.3	135.0	129.5	129.0	133.5	129.0	129.5		
A5	171.2	120.6	141.0	141.2	128.0	124.8	148.2	124.8	128.0		
A6	172.1	52.4	49.0	138.6	129.1	128.8	128.2	128.8	129.1		
A7	170.3	57.2	55.5	132.1	129.8	129.3	132.9	129.3	129.8		15.5
A8	169.9	83.2	48.3	129.7	129.0	113.8	159.5	113.8	129.0	56.8	55.2



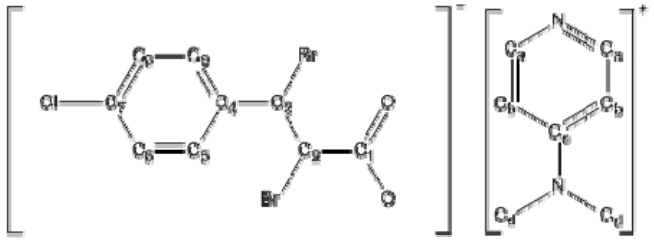
A1 – A5



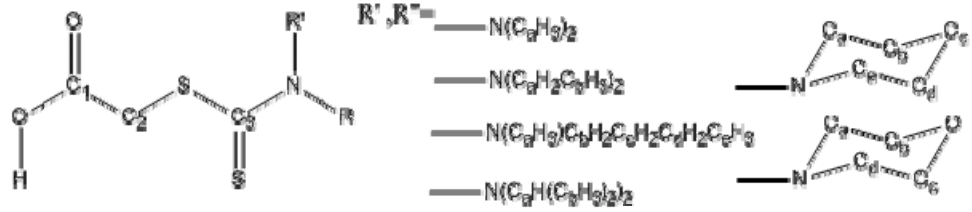
A6 – A8

Table 3.10 continued

Compounds	δ (^{13}C) / ppm													
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C_a**	**C_b**	**C_c**	**C_d**	**C_e**
A9	169.2	50.3	47.5	136.8	129.9	129.2	134.7	129.2	129.9	139.1	107.2	157.4	*	
A10	172.2	39.4	197.3							41.3				
A11	172.0	38.9	196.5							51.0	12.4			
A12	172.1	38.2	193.7							42.0	51.0	29.9	20.8	13.6
A13	172.0	38.9	196.7							27.0	17.1			
A14	172.8	38.6	193.6							53.9	24.2	25.5	26.1	52.0
A15	172.4	38.6	192.6							51.9	65.5	65.9	51.2	



A9

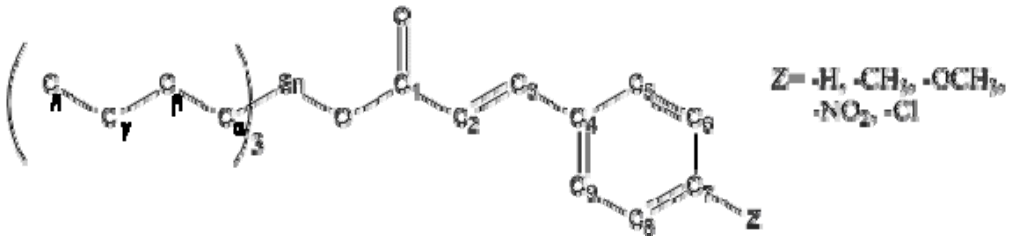


A10 – A15

***chemical shift is overlap with solvent**

Table 3.11 ^{13}C NMR data for triorganotin *p*-substituted cinnamates

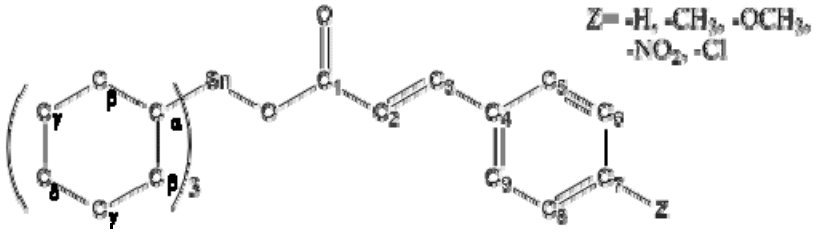
Compounds	δ (^{13}C) / ppm													
	Cα	**Cβ**	**Cγ**	**Cδ**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**Z**
C1	16.4	27.9	27.1	13.7	172.1	120.2	143.7	135.1	128.8	127.9	129.7	127.9	128.8	
C2	16.5	27.8	27.0	13.6	172.2	118.9	143.8	132.2	129.5	127.9	139.9	127.8	129.5	21.4
C3	16.4	27.8	27.0	13.6	172.2	117.3	143.6	127.6	129.4	114.2	160.8	114.2	129.3	55.1
C4	16.6	24.9	27.1	13.7	171.7	124.2	140.4	141.0	128.9	123.4	148.2	123.4	128.9	
C5	16.8	27.9	27.0	13.8	170.9	120.0	142.8	135.8	129.5	129.0	133.4	129.0	129.5	



C1: $J_{Sn\text{-}C\alpha}$ 335.8 Hz $J_{Sn\text{-}C\beta}$ 20.2 Hz $J_{Sn\text{-}C\gamma}$ 67.2 Hz $J_{Sn\text{-}C\delta}$ (<7 Hz)

Table 3.11 continued

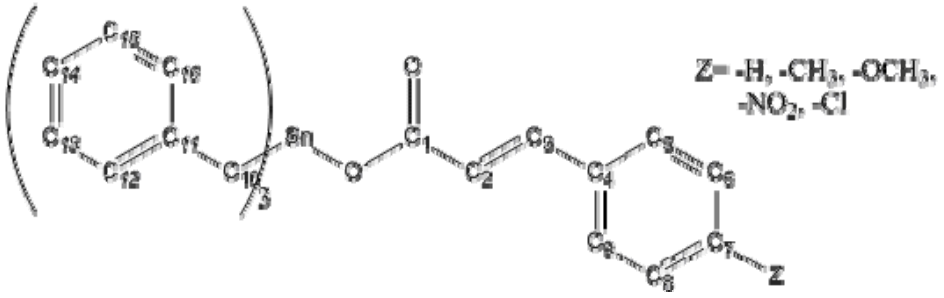
Compounds	δ (^{13}C) / ppm													
	Cα	**Cβ**	**Cγ**	**Cδ**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**Z**
C6*	33.8	31.2	29.4	27.0	172.0	120.3	143.7	135.2	128.0	128.8	129.8	128.8	128.0	
C7	34.5	31.1	29.0	27.0	172.2	119.5	144.2	132.2	129.5	127.8	140.0	127.8	129.5	21.8
C8	33.8	31.1	28.9	26.9	172.2	117.8	143.2	127.8	129.4	114.1	160.8	114.1	129.4	55.3
C9	31.3	31.2	29.0	27.0	170.9	125.0	140.5	141.5	128.5	124.1	148.2	124.1	128.5	
C10	34.0	31.2	28.7	27.0	171.7	121.0	142.1	135.5	129.1	129.2	133.7	129.2	129.1	



C6: $J_{Sn\text{-}C\alpha}$ 333.0 Hz $J_{Sn\text{-}C\beta}$ 14.7 Hz $J_{Sn\text{-}C\gamma}$ 68.8 Hz $J_{Sn\text{-}C\delta}$ 6.7 Hz

Table 3.11 continued

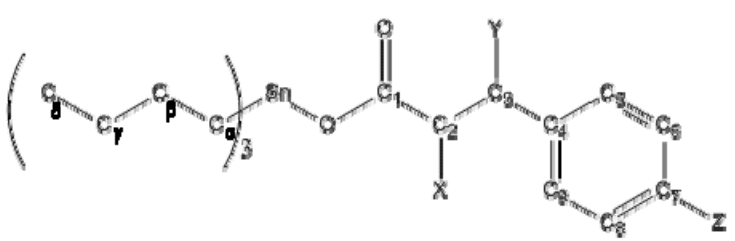
Compounds	δ (^{13}C) / ppm														
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**C13**	**C14**	**Z**
C11*	124.3	171.2	118.3	142.3	132.2	128.0	128.5	127.8	128.5	24.2	139.8	128.0	129.0	128.0	
C12	171.6	118.0	143.2	130.4	128.5	128.7	138.2	128.7	128.5	24.2	140.2	128.9	128.2	124.8	21.3
C13	173.4	116.2	145.0	127.5	129.8	114.4	161.4	114.4	129.8	24.2	139.0	128.8	128.0	124.5	55.5
C14	171.7	124.3	141.9	138.6	128.7	123.6	148.4	123.6	128.7	24.2	141.1	128.9	128.0	124.7	
C15	171.8	120.5	142.8	138.6	128.7	128.5	139.7	128.5	128.7	24.2	140.6	129.0	128.0	124.5	



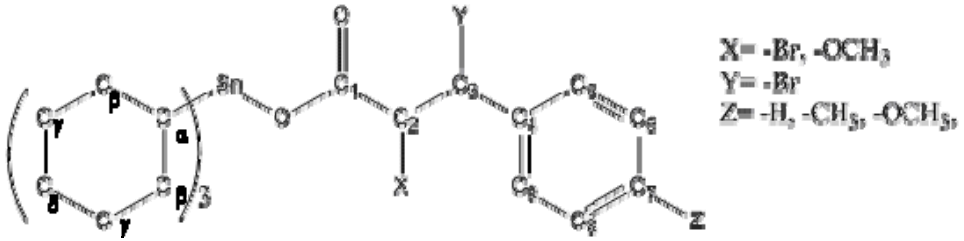
C11: $J_{Sn\text{-}C10}$ 316.9 Hz $J_{Sn\text{-}C11}$ 40.8 Hz $J_{Sn\text{-}C12}$ 31.6 Hz $J_{Sn\text{-}C13}$ 17.0 Hz $J_{Sn\text{-}C14}$ 20.6 Hz

Table 3.12 ^{13}C NMR data for triorganoltin substituted 3-phenylpropionates

Compounds	δ (^{13}C) / ppm														
	Cα	**Cβ**	**Cγ**	**Cδ**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**X**	**Z**
P1	16.6	27.8	27.0	13.6	172.2	48.6	52.8	138.8	128.9	129.2	127.9	129.2	128.9		
P2	16.5	27.8	27.0	13.6	172.2	48.2	54.8	143.8	132.2	129.5	128.0	140.0	128.0	129.5	21.4
P3	16.4	27.8	27.0	13.7	172.1	83.9	48.8	127.8	129.2	114.0	160.8	114.0	129.2	57.0	55.1
P4	34.6	31.0	29.0	26.2	172.1	48.9	52.4	138.6	128.8	129.1	128.2	129.1	128.8		
P5	34.4	31.0	28.8	26.4	172.2	48.2	54.2	136.7	128.6	128.9	138.4	128.9	128.6	21.6	
P6	34.2	31.0	28.9	26.9	173.5	84.6	49.4	129.3	129.6	113.6	159.7	113.6	129.6	57.3	55.2



P1 – P3

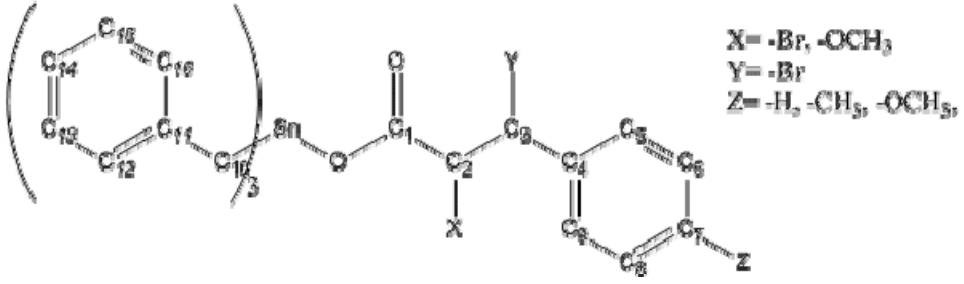


P4 – P6

P4: $J_{Sn\text{-}C\alpha}$ 328.4 Hz $J_{Sn\text{-}C\beta}$ 13.4 Hz $J_{Sn\text{-}C\gamma}$ 69.7 Hz $J_{Sn\text{-}C\delta}$ (<7 Hz)

Table 3.12 continued

Compounds	δ (^{13}C) / ppm															
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**C13**	**C14**	**X**	**Z**
P7	172.2	48.8	52.6	138.9	128.2	128.9	128.0	128.9	128.2	24.2	140.8	128.6	128.0	124.6		
P8	172.1	48.1	56.4	136.6	128.8	129.0	138.6	129.0	128.8	24.2	141.0	128.6	128.0	124.4	21.4	
P9	171.2	84.4	48.2	129.4	138.4	113.8	160.0	113.8	138.4	24.2	142.6	128.8	128.0	124.8	57.4	55.3

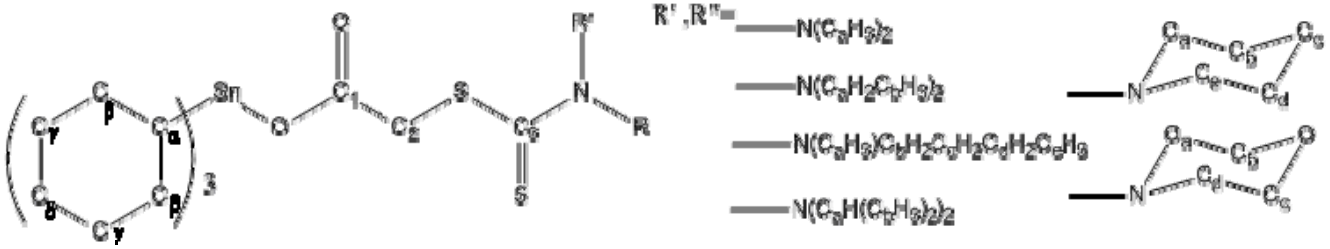


P7 – P9

P7: $J_{Sn\text{-}C10}$ 317.0 Hz $J_{Sn\text{-}C11}$ 40.2Hz $J_{Sn\text{-}C12}$ 31.4 Hz $J_{Sn\text{-}C13}$ 16.9 Hz $J_{Sn\text{-}C14}$ 19.8 Hz

Table 3.13 ^{13}C NMR data for tricyclohexyltin diorganodithiocarbamylacetates

Compounds	δ(^{13}C) / ppm											
	Cα	**Cβ**	**Cγ**	**Cδ**	**C1**	**C2**	**C3**	**C_a**	**C_b**	**C_c**	**C_d**	**C_e**
D1*	34.4	31.0	29.1	26.0	172.4	39.0	197.3	41.2				
D2	34.6	31.0	29.0	26.1	172.6	38.8	196.0	51.3	12.4			
D3	34.4	31.1	29.1	26.0	172.4	38.4	193.0	42.0	51.0	29.8	20.6	13.4
D4	34.4	31.1	29.1	26.2	172.6	38.9	196.0	27.0	17.2			
D5	34.6	31.1	29.0	26.1	172.8	38.9	193.4	53.9	24.4	25.5	26.1	52.1
D6	34.4	31.0	29.0	26.1	172.7	38.8	193.2	52.0	65.7	66.0	51.4	



D1: $J_{Sn\text{-}C\alpha}$ 333.0 Hz $J_{Sn\text{-}C\beta}$ 15.2 Hz $J_{Sn\text{-}C\gamma}$ 67.1 Hz $J_{Sn\text{-}C\delta}$ 6.4 Hz

3.5 X-ray structural studies

The X-ray crystal structures of *p*-nitrocinnamic acid **(A4)** and three of the bromination products of *p*-substituted cinnamic acid, namely 2,3-dibromo-3-phenylpropionic acid **(A6),** 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid **(A8)** and bis(4,4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)** were determined by using X-ray crystallographic technique. In addition, the crystal structure of triorganotin carboxylates namely tricyclohexyltin cinnamate **(C6),** tributyltin *p*-chlorocinnamate **(C5),** tribenzyltin *p*-nitrocinnamate **(C14),** tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)** and tricyclohexyltin dimethyldithiocarbamylacetate **(D1)** were also determined.

3.5.1 X-ray crystal structure of *p*-nitrocinnamic acid (A4)

The X-ray crystal structure of *p*-nitrocinnamic acid is depicted in **Fig. 3.18** as an ellipsoidal plot with 70% probability. The benzene ring is near planar (RMS: 0.009) and the carboxylate fragment comprising of C3=C2-C1 (=O2) O1 also lies on a plane (RMS: 0.01). These two planes are twisted, with the angle between the two planes equals to 5.62(8)^{o}. The nitro functional group is also twisted by 4.65(9)^{o} from the benzene ring. The bond distance of C2-C3 is 1.33(19) Å which is relatively shorter than C-C bond distance of 1.5 Å, clearly indicating the presence of ethylene group in this *p*-substituted cinnamic acid.

Inspection of the unit cell packing diagrams of this carboxylic acid (**Fig. 3.19a**, **Fig. 3.19b**, and **Fig. 3.19c**) shows that the molecules are linked together by H-bonding between the carboxylic acid functional groups (O1-H1… O2^{i} : 2.64(14) Å and symmetry code (i): -

x+1, -y+1, -z+1). In addition there exists non covalent O…O interaction between one of the nitro oxygen and the other nitro oxygen of adjacent molecules. This type of O…O interaction has been reported to be common in most aromatic nitro compounds (Kelly *et al.*, 2002). The resulting crystal packing of the molecules shows zigzag polymeric layers which propagated perpendicular to the *ac* plane.

There is no evidence of any intramolecular H-bonding between the ethylene hydrogen and the carboxylate oxygens (O1…H2 2.49 Å and O2…H3 2.55 Å). This is in contrast to similar compounds reported in the literature which claimed that there exist intramolecular H-bonding between the ethylene hydrogen and the carboxylate oxygens in 2-(4-ethoxybenzlindene)butanoic acid (Muhammed *et* al., 2008), 2-methyl-3-(3-methyl phenyl)acrylic acid (Muhammed *et* al., 2008) and 2-(4-isopropylbenzylindene) propanoic acid (Muhammed *et* al., 2008) with relatively shorter O…H distances of 2.30, 2.27 and 2.35 Å, respectively. The less polar ethylene hydrogen may be the reason for the insignificant H-bonding interaction in the title compound.

Table 3.14 Crystal data and structure refinement for *p*-nitrocinnamic acid **(A4)**

Identification code	**A4**
Empirical formula	$C_{18}H_{14}N_2O_8$
Formula weight	386.31
Temperature	123(2) K
Wavelength	0.71073 Å
Crystal system,	$P2_1/n$
Space group	Monoclinic
Unit cell dimensions	a = 6.136(10) Å $\alpha = 90^o$
	b = 4.954(10) Å $\beta = 93.274(10)^o$
	c = 27.022(5) Å $\gamma = 90^o$
Volume	820.24(3) $Å^3$
Z, Calculated density	2, 1.564 Mg/m^3
Absorption coefficient	0.126 mm^{-1}
F(000)	400
Crystal size	0.25 x 0.10 x 0.02 mm
θ range for data collection	1.51 to 27.50^o
Limiting indices	$-7\leq h\leq 7$, $-6\leq k\leq 6$, $-34\leq l\leq 35$
Reflections collected / unique	7370 / 1879 [$R_{(int)} = 0.0228$]
Completeness to θ = 27.50	100.0 %
Max. and min. transmission	0.9975 and 0.9693
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1879 / 1 / 131

Table 3.14 continued

Goodness-of-fit on F^2	1.059
Final R indices [I>2σ (I)]	$R_1 = 0.0352$, $wR_2 = 0.0921$
R indices (all data)	$R_1 = 0.0459$, $wR_2 = 0.0995$
Largest diff. peak and hole	0.298 and -0.277 $eÅ^{-3}$

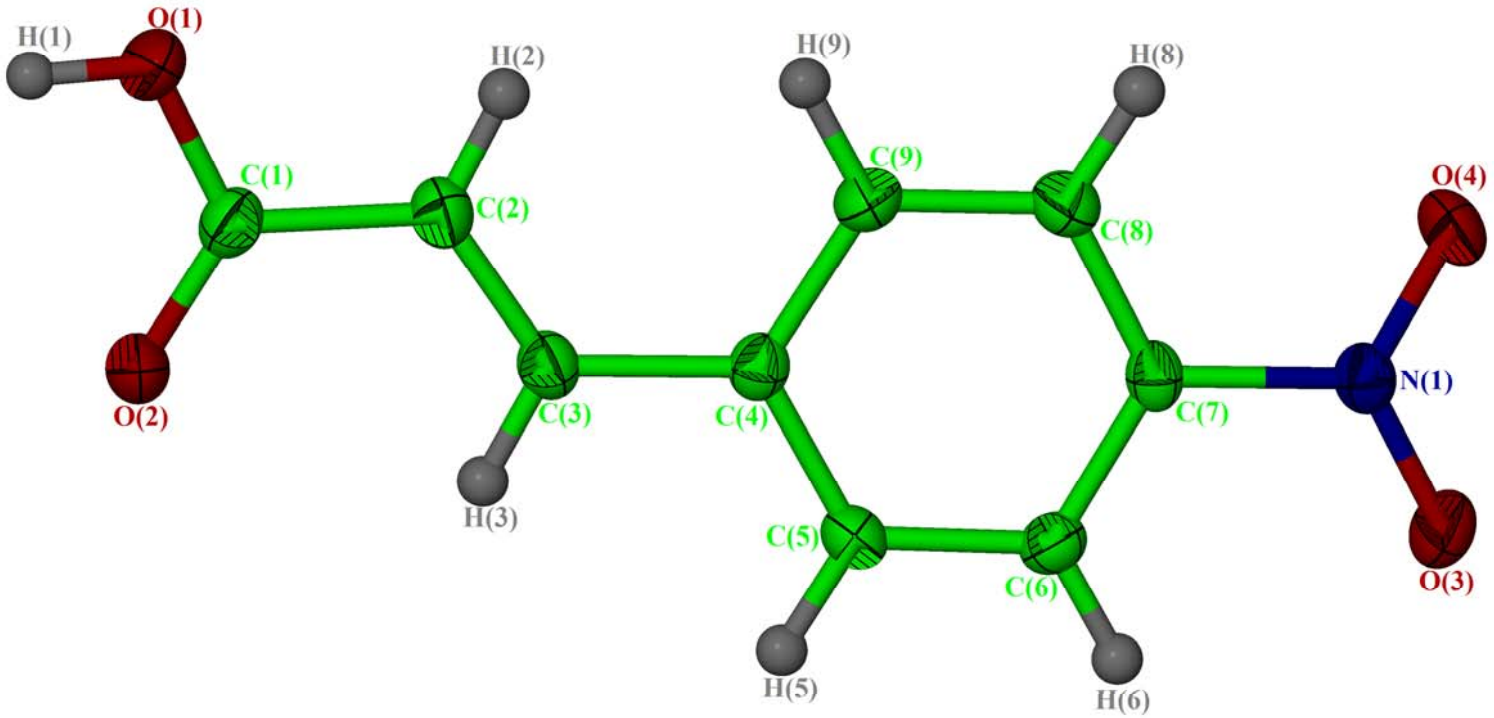


Figure 3.18 Molecular plot of *p*-nitrocinnamic acid **(A4)** at 70% probability.

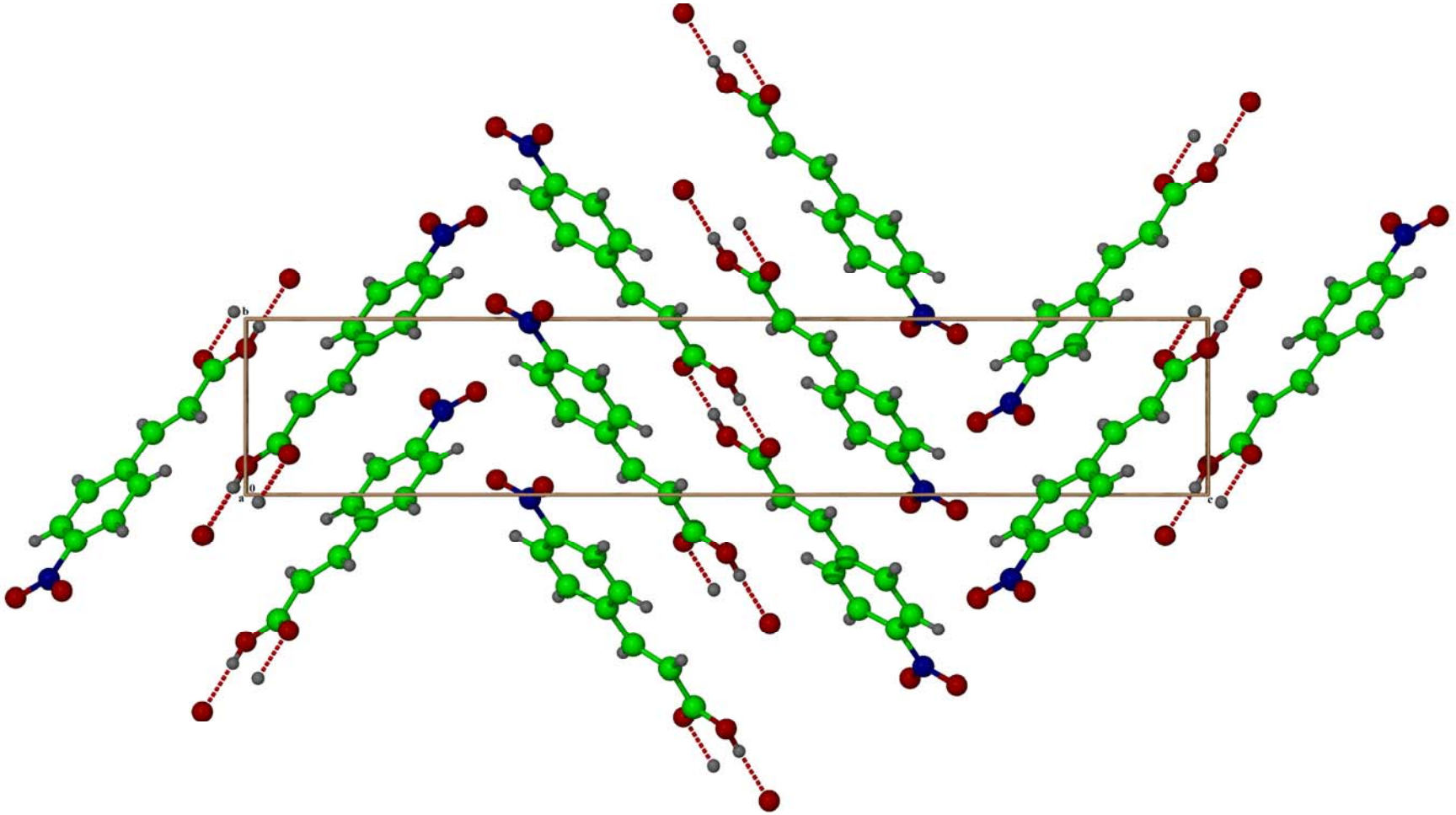


Figure 3.19a Close packing of *p*-nitrocinnamic acid **(A4)** viewed along *a*-axis.

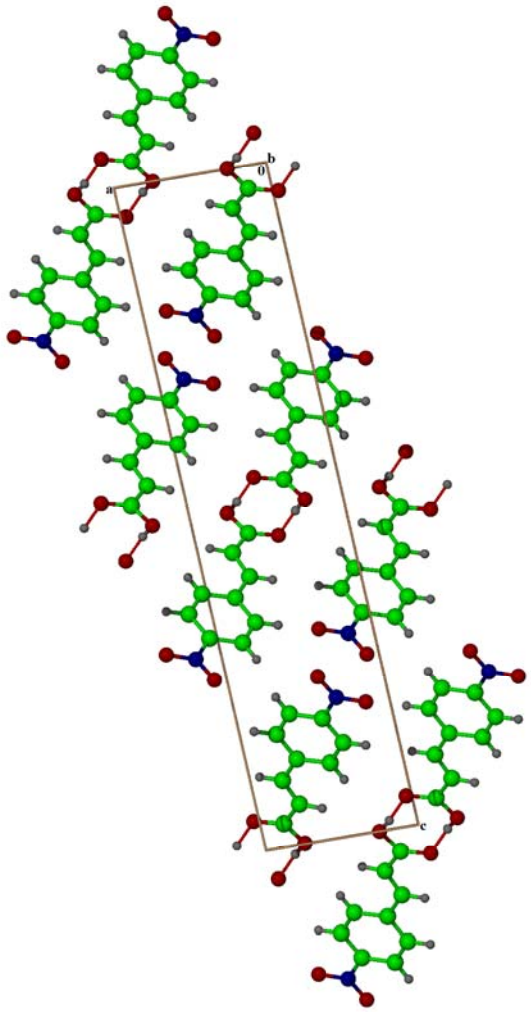


Figure 3.19b Close packing of *p*-nitrocinnamic acid **(A4)** viewed along *b*-axis.

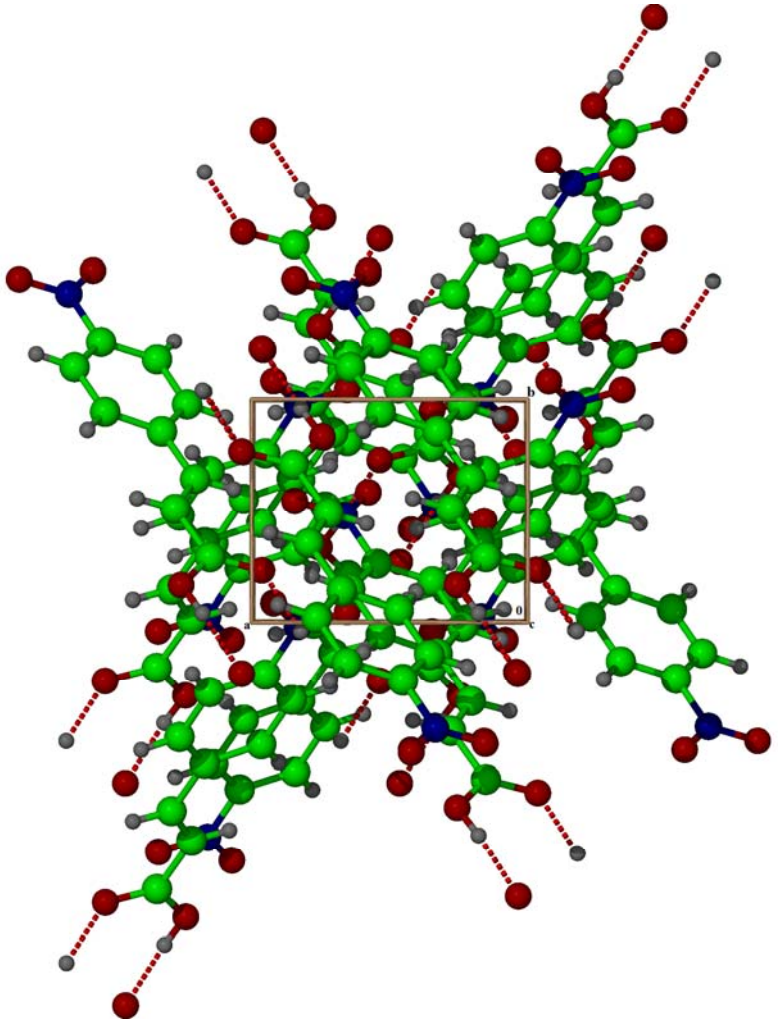


Figure 3.19c Close packing of *p*-nitrocinnamic acid **(A4)** viewed along *c*-axis.

3.5.2 X-ray crystal structure of 2,3-dibromo-3-phenylpropionic acid (A6)

The title compound, 2,3-dibromo-3-phenylpropionic acid is a product from the bromination of cinnamic acid. As shown in its molecular structure in **Fig. 3.20**, the addition of two bromine atoms across the ethylene double bond resulted in the lost of the double bond as evidenced from the longer C2-C3 bond distance of 1.49(5) Å compared to 1.33(19) Å in *p*-nitrocinnamic acid. The two bromine atoms are *trans* to each other and the plane occupied by Br1-C2-C3-Br2 is nearly flat with torsional angle of -177.59(16)^{o}. The benzene ring and the plane occupied by the carboxylate fragment are nearly flat (RMS are 0.0048 and 0.0194, respectively). The benzene ring and the plane defined by Br1-C2-C3-Br2 are approximately 90^{o} to each other. On the other hand, the plane occupied by the carboxylate fragment makes an angle of 83.7(4)^{o} with that of Br1-C2-C3-Br2 plane.

Inspection of the unit cell packing also reveals the presence of H-bonding between the carboxylate group of adjacent molecule, forming dimeric units in the unit cell (O1-H1o-O2^{i} and O1'-H1o'-O2^{i} are 2.68(1) Å and 2.69(1) Å respectively, symmetry code (i): -x+1, -y+1, -z+1). Since nitro substituent on the phenyl ring is absent in the title compound, a polymeric layer structure was not adopted in this case.

Detailed analysis of the structural solution of this compound shows that the structure is disordered over two positions with respect of the non-bromide atoms. The Br1 atom is connected to the carbon atom in the 2-position in the major component but is connected to the carbon atom in the 3-position in the minor component. Conversely, the Br2 atom is connected to the carbon atom in the 3-position in the major component but is connected to the carbon atom in the 2-position in the minor component. Hence, all

distances in the major component were restrained to within 0.01 Å of their equivalents in the minor component. The phenyl rings were restrained into rigid hexagons of 1.39 Å sides. Additionally, the four-atom carboxyl and seven-atom benzyl units were each restrained to be nearly flat. The anisotropic displacement parameters of the primed atoms were restrained to be equal to those of the unprimed atoms; these were also restrained to be nearly isotropic. In the initial stages of the refinement, the occupancy refined to an approximate 2:1 ratio. However, with the inclusion of hydrogen atoms, the refinement was unstable. Ratios that was either slightly smaller or slightly larger than 2:1 did not yield any significant differences in the final residual index. The ratio was then fixed to 2:1 Oxygen and carbon-bound H-atoms were placed in calculated positions (C-H 0.95 to 1.00 Å, O–H 0.84 Å) and were included in the refinement in the riding model approximation, with U (H) set to 1.2 to 1.5 U_{eq} (C,O).

Table 3.15 Crystal data and structure refinement for 2,3-dibromo-3-phenylpropionic acid **(A6)**

Identification code	**A6**	
Empirical formula	$C_9H_8Br_2O_2$	
Formula weight	307.97	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Pbca	
Space group	Orthorhombic	
Unit cell dimensions	a = 7.036(14) Å	$\alpha = 90^o$
	b = 9.721(2) Å	$\beta = 90^o$
	c = 29.278(6) Å	$\gamma = 90^o$
Volume	2002.9(7) $Å^3$	
Z, Calculated density	8, 2.043 Mg/m^3	
Absorption coefficient	8.058 mm^{-1}	
F(000)	1184	
Crystal size	0.36 x 0.10 x 0.08 mm	
θ range for data collection	1.39 to 27.50^o	
Limiting indices	$-9\leq h\leq 8$, $-12\leq k\leq 8$, $-38\leq l\leq 37$	
Reflections collected / unique	11596 / 2306 [$R_{(int)} = 0.0809$]	
Completeness to θ = 27.50	100.0 %	
Max. and min. transmission	0.5650 and 0.1595	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2306 / 0 / 118	

Table 3.15 continued

Goodness-of-fit on F^2	1.098
Final R indices [I>2σ (I)]	$R_1 = 0.0492$, $wR_2 = 0.1206$
R indices (all data)	$R_1 = 0.0889$, $wR_2 = 0.1514$
Largest diff. peak and hole	1.490 and -1.420 eÅ $^{-3}$

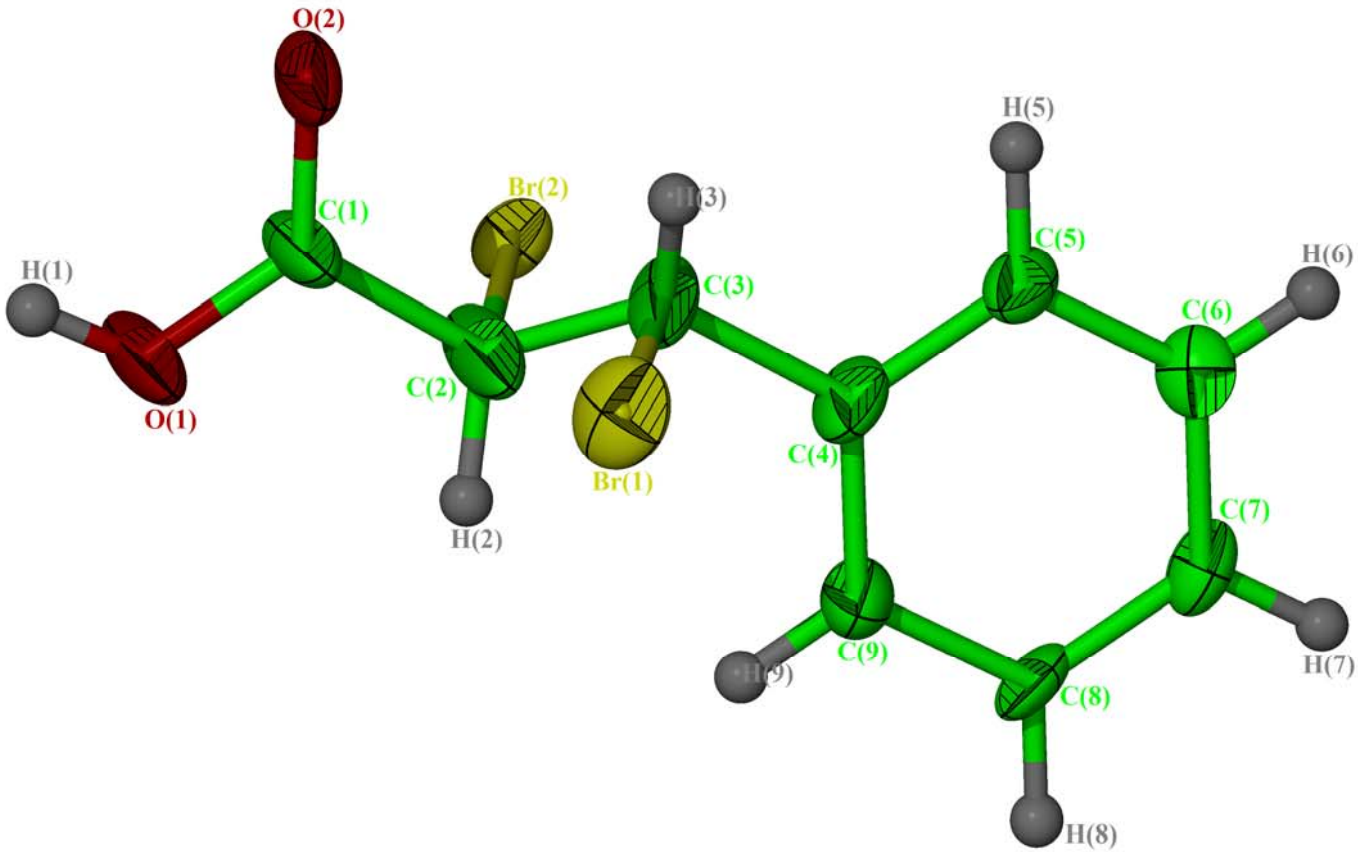


Figure 3.20 Molecular plots of 2,3-dibromo-3-phenylpropionic acid **(A6)** at 70% probability.

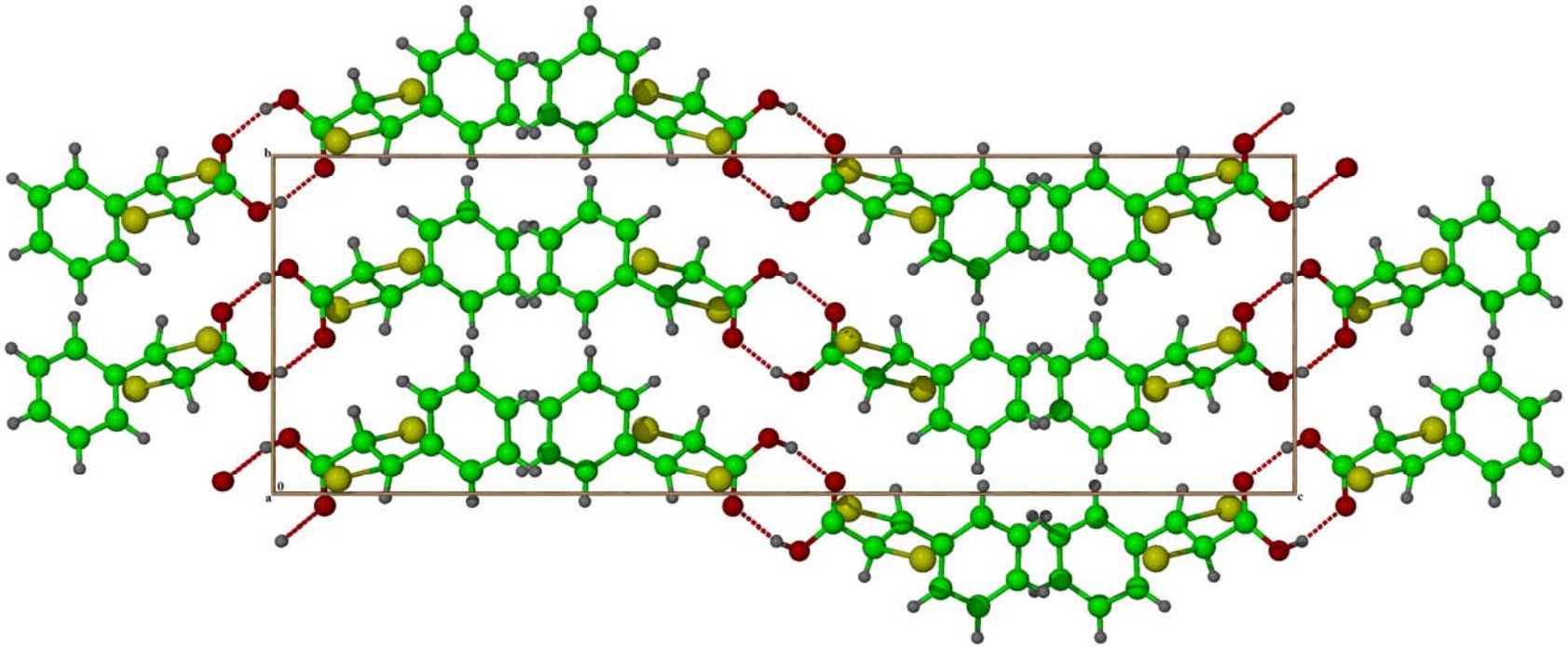


Figure 3.21a Close packing of 2,3-dibromo-3-phenylpropionic acid **(A6)** viewed along *a*-axis.

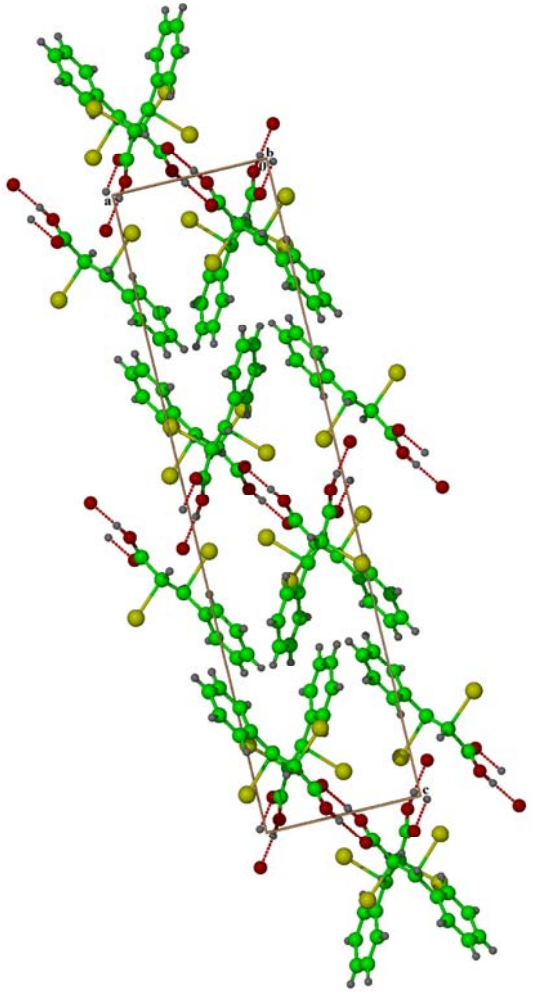


Figure 3.21b Close packing of 2,3-dibromo-3-phenylpropionic acid **(A6)** viewed along *b*-axis.

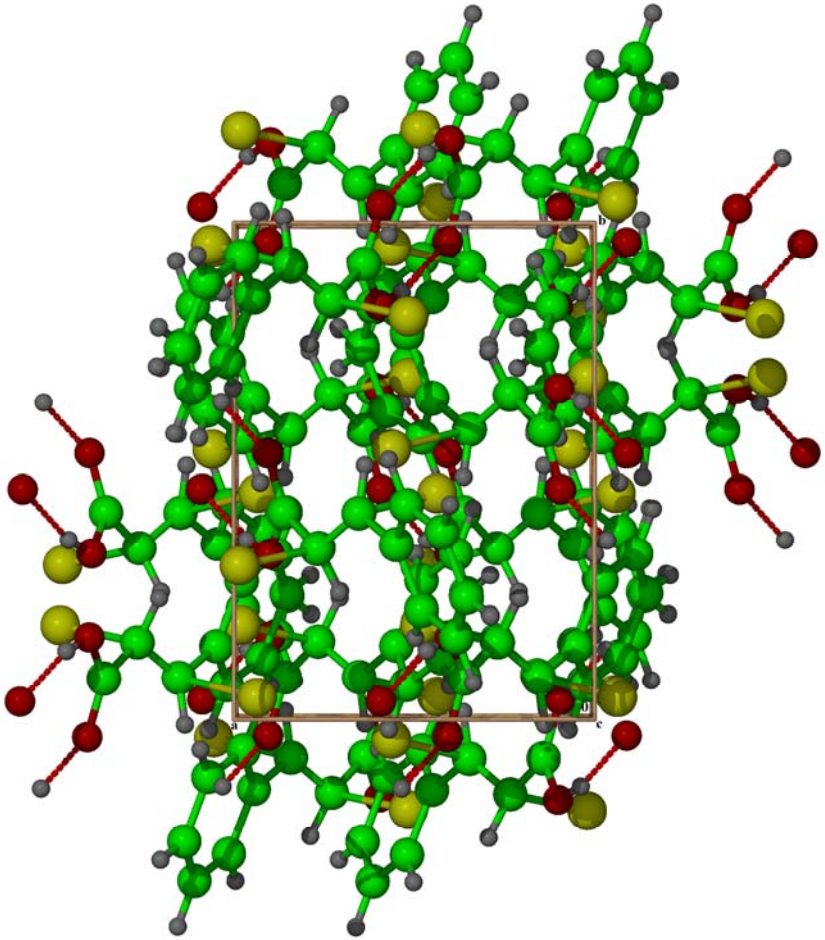


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Figure 3.21c Close packing of 2,3-dibromo-3-phenylpropionic acid **(A6)** viewed along *c*-axis.

3.5.3 X-ray structure of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid (A8)

This compound was formed as a result of the bromination of *p*-methoxycinnamic acid in the presence of methanol. Detailed mechanism of the formation of this product has been discussed in the earlier section on synthesis. As seen in the molecular structure of the compound (**Fig 3.22**), a bromide and methoxy substituents have been added across the double bond. This can be observed from the elongation of the C2-C3 bond distance to 1.51(5) Å. The methoxy and bromide substituents are *trans* to each other, with the plane occupied by Br1-C2-C3–O3 is nearly flat (RMS of plane: 0.0108). This plane makes an angle of 86.03(13)^{o} with the phenyl ring. The plane occupied by the carboxyl group makes an angle of 83.02(22)^{o} with the plane of Br1-C2-C3-O3, in the similar range as that of 2,3-dibromo-3-phenylpropionic acid.

A similar H-bonding between the carboxyl substituent of adjacent molecules, resulted in the formation dimeric molecular units in the unit cell is observed in this compound. The hydrogen bond distances are O1-H1o….O2^{i} 2.68(3) Å and O1'-H1o"…O2^{i} 2.68(3) Å, symmetry code (i): -x, 1-y, 1-z, within the range reported for O-H…O. There is a small H-bonding interaction between the carboxyl oxygen (O1) with the nearer hydrogen (H2) of the propyl chain as evidenced from the O1… H2 distance of 2.39 Å, which is in the similar range as those reported in the literature (Muhammad *et* al., 2008).

Table 3.16 Crystal data and structure refinement for 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid **(A8)**

Identification code	**A8**	
Empirical formula	$C_{11}H_{13}BrO_4$	
Formula weight	289.12	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	$P2_1/n$	
Space group	Monoclinic	
Unit cell dimensions	a = 16.659(4) Å	$\alpha = 90^o$
	b = 7.574(2) Å	$\beta = 106.037(2)^o$
	c = 9.863(3) Å	$\gamma = 90^o$
Volume	1196.18(6) $Å^3$	
Z, Calculated density	4, 1.605 Mg/m^3	
Absorption coefficient	3.432 mm^{-1}	
F(000)	584	
Crystal size	0.40 x 0.20 x 0.10 mm	
θ range for data collection	1.27 to 27.50°	
Limiting indices	$-21 \le h \le 20, -9 \le k \le 9, -12 \le l \le 12$	
Reflections collected / unique	7959 / 2729 [$R_{(int)} = 0.0326$]	
Completeness to θ = 27.50	99.3 %	
Max. and min. transmission	0.7253 and 0.3406	
Refinement method	Full-matrix least-squares on F^2	

Table 3.16 continued

Data / restraints / parameters	2729 / 0 / 147
Goodness-of-fit on F^2	1.052
Final R indices [I>2 σ (I)]	$R_1 = 0.0358$, $wR_2 = 0.0898$
R indices (all data)	$R_1 = 0.0501$, $wR_2 = 0.1021$
Largest diff. peak and hole	1.391 and -0.629 e. $Å^3$

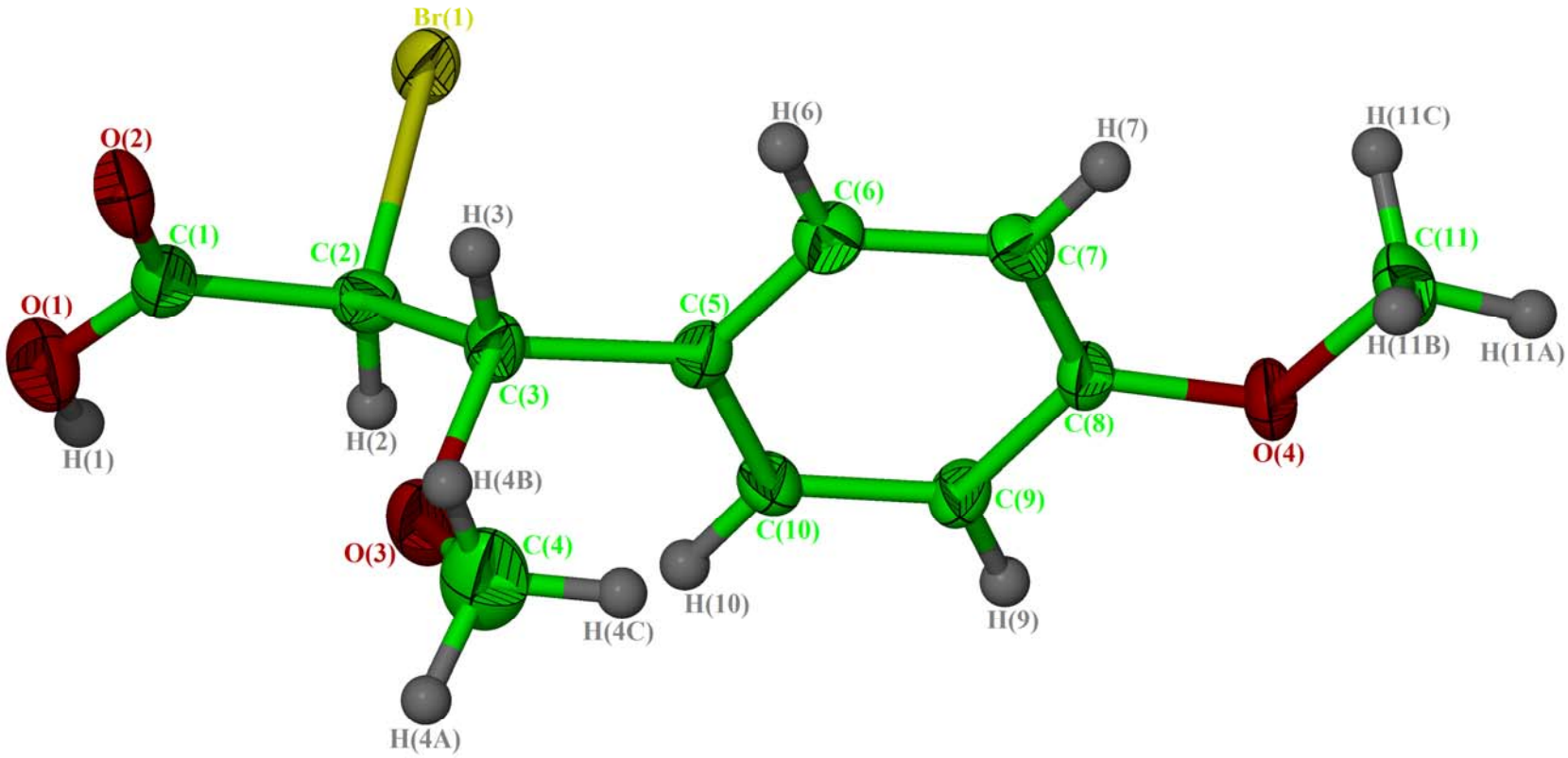

Figure 3.22 Molecular plot of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid (A8) at 70% probability.

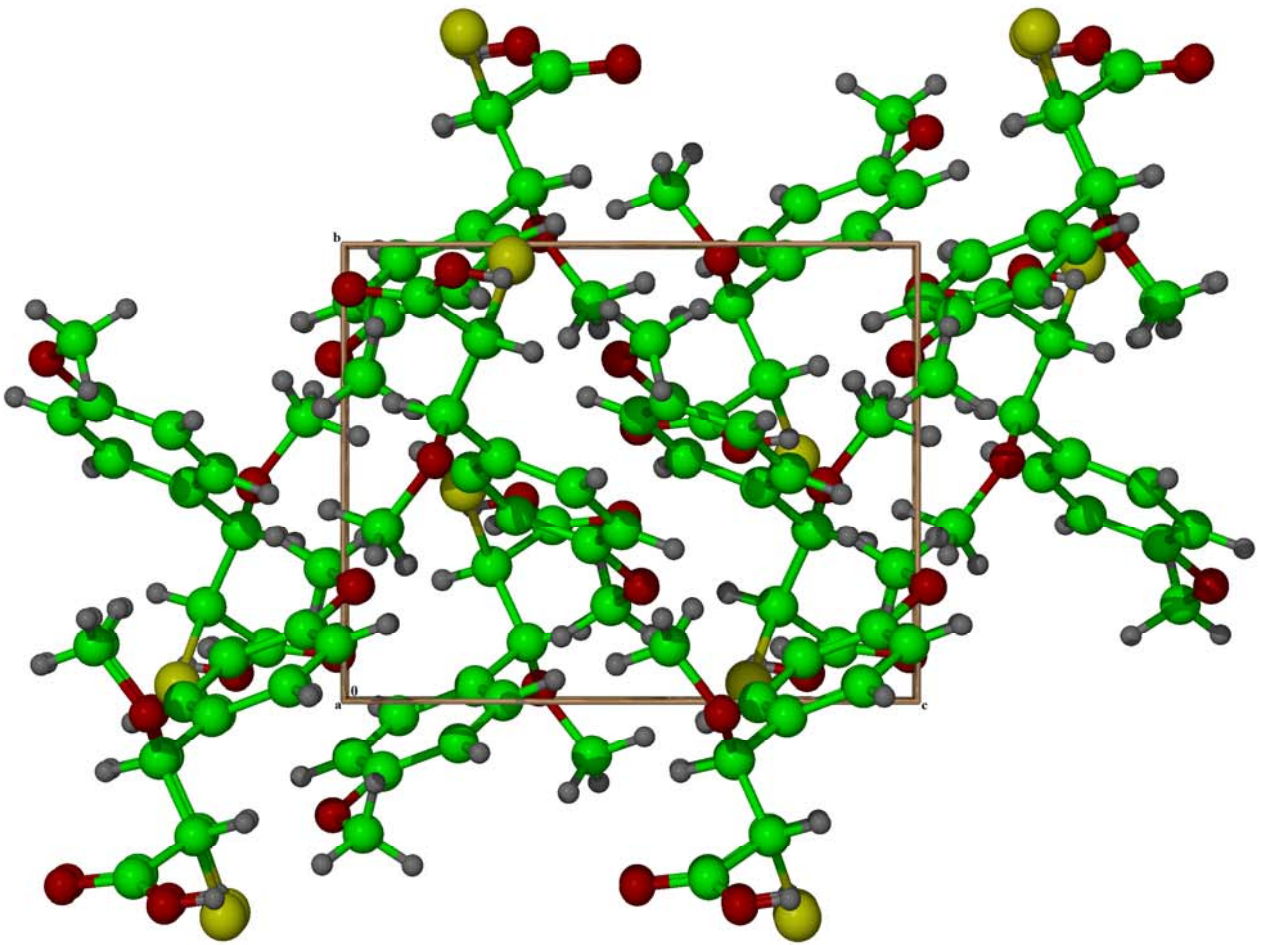

Figure 3.23a Close packing of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid **(A8)** viewed along *a*-axis.

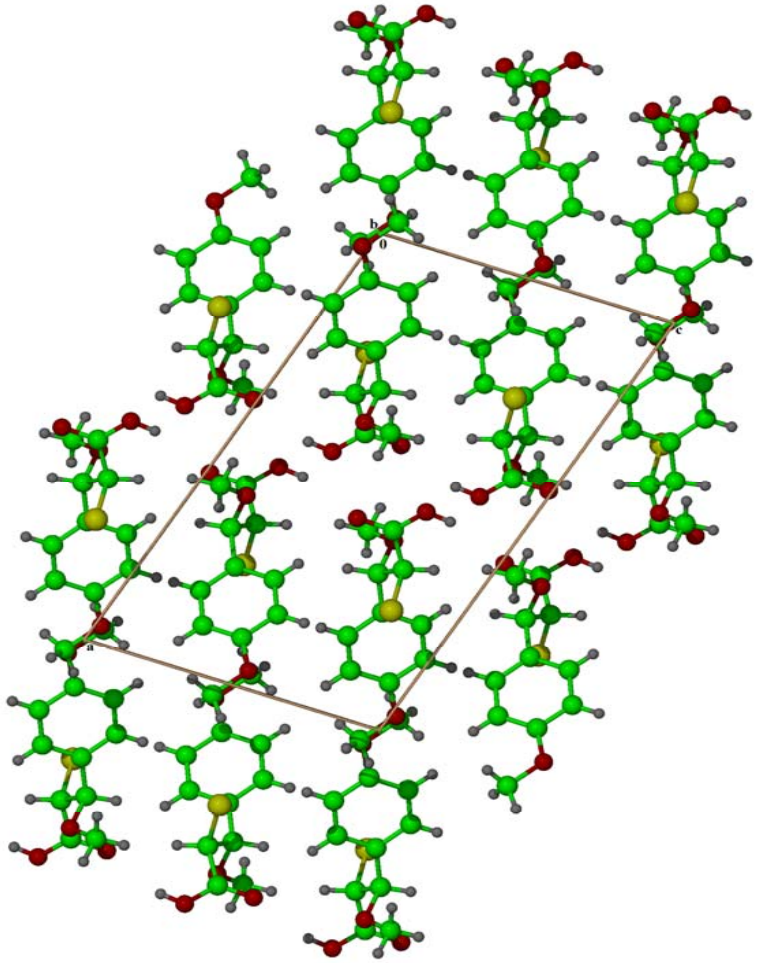

Figure 3.23b Close packing of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid **(A8)** viewed along *b*-axis.

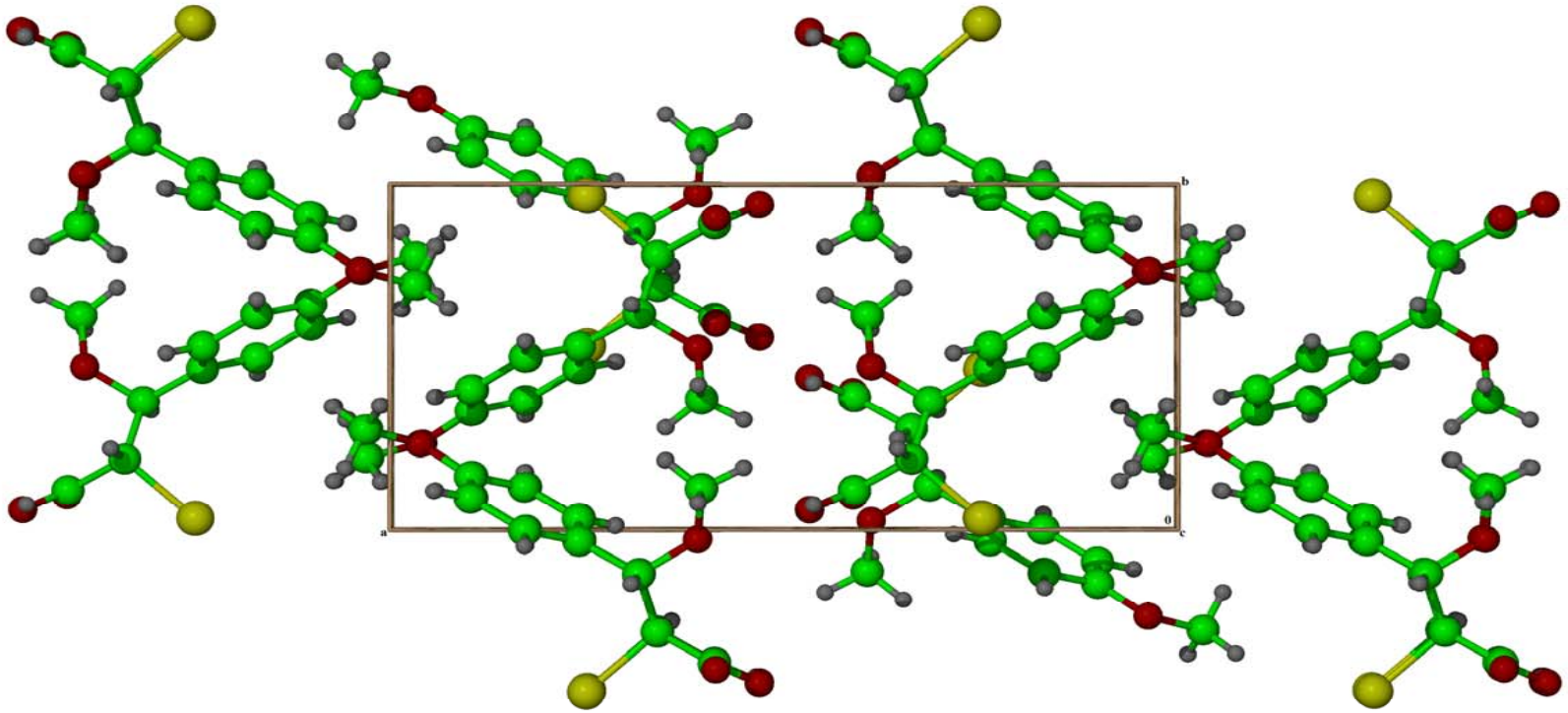

Figure 3.23c Close packing of 2-bromo-3-methoxy-3-(*p*-methoxyphenyl)propionic acid **(A8)** viewed along *c*-axis.

3.5.4 X-ray crystal structure of bis(4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide(A9)

The title compound was obtained from the bromination of *p*-chlorocinnamic acid by using 4-dimethylaminopyridinium tribromide. Inspection of the molecular structure (**Fig. 3.24**) seems to suggest that the bromination leads to the substitution at the ethylene hydrogen atoms instead of the addition of bromine atoms across the ethylene double bond. This is because of the short ethylene C=C bond of 1.28 (2) Å which is in the same range as the C=C bond distance in *p*-nitrocinnamic acid (**C5**). The C-C single bond distance obtained as a result of addition of bromine across the double bond in 2,3-dibromo-3-phenylpropionic acid is 1.49(5) Å. The compound was observed to be formed from the co-crystallization of the bromination products of 4-dimethylaminopyridinium bromide and 2,3-dibromo-3-(*p*-chlorophenyl)propionic acid. The molecules of these two products are found to link together by hydrogen bonding between the bromide ion and the pyridinium hydrogen as well as the carboxyl hydrogen atom as shown in **Fig. 3.25a** (N-H…Br 3.28(11) Å and O-H…..Br 3.10(10) Å). Because of this, intermolecular hydrogen bonding between the carboxylate groups of adjacent molecules was not observed in this case.

The 4-dimethylaminopyridinium cation is almost planar (RMS deviation is 0.0115), similar to those reported in the literature (Lo *et* al., 2008). The chlorine atom also lies in the same plane as the benzene ring.

Another important observation of the structural analysis of this compound is the existence of a number of strong residual peaks around the heavy bromine atoms, Br1, Br2 and Br3. This is probably due to the disorder bromine atoms in the structure and as a result,

a relatively large R factor of 9.33% was obtained after the final refinement process. Although a number of restraint have been applied to the refinement of the structure, it did not help to reduce the final R factor.

Table 3.17 Crystal data and structure refinement for bis(4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)**

Identification code	**A9**
Empirical formula	$C_{16}H_{15}Br_2ClN_2O_2$
Formula weight	462.57
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system,	$P2_1/n$
Space group	Monoclinic
Unit cell dimensions	a = 7.830(8) Å $\alpha = 90^o$
	b = 20.633(2) Å $\beta = 97.846(10)^o$
	c = 12.260(13) Å $\gamma = 90^o$
Volume	1962.4(4) $Å^3$
Z, Calculated density	4, 1.566 Mg/m^3
Absorption coefficient	4.275 mm^{-1}
F(000)	912
Crystal size	0.33 x 0.33 x 0.21 mm
θ range for data collection	1.95 to 27.50°
Limiting indices	$-10 \leq h \leq 10, -26 \leq k \leq 20, -15 \leq l \leq 15$
Reflections collected / unique	11638 / 4464 [$R_{(int)} = 0.0626$]
Completeness to θ = 27.50	99.1 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4464 / 0 / 217

Table 3.17 continued

Goodness-of-fit on F^2	1.106
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0990$, $wR_2 = 0.2875$
R indices (all data)	$R_1 = 0.1254$, $wR_2 = 0.3053$
Largest diff. peak and hole	3.924 and -1.659 $e.A^{-3}$

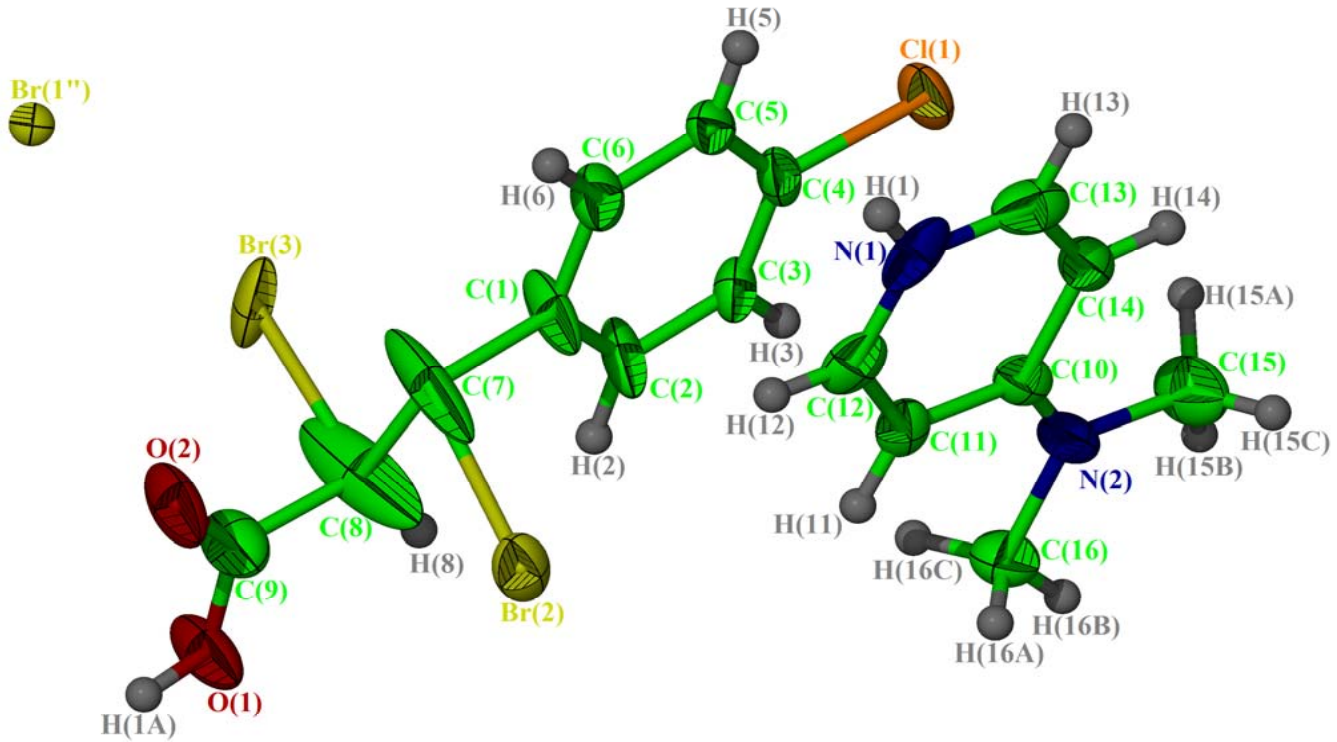

Figure 3.24 Molecular plot of bis(4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)**

at 70% probability.

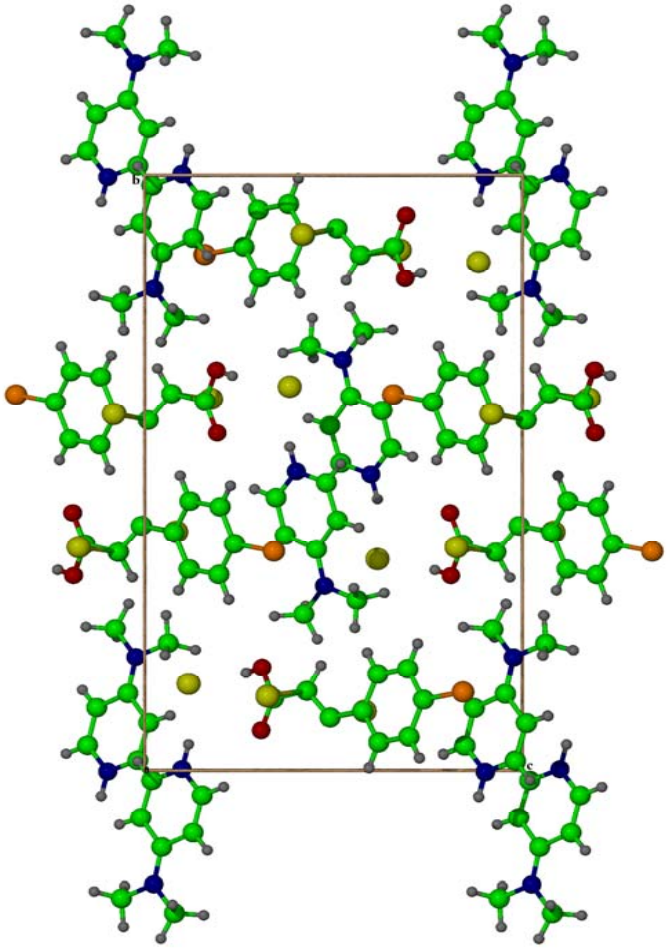

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Figure 3.25a Close packing of bis(4-dimethylaminopyridinium)2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)** viewed along *a*-axis

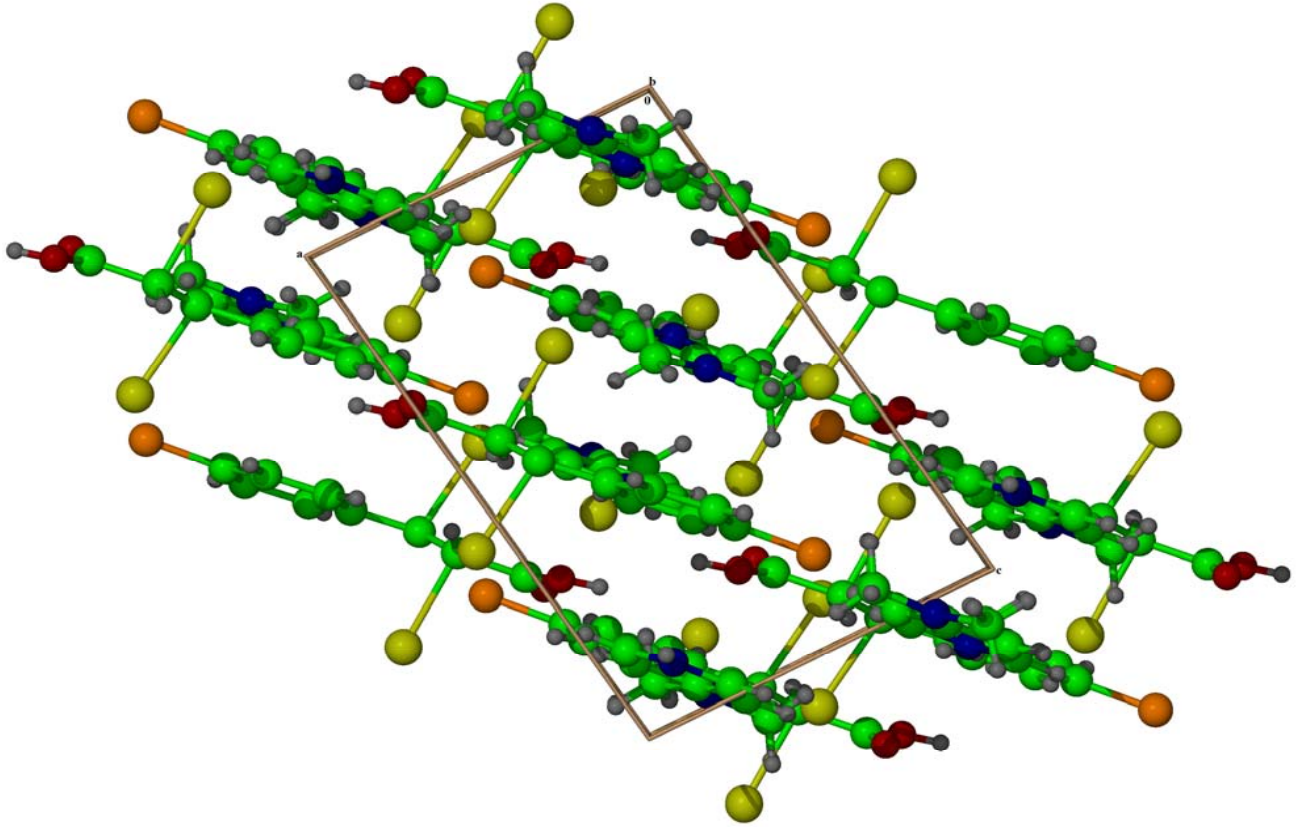

Figure 3.25b Close packing of bis(4-dimethylaminopyridinium)2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)** viewed along *b*-axis

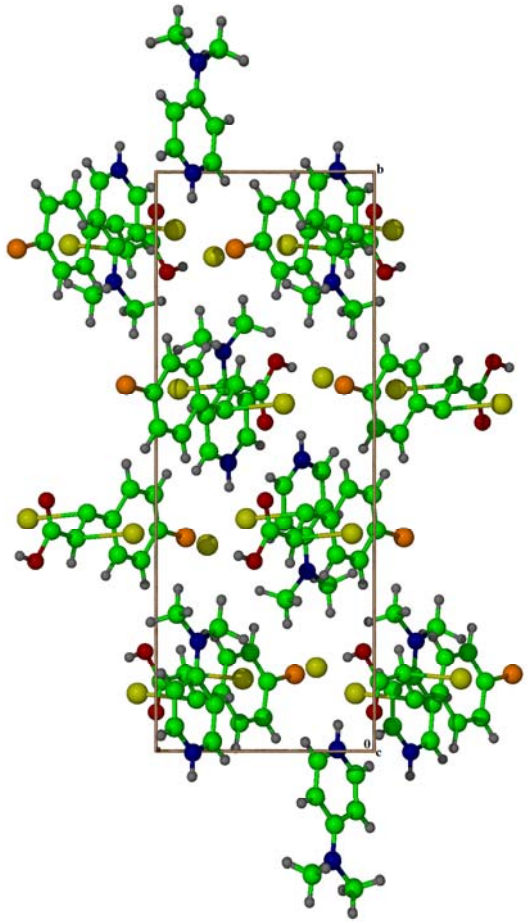

Figure 3.25c Close packing of bis(4-dimethylaminopyridinium)2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide **(A9)** viewed along *c*-axis

3.5.5 X-ray structure of tricyclohexyltin cinnamate (C6)

The title compound was obtained by the condensation reaction between tricyclohexyltin hydroxide and cinnamic acid. The crystals are monoclinic with, space group $P2_1/n$ and a = 9.406 (2), b = 55.073 (10), c = 10.624 (2) Å and $\beta = 114.807\ (10)^{o.}$ The molecular structure of the compound as depicted in **Fig. 3.26a** consists of two asymmetric discrete molecules containing four-coordinate tin atoms in a distorted tetrahedral configuration. The deviation from ideal tetrahedral geometry is evidenced from the four angles subtended at the tin atoms, that is C-Sn-C for one of the asymmetric unit are $92.4(10)^o$, $107.8(6)^o$, $113.9(6)^o$, $105.3(5)^o$ and $90.9(8)^o$, $110.0(6)^o$, $110.8(7)^o$, $115.9(8)^o$ for the other asymmetric molecule. There is no evidence of any intermolecular coordination between the acetate of an adjacent molecule and the tin atom as the significant steric hindrance by the cyclohexyl groups prevents close approached of the carboxylate oxygen towards the tin atoms. The intramolecular Sn-O2 and Sn-O4 distances of 2.82 Å and 2.85 Å, respectively are too long to be considered any interaction. The relative shorter C19-O2 and C46-O4 bond distances of 1.25(19) Å and 1.19(2) Å, respectively also support the non involvement of the carbonyl oxygen in any intra or intermolecular coordination with the tin atom. The C20-C21 and C47-C48 bond distances are 1.29(2) Å and 1.43(3), respectively, clearly indicates the presence of ethylene double bond in the cinnamate fragment. As seen in **Fig. 3.26b**, all the cyclohexyl groups adopt the chair conformation commonly found in most of th cyclohexyl derivatives.

Table 3.18 Crystal data and structure refinement for tricyclohexyltin cinnamate **(C6)**

Identification code	**C6**	
Empirical formula	$C_{27}H_{40}O_2Sn$	
Formula weight	514.78	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	$P2_1/n$	
Space group	Monoclinic	
Unit cell dimensions	a = 9.406(2) Å	$\alpha = 90^o$
	b = 55.073(10) Å	$\beta = 114.807(10)^o$
	c = 10.624(2) Å	$\gamma = 90^o$
Volume	4995.89(17) $Å^3$	
Z, Calculated density	8, 1.369 Mg/m^3	
Absorption coefficient	1.042 mm^{-1}	
F(000)	2140	
Crystal size	0.15 x 0.15 x 0.10 mm	
Theta range for data collection	2.14 to 27.50^o	
Limiting indices	$-12\leq h\leq 4$, $-15\leq k\leq 71$, $-5\leq l\leq 13$	
Reflections collected / unique	9425 / 8103 [$R_{(int)} = 0.0496$]	
Completeness to $\theta = 27.50$	70.7 %	
Max. and min. transmission	0.9029 and 0.8593	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8103 / 595 / 517	

Table 3.18 continued

Goodness-of-fit on F^2	1.648
Final R indices [I>2σ (I)]	$R_1 = 0.1433$, $wR_2 = 0.3224$
R indices (all data)	$R_1 = 0.2050$, $wR_2 = 0.3427$
Largest diff. peak and hole	1.863 and -1.695 $e.A^{-3}$

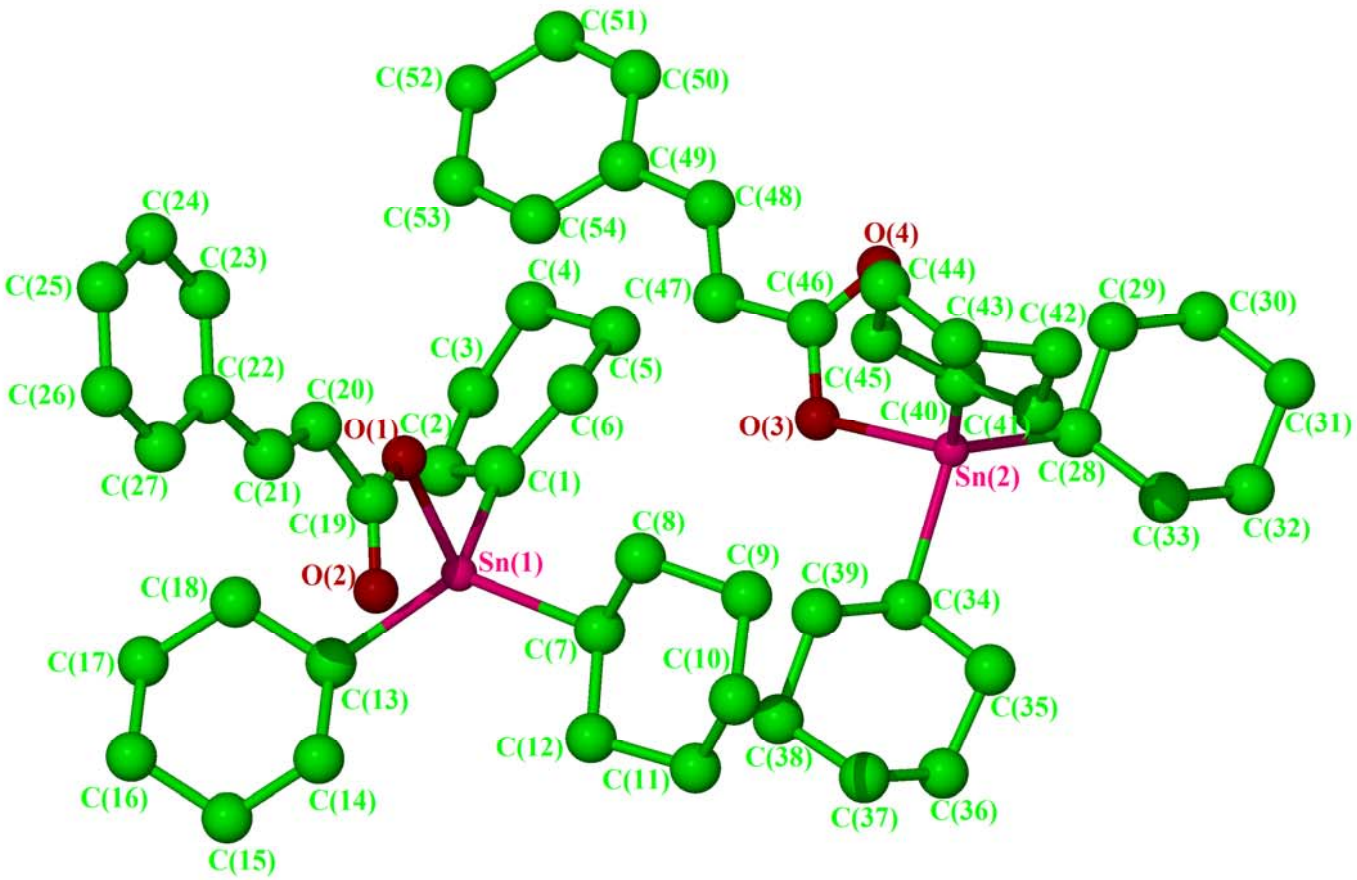

Figure 3.26a Molecular plot of tricyclohexyltin cinnamate **(C6).**

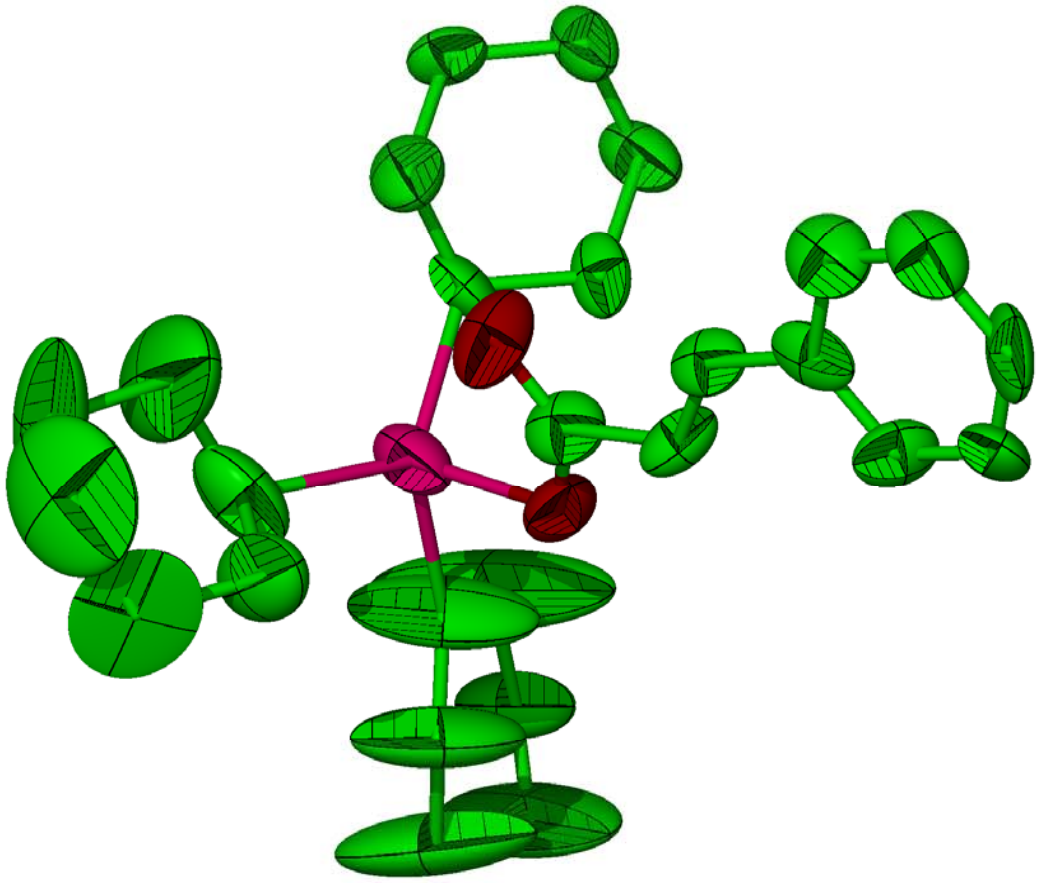

Figure 3.26b Ellipsoids drawn of tricyclohexyltin cinnamate **(C6)** at 70% probability.

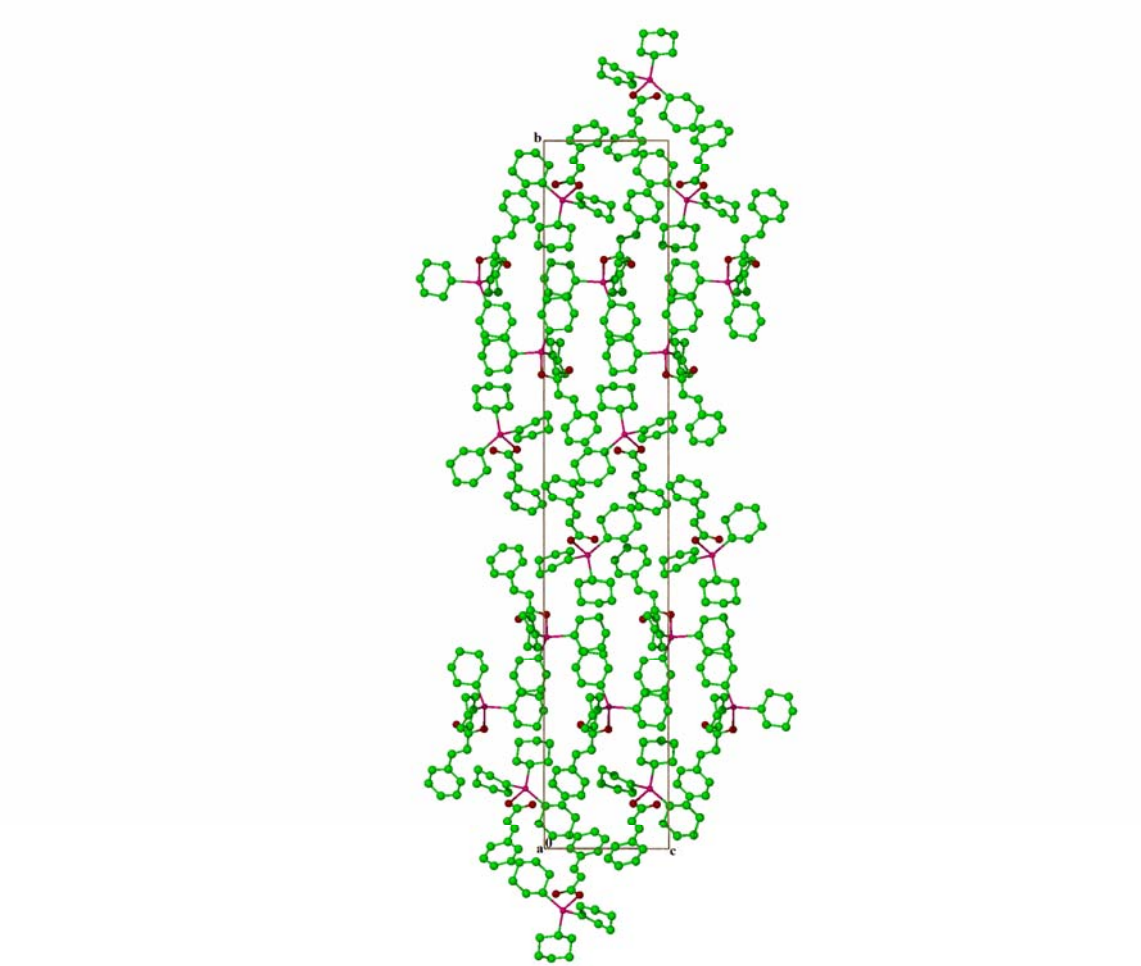

Figure 3.27a Close packing of tricyclohexyltin cinnamate **(C6)** viewed along *a*-axis.

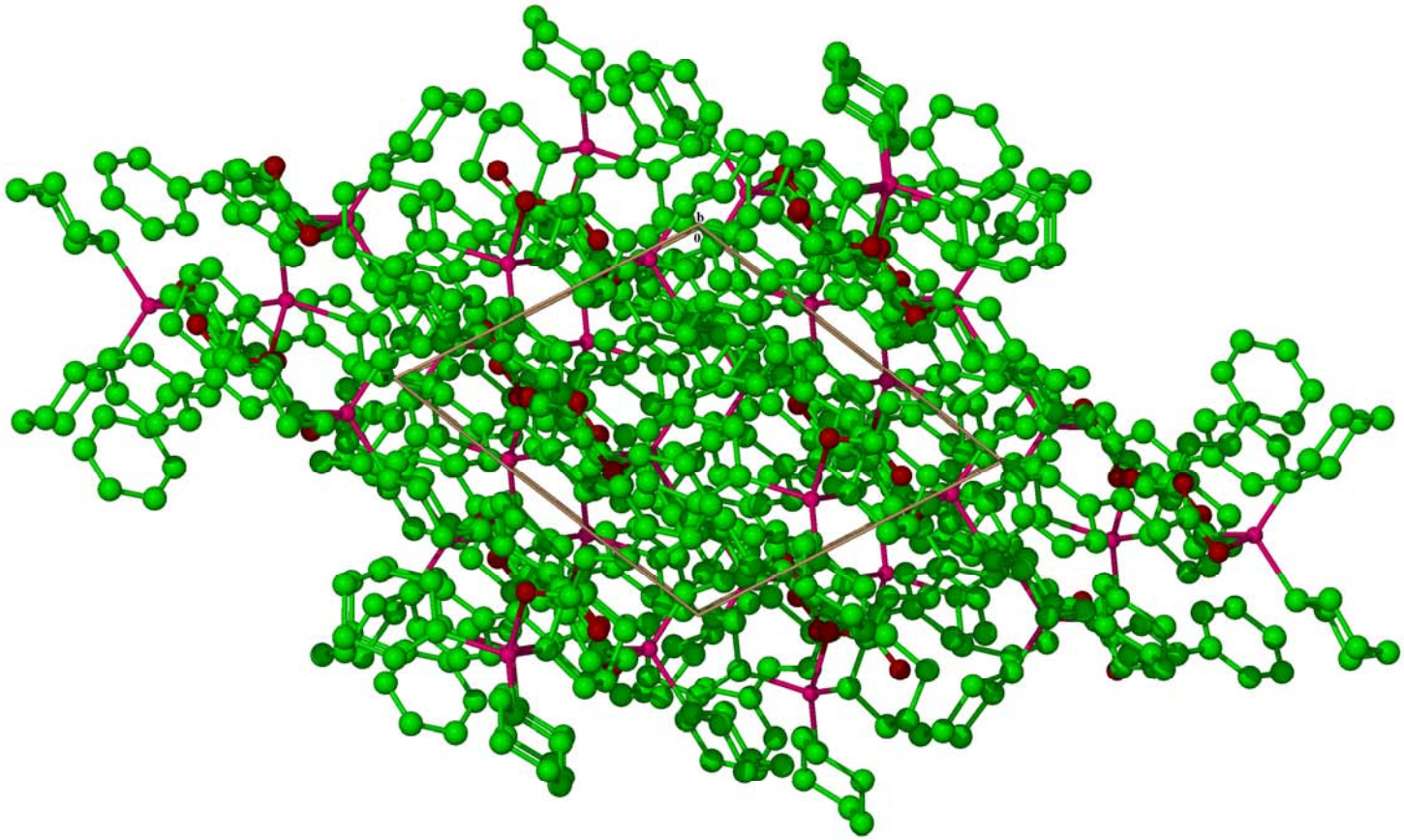

Figure 3.27b Close packing of tricyclohexyltin cinnamate **(C6)** viewed along *b*-axis.

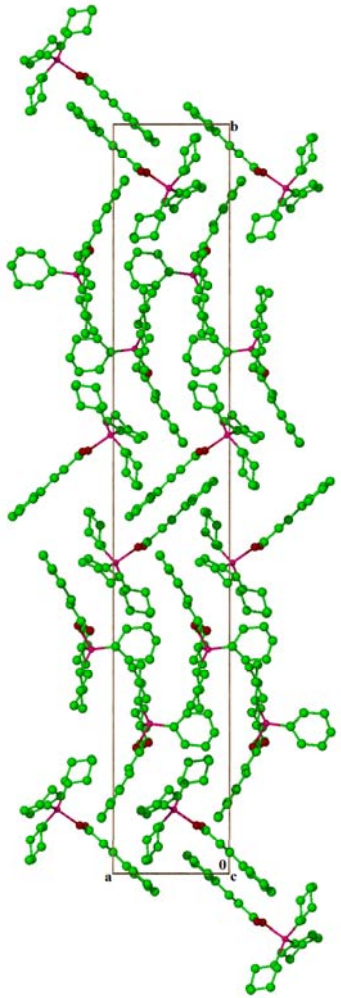

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Figure 3.27c Close packing of tricyclohexyltin cinnamate **(C6)** viewed along *c*-axis.

3.5.6 X-ray structure of tributyltin *p*-chlorocinnamate (C5)

The reaction of bis(tributyltin)oxide with *p*-chlorocinnamic acid afforded the title compound which also crystallizes in the monoclinic $P2_1/n$ space group. The cell parameter are a =12.834(6), b= 10.635(4), c= 18.080(11) Å, and β = 104.341(4)^o. In contrast to tricyclohexyltin cinnamate, the title compound adopts a five-coordinate tin configuration (**Fig. 3.28)** in which the tin atom are bonded to three butyl groups which Sn-C distances of 2.17(17), 2.26(2) and 2.19(17) Å, a carboxyl oxygen (Sn-O1 2.19 (9) Å) and a carboxyl oxygen from an adjacent molecule (Sn-O2' 2.40(11) Å). The geometry at tin can be regarded as a distorted trigonal bipyramid in which the equatorial plane occupied by Sn and the three butyl group while the two oxygen of the carboxyl groups form the axial positions. The O1-Sn-O2' bond angle of 172.1(3)^o confirmed the distortion from ideal trigonal bipyramidal geometry of the structure. The involvement of the intermolecular coordination resulted in the formation of polymeric chain structure (**Fig. 3.29a, 3.29b & 3.29c**). The C14-C15 bond distance of 1.29(15) Å also indicates that the C=C in the cinnamate fragment is retained. The chloro substituent is found to be situated on the plane of the phenyl ring (sum of angles subtended at C19 is 360^o).

There is a severe disorder found in the second, third and forth carbon atoms in the three butyl groups which is common among most butyl groups. As a result, the C-C bond distances of the butyl group varies over a wide range from 1.36(3) to 1.81(5) Å. This also caused a large R factor of 18.24 %.

Table 3.19 Crystal data and structure refinement for tributyltin *p*-chlorocinnamate **(C5)**

Identification code	**C5**	
Empirical formula	$C_{21}H_{33}ClO_2Sn$	
Formula weight	471.61	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	$P2_1/n$	
Space group	monoclinic	
Unit cell dimensions	a = 12.834 (6) Å	$\alpha = 90^o$
	b = 10.635(4) Å	$\beta = 104.341(4)^o$
	c = 18.080 (11) Å	$\gamma = 90^o$.
Volume	2390.8(2) A^3	
Z, Calculated density	4, 1.310 Mg/m^3	
Absorption coefficient	1.190 mm^{-1}	
F (000)	968	
Crystal size	0.33 x 0.33 x 0.21 mm	
θ range for data collection	1.76 to 27.49 ^{o}	
Limiting indices	$-16 \leq h \leq 16$, $0 \leq k \leq 12$, $-20 \leq l \leq 23$	
Reflections collected / unique	5168 / 4977 [$R_{(int)} = 0.0195$]	
Completeness to θ = 27.49	90.5 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4977 / 2 / 229	

Table 3.18 continued

Goodness-of-fit on F^2	0.951
Final R indices [I>2σ (I)]	$R_1 = 0.0588$, $wR_2 = 0.1416$
R indices (all data)	$R_1 = 0.1250$, $wR_2 = 0.1670$
Largest diff. peak and hole	0.358 and -0.346 e. $Å^{-3}$

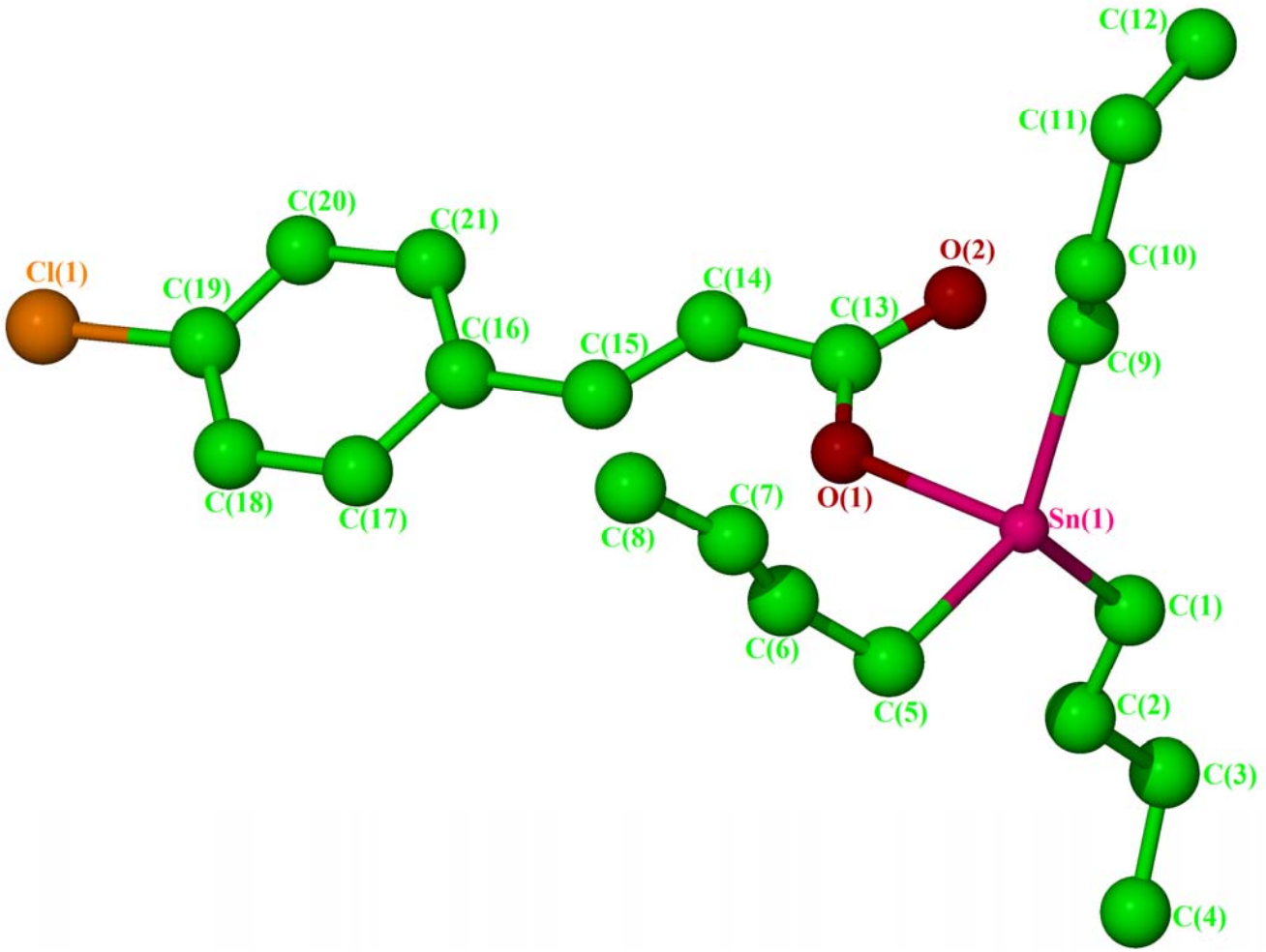

Figure 3.28 Molecular plot of tributyltin *p*-chlorocinnamate **(C5).**

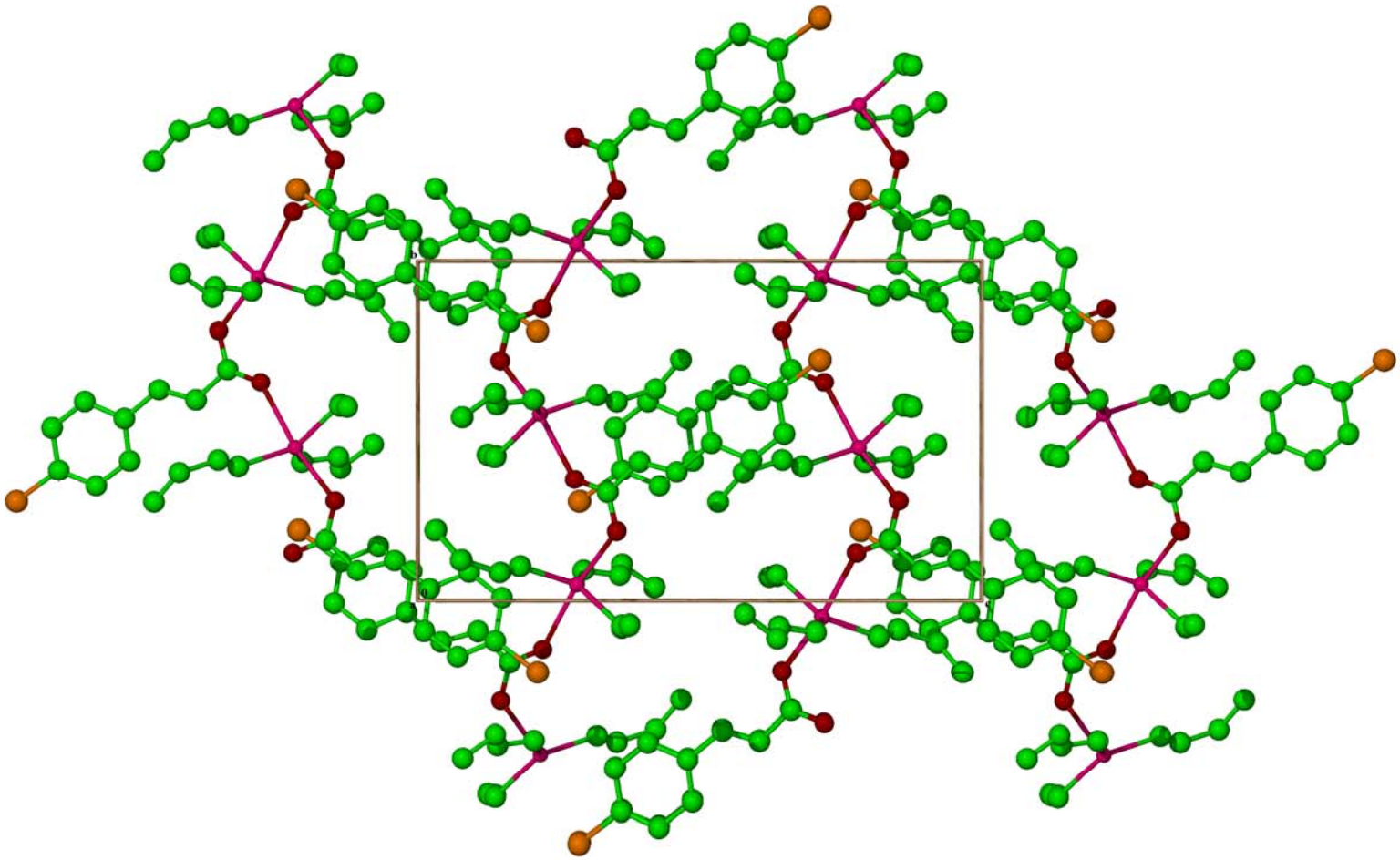

Figure 3.29a Close packing of tributyltin *p*-chlorocinnamate **(C5)** viewed along *a*-axis.

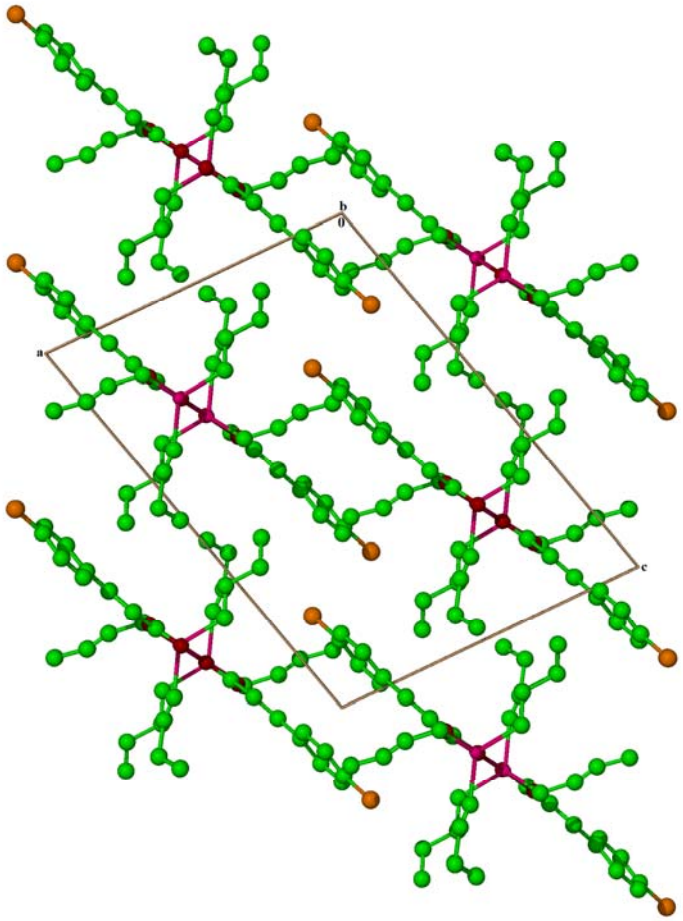

Figure 3.29b Close packing of tributyltin *p*-chlorocinnamate **(C5)** viewed along b-axis.

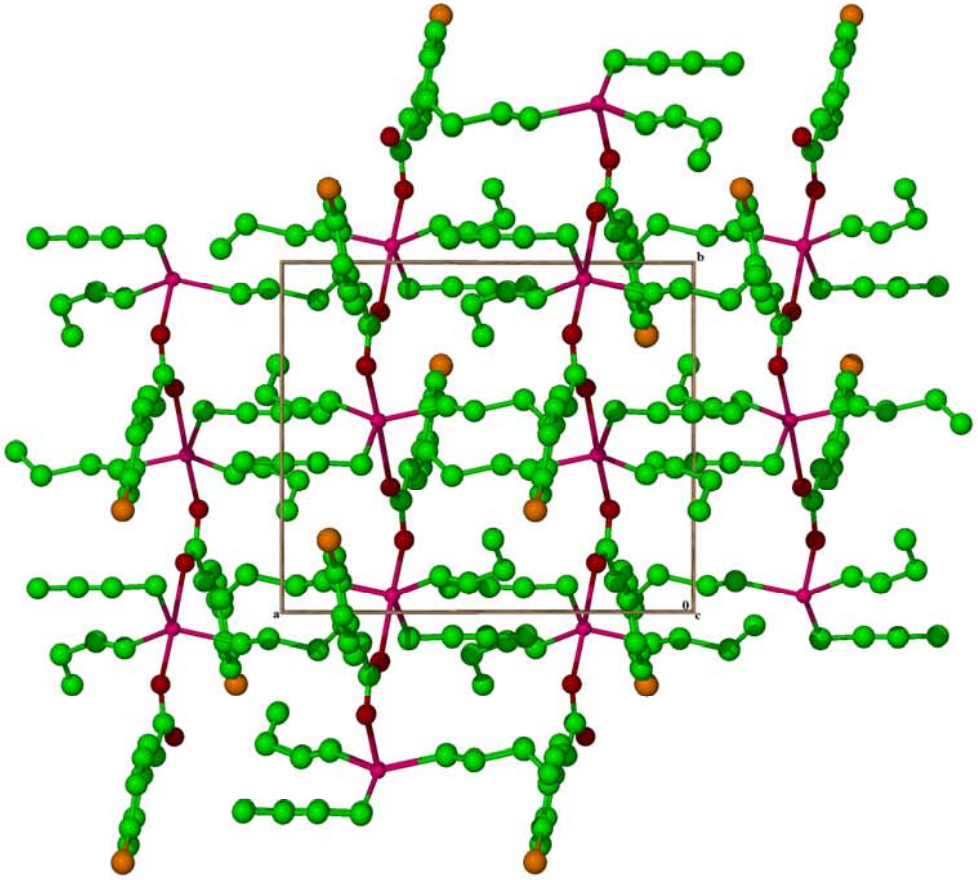

Figure 3.29c Close packing of tributyltin *p*-chlorocinnamate **(C5)** viewed along *c*-axis.

3.5.7 X-ray structure of tribenzyltin *p*-nitrocinnamate (C14)

Another of crystal structure triorganotin cinnamate from the reaction of tribenzyltin hydroxide with *p*-nitrocinnamic acid was determined. This compound again crystallizes in the monoclinic $P2_1/n$ space group with cell dimension of a = 21.483(3), b = 10.2154(1), c = 25.9562(4) Å and $\beta = 112.133(1)^o$. The molecular structure of the compound as shown in **Fig. 3.30** is found to consist of two asymmetric units. Each asymmetric unit contains a five-coordinate tin configuration in a distorted trigonal bipyramidal geometry. The trigonal bipyramid at tin is formed by the three benzyl groups in the equatorial plane and two oxygens atom, one from each adjacent carboxyl group in the axial position. The Sn-C bond distances for the two asymmetric units are 2.15(3), 2.15(3), 2.16(3) Å and 2.14(3) Å, 2.15(3) Å, 2.16(3) Å, respectively. The axial Sn-O bond distances are 2.18(2), 2.32(2) Å and 2.20(2), 2.33(2) Å, respectively. The distortion from ideal trigonal byramidal geometry can be seen from the deviation from 180^o of the O-Sn-O angle of the two asymmetric units (O1-Sn1-O2' $171.89(8)^o$ and O5-Sn2-O6' $173.04(8)^o$). The sums of C-Sn-C angles subtended at tin are 359.15^o indicating that the equatorial planes are virtually flat.

The carboxylate bridges found in the two asymmetric units resulted in the formation of two polymeric chains in the structure (**Fig. 3.31a, 3.31b** and **3.31c**). The intramolecular Sn1-O2 and Sn2-O6 bond distances of 2.32(2) Å and 2.33(2) Å, are relatively long and hence cannot be considered any significant interaction.

The C23-C24 and C53-C54 bond distances of 1.33(4) and 1.33(4) Å also indicates the presence of C-C double bond in the substituted cinnamate fragment. There is also no evidence of any involvement of the nitro oxygen in inter- or intramolecular bonding unlike

the case of the free *p*-nitrocinnamic acid as discussed in its X-ray structure. However, it was found that the nitro oxygen atoms in both asymmetric units are disordered over two positions with approximately occupancy of 50% in each position.

Table 3.20 Crystal data and structure refinement for tribenzyltin *p*-nitrocinnamate **(C14)**

Identification code	**C14**	
Empirical formula	$C_{30}H_{27}NO_4Sn$	
Formula weight	584.22	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system,	$P2_1/n$	
Space group	Monoclinic	
Unit cell dimensions	a = 21.485(3) Å	$\alpha = 90^o$
	b = 10.213 (1) Å	$\beta = 112.133(1)^o$
	c = 25.956 (4) Å	$\gamma = 90^o$
Volume	5275.99(12) $Å^3$	
Z, Calculated density	8, 1.471 Mg/m^3	
Absorption coefficient	1.004 mm^{-1}	
F(000)	2368	
Crystal size	0.36 x 0.03 x 0.03 mm	
θ range for data collection	1.05 to 27.50°	
Limiting indices	$-26\leq h\leq 27$, $-13\leq k\leq 13$, $-32\leq l\leq 33$	
Reflections collected / unique	48779 / 12115 [$R_{(int)} = 0.0316$]	
Completeness to $\theta = 27.50$	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9705 and 0.7139	

Table 3.20 continued

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12115 / 38 / 565
Goodness-of-fit on F^2	1.063
Final R indices [$I>2\sigma$ (I)]	$R_1 = 0.0330$, $wR_2 = 0.0774$
R indices (all data)	$R_1 = 0.0533$, $wR_2 = 0.0905$
Largest diff. peak and hole	0.812 and -0.798 $e.A^{-3}$

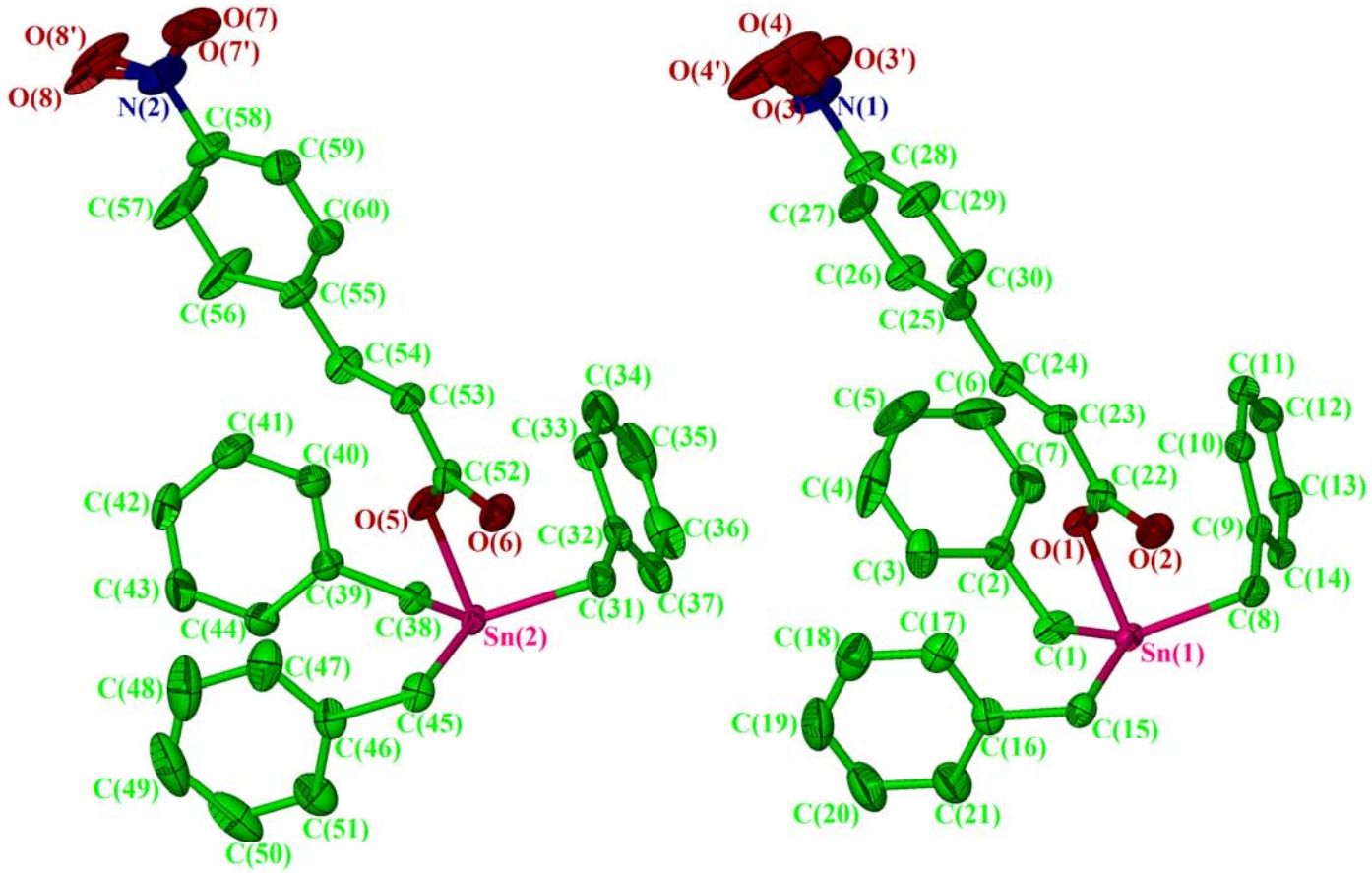

Figure 3.30 Molecular plot of tribenzyltin *p*-nitrocinnamate **(C14)** at 70% probability.

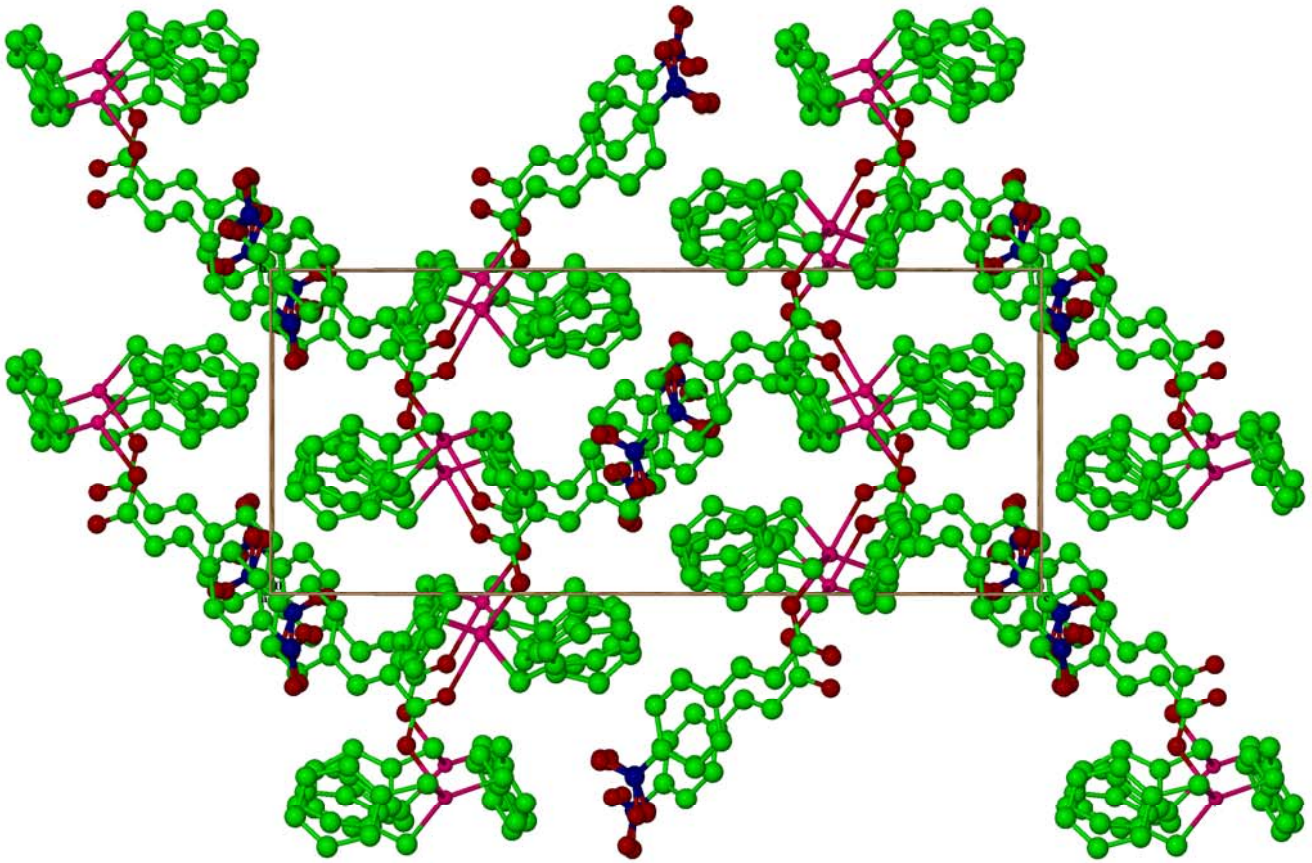

Figure 3.31a Close packing of tribenzyltin *p*-nitrocinnamate **(C14)** viewed along *a*-axis.

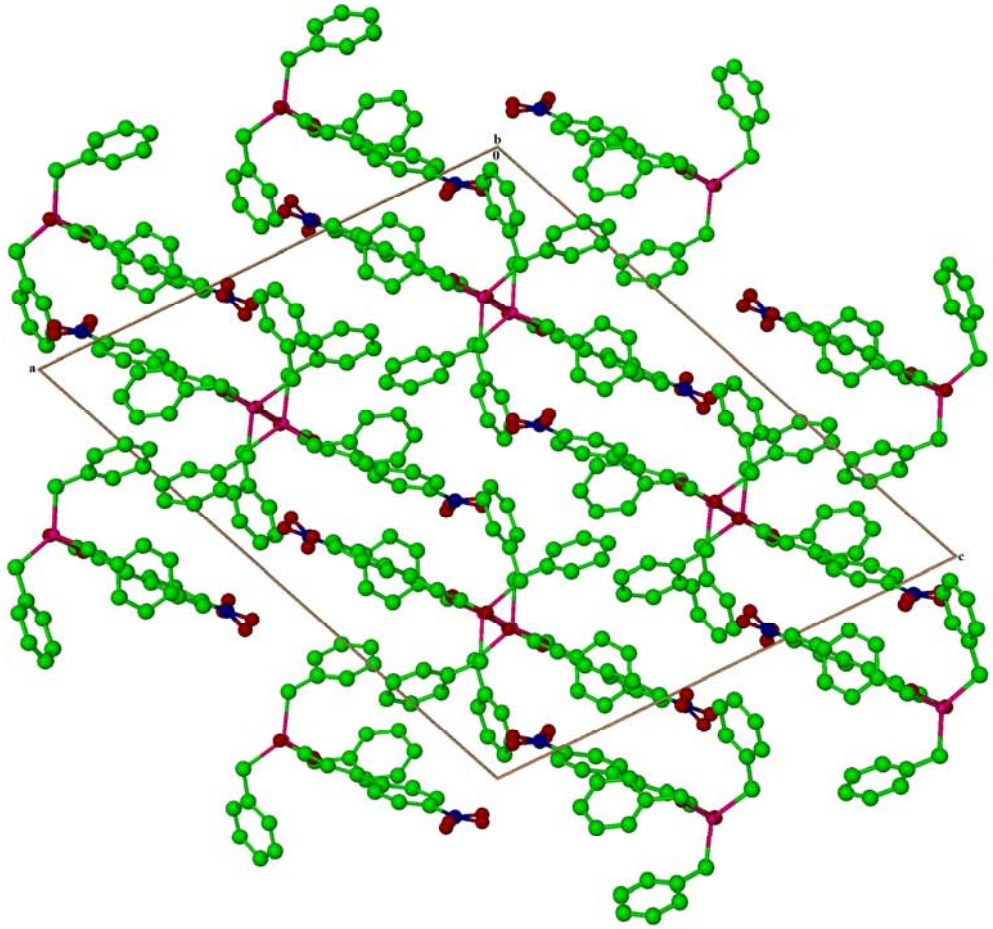

Figure 3.31b Close packing of tribenzyltin *p*-nitrocinnamate **(C14)** viewed along *b*-axis.

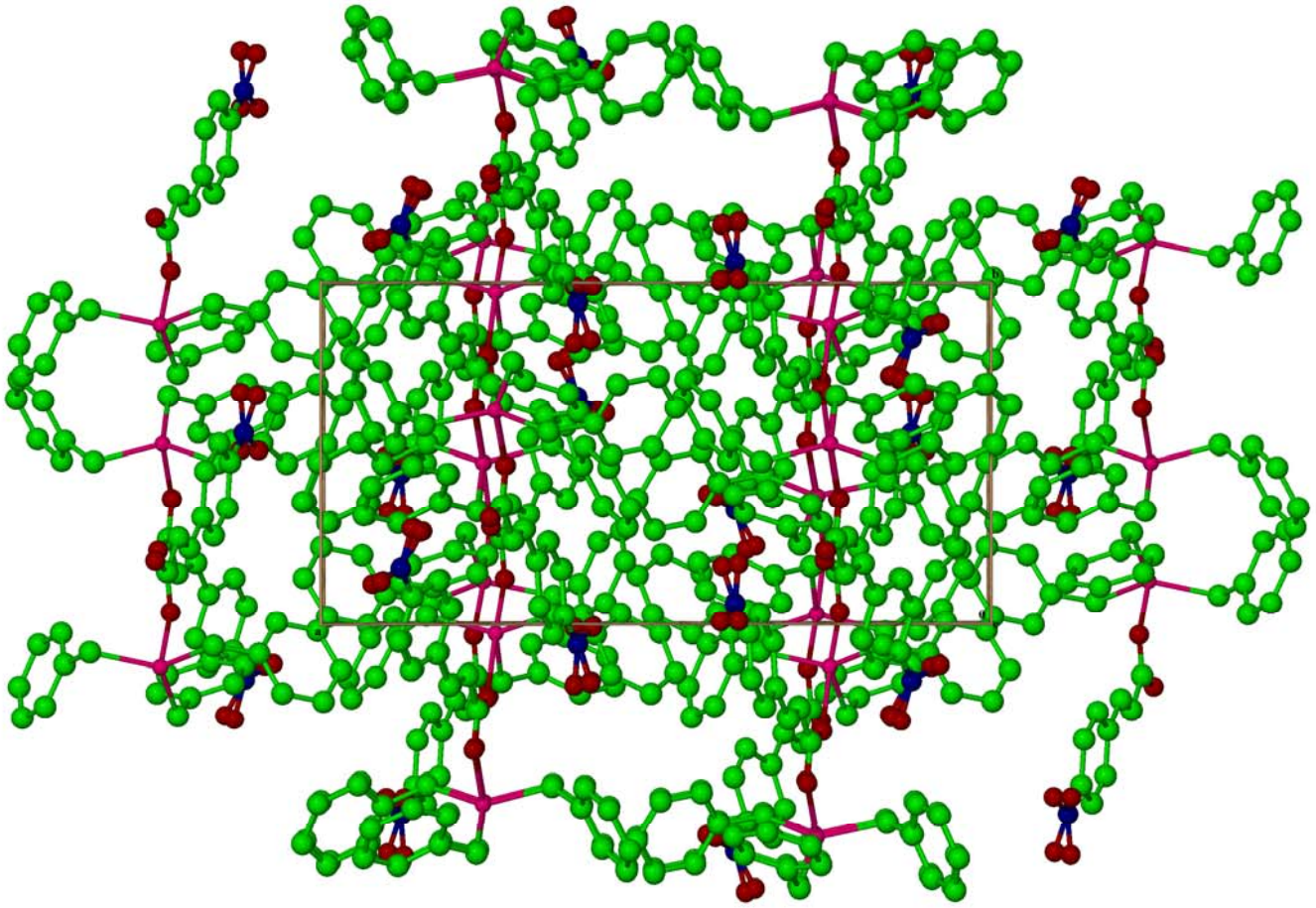

Figure 3.31c Close packing of tribenzyltin *p*-nitrocinnamate **(C14)** viewed along *c*-axis.

3.5.8 X-ray structure of tricyclohexyltin 2,3-dibromo-3-phenylpropionate (P4)

The title compound was prepared by the reaction of tricyclohexyltin hydroxide with 2,3-dibromo-3-phenylpropionic acid. The crystals are monoclinic, space group $P2_1/n$ with a = 21.253(3), b = 9.083(10), c = 15.055(2) Å and β = 108.287 (10)^o. The molecular structure as given in **Fig. 3.32** is a discrete monomeric molecule in which the tin atom is rendered four-coordinate in a tetrahedral geometry, similar to other tricyclohexyltin carboxylates (Molloy *et* al., 1986). The three Sn-C bond distances are 2.14(4), 2.16(3), 2.16(3) Å and a Sn-O bond with distance of 2.07(3) Å. The distorted tetrahedral geometry is revealed from the deviation of C-Sn-C angle from the ideal 109^o. In this case, the C-Sn-C bond angles at tin are C1-Sn-C7 = 118.36(14)^o, C7-Sn-C13 = 114.25(13)^o, C13-Sn-C1 = 107.13(13)^o. Significant difference was observed in the bond C-O distances of the carboxylate moiety (C19-O1 = 1.27(5) Å compared to C19-O2 = 1.20(6) Å. The observation shows that the carbonyl oxygen, O2 do not involve in any -inter or intermolecular bonding with the tin atom (**Fig 3.33a, Fig 3.33b** and **Fig3.33c**). The Sn-O2 is too long to have any intermolecular interaction with the tin atom. The two C-Br bonds in the molecule are not equal with bond distances of 1.99(7) Å and 2.05(8) Å, respectively.

Table 3.21 Crystal data and structure refinement for tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)**

Identification code	**P4**	
Empirical formula	$C_{27}H_{40}Br_2O_2Sn$	
Formula weight	675.10	
Temperature	118(2) K	
Wavelength	0.71073 Å	
Crystal system	$P2_1/n$	
Space group	Monoclinic	
Unit cell dimensions	a = 21.235(3) Å	$\alpha = 90^o$
	b = 9.083(10) Å	$\beta = 108.287(10)^o$
	c = 15.055(2) Å	$\gamma = 90^o$
Volume	2757.45(6) A^3	
Z, Calculated density	4, 1.626 Mg/m^3	
Absorption coefficient	3.846 mm^{-1}	
F(000)	1352	
Crystal size	0.30 x 0.20 x 0.10 mm	
θ range for data collection	1.01 to 27.50°	
Limiting indices	$-27 \leq h \leq 27$, $-11 \leq k \leq 11$, $-18 \leq l \leq 19$	
Reflections collected / unique	21967 / 6325 [$R_{(int)} = 0.0337$]	
Completeness to θ = 27.50	100.0 %	
Max. and min. transmission	0.6997 and 0.3916	
Refinement method	Full-matrix least-squares on F^2	

Table 3.21 continued

Data / restraints / parameters	6325 / 0 / 289
Goodness-of-fit on F^2	1.038
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0323$, $wR_2 = 0.0694$
R indices (all data)	$R_1 = 0.0503$, $wR_2 = 0.0826$
Largest diff. peak and hole	1.630 and -1.134 $e.A^{-3}$

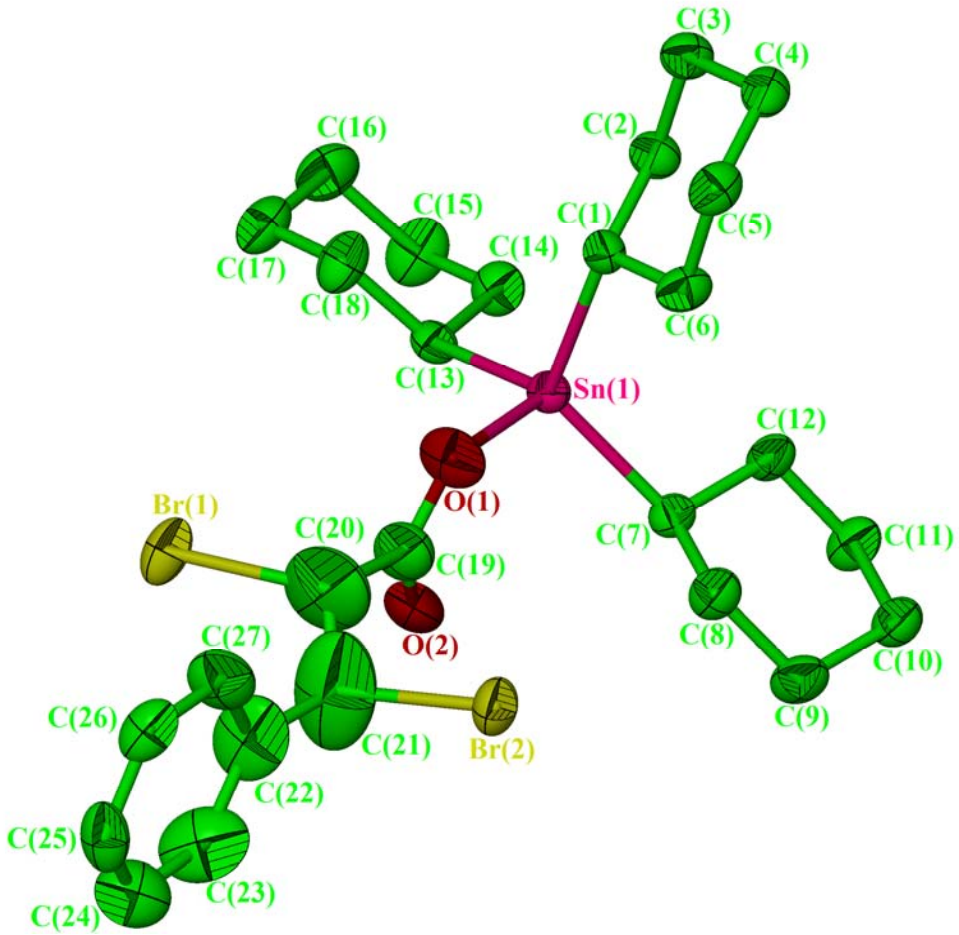

Figure 3.32 Molecular plot of tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)** at 70% probability.

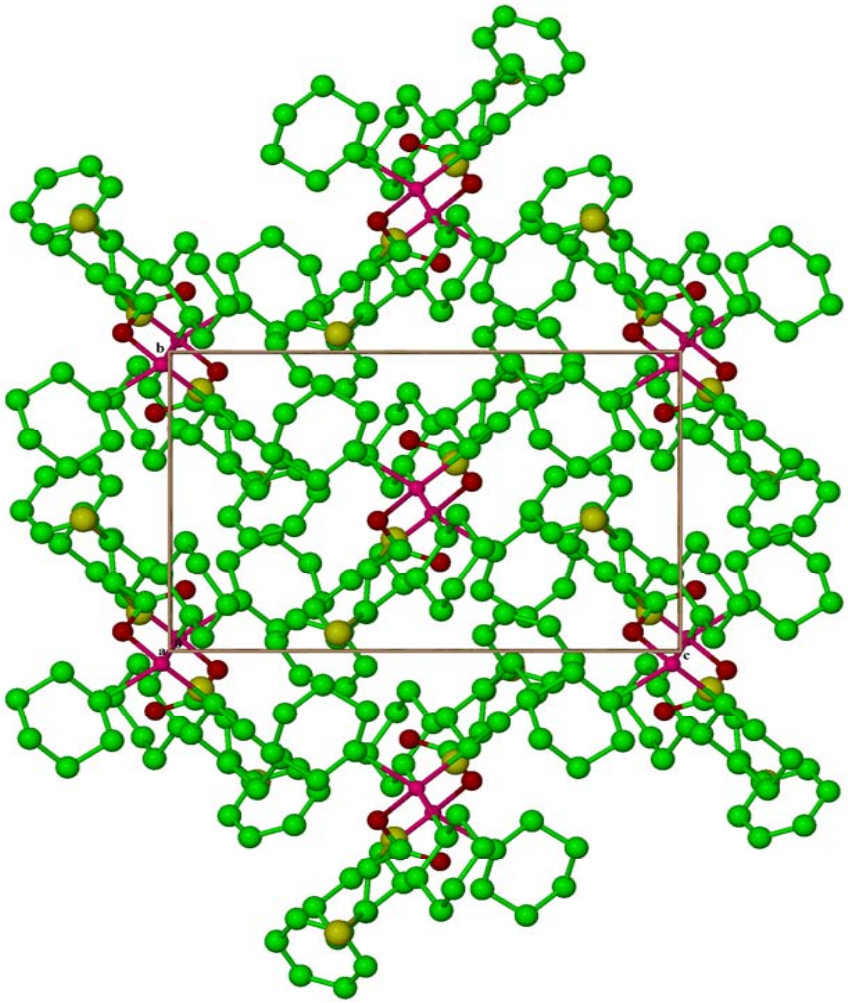

Figure 3.33a Close packing of tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)** viewed along *a*-axis.

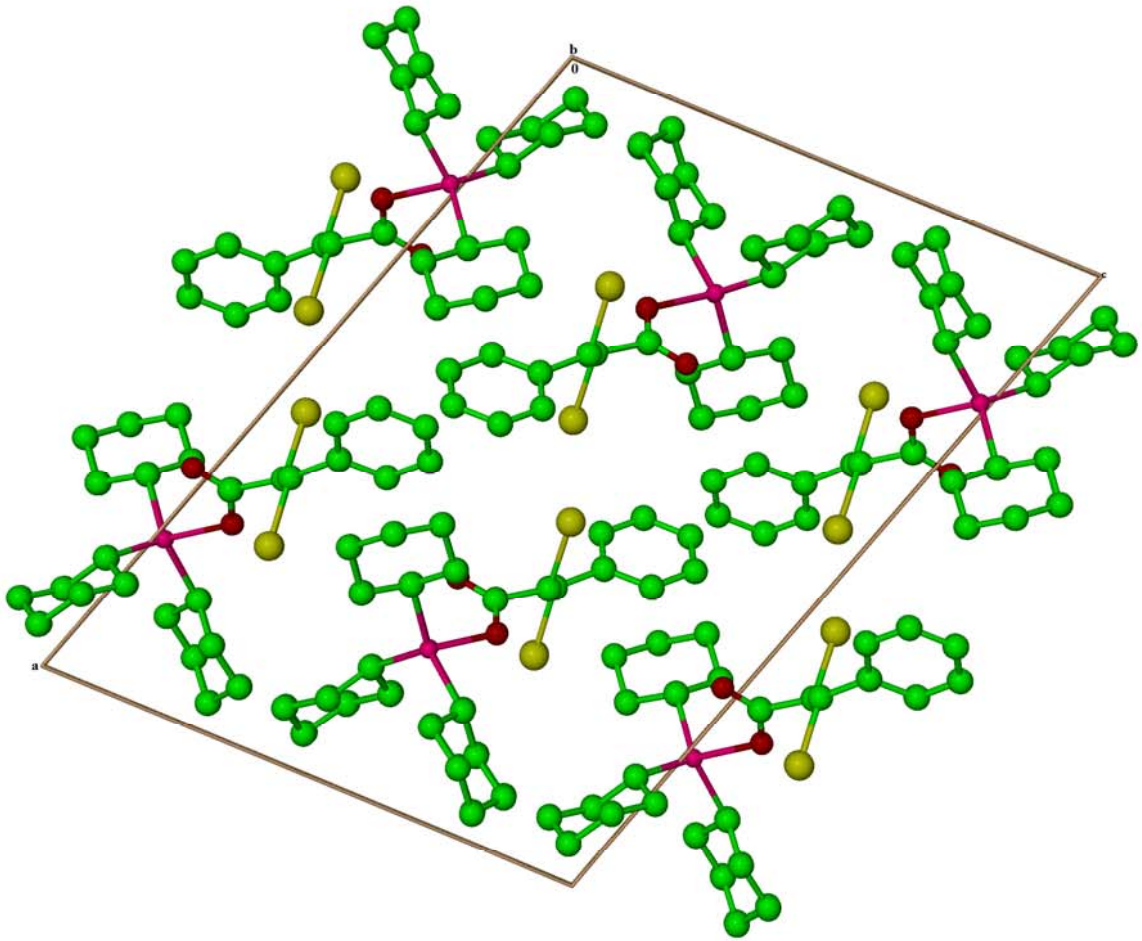

Figure 3.33b Close packing of tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)** viewed along *b*-axis.

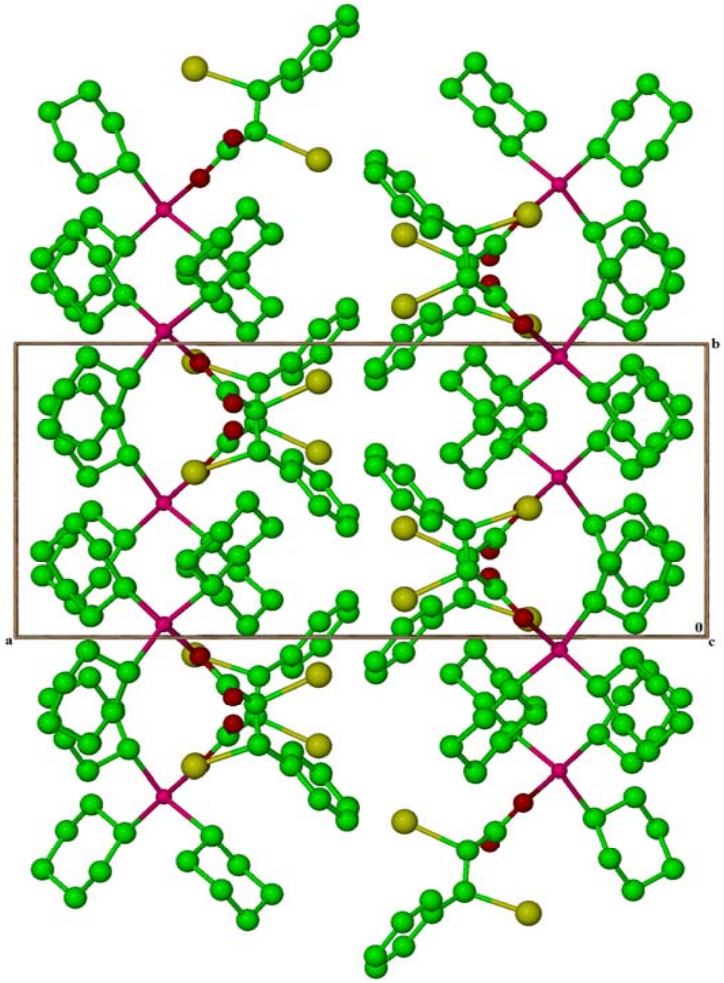

Figure 3.33c Close packing of tricyclohexyltin 2,3-dibromo-3-phenylpropionate **(P4)** viewed along *c*-axis.

3.5.9 X-ray crystal structure of tricyclohexyltin dimethyldithiocarbamylacetate (D1)

The title compound was obtained from the reaction of tricyclohexyltin hydroxide with dimethyldithiocarbamylacetic acid. The crystals is triclinic $P_{\bar{1}}$ space group with a = 10.827(14), b = 11.119(14), c = 22.952(2) Å, α = 77.422(8)^o, β = 83.007(7)^o, and γ = 73.007(7)^o. The crystal structure (**Fig. 3.34**) reveals two asymmetric molecules in the unit cell. Each asymmetric unit consists of a four coordinate tin with tetrahedral geometry. There is an enlargement of the three C-Sn-C bond angles from the ideal 109^o. (C1-Sn1-C7 = 107.6(6), C7-Sn1-C13 111.3(5), C13-Sn1-C1 = 126.8(6) and C24-Sn2-C30 = 119.1(9), C30-Sn2-C36 = 110.2(7)^o, C36-Sn2-C24 = 118.4(5)^o). The large C-Sn-C bond angles are due to the weak intermolecular interaction between the O2' and O4' of adjacent molecules with the tin atoms (Sn1-O2'= 2.89 and Sn2-O4' = 3.63 Å). A water molecule found in each of the asymmetric unit which is weakly hydrogen bonded to the carboxyl oxygen (O1w-H1w…O1 2.77 and O2w-H2w…O3 2.95 Å) (**Fig 3.35a, Fig 3.35b** and **Fig 3.35c**). The sulfur atom is not involved in any intra- or intermolecular coordination with the tin atom. The C=S bond distances are 1.67(11) Å and 1.67(14) Å while the C-S bond distances are 1.76(11) Å and 1.77(14) Å.

Table 3.22 Crystal data and structure refinement for tricyclohexyltin dimethyldithiocarbamylacetate **(D1)**

Identification code	**D1**	
Empirical formula	$C_{20}H_{20}N_4O_4S_2Sn$	
Formula weight	531.15	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	$P_{\bar{1}}$	
Space group	Triclinic	
Unit cell dimensions	a = 10.827(14) Å	α = 77.422(8)°
	b = 11.119(14) Å	β = 83.007(7)°
	c = 22.952(2) Å	γ = 73.115(7)°
Volume	2575.7(5) $Å^3$	
Z, Calculated density	4, 1.370 Mg/m^3	
Absorption coefficient	1.102 mm^{-1}	
F(000)	1064	
Crystal size	0.32 x 0.16 x 0.09 mm	
θ range for data collection	0.91 to 27.50°	
Limiting indices	$-14 \leq h \leq 14$, $-14 \leq k \leq 13$, $-29 \leq l \leq 29$	
Reflections collected / unique	17270 / 11255 [$R_{(int)}$ = 0.0476]	
Completeness to θ = 27.50	95.2 %	
Max. and min. transmission	0.9074 and 0.7194	
Refinement method	Full-matrix least-squares on F^2	

Table 3.22 continued

Data / restraints / parameters	11255 / 36 / 536
Goodness-of-fit on F^2	2.124
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.1316$, $wR_2 = 0.3552$
R indices (all data)	$R_1 = 0.1691$, $wR_2 = 0.3704$
Largest diff. peak and hole	2.301 and -3.876 $e.A^{-3}$

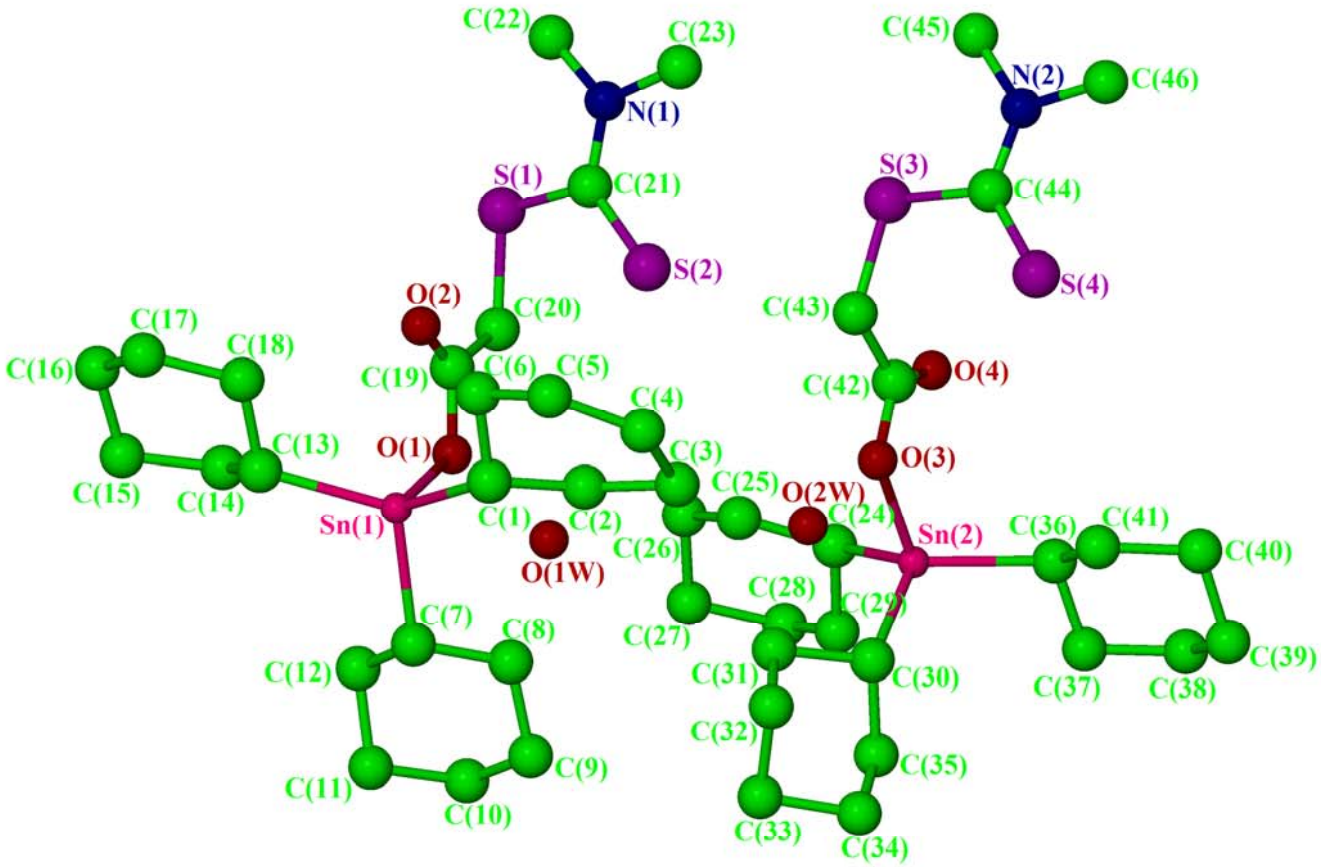

Figure 3.34 Molecular plot of tricyclohexyltin dimethyldithiocarbamylacetate **(D1)** at 70% probability.

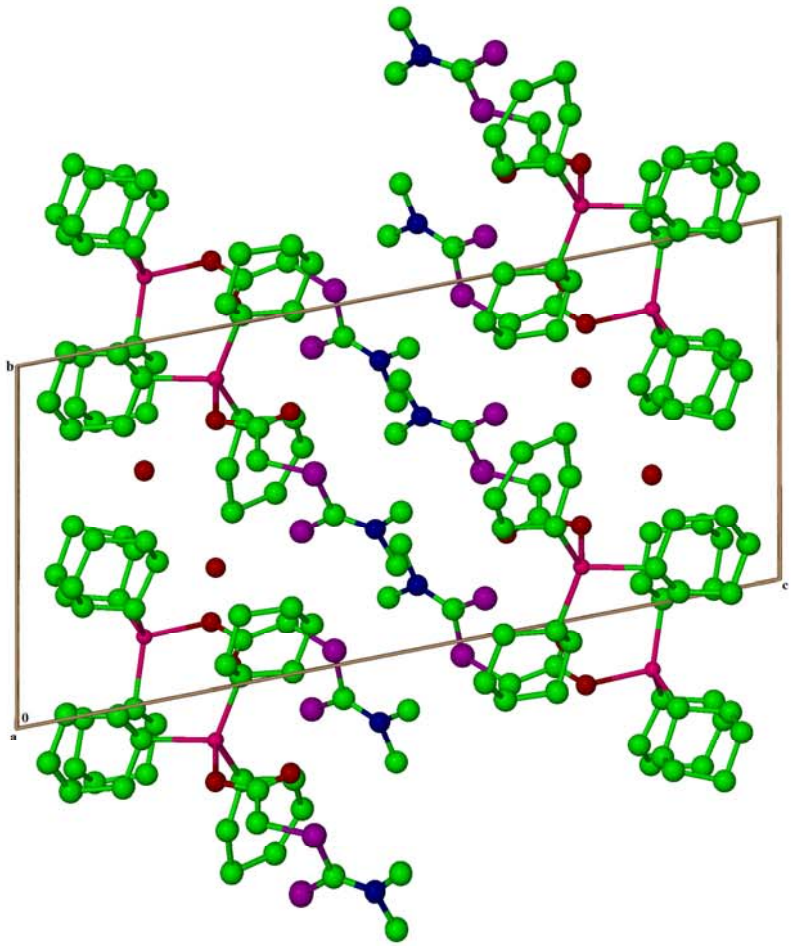

Figure 3.35a Close packing of tricyclohexyltin dimethyldithiocarbamylacetate **(D1)** viewed along *a*-axis.

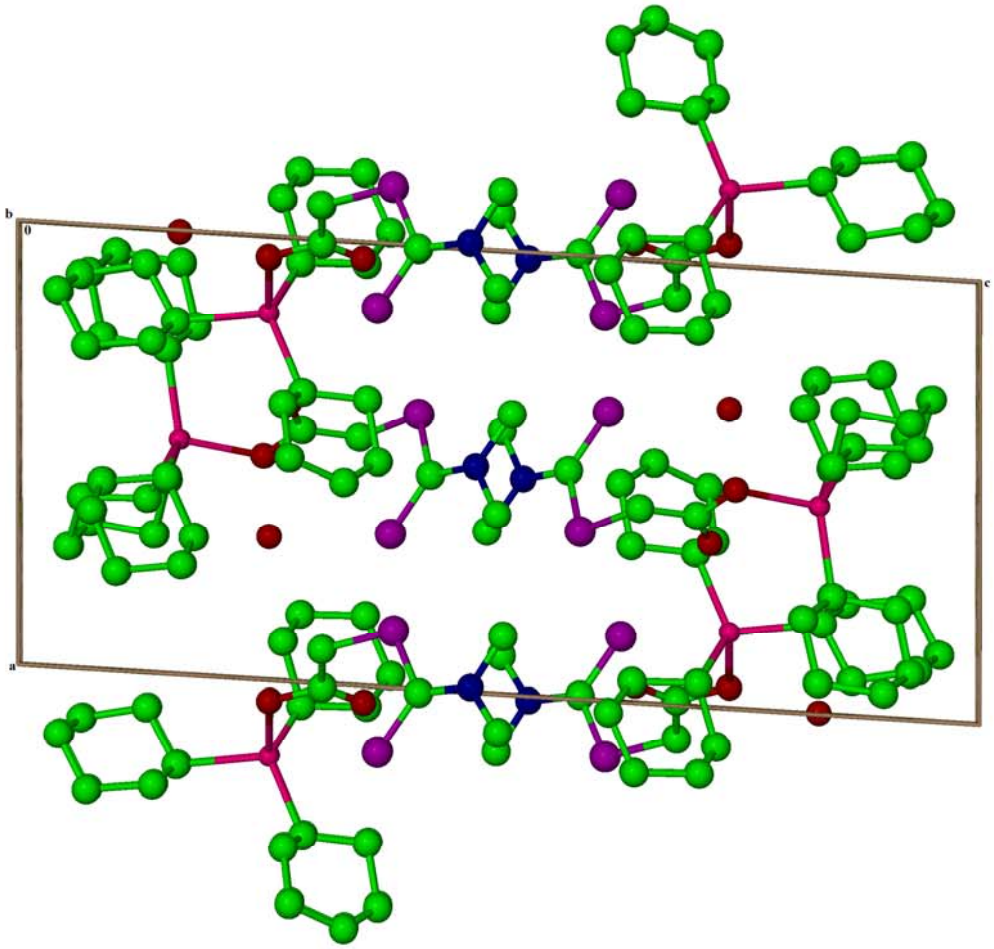

Figure 3.35b Close packing of tricyclohexyltin dimethyldithiocarbamylacetate **(D1)** viewed along *b*-axis.

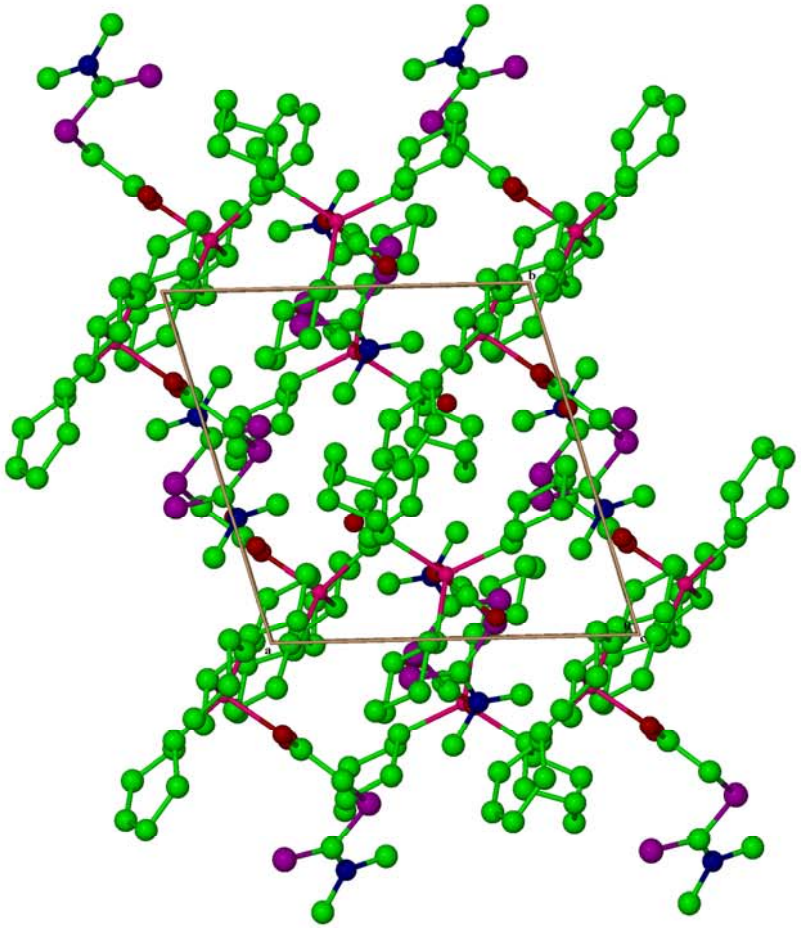

Figure 3.35c Close packing of tricyclohexyltin dimethyldithiocarbamylacetate **(D1)** viewed along *c*-axis.

3.6 Cytotoxicity activity

Table 3.23 compares the in-vitro cytotoxicity of the ten selected triorganotin carboxylate complexes against HL60 cells. The amount of formazan product, which was generated based on the reduction in the mitochondria, is proportional to the number of HL60 live cells in the culture. The MTT colorimetric assay was used for evaluation (Teo, 2005). As given in the experiment section, the result of cytotoxicity was compared to the control untreated cells and 1 μg/mL of the compound that used to inhibit the proliferation rate of the tumor cells was quoted in the percentage of viability.

As compared to the cytotoxic activity of cisplatin where the percentage of viability value is 1.17% or 1.19%, the selected triorganotin carboxylate complexes show a strong antiproliferation action. In general, the tricyclohexyltin carboxylates, except tricyclohexyltin *p*-nitrocinnamate (**C9**) and tricyclohexyltin 2,3-dibromo-3-phenyl propionate **(P5)**, showed comparable percentage viability as that for cisplatin. The tributyltin *p*-nitrocinnamate **(C4)** and tribenzyltin *p*-nitrocinnamate (**C14**) showed a slightly weaker antiproliferation action compared to the tricyclohexyltin cinnamates, thus indicating probably the organic group on the tin fragment play a role in the cytotoxicity activity.

The triorganotin compounds are able to inhibit mitochondrial oxidative phosphorylation and their biological activity pattern is probably due to their ability to bind to certain proteins. The cytotoxicity activity of the triorganotin compounds is mainly due to the ease of dissociation and the strength of the organotin fragment to bind with the tumor. However, tricyclohexyltin *p*-chlorocinnamate (**C10**) shows a weak antiproliferation action, which is 87.04% or 81.08% viability. This might be due to the presence of the chloro group in the phenyl ring of cinnamic acid. But the evidence to support the active reason for the

abnormal percentage viability needs further investigation. As shown in **Figure 3.36**, the brominated tricyclohexyltin substituted 3-phenylpropionates, which is tricyclohexyltin 2,3-dibromo-3-(*p*-methyl)phenylpropionate (**P5**) also show as a mild antiproliferation action, which is 43.40% or 48.41% of viability.

Table 3.23 The cytotoxicity of selected triorganotin carboxylates against human leukemia HL 60 cells.

Code	Compound	Set 1		Set 2	
		Viability %	**Standard deviation**	**Viability %**	**Standard deviation**
Ref	*Cisplatin*	1.17	1.21	1.19	0.80
C6	tricyclohexyltin cinnamate	3.06	2.24	1.95	1.24
C7	tricyclohexyltin *p*-methylcinnamate	2.58	3.68	1.09	0.80
C8	tricyclohexyltin *p*-methoxycinnamate	4.74	5.01	1.79	0.96
C9	tricyclohexyltin *p*-nitrocinnamate	3.55	4.45	2.69	1.35
C10	tricyclohexyltin *p*-chlorocinnamate	87.04	2.49	81.08	8.89
P4	tricyclohexyltin 2,3-dibromo-3-phenylpropionate	8.37	5.28	2.96	0.99
P5	tricyclohexyltin 2,3-dibromo-3-(*p*-methylphenyl)propionate	43.40	6.28	48.41	5.65
P6	tricyclohexyltin 2-methoxy-3-bromo-3-(*p*-methoxyphenyl) propionate	5.72	8.90	3.81	4.47
C4	tributyltin *p*-nitrocinnamate	3.98	3.02	3.33	2.51
C14	tribenzyltin *p*-nitrocinnamate	1.12	2.31	3.81	3.15

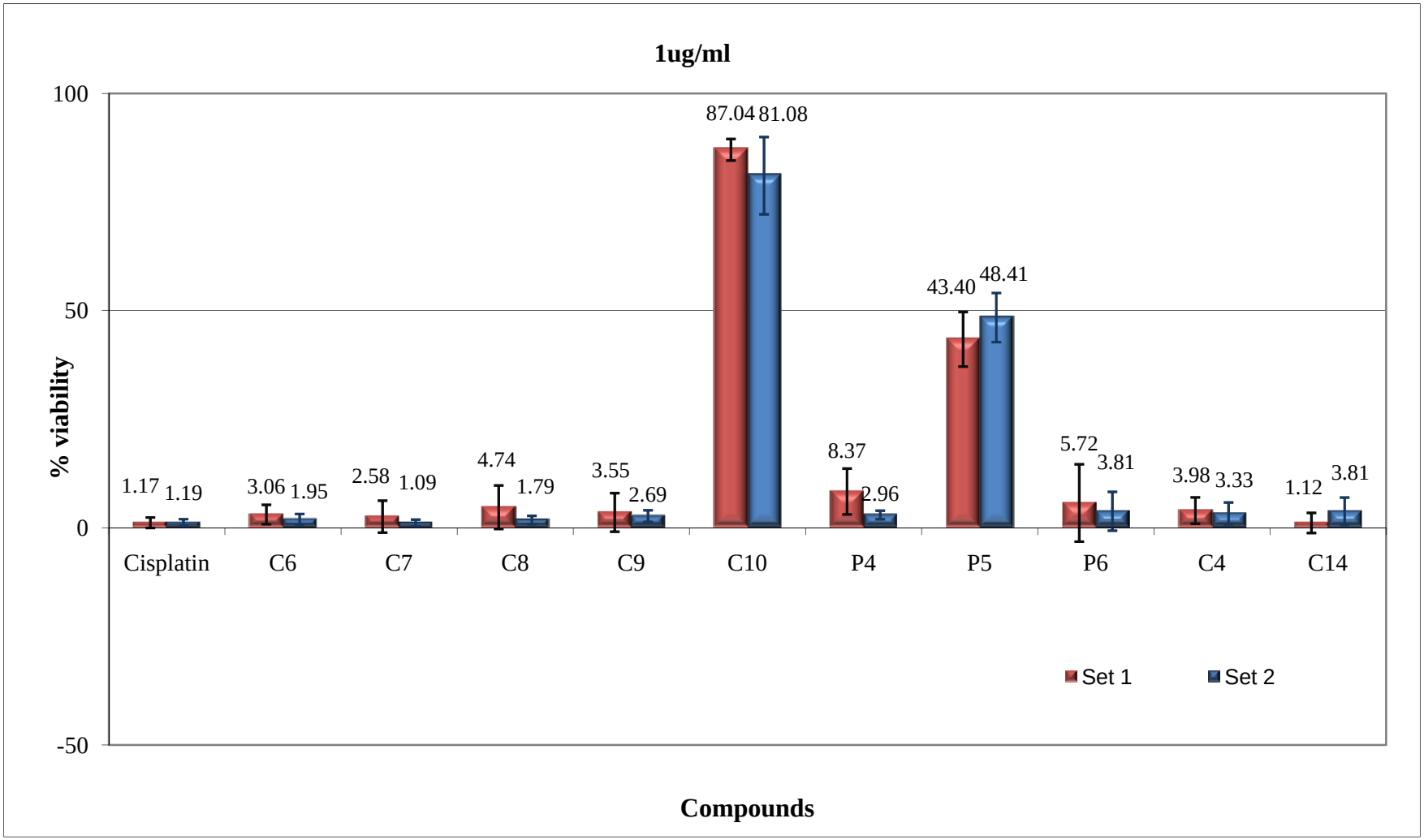

Figure 3.36 The cytotoxicity of selected triorganotin carboxylates against human leukemia HL 60 cells.

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Chapter 4

Conclusion

Chapter 4: Conclusion

The triorganotin carboxylates with the general formula of $R_3SnOCOCH=CHC_6H_5$-Z-*p* where R= Bu, Cyh, Bz; Z = -H, $-CH_3$, $-OCH_3$, $-NO_2$, -Cl were successfully synthesized by reacting triorganotin hydroxide with substituted cinnamic acids. These triorganotin carboxylates were then reacted with brominating agents such as bromine, *N*-(4-dimethylamino)pyridinium tribromide and *N*-bromosuccinimide. In general, the bromination reactions led to the cleavage of the Sn-O bond and the addition of bromide substituent at the C=C bond of the cinnamates. The products isolated are the carboxylic acids with the general formula $HOOCCH(X)CH(Y)C_6H_5$-Z-*p* where X= Br, $-OCH_3$; Y= Br; Z = -H, $-CH_3$, $-OCH_3$. In one case, the ionic compound [*p*-$ClC_6H_5CHBrCHBrCOO]^-$ $[(CH_3)_2NC_5H_4NH]^+$ was obtained. The triorganotin carboxylates and their bromination products were characterized by elemental analysis, infrared, ^1H and ^{13}C nuclear magnetic resonance spectroscopies. The results of the characterization supported the chemical formula proposed in this study. The X-ray structures of five of the compounds namely, bis(4-dimethylaminopyridinium) 2,3-dibromo-3-(*p*-chlorophenyl)propionate bromide, tributyltin *p*-chlorocinnamate, tricyclohexyltin cinnamate**,** tricyclohexyltin 2,3-dibromo-3-phenylpropionate and tribenzyltin *p*-nitrocinnamate were also determined by X-ray crystallography. In addition, ten selected triorganotin carboxylate **C4-C10**, **C14**, **P4-P6** against human leukemia HL60 cells were investigated and compared with *cisplatin*. Generally, the triorganotin carboxylates exhibit strong cytotoxic activities in the preliminary study.