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Synthesis, characterization and biological activities of Tricyclohexyltin (IV) complexes with various oxygen donor Ligands

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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF TRICYCLOHEXYLTIN (IV) COMPLEXES WITH VARIOUS OXYGEN DONOR LIGANDS

By
Lala Rukh
2009-GCUF-3112-320

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the requirements for the degree of

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DECLARATION

The work reported in this thesis was carried out by me under the supervision of **Dr. Saira Shahzadi,** Assistant professor, Department of Chemistry, GC University, Faisalabad, Pakistan.

I hereby declare that the title of thesis **"Synthesis, Characterization and Biological Activities of Tricyclohexyltin(IV) Complexes with Various Oxygen Donor Ligands"** and the content of thesis are the product of my own research and no part has been copied from any published source (except the references, standard mathematical or genetic models / equations / formulas / protocols etc. I further declare that this work has not been submitted for award of any other degree/diploma. The university may take action if the information provided is found inaccurate at any stage.

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To

PROPHET MUHAMMAD (Peace Be Upon Him)

Blessing on whole mankind,

MY LOVING PARENTS

Whom

Prayers, love and guidance lightens my whole life

and are the source of inspiration for me

And

MY FAMLIY

Without whom my life is incomplete

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ACKNOWLEDGEMENTS

All praises to almighty **ALLAH**, The benevolent, who bestowed upon me His blessings and through the mediation of his beloved **Prophet Muhammad** (**Peace Be Upon Him**) enlightened me with abundant resoluteness and perseverance, which enabled me to accomplish this scientific assignment objectively and successfully.

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(Lala Rukh)

ABSTRACT

Tricyclohexyltin(IV) complexes have been synthesized by reacting various oxygen donor ligands with Cy_3SnCl in 1:1/1:2 M/L ratio in anhydrous methanol under reflux conditions. The ligands and synthesized organotin(IV) complexes have been characterized by elemental analysis, FT-IR, ^1H NMR spectroscopy and semi-empirical analysis. FT-IR data explains the bidendate nature of ligands which is also confirmed by semi-empirical study. HOMO-LUMO calculations show that complex **4** is most stable with least chemical reactivity. Computed negative heat of formation shows that all complexes are thermodynamically stable. Organotin(IV) complexes exhibit significant antimicrobial and antifungal activities with few exceptions as compared to free ligands. Immunomodulatory data shows that complexes **1**, **4** and **7** are inactive immunomodulators.

Chapter-1

INTRODUCTION

1.1. Tin

Tin was known to ancient civilizations. Bronze is formed when tin is alloyed with copper which gave its name to the Bronze age. Tin is a silvery-white metal. Tin has highly crystalline structure. It is known as pliable and soft metal. Tin is commonly present in form of ore known as cassiterite. This ore is mainly found in Indonesia, Thailand, Bolivia, Malaya and Nigeria. Tin is obtained commercially when cassiterite is reduced with coal in reverberatory furnance (Abalos *et al.*, 1998). The general physical information about the tin is:

Atomic Number: 50

Relative Atomic Mass (^{12}C=12.000): 118.71

Melting Point/K: 505

Boiling Point/K: 2543

Density/kg m^{-3}: 7310 (293K)

Ground State Electron Configuration: $[Kr]4d^{10}5s^{2}5p^{2}$

Electron Affinity (M-M-)/kJ mol^{-1}: -121

Tin and its salts have many uses. It takes a high polish. To prevent corrosion, tin is mostly used to coat other metals. For example tin-cans actually steel having tin coating on them. Many alloys of tin are known which are important such as pewter, soft solder, bronze and phosphor bronze. Tin salts are also used as mordent as well as reducing agents. Tin(II) chloride is important salt of tin which is used as mordent in many industries. When tin salts are sprayed on the glass then this glass is used as electrically conductive coating. Flat surface of window glass is obtained by floating molten glass on molten tin. Tin alloys are also important as superconductive materials such as tin-nobidium alloy is important superconductive at low temperature (Tagliavini, 1992).

Tin is non-toxic. Tin compounds are also used as biocides such as trialkyl tin and triaryl tin. These compounds should be used with great care. Tin is protected with an oxide film therefore it does not react with oxygen and water. Tin reacst with acids as well as bases.

When tin is heated in air then it forms tin(IV) oxide. This is actually feebly acidic in nature. When tin crystals break then “tin cry” is heard due to breaking of crystals. This phenomenan is observed mostly in breaking of tin bar. Tin has two allotropic forms. When grey tin which has cubic structure is warmed then it changes into white tin which is ordinary form of metal.

1.2. Organotin

Organotin(IV) compounds are those compounds in which there is atleast one covalent C−Sn bond. The compounds contain a tetravalent Sn center and have the general formula R_4SnX_{4-n} (n = 1−4). Depending on the number of organic moieties, organotin complexes are classified as mono-, di-, tri- and tetraorganotin compounds ($RSnX_3$, R_2SnX_2, R_3SnX, R_4Sn), in which R is any alkyl or aryl group and X is an anionic species (halide, oxide, hydroxide, carboxylate, or thiolate) or a group attached to tin through oxygen, sulfur, nitrogen, halogen, etc. The first organotin compound was synthesized by ethyliodide and tin in the form of diethyltin diidodide Et_2SnI_2 (Frankland, 1852).

The reaction is shown as:

$$2EtI + Sn \longrightarrow Et_2SnI_2 \qquad (1.1)$$

Although the carbon tin bond (Sn−C) is weaker than the C−C or Si−C bond. Organotin compounds are mostly used in industry as polymers stabilizers, industrial and agricultural biocides. Thermal decomposition has no significanc under environmental conditions as well as many nucleophilic species (Mazhar, 2001). The physical properties of organotin compounds are affected by both the number of Sn-C bonds as well as the length of the alkyl chains. However, the Sn-C bonds are cleaved by UV radiation, different agents including strong acids, halogens, metal halides and electrophilic agents etc.

$$R_4Sn + Cl_2 \longrightarrow R_3SnCl + RCl \qquad (1.2)$$

$$R_4Sn + SnCl_4 \longrightarrow 2R_2SnCl_2 \qquad (1.3)$$

$$R_4Sn + HCl \longrightarrow R_3SnCl + RH \qquad (1.4)$$

The aryl, allyl or vinyl groups can be cleaved more easily from tin than the alkyl groups and lower alkyl groups are cleaved more readily than the higher alkyl groups. Tin in its compounds frequently shows coordination numbers greater than four, because of the availability of low lying empty $5d^o$ atomic orbitals and large atomic size (Buckton, 1859). Organotin compounds can be synthesized by standard methods of which the following are typical:

From Gignard

$$SnCl_4 + 4RMgCl \longrightarrow R_4Sn + 4MgCl \quad (1.5)$$

R= alkyl

From Organo Aluminium

$$SnCl_4 + 4R_3Al \longrightarrow 3R_4Sn + 4AlCl_3 \quad (1.6)$$

R= alkyl

From Direct method

$$Sn + 2RX \longrightarrow R_2SnX_2 \quad (1.7)$$

R= alkyl

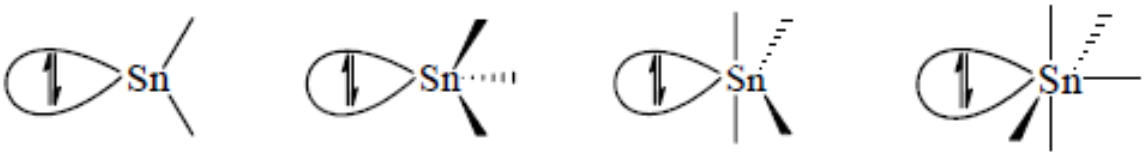
All these routes are used on an industrial scale but the Grignard method (or the equivalent organolithium reagent) is convenient for laboratory scale (Girasolo *et al.*, 2000). Rather less used is the modified Wurtz-type reaction.

$$SnCl_4 + 4RCl \xrightarrow{8Na} R_4Sn + 8NaCl \quad (1.8)$$

The conversion of R_4Sn to the partially halogenated species is readily achieved by scrambling reactions with $SnCl_4$. Reduction of R_4SnX_{4-n} with $LiAlH_4$ affords the corresponding hydrides and hydrostannation (addition of Sn−H) to C=C double bonds and triple bonds is an attractive route to unsymmetric or heterocyclic organotin compounds.

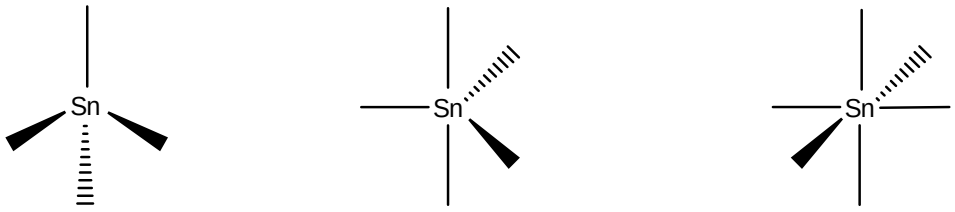
1.3. Principle co-ordination geometries at the tin centre in organotin compounds

Since the empty 5d orbitals of suitable energy may be involved in the hybridization in divalent and tetravalent tin, higher coordination numbers of tin are possible. Reactions of alkyltin chloride with appropriate nucleophiles give the alkyltin, alkoxides, amides, thioalkoxides, carboxylates, etc. (Gyurcsik and Nagy, 2000). The presence of these electronegative groups on tin renders the metal susceptibility for the coordination by Lewis bases, simple tetrahedral coordination is the exception rather than the rule.



Sn(II)

sp^2	sp^3	sp^3d	sp^3d^2
Trigonal Planer	Tetrahedral	Trigonal bipyramidal	Octahedral



Sn(IV)

sp^3	sp^3d	sp^3d^2
Tetrahedral	Trigonal bipyramidal	Octahedral

1.4. Physio-chemical Properties of organotin compounds

Organotin compounds are highly soluble in common organic solvents such as ethers, alcohols and halogenated hydrocarbons. However their solubility in water is of the order of 50 mg/L at ambient temperature. Experimentally determined data expaline that aqueous

solubilities range for Me_2SnCl_2 is 20 mg/L for readily soluble to 1 mg/L for sparingly soluble phenyl, cyclohexyl and octyltin compounds (Blunden *et al.,* 1984).

Tin complexes having lower molecular weight are mostly liquids at room temperature. Different compounds of tin exists in different states such as:

Tetraalkyltin (R_4Sn)

Tetraalkyltin compounds are colourless and liquids at room temperature.

Tetraaryltin (R_4Sn)

Tetraaryltin compounds are solids.

Tetramethyltin $(CH_3)_4Sn$

Tetramethyltin is volatile and toxic.

Tetrabutyltin $(C_4H_9)_4Sn$

Tetrabutyltin compound is colourless oily liquid with distinct odour.

Tetraphenyltin $(C_6H_5)_4Sn$

Tetraphenyltin is white crystalline powder and soluble in organic solvents.

Mostly organotin compounds are colourless and solid at room temperature. Their melting points range is from 97-105 ^oC. Their boiling points range is from 93-250 ^oC.

1.5. Synthesis of organotin compounds

Organotin compounds are prepared by number of methods. Organotin compounds are very important from biological and industrial point of view. Some important methods are given below which illustrate the synthesis of organotin compounds and its derivatives.

1.5.1. Direct synthesis of organotin compounds

The direct synthesis of organotin compounds involve the reaction between the metal and organic halides. The direct synthesis using a Gignard reagent or any other reagent was found more suitable and was regarded as customary methods (Sisdo *et al.,* 1960). The general reaction involving the tin chloride and benzyl is given below:

$$3C_6H_5CH_3Cl + 2Sn \xrightarrow{\text{water}} C_6H_5CH_2SnCl + SnCl_2 \qquad (1.9)$$

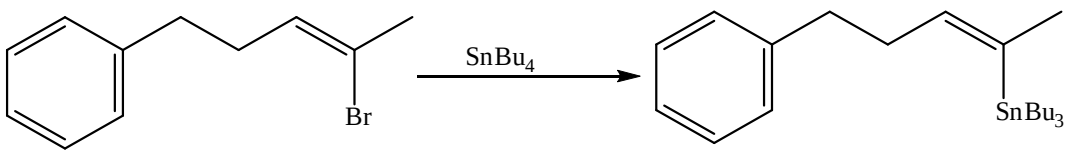
The above reaction takes place in the presence of water. The same reaction can also be take place in the presence of toluene but the products of the water as a solvent will be different from the toluene as:

$$3C_6H_5CH_3Cl + 2Sn \xrightarrow{\text{toulene}} C_6H_5CH_2SnCl_2 \qquad (1.10)$$

From above reaction it can be clearly noticed that the both products are different from one another.

1.5.2. Preparation of organotins from Gignard reagent

Organotin compounds can be synthesized by the reaction of gignard reagent with tin halides, for example tin tetrachlorides (Neumman and Liebigs, 1964). An example is the organic synthesis of tributyl-[5-phenyl-2-pentene-2]stannane. The reaction is given below:



(1.11)

The Wurtz-like coupling of alkyl sodium compounds with tin halides yield tetraorganotin compounds.

1.5.3. Preparation of organotin hydrides

Organotin hydrides can be prepared by the reaction of hydrochloric acid with he tin alloy or by the reduction of stannous salts, electrically. These compounds can also be prepared by the reaction of hydrochloric acid with metallic tin. Perhaps the most practical method involves the reduction of stannic chloride with lithium aluminium hydride under nitrogen containing oxygen at -70 ^{o}C. The presence of oxygen inhibits the decomposition at room temperature (Kuivila, 1964).

Reduction with the lithium aluminium hydride, can be extended to the preparation of a wide range of organotin hydrides and is generally the most convenient laboratory preparation.

$$RSnCl_4 + LiAlH_4 \longrightarrow RSnH_4 + LiAlCl_4 \quad (1.12)$$

Organotin halides are reduced to the corresponding hydrides smoothly and the products is obtained in the given halide form as:

$$RSnX_4 + R_2AlH \longrightarrow RSnH_4 + R_2AlX \quad (1.13)$$

1.5.4. Preparation of organotin carboxylates

The reaction of organotin halides with organic acids in the presence of a suitable base like triethylamine gives the corresponding organotin carboxylate (Lewis *et al.,* 1992).

$$R_3SnCl + RCO_2H + Et_3N \longrightarrow R_3SnOCOR + Et_3NHCl \quad (1.14)$$

The organotin carboxylates can also be prepared by the treatment of carboxylic acids with organotin oxides or hydroxides in boiling toluene or benzene.

$$R_3Sn_2O + 2RCO_2H \xrightarrow[H_2O]{PhMe} 2R_3SnOCOR \quad (1.15)$$

1.5.5. Preparation of organotin esters

Organotin esters can also be prepared by the cleavage of one or more organic groups from tetraorganotin compounds (R_4Sn) by carboxylic acids or mercury(I) or (II) carboxylates. The reaction by cleavage of a Sn−C bond with carboxylic acid occurs more readily when R is a vinyl, allyl or aryl group (Okawara and Yaruda, 1964).

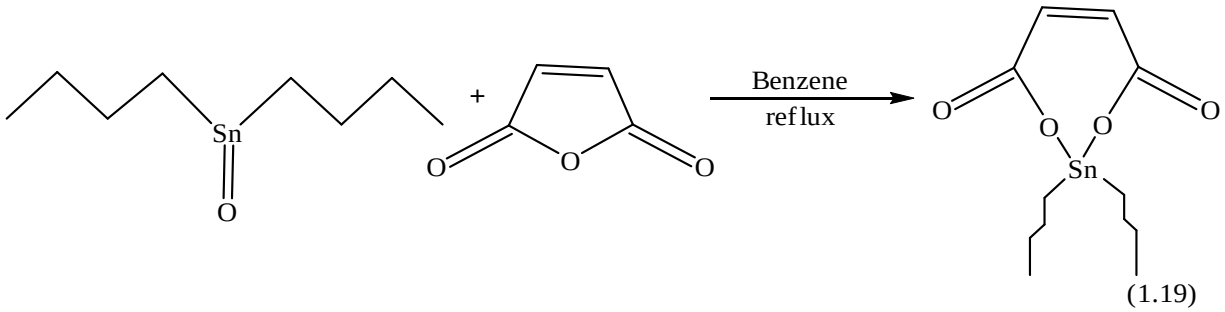
$$R_4Sn + nRCO_2H \longrightarrow R_4SnOCOR + nRH \quad (1.16)$$

$$Ph_4Sn + 2Cl_3CCO_2H \longrightarrow Ph_2SnOCOCCl_3 + 2PhH \quad (1.17)$$

$$2Me_4Sn + Hg_2OCOMe \longrightarrow 2Me_3SnOCOMe + 2Hg + C_2H_6 \quad (1.18)$$

1.5.6. Preparation of organotin monomers from maleic anhydride

Organotin monomers were prepared by the reaction of dibutyl tinoxide with the maleic anhydride or citraconic anhydride (Deyab *et al.*, 2010). The reaction scheme is given below:



(1.19)

1.6. Synthesis of organotin derivatives

It is observed that mostly organotin compounds occur as its derivatives. In these derivatives the organotin compounds are found to be bounded with heteroatoms such as oxygen, sulfur, halogens with tin metal.

1.6.1. Oxygen containing derivatives of organotin compounds

In this group of organotin compounds, the organotin derivatives are oxides, phenoxides, alkoxides, metallo stannoxanes and carboxylates. Organotin oxides are mostly synthesized by alkaline hydrolysis of halides (Pereyre *et al.*, 1987).

$$2(C_4H_9)_3SnCl + NaOH \longrightarrow 2(C_4H_9)_3SnOH + NaCl \longrightarrow 2(C_4H_9)_3SnOSn(C_4H_9)_3 \quad (1.20)$$

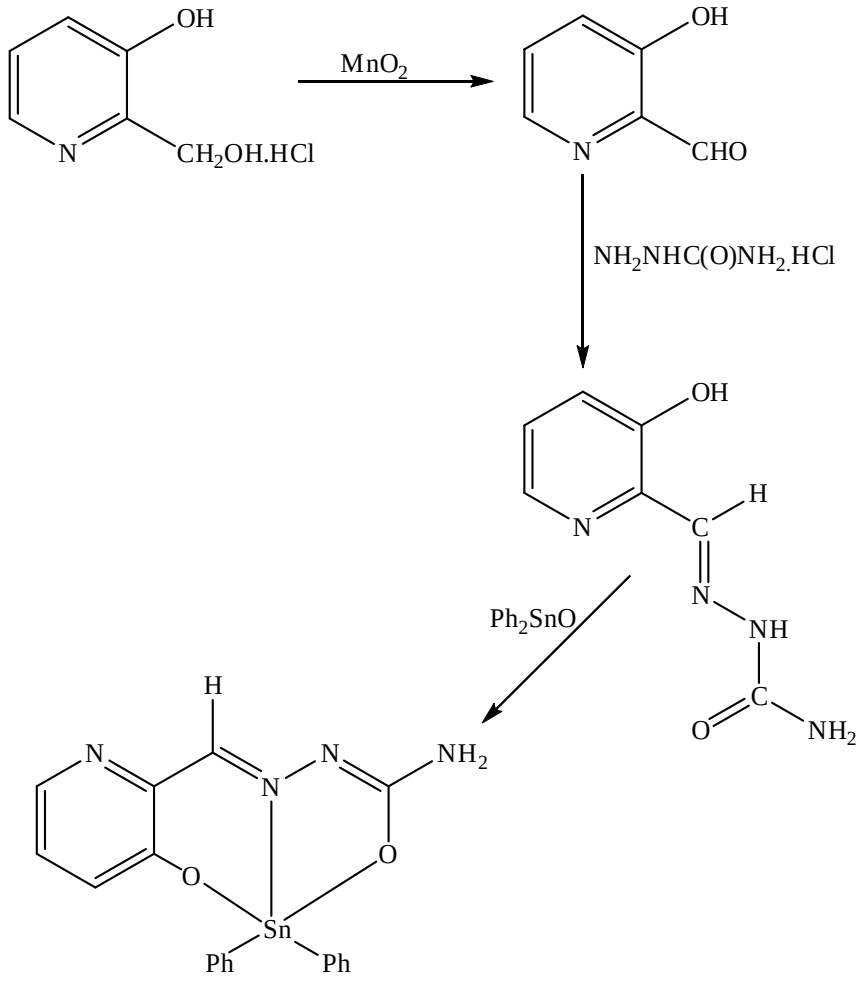
$$(C_4H_9)_2SnCl_2 + NaOH \longrightarrow (C_4H_9)_2SnO + NaCl \quad (1.21)$$

$$(C_4H_9)_3SnCl + NaOH \longrightarrow (C_4H_9)_3SnOOH + NaCl \quad (1.22)$$

$$(C_4H_9)_2SnCl_2 + 2C_7H_{15}COONa \rightleftharpoons (C_4H_9)_2Sn(COOC_7H_{15})_2 + 2NaCl \quad (1.23)$$

1.6.2. Synthesis of organotin compound derived from 3-hydroxy-2-formylpyridine semicarbazone

From 3-hydroxy-2-formylpyridine semicarbazone, the new diphenyltin(IV) compound is synthesized as:



(1.24)

1.6.3. Organotin compounds containing halogen atoms

By the cleavage reaction of hydrogen halides, $SnCl_4$ and halogen with tetraorganotin, the organotin halides can be prepared. Most important organotin compounds are mono-, di- and triorganotin halides.

$$3R_4Sn + SnCl_4 \longrightarrow 4R_3Sn \quad (1.25)$$

$$R_4Sn + SnCl_4 \longrightarrow 2R_2SnCl_2 \quad (1.26)$$

The synthesis of organotin halides by Kocheshkov redistribution reaction involves the reaction between tetraorganotin compounds and tin tetrahalides (Thoonenn *et al.*, 2004).

$$nR_4Sn + (4\text{-}n)SnCl_4 \longrightarrow 4R_nSnCl_{4-n} \qquad (1.27)$$

1.7. Reaction of organotin compounds

Important reactions involving organotin compounds are Stille reaction. This reaction is actually the coupling reaction with sp^2 hybridization organic halides catalyzed by palladium. Generally this reaction can be represented as

$$R{-}X + R^{-}{-}SnR_3^{--} \longrightarrow R{-}R^{-} + XSnR_3^{--} \qquad (1.28)$$

There are many reactions in which organotin compounds are involved. Some of those reactions are given below with their chemical reactions.

1.7.1. Reaction of organotin hydrides

The most important reaction of organotin hydride is the addition of hydrogen into alkene and alkynes. The direction of addition of hydrogen to the double bond has been established in few cases. For example the adduct obtained from styrene, identical to the product of reaction between 2-phenylethylmagnesium bromide and triphenyltin chloride (Kuivila, 1964).

$$(C_6H_5)_3SnH + H_2C{=}CH_2 \longrightarrow (C_6H_5)_3SnCH_2CH_2C_6H_5 \qquad (1.29)$$

$$(C_6H_5)_3SnCl + C_6H_5CH_2CH_2MgBr \longrightarrow (C_6H_5)_3SnCH_2CH_2C_6H_5 \qquad (1.30)$$

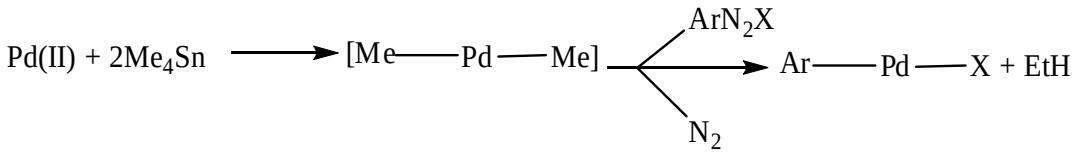
Similarly the adduct obtained from 1-octene is identical with the product of the reaction between triphenyl chloride and 1-octylmagnesium bromide.

1.7.2. Palladium catalyzed organotin reaction

Addition of a palladium catalyst to a solution of ArN_2X and Me_4Sn in acetonitrile afforded a methylarene (ArMe) with gas evolution.

(1.31)

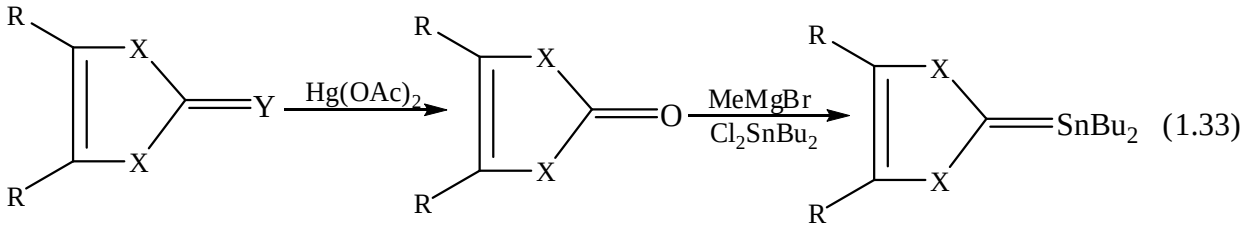
In this procedure the tin is added in the form of tetramethyltin and palladium in the form of palladium acetate (Carraher, 2008). The palladium acetate does not react with ArN_2X. The Pd catalyzed reaction scheme is given below:



(1.32)

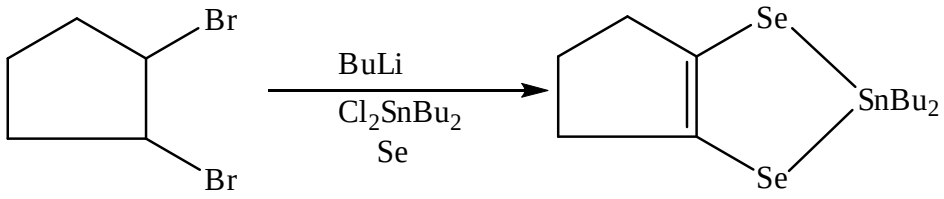
1.7.3. Reaction of organotin with esters

Organotin thiolates and selenolate could be prepared by trapping the corresponding dimagnesium salts with Cl_2SnBu_2. Treatment of thiones and selone with mercuric gives ketones. Two consecutive stepwise reaction was carried out by trapping Cl_2SnBu_2 at -78 ^oC temperature (Yamada *et al.*, 2002). Tin thiolate was used without purification through silica gel. The reaction is represented as:



(1.33)

Different examples showing the reactions between organotin and esters are given:



(1.34)

$$RCOCl + R_4^-Sn \xrightarrow{PhCH_2Pd(pph_3)_2Cl} RCOR^- + R_3^-SnCl \quad (1.35)$$

1.7.4. Reaction of organotin in the synthesis of ketone

Organotin compounds readily undergo a palladium catalyzed coupling with acid chlorides, thereby providing a general and simple method for the preparation of ketones (Seiky and Ishikawa, 1976). The reaction is general both with the respect to organotin compound and the acid chloride.

General representation of the reaction is

$$RCOX + R_4^-Sn \xrightarrow{PhCH_2Pd(pph_3)_2Cl} RCOR^- + R_3^-SnX \quad (1.36)$$

1.7.5. Reaction of organotin with metal-metal bond

Few compounds have been reported containing metal-metal bond. In these reaction the bond between Sn-Sn is cleaved and both the tin are attached to the carbons atoms therefore known as organotin compounds (Okawara and Yaruda, 1964). Inshortly, the bond between the two tin atoms in organotin compounds break forming the two fragments respective to the addition of the reactant.

Example of such type of reactions is:

$$(CH_3)_3Sn\text{—}Sn(CH_3)_3 + CF_3 \longrightarrow (CH_3)_3SnCF_6 + (CH_3)_3SnI \quad (1.37)$$

These types of reactions are actually carried out by the application of UV light on them. UV light causes the breaking of bond between them.

1.8. Applications of organotin compounds

Organotin(IV) compounds show a wide range of industrial, agricultural and biocidal applications. All these applications can be broadly categorized into two groups:

i. Biological Applications

ii. Non-Biological Applications

1.8.1. Biological applications

Organotin(IV) compounds are generally very toxic, even at low concentrations and display strong biological activities. The biological activity is essentially determined by the number and nature of the organic groups bound to the central Sn atom. The trialkyltin(IV) $[R_3Sn(IV)]^+$ and triaryltin(IV) $[Ar_3Sn(IV)]^+$ derivatives exert powerful toxic action on the central nervous system. Some of the important biological applications are given as under:

I. Leishmanicidal agents

An important pharmaceutical application of organotin(IV) complexes is in the chemotherapy of leishmaniasis, a parasitic infection of the skin, where $Oct_2Sn(IV)^{2+}$ maleate has shown promisingly high activity. The $Bu_2Sn(IV)^{2+}$ dilaurate, distearate, diolate, phenylethyl acetate and dipalmitate act as antihelminthic agents in cats suffering from dipulidiosis (Evans *et al.*, 1972).

II. Antilarvicidal agents

Triorganotin(IV) complexes have shown significant larvicidal activities against various species of mosquitoes. Some tributyltin complexes were screened against the fourth larval instar stage of the *Aedes aegypti* mosquito, responsible for the transmission of yellow fever, and were found to be more effective than the triphenyltin derivatives (Crowe, 1987).

III. Antiviral agents

A series of diorganotin compounds, diorganotin dichloride complexes, $R_2SnX_2L_2$, which were modeled after the antitumour agents like cis-platin showed antitumour activities. Since cisplatin has also shown to possess antiviral activity. The antiviral activity of the tin complexes was investigated and it has been found that $R_2SnX_2L_2$ complexes exhibited weak *in vitro* antiviral activity against certain DNA viruses (Gielen and Tiekink, 2005).

IV. Veterinary application

Organotin compounds have been used as anthelminthic agents for poultry as well as for animal husbandry and insecticides for sheep and cattle. Dibutyltin dilaurate is one of the constituents of a commercial product for combating worm infections in poultry and this compound has been used as a commercial formulation in combination with piperazine and phenothiazine (Islam *et al.,* 2008).

V. Dentistry

Tin chemicals are used in dentistry in different ways for solving various dental problems. For example, tin(II) fluoride is used in a number of toothpastes as an anti decaying agent and for a direct application to children's teeth. Tin(II) fluoride is also used in dentifrices (Evans *et al.,* 1972; Hattab, 1989).

VI. Antifouling coatings

Triorganotin compounds have been used in antifouling paints to restrict the attachment of the aquatic organisms such as Salime bacteria, algae or marine animals such as hydroids, crustanceans, mollusks and tunicates. These microorganisms can increase the weight of the drag leading to a greater consumption of fuel (Durr and Thomason, 2008).

VII. Crop protection

A number of triorganotin compounds have been developed as agrochemicals and they are successfully used in specialized applications. As organotin compounds have a low phyotoxicity, they are less harmful to non-targeted organism and they can easily degrade in the environment eventually forming harmless tin residues (Blunden *et al.,* 1985).

VIII. Antitumor activity

The uncontrolled cellular growth, causing cancer, can be prevented by arrested DNA replication. Various organometallic compounds have been used in this regard, however, organotin(IV) complexes exhibit attractive properties like enhanced water solubility, lower general toxicity than platinum drugs, better body clearance, fewer side effects, and no emetogenesis (Nath *et al.,* 2001; Crowe, 1989).

1.8.2. Non-biological applications

Organotin compounds were initially applied as stabilizers of transformer oils and vinyl plastics. The systematic research in the following decades, urged the commercial uses of organotin compounds, which are mainly used now-a-days as heat and light stabilizers in polyvinyl chloride (PVC) processing and as industrial catalysts in a variety of chemical reactions (Hoch, 2001). Some of the most important non-biological applications of organotin compounds are given below:

I. Polymer stabilizers

The organotin compounds are excellent stabilizers for polyvinylchloride (PVC), neoprene and other polymers against degradation by light, oxygen and decomposition during hot fabrication. Organotin compounds may act as suitable stabilizers for chlorinated polyethylenes, vinyl copolymers, silicones and polyamides (Lanigen and Weinberg, 1976).

II. Fire retardants

Both organic and inorganic tin compounds show promise as fire retardants. Polystyrene, cellulose acetate and polymethyl methacrylate in the presence of halogen is necessary to promote the degree of flame retardance. Anhydrous tin(IV) oxide produces improved flame retardance in unsaturated polyester thermostates when halogens are present (Vanderkerk, 1978).

III. Catalysts

Several tin compounds are used as homogeneous catalysts in the plastic industry. Stannous octoate is used in flexible polyurethane foams and di-*n*-butyltin dilaurate is employed in specialized ‘high resilience’ flexible foams and also in certain rigid foams, elastomers and coatings (Tagliavini, 1992). Friedel Crafts alkylation and acylation and liquid-phase hydrogenation, dehydrogenation and isomerization Organotin halides of the general formula R_4SnX_{4-n} have been used as catalytic precursors for dehydration processes (Davies, 1982).

IV. Water repellents

Water repellent properties have been exhibited by certain monoalkyltin compounds and these have been tested on building materials (limestone) bricks and concrete and on cellulosic substrates such as cotton, paper and wood. Octyltin trilaurate has been shown to impart water

repellency to limestone comparable to that shown by a commercial silicon treatment (Hobbs and Smith, 1982).

V. Natural fiber treatment

Tin(II) chloride, ammonium hydrogen fluoride isopropanol and polishing agents are used to protect the sheepskin wool in the spray treatment process. K_2ZrF_6, tin(II) chloride and hydrochloric acid have been used for protection purposes in an immersion treatment process (Fuller, 2003).

VI. Glass melting

Tin(IV) oxide electrodes are used in the manufacture of lead containing crystal glass by electric melting. As the glass melts, they do not become electrically conductive until the temperature rises above 800 ^oC (Poller and Mufti, 1967).

VII. Precursors for forming SnO_2 films on glass

Thin coating of tin(IV) oxide on glass are used to strengthen glassware and returnable bottles and jars. Tin(IV) oxide coating also assists in the adherence of organic lubricant films which improve the scuff resistance of the glassware (Davies, 2008).

VIII. Electroplating

The most commonly used compounds in electroplating are tin(IV) sulfate, tin(II) chloride, tin(II) fluoroborates and sodium/potassium stannates. These are used to produce a range of deposits containing tin, generally on a metallic surface. Similar other coatings, which are normally used in tin-alloy plating, are tin-nickel, tin-zinc, tin-copper, tin-cadmium and tin-cobalt (Evans, 1978).

New and safe organotin(IV) complexes with reduced toxicity have been synthesized with various oxygen donor ligands which are highly effective even at very low concentration and cheaper with fewer side effects. Organotin(IV) complexes have been prepared which are more biological active as compared to their free ligands.

Chapter-2

REVIEW OF LITERATURE

Ronconi *et al.* (2002) described the synthesis and characterization of noval organotins(IV) with *N*-methylglycine. All these derivatives are supposed to be forming ring structures which are stable. As single crystal was not obtained. Many techniques were used to describe the structure of the compounds. The compounds were also analyzed by ($^{1}H/^{119}Sn$) NMR, FT-IR and Sn-Mossbauer spectroscopy and thermogravimetery. Finally, the synthesized complexes were tested for their *in vivo* cyotoxic activity against human adenocarcinoma Hella cells. In some cases it shows strong activity even at low concentration.

Tarassoli *et al.* (2002) prepared the dithiocarboxylato compounds of tin by reacting dibenzyl tin dichloride with 2-N-ethylamino-1-cyclopentene-1-carbodithioic acid. Reaction of benzylamine with 2-amino-1-cyclopentene-1-carbodithioic acid gave 2-N-benzylamino-1-cyclopentene-1-carbodithioic acid. This acid further reacts with di- or tribenzyl tin chlorides to yield desired products. The synthesized complexes were studied by IR and NMR (^{1}H, ^{13}C and ^{119}Sn) spectroscopic techniques. Elemental analysis was also done. The crystal structure of three compounds were also obtained. It was noticed that in all complexes the tin was bounded asymmetrically to the dithiocarboxylato ligand. This bonding occurred due to two sulfur atoms. By observing NH…S bond the orientation of ligand was studied.

Ma *et al.* (2003) synthesized diphenyltin marocycles compounds which were actually 18-memberd stereoregular compounds. These compounds were prepared by the reaction of 2-mercaptonicotinic acid with diphenyltin dichloride. Three compounds were characterized by IR, NMR and elemental analysis. Two complexes were also observed by crystallography. The single crystal diffraction data of these two compounds explained that both compounds were highly symmetrical tri-nuclear cyclic complexes. Cis-trigonal bipyramid environment of tin was distorted. Between tin and oxygen, weak interaction was observed.

Pruchnik *et al.* (2003) explained the properties of butyltin complexes $[Sn(C_4H_{9-n})_3\{OOCC_6H_3(NH_2)_{2-3,4}\}]_n$, $[Sn(C_4H_{9-n})_3\{OOCC_6H_3(NH_2)_{2-3,5}\}]$, $[Sn(C_4H_{9-n})_3\{OOCC_6H_4N\text{-}NC_6H_4N(CH_3)_{2-4}\}]$ and $[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_{2-3,5}\}]_n$. The compounds were characterized by ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy. The results show that complexes in

chloroform have distorted tetrahedral geometery but in the strong co-ordinating solvents show the trigonalbipyramidal geometry. One compound is also studied by X-ray crystallography. This complex exhibit trigonal bipyramidal geometery having carboxylato ligand in bridging manner. Ligand bounded with tin atoms in axial positions. These compounds showed better cytostatic activity.

Benetollo *et al.* (2004) synthesized new sodium bis (2-pyridylthio)acetate ligand by using 2-mercaptopyridine, dibromoacetic acid and NaOH in ethanol solution. By the reaction between $SnCl_{4-n}$ acceptors and $Na[(pyS)_2CHCO_2]$, the new mono- and diorganotin derivatives have been synthesized. These derivatives have contained the anionic bis(2-pyridylthio)acetate. Mostly mononuclear complexes have been obtained. These complexes have been analyzed by elemental analysis, IR, NMR data and single crystal X-ray crystallography. Existance of hydrolysed species have been confirmed by E.I.MS spectra of compound containing methanol solvent. The dimeric dicarboxylatotetramethyldistannoxane product was obtained by using acetonitrile solution. Obtained product was characterized by single crystal diffraction analysis.

Li *et al.* (2004) synthesized three diorganotin(IV) complexes of 4-X-benzohydroxamic acid [X = NH_2 (HL_1), NO_2 (HL_2) or F (HL_3)] denoted as $[R_2SnL_2]$ and $[R_2Sn(L)]_2O$ (R = Me, Et, *n*-Bu or Ph). These complexes have been analyzed by elemental analysis, FT-IR, ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopic techniques and FAB-MS. These complexes have also been confirmed by their melting points. Results show the stability of complexes in air. Antitumor activity of these complexes against human cells was also checked. By increasing chain length of carbon in alkyl ligands, the activity of synthesized complexes increases. There is no recognition of structure- activity of these compounds.

Mishra *et al.* (2005) synthesized some organotin complexes with salicylaldehyde and hydrazone. Many techniques were used to study the characterization of complexes which involved elemental analysis, IR, NMR and UV-vis spectroscopy. The ligand and metal have reacted in 1:1 molar ratio. The ligand acts as a bidendate ligand and complexes showed the antibacterial activity against different bacteria.

Szorcsik *et al.* (2005) synthesized twenty two new compounds by metathetical reactions having ligands containing –OH, (-C=O) group and an aromatic nitrogen donor atom. On the

basis of FT-IR and Mossbauer spectroscopy, the molecular structures were assigned to these complexes. FT-IR spectroscopy data of complex has confirmed the binding sites of ligand. It was observed that in complexation mostly the phenolic side of ligand is used for attachment. Trigonal bipyramidal and octahedral geometries of complexes were confirmed by ^{119}Sn NMR spectroscopy. X-ray diffraction analysis was also done.

Pellei *et al.* (2006) synthesized new organotin complexes of neutral bis(2-pyridylthio)methane ligand with SnR_nCl_{4-n} (R = Cy, Ph, Bu and Me n = 1-3) acceptors containing mono-, di- and triorganotin derivatives. Products were mono-nuclear and analyzed by elemental analysis, FT-IR, E.I.MS, multinuclear NMR (^{1}H, ^{13}C and ^{119}Sn). The complete and appropriate dissociation of complexes in solution was confirmed by ^{1}H and ^{119}Sn NMR. The greatest stability of mono and diorganotin(IV) complexes was observed in solution state. The spectroscopic data of mono and diorganotin(IV) derivatives reveals with the six coordinated geometery of these derivatives.

Rehman *et al.* (2006) prepared some noval organotin compounds by reacting organotin(IV) chlorides with monomethyl phthalate. Tin is supposed to be bounded with the ligand molecules through the carbon oxygen bond. Many analytical techniques have been employed to these compounds such as elemental analysis, molar conductance and the structures of these complexes have been discussed by IR, (^{1}H, ^{13}C, ^{119}Sn) NMR and ^{119m}Sn Mossbauer spectroscopy.

Hussain *et al.* (2007) introduced a series of some diorganotin(IV) and triorganotin(IV) complexes. These complexes have been synthesized by reaction with monoisopropyl and monomethyl maleate with tin. Then these synthesized complexes were characterized by different spectroscopic techniques such as IR, ^{1}H, ^{13}C, ^{119}Sn-NMR, UV and mass spectroscopy. Results of spectroscopic study explain bidendate action of carboxylate ligand in diorganotin(IV). This ligad acts as monodendate ligand in triorganotin(IV) compounds. Biological evaluation against various microorganisms reveals that that the reactivity of triorganotin are slightly higher than that of diorganotin compounds.

Shankar *et al.* (2007) synthesized various stable ligand containing dibutyl alkanesulfonates. The dibutyl alkanesulfonates reacted with acetylacetone or 4-methoxy-2-quinoline carboxylic acid. Both reacted having equal number of moles in acetonitril solvent under normal

temperature pressure conditions. Distorted octahedral geometery around the tin atoms was observed. Crystal structure of three complexes confirms the bridging bidendate mode of attachment with tin atoms. The great covalent character was observed in bonding between tin atoms and alkanesulfonates.

Nath *et al.* (2008) synthesized new di- and triorganotin derivatives of tyrosinylphenylalanine. FT-IR, multinuclear NMR (^{1}H, ^{13}C and ^{119}Sn) spectroscopy studies were used to explain the coordination and bonding mode in these derivatives. The action behavior of dipeptide bond as dianionic bond was confirmed through above spectroscopy technique. Distorted trigonal-pyramidal geometery of tin was observed having monodendate ligand. This distorted geometry was further confirmed by X-ray crystallography.

Xanthopoulou *et al.* (2008) synthesized new organotin(IV) compounds with heterocyclic thioamides 2-mercapto-benzothiazole (Hmbzt), 5-chloro-2-mercapto-benzothiazole (Hcmbzt) and 2-mercapto-benzoxazole (Hmbzo) of formulae $[(Ph)_3Sn(mbzt)]$ (1), $[(Ph)_3Sn(cmbzt)]$ (3) and $[(Ph)_2Sn(cmbzt)_2]$ (4), together with the already prepared $[(Ph)_3Sn(mbzo)]$ (2), $[(n\text{-}Bu)_2Sn(cmbzt)_2]$ (5) and $[(Me)_2Sn(cmbzt)_2]$ (6) were utilized to investigate their effect on peroxidation of oleic acid. Compounds 3 and 6 showed that the reactive radicals are responsible for the chain radical oxidation of substrate. The compound 1 showed the peroxidation by having a catalyst. This was also studied and then compared to the cis-platin. Then these all compounds were tested against the antitumor activity against various cells.

Affan *et al.* (2009) studied the reaction of thiophene-2-carboxaldehyde benzhydrazone ligand base organotin(IV) chloride. The organotin(IV) complexes were studied by using many techniques such as elemental analysis, UV-vis, FT-IR, ^{1}H, ^{13}C NMR and molar conductivity. Diphenyltin(IV) complex was only characterized by X-ray crystallography. Organotin complexes were also checked for antibacterial activities using five types of bacteria.

Zia-ur-Rehman *et al.* (2009) synthesized diphenyltin(IV) derivative and two chlorodiorganotin(IV) compounds. Spectroscopy study was done to these complexes which include FT-IR, multinuclear NMR, Raman, elemental analysis and mass spectroscopy. Tin atom, in both solid and solution state was assigned to have five and six coordinated geometry. This statement was confirmed by spectroscopy measurements. Cyclic voltametry technique was used to explain the thermodynamic, electrochemical and kinetic behavior of

complexes. Cyclic volametery data showed that these complexes were diffusion controlled. Charge transfer coefficients were determined by the application of Kochi equation.

Deyab *et al.* (2010) explained the synthesis of organotin monomers which contains the dibutyltin moieties and citraconate as a monomer. Free radical copolymerizations of organotin monomers was also carried out between styrene (ST) and butyl acrylate (BA). The total conversion was kept low (≤15% wt/wt) for all synthesized complexes and the copolymers composition was studied by tin determination using the Gillman and Rosenberg method. Fineman-Ross (FR) method was utilized to study the reactivity ratios which was calculated from the copolymer composition. The new formed monomers were characterized by elemental analysis, (^{1}H, ^{13}C) NMR and FTIR spectroscopy.

Muhammad *et al.* (2010) synthesized organotin monomers containing titaconate and monoethyl tributyltin fumarate. Styrene was used to copolymerize these organotin monomers. Methyl methacrylate was also used to copolymerize the organotin monomers which involves the free radical mechanism. Through tin analysis the overall copolymer composition was determined. Many spectroscopic techniques were used to to characterized and discuss these synthesized polymers. These techniques involve FT-IR, NMR and mass spectroscopy.

Affan *et al.* (2011) explained the synthesis of three new organotin(IV) compounds by the reaction between 2-benzoylpyridine-*N*(4)-cyclohexylthiosemicarbazone [HBPCT, (**1**)] ligand and organotin(IV) chloride. The general representation of the new three complexes are [(CH_3)$SnCl_2$(BPCT)] (**2**), [(C_6H_5)$SnCl_2$(BPCT)] (**3**) and [(C_6H_5)$_2$SnCl(BPCT)] (**4**). The new formed compounds have been analyzed by CHN analysis, molar conductivity, UV-vis, FT-IR and ^{1}H NMR spectroscopic techniques. The complex 3 is subjected toward the single crystal X-ray diffraction. Results showed that this complex is six coordinated and posses strongly a distorted octahedral geometry. The crystal system of [(C_6H_5)$SnCl_2$(BPCT)] (**3**) is orthorhombic with space group *P*2*ac*2*n* and the unit cell dimensions: a = 28.1363(5) Å, b = 9.5970(2) Å, c = 9.4353(2) Å.

Zhu *et al.* (2011) synthesized four new organotin(IV) complexes. The complexes were then analyzed by elemental analysis, IR, (^{1}H and ^{13}C) NMR spectroscopy. X-ray single crystal diffraction study was also carried out for some complexes. Trigonal bipyramid geometry of

tin in all complexes having 5 coordinted attachment was confirmed by structural analysis. In methanol solution, one electron oxidation reversible reaction of complexes was also studied. The complexes have also been screened for their antitumor activities. Complexes 3 and 4 have showed greatest activity against Hella cells due to the presence of neutral 1,10-phenanthroline which was absent in complex 1 and 2 which showed lower activity against cancer cells .

Affan *et al.* (2012) synthesized the few organotin complexes with formula [AScCl(dact)] where A= Me, Bu, Ph. Organotin(IV) complexes were characterized by many techniques such as CHN analysis, NMR, mass, IR, FT-IR and UV-vis spectroscopy. Complexes were also characterized by X-ray diffraction. Cytotoxicity of these complexes was also studied. Antimicrobial study suggested that these complexes are better antimicrobial agents than that of free radicals.

Dehghan and Khoshkam (2012) synthesized complexes by the reaction of quercetin and stannous chloride. The complexation was observed by different spectroscopic techniques such as elemental analysis, FT-IR, NMR and mass spectrometery. The chelate formation between tin atom and quercetin was confirmed by spectroscopy measurements. In these complexes 3-hydroxy-4-carbonyl and catechol both provide chletaion sites. It was observed that after chelation of tin atom the scavenging activity of tin atom was decreased.

Wang *et al.* (2013) synthesized six new tin complexes. These complexes have been synthesized by the reaction of organotin oxide or organotinchloride with 3,5,6-trichlorosalicylic acid. Various spectroscopy techniques were used to study these complexes such as FT-IR, multinuclear NMR. These complexes were also characterized by their elemental analysis. Two complexes were also characterized by single crystal X-ray crystallography. X-ray structure of complex 1 showed that it has cage like structure having two triphenyl nuclei, 10 monophenyl nuclei and two inorganic tin nuclei. Complex 3 showed infinite chain like structure and complex 6 showed typical complex ladder like structure.

Chapter-3

MATERIALS AND METHODS

3.1. Chemicals and Instrumentation

Acetylenedicarboxylic acid, 5-Aminoisophthalic acid, Imminodiacetic acid monohydrate, Isonepecotic acid, *l*-Lysin monohydrate and 4-Aminophenylacetic acid were purchased from Merck (Germany). Sarcosine and tricyclohexyltinchloride were purchased from Sigma Aldrich (USA). Methanol, Acetone, Ethanol and DMSO were purchased from Sigma Aldrich (USA). Chloroform, *n*-Hexane and petroleum ether were purchased from Merck (USA). Nutrient agar, Nutrient broth and Potato dextrose agar were purchased from Oxoid Company (UK). All reagents and solvents were purchased commercially and used without any further purification. Solvents were dried by standard procedure (Armarego and Chai, 2003).

Infrared spectra were recorded using Perkin–Elmer 1000 FT-IR spectrophotometer as KBr discs in the range of 4000-400 cm^{-1}. The percentage composition of elements (CHN) were determined by using CHNS-932 elemental analyzer, Leco corporation (USA). NMR spectra were recorded on a Bruker ARX 300 MHz FT-NMR spectrometer using deuterated $CDCl_3$ as internal reference. The melting points of samples were determined by taking them in the capillary tubes with the help of electrothermal melting point apparatus, model staurt (SMP3 USA).

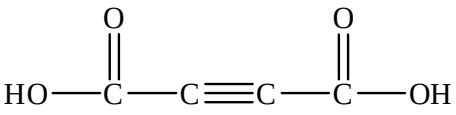
The antimicrobial activities of the ligand and organotin(IV) complexes were observed in an incubator (Sanyo, Germany), laminar air flow (Dalton, Japan) and sterilized in an autoclave (Omron, Japan). The Luminometer used in oxidative burst assay was Luminoskan EL, RT, RS (Helsinki, Finland). The semi-empirical calculations were done by MOPAC 2007 (Stewart, 2007) program in gas phase using the PM3 method (Stewart, 2007).

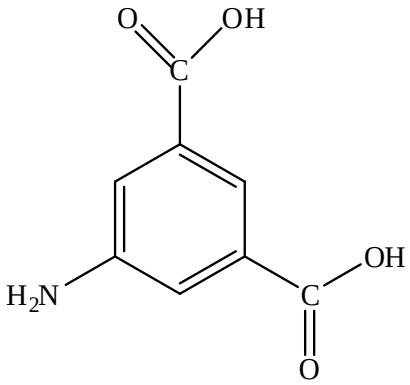
3.2. General procedure for the synthesis of organotin(IV) complexes

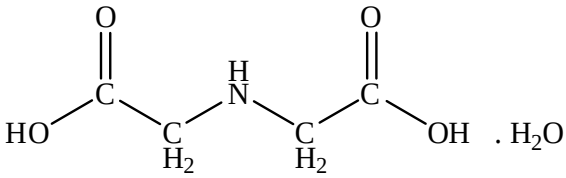
The ligands $\mathbf{L^{1\text{-}7}}$ (1 mmol) was dissolved in a methanol (70 mL) in a round bottom flask (250 mL) with continuous stirring at room temperature. Then tricyclohexyltinchloride (1 mmol)/(2 mmol) was added as solid in portions to above solution. The reaction mixture was refluxed with continous sitirring for 4-6 hours. Solvent was evaporated through rotary evaporator

under reduced pressure. Solid product obtained, was dried in air and recrystallized in methanol: pet. ether mixture.

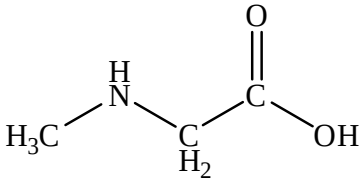
$$H_2L^{1\text{-}3} + 2Cy_3SnCl \xrightarrow{\text{Reflux}} (Cy_3Sn)_2L^{1\text{-}3}$$

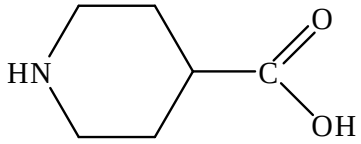
$L^1 =$ 

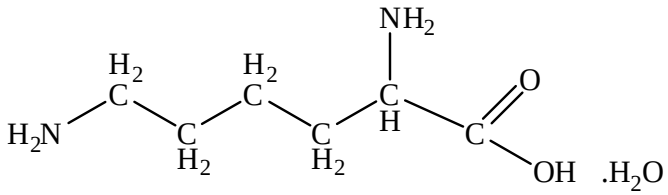
$L^2 =$ 

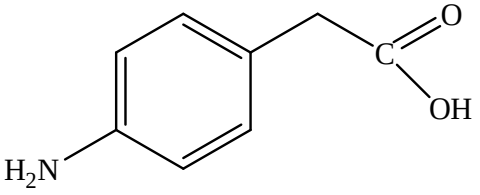
$L^3 =$  $. H_2O$

$$HL^{4\text{-}7} + Cy_3SnCl \xrightarrow{\text{Reflux}} Cy_3SnL^{4\text{-}7}$$

$L^4 =$ 

L^5 = 

L^6 = 

L^7 = 

3.3. Antimicrobial Activities of ligands and complexes

3.3.1. Antibacterial activity

The synthesized complexes were screened for their *in vitro* antibacterial activity against four bacterial strains such as *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pasturella multocida* by measuring inhibition zones using disc diffusion method (CLSI, 2007).

I. Nutrient agar (2.8%)

Nutrient agar 2.8 g was dissolved in a small amount of distilled water and then volume of the solution was made up to 100 mL by adding water. The prepared nutrient agar medium was autoclaved for 15 min at 121 ^{0}C. This medium was used to culture the bacterial strains.

II. Bacterial growth medium, culture and inoculums preparation

Pure cultures were maintained on nutrient agar medium in petri plates. For the inoculum preparations, 13 g/L of nutrient broth was suspended in distilled water, mixed well and

autoclaved. 10 µL of pure culture of a bacterial strain was mixed in medium and placed in shaker for 24 h at 27 ºC. The inocula were stored at 0 ºC in refrigerator.

III. Disc diffusion method

Nutrient agar, 28 g/L was suspended in distilled water, mixed well and distributed homogenously. The medium was sterilized by autoclaving at 121 ºC for 15 min. Before the medium was transferred to petri plates; inoculums (100 µL/100 mL) were added to the medium and poured in sterilized petri plates. After this, small filter paper discs were laid flat on growth medium containing 100 µL of sample. The recommended concentration 100 µL of the test sample (2 mg/mL in DMSO) was introduced into the respective wells. The petri plates were then incubated at 37 ºC for 24 hrs, for the growth of bacteria. The complexes having antibacterial activity inhibited the bacterial growth and clear zones were formed. The zones of inhibition were measured in millimeters using zone reader (Huang *et al*., 2001).

3.3.2. Antifungal activity

The synthesized complexes were screened for their *in vitro* antifungal activity against four fungal strains such as *A. flavis, A. niger, A. alternata and H. myedis* using disc diffusion method (CLSI, 2007). Pure culture of the fungi was maintained on potato dextrose agar (PDA) medium in petri plates that were presterilized in hot air oven at 100 ºC for 3 hours.

I. Nutrient broth (1.3%)

Nutrient broth (1.3 g) was dissolved in 25 ml of distilled water and made the volume upto 100 ml. The prepared nutrient medium was autoclaved for 15 min at 121 ^{0}C. This medium was used to culture the fungus.

II. Potato dextrose agar (3.9%)

Potato dextrose was dissolved in 25 ml of distilled water and made the volume up to 100 ml. The prepared medium was autoclaved for 15 min at 121 ^{0}C. This medium was used for activity of fungal strains.

III. Growth medium, culture and inoculums preparation

The fungus was cultured on potato dextrose agar medium in petri plates. These culture plates were incubated at 28 ºC for 2 days for the multiplication of fungal strains. The prepared

sterilized growth medium was transferred to the sterilized petri plates. The petri plates were then incubated at 28 ºC for 48 h, for the growth of fungus (Sarker *et al.,* 2007).

IV. Disc diffusion method

Small filter paper discs were laid flat on growth medium having fungal growth and 100 µL of sample was applied on each disc. The petri plates were again incubated. The sample having antifungal activity exhibited clear zones around the discs. The zones of inhibition were measured in mm against reference fluconazol using zone reader (Huynh *et al.,* 2001).

3.4. Semi-empirical Analysis

The semiempirical studies were done by MOPAC 2007 (Stewart, 2007) program in gas phase using PM3 method (Stewart, 2007). Selected parts of the complexes not containing the metal ion were preoptimised using molecular mechanics methods. Several cycles of energy minimization had to be carried for each of the molecules. Geometry was optimized using Eigen Vector following. The Root Mean Square Gradient for molecules was all less than one. Self Consistent Field was achieved in each case. Absences of imaginary frequencies were checked consistently.

3.5. Immunomodulatory activity (oxidative burst study)

Immunomodulatory activity was checked by Luminal enhanced chemiluminescence assay (Helfand *et al.*,1982; Halker *et al*., 2001). Precisely, 25 µL of serially diluted compounds with concentration ranges between 1-100 mg/mL was incubated with 25 µL diluted whole blood in 1:50 dilution in sterile $HBSS^{++}$ ($HBSS^{++}$ = Hank's balanced salt solution with Ca^{+2} and Mg^{+2} ions). These tests were carried out in white 96-well plates which were incubated at 37 ^{o}C for 30 minutes in the thermostated chamber of the luminometer. $HBSS^{++}$ and cells without compounds were used as negative and positive control, respectively. After 15 minutes of incubation of whole blood Opsonized zymosan-A, 25 µL, followed by 25 µL luminol (7×10^{-5} M) along with $HBSS^{++}$ was added to each well to get a volume of 100 mL of each well. The total ROS level was recorded as total light produced and recorded during the 50 minutes scan. The luminometer results were monitored as chemiluminescence relative high unit (RLU) with peak and total integral values set for 50 minutes repeated scans at 30 s

intervals and 1 s points measuring time. The percentage of inhibition was calculated by the following formula:

% Inhibition = 100 - (RLU of test sample/RLU of the control) × 100

3.6. Statistical Analysis

The collected data was presented in tabular form along with their mean and standard error. Where appropriate, the data were tested by one-way ANOVA using Minitab 13. Pearson correlation coefficients and *p*-values were used to show correlation and their significance. Differences of p were considered significant (Steel *et al.*, 1997).

Immunomodulatory avtivity results were processed by using SoftMax Pro 4.8 software (Molecular Devices, CA, USA) and then by MS Excel. Results were presented as means ± standard error mean from triplicate (n = 3) observation. IC_{50} values were determined by using EZ-FIT, Enzyme kinetics software by Perrella Scientific, Inc. USA.

Chapter-4

RESULTS AND DISCUSSION

All synthesized organotin(IV) complexes are solid and stable in air. They have sharp melting points and are soluble in common organic solvents. Elemental analysis (C, H and N) data of parent acids and synthesized complexes shows good agreement between the calculated and found values. Physical data of ligands and synthesized organotin(IV) complexes is given in Table 4.1.

4.1. Infrared Spectroscopy

Infrared spectroscopy is one of the most frequent employed technique used for the characterization of organotin(IV) compounds (Jamil *et al.,* 2009). Infrared spectra of ligands **L^1-L^7** and complexes **1-7** were recorded as KBr discs in the range of 4000-400 cm^{-1} in order to confirm the complexation.

The absence of υ(OH) vibration in organotin complexes **1-7**, in range of 3520-3580 cm^{-1} indicates the deprotonation of carboxylic acid group and consequent co-ordination of carboylate group with the tin metal (Hussain *et al.,* 2007).

The nature of coordination of carboxyl group is decided on the basis of ($\Delta\upsilon$) value, which is separation value of υ_{asym}(COO) and υ_{sym}(COO) peaks (Hussain *et al.,* 2012).

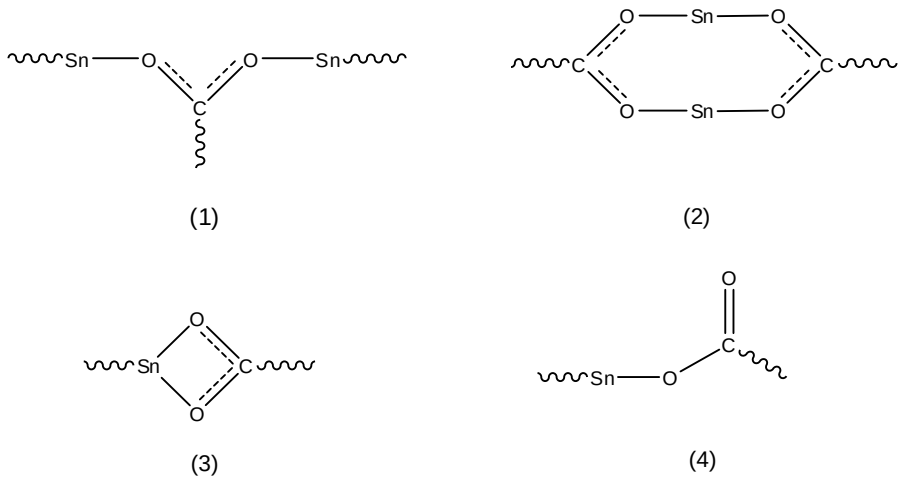


Fig. 4.1: Different modes of attachment between tin and oxygen

It was observed that complexes where difference of (Δυ) is less than 350 cm^{-1} and greater than 200 cm^{-1} exhibit five coordinated polymeric structure. However when (Δυ) is less than 200 cm^{-1}, the carboxylate group in such complexes can be consider to be practically by bidendate indicating chelation (Khan *et al.,* 2006) (Fig. 4.1).

The value of (Δυ) for all synthesized organotin(IV) complexes **1-7** was found to be less than 200 cm^{-1} which confirms bidendate nature of carboxylate group. The synthesized complexes **2, 6** and **7** exhibit strong to weak absorption bands in region of 3410-3455 cm^{-1} due to $\upsilon(NH_2)$ stretching vibrations (Pruchnik *et al.,* 2003; Chauhan and Shaik, 2005).

The υ(NH) band was observed in range of 3339-3368 cm^{-1} and 3335-3360 cm^{-1} in ligands $\mathbf{L^3}$-$\mathbf{L^5}$ and complexes **3-5**, respectively. The absence of large systematic shifts of υ(NH) band in spectra of complexes indicates that there is no interaction between -NH group and metal ion as oxygen atom is more electronegative than nitrogen so, electron density of Sn(IV) moves toward oxygen than nitrogen (Demertzi *et al.,* 2005; Shahzadi *et al.,* 2010).

Moreover the complexation was further confirmed by the presence of υ(Sn-C) and υ(Sn-O) bands in range of 585-525 cm^{-1} and 441-418 cm^{-1}, respectively (Rehman *et al.,* 2005; Singh *et al.,* 2008). The IR spectra of synthesized organotin(IV) complexes **1-7** are given in Figures 4.2-4.5.

4.2. ^{1}H NMR Spectroscopy

^{1}H NMR spectra of the ligands $\mathbf{L^1}$, $\mathbf{L^4}$, $\mathbf{L^7}$ and complexes **1**, **4**, **7** were recorded in deuterated DMSO to find the behaviour of magnetically nonequivalent protons. The data is given in Table 4.3.

The disappearance of -OH signal at 10.2, 12.1, 12.2 ppm in complexes **1**, **4** and **7**, respectively confirm the replacement of carboxylic proton by organotin(IV) moiety (Jabeen *et al.,* 2012). All protons present in synthesized complexes have been identified in position and numbered with protons calculated from incremental method (Kalinowski *et al.,*1984).

The -NH group in the spectrum of ligand $\mathbf{L^4}$ appeared at 2.08 as singlet which does not show any shift upon complexation. It confirms that –NH group does not participate in bonding with tin(IV) (Xanthopoulo *et al.,* 2003; Shahzadi *et al.,* 2010).

For ligand $\mathbf{L}^7$ the appearance of signals in the region of 6.48-6.90 ppm as doublet are ascribed to the protons of phenyl group with $^2J[^1H, ^1H]$ of 8.4 Hz (Willem *et al.*, 1997; Hussain *et al.*, 2008). The $–NH_2$ group in the spectra of $\mathbf{L}^7$ appeared at 3.33 ppm as singlet and in the region of 3.32-3.37 ppm as doublet with $^2J[^1H, ^1H]$ of 5.4 Hz in complex **7**, respectively. This describes that there might be formation of zwitter ion in complex **7**.

Furthermore, complexation of Sn(IV) moiety with carboxylate group is confirmed by appearance of signals of tricyclohexyl protons in range of 1.19-1.85 ppm, 1.20-1.85 ppm and 1.20-1.83 ppm as multiplet in complex **1**, **4** and **7**, respectively (Tian *et al.*, 2013). The ^1H NMR spectra of $\mathbf{L}^7$ and Complex **7** are given in Figures 4.6 and 4.7, respectively.

4.3. Semi-empirical Study

In the geometry optimized structures, the carboxylate oxygen (with the short C-O bond) is bounded to the tin with a longer Sn-O bond, while the carboxylate oxygen (with the long C-O bond) is bounded to tin with a shorter Sn-O bond. This kind of asymmetric coordination behavior is documented in the X-ray crystal structures of organotin carboxylates (Stewart, 2007). The selected bond lengths (Å) and bond angles (^{o}) of complexes **1-7** are tabulated in Table 4.4 and 4.5, respectively.

Computed negative heats of formation indicate that all molecules are thermodynamically stable Table 4.6. The calculated HOMO and LUMO of each of the complex is shown in Figures 4.8-4.14. Notice that in all structures except complex **2**, the LUMO is primarily located on a tin moiety. In complex **2** both the HOMO and LUMO are located on the bridging aniline group. The calculated HOMO and LUMO energies are shown in Table 4.7. It is well known that a large HOMO-LUMO gap indicates stable molecule with less chemical reactivity, while a small HOMO-LUMO gap is associated with unstable molecule with high chemical reactivity. The ability of the molecule to donate electrons, (Ionization potential), E_{LUMO} represents (Electron Affinity) and electrophilicity values ($\omega=\mu^2/2\eta$) (Parr *et al.*, 1999), chemical potential values $\mu = -(I+A)/2$ (Parr *et al.*, 1978), global hardness ($\eta = I-A/2$) (Parr *et al.*, 1983) values and global softness values ($S=1/2\eta$) (Yang *et al.*, 1985) have been calculated in each case.

Table 4.1: Physical data of organotin(IV) complexes

Compound No.	Molecular Formula	Molecular Weight (g/mol)	Melting point (^{o}C)	Yield (%)	Elemental analysis		
					%		
					Element	Calculated	Found
L^1	$C_4H_2O_4$	114.05	180-187	-	C	42.11	
					H	1.76	
					N	-	-
1	$C_{40}H_{66}O_4Sn_2$	848.37	119-124	90	C	56.63	55.60
					H	7.84	7.81
					N	-	-
L^2	$C_8H_7NO_4$	181.15	>300	-	C	53.03	53.08
					H	3.89	3.85
					N	7.72	7.69
2	$C_{44}H_{71}NO_4Sn_2$	915.46	126-129	81	C	57.79	57.77
					H	7.72	7. 86
					N	1.53	1.50
L^3	$C_4H_7NNa_2O_5$	195.08	172-177	-	C	24.62	24.67
					H	3.61	3.67
					N	7.17	7.22
3	$C_{40}H_{71}NO_4Sn_2$	867.42	114-119	82	C	55.39	55.31
					H	8.25	8.29
					N	1.61	1.64

Compound No.	Molecular Formula	Molecular Weight (g/mol)	Melting point (^{o}C)	Yield (%)	Elemental analysis		
					%		
					Element	Calculated	Found
L[4]	$C_3H_7NO_2$	89.08	208-213	-	C	40.44	40.42
					H	7.92	7.95
					N	15.71	15.68
4	$C_{21}H_{39}NO_2Sn$	456.25	132-134	89	C	55.28	55.32
					H	8.61	8.59
					N	3.07	3.03
L[5]	$C_6H_{11}NO_2$	129.16	>300	-	C	55.79	55.76
					H	8.58	8.54
					N	10.83	10.89
5	$C_{24}H_{43}NO_2Sn$	496.31	129-133	86	C	58.08	58.12
					H	8.73	8.77
					N	2.82	2.78
L[6]	$C_6H_{16}N_2O_3$	164.21	215 (dec)	-	C	43.88	43.90
					H	9.82	9.83
					N	17.05	17.08
6	$C_{24}H_{46}N_2O_2Sn$	513.34	118-122	83	C	56.16	56.19
					H	9.03	9.07
					N	5.46	5.41

Compound No.	Molecular Formula	Molecular Weight (g/mol)	Melting point (^{o}C)	Yield (%)	Elemental analysis		
					%		
					Element	Calculated	Found
L^7	$C_8H_9NO_2$	151.16	201 (dec)	-	C	63.56	63.54
					H	6.00	5.96
					N	9.26	9.30
7	$C_{26}H_{41}NO_2Sn$	518.28	129-139	90	C	60.25	60.29
					H	7.97	7.93
					N	2.70	2.66

Table 4.2: IR spectral data[a] (cm^{-1}) of organotin(IV) complexes

Compound No.	υ(O-H)	$\upsilon(COO)_{asym}$	$\upsilon(COO)_{sym}$	(Δυ)	υ(N-H)	$\upsilon(-NH_2)$	υ(Sn-C)	υ(Sn-O)
L^1	3535w	1570s	1274m	296	-	-	-	-
1	-	1560s	1439s	121	-	-	528s	441s
L^2	3560m	1519m	1282m	237	-	3439w	-	-
2	-	1558s	1440s	118	-	3435s	551s	418s
L^3	3529m	1575m	1298m	277	3368w	-	-	-
3	-	1570s	1441s	129	3360s	-	551m	418s
L^4	3550m	1601m	1373s	228	3339w	-	-	-
4	-	1565s	1441s	124	3335m	-	535s	422m
L^5	3539m	1548m	1288w	260	3365w	-	-	-
5	-	1539s	1412s	127	3355s	-	585s	441s
L^6	3520s	1596s	1385s	211	-	3455s	-	-
6	-	1572w	1445s	127	-	3449m	527s	432m
L^7	3580s	1578s	1375m	203	-	3415s	-	-
7	-	1576m	1441s	135	-	3410s	525s	423s

[a]s = strong; m = medium; w = weak

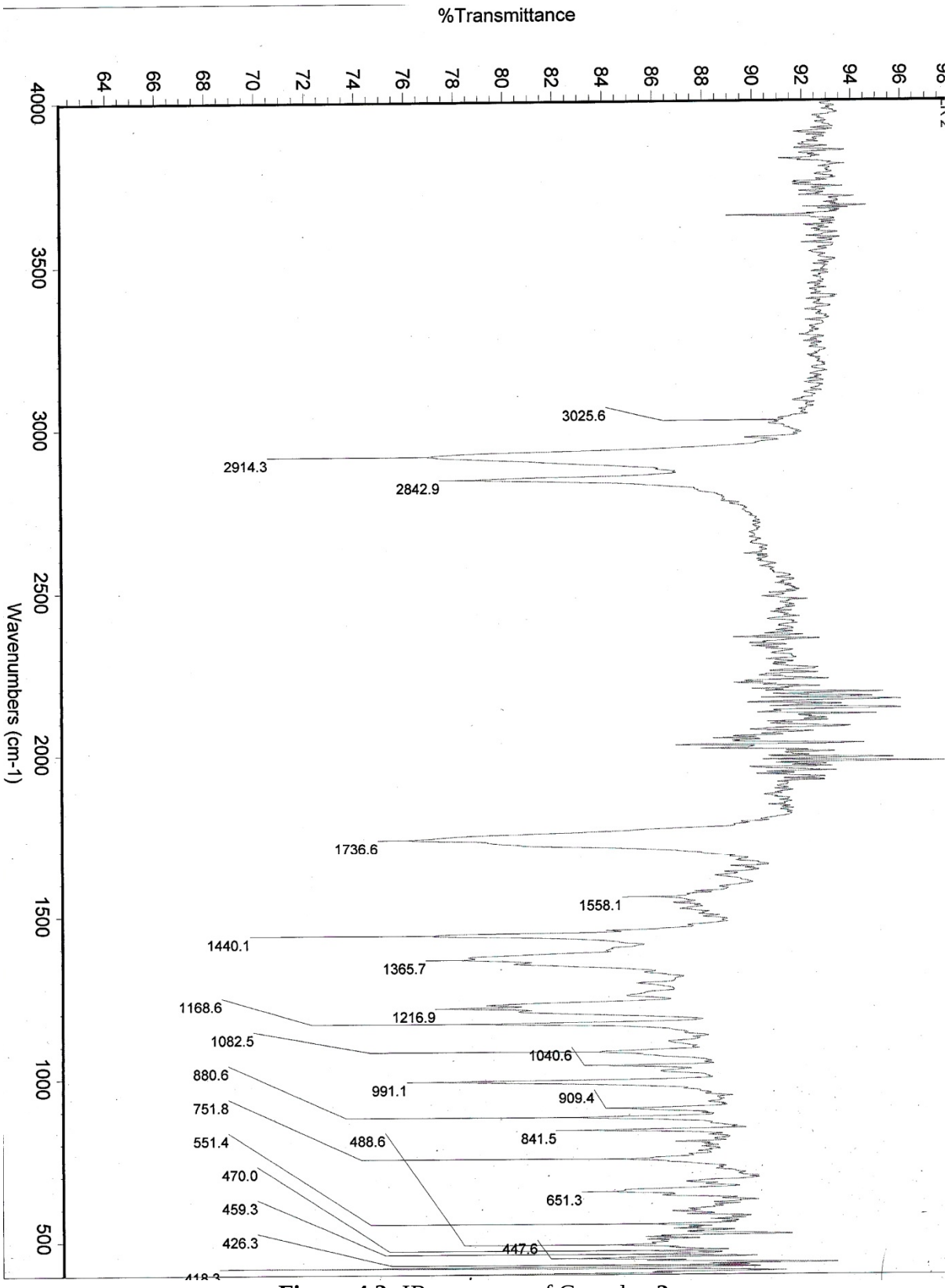


Figure 4.2: IR spectrum of Complex **2**

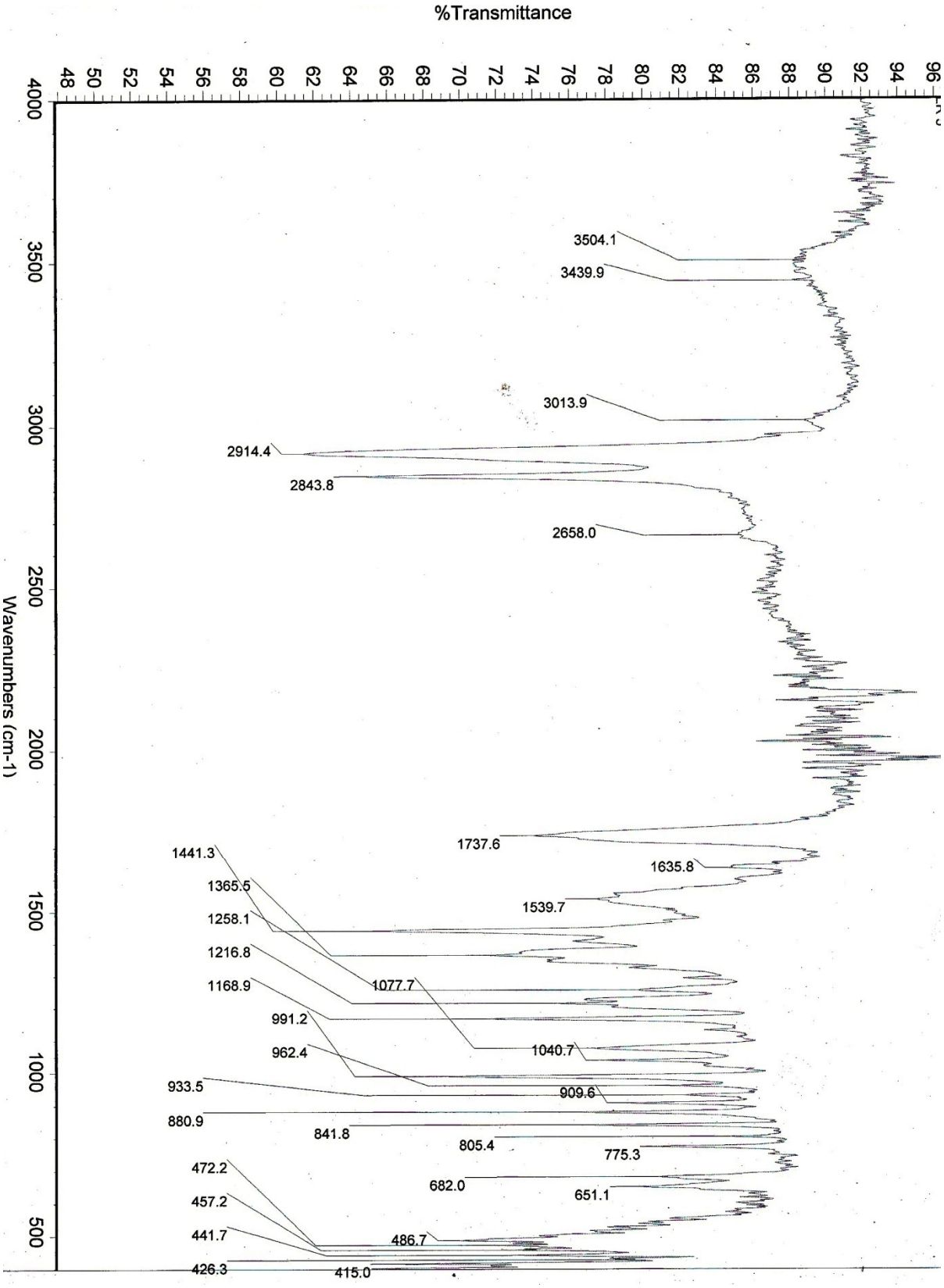


Figure 4.3: IR spectrum of Complex **5**

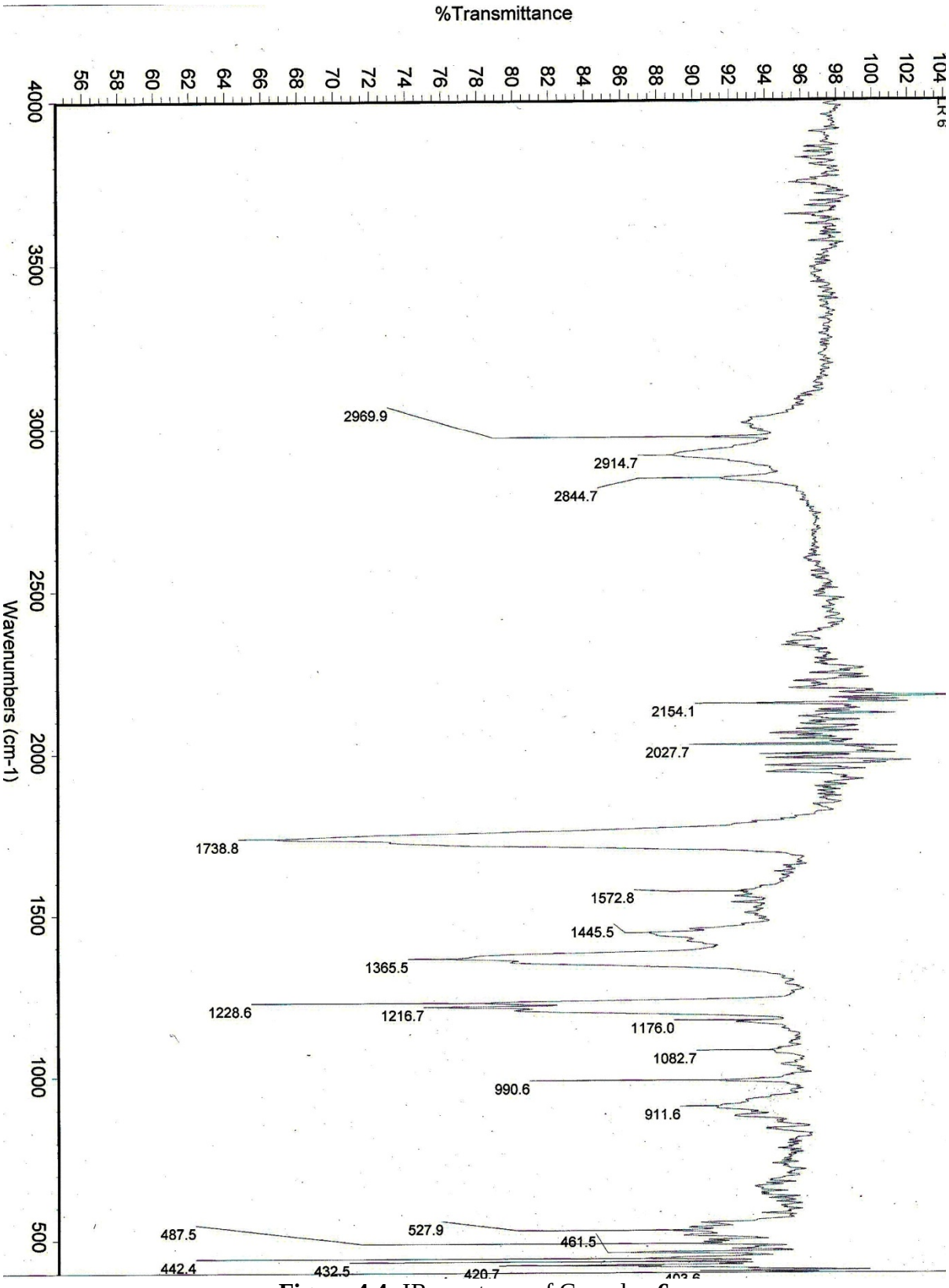


Figure 4.4: IR spectrum of Complex **6**

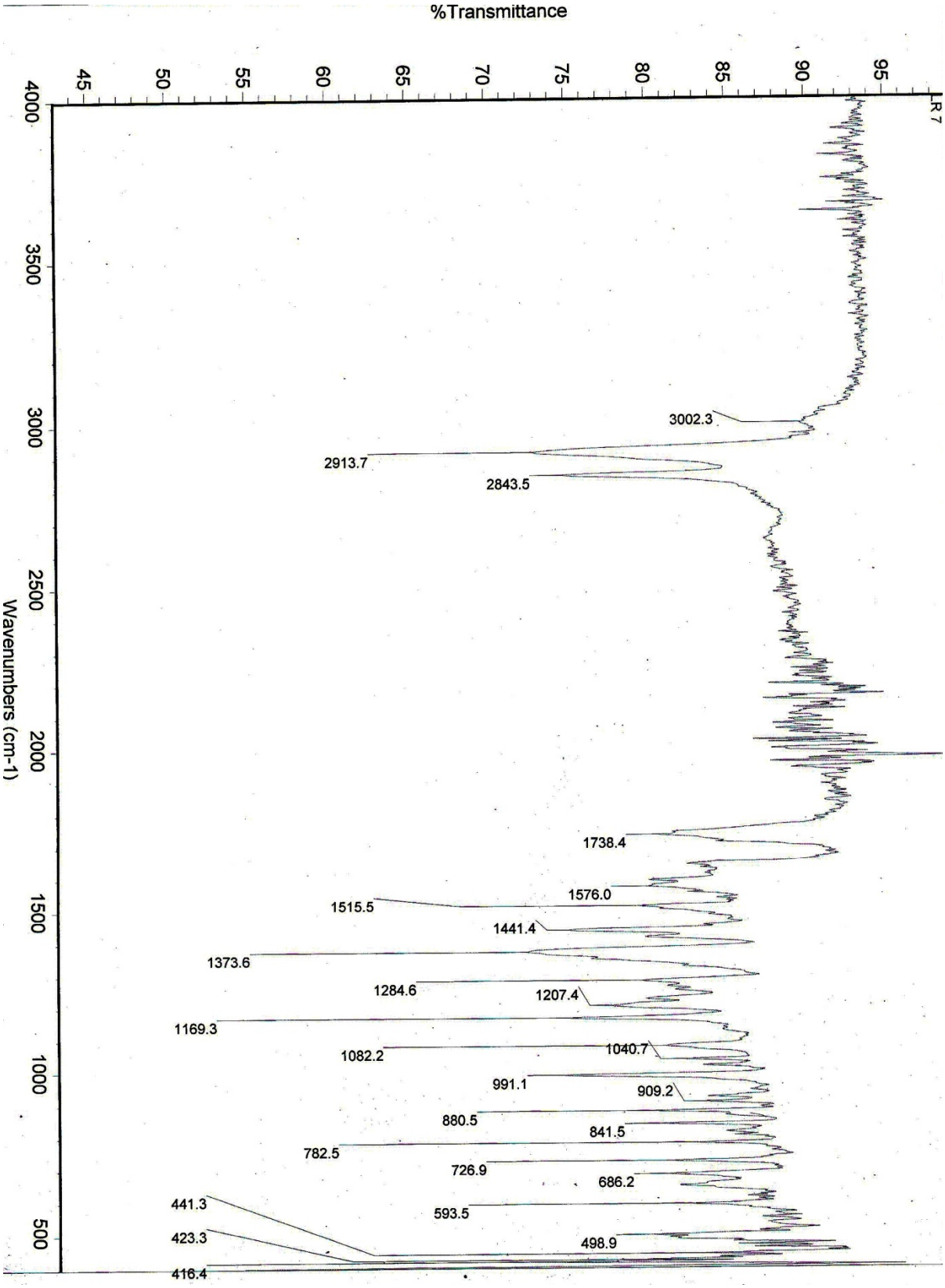


Figure 4.5: IR spectrum of Complex **7**

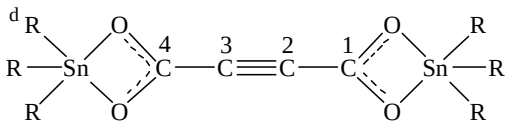
Table 4.3: ^{1}H NMR data[a-e] (ppm) of organotin(IV) complexes

Proton No.	L^1	Complex 1	L^4	Complex 4	L^7	Complex 7
2	-	-	2.45-2.51m	2.46-2.50m	2.50s	2.50s
3	-	-	0.87s	0.87s	-	-
4,8	-	-			6.48-6.51d (8.4)	6.48-6.50d (8.4)
5,7	-	-	-	-	6.87-6.90d (8.4)	6.87-6.90d (8.4)
-NH	-	-	2.08s	2.08s	-	-
$-NH_2$	-	-	-	-	3.33s	3.32
R	-	1.19-1.85m	-	1.20-1.85m	-	1.20-1.83m

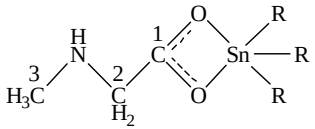
[a]Multiplicity is given as: s = singlet, d = doublet, m = multiplet

[b]Chemical shifts (δ) in ppm

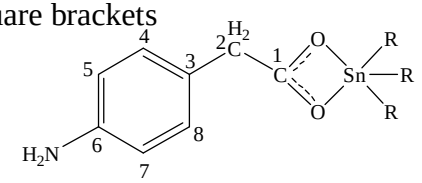
[c]Coupling constant, $^{2}J[^{1}H, ^{1}H]$ in Hz is given in square brackets



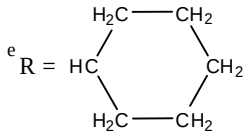
Complex **1**



Complex **4**



Complex **7**



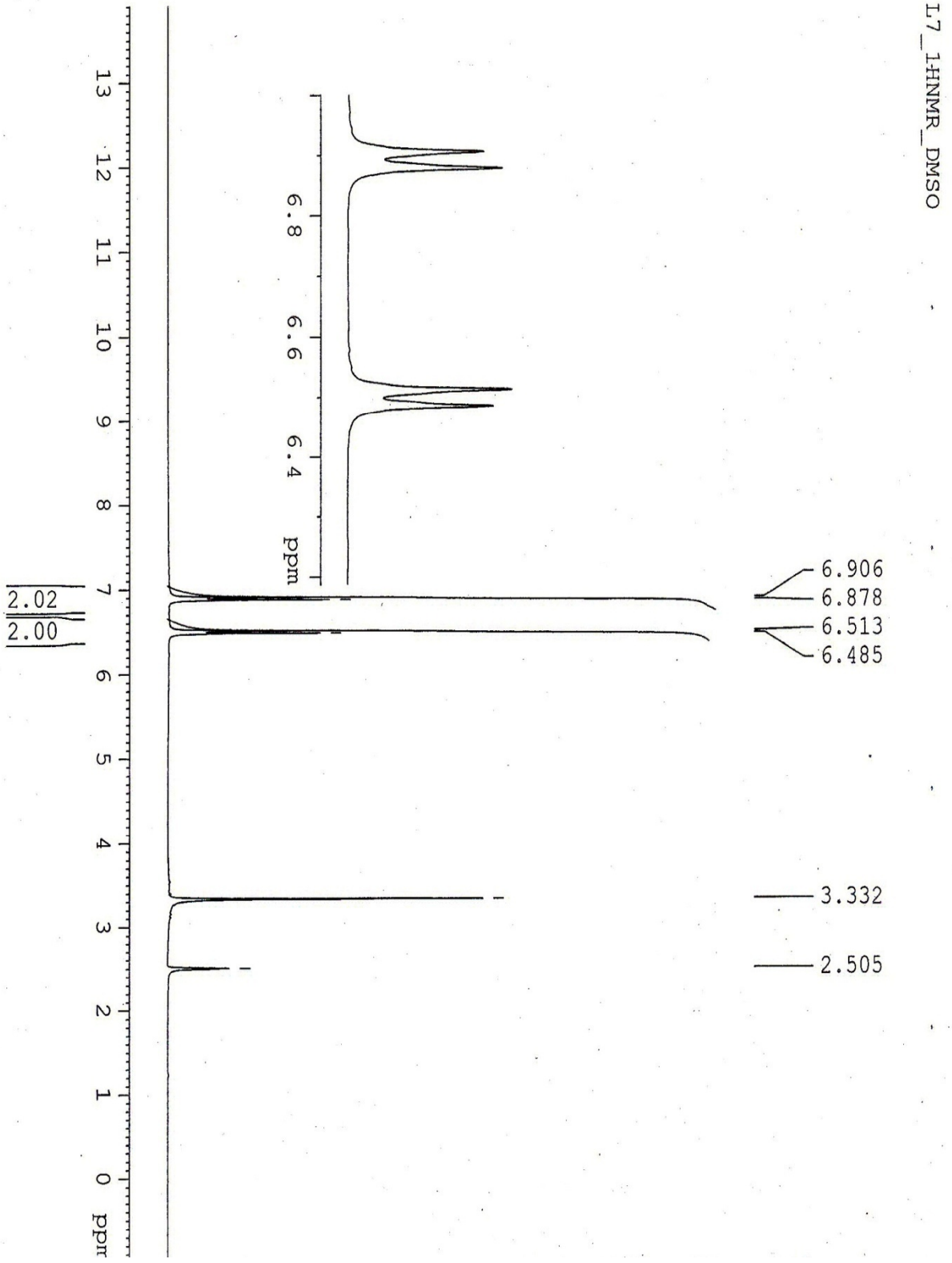


Figure 4.6: ^{1}H NMR spectrum of **L^{7}**

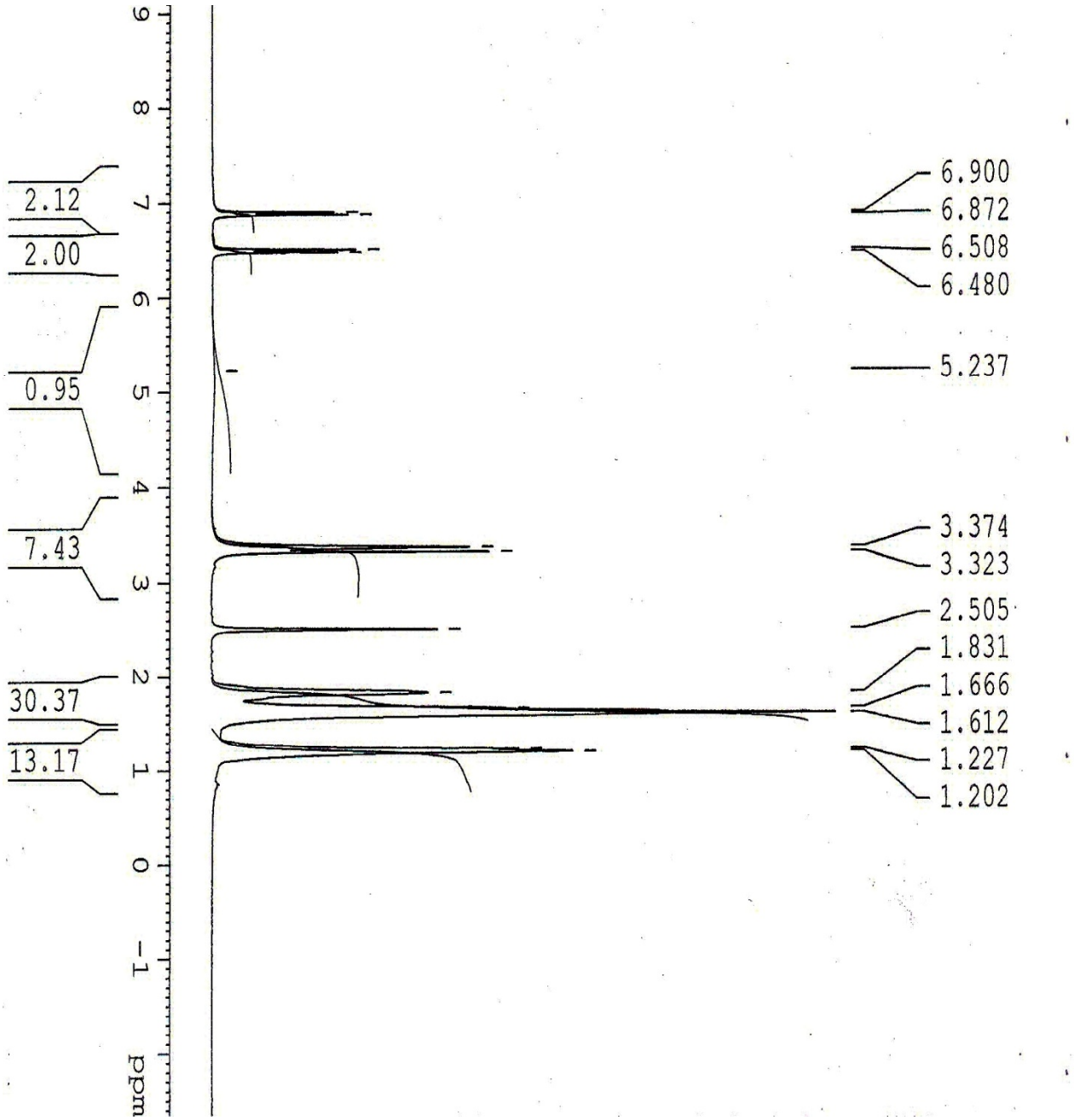


Figure 4.7: ^{1}H NMR spectrum of Complex **7**

Table 4.4: Selected Bond Lengths (Å) of organotin(IV) complexes

Bond Lengths	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Sn-O	2.03, 2.08	2.71, 2.03 2.03, 2.71	2.73, 2.03 2.03, 2.71	2.72, 2.03	2.72, 2.03	2.72, 2.03	2.73, 2.01
C-O	1.23, 1.32	1.24, 1.32 1.24, 1.32	1.24, 1.32 1.24, 1.32	1.24, 1.32	1.24, 1.32	1.24, 1.32	1.24, 1.32
C-N	-	1.43	1.48, 1.48	1.47, 1.48	1.49, 1.48 1.49	1.49, 1.48	1.43

Table 4.5: Selected Bond Angles (^{o}) of organotin(IV) complexes

Bond Angles	**1**	**2**	**3**	**4**	**5**	**6**	**7**
O-Sn-O	49.6, 49.5	50.2, 49.7	50.1, 49.9	50.0	50.0	50.0	50.1
O-C-O	112.5, 112.7	110.6, 110.4	111.0, 110.7	111.0	111.0	110.83	110.8
C-Sn-C	119.7, 112.8 101.6, 108.3 110.8, 111.6	119.5, 112.4 101.4, 107.9 106.7,113.0	102.2, 111.8 118.0, 108.2 111.6, 110.4	102.2, 118.0 111.7	102.0, 111.9 108.9	102.2, 118.1 111.7	102.1, 118.0 111.7
SnOCO/SnOCO Interplaner angle	84.74	16.0	44.5	-	-	-	-

Table 4.6: Computed thermodynamic parameters of organotin(IV) complexes

Parameters At 298K	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Heat of Formation (Kcal/mole)	-207.449	-239.868	-269.702	-136.501	-139.164	-148.187	-116.315
Enthalpy (Kcal/mole-K)	19907.663	24580.764	23224.909	13408.080	15373.186	15812.248	15119.295
Entropy (Kcal/mole-K)	198.781	212.285	203.963	142.190	155.379	158.306	153.403
Heat Capacity (Cp) (Kcal/mole-K)	158.331	175.338	165.770	91.301	107.125	107.781	104.567

Table 4.7: Computed molecular descriptors of organotin(IV) complexes

Compound No.	**1**	**2**	**3**	**4**	**5**	**6**	**7**
HOMO energy (eV)	-9.64602	-9.01145	-9.58535	-9.51956	-9.20387	9.48253	-8.65916
LUMO energy (eV)	-0.79959	-0.71980	-0.68649	-0.55025	-0.62552	-0.57201	-0.58400
HUMO-LUMO (eV)	8.84643	8.29165	8.89886	8.96931	8.57835	8.91052	8.07516
Dipole Moment (debyes)	1.326	1.718	1.808	1.558	1.952	2.241	1.394
Global Hardness (η, eV)	4.42321	4.14582	4.43943	4.48465	4.28917	4.45526	4.03758
Global Softness (S, eV)	0.11303	0.12060	0.11237	0.11149	0.11657	0.11222	0.13836
Chemical Potential (μ, eV)	-5.22280	-4.86562	-5.13592	-5.03490	-4.91469	-5.02727	-4.62158
Electrophilicity (ω)	3.08346	2.85515	2.96416	2.82633	2.81571	2.83636	2.64502

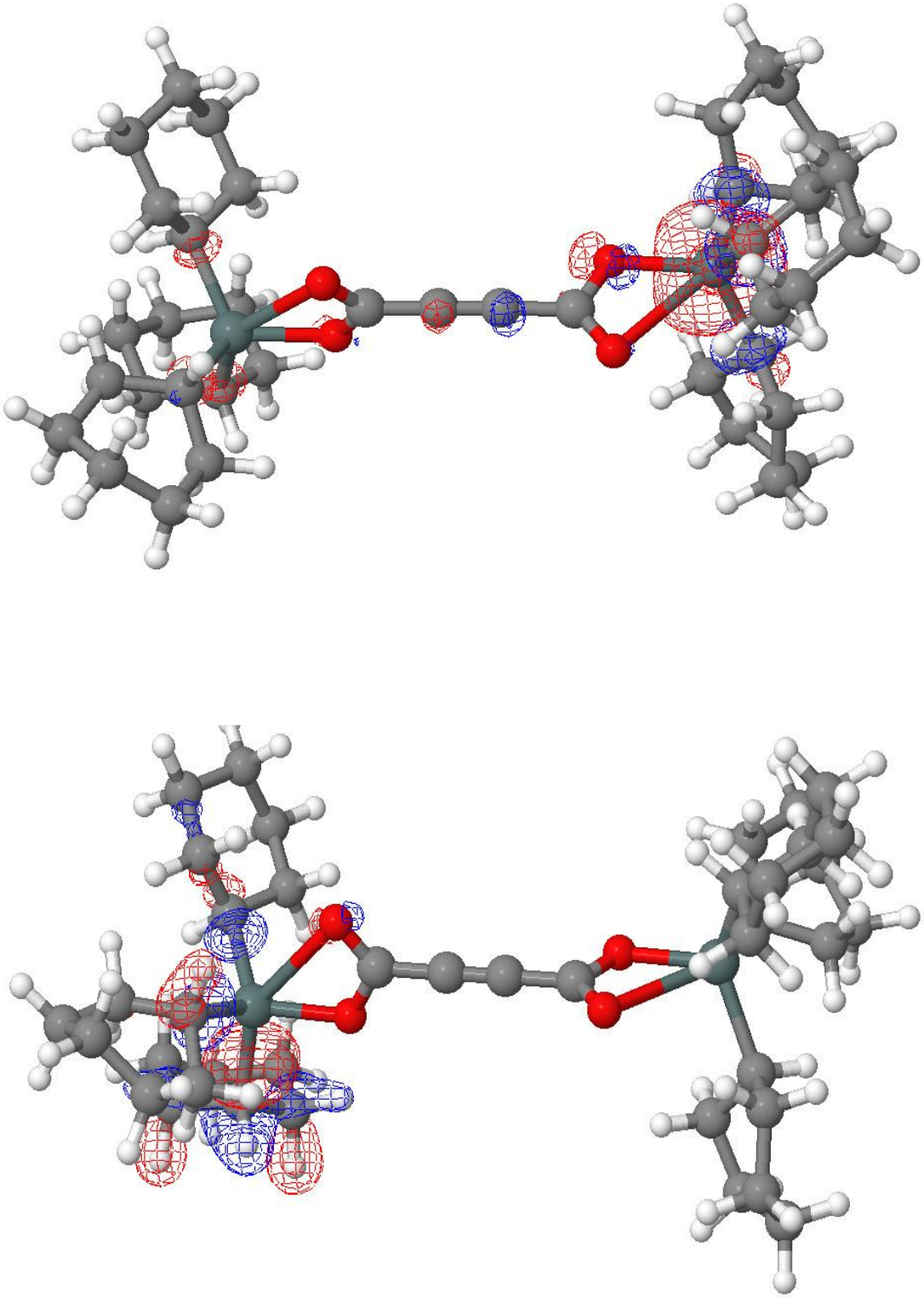


Figure 4.8: HOMO-LUMO of Complex **1**

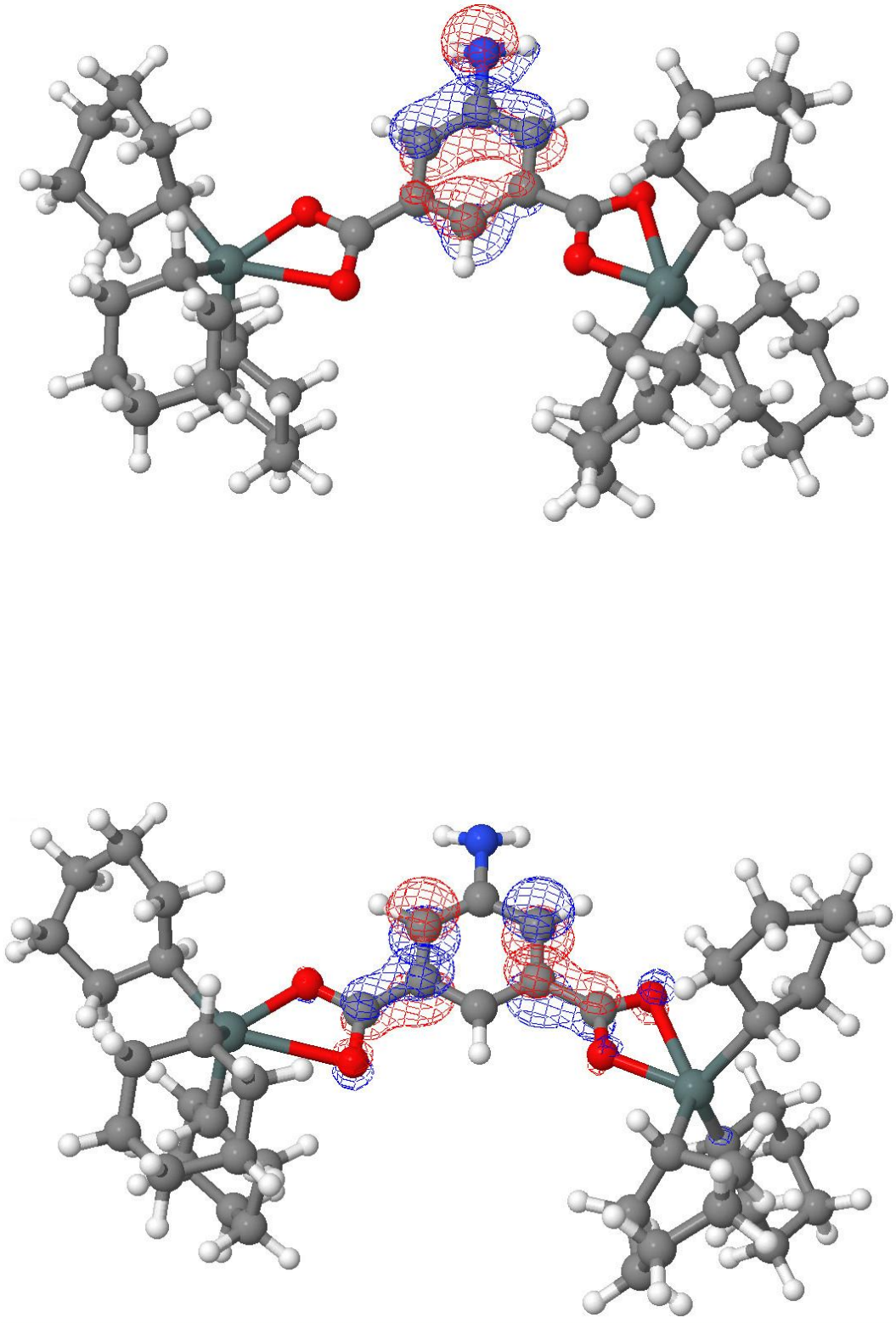


Figure 4.9: HOMO-LUMO of Complex **2**

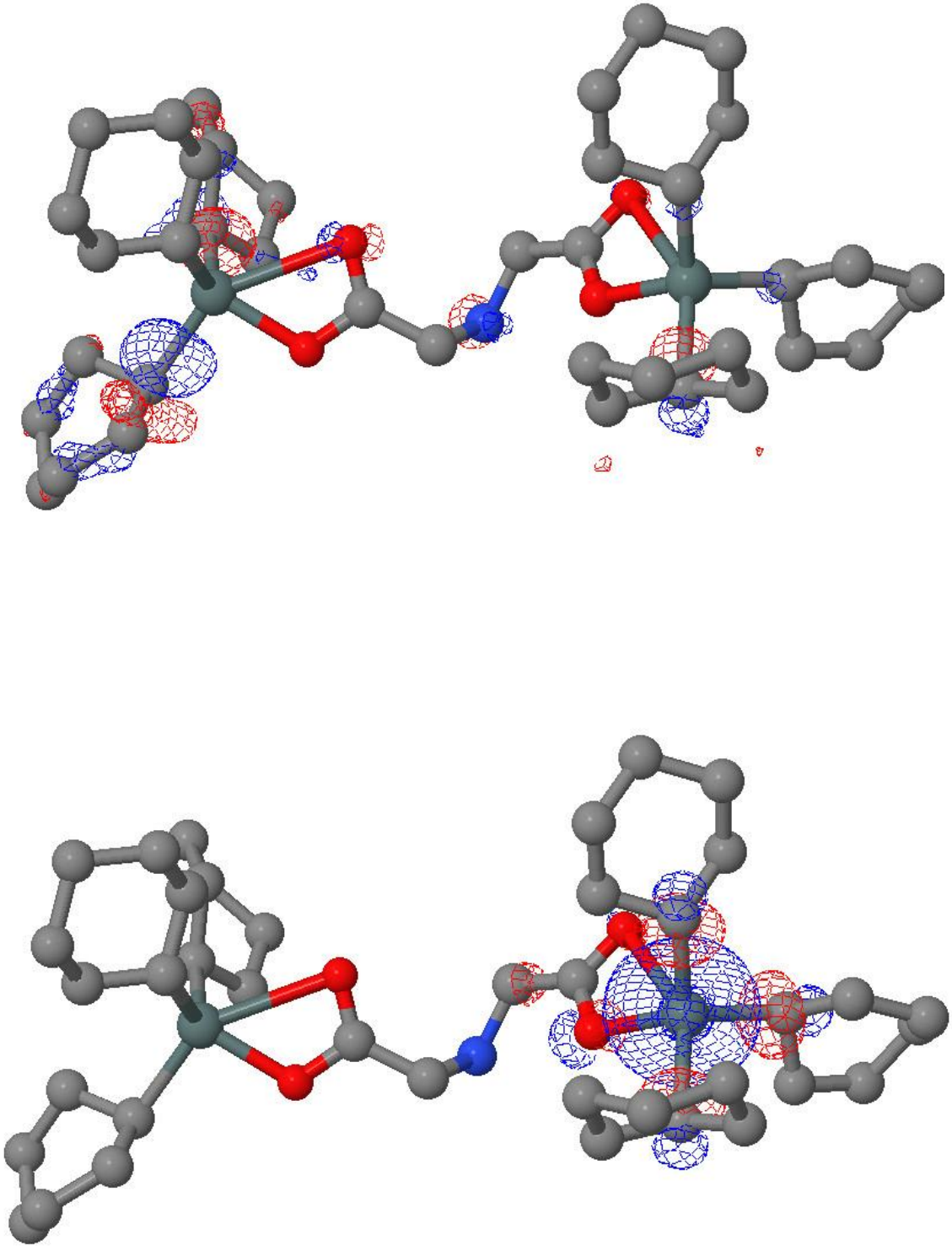


Figure 4.10: HOMO-LUMO of Complex **3**

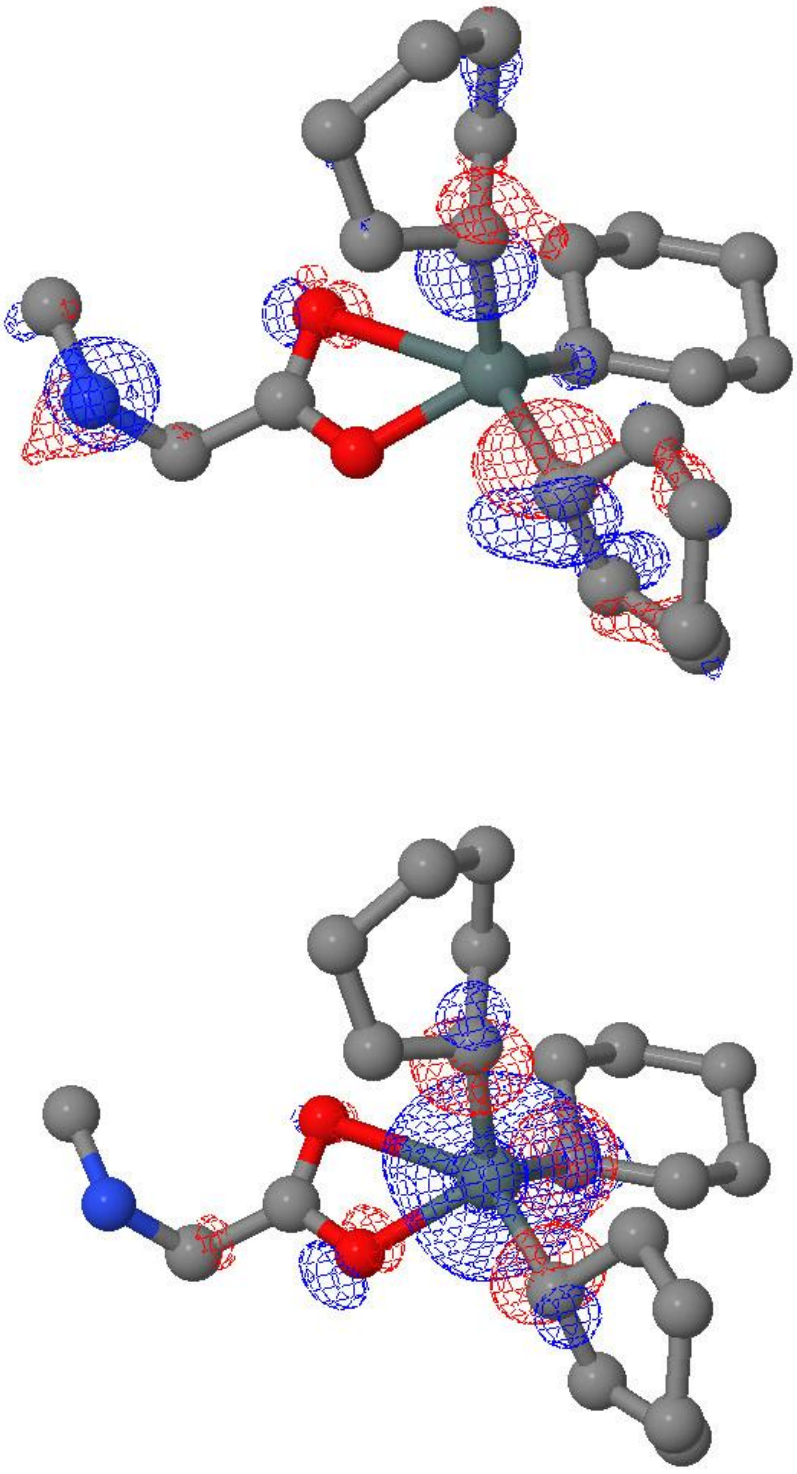


Figure 4.11: HOMO-LUMO of Complex **4**

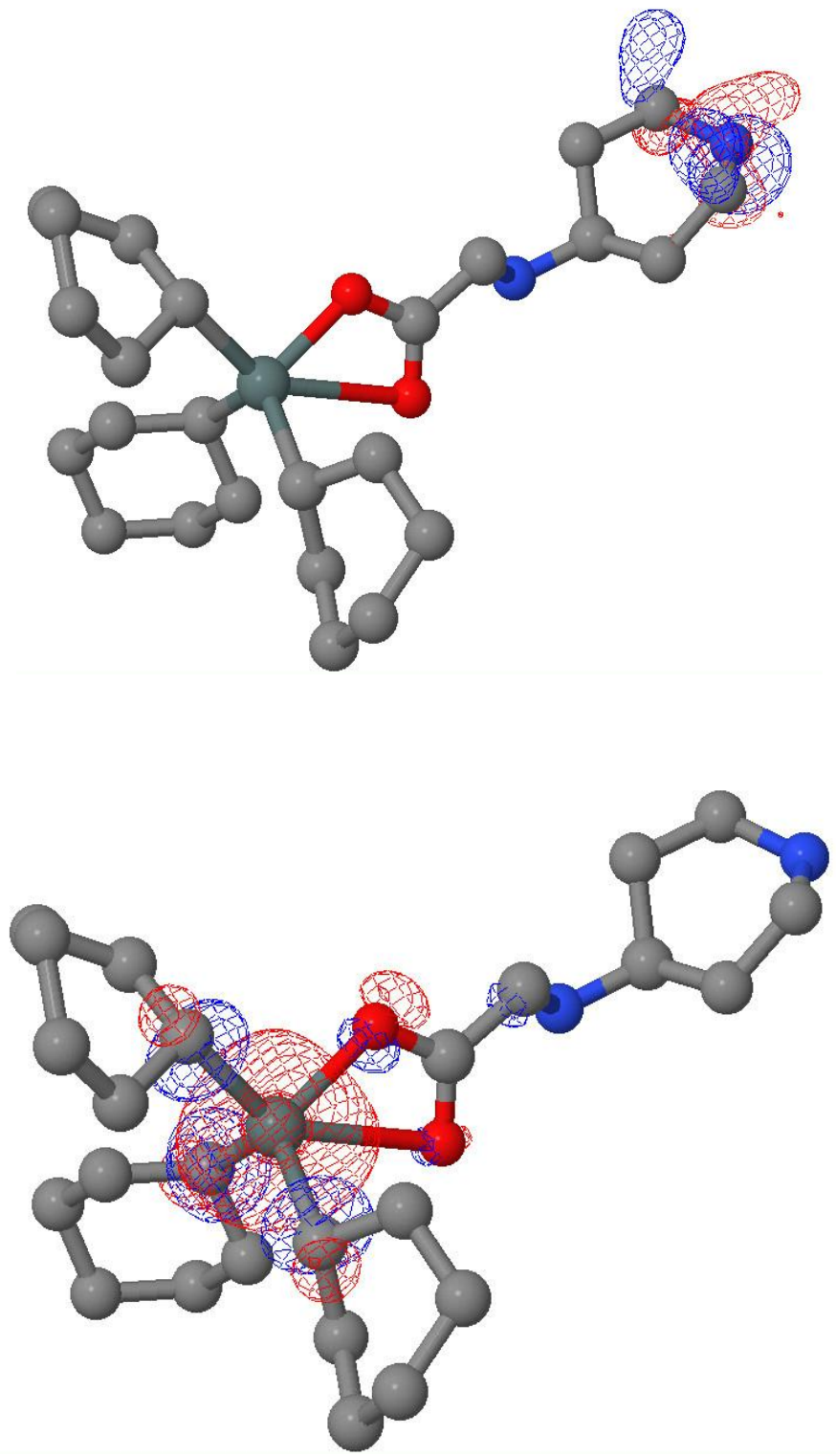


Figure 4.12: HOMO-LUMO of Complex **5**

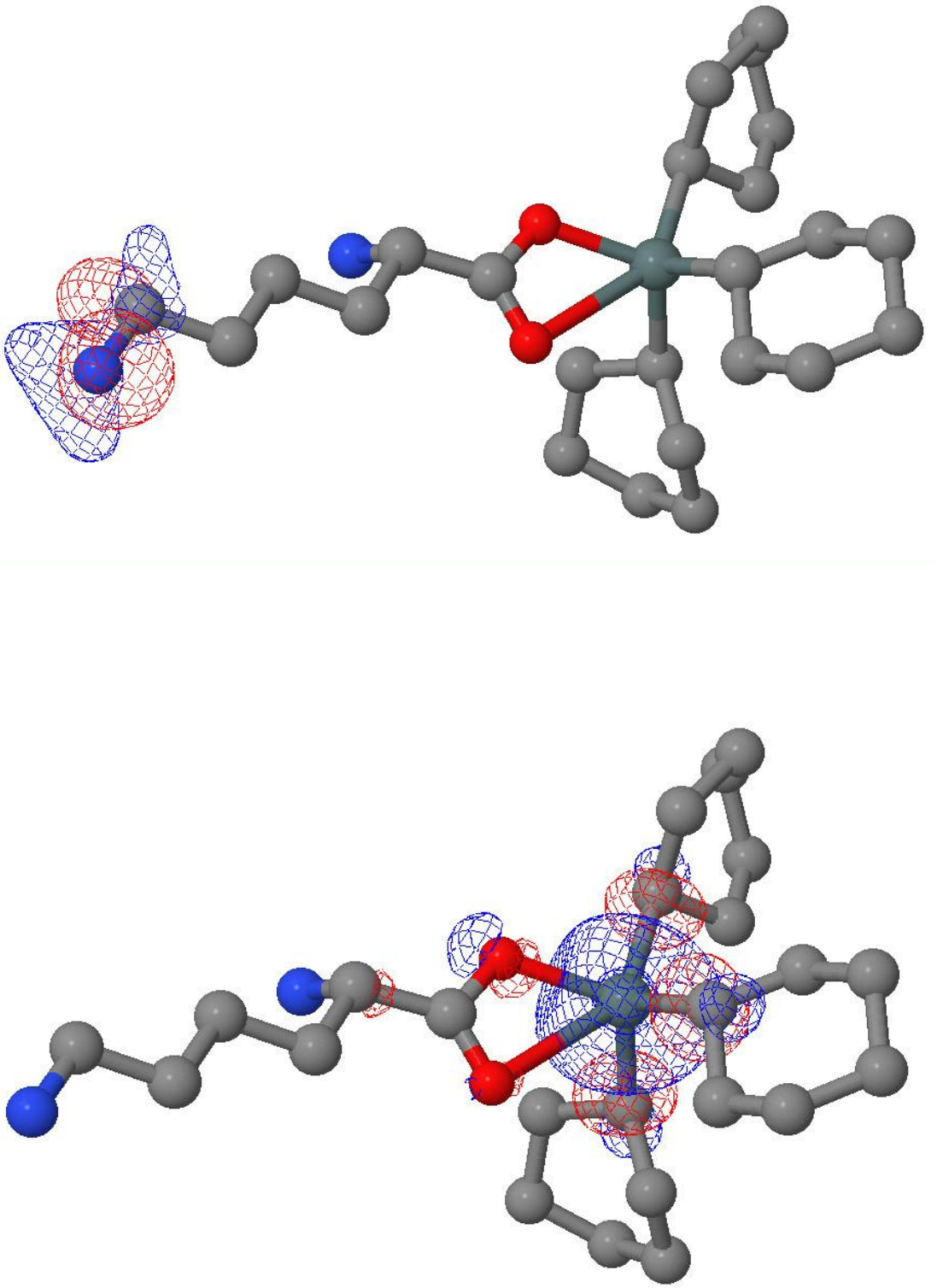


Figure 4.13: HOMO-LUMO of Complex **6**

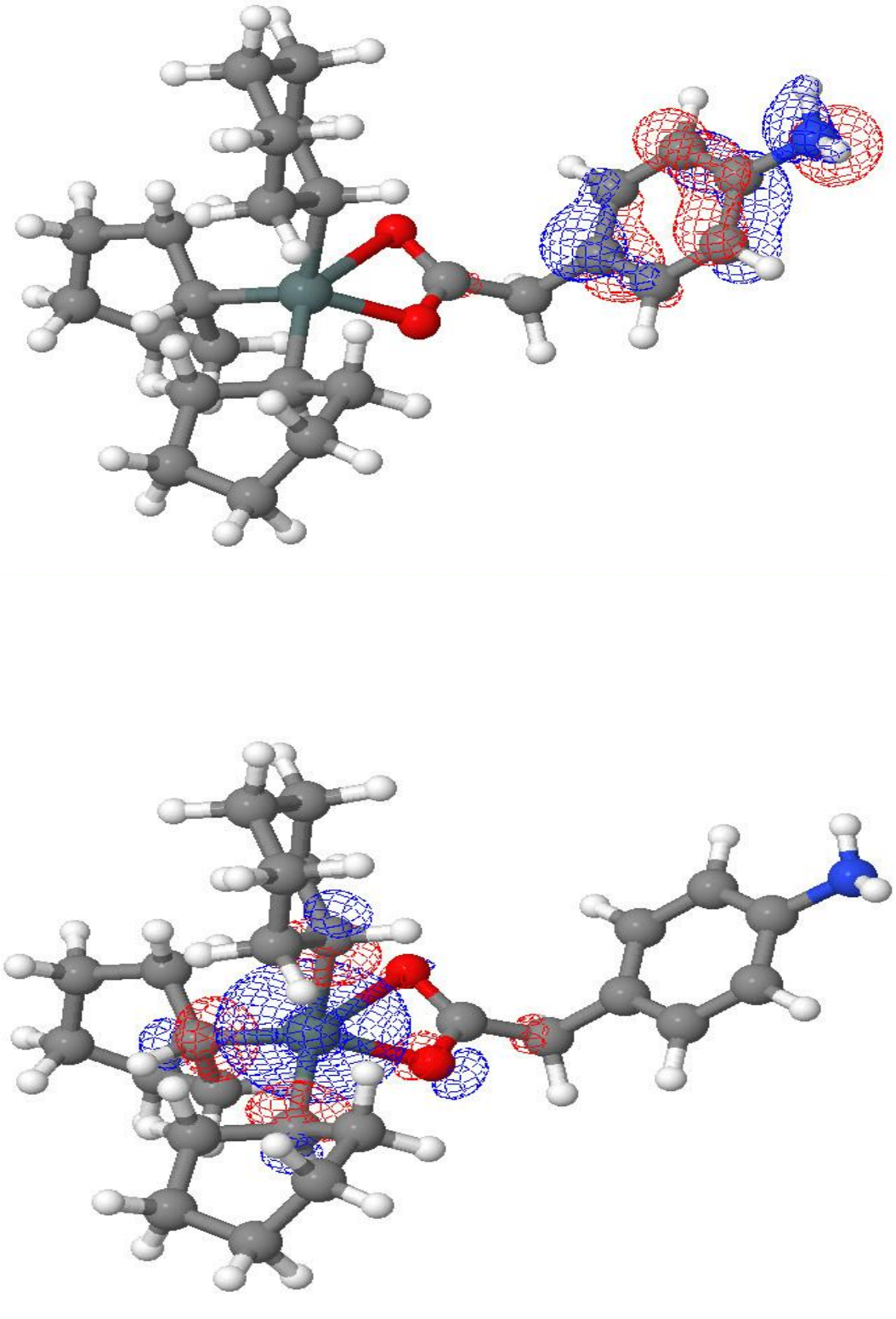


Figure 4.14: HOMO-LUMO of Complex **7**

4.4. Antimicrobial Activity

4.4.1. Antibacterial Activity

The ligands $\mathbf{L^1}$-$\mathbf{L^7}$ and its organotin(IV) complexes **1-7** were tested for antibacterial activity using two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative bacterial (*Escherichia coli* and *Pasturella multocida*) strains. The inhibition zone diameters were measured and compared with the results of standard drug, Rifampicine (positive control) (Sarkar *et al.,* 2007). Data revealed that ligands $\mathbf{L^4}$ and $\mathbf{L^6}$ exhibit significant activities against all pathogenic bacteria. Furthermore complexes **1**, **2** and **4** are found to be more active as compared to their free ligands $\mathbf{L^1}$, $\mathbf{L^2}$ and $\mathbf{L^4}$ which indicate that metallation increases the antimicrobial activity (Singh and Varshney, 2006). These complexes show moderate activity against Gram-positive bacteria but relatively high activity against Gram-negative bacteria (Sharma *et al.,* 2010). This can be attributed to the difference in structure of cell walls. The lipopolysaccharides forms an outer lipid membrane and contributes to complex antigenic specificity for Gram (-) cells (Shahzadi *et al.,* 2005).

The variation in the toxicity of different antibacterial agents against different organisms depend either on the impermeability of the cells or differences in ribosomes to the antimicrobial agents (Garrod *et al.,* 1981). The antibacterial results are summarized in Table 4.8.

4.4.2. Antifungal Activity

Organotin complexes act as antifungal agents so the ligands $\mathbf{L^1}$-$\mathbf{L^7}$ alongwith their organotin(IV) complexes **1-7** were also screened for their antifungal activity against different fungal strains. Fluconazol (positive control) was used as standard drug (Singh *et al.,* 2008). The screening data of ligands and its synthesized organotin(IV) complexes show that complexes exhibit signifacnt activity as compared to their respective ligands (Singh *et al.,* 2010).

Complexes **1**, **2** and **4** are found to be more potent inhibitors of fungal growth. Apparently, function of ligand is only to support the transport of active organotin(IV) moiety to the site of action where it is released by hydrolysis (Jain *et al.,* 2004; Singh *et al.,* 2009). The antifungal activity of complexes **1**, **2** and **4** against *A. alternata was* comparable to that of standard drug.

On comparing the results in general, it may be concluded that organotin(IV) complexes have greater inhibiting power than their respective free ligands against all microbes (Singh and Varshney, 2006). The complexes show less fungicidal effects as compared with the bacterial effects. The inhibition zone diameters of antifungal activity was given in Table 4.9.

4.4.3. Immunomodulatory Activity (Oxidative Burst Study)

Immunomodulatory activity of ligands and organotin(IV) complexes was carried out by luminol based chemiluminescence assay (Helfand *et al.*,1982; Halker *et al*., 2001). Ligands $\mathbf{L^1}$, $\mathbf{L^4}$ and $\mathbf{L^7}$ and complexes **1**, **4** and **7** exhibit IC_{50} value greater than 100 mg/mL. The Immunomodulatory data of ligands and complexes is given in the Table 4.10.

Ligands $\mathbf{L^1}$, $\mathbf{L^4}$ and $\mathbf{L^7}$ and complexes **1**, **4** and **7** did not show Immunomodulatory activity due to unavailability of supplementary binding sites in drug molecules (Ettouhami *et al.*, 2011). In ligand $\mathbf{L^7}$ and complex **7** no responce of Immunomodulatory activity might also be due to fact that amino group has no ability to be protonated at physiological (pH = 7.4) to form ionic bonding such as hydrogen bonding with target molecule which enhances its pharmacodynamic properties (Sultana *et al*., 2013).

Results suggested that ligands and synthesized organotin(IV) complexes have no ability to form carboxylate ion. The binding ability of organotin(IV) complexes toward target molecule depends upon the co-ordination number and nature of groups bounded to central tin atom (Sultana *et al*., 2013).

Table 4.8: Antibacterial activity of organotin(IV) complexes[a-e]

Compound No.	Inhibition Zone (mm)			
	E. coli	***B. subtilus***	***S. aureus***	***P. multocida***
	Mean ± S.D	**Mean ± S.D**	**Mean ± S.D**	**Mean ±S.D**
L^1	0^{c}	0^{c}	0^{c}	0^{c}
1	$15^{bc} \pm 1.3$	$13^{bc} \pm 1.1$	$14^{bc} \pm 1.2$	$15^{b} \pm 1.1$
L^2	0^{c}	0^{c}	0^{c}	0^{c}
2	$16^{b} \pm 1.5$	$13^{bc} \pm 1.8$	$13^{bc} \pm 1.4$	$17^{ab} \pm 1.7$
L^3	0^{c}	0^{c}	0^{c}	0^{c}
3	0^{c}	0^{c}	0^{c}	0^{c}
L^4	$12.5^{bc} \pm 1.7$	$13^{bc} \pm 0.8$	$12.5^{bc} \pm 1.7$	$12^{bc} \pm 1.8$
4	$17^{b} \pm 1.3$	$15^{b} \pm 1.3$	$14^{bc} \pm 1.3$	$17^{ab} \pm 1.5$
L^5	0^{c}	0^{c}	0^{c}	0^{c}
5	0^{c}	0^{c}	0^{c}	0^{c}
L^6	$21^{ab} \pm 1.6$	$22^{ab} \pm 1.5$	$24^{ab} \pm 1.5$	$13^{bc} \pm 1.9$
6	0^{c}	0^{c}	0^{c}	0^{c}
L^7	14^{bc}	0^{c}	0^{c}	0^{c}
7	0^{c}	0^{c}	0^{c}	0^{c}
Standard drug	$35^{a} \pm 1.8$	$32^{a} \pm 1.9$	$40^{a} \pm 1.5$	$30^{a} \pm 1.7$

[a]Standard Drug, Rifampicine (Positive control)

[b]Concentration 10 mg/mL in DMSO

[c]Different letters in superscript indicate significant and non-significant differences with sample

[d]Values are mean ± SD of three samples analyzed individually in triplicate at $p< 0.1$

[e]No activity

Table 4.9: Antifungal activity of organotin(IV) complexes[a-e]

Compound No.	Inhibition Zone (mm)			
	A. niger	***A. flavus***	***H. myedis***	***A. alternata***
	Mean ± S.D	**Mean ± S.D**	**Mean ± S.D**	**Mean ±S.D**
L^1	0^{c}	0^{c}	0^{c}	0^{c}
1	$12^{bc} \pm 1.2$	$13^{bc} \pm 1.9$	$15^{ab} \pm 1.5$	$14^{b} \pm 1.0$
L^2	$20^{ab} \pm 1.5$	0^{c}	0^{c}	$20^{bc} \pm 1.2$
2	$10^{bc} \pm 1.4$	$11^{bc} \pm 1.6$	$12^{bc} \pm 1.1$	$15^{bc} \pm 0.9$
L^3	0^{c}	0^{c}	0^{c}	0^{c}
3	0^{c}	0^{c}	0^{c}	0^{c}
L^4	$14.5^{b} \pm 1.1$	$37.5^{a} \pm 1.5$	0^{c}	$27^{a} \pm 1.7$
4	$14^{b} \pm 1.4$	$13^{bc} \pm 1.1$	$14^{bc} \pm 1.7$	$13^{bc} \pm 1.6$
L^5	0^{c}	0^{c}	0^{c}	0^{c}
5	$10^{bc} \pm 1.7$	$10^{bc} \pm 1.2$	$11^{bc} \pm 1.8$	$10^{bc} \pm 1.1$
L^6	$24^{ab} \pm 1.3$	$27^{ab} \pm 1.8$	0^{c}	$19^{ab} \pm 1.4$
6	0^{c}	0^{c}	0^{c}	0^{c}
L^7	$28^{a} \pm 1.6$	$24^{ab} \pm 1.3$	0^{c}	$26^{ab} \pm 1.4$
7	0^{c}	0^{c}	0^{c}	0^{c}
Standard drug	$25^{a} \pm 1.4$	$26^{a} \pm 1.5$	$25^{a} \pm 1.2$	$28^{a} \pm 1.7$

[a]Standard Drug, Fluconazol (Positive control)

[b]Concentration 10 mg/mL in DMSO

[c]Different letters in superscript indicate significant and non-significant differences with sample

[d]Values are mean ± SD of three samples analyzed individually in triplicate at $p< 0.1$

[e]No activity

Table 4.10: Immunomodulatory activity of organotin(IV) complexes[a-c]

Compound No.	IC_{50} ± SD (μg/mL)
L^1	>100
1	>100
L^4	>100
4	>100
L^7	>100
7	>100
Standard drug	11.8 ± 1.2

[a]Standard drug: Ibuprofen, (Positive control)

[b]Concentration 1 mg/mL in DMSO

[c]Values are mean ± SD of three samples analyzed individually in triplicate at $p< 0.005$

4.5. Conclusion

Organotin(IV) complexes with different oxygen donor ligands and tricyclohexyltin chloride have been synthesized in good yield. IR data clearly demonstrated the bidendate mode of attachment between tin and oxygen atom in synthesized organotin(IV) complexes which is also confirmed by Semi-empirical study. HOMO-LUMO calculations show that all complexes are thermodynamically stable and chemically inert.

The antimicrobial assay of ligands and organotin(IV) complexes shows that complexes are more active as compared to their respective ligands with few exceptions. The complexes **1**, **2** and **4** were found to be more potent inhibitors toward bacterial strains as compared to fungal culture with few exceptions. None of ligands and complexes show any Immunomodulatory activity which confirm that ligands and complexes are inactive immunomodulators.

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