# CHAPTER I

INTRODUCTION

Tin was discovered in old tombs from the ancient Egyptian or Babylonian dynasty before 3000 B.C., in various forms of vessels and ornament made of bronze which is an alloy of copper and tin that usually contains 2-35 % of tin.[1]

Tin metal is defined mainly from the mineral Cassiterite (SnO_2) or, to a lesser extent, from the sulphide ore Stannite ($Cu_2S.FeS.SnS_2$) and Malayanite ($CaSnSiO_5$). At present, tin requirements are running at between 150,000 - 160,000 tons per year. There are many uses of tin such as in can-making industries, solder and tin chemicals etc.[2]

Organotin compounds are defined as compounds containing at least one tin - carbon bond which was discovered by Lowing in 1852. The first description dates back to 1849, when Sir Edward Frankland synthesized diethyltin diiodide.[3] Since then the studies of organotin chemistry were begun to be developed for industrial applications. By the end of 1965 about 3000 papers on organotins had been published and by 1980 some 1000 papers were appearing annually.[4] Tin is an element in group IV of the

periodic table with a $5s^2 5p^2$ electronic configuration. Quadrivalent organotins often present the tetrahedral sp^3 hybridization. This is so far tetraorganotin, hexaorgano ditins, organotin hydrides and most of thiotin derivatives.
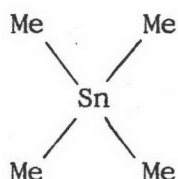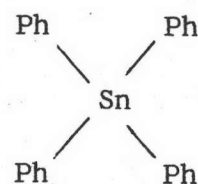

Tetramethyltin   Tetraphenyltin

Most organotin compounds of interest for organic synthesis are liquid or solid and soluble in most organic solvents. The covalent radius of tin is 0.14 nm. and consequently bond lengths of tin are long; average value in nm. are Sn-C 0.22, Sn-H 0.17, Sn-Cl 0.24, Sn-O 0.21, Sn-S 0.24, Sn-Sn 0.28 nm. Inspite of the differences in electronegativity the bonds are commonly considered as essentially covalent by easily polarizable. In consequence, organotins show little ionization in solution.

$$\overset{\delta^+}{Sn} \longrightarrow \overset{\delta^-}{Y}$$
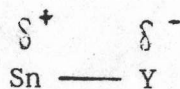
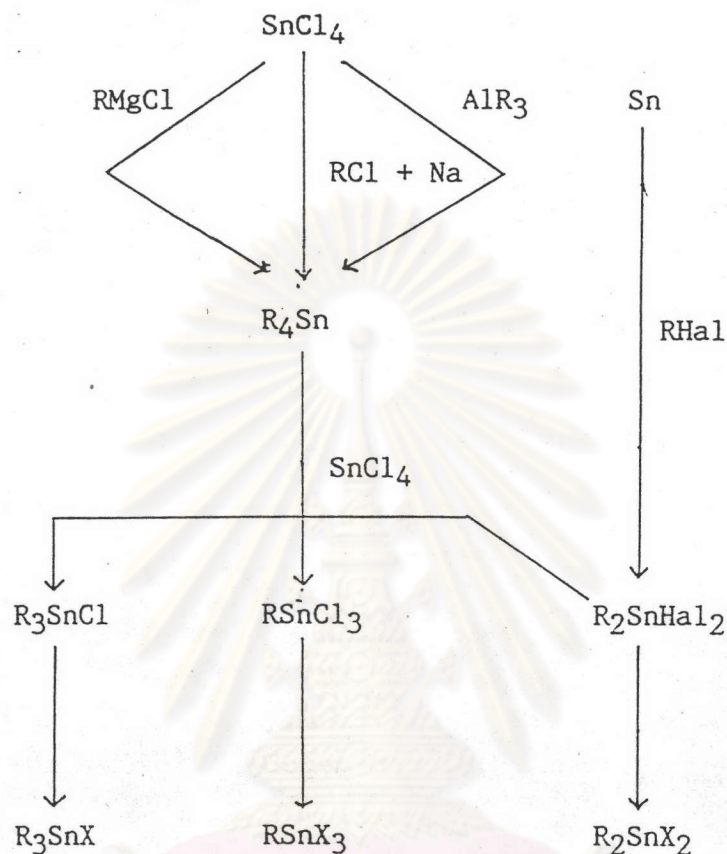The important methods of preparation of R_xSnX_{4-x} (X= 1-3) compounds are illustrated in Figure 1.

Fig. 1 Principal industrial manufacturing processes for organotin compounds

Most of industrially important processes produce the tetraorganotin compounds, from which other compounds are made by subsequent further reactions. The main process routes are the following:

1) Grignard method

$$SnX_4 \ + \ 4 \ RMgX \ \longrightarrow \ R_4Sn \ + \ 4 \ MgX_2 \qquad (1)$$
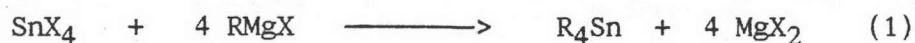
Mixed solvent systems are needed and large volumes are required, but the process is flexible, with high yields. It is the only feasible method for phenyltin compounds, but this method might not be available for other organotin compounds.

2) Wurtz method

$$SnCl_4 \ + \ 8 \ Na \ + \ 4 \ RCl \ \longrightarrow \ R_4Sn \ + \ 8 \ NaCl \qquad (2)$$

Again, large volume of solvent is required in this method to suppress the conversion of alkyl chloride, RCl, to hydrocarbon, R-R. The yields are usually only fair, and various kinds of side reaction also proceed.

The basic Wurtz reaction is applicable to almost all simple alkyl and aryl chlorides.

3) Aluminium alkyl method

$$3 \ SnCl_4 + 4 \ R_3Al + 4 \ R'_2O \ \longrightarrow \ 3 \ R_4Sn + 4 \ AlCl_3.R'_2O \qquad (3)$$
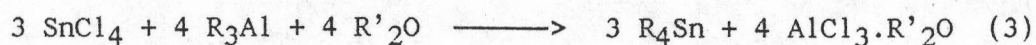
Only a small reaction volume is required, since no solvent is necessary, and the process can also be operated continuously. The presence of a complexing agent (such as an ether) is necessary for high efficiency. This method can be used to produce a wide range of tetraorganotins.

4) Direct Synthesis

One direct synthesis that can be used is the reaction between metallic tin and an alkyl iodide, using a suitable catalyst :

$$Sn + 2 RI \longrightarrow R_2SnI_2 \qquad (4)$$
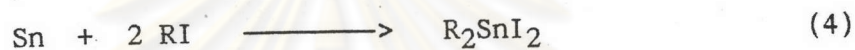
Only iodides give a suitable high reaction rate, and only dialkyltin species can be produced.

1.1 Organotin compounds

Organotin compounds are divided in four main groups.

1. Tetraorganotin compounds

2. Trioraganotin compounds

3. Diorganotin compounds

4. Monoorganotin compounds

### 1.1.1 Tetraorganotin compounds

Tetraorganotin compounds are substances of the

type R_4Sn in which the R groups may be alkyl or aryl. The tetraalkyltins are colorless, and the compounds of lower molecular weight are liquids at room temperature. The tetraaryltins are solids with melting points above 170 ^{O}C. The lower tetraalkyltins can be distilled at atmospheric pressure without decomposition. The lower molecular-weight compounds are soluble in the compare organic solvents. The higher molecular-weight substances are only sparingly soluble in many of the more common solvents and solution can be affected only by such solvents as benzene, pyridine or chloroform. These compounds are typical covalent bonds. They are quite stable in the presence of air or water and are unreactive in such organometallic reactions as addition to a carbonyl group. They are not highly sensitive toward strong aqueous bases but cleavage of the carbon-tin bond occurs readily with halogens, hydrogen halides, or strong aqueous acids.[5]

Tetraorganotin compounds have been prepared in numerous ways but two procedures have been employed most frequently. These are preparations involving the action of a moderately reactive organometallic compounds (such as Grignard reagents or an organolithium compounds) with tin(IV) chloride, and another preparation employing a tin-sodium alloy and an alkyl halides. The former method is superior either for laboratory

syntheses or for commercial processes, for example:

$$4RLi + SnCl_4 \longrightarrow R_4Sn + 4LiCl \qquad (5)$$

$$4RNa + SnCl_4 \longrightarrow R_4Sn + 4NaCl \qquad (6)$$
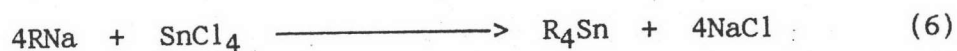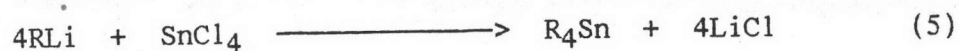
the aryl and allyllithiums can be prepared from the corresponding halides by reaction with lithium metal. A mole of lithium halide is produced as a by-product.

$$2Li + RX \longrightarrow RLi + LiX \qquad (7)$$
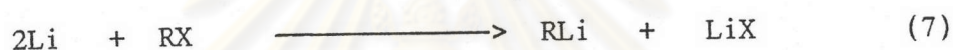
The similarity of the reaction of Grignard reagents and aryl lithium suggests that the latter might be useful in the synthesis of other organometallic compounds, especially since lithium derivatives of unusual types may be prepared. It has been shown that mercuric chlorides react readily with benzyllithium to form dibenzylmercury. In preliminary studies it was found that di-p-tolylmercury and tetra-p-tolyl tin could be easily prepared from p-tolyllithium and the corresponding metallic halides.[6]

$$2 RLi + HgCl_2 \longrightarrow R_2Hg + 2 LiCl \qquad (8)$$

$$4 RLi + SnCl_4 \longrightarrow R_4Sn + 4 LiCl \qquad (9)$$
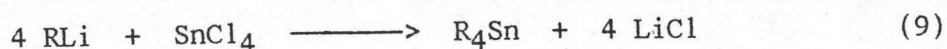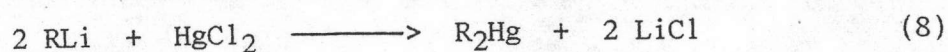
For the synthesis of the amino compounds, p-dimethylaminophenyl-lithium, $(CH_3)_2NC_6H_4Li$, was prepared from p-bromodimethylaniline. Unlike the Grignard reagent from this bromide, the lithium derivative could be prepared easily and smoothly in good yields. This reagent readily yielded tetra-(p-dimethylaminophenyl)-tin, $[(CH_3)_2NC_6H_4]_4Sn$, this amino compound was found to be well-characterized solids with definite melting points and was easily recrystallized from appropiate solvents.

The lithium derivatives can also be prepared by metal-halogen exchange. As a method for preparing organolithium compounds, the metal-halogen exchange reaction

$$R-Hal \ + \ R'-Li \ \longrightarrow \ R-Li \ + \ R'-Hal \qquad (10)$$
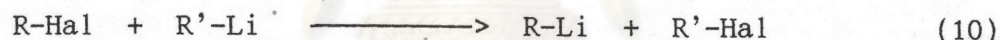
rival metallation. Because of the complexities by the constitution of organolithium compounds and by side reaction, the measuremant and interpretation of the kinetics of metal-halogen exchange reactions are extremely difficult. Nevertheless, the metal-halogen exchange reaction has generally been considered as polar (or concerted), and some possible representations for its mechanism are pictured below.[7]
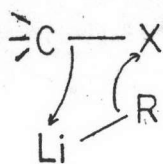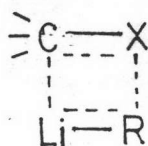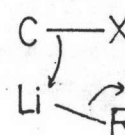
(I)   (II)   (III)

These diagrams represent variations on one theme a four-centered transition state. In (I), the dominating process is pictured as nucleophilic attack on halogen; in (III), the dominating process is pictured as electrophilic attack on carbon, and (II) represents a concerted process, with a true four-centered transition state. The available evidence does not enable a clear distinction to be made between these processes, although (I) and (II) are generally favored.
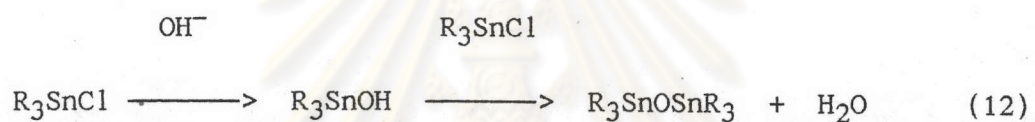
1.1.2 Triorganotin compounds

Triorganotin compounds are substances of the type R_3SnX in which the R groups may be alkyl or aryl and X may be halide, oxide, carboxylate etc. The compounds may be directly prepared by the reaction between organic halide compounds with tin metal. This reaction is especially for preparing tribenzyltin chloride as shown in Eq.(11).

$$3\ C_6H_5CH_2Cl\ +\ Sn\ \longrightarrow\ (C_6H_5CH_2)_3SnCl\ +\ SnCl_2 \qquad (11)$$
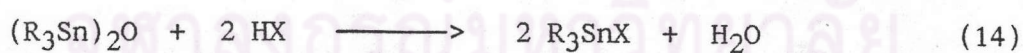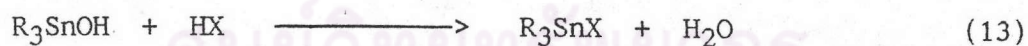
This reaction gives a good yield when water is used as solvent. If toluene is used as solvent, the reaction gives dibenzyltin dichloride instead.

Three alkyl or aryl groups of organotin halides can be hydrolysed with aqueous solution of sodium, potassium or ammonium hydroxide as shown in Eq.(12).

$$R_3SnCl\ \xrightarrow{\ OH^-\ }\ R_3SnOH\ \xrightarrow{\ R_3SnCl\ }\ R_3SnOSnR_3\ +\ H_2O \qquad (12)$$

Triorganotin hydroxide and oxide compounds are basic compounds which can react with an acid as shown in Eq.(13)-(14).

$$R_3SnOH\ +\ HX\ \longrightarrow\ R_3SnX\ +\ H_2O \qquad (13)$$

$$(R_3Sn)_2O\ +\ 2\ HX\ \longrightarrow\ 2\ R_3SnX\ +\ H_2O \qquad (14)$$

1.1.3 Diorganotin compounds

Diorganotin compounds are substances of the type

R_2SnX_2 in which the R groups may be alkyl or aryl and X may be halide, oxide, hydroxide and carboxylate, etc. The compounds may be directly prepared by the reaction between organic halide compounds with tin metal and copper or zinc as catalyst to give a good yield of dialkyldihalide.

$$2\ RX\ +\ Sn\ \xrightarrow{\quad Cu/Zn \quad}\ R_2SnX_2 \qquad\qquad (15)$$
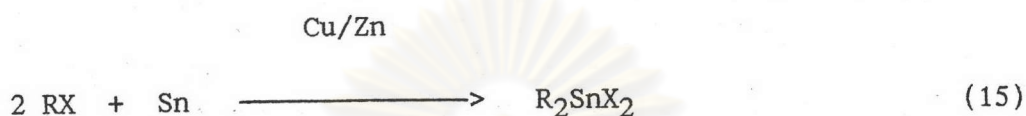
This classe of tin compounds is very important industrially, usage being prominant in the plastics field with application such as PVC stabilisers and catalysts for polyurethane and silicone production. They are characterised by generally low mammalian toxicity, and several compounds are approved for use in food-contact materials.[8]

1.1.4 Monoorganotin compounds

Monoorganoin compounds are substances of the type $RSnX_3$ in which the R group may be alkyl or aryl and X may be halide, oxide, hydroxide and carboxylate etc. The compounds can be prepared by the reaction between diorganotin dihalides with tin tetrachloride as shown in Eq.(16).

$$R_2SnCl_2 + SnCl_4 \longrightarrow 2 RSnCl_3 \qquad (16)$$
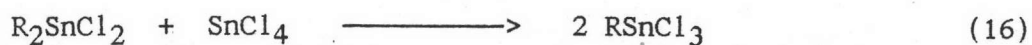
Monoorganotins have been comparatively little studied until recently, and their full potential has yet to be realised, their low mammalian toxicity is a notable advantage for future growth, and possible new application. The major industrial use of monoorganotins is for heat stabilisers in PVC, where they are used along with their dialkyltin analogues.

Beside the methods for preparing organotin compounds which were described above, there is another important method for preparing organotin compounds especially organotin halides. This reaction is redistribution reaction.

1.2 Redistribution reaction

The term "redistribution reaction" generally describes a chemical reaction in which two (or more) kinds of exchangeable substituents change sites with each other on one (or more) kinds of polyfunctional central moieties. The substituents as well as the central moieties may be made up of a number of atom which, however, under the specified experimental conditions, remain as intact entities. If allowed to proceed sufficiently long time at a proper reaction temperature, these reactions generally reach

an equilibrium state.

Redistribution reaction is meant to encompass such term as exchange, substituent exchange, scrambling, and ligand exchange reactions or ligand interchange, recognization, and distribution reactions and also the terms symmetrizations, dissymmetrizations, dispropotionations, compropotionations, or metatheses. Some of these latter ones have been used to name special phases of the general redistribution reaction (e.g. if the term compropotionation is used to describe a given reaction, its back reaction is then a dispropotionation).[9]
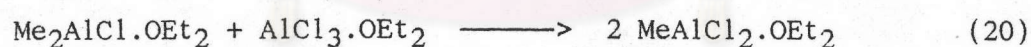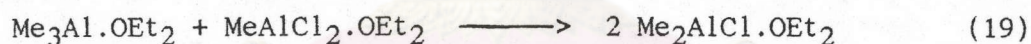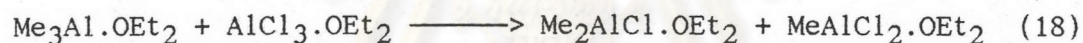
In the simplest form the redistribution reaction is defined by Eq (18):

$$M-R \; + \; M'-R' \; \longrightarrow \; M-R' \; + \; M'-R \qquad (17)$$
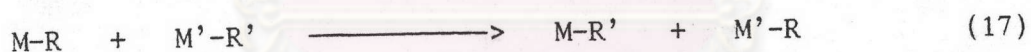
A group R on metal atom M moves to another metal atom M', while a group R' on M' moves to M. The significance and generality of the reaction appear to have been first realized by Calingaert and Beatty.[10] In recent years Lockhart [11] and Moedritzer [12] have reviewed the reaction generally. Van Wazer and Moedritzer have dealt in detail with the redistribution reactions of the organometallic compounds of silicon and germanium, [13] giving

particularly valuable treatments of the equilibrium aspects of redistribution, but devoting little attention to the kinetic features of the reaction.

In general the metal atoms, M and M', of Eq.(17) are multivalent. Hence in practice, redistribution is often not a single reaction, but a sequence of related reactions. For example, reaction of trimethylaluminium with aluminum chloride in ether to produce either dimethylaluminum chloride or methyl-aluminum dichloride require two redistributions: either Eq.(18) followed by Eq.(19), or Eq.(18) followed by Eq.(20).[14]

$$Me_3Al.OEt_2 + AlCl_3.OEt_2 \longrightarrow Me_2AlCl.OEt_2 + MeAlCl_2.OEt_2 \quad (18)$$

$$Me_3Al.OEt_2 + MeAlCl_2.OEt_2 \longrightarrow 2 Me_2AlCl.OEt_2 \quad (19)$$

$$Me_2AlCl.OEt_2 + AlCl_3.OEt_2 \longrightarrow 2 MeAlCl_2.OEt_2 \quad (20)$$

Furthermore, the groups R, exchanged in a redistribution, are not neccessarily monovalent. The formation of silicone polymers depends upon repeated redistribution reactions in which the exchanging groups are divalent oxygen atoms. Even if R is nominally monovalent (e.g., CH_3-, $Cl-$, $PhC=C-$), it is not neccessarily monocoordinate.
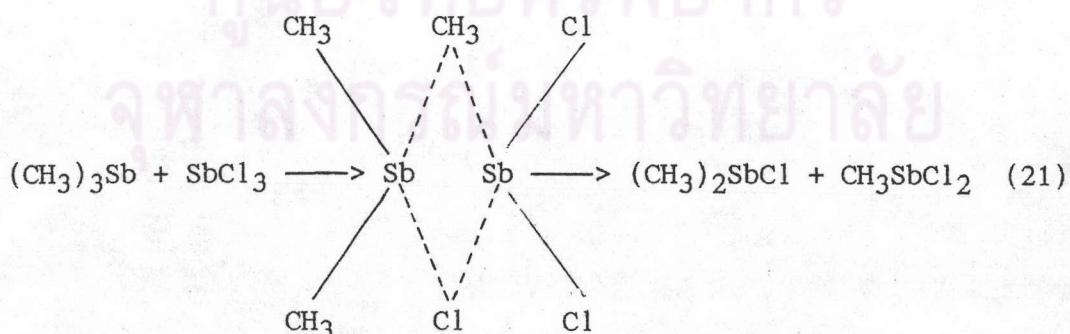
Redistribution reactions originally served as a synthetic method for the preparation of certain classes of compounds. Recently, however,[15,16] a large body of information was collected which was aimed toward the quantitative study of redistribution equilibria by physical tools such as nuclear magnetic resonance, gas chromatography, mass spectrometry, etc. In many of the latter studies, however, these reactions have not been examined in detail with respect to their synthetic utility.

1.2.1 Mechanism of the reaction

Although redistribution reactions have been observed as early as more than a hundred years ago, it is rather surprising that it was not until about 1940 that the equilibrium nature of this type of reaction was recognized. Calingaert and his co-workers have applied the laws of probability to a quantitative interpretation of the "random distribution" of exchanging substituents found in certain systems such as the lead alkyls. An outstanding early landmark in developing the logic of this type of reactions applied to the redistribution of molecular segments in large molecules was made by Flory,[18] also in this period.

Redistribution reactions in general may be acid catalyzed, base catalyzed, or thermally induced. The rates of redistribution reactions may vary greatly depending on the nature of the central atoms or moieties and of the exchanging substituents. As a rule of thumb, redistribution involving First-Row element as the central atom generally proceed slower than those Second-Row elements, and the latter are slower than those of a Third- or Fourth-Row element. Also exchanges involving carbon-metal bonds are much slower than exchanges involving hydrogen, halogen, sulfur, oxygen, or nitrogen bonds to the metal.

It is generally assumed that the interchange of substituents between central moieties are bimolecular and proceed through a four-center activated complex. For the system of antimony trichloride-trimethylantimony, initial rate measurements have shown that the first step reaction is first order in each

$$(CH_3)_3Sb + SbCl_3 \longrightarrow \begin{array}{c} CH_3 \quad CH_3 \quad Cl \\ Sb \quad\quad Sb \\ CH_3 \quad Cl \quad Cl \end{array} \longrightarrow (CH_3)_2SbCl + CH_3SbCl_2 \quad (21)$$

component and that the rate constants are consistent with a mechanism involving the formation of the four-center transition state as shown in Eq. (21). The relatively large negative activation entropy (-25 e.u.) for this reaction is in agreement with values obtained for other bimolecular reactions believed to involve two sites for attachment in the transition state.

Also, catalytic reactions are likely to proceed via four-center activated intermediates. Exchanges involving boron-carbon bonds generally require strongly forcing conditions, often temperatures in the range of 200-300 $^{\circ}$C. However, in the presence of B-H containing substances, such as diborane or tetraalkyldiboranes, the exchange of B-C bonds with B-X bonds (X = alkyl, halogen, OR, SR) proceeds under mild conditions probably with the catalyst participating in a bridge mechanism. [18]
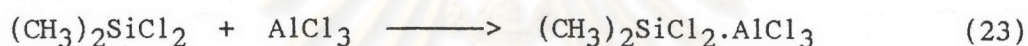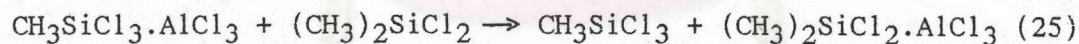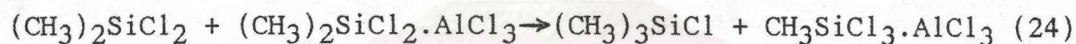

$$(22)$$
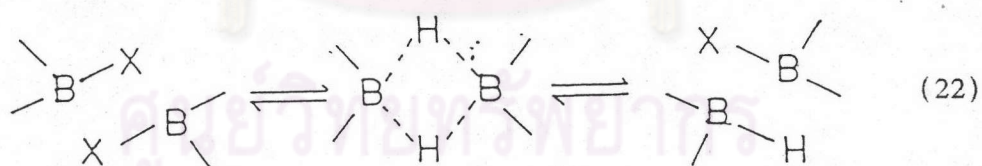
Another example of a catalytic dispropotionation is the redistribution of methyl groups and chlorines in the methylchlorosilanes in the presences of AlCl$_3$. Based on a thorough kinetic study,[19] any mechanism will have to take into

account the following facts: (a) the rate is a linear function of the $AlCl_3$ concentration; (b) the reaction is first order in chlorosilanes; (c) the rate equation must reduce to equilibrium constants when the change in concentration with time is zero; (d) substantially all the aluminum chloride is associated in some manner with the chlorosilanes.

A most reasonable mechanism which fits all these requirements is the following. The reaction

$$(CH_3)_2SiCl_2 + AlCl_3 \longrightarrow (CH_3)_2SiCl_2.AlCl_3 \qquad (23)$$

goes to completion before either one of the two reactions

$$(CH_3)_2SiCl_2 + (CH_3)_2SiCl_2.AlCl_3 \rightarrow (CH_3)_3SiCl + CH_3SiCl_3.AlCl_3 \quad (24)$$

$$CH_3SiCl_3.AlCl_3 + (CH_3)_2SiCl_2 \rightarrow CH_3SiCl_3 + (CH_3)_2SiCl_2.AlCl_3 \quad (25)$$

start to take place. The latter reaction, which merely involves the transfer of aluminium chloride from one silane to another, must be very much more mobile than the preceding reaction, where rupture and formation of both silicon-carbon and silicon-chlorine bonds are involved. Very probably the aluminum chloride is attached to the chloride of the chlorosilane. This weakens the

Si-Cl bond and when a collision occurs with another chlorosilane molecule, the two silicons exchange $AlCl_4^-$ and CH_3^- or $AlCl_4^-$ and Cl^-. Since halogen attached to silicon exchange quite easily, only a relatively few collision will have the correct orientation implies a low entropy of activation.
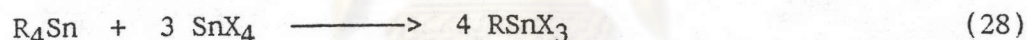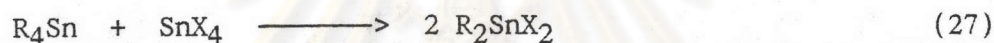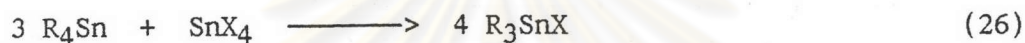
These few studies make it appear very likely that mechanism involving four-center transition states will be common in redistribution reactions. However, it is not yet possible to predict a mechanism on an a priori basis.

Somewhat more complicated mechanisms are involved when one of the exchanging substituents is difunctional, thus resulting in various kinds of oligomeric and polymeric structures. Although the synthetic utility of these kinds of redistribution reactions is obvious, very little work has been done toward the elucidation of mechanisms in these systems.

### 1.2.2 Redistribution reaction of organotin compounds

The redistribution of tin tetralkyls or aryls with tin tetrahalides is perhaps the most thoroughly studied reaction of this type. As early as 1859 and 1862, reports have appeared describing the reaction of tetrabutyltin and tin tetrachloride.

Subsequently many papers were published reporting the preparation of alkyl or arylchlorostannanes by compropotionation of the tetraalkyl or aryl compounds with the tetrahalides. These reactions generally proceed with remarkable ease, sometimes even at room temperature. This method was first introduced by Kocheskov to obtain mono-, di- or tri-organotin halides. Depending on the molar ratio of the reactants one out of the three following reactions seems to proceed :

$$3 R_4Sn + SnX_4 \longrightarrow 4 R_3SnX \qquad (26)$$

$$R_4Sn + SnX_4 \longrightarrow 2 R_2SnX_2 \qquad (27)$$

$$R_4Sn + 3 SnX_4 \longrightarrow 4 RSnX_3 \qquad (28)$$

For R= C_6H_5, $C_6H_4CH_3$, $CH_2=CH-$, and X= Cl and Br, very good yields of the various reaction products could be obtained. When R is CH_3, $n-C_3H_7$ and $CH_3-CH = CH-$ only the reactions of types (26) and (27) are effective. In general the reaction is carried out by heating a mixture of suitable mole ratio of tetra-organotin and stannic tetrachloride with or without solvent. The temperature usually reaches 200 $^{\circ}C$ unless a catalyst, for example SnF_2, is used to lower the temperature.[20] Nevertheless, the reaction condition is still too rigorous for the thermally
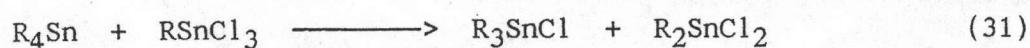
unstable groups which may be present in the tetraorganotin compounds such as tetrakis-(4-dimethylaminophenyl)stannane. Industrially, the di-, and tri-alkyltin chloride are manufactured by this redistribution method, simply by heating the components, in the absence of solvent, to approximately 200 ^{o}C for a period of hours. With regard to the monoorganotin compounds, $RSnX_3$, only phenyltin trichloride may be successfully produced by this method. The reason for this becomes clear when additional reactions to those above are considered. In all cases, a reaction between R_4Sn and $SnCl_4$ proceeds very rapidly. [21] :

$$R_4Sn \ + \ SnCl_4 \ \longrightarrow \ R_3SnCl \ + \ RSnCl_3 \qquad\qquad (29)$$
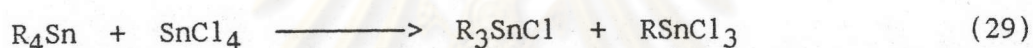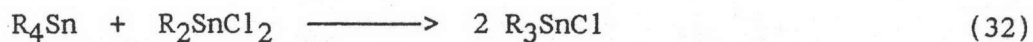
At elevated temperatures, secondary reactions then take place. For example, when equimolar amounts of R_4Sn and $SnCl_4$ are present the following reaction occurs :
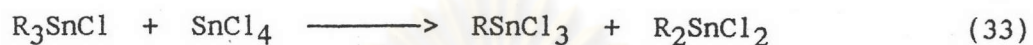
$$R_3SnCl \ + \ RSnCl_3 \ \longrightarrow \ 2\ R_2SnCl_2 \qquad\qquad (30)$$
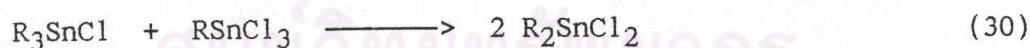
whereas when an excess of R_4Sn is present, the secondary reactions are as follows :

$$R_4Sn \ + \ RSnCl_3 \ \longrightarrow \ R_3SnCl \ + \ R_2SnCl_2 \qquad\qquad (31)$$

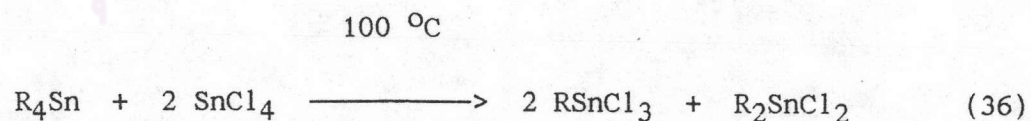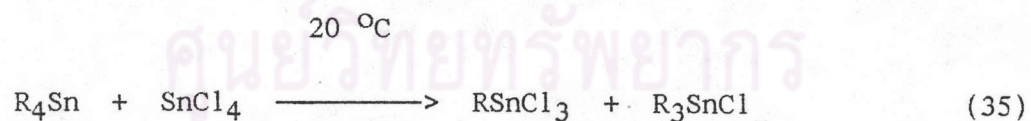$$R_4Sn \ + \ R_2SnCl_2 \ \longrightarrow \ 2 \ R_3SnCl \tag{32}$$

However, in an excess of $SnCl_4$, the following additional reactions must occur, in order to achieve complete formation of the monoorganotin compound :

$$R_3SnCl \ + \ SnCl_4 \ \longrightarrow \ RSnCl_3 \ + \ R_2SnCl_2 \tag{33}$$

$$R_2SnCl_2 \ + \ SnCl_4 \ \longrightarrow \ 2 \ RSnCl_3 \tag{34}$$

Unfortunately, the reaction between R_2SnCl_2 and $SnCl_4$ is extremely slow, except when R= Ph. Consequently, the monoalkyltin trichlorides are produced industrially by partial redistribution, by reaction of tetraorganotin and tin (IV) chloride, either in equimolar amounts at approximately 20 ^{O}C, or in 1:2 ratio at approximately 100 ^{O}C.

$$R_4Sn \ + \ SnCl_4 \ \xrightarrow{\text{20 }^{O}C} \ RSnCl_3 \ + \ R_3SnCl \tag{35}$$

$$R_4Sn \ + \ 2 \ SnCl_4 \ \xrightarrow{\text{100 }^{O}C} \ 2 \ RSnCl_3 \ + \ R_2SnCl_2 \tag{36}$$

The monoorganotin compound is seperated from the reaction

products by vacuum distillation.

In 1953, it was shown that when the redistribution between Bu_4Sn and $SnCl_4$ is carried out at temperatures between 0 °C and 20 °C an equimolar mixture was obtained of Bu_3SnCl and $BuSnCl_3$, which corresponds to the following reaction equation

$$Bu_4Sn + SnCl_4 \longrightarrow Bu_3SnCl + BuSnCl_3 \qquad (37)$$
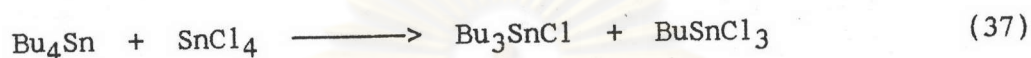
Although it has been stated that these redistribution reactions are "undesirable for the preparation of organotin halides in which all of the organic groups are not identical,"[22] they have not been investigated in detail.

It was found that under appropiate conditions redistribution analogous to that of Eq.(30) can provide an easy route for the preparation of mixed organotin dihalides, $RR'SnX_2$. In some cases even organotin monohalides with three different alkyl or aryl groups can be prepared. The alkylation of butyltin trichloride with tetramethyltin was exothermic yielding trimethyltin chloride and butylmethyltin dichloride. However, some dimethyltin dichloride and butyldimethyltin chloride were formed as shown in Eq.(38).

$$Me_4Sn + BuSnCl_3$$

$$\downarrow$$

$$Me_3SnCl + BuMeSnCl_2 + Me_2SnCl_2 + BuMe_2SnCl \qquad (38)$$
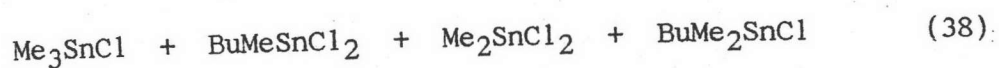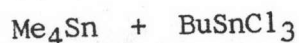
1.3 Applications of organotin compounds

Organotin compounds have found applications in several areas and hence are made industrially in large scale. The first application of organotin compounds has been in the stabilization of polyvinyl chloride (PVC) to prevent thermal degradation during processing and long-term photodegradation.

The organotin compounds are used as PVC stabilizers, antifoulants, agrochemicals, pharmaceuticals, etc. The major applications are found by taking of two properties of tin: the first is the strong affinity for donor atoms such as oxygen and sulfur, and the second is its physiological activity as in biocides and rodent repellents. The first property can be used for PVC stabilizers, other polymer stabilizers and reagents for organic synthesis. The other uses involve the application of mainly the second property. The wide range of industrial applications of organotin chemicals, and the specific compounds

used are shown in Table 1. Organotin compounds are often effective in very low concentrations in many applications, which is advantageous from a formulation and cost effectiveness point of view. The biocide properties of triorganotin derivatives are used in area like textile, wood or paint protection, antifouling paint and pesticide or insecticides in agriculture. Triorganotin compounds are the most popular, but triphenyl or tricyclohexyl derivatives are also in used while other organotins have more limited applications.

The applications of organotin compounds in the pharmaceuticals fields are veterinary medicine, and recently there have been additional developments in radiopharmacology and chemotherapy. Although not used at the present time, certain organotin complexes have shown potential as an antitumour drugs. Another potential medical use for organotin compounds is in the chemotherapy of leishmaniasis, a parasitic infection which affects the skin. In a screening program of 68 compounds, dioctyltin maleate showed one of the highest in vivo activities when tested against Lieshmania major, a close relative to Trypanosoma, in mice.[23]

Table 1 Industrial applications of organotin compounds

Application	Compound
	R_3SnX
Agriculture (fungicides)	$(C_6H_5)_3SnX$ (X = OH, OAc)
(antifeedants)	$(C_6H_5)_3SnX$ (X = OH, OAc)
(acaricides)	$(c\text{-}C_6H_{11})_3SnX$
	$(X = OH, -\overline{N.C{=}N.C{=}N})$
	$\quad\quad\quad\quad\quad\quad\,\underset{H}{|}\quad\underset{H}{|}$
	$(C_6H_5(CH_3)_2CCH_2)_3Sn)_2O$
Antifouling paint biocides	$(C_4H_9)_3SnX$ (X = OH, OAc, F, Cl, SCS.N(CH_3)_2, OCOCH_2Cl, OCOC_6H_4N\text{-}3)
	$(C_4H_9)_3SnOCOCH_2CBr_2COOSn(C_4H_9)_3$
	$(C_6H_5)_3SnX$ (X = F, Cl, OAc)
	$((C_4H_9)_3Sn)_2O$
	$(C_4H_9)_3SnOCOCH_2CBr_2COOSn(C_4H_9)_3$
	$(C_4H_9)_3SnOCO(CH_2)_4COOSn(C_4H_9)_3$
	$(-CH_2C(CH_3)(COOSn(C_4H_9)_3)-)_n$
Wood preservative fungicides	$((C_4H_9)_3Sn)_2O$
	$(C_4H_9)_3Sn(naphthenate)$
	$((C_4H_9)_3Sn)_3PO_4$
Stone preservation	$((C_4H_9)_3Sn)_2O$
Disinfectants	$(C_4H_9)_3SnOCOC_6H_5$
	$((C_4H_9)_3Sn)_2O$
Molluscicides (field trials)	$(C_4H_9)_3SnF$
	$((C_4H_9)_3Sn)_2O$
	R_2SnX_2
Heat and light stabilizers for rigid PVC	$R_2Sn(SCH_2COO\text{-}i\text{-}C_8H_{17})_2$ (R = CH_3, C_4H_9, C_8H_{17}, (C_4H_9)OCOCH_2CH_3)
	$(R_2SnOCOCH{=}CHCOO)_n$ (R = C_4H_9, C_8H_{17})
	$(C_4H_9)_2Sn(OCOCH{=}CHCOOC_8H_{17})_2$
	$(C_4H_9)_2Sn(OCOC_{11}H_{23})_2$
	$(C_4H_9)_2Sn(SC_{12}H_{25})_2$
Homogeneous catalysts for RTV silicones, polyurethane foams and transesterification reactions	$(C_4H_9)_2Sn(OCOCH_3)_2$
	$(C_4H_9)_2Sn(COO^iC_8H_{17})_2$
	$(C_4H_9)_2Sn(OCOC_{11}H_{23})_2$
	$(C_4H_9)_2Sn(OCOC_{12}H_{25})_2$
	$((C_4H_9)_2SnO)_n$
Precursor for forming SnO_2 films on glass	$(CH_3)_2SnCl_2$
Anthelmintics for poultry	$(C_4H_9)_2Sn(OCOC_{11}H_{23})_2$

1.4 Trypanosomal disease

Trypanosomal diseases have been one of the major problems in tropical area especially in Africa, central and south America. In Africa, Trypanosoma brucei rhodensiense (east Africa) and T.b.gambiense (central and west Africa) are the causative agents for sleeping sickness. A study by WHO between 1989-1990 estimates that as many as 25,000 cases reported each year and 50 millions people in 36 countries are on the risk to this disease.[24] Chagas disease, widely spreads in central and south America, is caused by another species of trypanosome, T.cruzi. There is no effective way to treat Chagas disease eventhough this disease has been recognized since 1909. The diseases can be transmitted from man-to-man, animal-to-man or vice versa by blood sucking insect, i.e. tse'-tse' fly, triatome. Thus, controlling these diseases is very difficult. The figures of Trypanosoma and Trypanosoma's life cycle were shown in Fig 2 and 3, respectively.

Treatment of trypanocidal diseases are always difficult especially when the diseases invade central nervous system. The people who are infected with this disease usually died.

In 1901, Lansberger found a drug for treatment of sleeping sickness, Atoxyl or sodium salt of 4-aminophenylar-senate, but it was toxic when administered continuously.[25]
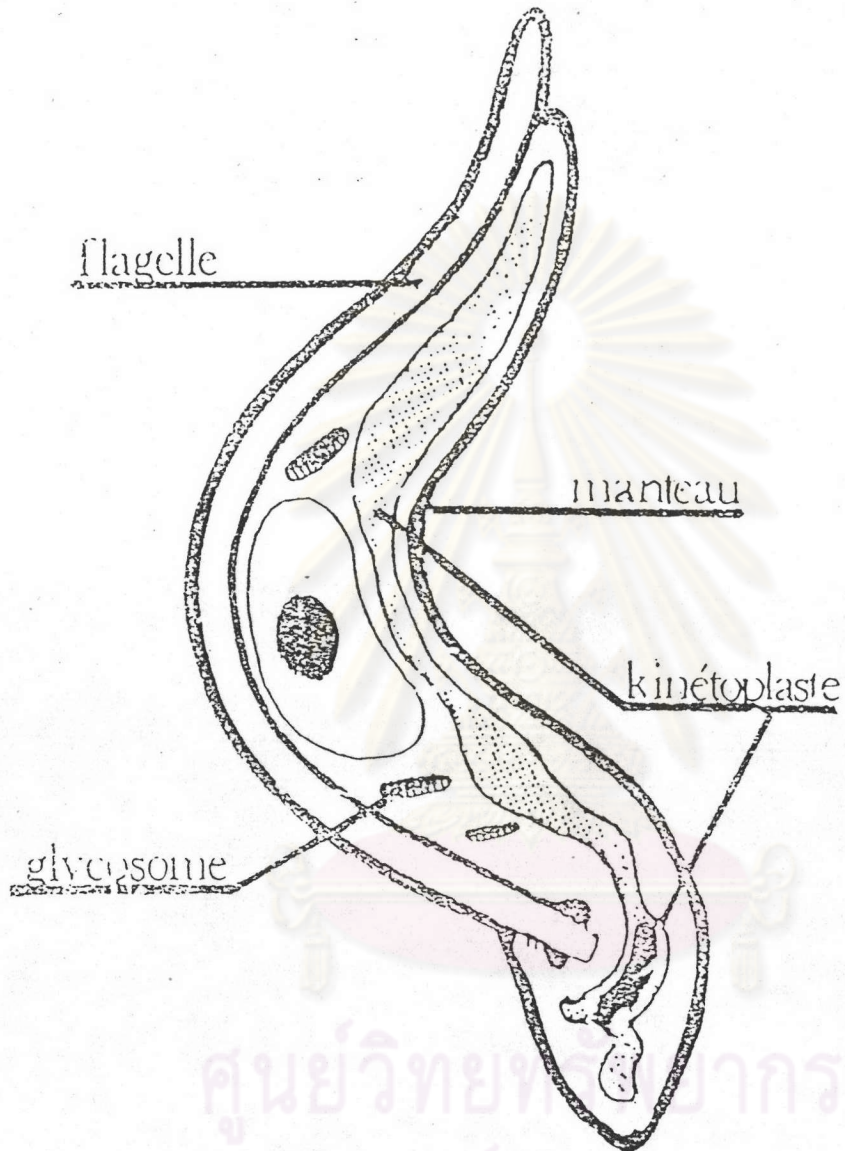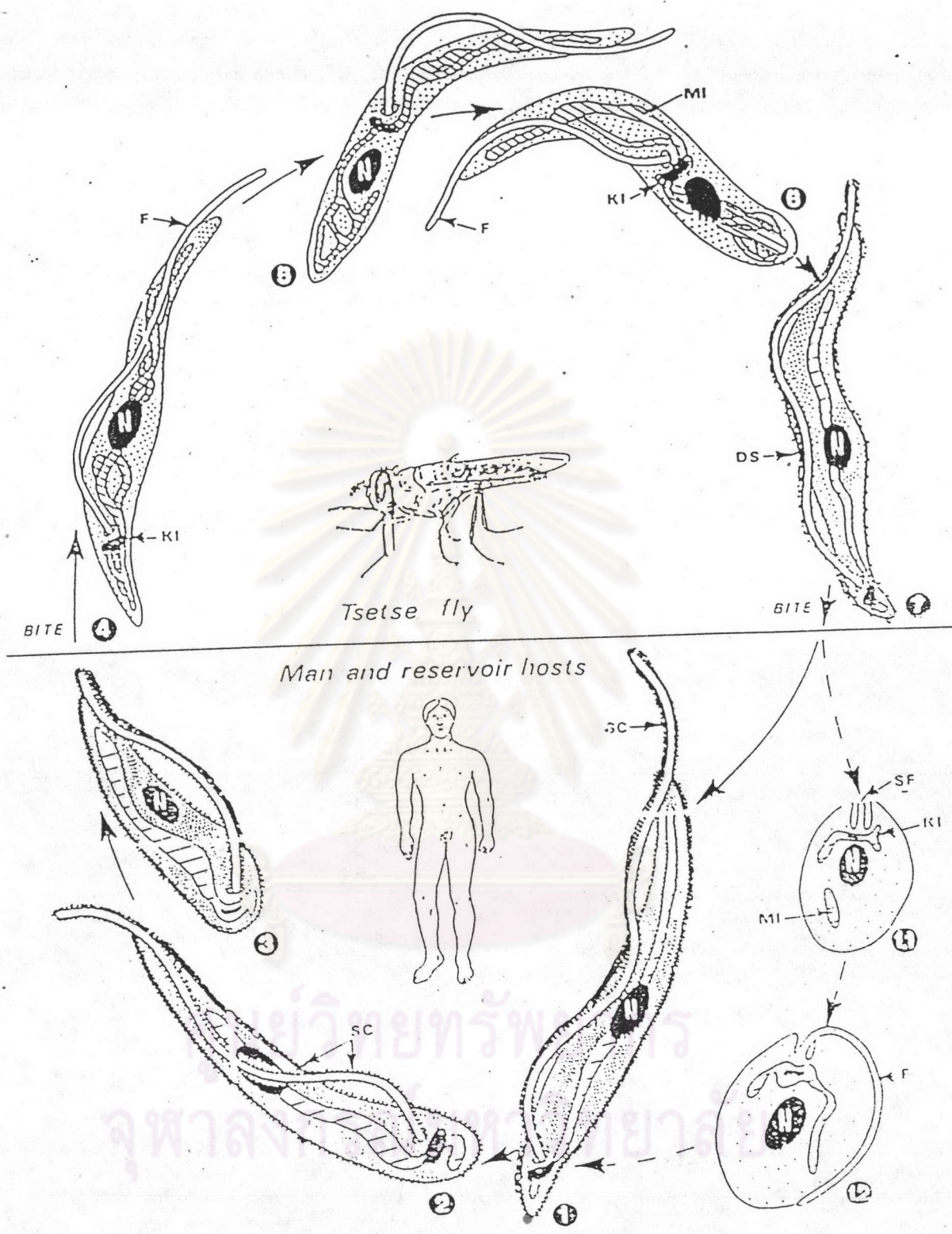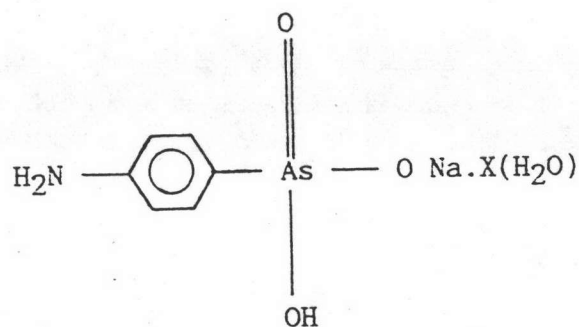
Figure 2   The figure of Trypanosoma

Figure 3 Life cycle of Trypanosoma

$$H_2N - \underset{\underset{OH}{\overset{\overset{O}{\parallel}}{As}}}{} - O \; Na.X(H_2O)$$

Sodium 4-aminophenylarsenate

In 1910, Plimmer and Bateman studied the curative effects of the drugs against nagana, disease which is caused by T.b. brucei, and surra in rats and dogs. The metallic antimony (Sb) was found to give the most favorable results.[26]

Treatments of trypanosomal diseases were studied in many cases. However, at present, there are a few drugs that are effective in treatment of this disease. Pentamidine, a drug used to treat the first period of infection by T.b.gambiense, is not effective in the second period of infection. Moreover, the parasites develope their resistant to pentamidine. Suramine is very effective in treatment of the early state of infection from T.b.rhodensiense and T.b.gambiense but this drug sometime creates undesire secondary effect, i.e. renal problem. A few arsenical compounds, for example, melarsoprol (Mel W) are used to treat trypanocidal infection to the central nervous system but their

toxicity prohibit prolonged usage. Structures of pentamidine, suramine and melarsoprol were shown in Table 2.

Table 2 The structures of drugs for treatment of trypanosomal diseases.

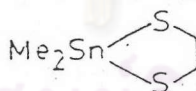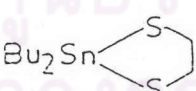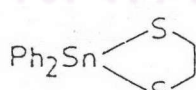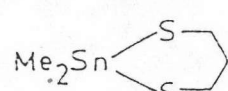| Drugs	Structure
Pentamidines	
Suramine	
Melarsoprol (Mel W)	

Organotin compounds are known to form strong Sn–S bond with the thiol group.[27] The biological activity of diorganotin compounds and enzymes has to contain active dithiol moiety. Many biological activities of organotin compounds are known, for

example fungicides, bacteriocides, ascaricides, and anti-tumour. Therefore, in 1991, A. petsom and G.Deleris [28] studied trypanocidal activity of organotin compounds. The results of the study of the in vitro trypanocidal activity of diorganotin disulfides were reported in Table 3.

The in vitro trypanocidal activity of organotin sulfides from Table 3 showed that organotin sulfides were effective against T.cruzi. Selected samples that showed strong activity were tested in mices infected with T.cruzi, but none of them showed activity in vivo because organotin compounds are not soluble in water , so they could not be dissolved in blood but Mel W could because of aminotriazine group. Thus such organotin compounds should have amino groups. Since these organotin compounds could not be prepared by the general methods, redistribution reaction was studied and this reaction of organotin compounds containing amino groups never been studied, it is valuable to study. Furthermore, organotin compounds are cheaper, less toxic and similar to oraganoarsenic or organoantimony compounds. Therefore, organotin compounds containing amino groups were studied by synthesis the compounds, which were similar to melarsoprol structure, might have trypanocidal activity.

Table 3 In vitro trypanocidal activity of diorganotin disulfides
against T.cruzi.

COMPOUND NO.	STRUCTURE	*conc.(μg/mL)
1	$Me_2Sn(SCH_2CH_2CH_3)_2$	2.5
2	$Bu_2Sn(SCH_2CH_2CH_3)_2$	$3*10^{-3}$
3	$Ph_2Sn(SCH_2CH_2CH_3)_2$	$25*10^{-3}$
4	$Me_2Sn[S(CH_2)_7CH_3]_2$	2.5
5	$Bu_2Sn[S(CH_2)_7CH_3]_2$	$4.8*10^{-3}$
6	$Ph_2Sn[S(CH_2)_7CH_3]_2$	$78*10^{-3}$
7	$Me_2Sn{\Large\langle}\begin{smallmatrix}S\\S\end{smallmatrix}{\Large\rangle}$	2.5
8	$Bu_2Sn{\Large\langle}\begin{smallmatrix}S\\S\end{smallmatrix}{\Large\rangle}$	$9.7*10^{-3}$
9	$Ph_2Sn{\Large\langle}\begin{smallmatrix}S\\S\end{smallmatrix}{\Large\rangle}$	1.25
10	$Me_2Sn{\Large\langle}\begin{smallmatrix}S\\S\end{smallmatrix}{\Large\rangle}$	2.5

(continued)

COMPOUND NO.	STRUCTURE	* conc.(μg/mL)
11	Bu$_2$Sn(S-CH$_2$CH$_2$-S)	$0.75*10^{-6}$
12	Ph$_2$Sn(S-CH$_2$CH$_2$-S)	$3*10^{-3}$
13	Bu$_2$Sn(S-CH$_2$-CH(CH$_2$OH)-S)	$19.5*10^{-3}$
14	Bu$_2$Sn(S-pyridyl)$_2$	$78*10^{-3}$
15	Bu$_2$Sn(S-pyrimidinyl)$_2$	$15*10^{-3}$
16	Bu$_2$Sn(S-benzoxazolyl)$_2$	$0.4*10^{-3}$
17	Bu$_2$Sn(S-benzothiazolyl)$_2$	$0.4*10^{-3}$
18	Bu$_2$Sn(S-chlorobenzothiazolyl)$_2$	$31*10^{-3}$
19	(Me$_2$N-C$_6$H$_4$)$_{1/2}$Sn-(SCH$_2$CH$_2$CH$_3$)$_2$	1.25
20	ARSOBAL	$2*10^{-3}<CA<25*10^{-3}$
21	CYMELARSAN	$0.25*10^{-3}<CA<1.6*10^{-3}$

1.5 Objectives

The objectives are the studying of redistribution reaction of organotin compounds containing amino groups for synthesizing organotin derivatives which may have trypanocidal activity.