ORGANOTIN REAGENTS TOWARD THE PREPARATION OF CYCLIC DISULFIDES AND RELATED COMPOUNDS

by

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ABSTRACT

Aspects of the chemistry of organotin-sulfur derivatives have been investigated. A series of symmetrical disulfides was prepared by halogen oxidation of the corresponding tri-n-butyl alkylthio or tri-n-butyl arylthiotin(IV) compounds. Similarly, cyclic disulfides (5- to 12-membered size ring) were prepared using the appropriate μ-α,ω-alkyldithiohexa-n-butylditin(IV) species or 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes. The synthesis of the cyclic disulfides did not require any special high dilution techniques. Synthetic procedures for the synthesis of the tin-sulfur derivatives are described. The effectiveness of organotin reagents in the synthesis of cyclic disulfides is examined. Studies on reaction kinetics and competition reactions were carried out to provide information on the mechanism of halogen oxidation of the tin-sulfur species.

The coupling of sulfinyl chlorides with tri-n-butyltin lithium afforded symmetrical thiosulfonates; these thiosulfonates were likely provided via rearrangement of vic-disulfoxides. Low temperature ^{13}C-NMR supports this.

The use of organotin-sulfur derivatives as sulfhydryl protecting groups or as reagents for the synthesis of substituted thiophenes was examined.

The desulfurization of 1,2-dithiepane 1,1-dioxide was accomplished; this provided insight on the desulfurization of cyclic thiosulfonates.

Ph.D. Steve J. Bodzay Chimie

L'EMPLOI DE REACTIFS ORGANOSTANNIQUES DANS LA PREPARATION DE DISULFURES CYCLIQUES ET DE COMPOSES APPARENTES

RESUME

Plusieurs aspects de la chimie des dérivés organostanniques furent étudiés. Une série de disulfures symétriques ont été préparés par oxydation halogénique des composés tri-n-butyle alkylthiostanniques(IV) ou tri-n-butylarylthiostanniques(IV) correspondants. De même, des disulfures cycliques de 5 à 12 membres furent préparés à partir des espèces μ-alkyldithio-α,ω hexa-n-butylbisstanniques(IV) ou de di-n-butyl-2,2 dithiastanna-1,3,2 cycloalkanes sans exiger de grandes dilutions. Les dérivés stannosulfurés furent synthétisés et l'efficacité des réactifs organostanniques dans la synthèse de disulfures cycliques fut évaluée. L'étude de la cinétique réactionnelle et des réactions compétitives ont été effectuées dans le but d'éclaircir le mécanisme d'oxidation halogénique de l'espèce stannosulfurée.

La réaction des chlorures sulfiniques avec le tri-n-butylstannure de lithium a produit des thiosulfonates symétriques résultant vraisemblablement du réarrangement de disulfoxydes vicinaux (études de RMN ^{13}C à basse température à l'appui).

L'utilisation de dérivés organostannosulfurés comme groupements protecteurs des fonctions sulfhydriles ou comme réactifs dans la synthèse de thiophènes substitués a été mise à l'épreuve.

La désulfurisation du dioxyde-1,1 de dithiépane-1,2 fut effectuée; ceci a fourni quelques indications en ce qui a attrait à la désulfurisation de thiosulfonates cycliques.

To Deborah

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S.J. Bodzay

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LIST OF ABBREVIATIONS

Å	angstrom
bp	boiling point
Bu	butyl
Bz	benzyl
cm	centimeter
Et	ethyl
FT	Fourrier transform
g	gram
GC	gas chromatography
h	hour
IR	infrared
kg	kilogram
lit	literature
m	meter
M	molar
Me	methyl
mg	milligram
min	minute
ml	milliliter
mm	millimeter
mmol	millimole
mp	melting point
MS	mass spectroscopy
nm	nanometer
NMR	nuclear magnetic resonance

Ph	phenyl
ppm	parts per million
RT	retention time
s	second
$t_{\frac{1}{2}}$	half life
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	tetramethylsilane
Trityl	triphenylmethyl
UV	ultraviolet

CHAPTER 1

INTRODUCTION

1.1 A Brief History of Sulfur and Tin.

It is of interest that while sulfur and tin have been known since antiquity, little research into the combination of these two elements has been carried out until very recently.

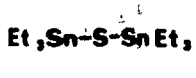
In the Bible, sulfur is referred to as brimstone. The Chinese adeptly experimented with combinations of saltpetre (potassium nitrate), charcoal and sulfur for use firstly in public firework displays and then for military purposes.[1] This formulation for gunpowder may have been used as early as ca. 2000 B.C. by the Chinese mandarin Wan Pou, but more conservative estimates place the first use of this explosive at about the first century A.D.[2] Tin is a component of the alloy bronze from which the era of ca. 3500-2500 B.C. takes its name.[3]

Organosulfur chemistry began in 1833-1834 when the Copenhagen professor Zeise prepared ethanethiol (C_2H_5SH).[4,5] After obtaining the mercaptan (thiol), Zeise also prepared diethyl disulfide.[6] There was no looking back and organosulfur chemistry is now an important branch of organic chemistry.

The first organotin compounds were diethyltin species. Frankland prepared diethyltin diiodide in 1849, but it was not characterized as such until a few years later. He synthesized diethyltin dichloride and diethyltin oxide in 1853.[7] In 1861 Kekulé pronounced the following: " I cannot resist the opportunity of once again drawing the attention of chemists to the analogy between tin compounds and carbon compounds...."[7]

After 1880, the study of alkyltin compounds faded but the discovery of industrial applications for organotins brought about a renaissance which started around 1949.[7]

In 1860, Kulmitz investigated the reaction of triethyltin bromide and hydrogen sulfide, which afforded "stannethyl sulfide" (1), [bis(triethyltin) sulfide]. This was the first reported compound containing a covalent tin-sulfur bond.[8] The discovery in 1950 that compounds of the type (2) stabilized polyvinyl chloride stimulated the modern interest in tin-sulfur chemistry.[9]



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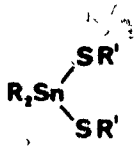


(2)

1.2 Odor of Sulfur Chemistry and Sulfur Chemists.

The adjectives used to describe the unpleasant odor of organosulfur compounds and the chemists who work with these compounds are many. All convey the notion that sulfur chemists are bearers of ill wind. The obnoxious odor from one notorious class of sulfur derivatives has led to the evacuation of buildings and on at least one occasion the flight of commuters from an entire section of a subway train.

Low molecular weight thiols are the most notorious, as Field points out[10] in the following fashion: "A few bigots complain that volatile disulfides have disagreeable odors, but at least complaints are much less strident than against thiols." In conjunction with their work on sulfur compounds in plants, Ettlinger and Kjaer pronounced: "The odors

of divalent sulfur compounds are not always pleasant, but they confer on this area of natural products a homely appeal...".[11] Lastly, concerning a ton of butanethiol which was shipped to France during World War I to be used as a camouflage gas, Reid offers," There is no record to its fate, though it should have been possible to trace it."[4]

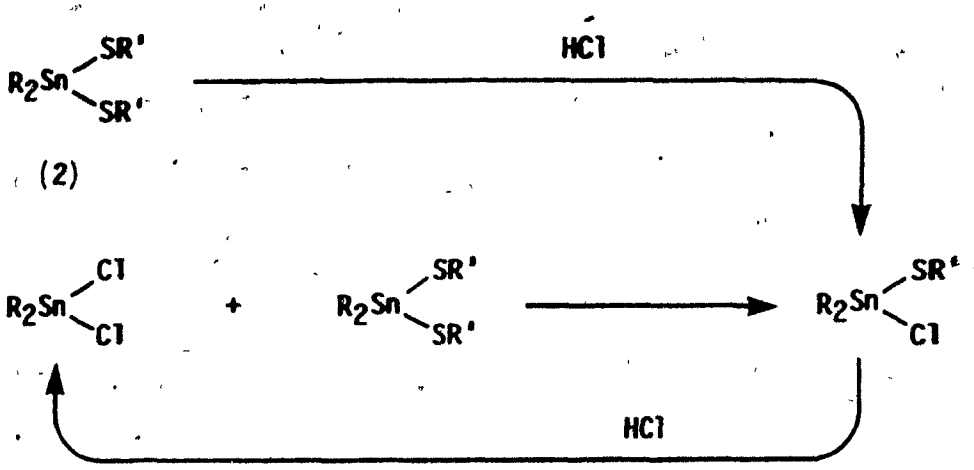
It should be emphasized that only low molecular weight sulfur compounds are offensive, and of these, thiols in particular. Furthermore, since many products of biological decay contain these compounds, it has been speculated that heightened sensitivity to these odors has served to protect organisms from potentially toxic, rotting or decomposing foods.[12] As little as 1 part in 50,000,000,000 of ethanethiol in air can be detected by the human olfactory system.[4]

1.3 Uses of Organotin Compounds.

As was mentioned above (Section 1.1), compounds of type (2) are used to stabilize PVC. They do so by preventing thermal dehydrochlorination of the polymer during processing and subsequent exposure to sunlight.[13] Dialkyltin bis(S,S'-isooctylthioglycollate) [$R_2Sn(SCH_2CO_2$-i-Oct$)_2$] exhibits low mammalian toxicity; hence it is used as a PVC additive for applications in which the polymer will contact water, food and beverages.[13] The mechanism of heat stabilization is provided in Scheme 1.

Organotins of the type $RSnX_3$, R_2SnX_2 and R_3SnX, some of these being organotin-sulfur derivatives, have been used as fungicides, miticides, disinfectants, biocides in marine paints, and wood preservatives.[13] Tin-oxygen compounds have been shown to have water repellent properties.[13]

Scheme 1.



1.4 Toxicity of Organotins.

The toxicity of organotins varies with the number of alkyl groups attached; toxicity is greatest when there are three Sn-C bonds, that is compounds of type R_3SnX.[14] Toxicity decreases as the alkyl groups at tin increase in size. Thus Me_3SnX is more toxic than Et_3SnX which in turn is more harmful than Bu_3SnX.[15]

While organotins exhibit toxic properties, inorganic tin is non-toxic; similar behavior is not observed for lead, mercury and arsenic.[14] This phenomenon can be understood by considering the mechanism by which organotins manifest their toxicity. Trialkyltins and tetraalkyltins (which rapidly dealkylate to the corresponding trialkyl derivatives) bind to proteins; possibly to cysteine and histidine residues. Dialkyltins can also combine with proteins and further, may bind to reduced lipoic acid.[13,14] Organotins concentrate in the blood, liver and brain.[14]

Almost all volatile organotin compounds cause headaches, this along with its strong unpleasant smell are early warning signs to local atmosphere contamination.[16]

1.5 Bond Strengths.

The most important bond dissociation energy in the study of tin-sulfur species is, of course, that of the tin-sulfur bond. Unfortunately this value is difficult to locate in the literature, as Smith and Davies have pointed out: "Accurate values for the Sn-S bond dissociation energy do not appear available...."[17] Nevertheless, a thorough survey of the literature indicates that a value of 52 kcal/mol is reasonable for this bond energy.[18]

Table 1. Relevant Bond Dissociation Energies.[18,19]

Bond	Bond Dissociation Energy (kcal/mol)	Compound
S-C	77	MeSMe
S-H	92	MeSH
S-S	74	MeSSMe
S-Cl	70	MeSCl
S-O	63-68	Divalent Sulfur, Various Sulfites[20]
Sn-S	52	Me_3SnSBu
Sn-O	66	Me_3SnOEt
Sn-N	41	Me_3SnNMe_2
Sn-F	99	SnF_4
Sn-Cl	75	Me_3SnCl
Sn-Br	61	Me_3SnBr
Sn-I	45	Me_3SnI
Br-Br	46	
I-I	36	

An empirical method for the determination of bond dissociation energies has been developed by Sanderson; a series of formulae are given to obtain the bond strength of almost any bond.[21] His system utilizes the concept of the equalization of electronegativities of all bonded atoms in a molecule. For Sn-S, the calculated bond dissociation energy is 56.0 kcal/mol.[21,22]

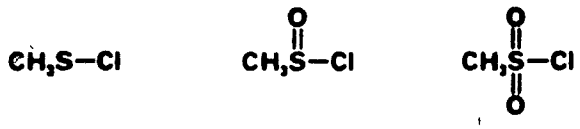
The compound used to obtain the Sn-F bond strength was SnF_4, however, the bond energies for the other tin halides were found using the respective trimethyltin halide. When performing calculations with bond energies it is important that the values be "internally" consistent; since the Sn-F bond energy determined from Me_3SnF can not be found, it is of interest to know the other tin halide bond energies as determined from tin tetrahalides. These energies, in kcal/mol, are: Sn-Cl, 77 ($SnCl_4$); Sn-Br, 65 ($SnBr_4$); Sn-I, 49 (SnI_4).[23] These values are very similar to those obtained using Me_3SnX, as shown in Table 1.

1.6 Nomenclature.

The nomenclature of organosulfur compounds can, at the very least, be perplexing. Eric Block writes "The difficulties stem not only from the myriad of known structural types but also from disagreement among the experts on the proper choice of names."[24] Further obstacles arise when one deals with organosulfur species that also contain metals. In this thesis the IUPAC method of naming compounds will be used.

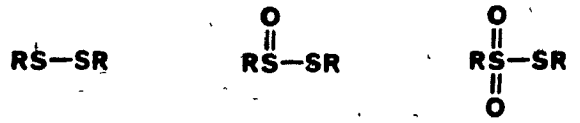
Often the suffixes for organosulfur compounds contain one of the vowels e, i or o. These suffixes indicate the oxidation number at sulfur, and there is a direct correspondence between alphabetical order and

increasing oxidation number. Thus the letter e in a suffix designates a divalent sulfur species (no double bond to oxygen). The letter i implies tetravalent sulfur (one sulfur-oxygen double bond) while the letter o refers to hexavalent sulfur (two sulfur-oxygen double bonds). This is exemplified by these organosulfur chlorides: methanesulfenyl chloride (3), methanesulfinyl chloride (4) and methanesulfonyl chloride (5).



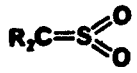
(3) (4) (5)

Similarly, disulfides (6), thiosulfinates (7) and thiosulfonates (8) differ only in oxidation number at one of the two adjacent sulfur atoms.



(6) (7) (8)

Strict adherence to the e-i-o rule would suggest that disulfides should be called thiosulfenates, however this is not the case. Convention allows for this and other exceptions. An example of a far greater inconsistency is the following: sulfenes (9), sulfines (10) and sulfones (11). In this instance, the common names for these quite diverse compounds are implied to have related structures.



(9)

(10)

(11)

A partial listing of IUPAC nomenclature for organosulfur compounds is given on the next page. It includes compounds of the type discussed in this thesis; a more extensive collection is also available.[24]

The nomenclature of organosulfur derivatives of tin can be confusing because they can be named with an "organic nomenclature" or an "inorganic nomenclature".[25] This has been been noted in the following: "Occasionally, the comments (on both nomenclature systems) turn to complaints about the inflexibility of one group or the other, and the unwillingness of one to accept the principles followed by the other. Such complaints are especially common in borderline fields such as organometallic compounds."[25] By the "inorganic" method, the sulfur containing group at tin can be considered as either an anion or as a ligand. In the former case the tin-sulfur compounds are called tin alkanethiolates; for instance, by this nomenclature system, compound **(12)** below is called tri-n-butylstannyl ethanethiolate. When the sulfur group is considered as a ligand then the C_2H_5S moiety is called ethylthio or ethanethiolato. Thus compound **(13)** below can be named di-n-butyl diethanethiolatotin(IV) or di-n-butyl diethylthiotin(IV).[26,27]

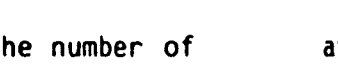
Type	Example	IUPAC name
Thiol, (mercaptan)	EtSH	Ethanethiol
Sulfide, (thioether)	EtSMe	Ethyl methyl sulfide
Sulfoxide	MeS(O)Me	Dimethyl sulfoxide
Sulfone	$EtSO_2Et$	Diethyl sulfone
Sulfenic acid	MeSOH	Methanesulfenic acid
Sulfinic acid	MeS(O)OH	Methanesulfinic acid
Sulfonic acid	$MeSO_2OH$	Methanesulfonic acid
Sulfenate ester	MeSOPh	Phenyl methanesulfenate
Sulfinate ester	PhS(O)OMe	Methyl benzenesulfinate
Sulfonate ester	$MeSO_2OMe$	Methyl methanesulfonate
Disulfide	EtSSMe	Ethyl methyl disulfide
Trisulfide	MeSSSMe	Dimethyl trisulfide
Thiosulfinate	n-BuS(O)SBz	Benzyl n-butanethiosulfinate
Thiosulfonate	$MeSO_2SEt$	Ethyl methanethiosulfonate
Sulfenamide	$EtSNH_2$	Ethanesulfenamide
Sulfinamide	$BzS(O)NH_2$	Phenylmethanesulfinamide
Sulfonamide	$PhSO_2NH_2$	Benzenesulfonamide
Sulfenyl halide	PhSCl	Benzenesulfenyl chloride
Sulfinyl halide	BzS(O)Cl	Phenylmethanesulfinyl chloride
Sulfonyl halide	$BzSO_2Br$	Phenylmethanesulfonyl bromide
vic-Disulfoxide	MeS(O)S(O)Me	Dimethyl vic-disulfoxide
O,S-Sulfenyl sulfinate	EtS(O)OSMe	Methanesulfenyl ethanesulfinate
vic-Disulfone	$MeSO_2SO_2Me$	Dimethyl vic-disulfone
Sulfonium salts	$Me_3S^+I^-$	Trimethylsulfonium iodide
Sulfurane	Me_4S	Tetramethylsulfurane

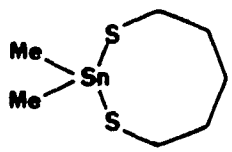
(12) (13)

In this thesis, tin-sulfur compounds will usually be named as alkylthiotin(IV) species. Compounds of type (12) will be commonly referred to as thiotins, while compounds of type (13) will be commonly called dithiotin species.

Compounds of type (14) can be similarly named, however, the bridging dithio moiety must be considered; thus, compound (14) is named μ-1,4-butyldithiohexamethyldiitin(IV). This type of compound will be commonly referred to as a dithioditin species.

Cyclic compounds of the type depicted below (15) are named according to the number of atoms in the ring, with the appropriate





(14) (15)

prefixes for sulfur or tin. Thus compound (15) is named 2,2-dimethyl-1,3,2-dithiastannacyclooctane. These will be commonly referred to as a cyclic dithiastanna species.

1.7 Bonding and Stereochemistry of Disulfides.

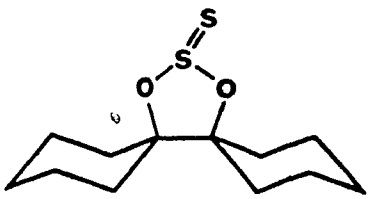
It was once a controversy as to whether the disulfide linkages are branched (**16**) or unbranched (**6**). Raman and infrared spectra, ultraviolet, X-ray and dipole moments all show quite clearly that the unbranched

(**16**)

RS—SR

(**6**)

(**6**) system is favored.[28,29] "The availability of sulfur to form chains is displayed in the allotropes of the element, and in a variety of compounds built up of sulfur chains terminated by other atoms or groups."[29] Sulfur monofluoride (S_2F_2) is a notable exception, it exists in the branched form[28] as well as the unbranched form.[30] It is likely that the strong electron pull transmitted by the two fluorines



(**17**)

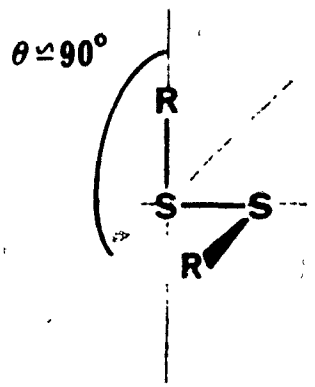
allows for d-orbital utilization, hence double bond character. Cyclic thiosulfite 0,0'diesters can also have a branched sulfur; the X-ray structure of 0,0'-bicyclohexyl-1,1'-diyl thiosulfite (**17**) confirms this.[31]

It is not always wise to base explanations of bonding on the availability of d orbitals, but the presence of electronegative atoms on sulfur such as fluorine or oxygen can increase the effective nuclear charge on sulfur thus contracting orbitals and lowering orbital energies of the sulfur atom in question.[32]. Nuclear effects seem to sensitize 3d orbitals more than others thus they are apt to shrink more than the 3s or 3p orbitals.[33] This allows for the 3d and other orbitals to mix, so that a $3d\pi - 3p\pi$ bond may form.[32,34]

The bonding in so-called hypervalent sulfur compounds SF_4 (includes one lone pair of electrons on sulfur) and SF_6 also invoke the use of d-orbitals. Hybridization of the unfilled 3d orbitals occurs to afford the trigonal bipyramidal SF_4 (sp^3d hybrid) while SF_6 exhibits octahedral symmetry (sp^3d^2).[32] An alternate approach to the bonding in these molecules suggests that they are hypovalent; thus, for SF_6, the central sulfur atom has a +3 charge while each fluorine supports a one-half negative charge.[35]

Disulfides are generally non-planar with a R-S-S-R dihedral angle of ca. 90° (Figure 1).[34,36] The barrier to rotation varies, typical values are 9.5 kcal/mol for Me_2S_2 and 13.2 kcal/mol for Et_2S_2. The

Figure 1. Stereochemistry of the Disulfide Linkage

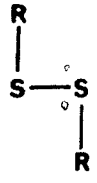


barrier for H_2S_2 is a low 2.7 kcal/mol while that of S_2Cl_2 is a relatively high 14.2 kcal/mol.[29,34] Significantly lower values were attained by Boyd[37] who calculated a barrier of 2.2 kcal/mol for Me_2S_2 and an upward limit of 7.0 kcal/mol for acyclic disulfides; his calculation for H_2S_2 predicts a barrier of 0.9 kcal/mol. Generally lower values have been similarly calculated by Snyder and Carlsen.[38]

A postulate on the nature of the bonding of disulfides is that the σ bond between the two sulfurs and the σ bond joining sulfur and carbon atoms are nearly pure p in character. Of the two lone pairs of electrons on sulfur one is in the 3s orbital spherically distributed about the nucleus while the other occupies the remaining 3p orbital.[29,39] In disulfides, these nonbonded 3p electrons are repelled, the minimum repulsion being when the dihedral angle is at 90°. Said in a different way, the S-S bond strength is greatest when there is a CSSC dihedral angle of 90° because the negative contributions ($S_1 3p\pi - S_2 3p\pi$) are diminished relative to other bonding contributions.[37] Another possibility is that the orbitals are sp^3 hybridized and the 90° dihedral angle results from repulsive interaction of the nonbonded sp^3 orbitals.[34]

Due to the skew conformation of disulfides two enantiomeric conformers are possible. Interconversion of the conformers may occur through a cis (**18**) or trans (**19**) transition state. The trans transition state is energetically favored.[36,37,40] In addition, as expected, when the

(18)



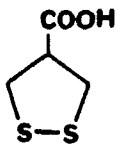
(19)

size of substituents on sulfur increase, the cis barrier to rotation increases relative to the trans barrier.[36,38] Boyd[36] has calculated that the disulfide dihedral angle is determined by electronic effects while both steric and electronic effects control the relative magnitude of cis and trans rotational barriers. It should be noted however that the CSSC dihedral angle for acyclic disulfides is not always 90°, in fact it may vary from 74° to 105°.[41] Also, others claim that the dihedral angle is indeed affected by steric as well as electronic effects.[41] In the absence of steric effects the cis barrier appears to be of lower energy than the trans.[34]

It has been suggested that the inherent chirality of the disulfide moiety contributes to the high specific rotation of L-cystine relative to other amino acids.[34,42]

In the presence of a fixed asymmetric center, an unequal distribution of M (left-handed helix) and P (right-handed helix) of the disulfide can be maintained. This unequal allotment of diastereomeric forms occurs in many naturally-occurring compounds.[43,44]

Small cyclic disulfides such as 1,2-dithiolane-4-carboxylic acid (20) are constrained and cannot achieve a CSSC dihedral angle of 90°. For compound (21) the dihedral angle is 26.6° while for 1,2-dithiane-3,6-dicarboxylic acid it is 60.3°.[30] This greatly affects the stability of the disulfide; for instance 1,2-dithiolane readily polymerizes on efforts to purify and isolate it.[45]



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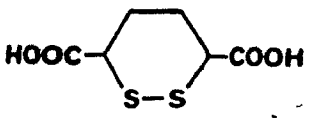
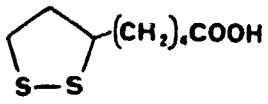


(21)

1.8 Naturally-Occurring and Other Interesting Cyclic Disulfides.

One of the most important and widely known cyclic disulfides is α-lipoic acid (22). It is isolated from liver tissue and is required for metabolism and growth. Furthermore, there is a possible need for α-lipoic acid in the photosynthetic processes of plants.[46] The 1,2-dithiolane (23) moiety is also present in nereistoxin (24), a neurotoxin found in the marine worm Lumbriconereis heteropoda[47], in 3,3-dimethyl-1,2-dithiolane (25) which is a constituent of in mink secretion[48] and in the plant growth regulator asparagusic acid (20) found in asparagus.[49] Asparagus also contains the methyl (26) and ethyl (27) esters of



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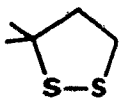

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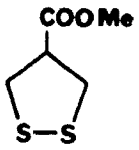

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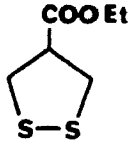
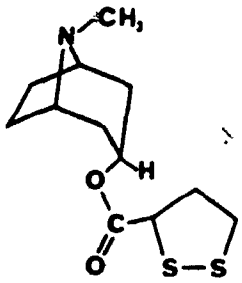


(27)

asparagusic acid.[49] Brugine (28), 4-hydroxy-1,2-dithiolane (29) and gerrardine (30) which are present in species of mangrove trees [11,48] also have the 1,2-dithiolane sub-structure.



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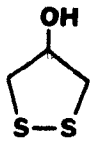

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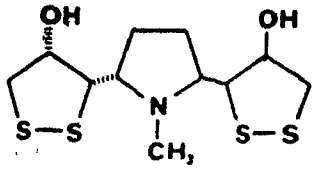
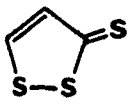


(30)

Cabbage harbors 1,2-dithiole-3-thione (**31**) [46] while the parent compound 1,2-dithiole (**32**) contributes to the characteristic odor of cooked asparagus.[50] Asparagus (cooked or uncooked) also contains the following six membered ring disulfides: 1,2-dithiane-4-carboxylic acid (**33**), 5-methyl-1,2-dithiane-4-carboxylic acid (**34**)[49], 3-vinyl-3,4-dihydro-1,2-dithiin (**35**) and 3-vinyl-3,6-dihydro-1,2-dithiin (**36**).[50] Red dithiin (**37**) occurs in several species of plants.[46]



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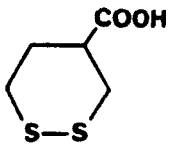

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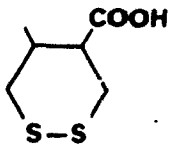

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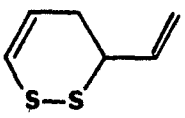

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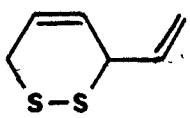

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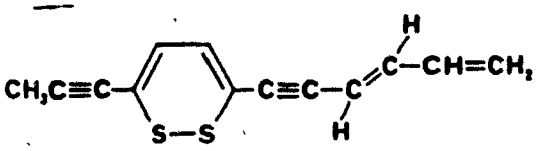
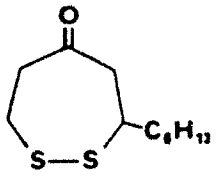


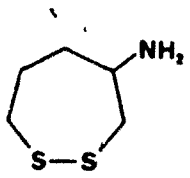
(37)

The seven-membered cyclic disulfide 3-hexyl-1,2-dithiepan-5-one (**38**) has been detected in the Hawaiian brown the alga Dictyopteris plagiogramma.[51] 1,2-dithiepan-4-amine (**39**) along with its methanesulfonyl (**40**) and benzenesulfonyl (**41**) derivatives have been studied as possible radiation drugs.[52]

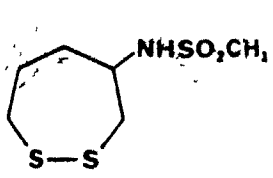
Cyclic disulfides with additional sulfur atoms in the ring are also known. The red alga Chondria californica and the mushroom Lentinus edodes contain 1,2,4-trithiolane (**42**), Chondria californica also contains the corresponding sulfoxide (**43**).[47,53] cis-3,5-Dimethyl-1,2,4-trithiolane (**44**) and the trans isomer (**45**) have been detected in potato oil, roasted filberts, cooked beef, cheese, dry red beans and the mushroom Boletus edulis.[50,54]



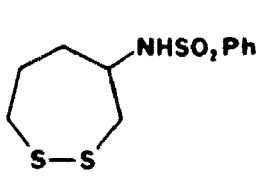
(**38**)



(**39**)



(**40**)



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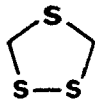
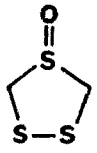
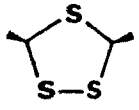


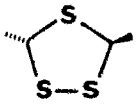
(**42**)



(**43**)



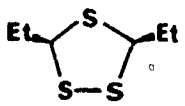
(**44**)



(**45**)

Similar compounds, cis-3,5-diethyl-1,2,4-trithiolane (**46**) and trans-3,5-diethyl-1,2,4-trithiolane (**47**), are found the onion Allium

cepa[55], while trithiolaniacin (48) occurs in root material of guinea-hen weed Petiveria alliacea.[48,50]



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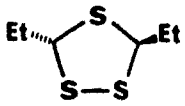

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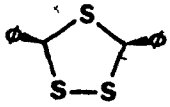
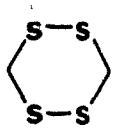


(48)

From Chondria californica, the red alga which contains (42), have been identified 1,2,4,5-tetrathiane (49), lenthionine (50), 1,2,4,6-tetrathiepane (51) and the corresponding sulfone (52).[47] Lenthionine and 1,2,4,6-tetrathiepane are also found in the highly prized edible mushroom Lentinus edodes (Shiitake)[53,56] from which the former derives its name. Lenthionine also occurs in cooked mutton.[57]



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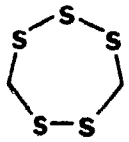

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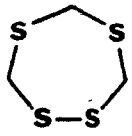

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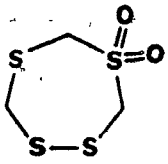
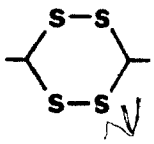


(52)

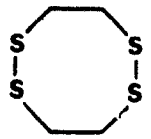
From processed ham [54] and cooked mutton [57] one finds 3,6-dimethyl-1,2,4,5-tetrathiane (53), a compound similar to (49). Other bis(disulfides) are the dimer of 1,2-dithiacyclobutane (54), 1,2,5,6-tetrathiocane (55) which is found in 'Chenin Blanc' grape leaves [50] and the alkaloid cassipourine (56) from Cassipourea gummiflua.[11] An example of a

compound with four disulfide linkages is 1,2,4,5,7,8,10,11-octathiacyclododecane (**57**) which is found in the red alga Chondria californica.[47]

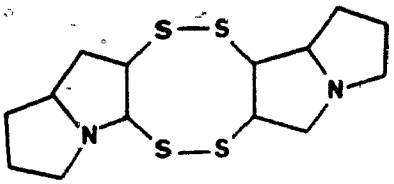


(**53**)

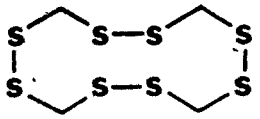
(**54**)



(**55**)

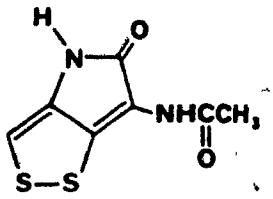


(**56**)

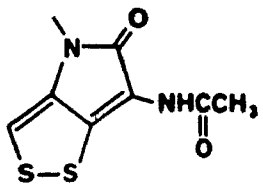


(**57**)

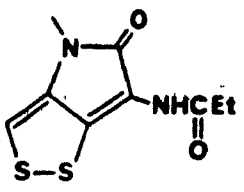
The very active antibiotics holomycin (**58**), thiolutin (**59**) and aureothricin (**60**), which also contain a cyclic disulfide moiety, are all isolated from Streptomyces, unfortunately these compounds also exhibit



(**58**)

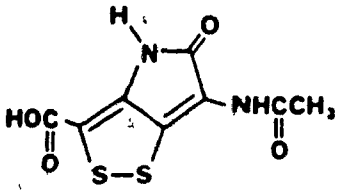


(**59**)

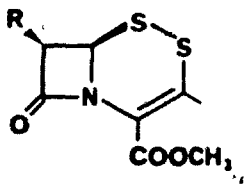


(**60**)

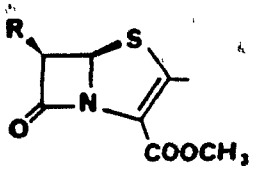
considerable toxicity.[46] A derivative of holomycin, 3-carboxyholomycin (**61**), also resembles the penicillins; this compound shows far less antibiotic activity.[58] Cyclic disulfides of the type (**62**) have been synthesized by Perrone and co-workers[59]; these were used to prepare penicillins (**63**) using desulfurizaton techniques.



(**61**)

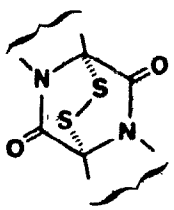


(**62**)

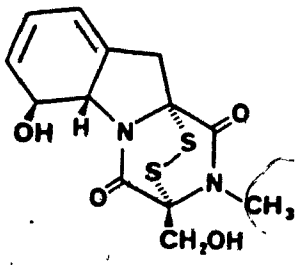


(**63**)

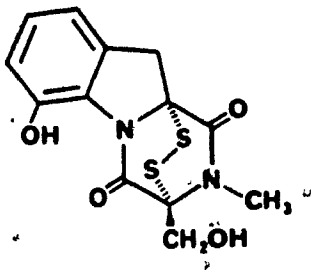
More complex cyclic disulfides are the bicyclic compounds that contain the epidithiodioxopiperazine ring system (**64**). Many of these compounds exhibit antiviral, antibiotic or antifungal activity. the site of this activity is thought to be the epidithiodioxopiperazine ring.[60] Two examples are the antibiotics gliotoxin (**65**) and dehydrogliotoxin (**66**).[61] An analogue of dehydrogliotoxin, compound (**67**), inhibits the enzyme reverse transcriptase.[60,62] Aranotin (**68**), apoaranotin (**69**) and acetylaranotin (**70**), all produced by the fungus Arachniotus aureus, have antiviral activity.[63,64] Hyalodendrin (**71**), a



(**64**)



(65)



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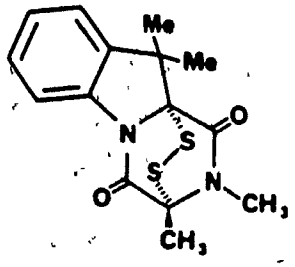
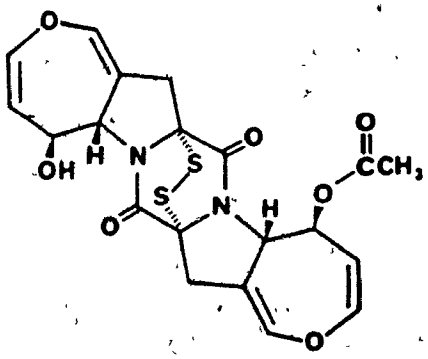
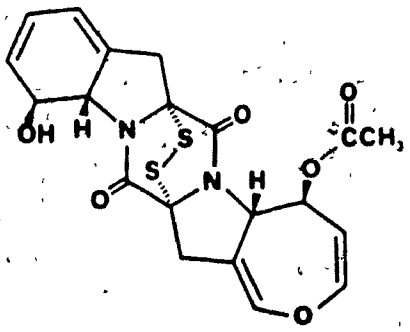


(67)

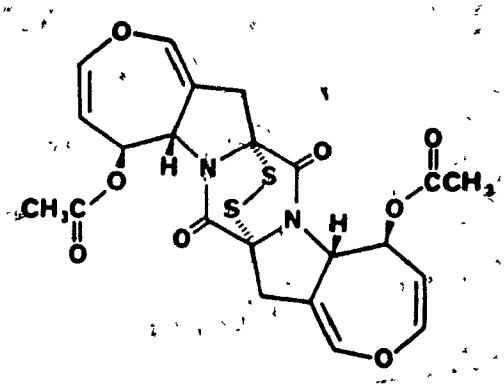
fungitoxic metabolite, is produced by the imperfect fungus Hyalodendron.[12] Many other epidithiodioxopiperazines such as sporidesmin (72) have been listed by Sammes.[65]



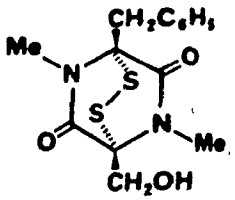
(68)



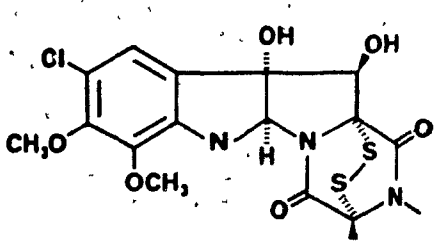
(69)



(70)



(71)

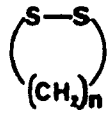


(72)

The nonapeptides oxytocin and vasopressin contain two cysteine residues that are linked to form a cyclic disulfide. Oxytocin is required for milk flow in lactating animals and for uterine contraction. It was the first polypeptide hormone to be synthesized. Vasopressin increases blood pressure and suppresses urine flow.[46,66] There are several polypeptides that are cyclic disulfides; their primary structure is partially determined by the oxidized cysteine residues. Likely the best known of these polypeptides is the pancreatic hormone insulin. It is composed of two chains, A and B, that are joined by two disulfide linkages to form a ring. Furthermore, the A chain is itself a cyclic disulfide since it contains a pair of cysteine residues that are oxidatively coupled.[66,67]

1.9 Previous Preparations of Cyclic Disulfides.

The earliest method[68] used to prepare a series of cyclic disulfides (73) was developed by Davis and Fettes.[69] They showed that the steam distillation of aqueous dispersions of disulfide polymers afforded very small amounts of the respective monomers. The rate of depolymerization was very slow, however, it was noted that the addition of sodium hydroxide significantly increased this rate.



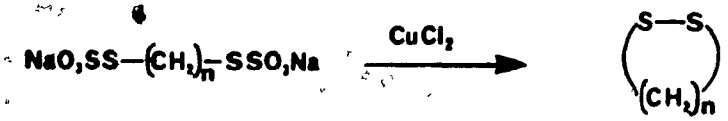
(73)

for, n = 3, (23); n = 4, (74); n = 5, (75); n = 6, (76)
n = 7, (77); n = 8, (78); n = 9, (79); n = 10, (80)

The preparation of cyclic disulfides by reverse polymerization was also achieved by Nelander[70] who placed ca. 100 mg of polymer latex on a twofold excess of solid iodine. Small droplets of liquid monomer appeared at room temperature or with gentle heating. The yields for the five-membered ring disulfide 1,2-dithiolane (23), the six-membered ring 1,2-dithiane (74) and the seven-membered ring disulfide 1,2-dithiepane (75) were 72%, 92% and 81% respectively. Yields for medium ring size cyclic disulfides were not as good; 4% of 1,2-dithiacyclooctane (76) was prepared while a slightly better 8% was obtained for 1,2-dithiacyclododecane (80).

The treatment of Bunte salts (81) with $CuCl_2$ has also been used to synthesize cyclic disulfides (Scheme 2).[68] The yields of monomers are generally low, and very low (0.2-4.0 %) for medium ring size cyclic disulfides (eight- to twelve-membered rings). Treatment of the Bunte salts with zinc chloride has been found less successful, while iodine or hydrogen peroxide oxidations have been unsuccessful.

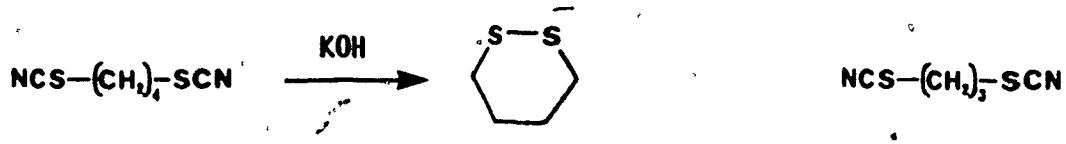
Scheme 2.



(81) (73)

The reaction of tetramethylenedithiocyanate (82) with potassium hydroxide provides 1,2-dithiane (74) in good yields (Scheme 3); however, attempts to prepare 1,2-dithiacyclooctane (76) using the hexamethylene derivative lead to polymerization.[71] Gagnon, Boivin and Brown[72] claim to have prepared 1,2-dithiolane in 95% yield by adding hydrazine hydrate to trimethylenedithiocyanate (83).

Scheme 3.



(82) (74) (83)

Barltrop, Hayes and Calvin[45] prepared 1,2-dithiolane (23) and 1,2-dithiane (74) by adding the respective dibromides to a refluxing solution of sodium disulfide nonahydrate and elemental sulfur. Polymers of 1,2-dithiolane were depolymerized by steam distillation in the presence of strong alkali.

Oxidation of thiols using common oxidants such as O_2, H_2O_2, I_2, SO_2Cl_2, $K_3Fe(CN)_6$ and $FeCl_3$ is routinely used to prepare symmetrical disulfides.[73] Careful oxidation of dithiols using long addition times

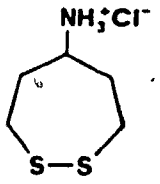
of the oxidant and high dilution conditions should afford good yields of monomer as opposed to polymer. It is precisely this type of methodology which is most frequently used to prepare cyclic disulfides.

Cyclic disulfides containing 5-10, 12 and 15-membered rings have been prepared by the slow addition of ferric chloride to dithiols.[74] 1,2-Dithiolane (**23**) was isolated as a polymeric gum. 1,2-Dithiane (**74**) and 1,2-dithiepane (**75**) were obtained in good yields; however, to obtain (**75**) it was necessary to add the oxidant over a period of two days. The eight-membered cyclic disulfide (**76**) was obtained in 30% yield but the addition of $FeCl_3$ required 6 days. For larger homologues, the following results were obtained: nine-membered ring (**77**), 45% after 7 days; ten-membered ring (**78**), 50% after 9 days; twelve-membered ring (**80**), 60% after 7 days; fifteen-membered ring, 60% after 3 days.

The efficiency of iodine oxidation of a thiol is increased by adding triethylamine. This is due to the uptake, by the base, of the hydroiodic acid which is formed in the reaction. Iodine and triethylamine were used by Isenberg and Herbrandson[75] to obtain the six membered cycle 1,2-dithiane (**74**) in 96% yield.

The formation of monomeric disulfides using prolonged oxidant addition times is tedious, while high dilution suffers from the disadvantage of requiring copious amounts of solvent. An improved method based on high dilution principle is titrimetry.[76] By using two addition funnels the dithiol and oxidant can be added simultaneously to a flask containing solvent. When this procedure is used the effective concentrations of dithiol and oxidant remain very low but the final concentration of disulfide is high. Herbrandson and Wood[77] prepared 1,2-dithiepane-5-amine hydrochloride (**84**) in 75% yield by simultaneous

dropwise addition of the appropriate dithiol and an aqueous solution of I_2/KI to a reaction flask. Total addition time was 3 h and the final concentration of the disulfide in solution was ca. 0.04 M. Oxidation of this dithiol without high dilution using $FeCl_3$, I_2 or O_2 under basic conditions, yielded polymer or starting material.



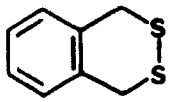
(84)

Similarly, Goodrow and Musker[76] synthesized a series of cyclic disulfides (7-9 membered rings) in good yield (73-86%) using simultaneous addition of solutions of dithiol and I_2 to a solution of triethylamine. The final concentration of disulfide ranged from 0.03 M to 0.07 M, and the addition took 3-5 h. The same disulfides were prepared in far lower yields either by $FeCl_3$ oxidation of the dithiols (under high dilution conditions) or $CuCl_2$ oxidation of the Bunte salts. Field and Barbee[78] have also used the titrimetric technique although with limited success.

A series of cyclic disulfides was prepared by first functionalizing the dithiols with lead(II) acetate to form the lead dithiolates (**85**), which were then treated with elemental sulfur to afford the respective cyclic disulfides.[79] Using this methodology, 1,2-dithiolane (**23**) was prepared in 90% yield, 1,2-dithiane (**74**) in 96%, 1,2-dithiepane (**75**) in 82%, 1,2-dithiacyclooctane (**76**) in 86% and 4,5-benza-1,2-

dithiane (86) in 88%. Unfortunately, the literature reference does not contain any experimental details nor does it include physical data for the disulfides which were prepared. Using this same method, Field and Barbee[78] reported the preparation of the six-membered cyclic disulfide (74) in 96% yield; however, the seven membered-cyclic disulfide, 1,2-dithiepane (75), was prepared in only 6% yield.

(85)



(86)

A study of the yields obtained for 1,2-dithiolane (23), 1,2-dithiane (74) and 1,2-dithiepane (75) by a variety of preparative techniques, including many already discussed, was performed by Field and Barbee[78]. It is of interest to compare the methods in terms of the yields of monomer produced; further, this information will serve to summarize much of what as been described in this section. The five-membered cyclic disulfide, 1,2-dithiolane, (23) was obtained in 90% via depolymerization. It was obtained in 84% yield by slow addition of H_2O_2 and dithiol using titrimetric conditions to a solution of KI; 26% using iodine and ferric chloride, 21-40% using lead tetraacetate and no yield with p-toluenesulfonyl chloride in aqueous alkali. Addition of elemental sulfur to the lead dithiolate also, did not afford any (23). 1,2-Dithiane (74) was best prepared by adding sulfur to the lead dithiolate, the yield being 95%. p-Toluenesulfonyl chloride in aqueous alkali afforded (74) in 93% yield. The yield of (74) was 87% using p-tolue-

nesulfonyl chloride with no alkali, 81% using t-butyl hydroperoxide, 77% using I_2/KI and 77% using iodine and triethylamine. The highest yield for 1,2-dithiepane (75), 54%, came from dropwise addition (1.5 days) of dithiol to a solution of $FeCl_3$. A yield of 17% of (75) was obtained using p-toluenesulfonyl chloride in aqueous alkali, 7% from the titrimetric addition of dithiol and H_2O_2, and 6% via the addition of sulfur to the lead dithiolate.

In summary, moderate to good yields are usually obtained for the smaller sized cyclic disulfides, in particular the six-membered ring disulfide (1,2-dithiane). However, the medium sized cyclic disulfides (8- to 12-membered rings) are difficult to prepare in good yields even when specialized techniques are used.

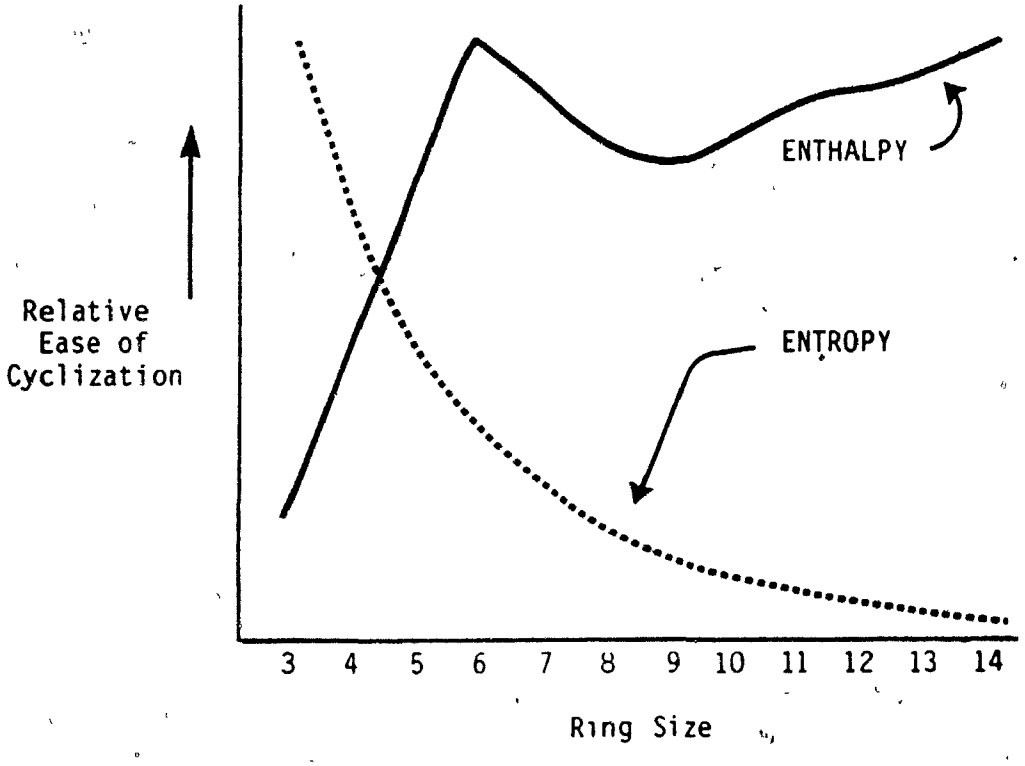
1.10 Difficulties with Cyclization Reactions.

When considering the intramolecular process of a cyclization reaction it is important to acknowledge the potential for problems arising from a competing intermolecular reaction. Galli and Mandolini[80] describe the fundamental quantity in cyclization reactions as the effective molarity (EM) or k intramolecular/k intermolecular for a given reaction at a determined concentration. For a given concentration, an EM of 1 for a reaction indicates that cyclization (k intramolecular) and polymerization (k intermolecular) are occurring at the same rate.[80]

It is profitable to be able to determine, or at least to postulate, what the relative ease of formation of a large ring system(s) such as a series of macrolides of varying ring sizes may be. To do this, we must compare the components of total free energy of formation for the intramolecular process with those of the intermolecular one. The total free

energy involved can be broken down into three components: the differences in individual bond energies which takes into consideration the energies of bonds that are broken and formed, the difference in total strain energy, and lastly an entropy term.[81] The bond energies for cyclization should be the same as those for polymerization. The differences in strain energy are those contributing to ring strain; this compromises ring formation. Ring strain arises from a combination of Pitzer strain (bond opposition forces due to imperfect staggering), Baeyer strain (deformation of ring bond angles) and strain which occurs due to transannular interactions.[82] Intuitively, we know that entropy discourages polymerization; for an intermolecular reaction to take place, two molecules must be brought close enough together to react.

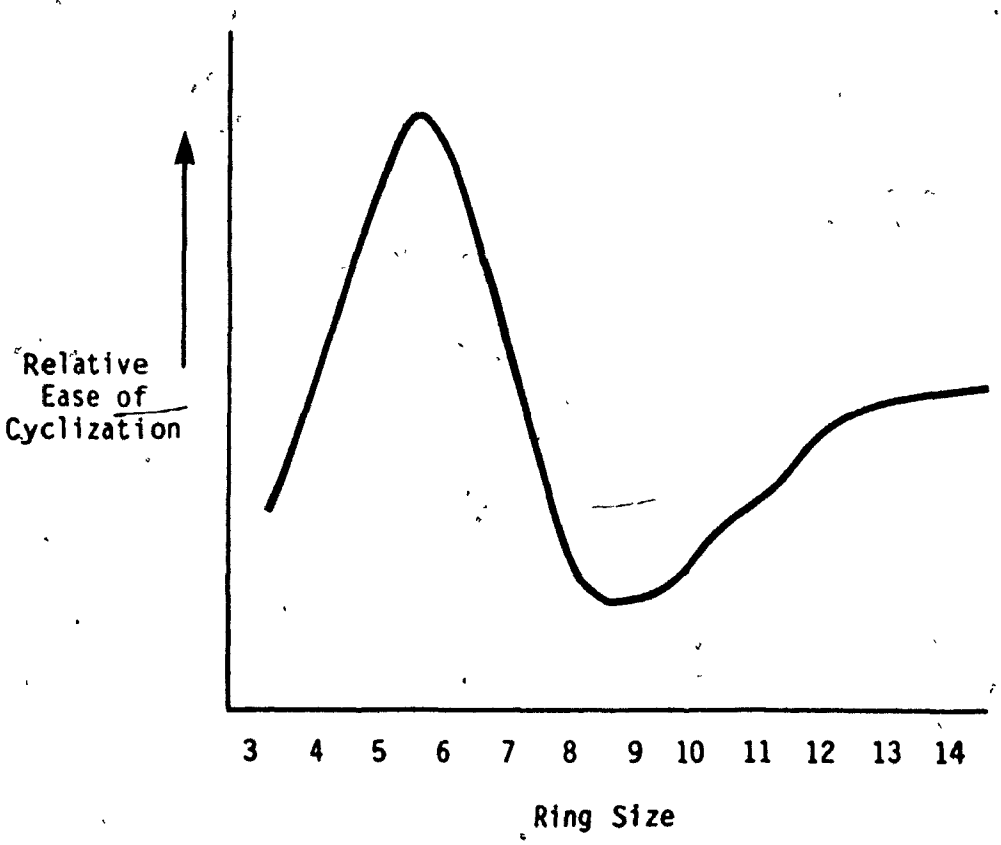
Figure 2. Enthalpy and Entropy Effects for Cyclization.[83]



This requires a decrease in net entropy and costs energy. For the intramolecular process the reactants are relatively close, both being in the same molecule; hence, entropy does not change significantly.[81] In addition, the entropy term discourages monomer ring formation with an increase in potential ring size of the monomer.[83]

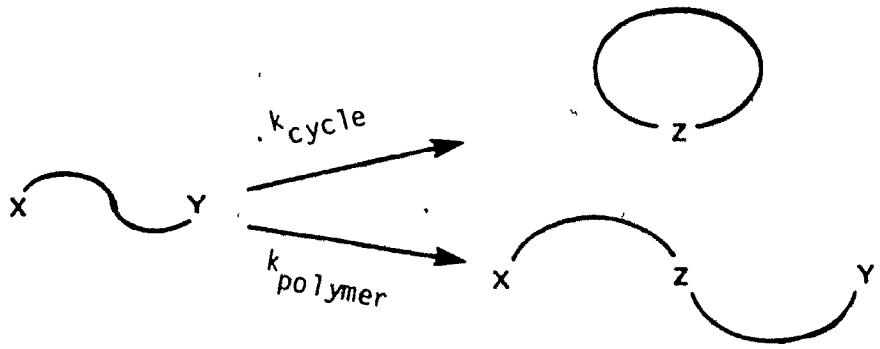
Note the dip in the enthalpy curve of Figure 2 above for ring sizes 8-12. These medium size rings (8-12) are often the most difficult to make[82] and this is due in large part to enthalpy effects. The relative ease of cyclization using a combination of enthalpy and entropy effects as a function of ring size is shown below (Figure 3).

Figure 3. Relative Ease of Cyclization in Terms of Combined Energy Effects.



Mandolini and co-workers have published many reports concerning macrolide formation[80,82,84,85]; the difficulty in forming medium sized rings is well documented in these articles. The reactivity plots presented in these reports, that is plots of EM or log EM versus ring size, compare well with the relative ease of cyclization plot above (Figure 3).

Ring formation by an intramolecular process, that is, cyclization of a bifunctional reagent, is a first-order process. The competing polymerization reaction is bimolecular or second-order.[82] This is exemplified by the following diagram.



The rates for cyclization and polymerization are:

$$\text{Rate of cyclization} = k_{cycle}[\text{substrate}]$$

$$\text{Rate of polymerization} = k_{polymer}[\text{substrate}]^2$$

Assuming that polymerization is the only competing reaction, then we can establish with a simple mathematical argument the ratio of the the rate of cyclization to the rate of polymerization[83]; that is we can establish a relative rate of cyclization.

$$\text{Relative rate of cyclization} = \frac{k_{cycle}[\text{substrate}]}{k_{polymer}[\text{substrate}]^2}$$

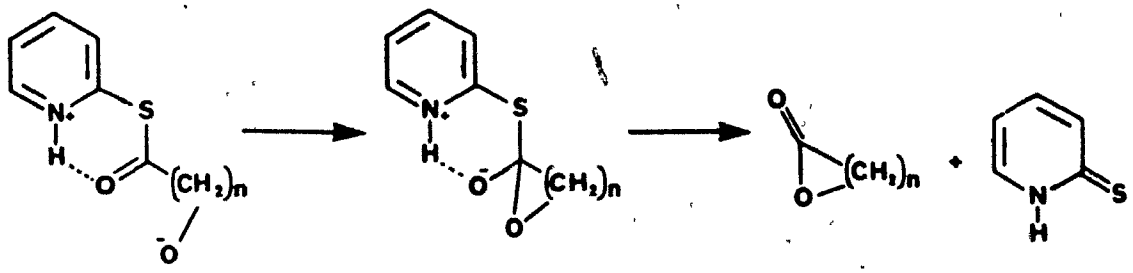
$$\text{Relative rate of cyclization} = k \cdot \frac{1}{[\text{substrate}]}$$

The principle that high substrate concentrations favor polymerization while dilution favors cyclization is now quite clear. Put in a different way, cyclization can occur without strong competition only at low concentrations of bifunctional substrate.[82] High dilution to encourage cyclization is usually effected in two ways. The first entails simple addition of a bifunctional reagent to a large volume of solvent over a short period of time. The second is the Ziegler[85] high dilution technique in which a bifunctional reagent is added very slowly to a solution containing a reaction stimulant such as an oxidizing reagent or heat. The accumulation of the bifunctional reagent is prevented; hence, by simply controlling the rate of feed, polymerization can be discouraged.[87]

1.11 Newer Methods to Enhance Monomer Formation.

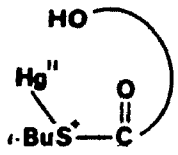
Corey and co-workers[88,89] have recently used double activation methods to improve yields in lactonization procedures. This is done by simultaneously activating both the carboxyl and hydroxyl sites by forming the 2-pyridinethiol ester (**87**) of a hydroxy acid. In this compound, proton transfer from the hydroxy moiety to the carbonyl is more efficient than for simple esters. This can be seen below (Scheme 4).

Scheme 4.

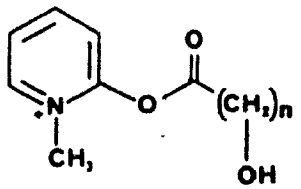


(87)

Similar systems are used by Masamune[90,91] and Mukaiyama[92] as reported by Nicolaou.[93] In the former case lactonization is improved by first forming the S-t-butyl thiolester and then allowing cyclization to occur in the presence of mercuric trifluoroacetate. It is likely that the electrophilic mercury forms a complex (88) with sulfur. Mukaiyama reacts N-methyl-2-chloropyridinium iodide with a hydroxy acid; this effects his lactonization procedures via the reactive species (89).[93]



(88)

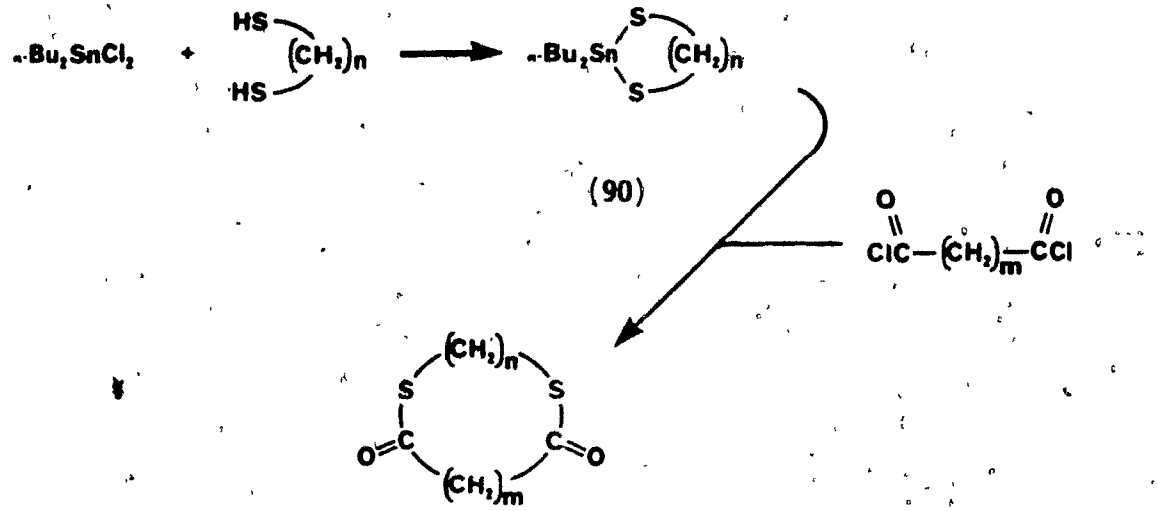


(89)

Tin derivatives have been used to prepare a variety of macrocycles. Shanzer and co-workers have prepared a number of large ring systems by exploiting the fact that tin reacts readily with heterocyclic intermediates to yield highly reactive reagents.[94,95] Firstly, dialkyl tin species are used to prepared cyclic stannadioxanes[95-97], cyclic stanna-

dithianes (90)[98] and cyclic stannoxathianes[99] which serve as covalent templates for intramolecular condensation. The metalloid is then expelled to afford the target ring.[100] An example of a sulfur-containing macrocycle (91) that has been formed by this method is given below in Scheme 5.[98]

Scheme 5.



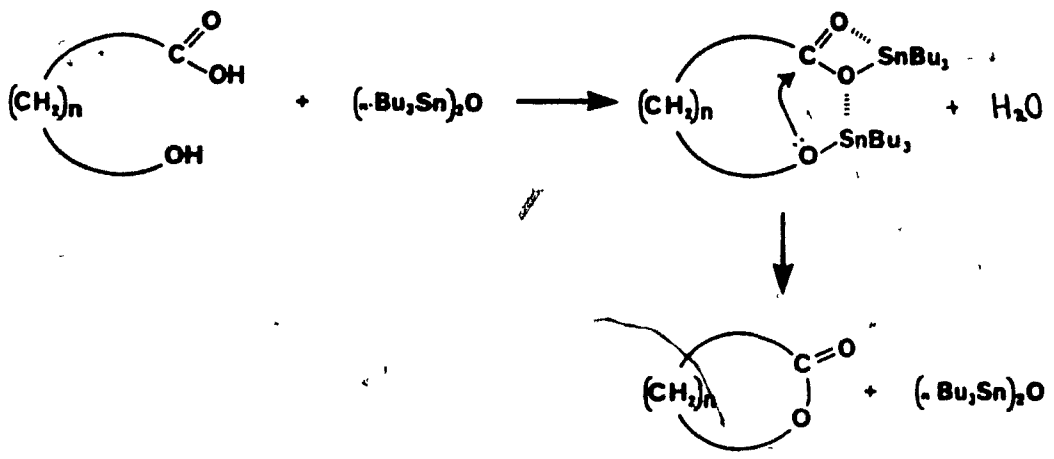
(90)

(91)

Shanzer has also used silicon as the metalloid to serve as the covalent template to synthesize macrocycles.[101,102] Further, the covalent template technique has been applied to the synthesis of chiral and diastereomeric macrocycles.[103,104]

Macrocyclic lactones and lactams have been prepared by Steliou and Poupart[105] using tin derivatives (Scheme 6). In these examples template and double activation effects are imparted by tin. Double activation results from an increase in nucleophilicity of the alkoxy group due to bonding to tin, while the carboxyl moiety is activated by the enhance-

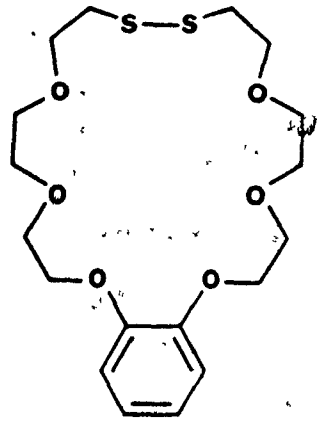
Scheme 6.



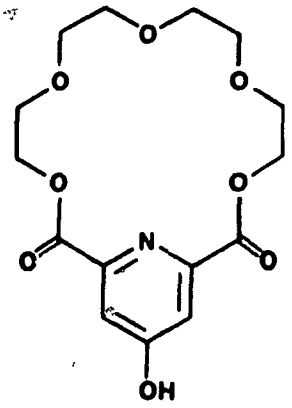
ment of the anticipated leaving group (di-n-butyltin oxide).[105,106] Scheme 6, above (Steliou and co-workers[106]), clearly illustrates this.

Alkali metals have been used to good effect in the synthesis of macrocycles. For instance, cyclic disulfide (**92**) was prepared in a ratio of 1 : 2 (monomer / polymer) in the absence of Cs^+. However, with the addition of Cs^+ the ratio was 4 : 1 (monomer / polymer) or eight-fold improvement.[107,108] The cesium ion apparently acts as a site for a reverse host-guest relationship, a type of template. The ability of alkali metals to promote monomer formation (for compound **92**) decreases in the order Cs^+/ Rb^+/ Na^+.[108] Association between alkali metals and crown ethers depends on both the nature of the ion and the crown ether ring size.[109] In the same way that the proper crown ether must be chosen to suit a particular ion, so must the appropriate ion be chosen to facilitate a given crown ether synthesis. Bradshaw and co-workers used K^+ to elegantly prepare crown ethers (**93**) and (**94**).[110]

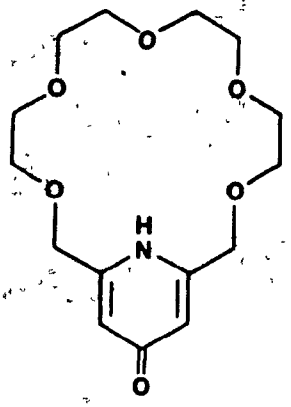
Rastetter and Phillion have employed thiol-functionalized crown ethers as reagents for macrolide closures.[111] The thiol moiety is reacted with a α,ω-hydroxy carboxylic acid to form a thioester. This



(92)



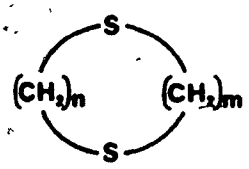
(93)



(94)

thioester is then treated with potassium t-butoxide to afford the α-alkoxide which cycles around to attack the thioester and yield the required lactone; "the cyclization reaction proceeds via a template conformation in which the α-alkoxide is held proximate to the thioester through ionic bonding to the crown-bound potassium cation."[111]

Cesium has been used by Buter and Kellogg[112] to prepare sulfur containing macrocycles (95). The cesium serves as a counterion for the thiolate nucleophile under the polar reaction conditions. Lactones[113] and some sulfur containing metacyclophanes[113a] have been similarly synthesized.



(95)

CHAPTER 2

RESULTS and DISCUSSION

2.1 Symmetrical Disulfides

2.1.1 The Preparation of Thiotin(IV) Species

tri-n-Butyl alkylthiotin(IV) compounds (**96**) and tri-n-butyl phenylthiotin(IV) (**96g**) were prepared in very high yield and purity by mixing tri-n-butyltin chloride (**97**) and the respective thiols in the presence of a slight excess of triethylamine (Scheme 7). The procedure is similar to that presented by Wieber and Schmidt[114,115] as well as Harpp, Aida and Chan.[116] Triethylamine hydrochloride precipitated immediately indicating the facility of the reaction. However the solution was allowed to stir for a further 3-4 h to ensure completion.

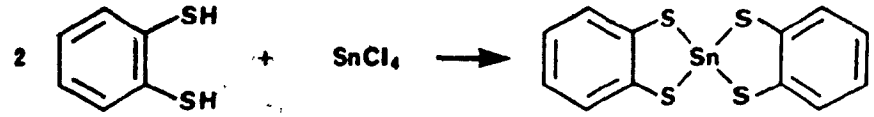
Scheme 7.

$$\underset{\textbf{(97)}}{n\text{-}Bu_3SnCl} + RSH \xrightarrow{Et_3N} \underset{\textbf{(96)}}{n\text{-}Bu_3Sn\text{-}SR} + Et_3NHCl$$

No significant increase in yield was achieved with a longer reaction time. The triethylamine hydrochloride salt was removed by filtration, and could be dried and weighed; when this was done, the yield of solid was ca. one equivalent of the hydrochloride (95-98%). The high and relatively clean yields of the thiotins was not unexpected. In 1940, Brown and Austin[117] suggested that the completeness of a similar reaction of thiols with tin might be useful for quantitative

determination of tin. The reaction that they considered was the mixing of dithiocathechol (**98**) with stannic chloride (**99**), shown in Scheme 8.

Scheme 8.



(**98**) (**99**)

The alkyl and arylthiotin(IV) compounds were obtained as liquids or waxy solids by placing the samples under vacuum overnight. The compounds were subjected to a variety of structural determination techniques, including ^{1}H-NMR, ^{119}Sn-NMR, MS and Raman spectroscopy. These

Table 2. Yields of tri-n-Butyl Alkylthiotin(IV) Species and tri-n-Butyl Phenylthiotin(IV).

Entry	% Yield
tri-n-butyl benzylthiotin(IV) (**96a**)	95
tri-n-butyl n-butylthiotin(IV) (**96b**)	98
tri-n-butyl s-butylthiotin(IV) (**96c**)	97
tri-n-butyl t-butylthiotin(IV) (**96d**)	95
tri-n-butyl cyclohexylthiotin(IV) (**96e**)	97
tri-n-butyl n-decylthiotin(IV) (**96f**)	94
tri-n-butyl phenylthiotin(IV) (**96g**)	93

data indicate that the purity of the thiotin(IV) compounds is high although the waxy solids show wide melting ranges (4-8°C). Spectroscopic data from all thiotin(IV) species and related compounds is presented in Section 2.4.

2.1.2 Bond Strength Considerations

A quick calculation based on bond strengths indicates that iodine or bromine should easily oxidize the tri-n-butyl alkyl or arylthiotin(IV) compounds to the respective symmetrical disulfides. The published bond energies shown below in kcal/mol [18,19], were determined using species similar in structure to those prepared in the present study, and thus can be used to provide useful approximations of energy changes involved in forming the disulfides. The reaction of trialkyl alkylthiotin(IV) compounds with iodine results in a reaction enthalpy of approximately 24 kcal/mol, while their reaction with bromine favors disulfide formation by 46 kcal/mol.

$$\underset{52}{2\ R_3Sn\text{-}SR'} + \underset{36}{I\text{-}I} \longrightarrow \underset{45}{2\ R_3Sn\text{-}I} + \underset{74}{R'S\text{-}SR'}$$

$$\text{or } -164 - (-140) = -24 \text{ kcal/mol}$$

$$\underset{52}{2\ R_3Sn\text{-}SR'} + \underset{46}{Br\text{-}Br} \longrightarrow \underset{61}{2\ R_3Sn\text{-}Br} + \underset{74}{R'S\text{-}SR'}$$

$$\text{or } -196 - (-150) = -46 \text{ kcal/mol}$$

Thus bromine and iodine were used to prepare disulfides from the thiotin(IV) compounds.

2.1.3 Oxidation of Thiotin(IV) Species to Disulfides

Symmetrical disulfides (6) were synthesized from the tin-sulfur derivatives (96) by the dropwise addition of bromine or iodine in carbon tetrachloride (Scheme 9). Yields of disulfides were highest when one equivalent of halogen was added per two equivalents of thiotin species. This amounted to the same quantity of oxidant required for the color of bromine or iodine to become apparent in solution. Thus, a simplified procedure requires the addition of oxidant until the bromine or iodine color persisted in the solution. The quantitative addition of iodine to thiotin(IV) compounds has also been observed by Abel and Brady.[118]

Scheme 9.

$$\underset{(96)}{2\ \underline{n}\text{-}Bu_3Sn\text{-}SR} + X_2 \longrightarrow \underset{(6)}{RS\text{-}SR} + 2\ \underline{n}\text{-}Bu_3SnX$$

The reaction, which took no more than five minutes, was washed with sodium thiosulfate, dried and the solvent was removed. The resultant oil was chromatographed on neutral alumina and eluted with hexanes/dichloromethane.

Isolation of the disulfides using column chromatography was easier when Br_2 rather than I_2 was used as the oxidant. The reason for this is twofold: firstly, tri-n-butyltin bromide which formed on oxidation appeared to be more soluble in the thiosulfate wash than tri-n-butyltin iodide; secondly, a smaller mass of tin halide is formed when Br_2 is used (the molecular weight of $\underline{n}\text{-}Bu_3SnBr$ being 369 while the iodine derivative is 416). Thus, a series of disulfides was prepared using bromine as oxidant (Table 3).

Table 3. Isolated Yields of Symmetrical Disulfides

Disulfide	% Yield	Disulfide	% Yield
benzyl (**8a**)	94	cyclohexyl (**8e**)	94
n-butyl (**8b**)	96	n-decyl (**8f**)	84
s-butyl(**8c**)	97	phenyl (**8g**)	91
t-butyl(**8d**)	89		

A close survey of the literature shows that bromine and/or iodine oxidation of thiotins have been used to prepare a few symmetrical disulfides (di-p-tolyl disulfide and diphenyl disulfide) from tin-sulfur derivatives.[118-120] However, experimental procedures, if mentioned at all, are lacking in detail since interest is directed toward the tin derivative and its chemistry rather than the disulfide.

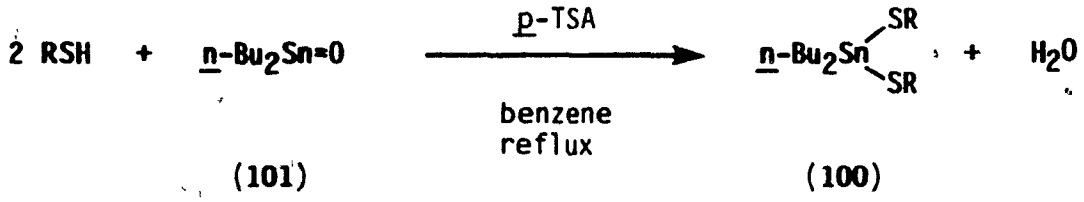
2.1.4 Symmetrical Disulfides from Dithio and Tetrathiotin(IV) Compounds

One of the problems that arises during the purification of disulfides is the large amount of tin by-product which is present in the reaction mixture. For instance, from a bromine oxidation of 1 g of tri-n-butyl t-butylthiotin(IV) (**96d**) there results a maximum of 0.24 g of disulfide and 0.98 g of tri-n-butyltin bromide (4.1 g of tin bromide per 1 g of t-butyl disulfide). The tin derivative adheres strongly to neutral alumina; hence purification is facilitated with alumina and nonpolar eluting solvents. Nevertheless, the large amount of tin by-product is annoying. This can be alleviated somewhat by using dithiotin

or better still, tetrathiotin compounds. Whereas bromine oxidation of tri-n-butyl n-butylthiotin(IV) results in 4.1 g of tin bromide per 1 g of dibutyl disulfide, the use of di-n-butyl di-n-butylthiotin(IV) affords, upon bromine oxidation, 2.2 g of tin dibromide per 1 g of dibutyl disulfide. Bromine oxidation of tetra-n-butylthiotin(IV) yields 1.3 g of stannic bromide per 1 g of dibutyl disulfide.

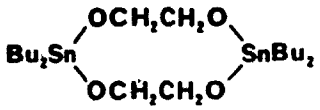
di-n-Butyl di-n-butylthiotin(IV) (**100a**) and di-n-butyl dibenzylthiotin(IV) (**100b**) were prepared by refluxing 2 equivalents of the respective thiols with 1 equivalent of di-n-butyltin oxide (**101**) in the presence of catalytic amounts of p-toluenesulfonic acid (Scheme 10). The apparatus was equipped with a Dean-Stark condenser to remove water.

Scheme 10.



(**101**) (**100**)

The products were thick opaque liquids. This preparation is not unlike that of Considine[121] who reacted di-n-butyltin oxide with 1,2-ethanediol (ethylene glycol) and obtained 1,1,6,6-tetra-n-butyl-1,6-distanna-2,5,7,10-tetraoxacyclodecane (**102**).



(**102**)

tetra-n-Butylthiotin(IV) (**103a**) and tetrabenzylthiotin(IV) (**103b**) were synthesized by adding 1 equivalent of the corresponding thiol in the presence of freshly distilled triethylamine to slightly less than 1/4 equivalent of stannic chloride (**99**) (Scheme 11). After typical work up procedures, the tetraalkylthiotin compounds were obtained as thick, gummy liquids. These compounds were not very stable; after 1 week ^{1}H-NMR and GC showed evidence for the corresponding symmetrical disulfide.

Scheme 11.

$$4\ \underline{n}\text{-BuSH} + SnCl_4 \xrightarrow{Et_3N} (\underline{n}\text{-BuS})_4Sn + 4\ Et_3NHCl$$

(**99**) (**103**)

di-n-Butyl disulfide and dibenzyl disulfide were obtained in good yields by oxidizing the pertinent dithiotin and tetrathiotin species with 1 and 2 equivalents of bromine respectively. As before, the oxidation was carried out in CCl_4; addition of oxidant was stopped once the red-brown bromine color persisted. The yields are summarized below.

Table 4. Isolated Yields of Symmetrical Disulfides Prepared from the Corresponding Dithiotin and Tetrathiotin Derivatives.

	from dithiotin compound	from tetrathiotin compound
di-n-butyl disulfide	94%	80%
dibenzyl disulfide	96%	74%

The lower yield of symmetrical disulfide obtained from the oxidation of tetrathiotin derivatives may be a reflection of the lower stability of these compounds as opposed to the dithiotin species. Kennedy and McFarlane[122] have noted that, unlike monothiotin(IV) and dithiotin(IV) species, trithiotin(IV) and tetrathiotin(IV) compounds are susceptible to slow atmospheric hydrolysis. Nevertheless, as anticipated, very good yields of symmetrical disulfides were obtained and work-up procedures were simplified.

2.1.5 Bis(triphenylmethyl) Disulfide; (Dityityl Disulfide)

It was of interest to investigate the preparation of dityityl disulfide (**8h**) via an organotin reagent since triphenylmethanethiol (**104**) itself is not readily oxidized by iodine to the disulfide, as is

$$\underset{(104)}{Ph_3CSH} + Bu_3SnCl \longrightarrow \underset{(96h)}{Bu_3Sn\text{-}SCPh_3} \xrightarrow{\frac{1}{2}\ I_2} \underset{(8h)}{\frac{1}{2}\ (Ph_3CS)_2} + Bu_3SnI$$

the case with most other thiols.[123] The mechanism for iodine oxidation of thiols is thought to be as follows.[123]

$$RSH + I_2 \rightleftharpoons RSI + HI$$

$$RSH + RSI \rightleftharpoons RSSR + HI$$

net... $$2\ RSH + I_2 \rightleftharpoons RSSR + 2HI$$

Provided that HI (strong reducing agent) is taken up in an aqueous solution or by the action of a base then the reaction proceeds and disulfide is formed.[73] However, for R = triphenylmethyl (trityl), the initial equilibrium disfavors sulfenyl iodide formation. It has been argued that inductive effects withdraw electrons from sulfur, hence weakening its effectiveness as a nucleophile.[123]

In preparing the trialkyl thiotin(IV) compound we are dealing with a sufficiently different situation, so halogen oxidation may afford the disulfide.

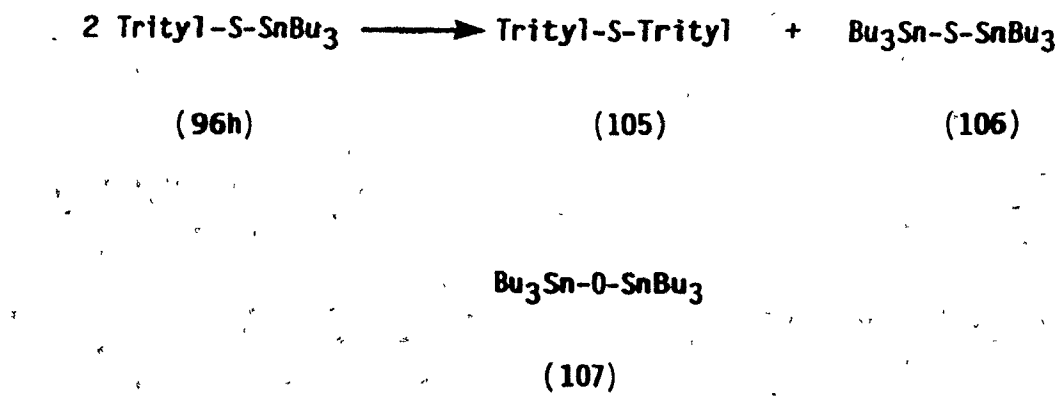
Triphenylmethanethiol (**104**) was prepared by passing hydrogen sulfide through an acetic acid solution of triphenylmethanol (triphenylcarbinol) containing a catalytic amount of sulfuric acid. This preparation, based on that of Vorländer and Mittag[124], easily afforded the odorless thiol in 91% yield.

The thiol was then reacted with tri-n-butyltin chloride by using procedures similar to those already presented except that the solution was stirred vigorously for 20 h. Proton NMR, mass spectrometry and ^{119}Sn-NMR showed that after this lengthy time the mixture was non-homogeneous. The resultant orange mixture streaked on silica and alumina while attempts at distillation led to decomposition. ^{119}Sn-NMR of the crude showed three peaks : 54.7 ppm (46%, thiotin); 104.9 ppm (16%); and 154.6 ppm (38%, tri-n-butyltin chloride). The ^{119}Sn-NMR integrations appear to reflect relative abundances reasonably well; for instance the (1:1), (10:1) and (1:10) molar mixtures of tri-n-butyltin chloride and tri-n-butyl phenylthiotin(IV) provided the following integrations: (1.1 : 1); (11.4 : 1); (1 : 9.2). Tin NMR data are tabulated

later in Section 2.4.1. MS also showed evidence of unreacted tri-n-butyltin chloride.

A small amount of fine white crystals (mp 160-164°C) precipitated when the crude mixture was taken up in cold hexanes. This solid was bis(triphenylmethyl) sulfide (**105**, dityityl sulfide), obtained in 3% yield; the mixed melting point with authentic bis(triphenylmethyl) sulfide[125] (mp 158-165°C) was 159-164°C. Furthermore, the proton NMR of these white crystals and authentic sulfide (**105**) were identical. Disproportionation of tri-n-butyl triphenylmethylthiotin(IV) (**96h**) may well have given bis(triphenylmethyl) sulfide and bis (tri-n-butyltin) sulfide (**106**) (Scheme 12). It was thought that this may account for the third peak found in the ^{119}Sn-NMR at 104.9 ppm; however, an authentic sample of (**106**) showed a ^{119}Sn-NMR resonance at 82.6 ppm. In fact, the peak at 104.9 ppm corresponds to bis(tri-n-butyltin) oxide (**107**), which likely resulted from the hydrolysis of residual tri-n-butyltin chloride during aqueous work-up procedures. The 3 % of bis(triphenylmethyl) sulfide found could be due to air oxidation of the tin-sulfur reagent.

Scheme 12.



This crude mixture was oxidized with bromine or iodine in an attempt to form the disulfide from tri-n-butyl triphenylmethylthiotin(IV) in the mix. Typical work-up procedures afforded an oily blend. Proton NMR of this mix showed upfield resonances corresponding to n-butyl and a resonance in the aromatic region at 7.29 ppm. The latter peak may have been that of bis(triphenylmethyl) disulfide.

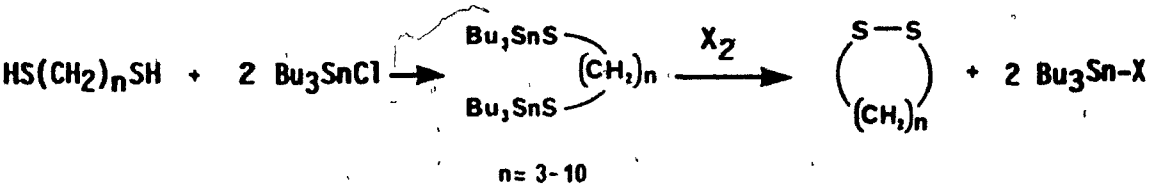
After the addition to the mixture of hexanes/dichloromethane (7:1) white crystals slowly appeared; these were recrystallized to afford 43% of bis(triphenylmethyl) sulfide. The solid decomposed at 159-164°C. A mixed melting point with authentic bis(triphenylmethyl) sulfide[125] was in the same range. The literature melting point of the disulfide is 155°C while that of the sulfide is 165°C.[126] ^{1}H-NMR showed a singlet at 7.23 ppm. Lastly, the osmometric molecular weight determination of these crystals indicated a molecular weight of 497 g/mol, the calculated weight of the sulfide is 519.4 g/mol while that of the disulfide is 551.5 g/mol. Clearly, the isolated product was the sulfide and not the disulfide. The differences in proton NMR between the crude mixture and the isolated product (7.29 ppm versus 7.23 ppm) suggest that the disulfide may have been formed initially. By analogy with phenyl sulfides and disulfides, one would expect the proton resonance for the disulfide to be slightly downfield from the sulfide. The aromatic resonance for diphenyl sulfide is 7.28 ppm, for diphenyl disulfide it is 7.31 ppm. It is likely that if the disulfide was part of the oily crude, after oxidation, then purification attempts led to decomposition. There have been previous reports stating the low stability of bis(triphenylmethyl) disulfide;[126,127] the disulfide was prepared by condensing triphenylmethanesulfenyl chloride with thiphenylmethanethiol.[127] It has

also been noted that the disulfide is surprisingly less stable than the corresponding trisulfide and tetrasulfide.[121] Generally, when considering a series of polysulfides, the opposite is true. As an example, the energy of the sulfur sulfur (S-S) bond in dimethyl disulfide is 74 kcal/mol[19] while the average S-S bond energy for dimethyl tetrasulfide is 36 kcal/mol.[127] Steric interference is introduced to explain the anomaly presented.

2.2 Cyclic Disulfides

Cyclic disulfides (**73**) where n=3-10 were prepared via two routes. In the first method the respective dithiols (**108**) were treated with 2 equivalents of tri-n-butyltin chloride to afford μ-α,ω-alkyldithiohexa-n-butylditin(IV) compounds (**109**). These were subsequently oxidized with bromine or iodine to yield the cyclic disulfides (Scheme 13). This preparation is not unlike that used to make the tri-n-butyl alkylthiotin(IV) compounds.

Scheme 13.

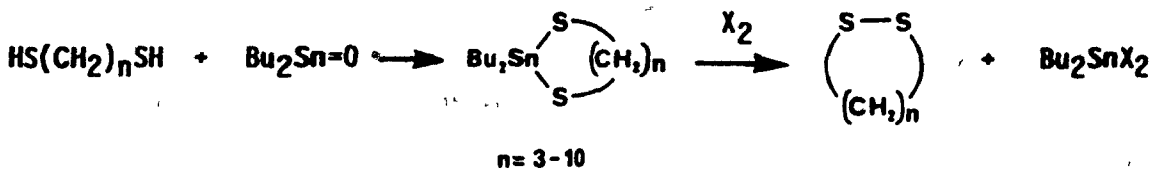


(**108**) (**97**) (**109**) (**73**)

For the second approach it was first necessary to synthesize 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes (**110**) by refluxing the appropriate dithiols with di-n-butyltin oxide (**101**). The compounds were then oxidized with bromine or iodine to give the corresponding cyclic

disulfides (Scheme 14). This procedure parallels that in which di-n-butyl di-n-butylthiotin(IV) (**100a**) and di-n-butyl dibenzylthiotin(IV) (**100b**) were prepared and then oxidized to afford di-n-butyl disulfide and dibenzyl disulfide.

Scheme 14.



(108) **(101)** **(110)** **(73)**

Before we consider each of these preparations in more detail it is important to realize that although the two methods are similar, in that firstly a tin-sulfur derivative is prepared followed by an oxidation step yielding the disulfide, there is an important difference between these two procedures. In the first synthesis (Scheme 13) cyclization occurs during the oxidation step, whereas in the second (Scheme 14), cyclization occurs during the synthesis of the tin-sulfur derivative.

All of the required α,ω-alkane dithiols were available from commercial sources except 1,7-heptanedithiol and 1,9-nonanedithiol; these were prepared in good yields, 81% and 78% respectively, using the thiouronium salt method.[128] This involves treatment of the corresponding dibromides with thiourea in refluxing ethanol. The thiduronium salt, which formed, was decomposed to the dithiols by refluxing in dilute aqueous potassium hydroxide. The resultant dithiols had boiling points that matched literature values and proton NMR was correct for each.

2.2.1 Cyclic Disulfides Prepared from μ-Dithioditins

The μ-α,ω-alkyldithiohexa-n-butylditin(IV) compounds were viscous liquids or waxy solids; they were difficult to purify because they streaked severely on alumina or silica gel and they were not readily distillable. Fortunately, after the samples had been placed under vacuum overnight, proton NMR, ^{119}Sn-NMR and MS showed that these dithioditin species were homogeneous; hence they were used without further purification.

The μ-dithioditin(IV) compounds were oxidized with bromine or iodine in CH_2Cl_2 to yield the cyclic disulfides. The oxidant (0.20 M in CH_2Cl_2) was added at a rate of 2 ml/min to a 0.05 M dichloromethane solution of the tin-sulfur derivative. Bromine or iodine were taken up as quickly as they were added, as shown by the fast dispersal of the oxidant's color in solution. With this rate of feed, a potential of 4.0 mmol of cyclic disulfide can be prepared in 10 min. Table 5, below, shows the monomer yields, which compare well with previous preparations of these cyclic disulfides. As was indicated in the introduction to this thesis, former syntheses required long addition times, as much as days, or high dilution (many liters of solvent). Often, literature yields are much lower than those achieved in this work.[129]

The yields of the cyclic disulfides are all for isolated compounds except for 1,2-dithiolane (23). The yields for this compound are based on ultraviolet spectra of dichloromethane solutions (various dilutions), (λ_{max} 330 nm, ϵ=142).[130] This UV data may be compared with the value obtained by Barltrop, Hayes and Calvin[45], (EtOH, λ_{max} 334 nm, ϵ=150). Attempts to isolate this compound by gentle evaporation of the solvent under a stream of nitrogen led to polymerization.

Table 5. Yields of Cyclic Disulfides Prepared by the Method in Scheme 13.

Disulfide	Ring Size	% Yields with Br_2	% Yields with I_2
1,2-Dithiolane (**23**)	5	88	92
1,2-Dithiane (**74**)	6	95	96
1,2-Dithiepane (**75**)	7	76	74
1,2-Dithiacyclooctane (**76**)	8	36	37
1,2-Dithiacyclononane (**77**)	9	39	42
1,2-Dithiacyclodecane (**78**)	10	59	61
1,2-Dithiacycloundecane (**79**)	11	(34)*	(38)*
1,2-Dithiacyclododecane (**80**)	12	1.5, (59)*	(61)*

* these entries were isolated as dimers, GC evidence shows that the monomers were initially formed but isolation resulted in dimerization.

Except for a low yield (1.5 %) of (**80**) when Br_2 was used as an oxidant, 1,2-dithiacycloundecane (**79**) and 1,2-dithiacyclododecane (**80**) were obtained as dimers. Gas chromatographic analyses showed that both of these cyclic disulfides were formed to some degree as monomers. It appears that work-up procedures (chromatography and the removal of solvent) yielded the dimers. It is difficult to say what amount of monomer was initially formed because the GC response factor of the monomer is unknown. Without this, GC integrations can only be estimates based on analogous compounds. It is possible to analyze the chromatograms of the crude mixtures and extrapolate from isolated dimer yields;

doing this indicates that a good deal of the dimer obtained after chromatography resulted from the monomer, as much as 80% of the isolated amount of dimer in both cases.

Structural studies were carried out to discriminate between monomer and dimers or possibly higher polymers, these are detailed in section 2.2.5. It is worth noting however, that these studies were difficult for the eight-membered (**76**), nine-membered (**77**) and ten-membered ring disulfide (**79**), since these three polymerized in a few hours. The eleven-membered ring and the twelve-membered ring disulfides [(**79**) and (**80**)], which were isolated as dimers, continued to polymerize to higher polymers; compound (**79**) appeared to be more prone to further polymerization than compound (**80**). In contrast, 1,2-dithiane (**74**), the six-membered ring disulfide could be kept for weeks with little polymerization while 1,2-dithiepane (**75**) the seven-membered ring disulfide could be kept for about one week before polymerization became noticeable. The various stabilities in the cyclic disulfide series likely reflects ring effects on the sulfur-sulfur bond. The low stability of the medium-size ring disulfides has also been noted by Schöberl and Gräje[74] as well as Affleck and Dougherty.[68]

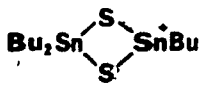
The lower yields obtained for the eight- and nine-membered ring disulfides coincides with the enthalpy "dip" on the ease of cyclization curves (pages 29 and 30). Furthermore, the greatest yields were obtained for the five- six- and seven-membered ring disulfides; this too was predicted from the ease of cyclization curve on page 30.

2.2.2 Cyclic Disulfides from 2,2-di-n-Butyl-1,2,3-Dithiastannacycloalkanes

The 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes (**110**) were prepared by adding the respective dithiols to benzene solutions of di-n-butyltin oxide and catalytic amounts of para-toluenesulfonic acid. Two different final concentrations of benzene solutions were used (0.05 M, 0.20 M). The dithiols were added as 1.0 M benzene solutions at a rate of 2 ml/min. The reaction is a straightforward nucleophilic displacement of the oxygen by two sulfhydryl moieties. The water that is formed in this reaction was removed as a water/benzene binary azeotrope (bp. 69 °C) and collected in a Dean-Stark condensing apparatus.

2,2-di-n-Butyl-1,3,2-dithiastannacyclohexane (**110a**) was obtained as fine white crystals in 97% yield. This compound was clearly monomeric, as attested by mass spectrometry and, more important, osmometric molecular weight determinations. The other dithiastannacycloalkanes were very thick liquids or gums. These compounds streaked on silica and alumina column chromatography. Attempts at distillation using very high vacuum charred the samples; the vacuum was acquired with an oil diffusion pump (10^{-5} mm/Hg). It is surprising that these monotin species could not be distilled; since, tri-n-butyl benzylthiotin(IV) (**96a**) distilled at 139 °C/0.3 mm. Heating the neat samples during distillation may have caused them to polymerize. These polymers would then decompose upon further heating (180°-200°C). Alternatively, the dithiastanna compounds may have been prepared solely as dimers or higher polymers; however, the good yields of monomeric cyclic disulfides, which were achieved by oxidizing these compounds, largely discredits this

possibility. It should be noted that mass spectral evidence for many of the dithiastanna systems indicates that they were obtained, to some degree, as dimers (polymers); there is no reason to believe that they were obtained fully in this manner. The mass spectra for 2,2-di-n-butyl-1,3,2-dithiastannacyclooctane (**110c**), 2,2-di-n-butyl-1,3,2-dithiastannacyclononane (**110d**), 2,2-di-n-butyl-1,3,2-dithiastannacyclodecane (**110e**), 2,2-di-n-butyl-1,3,2-dithiastannacycloundecane (**110f**), 2,2-di-n-butyl-1,3,2-dithiastannacyclododecane (**110g**) and 2,2-di-n-butyl-1,3,2-dithiastannacyclotridecane (**110h**) all showed peaks with m/z greater than the respective parent ions for the monomers. The peaks in question are a cluster whose largest components are m/z: 475, 473 and 471. This cluster corresponds to $n\text{-}Bu_3Sn_2S_2^+$, which may appear as (**111**) depicted below. The peaks match the isotopic cluster that can be calculated for a ditin species using all of the naturally occurring isotopes of tin. A broader discussion on the mass spectral behavior of tin species, including calculated clusters, is included later in this chapter (Section 2.4.2).



(111)

It was desired to isolate all of the dithiastannacycloalkanes in pure monomeric form so that a study on the amount of monomeric cyclic disulfide resulting from the subsequent oxidation could have been performed; unfortunately, as indicated above, this could not be done. Nonetheless, cyclic disulfides were prepared by bromine or iodine oxida-

tions of the 2,2-di-n-butyl-1,3,2-dithiastannaycloalkanes (prepared in 0.05 M or 0.20 M solutions) as they were obtained. That is, those mixtures which were known to contain appreciable amounts of polymeric dithiastanna compounds were used as such. The oxidative procedure is much the same as the previous method described to form cyclic disulfides by oxidatively coupling μ-α,ω-alkyldithiohexa-n-butylditin(IV) compounds. The yield of 1,2-dithiolane (**23**) was once again determined by ultraviolet spectroscopy. As before 1,2-dithiacycloundecane (**79**) and

Table 6. Yields of Cyclic Disulfides as Obtained by the Oxidation of 2,2-di-n-Butyl-1,3,2-Dithiastannacycloalkanes Which had Been Prepared in 0.05 M and 0.20 M Solutions.

Disulfide	Ring size	% Yields 0.05 M		0.20 M	
		Br_2	I_2	Br_2	I_2
(23)	5	97	97	91	93
(74)	6	96	96	95	96
(75)	7	80	77	53	49
(76)	8	22	26	16	16
(77)	9	36	31	18	14
(78)	10	45	49	20	21
(79)	11	(47)*	(40)*	(34)*	(38)*
(80)	12	(44)*	(43)*	(39)*	(37)*

* These entries were isolated as dimers.

1,2-dithiacyclododecane (**80**) were formed as dimers; again, GC indicated that appreciable amounts of the monomers were formed in situ. As much as 80 % of the isolated dimer yields were initially in monomeric form; however, for reasons noted earlier (page 51), only estimates of the amount of monomer formed can be made. The yields for the cyclic disulfides are summarized in Table 6 above. The relation between yields and ring size is similar to that noted before (page 52). Noteworthy, is the fact that the yields of the cyclic disulfides were greater when the dithiastannacycloalkanes prepared in the more dilute solution (0.05 M) were used. This was the anticipated result suggesting that dilution aids in monomer formation; the effects of dilution in conjunction with tin reagents is presented in Section 2.2.4.

2.2.3 Comparison of Yields of Cyclic Disulfides Prepared from the Oxidation of Thiotin Species Versus Oxidation of the Dithiol

A GC study was undertaken to compare the efficacy of synthesizing cyclic disulfides using thiotins versus the preparation of these disulfides without tin . One equivalent of bromine was slowly added to 0.05 M CH_2Cl_2 solutions of the μ-α,ω-alkyldithiohexa-n-butylditin compounds (**109**). This preparation is a duplicate to the procedures presented above except the dichloromethane contained 2% v/v of 2,5-dimethyl thiophene. This additive served as an inert internal standard for gas chromatographic analyses. Using identical conditions (solvent, time, concentrations and temperature) the cyclic disulfides were also furnished by directly oxidizing the respective dithiols. In the latter set of experiments 2 equivalents of triethylamine were added to the solution prior to a slow introduction of bromine. The triethylamine is

Table 7. Relative Yields of Cyclic Disulfides; With and Without Tin.

Disulfide	Ring Size	Relative Amounts with tin : without
1,2-Dithiolane (23)	5	1.8 : 1
1,2-Dithiane (74)	6	1.1 : 1
1,2-Dithiepane (75)	7	2.7 : 1
1,2-Dithiacyclooctane (76)	8	12 : 1
1,2-Dithiacyclononane (77)	9	10 : 1
1,2-Dithiacyclodecane (78)	10	11 : 1
1,2-Dithiacycloundecane (79)	11	8.0 : 1
1,2-Dithiacyclododecane (80)	12	6.5 : 1

required to neutralize hydrobromic acid which forms; this acid hinders disulfide formation.[73] Table 7 above, summarizes the relative yields for cyclic disulfides of five to twelve-membered size rings as obtained with, and without the aid of thiotins.

These experiments show that for small rings, 5 and 6 members, tin-sulfur derivatives improve yields somewhat. Good yields for these cyclic disulfides, particularly 1,2-dithiane (**74**), have been achieved in the past by simple oxidative procedures.[71,74,75,78,79]

1,2-Dithiepane (**75**) was formed in better yields when the corresponding thiotin compound was used, although this compound can also be attained in moderate yields with straight forward oxidation.[78] The relative yields of the medium size rings (8 to 12-membered rings) clearly show that thiotin(IV) compounds greatly aid in the formation of monomeric cyclic disulfide. The medium size rings are the most difficult

Table 8. Yields of Cyclic Disulfides Attained Using Bunte Salts.[68]

Disulfide	Ring Size	Yield(%)	Authors' Comments[68]
1,2-Dithiepane (75)	7	13	
1,2-Dithiacyclooctane (76)	8	4	Quickly polymerized to a sticky rubber.
1,2-Dithiacyclononane (77)	9	2	
1,2-Dithiacyclodecane (78)	10	3	
1,2-Dithiacycloundecane (79)	11	0.2	Trace of oil, too little to purify.
1,2-Dithiacyclododecane (80)	12	2-3	Polymerized almost spontaneously.

to make; for instance, Affleck and Dougherthy[68] prepared these medium ring disulfides in low yields by oxidation of the respective Bunte salts. The concentration of the solution was 0.2-0.4 M and the oxidant was added over quite a short period of time (1.50 moles of $CuCl_2$ added in 2 h). The yields that these workers attained are given above (Table 8).

2.2.4 Oxidation of μ-1,7-Heptyldithiohexa-n-Butylditin(IV) (109e) in a Variety of Solution Concentrations

Solution concentration plays an important role in preparation of monomers. A combination of dilution and tin effects should afford even greater yields of monomeric macrocycles. This was indicated earlier when a comparison was made between the yields of monomeric cyclic disulfides synthesized by the oxidation of the 2,2-di-n-butyl-1,3,2-dithiastanna compounds which were prepared in two different solution concentrations, 0.05 M and 0.20 M. Higher yields of disulfides

were achieved when the dithiastannacycloalkanes prepared in a 0.05 M benzene solution were used. To further investigate combinations of dilution and tin effects, 1,2-dithiacyclononane (**77**) was prepared using a series of diluted solutions containing either μ-1,7-heptyldithiohexa-n-butylditin(IV) (**109e**) or just the dithiol (1,7-heptanedithiol). Five different solutions of 1,7-heptane dithiol in the presence of 2 equivalents of triethylamine were oxidized with one equivalent of bromine. Using similar reaction conditions, without triethylamine, a series of solutions of the tin-sulfur derivative (**109e**) were concomitantly oxidized. The reaction concentrations were; 0.50 M, 0.10 M, 0.05 M, 0.01 M and 0.005 M. The solutions were prepared by appropriately diluting stock solutions which contained an equal amount of 2,5-dimethylthiophene, an internal GC standard . In this way all ten solutions contained the same amount of 2,5-dimethylthiophene. Only three of the entries were isolated; 0.05 M with tin, 0.005 M with tin and 0.005 M without tin. The yields of the other entries were deduced by using the internal standard and comparing GC data for these entries with GC data obtained for the three solutions noted above.

At the higher concentrations, 0.50 M and 0.10 M, no monomeric disulfide was detected after oxidation of the dithiol. Oxidation of the thiotin at these concentrations resulted in 7 % and 21 % yields of the monomer respectively. In 0.05 M dichloromethane solutions, the yield of 1,2-dithiacyclononane (**77**) from the dithiol was 4% while from the thiotin the yield was 42%. The more dilute solutions showed even further improvement in monomer formation; at 0.01 M and 0.005 M the respective yields from the dithiol were 8% and 9%, from the thiotin the yields were 63% and 66% (Table 9).

Table 9. Yields of 1,2-Dithiacyclononane Obtained With and Without Tin Reagents in Various Solution Concentrations.

Solution Concentration (mol/l)	% Yield With Tin	% Yield Without Tin
0.50	7	-
0.10	21	-
0.05	42	4
0.01	63	8
0.005	66	9

Examining the results from the last two solution concentrations, 0.01 M and 0.005 M, it is interesting to note that while there was a doubling in the dilution factor there was no significant improvement in yields. It is evident that a consideration of cost and time effectiveness of these types of reactions is warranted. While further dilution does improve yields it may not be sufficient to substantiate uses of large quantities of solvent or time which would be required. Nevertheless, it is clear that dilution which is important for the formation of monomers from the dithiols is also very useful when oxidizing the tin-sulfur reagents. Hence cyclic disulfides are best prepared with the conjunction of the use of tin-sulfur compounds and dilution. Dilution may be as straightforward as presented above, or it may involve high-dilution methods including titrimetry.[76]

2.2.5 Discrimination Between Monomers and Dimers

It is imperative to establish whether the cyclic disulfides which were isolated, were prepared as monomers, dimers or possibly higher polymers. A wide variety of physical methods were used to discriminate between monomers and dimers. Individually these methods may not be sufficient proof, but together they provide strong evidence.

2.2.5.1 Physical Properties of Cyclic Disulfides

Many of the isolated cyclic disulfides had physical properties similar to those published. 1,2-Dithiane (**74**) was isolated as a white solid whose melting point was 30-31°C; some literature values are 29°C[71], 29-30°C[75], 31-31.5°C[74] and 30-32°C[78]. 1,2-Dithiepane (**75**) had a boiling point of 47°C/1.0 mm; literature values include 55-60°C/1.7 mm[78], 42°C/2 mm[74] and 57-60°C/5 mm[68]. The refractive indices of those compounds which were obtained as liquids also compares well with published results; these data are summarized below in Table 10.

Table 10. Refractive Indices of Some Cyclic Disulfides.

Disulfide	Refractive Index (n_D^{25})	
	Found	Literature
1,2-Dithiepane (**75**)	1.5681	1.570[a], 1.5690[b]
1,2-Dithiacyclooctane (**76**)	1.567	1.5698[a]
1,2-Dithiacyclononane (**77**)	1.5627	1.5642[a], 1.5623[c]
1,2-Dithiacyclodecane (**78**)	1.5407	1.5461[a]

a: n_D^{25}, reference (74); b: n_D^{25}, reference (78); c: n_D^{25}, reference (76).

2.2.5.2 Molecular Refractivity Study

The density of 1,2-dithiepane (**75**) was determined to be 1.14765 g/ml using a Sodev inc. vibrating cell densitometer.[131] Knowing this value and the refractive index it is possible to compute the molecular refractivity using the Lorentz and Lorentz equation[132], where n is the

$$\text{Molecular Refractivity} = \frac{M}{d} \cdot \frac{[(n_D^{25})^2 - 1]}{[(n_D^{25})^2 + 2]}$$

refractive index, d is the density and M is the molecular weight. In this way the value obtained for the monomer is 38.27 ml/mol; for the dimer it would be twice that, 76.55 ml/ mole, by virtue of the molecular weight. The molecular refractivity can be provided by a second method: the summation of atomic and structural constants or bond refractions. These values are provided in many reference texts. Ordinarily one cannot differentiate between a monomer and a dimer in this fashion, since the calculated molecular refractivity of a dimer is twice that of the monomer (as with the computed molecular refractivity). The calculation consists of twice as many bond refractions, that is the dimer will have twice as many C-H bonds, twice as many C-S bonds and so on. However, the C-C bond refractivity for small rings is sufficiently different from large ring or alicyclic C-C bond refractivity; thus a comparison between computed and calculated molecular refractivities of the smaller seven-membered ring (1,2-dithiepane (**75**)) versus its dimer can be made to assist us in discriminating between monomer or dimer.

The calculated value for the monomer is 39.17 ml/mole or 2.30% higher than the computed value, while that calculated for the dimer is 78.55 ml/mole or 2.54 % higher than the computed value of 76.55. This

for monomer:						for dimer:					
4	C-C	@	1.27*	=	5.08	8	C-C	@	1.296	=	10.37
10	C-H	@	1.676	=	16.76	20	C-H	@	1.676	=	33.52
2	C-S	@	4.61	=	9.22	4	C-S	@	4.61	=	18.44
1	S-S	@	8.11	=	8.11	2	S-S	@	8.11	=	16.22
					39.17						78.55

* C-C value for small rings

appears to suggest that the liquid is monomeric 1,2-dithiepane, however the percent differences are so close as to make this study inconclusive.

Table 11. Calculated and Computed Molecular Refractivities of 1,2-Dithiepane.

	Refractivity		% Difference
	Calculated	Computed	
monomer	39.17	38.27	2.30
dimer	78.55	76.55	2.54

2.2.5.3 Molecular Weight Study

Molecular weight determinations were attempted using a Corona-Wescan Osmometric Molecular Weight Apparatus. The principle applied by

the system is as follows.[133] The vapor pressure of a solution is lower than that of a pure solvent at the same temperature. This is a direct consequence of Raoult's law, where P_1 is the partial pressure of solvent

$$P_1 = x_1 \cdot P_1^{\circ}$$

P_1° the vapor pressure of pure solvent and x_1, the mole fraction of solvent.

The instrument consists of two thermistors that are connected by a bridge; any unbalance can be measured with a sensitive detector. The thermistors are enclosed in a heated bath with a saturated atmosphere of pure solvent. The pure solvent in this case was toluene and the bath temperature was 50°C. When a solution is dropped on one of the thermistors, condensation of solvent into the solution from the surrounding atmosphere occurs. This happens because of the lower vapor pressure of the solution. This condensation releases heat, thus warming the thermistor. All the while, pure solvent is dropped unto the second thermistor; hence a temperature difference may be measured. From this difference (ΔT) the molecular weight of the solute can be measured. K is a constant which must be determined prior to the experiment by

$$\Delta T = K \cdot \frac{C}{m}$$

running a series of controls, C is the solute concentration in g/l and m is the molecular weight of the solute. The accuracy of the calibration curve required to find K could be confirmed by doing experiments on samples of known molecular weight; when this was done errors of 1-2% of the actual molecular weight were usually found, in some instances deviations of up to 5% were noted.

The system will not stabilize unless the solvent is sufficiently more volatile than the solute being investigated.[133] Unfortunately all of the monomeric cyclic disulfides were too volatile so that measurement of their molecular weights with this instrument proved to be impossible. Attempts to operate the instrument at lower temperatures by using more volatile solvents were also unsuccessful. It is recommended that the apparatus be operated at such a temperature so that the solvent vapor pressure be 50-200 mm Hg. For dichloromethane this temperature is 20°C.[133] Unluckily, mechanical pumping of the necessary coolant around the block containing the thermistors could not be affected with the needed precision to get the required stability. With n-pentane as solvent the required temperature is about 5°C; again the instrument was too noisy, although less so than before. For the latter case, the coolant used was a steady stream of cold tap water.

The instrument was useful for larger, less volatile compounds; for instance, it indicated that 1,2-dithiacycloundecane (**79**) and 1,2-dithiacyclododecane (**80**) were obtained as dimers. The molecular weight for (**79**) was determined to be 398, the calculated weight for the dimer is 380.7. The weight obtained for (**80**) was 418, the calculated dimer weight is 408.8 (Table 12). Noteworthy is the fact that 1,2-dithiacyclododecane which is isolated as a dimer had a melting point of 37-39°C. Schöberl and Gräfje isolated 1,2-dithiacyclododecane in 60% yield; they believed it to be monomeric, however the reported melting point (40-42°C[74]) suggests that they had actually isolated the dimer.

Table 12. Osmometric Molecular Weight Determination of (79) and (80).

Entry	Calculated Molecular Weight for Monomer	for Dimer	Molecular Weight Found
(79)	190.4	380.7	398
(80)	204.4	408.8	418

2.2.5.4 Proton NMR Study

All of the cyclic disulfides had the appropriate proton NMR spectrum. Usually, a resonance (triplet) at about 2.70 ppm downfield from TMS was found; this triplet was assigned to the methylenes adjacent to the disulfide linkage. This peak (2.70 ppm) is similar to the one found in straight chain aliphatic disulfides. Proton NMR is not very effective in discriminating between monomers and dimers or higher polymers of the medium or large ring disulfides. For the smaller ring disulfides, resonances for these methylenes next to sulfur were slightly further downfield. For 1,2-dithiane (**74**) and 1,2-dithiepane (**75**) this peak was observed at 2.83 ppm. For 1,2-dithiolane (**23**), the corresponding peak was at 2.95 ppm; polymers of (**23**) also showed a resonance at *ca.* 2.95 ppm. The extra deshielding seen for 1,2-dithiolane (**23**) appears to be a result of the proximity of other sulfur atoms and not due to decreasing ring size. Polymers of 1,2-dithiepane (**75**) showed a resonance at 2.73 ppm; so for this one compound at least ^{1}H-NMR appears useful in discriminating between monomer and dimer (polymer). For all of the cyclic disulfides in this study, the other methylene resonances, those not adjacent to sulfur, were seen at 1.30-1.90 ppm.; integrations were correct throughout.

2.2.5.5 Raman Study

The usual Raman S-S symmetrical stretch is at about 510 cm^{-1}.[134,135] It may appear that this could be useful in contrasting between monomers and dimers, since there is an approximate linear relationship between the frequency of the S-S stretch and the CS-SC dihedral angle.[136] The explanation for this being that as the CS-SC dihedral angle decreases from the expected 90° there is more $p\pi - p\pi$ interference. This serves to destabilize or weaken the sulfur-sulfur bond.[136,137] Thus, disulfides with dihedral angles smaller than usual should therefore show lower frequency S-S stretches. Bastian and Martin[138], as well as Van Wart and Sheraga[137] have shown that substituted 1,2-dithiolanes have S-S stretches below 500 cm^{-1}. Unfortunately, this effect seems to only become prominent or noticeable for compounds with a CS-SC dihedral angle below 60°.[137] The dihedral angles

Table 13. S-S and C-S (Neat) Raman Stretch for Cyclic Disulfides.

Disulfide	S-S cm^{-1}	C-S cm^{-1}
1,2-Dithiane (**74**)	509	659
1,2-Dithiepane (**75**)	515	638
1,2-Dithiacyclooctane (**76**)	509	635
1,2-Dithiacyclononane (**77**)	506	633
1,2-Dithiacyclodecane (**78**)	506	635
1,2-Dithiacycloundecane * (**79**)	506	635
1,2-Dithiacyclododecane * (**80**)	509	638

* Performed on neat sample of dimer.

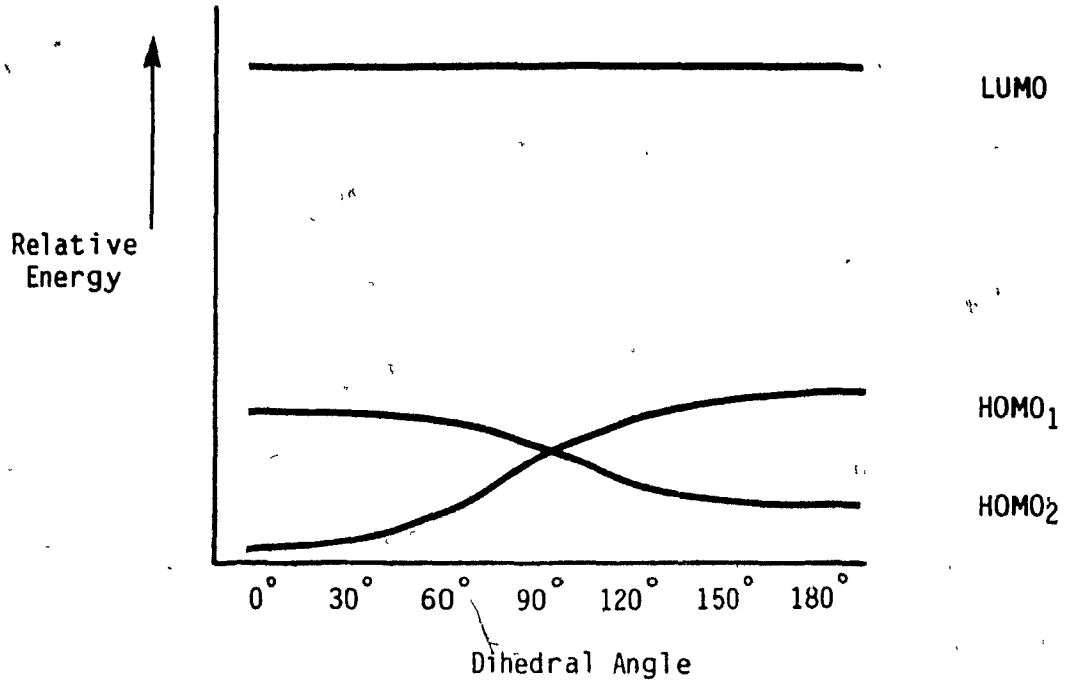
for a variety of substituted 1,2-dithianes are ca. 60°.[41,139] Consequently, Raman spectroscopy proves to be of little use for contrasting between monomers and dimers for 1,2-dithiane (**74**) or larger ring disulfides. Experimental results for some of the compounds prepared in this study are provided in Table 13.

2.2.5.6 Ultraviolet Spectroscopy Study

The usual first ultraviolet absorption for disulfides is at ca. 250 nm.[140,141] With decreasing ring size, this transition shows a bathochromic shift. For example, seven-membered ring disulfides show an absorption at ca. 260 nm. 1,2-Dithianes have a first transition at ca. 285 nm. Five-membered ring disulfides show this peak at ca. 330 nm.[141] Calvin and co-workers[45,142], who reported that 1,2-dithiolanes absorbed at 330 nm, were the first to point out the relationship between the first absorption band and ring size. They applied ring strain arguments to account for this. A more likely cause for this red shift is explained by the 'Bergson' model in which the energy of the highest occupied molecular orbital is dependent on the CS-SC dihedral angle.[140] His calculations were carried out to include dihedral angles between 0 and 90°. Recently these calculations have been extended to include the dihedral angles between 90 and 180°.[37,143] The energy diagram is given in Figure 4. The two highest occupied molecular orbitals ($HOMO_1$ and $HOMO_2$) are made up of four lone pair electrons from the sulfur atoms; they are described as a nonbonding combinations of $3p\pi$ atomic orbitals. These orbitals vary with the CS-SC dihedral angle as indicated above. The lowest unoccupied MO (LUMO) is characterized as a σ^* MO.[37] The

first transition then is a $n \rightarrow \sigma^*$ band.[37,141,143] It is because of this transition to an antibonding orbital that S-S bond cleavage occurs when disulfides are exposed to UV light.[140] An analysis of Figure 4[37] clearly shows that a red shift is expected as the disulfide dihedral angle deviates from 90°.

Figure 4. Correlation of Molecular Orbitals for the Disulfide Linkage with Dihedral Angle



Although isolated as a polymer, in solution, prior to isolation attempts, the first band for 1,2-dithiolane (**23**) was 331 nm. For 1,2-dithiane (**74**) this absorption occurred at 290 nm. The seven-membered 1,2-dithiepane (**75**) showed a peak at 262 nm. These compounds were shown to be monomers. If these three were dimers then it is reasonable to assume that the size of these dimeric rings would allow the disul-

fide(s) to approach the more favorable 90° dihedral angle, hence the first ultraviolet absorption would have been expected to be about 250 nm. For the larger cyclic disulfides, eight-membered rings or greater, UV experiments cannot ascertain whether they were isolated as monomers, dimers or even higher polymers. These larger rings may have been isolated as monomers but their CS-SC dihedral angles approach or are at 90°, similar to polymeric forms.

2.2.5.7 Mass Spectral Study

Mass spectroscopic information was obtained for all the cyclic disulfides in this study except for 1,2-dithiolane (**23**). The cyclic disulfides showed highly abundant parent ions. The cyclic disulfides of six- to ten-membered ring sizes showed parent ions for the monomeric species without any peaks of higher mass to charge ratio. This was taken as evidence, although inconclusive, that there were no dimers or higher polymers. It must be realized that lack of evidence for dimers in the MS does not preclude their presence. Dimers or higher polymers may have fragmented into monomeric moieties in the spectrometer. It should be noted however, that when compounds (**76**), (**77**) and (**78**), the eight-, nine- and ten-membered rings, were left standing to polymerize, the subsequent mass spectra showed parent ion peaks for both dimeric and monomeric species. 1,2-Dithiacycloundecane (**79**) and 1,2-dithiacyclododecane (**80**) which were isolated as dimers showed peaks at m/z 380 and 408 respectively; these being the parent ions for the dimer. While it is unlikely, peaks attributed to monomeric parent ions may well correspond to doubly charged dimeric parent ions.

In general, mass spectra of these compounds showed prominent loss of neutral sulfur ($M^+ - S$). Other fragments that were observed include the loss of a SH radical and the loss of $CH_2SH\cdot$. Losses of $C_2H_5S\cdot$, $C_3H_7S\cdot$ and $C_4H_9S\cdot$ occur for the larger nine- and ten-membered rings. The rest of the spectra are mostly composed of hydrocarbon fragments and a peak at m/z= 45 (CHS^+).

2.2.5.8 Gas Chromatographic Study and Summary

Thus far we have seen that the structural evidence suggests monomeric forms for the smaller disulfides but very little information is available for the larger ones. 1,2-Dithiolane is synthesized as the monomer but polymerizes on isolation. 1,2-Dithiane (**74**) and 1,2-dithiepane (**75**) are both monomeric. Mass spectral evidence and comparison of refractive indices to published values suggest that the medium sized rings, 8, 9 and 10, are also monomeric. However, further proof is required.

Gas chromatographic data suggests that all of the disulfides were prepared as monomers, including the 11 and 12-membered rings. After oxidation, the crude mixtures (disulfide and tin derivative in CCl_4) were injected into a 10 m capillary bonded column containing 3% Silicone OV-101. The temperature program was 80-225°C at a rate of 20°/ min, the carrier gas pressure was 0.7 kg/cm^2. The retention times, shown below in Table 14, compare well with retention times of straight chain alkyl disulfides containing the same number of carbon atoms. Furthermore, these retention times when plotted against ring size show a well aligned linear relationship (Figure 5). Since we have established that

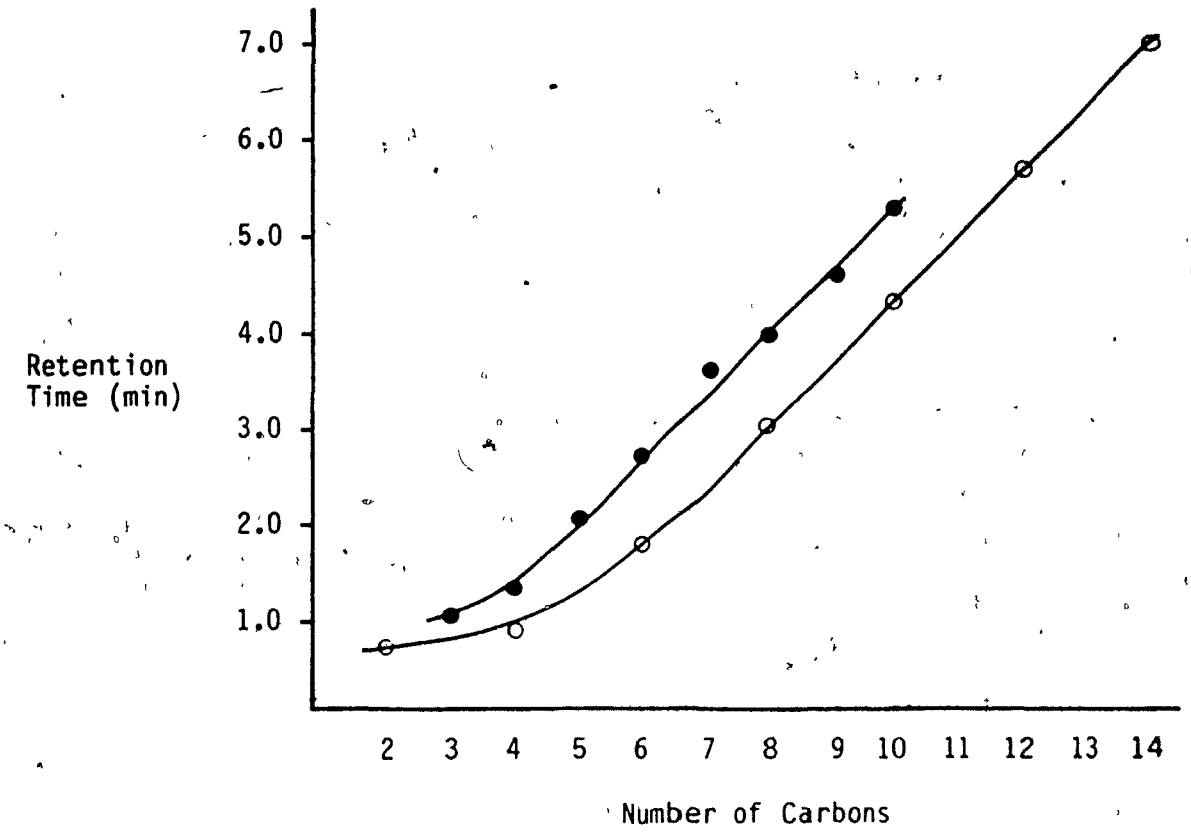
1,2-dithiolane (**23**), 1,2-dithiane (**74**) and 1,2-dithiepane (**75**) are monomeric it follows from Figure 5, page 73, that the larger cyclic disulfides were also prepared as monomeric species.

Table 14. Gas Chromatographic Retention Times of Cyclic Disulfides in Minutes; 10 m OV-101 Capillary Column, 80-225°C at 20°/min.

Disulfide	# of carbon atoms	retention time
Dimethyl disulfide	2	0.52
1,2-Dithiolane (**23**)	3	1.04
Diethyl disulfide	4	0.89
1,2-Dithiane (**74**)	4	1.33
1,2-Dithiepane (**75**)	5	2.01
di-n-Propyl disulfide	6	1.71
1,2-Dithiacyclooctane (**76**)	6	2.67
1,2-Dithiacyclononane (**77**)	7	3.62
di-n-Butyl disulfide	8	3.00
1,2-Dithiacyclodecane (**78**)	8	3.98
1,2-Dithiacycloundecane (**79**)	9	4.60
di-n-Pentyl disulfide	10	4.33
1,2-Dithiacyclododecane (**80**)	10	5.35
di-n-Hexyl disulfide	12	5.72
di-n-Heptyl disulfide	14	7.01
Dimer of (**79**)	18	10.39
Dimer of (**80**)	20	11.63
di-n-Decyl disulfide	20	11.74

The retention times of the isolated cyclic disulfides, after column chromatography, are similar to those found for crude GC analyses except for 1,2-dithiolane (**23**) which polymerized, 1,2-dithiacycloundecane (**79**) which dimerized and 1,2-dithiacyclododecane (**80**) which also dimerized. The GC retention times for the dimers of (**79**) and (**80**) are 10.39 and 11.63 min respectively; these species have been acknowledged to be dimeric using osmometric molecular weight determination.

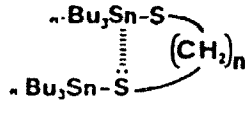
Figure 5. Plot of Cyclic Disulfide (—●—) and Straight Chain Symmetrical Disulfide (—○—) GC Retention Times as a Function of Ring Size.



2.2.6 Mechanism for a "Tin Effect"

The use of organotin compounds clearly enhances the isolated yields of cyclic disulfides; there appears to be some kind of effect imparted by tin. It is of interest to postulate a mechanism by which tin provides such good yields of monomeric cyclic disulfides, without the necessity of employing high dilution or titrimetric techniques. This behavior suggests a 'template effect' of sort; as mentioned in the introduction to this thesis there have been a number of recent reports on tin-directed cyclization reactions.[100,104-106,108]

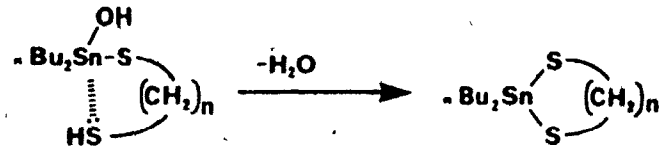
Table 7 on page 57 reported the relative yields of cyclic disulfides that were achieved by using thiotin species versus simple oxidation of dithiols. The use of tin provided higher yields of monomers; the effect was most prominent for the medium ring disulfides. Further, Figure 3 on page 30 shows that for medium size rings there is a dip in the enthalpy curve resulting from strain; this discourages monomer formation. One way in which tin may provide a template effect is through an auto-association mechanism as portrayed below, (112). In this structure (112) the two sulfurs are brought close together by a donation of the lone pair(s) of electrons on sulfur to the tin atom which is known to expand its valency.[106,144] Bromine or iodine oxidation may then act on this associated system. The μ-α,ω-alkyldithiohexa-



(112)

n-butylditin(IV) compounds (**109**) can approach cyclization without strong strain energy constraints. The dip in the enthalpy curve is raised somewhat, sufficient to improve the yields of monomers formed. Provided that entropy effects encourage monomer formation then good yields of these monomers may be observed.

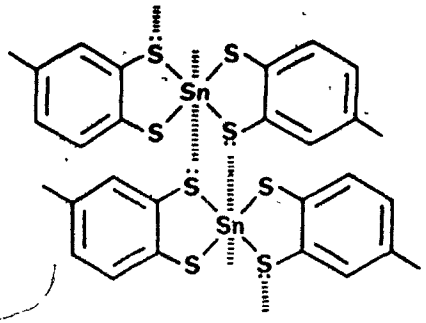
The good yields of cyclic disulfides formed from the oxidation of 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes (**110**) may be similarly explained. In this instance tin may impart its effect during the formation of the dithiastanna species (the cyclization step) and not during oxidation. The associated system may well resemble structure (**113**).



(**113**) (**110**)

Whereas X-ray and ^{119}Sn-NMR studies show that tin alkoxides auto-associate[144,145], it has been shown that some thiotin(IV) compounds do not.[122] The argument given to explain the lack of auto-association for these thiotin species is based on the lower electronegativity of sulfur and hence the lower Lewis acidity of tin. This lack of auto-association found for some thiotins disagrees with the proposed mechanisms of the 'template effect' given above. Recently, Zuckerman and co-workers[146] have shown that tin-sulfur species do auto-associate; they have found bis(tolyl-3,4-dithio)tin(IV) (**114**) exists as depicted below. While the auto-association of thiotins may be so small as to usually not be

noticeable by tin NMR, a weak association may be adequate for the purposes of a 'template effect'.



(114)

The presence of tin may also serve to mask the thiol moiety thus preventing rapid thiol-disulfide exchange which would lead to polymerization. Whereas monosulfides do not exchange with thiols in even extreme conditions, with disulfides "...the exchange is measurably fast and free of side reactions."[147] Rates of interchange between 1.3×10^4 and 9.0×10^5 $M^{-1}s^{-1}$ have been observed.[148] The reaction of cyclic disulfides and thiols has also been noted.[45,147]

Many of the monomeric cyclic disulfides polymerize quickly; some of the monomeric material formed during a very slow oxidative process may begin to polymerize before the full addition of the oxidant is complete. Hence, a fast reaction could afford a higher isolable yield of a given monomer. The bromine or iodine oxidations of thiotin(IV) species are very fast, so fast that attempts at measuring the rates was unsuccessful; kinetic experiments will be described in more detail later (Section 2.3.2). Since this oxidation is so quick there is a lower probability for the monomers to polymerize before isolation procedures are carried out, thus better potential yields of the monomers.

To summarize, the good yields of monomeric cyclic disulfides may result from a contribution of auto-association, the masking of the thiol moiety and the rapidity of the oxidation step. All of these result from the tin-sulfur reagent; hence, a 'tin effect'.

2.3 Oxidation Mechanism

2.3.1 Possible Mechanisms and Literature Precedent

There are three likely mechanisms by which the bimolecular cleavage of a tin-sulfur bond by halogen may occur. These mechanisms are acceptable for the generalized cleavage of a group IVb group VIb bond.[149]

The first mechanism entails nucleophilic attack on iodine by the sulfur atom, thus generating the charged sulfonium iodide ion (**115**). Iodide would then attack tin and displace sulfenyl iodide as shown. In a similar mode, a second molecule of thiotin (**96**) could then attack the sulfenyl iodide affording another sulfonium ion (**116**) which then proceeds to the disulfide (**6**). The development of a positive center

Scheme 15.

1) $R_3Sn\text{-}SR' + I_2 \longrightarrow \left[R_3Sn\text{-}\overset{I}{\underset{|}{S^+}}R' \;\; I^- \right] \longrightarrow R_3Sn\text{-}I + I\text{-}SR'$

(**96**) (**115**)

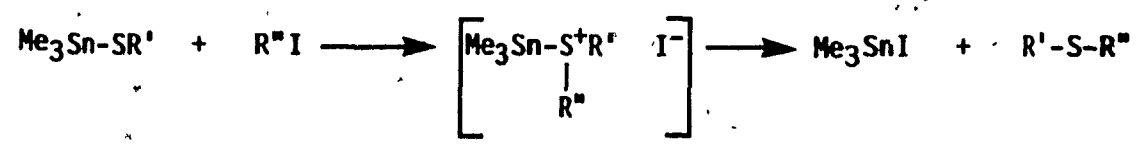
2) $R_3Sn\text{-}SR' + I\text{-}SR' \longrightarrow \left[R_3Sn\text{-}\overset{SR'}{\underset{|}{S^+}}R' \;\; I^- \right] \longrightarrow R_3Sn\text{-}I + R'S\text{-}SR'$

(**96**) (**116**) (**6**)

suggests that a Hammett plot would reveal a rather large negative substituent effect ($-\rho$). A reaction proceeding by this mechanism would also show a strong solvent dependence. The rates in polar solvents would be expected to be considerably faster than in nonpolar solvents.

A reaction which appears to proceed in this fashion is the synthesis of unsymmetrical sulfides (**117**) from trimethyl alkylthiotin(IV) compounds (**118**) and alkyl halides (**119**) (Scheme 16).[150,151] Studies on trimethyl methylthiotin(IV) showed rate acceleration in polar solvents ($k_{PhCN}/k_{Benzene}$ = ca. 100) and a significant negative ρ value of -1.4.

Scheme 16.



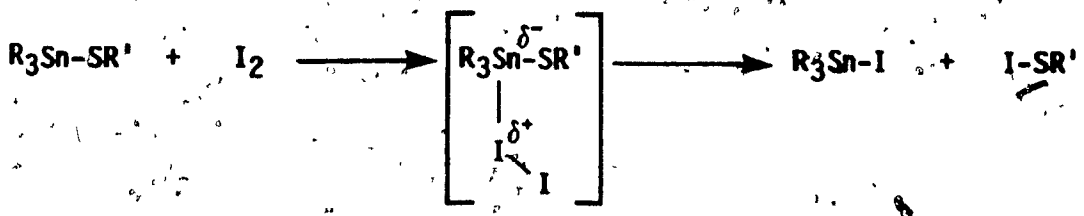
(**118**) (**119**) (**117**)

When (+)-2-bromo-n-octane was used there was an inversion of configuration at the carbon of the alkyl halide; this is expected to occur for the proposed mechanism. Other mechanisms which we will examine would show either retention or partial racemization.

The second possible mechanism is five-coordination of tin to iodine (**120**) (Scheme 17).

The sulfenyl iodide which is generated may then react with a second molecule of the thiotin(IV) compound, perhaps via a similar mechanism to generate the disulfide. This provides some negative charge on tin, hence a positive value is expected from a linear free energy plot.[152]

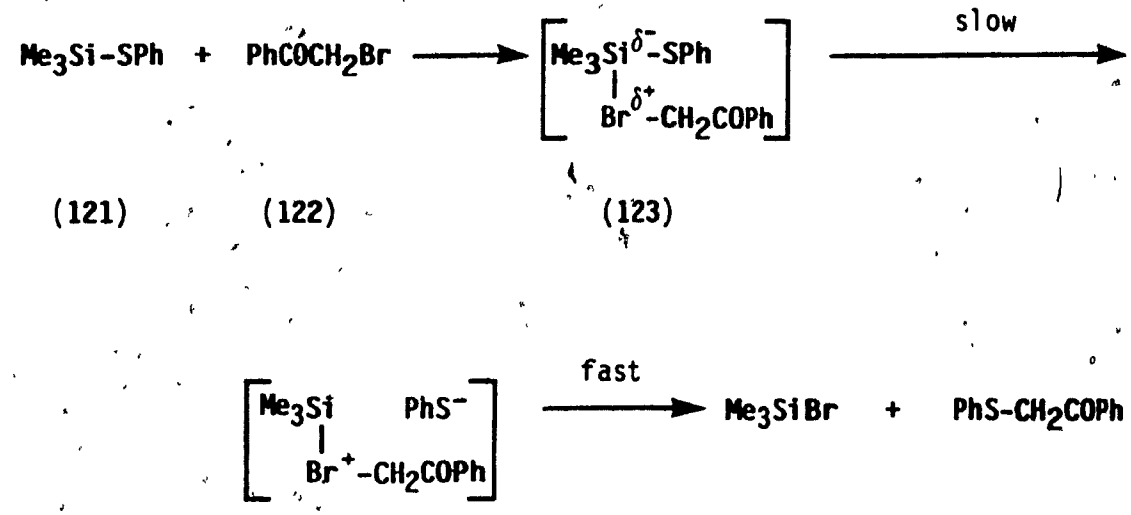
Scheme 17.



(120)

The reaction of trimethyl methylthiosilicon(IV) (121) with α-bromoacetophenone (122) appears to proceed through such a five-coordinated silicon species (123) (Scheme 18).[153] A ρ of + 2.2 has been observed for this reaction.

Scheme 18.



(121) (122) (123)

The third possibility is a four-centered non-ionic mechanism. Iodine approaches the thiotin species giving a four-centered transition state (124) which in turn leads to a sulfenyl iodide and tin iodide. The next step may then involve a second four-centered transition state (125) between sulfenyl iodide and a second molecule of the thiotin species (Scheme 19).

Scheme 19.

1) $R_3Sn\text{-}SR' + I_2 \longrightarrow \left[R_3Sn\cdots SR' \;\; I\cdots I \right] \longrightarrow R_3Sn\text{-}I + I\text{-}SR'$

(124)

2) $R_3Sn\text{-}SR' + I\text{-}SR' \longrightarrow \left[R_3Sn\cdots SR' \;\; I\cdots SR' \right] \longrightarrow R_3Sn\text{-}I + R'S\text{-}RS'$

(125)

A four-centered concerted mechanism is not expected to be highly influenced by solvent effects nor would there be a large value for ρ.[152] The transition state may be polarized such that there is a partial positive charge on sulfur; thus, there is potential for a small negative ρ value.[154]

The formation of sulfonates (126) from the combination of aryloxytrimethyltin(IV) (127) and methanesulfonyl chloride (5) is explained using such a mechanism (Scheme 20).[154] There is small rate enhancement observed with polar solvents, the ρ value is - 1.03.

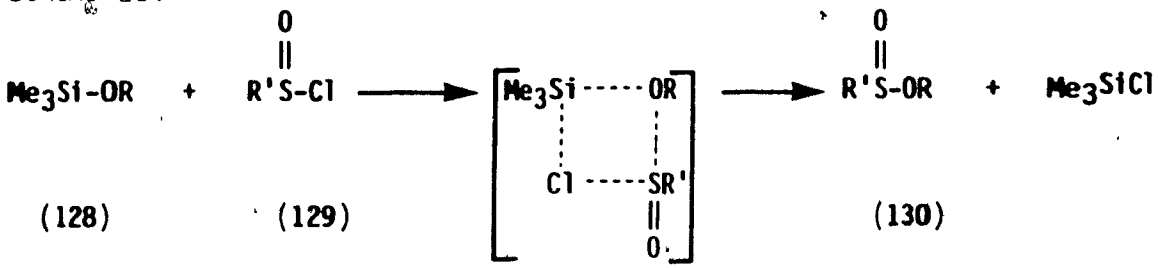
Scheme 20.

$$Me_3Sn\text{-}OC_6H_4X + MeSO_2Cl \longrightarrow \left[Me_3Sn\cdots OC_6H_4X \;\; Cl\text{---}SMe(=O)(=O) \right] \longrightarrow Me_3SnCl + MeSO_2\text{-}OC_6H_4X$$

(127) (5) (126)

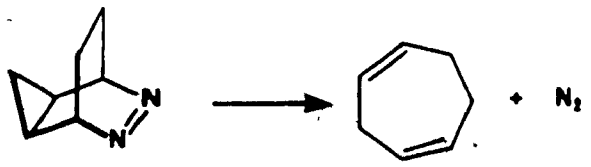
Harpp and co-workers postulated a four-centered mechanism for the reaction of alkyloxytrimethylsilane (**128**) and sulfinyl chlorides (**129**) which provides sulfinate ester (**130**) (Scheme 21).[155] A ninefold rate

Scheme 21.



(**128**) (**129**) (**130**)

increase observed in going from C_6D_{12} to CH_2Cl_2 promoted the proposal of a nonionic mechanism. As a comparison of solvent effects, the chelotropic decomposition of (**131**) has been studied over a wide range of solvent polarities; from isooctane to 96% ethanol there is only a 15-fold rate change.[156] Thus a ninefold change for the production of ester (**130**) is consistent with minimal charge production in its transition state.

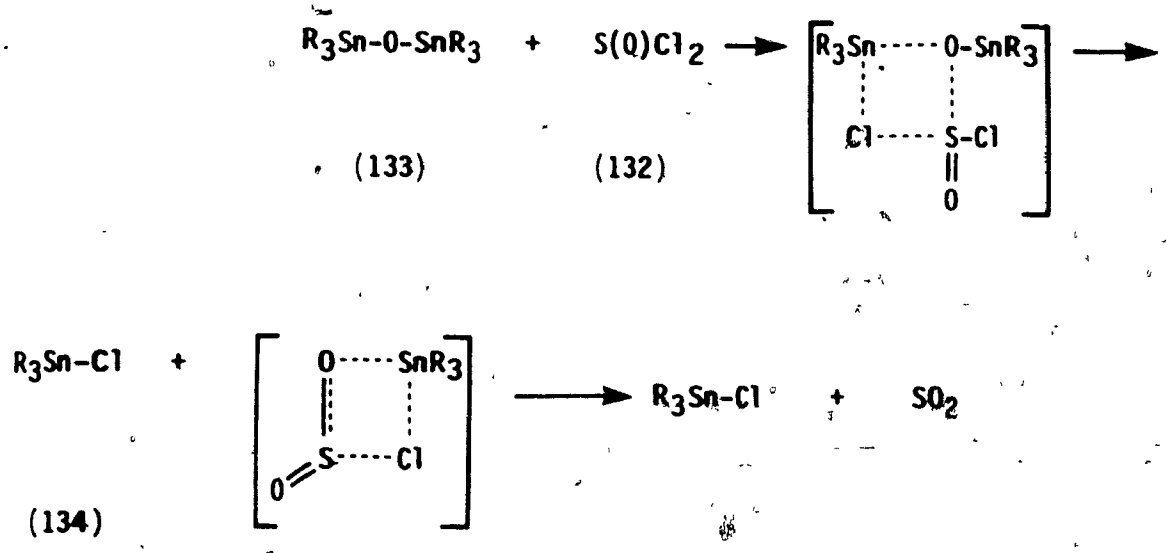


(**131**)

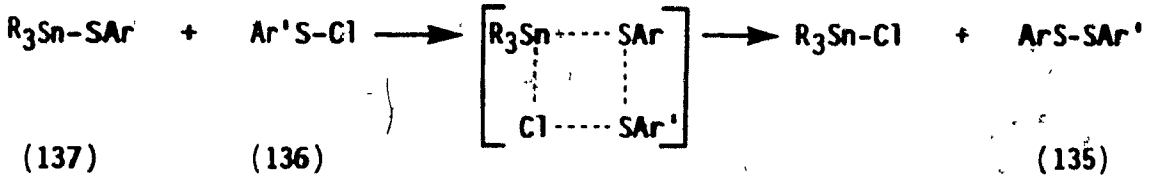
Similar four-centered transition state mechanisms have been proposed for the reaction of thionyl chloride (**132**) with bis(trialkyltin) oxides (**133**) or dialkyltin oxides to yield SO_2 and organotin chlorides[148] (**157**) (Scheme 22), and for the formation of unsymmetrical

disulfides (135) from aryl sulfenyl chlorides (136) and trialkyl alkylthiotin(IV) compounds (137) (Scheme 23).[158]

Scheme 22.



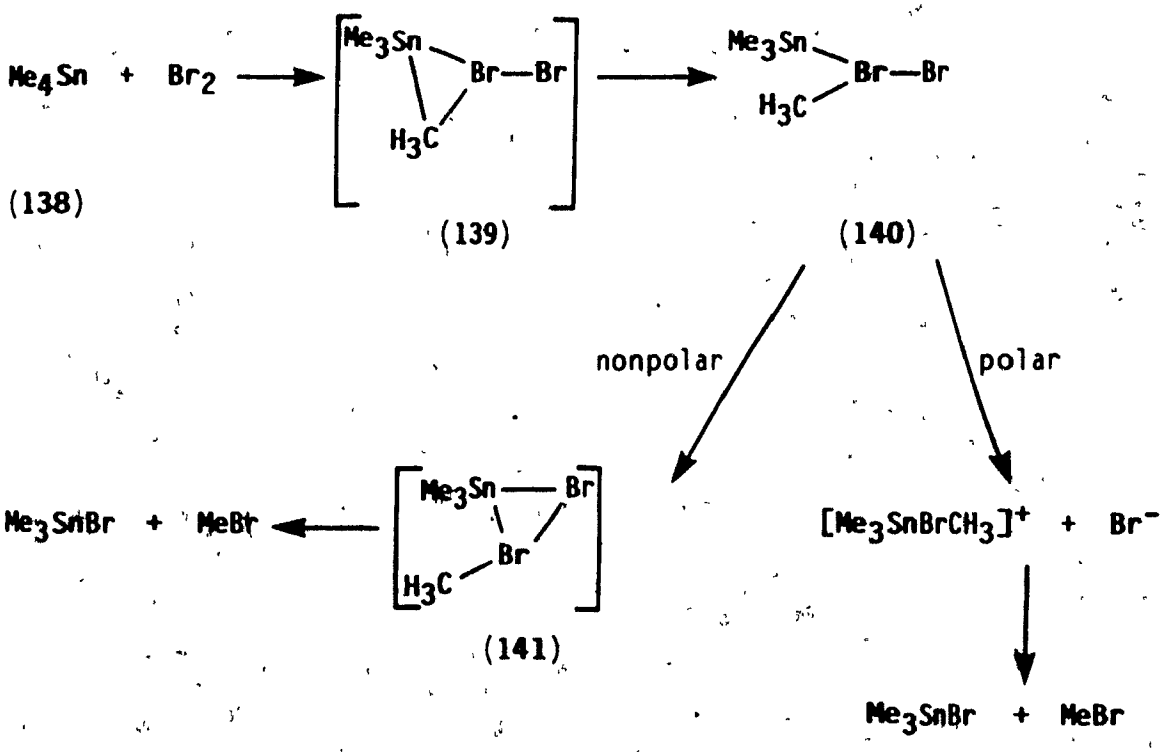
Scheme 23.



The reaction of tetraalkyltin(IV) compounds with bromine or iodine is believed to go through a four-centered transition state in nonpolar solvents and a stepwise mechanism in polar solvents.[159-161] These mechanisms are based on kinetic measurements and particularly stereochemical aspects of the reaction. Recently, Dewar and Kuhn[162] have calculated that brominolysis of tetramethyltin(IV) (138) may proceed by a single transition state (139) in all solvents. The transition state (139) leads to a hypervalent intermediate (140) which could decompose

via (141) to the observed products, this would occur with retention of configuration at carbon and does not necessitate a four-centered mechanism (Scheme 24). In polar solvents the bromine bromine bond of inter-

Scheme 24.



mediate (140) could cleave and then attack of Br^- at carbon to generate the products with inversion of configuration at carbon.

For tetraalkyltins, the status of the four-centered mechanism is not clear. Whether this ambiguity applies for thiotin species is inevident. For the oxjdation of thiotins with halogen a four-centered concerted or perhaps synchronous[163] mechanism is possible.

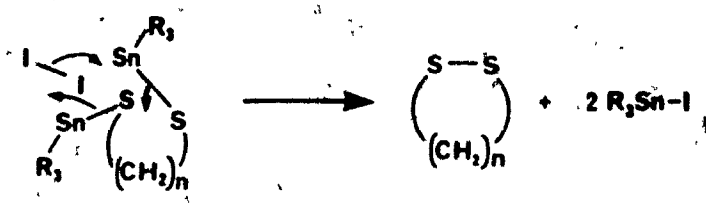
As was discussed, the formation of disulfides from organotin-sulfur derivatives and bromine or iodine is a two step process. The first step is cleavage of one tin-sulfur bond to give a sulfenyl halide and a tin

halide, followed by reaction of the sulfenyl halide with a second molecule of the thiotin reagent to yield the disulfide and a second tin halide.

In summary, the three proposed mechanisms are: sulfonium ion, five-coordinate tin and four-centered transition state. There is no reason to believe that both steps in the synthesis of disulfides experience the same mechanism. The first step may proceed through a sulfonium ion while the second may occur via a four-centered transition state. Kinetic measurements would give evidence for the mechanism of the rate determining step only.

There is a fourth likely mechanism which we have as yet discussed; this being a six electron concerted or perhaps synchronous mechanism. The disulfide would form in a single step by this process. Kinetics would show little effect of solvent polarity on reaction rate and a linear free energy plot should show a small value for ρ. For simple disulfides, the mechanism requires a termolecular collision. This is far less likely than a bimolecular collision, but auto-association may alleviate the energetic constraints of the three collision mechanism. Further, for μ-α,ω-alkyldithiohexa-n-butyltin(IV) species and 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes the required collision is only bimolecular (Scheme 25).

Scheme 25.



Lastly, a free radical process should be considered as a potential mechanism for halogen oxidation of thiotin species. While, the chemistry of organotin hydrides is known to proceed via free radicals[164], the literature indicates that such behavior for organotin-sulfur derivatives is less likely.[149-151,154] Nevertheless, this type of mechanism should be kept in mind.

2.3.2 Attempted Kinetic Measurements

A kinetic study was undertaken to elucidate the mechanism of halogen oxidation of tin-sulfur reagents. The uptake of iodine was monitored by UV (I_2 λ_{max} = 520, in CH_2Cl_2) using a stopped-flow apparatus. The iodine was added to tri-n-butyl phenylthiotin(IV) (96g); under pseudo first order conditions which were maintained by having ca. a tenfold excess of thiotin compound. Unfortunately the reaction proceeded more rapidly than could be measured; the time interval between scans by the stopped-flow apparatus was set at 0.005 s. The optical density resolution of the instrument is ca. 0.001.

An increase in steric bulk should slow the reaction down sufficiently to be observable by stopped-flow. Thus, tricyclohexyl t-butylthiotin(IV) (142) was prepared from tricyclohexyltin chloride and t-butanethiol. Furthermore, isooctane, a less polar solvent, was used for these and subsequent kinetic studies.

(142)

The oxidation of the thiotin reagent with ca. one-seventh equivalent of iodine occurred too rapidly to be measured. The concentration of the iodine was 1.57×10^{-4} M; the thiotin(IV) reagent was 1.15×10^{-3} M. Since pseudo first order conditions were applied, the maximum first order rate constant (k) is 138.6 s^{-1}

$$k = \frac{\ln 2}{t_{\frac{1}{2}}} = \frac{.693}{0.005\ s} = 138.6\ s^{-1}$$

The greatest observable second order rate constant (k') is given below.

$$k' = \frac{138.6\ s^{-1}}{0.00115\ M \times \frac{1}{2}} = 2.42 \times 10^{5}\ M^{-1}s^{-1}$$

The maximum observable rate constant is ca. 2.4×10^{5} $M^{-1}s^{-1}$ (the molarity of the tin reagent is multiplied by 1/2 since it is diluted to this extent in the stopped-flow apparatus). The rate constant for the reaction must then be greater than this value; the oxidation of thiotins with iodine is very fast indeed!

It is possible that the halogen is forming a charge transfer complex with the sulfur of the thiotin, similar to the charge transfer complex that is formed between sulfides and iodine. Studies on sulfides and iodine have shown considerable hypsochromic shifts of the iodine absorption.[165-167] For instance, the visible band for iodine in n-heptane occurs at 525 nm, with the presence of 40 molar equivalents of diethyl sulfide this band shifts to 435 nm[165], intense charge transfer peaks show up at about 300-310 nm. Some of this information is summarized in Table 15.

Charge transfer complexes can also be formed between disulfides and iodine; however, they are much weaker than those formed by sulfides.[166] This is a consequence of the relative base strengths of the donors. Nevertheless, as disulfide is being formed it too may complex with iodine. Thus it is possible that kinetic studies show interference caused by complexations of the iodine in the presence of a variety of electron donors.

Table 15. Absorption Maxima of Various Sulfur Containing Donors with Iodine in Carbon Tetrachloride.[166]

Donor	λI_2, nm	λ Charge Transfer, nm
Diethyl Sulfide	430 435*	305 302*
Diallyl Sulfide	435	306
Dibenzyl Sulfide	440	307
Diethyl Disulfide	450 460*	302 304*

* In n-heptane, reference 165.

It follows then that kinetic studies should be performed by monitoring product formation rather than substrate consumption. Disulfides absorb at ca. 250 nm; there is considerable interference between this band and those from thiotins and tin halide; however, 1,2-dithiolane absorbs at 330 nm and is useful for product studies. There may be concern for charge transfer problems; however, by adding a tenfold (pseudo first order conditions) excess of organotin-sulfur reagent it is clear that once the reaction is complete there would be no residual

halogen; the halide is reduced and covalently bonded to tin as trialkyltin halide.

Using a diode array spectrophotometer, the band at 330 nm from 1,2-dithiolane was observed directly on addition of iodine, but so rapidly that no rate constant could be determined. This kinetic measurement was repeated at -20°C, but the low temperature did not slow the reaction down sufficiently to be observable. The initial scan can be achieved only after ca. 1 s but the resolution is far better than that which can be observed using the stopped-flow apparatus; the experiment was carried out so that a change in absorbance of only ca. 0.004 would occur. This high resolution allows for the use or far more dilute solutions, hence faster relative observable rates. The final concentration of iodine was 3.33×10^{-6} M while the final concentration of μ-1,3-propyldithio-hexa-n-butylditin(IV) was about seven times that at 2.42×10^{-5} M.

A consideration of the efficacy of the instrument again affords a maximum measurable value.

$$k = \frac{.693}{1\ s} = .693\ s^{-1}\ , \quad k' = \frac{.693}{0.0000242} = 2.86 \times 10^{4}$$

The maximum observable second order rate constant for this reaction is ca. $2.9 \times 10^{4}\ M^{-1}s^{-1}$ at -20°C. To attain this value, the instrument was pushed to the limit. A more conservative and perhaps more accurate maximum rate constant is ca. $1.5 \times 10^{4}\ M^{-1}s^{-1}$ at -20°C.

Again it must be concluded that the reaction of iodine with thiotins is very fast; far faster than can be easily measured.

The lower molecular absorptivity for bromine ($\epsilon = 200$)[168] as opposed to iodine ($\epsilon = 950$)[168] means that only slower rates (ca. 5-fold

less) would be observable if Br_2 was used as the oxidant. Furthermore, the energetics of the reaction suggest that bromine oxidation should proceed faster (see page 39). For these two reasons the kinetics of Br_2 oxidation of thiotins was not examined.

The kinetic studies on the oxidation of tricyclohexyl t-butylthiotin(IV) and μ-1,3-propyldithiohexa-n-butylditin(IV) were repeated with the addition of a free radical trap (BHT). The procedures were identical except that 2 equivalents of 2,6-di-t-butyl-4-methylphenol (BHT) were added to the isooctane solution of thiotin reagent. Once again oxidation was too rapid to be measured. This result disfavors a free radical mechanism.

2.3.3 Mixed Reaction Studies and Stereochemical Considerations.

Various amounts of IBr or a 1:1 mixture of bromine and iodine were added to di-n-butyl di-n-butylthiotin(IV) (**100a**) in an attempt to distinguish between a six electron concerted mechanism and a stepwise mechanism (ionic, five-coordinate at tin or four-centered). A six electron concerted mechanism requires that when one equivalent of bromine/iodine (1:1) mixture is added only tin dibromide (**143**) and tin diodide (**144**) should be observed. Furthermore, when 1 equivalent of IBr is added, a six electron concerted mechanism predicts that only di-n-butylbromoiodotin(IV) (**145**) would be produced. Alternatively, in a stepwise mechanism, tin dibromide, bromoiodotin and tin diiodide should be seen in a ratio of 1:2:1 (fully random) when either one equivalent of Br_2/I_2 (1:1) mixture or of IBr is added to the dithiotin species.

The products were identified by ^{119}Sn-NMR; ^{119}Sn-NMR integrations were used to determine the relative molar ratios of the products pro-

duced. The addition of either one equivalent of bromine or iodine to di-n-butyl di-n-butylthiotin(IV), gave the following ^{119}Sn-NMR resonances, relative to tetramethyltin: 88.4 ppm, di-n-butyltin dibromide (**143**); -54.6 ppm, di-n-butyltin diiodide (**144**). To determine the resonance for the bromoiodotin compound, one equivalent of IBr was added to the dithiotin reagent; ^{119}Sn-NMR: 88.7 ppm (**143**); 22.1 ppm; -57.7 ppm (**144**). The second peak (22 ppm) results from di-n-butylbromoiodotin(IV) (**145**).

n-Bu_2SnBr_2	n-Bu_2SnI_2	n-BuSnIBr
(143)	(144)	(145)

Table 16. ^{119}Sn-NMR Data for the Reaction of di-n-Butyl Dialkylthiotin(IV) with Br_2/I_2 or IBr.

Oxidant	Total Amount of Oxidant		
	1 mole	1½ moles	XS of 2 moles
I_2/Br_2	88.5 ppm (27%)	88.4 ppm (50%)	86.4 ppm (100%)
	22.4 ppm (45%)	21.7 ppm (44%)	
	-56.7 ppm (28%)	-59.1 ppm (6%)	
IBr	89.6 ppm (25%)	88.0 ppm (43%)	88.9 ppm (100%)
	21.5 ppm (50%)	22.2 ppm (46%)	
	-58.4 ppm (25%)	-55.7 ppm (11%)	

When a total of one mole of oxidant was added, that is, one-half an equivalent of iodine and one-half an equivalent of bromine or one equivalent of IBr, all three possible organotin halide derivatives were found in ca. 1 : 2 : 1, (143):(145):(144). This mixing suggests that the reaction proceeds in a stepwise fashion. An experiment to confirm this result, that is to see if this mixing may not have resulted from randomization of the tin halides once they had formed, was performed. The dibromide (143) and the diiodide (144) were each individually prepared by adding the corresponding halogen to di-n-butyl dialkylthiotin(IV); they were then added to a single NMR tube and a tin spectrum was acquired. The acquisition took 90 min as did those summarized above; the results are as follows: 88.8 ppm (26%), 23.4 ppm (51%) and -57.0 ppm (23%). Thus, the disulfide synthesis mechanism may well have

$$\underset{(143)}{Bu_2SnBr_2} + \underset{(144)}{Bu_2SnI_2} \longrightarrow (143) + \underset{(145)}{Bu_2SnIBr} + (144)$$

$$1 \quad : \quad 2 \quad : \quad 1$$

been six electron concerted; halide randomization does not permit a discernment between this and a stepwise mechanism. Complete randomization between dialkyltin dihalides has also been observed by Van den Berghe, Van der Kelen and Eeckhaut.[169]

Table 16 above, shows that as further oxidant is added, either the bromine iodine mixture or IBr, the dibromide (143) predominates over the diiodide. Once an excess of two equivalents of oxidant is added only the dibromide is noticeable, the iodine stays in solution. This result

is predicted by bond energy considerations. Also, Fukuto and Jensen have observed that the reaction of tetraalkyltins with IBr affords alkyl iodide and trialkyltin bromide exclusively.[160]

The investigation of stereochemical effects of the reaction could have been of assistance in elucidating the reaction mechanism. With a chiral tin reagent it would have been possible to see if the oxidation of the thiotin proceeds with retention, inversion or racemization at tin. Unfortunately, as we have just seen, organotin halides undergo facile halogen-halogen exchange[169]; the tin derivative of the reaction of thiotin(IV) species and halogens is of course a tin halide. In addition, Peddle and Redl determined the stereochemical stability of organotin compounds and found that "...while it should be possible to resolve an optically active organotin compound with four carbon-tin bonds...", the same is not true for trialkyltin halides.[170] Hence, a stereochemical investigation was not undertaken.

2.3.4 Determination of Rho (ρ) by Competition Studies.

To obtain a value for ρ for the reaction of thiotins with halogen, the competition of a variety of phenyl substituted tri-n-butyl arylthiotin(IV) compounds for iodine was examined. A comparison of relative yields of the resultant respective disulfides was determined by gas chromatography. The phenyl substituents were: p-t-butyl, σ_p = -0.15; p-methyl, σ_p = -0.14; H, σ = 0.00; p-fluoro, σ_p = 0.15; p-chloro, σ_p = 0.24; m-trifluoromethyl, σ_m = 0.46; (for clarity these six tri-n-butyl arylthiotins will be referred to as A, B, C, D, E and F).[152,171] The GC retention times and response factors for the respective disulfides were first determined as follows: a solution containing equal molar amounts

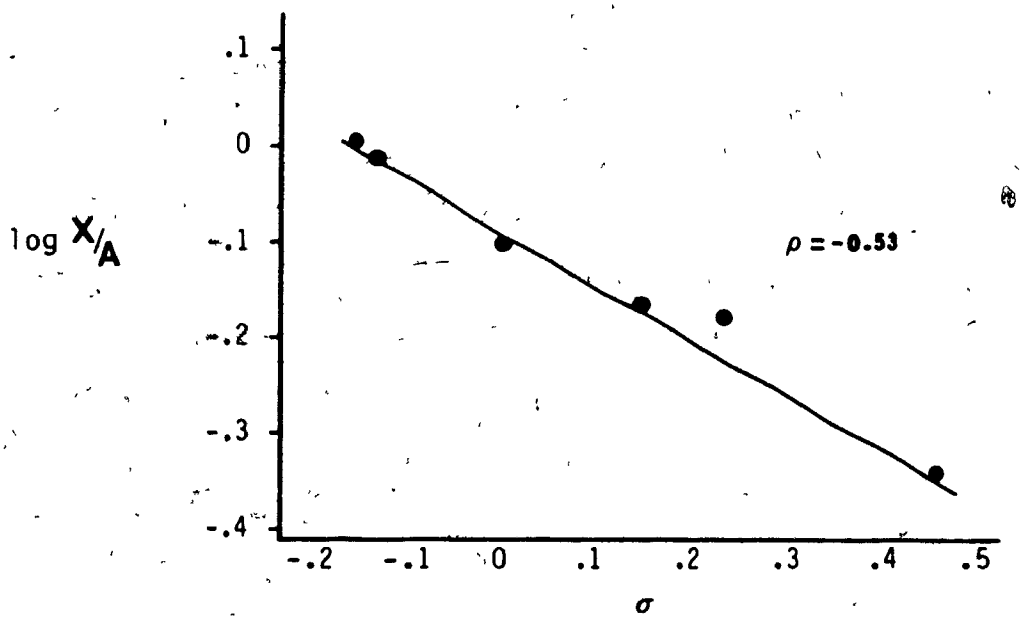
of all six organotin-sulfur reagents was reacted with slightly more than six equivalents of iodine which was sufficient to fully oxidize all of the thiotins. Assuming the yields of disulfides prepared in this manner approached 100%, then a consideration of the integrator output enabled the realization of the relative GC sensitivities of the corresponding disulfides.

The competition reactions were carried out by mixing 1 equivalent each of A and of B in dichloromethane. To this was added 1/2 an equivalent of iodine and the solution was immediately injected into the GC. The process was repeated for A with C, A with D, A with E and for A with F. Knowing the relative sensitivities of the individual disulfides, the ratios of disulfides formed B vs. A, C vs. A, E vs. A and F vs. A were determined. The log of the ratios of the disulfides formed was then plotted against substituent constants (σ). A similar plot was established for ratios versus B; A vs. B (calculated above), C vs. B, D vs. B and so on. Similarly the ratios of each disulfide formed against C, D, E and F was realized. A typical plot is shown below (Figure 6). The average ρ value was -0.45. This negative value dissuades the five-coordinate mechanism; but it does not discriminate between the other three, two possible concerted mechanisms and the ionic mechanism. Nevertheless, the low number favors one of the concerted mechanisms, four-centered or six electron concerted.

For comparative purposes, it is of interest to consider the ρ value(s) obtained for other reactions. For the dissociation of benzoic acid (negative charge formation) in ethanol ρ = 1.96, while for the dissociation of the same acid in water ρ = 1.00. A ρ of -4.07 is found for the formation of the methylether $Ar_2CH\text{-}OCH_3$ from $Ar_2CH\text{-}Cl$ in MeOH

For the SN_2 attack of hydroxide ion on $ArCH_2$-Cl to form $ArCH_2$-OH in 48% ethanol ρ = -2.18. The latter two reactions proceed through a positively charged aryl species.[172] Concerted or synchronous mechanisms normally have a low absolute value of ρ, less than one[171], as was found for the oxidation of arylthiotins above. An extensive listing of reaction ρ values is available.[172]

Figure 6. Linear Free Energy Plot for the I_2 Oxidation of Arylthiotin(IV) Species in CH_2Cl_2.



2.4 Spectroscopic Properties of Organotin-Sulfur Derivatives

2.4.1 Tin NMR

There are ten naturally occurring tin isotopes, three of them (^{115}Sn, ^{117}Sn, ^{119}Sn) are amenable to study by nuclear magnetic spectroscopy. All three have a nuclear spin I = ½. ^{119}Sn is the most

abundant and is slightly more sensitive than the other two nuclides; for this reason tin NMR is most often carried out using this isotope[145,173]; Table 17, summarizes some physical properties for all three.

Table 17. NMR Parameters for Tin Isotopes.[173]

Isotope	% Natural Abundance	Nuclear Spin	NMR Frequency MHz at 2.349 Tesla
^{115}Sn	0.35	½	32.86
^{117}Sn	7.61	½	35.63
^{119}Sn	8.58	½	37.29

Tetramethyltin, $(CH_3)_4Sn$, is the accepted chemical shift reference standard for ^{119}Sn-NMR. By IUPAC convention, resonances at higher fields than tetramethyltin are reported in negative ppm, those of lower field are given positive ppm values.[173] The reader should be aware that not all publications adhere to this rule, particularly those that are less recent.

Chlorinated solvents are very good for ^{119}Sn-NMR studies; polar solvents such as acetone or dimethylsulfoxide coordinate with tin, this serves to shield the tin species resulting in an upfield resonance.[145] In general, six-coordinate tin species are upfield from five-coordinate species which are in turn upfield of four-coordinate tin compounds.

The ^{119}Sn-NMR spectra were obtained using dilute samples to prevent auto-association. Typically, 150-300 mg of tin-sulfur compound was used in ca. 4 ml of $CDCl_3$, the solutions were thus ca. 0.05 to 0.1 M. Tetramethyltin was used as an external standard. Trends can be observed from the data in Table 18. Tri-n-butyl thiotin(IV) compounds

Table 18. ^{119}Sn Resonances of Thiotins Relative to Tetramethyltin.

n-Bu_3Sn-SR

R		R	
Benzyl (96a)	70.9	n-Butyl (96b)	69.8
s-Butyl (96c)	66.2	t-Butyl (96d)	51.8
Cyclohexyl (96e)	63.5	n-Decyl (96f)	70.5
Phenyl (96g)	74.6	Trityl (96h)	54.7
p-t-Butylphenyl (96i)	82.6	p-Tolyl (96j)	79.7
p-Fluorophenyl (96k)	82.3	p-Chlorophenyl (96l)	80.7
m-Trifluoromethyl-phenyl (96m)	85.2	CH_2COOMe (165)	84.7
$CH_2CH(COOEt)$-NH(BOC) (167)	86.3		

n-Bu_3Sn-S$(CH_2)_n$S-Sn-n-Bu_3

n=		n=	
3 (109a)	77.6	4 (109b)	77.9
5 (109c)	75.5	6 (109d)	76.6
7 (109e)	76.5	8 (109f)	76.6
9 (109g)	75.0	10 (109h)	75.6

n-Bu_2Sn-S$(CH_2)_n$S

n=		n=	
3 (110a)	149.8	4 (110b)	129.5
5 (110c)	127.4	6 (110d)	127.8
7 (110e)	127.5	8 (110f)	127.4
9 (110g)	128.0	10 (110h)	127.8

Table 18. Continued

Other Thiotins			
n-$Bu_2Sn(S\text{-}n\text{-}Bu)_2$ (**100a**)	127.0	n-$Bu_2Sn(SBenzyl)_2$ (**100b**)	125.6
$Sn(S\text{-}n\text{-}Bu)_4$ (**103a**)	130.5	$Sn(SBenzyl)_4$ (**103b**)	139.2
n-$Bu_3Sn\text{-}S\text{-}Sn\text{-}n\text{-}Bu_3$ (**106**)	82.6	Tricyclohexyl t-butylthiotin(IV) (**142**)	148.7
1,4,6,9-Tetrathio-5-stannaspiro[4,4]nonane (**146**)	279.2		

show resonances from ca. 50 to 78 ppm; thiotins with a primary carbon attached to sulfur resonated at 70-76 ppm while the bulkier thiotins are shielded somewhat; R = s-butyl, 63.5 ppm, R = cyclohexyl, 63.5 ppm, R = trityl, 54.7 ppm and R = t-butyl, 51.8 ppm.

Bulky groups directly bonded to tin tend to deshield the metal, however, the mechanism for this is not understood.[174] This is also seen above, the resonance for tricyclohexyl t-butylthiotin(IV) is 148.7 ppm, for tri-n-butyl t-butylthiotin(IV) the value is 51.8 ppm

Table 19. ^{119}Sn-NMR of Other Compounds of Interest.

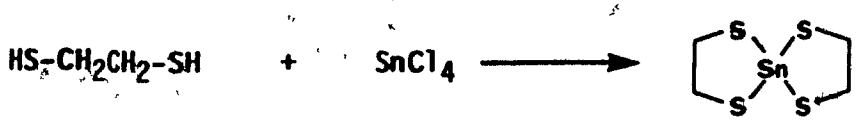
Entry	Resonance (ppm)
n-Bu_3SnCl (**97**)	155.4
n-$Bu_3SnOSn\text{-}n\text{-}Bu_3$ (**107**)	105.0
n-Bu_3SnOMe (**166**)	104.5
n-Bu_2SnBr_2 (**143**)	88.4
n-Bu_2SnIBr (**145**)	22.0
n-Bu_2SnI_2 (**144**)	-54.6

As expected, dithiotin compounds are deshielded more than the monothiotin species. However, tetrathiotin species are only slightly more deshielded than the dithio compounds; the electron removal by sulfur is not additive; this observation is in accordance with the literature.[174,175] Kennedy and McFarlane[122] have shown that for phenylthiotins and t-butylthiotins the tetrathiotin compounds are more shielded than the dithiotin species. To account for this it is suggested that there may be more p -d back donation as the tin atom becomes more electropositive.[122]

Of interest are the resonances for the 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes; for the most part they are between 127 and 128 ppm. However, for 2,2-di-n-butyl-1,3,2-dithiastannacycloheptane (**110b**) the peak is at 129.5 ppm, more significantly for 2,2-di-n-butyl-1,3,2-dithiastannacyclohexane (**110a**) the peak is at 149.8 ppm. The smaller rings put constraints on tin, deforming the S-Sn-S bond angle. This deshielding has also been noted in the literature.[176,177] Since no other ^{119}Sn-NMR peaks were noted for (**110a**) and (**110b**), this data suggests that these two dithiastannacycloalkanes were prepared as monomeric species, with no or very little polymer.

Similar deviations are observed for tetraalkyltins when the C-Sn-C interbond angles are reduced.[174,177] 1,4,6,9-Tetrathia-5-stannaspiro[4,4]nonane (**146**) was prepared from ethanedithiol and stannic chloride (Scheme 26); it contains two five-membered rings attached to tin and should show a large deshielding effect. Indeed the resonance for this compound was 279.2 ppm.

Scheme 26.

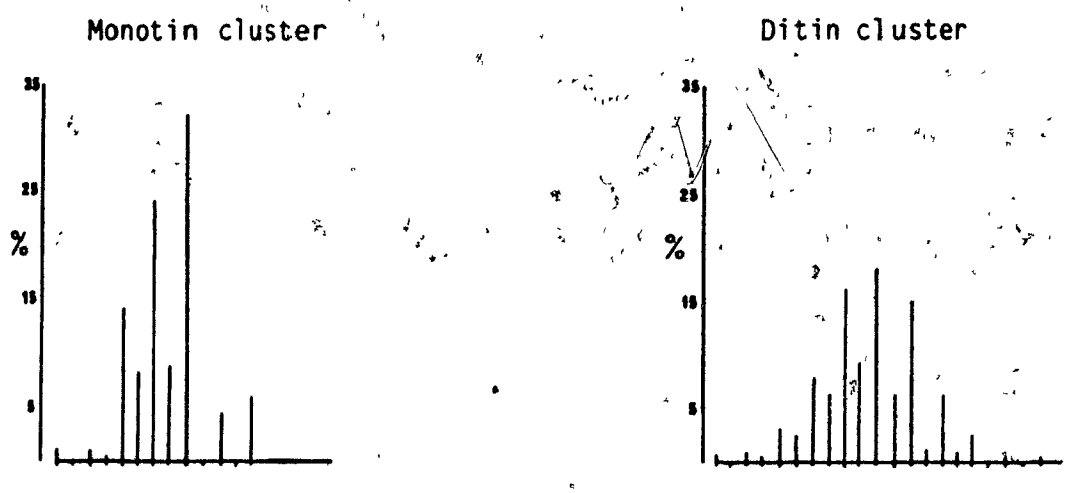


(146)

2.4.2 Mass Spectra of Thiotin(IV) Compounds.

It was noted above that tin has ten naturally occurring isotopes; this is the most for any element.[145] Thus, tin clusters should be observed in the mass spectrum for any tin containing compound. These clusters are easily spotted and facilitate the interpretation of the spectrum. The expected cluster for a monotin compound and the calculated cluster for a ditin compound is shown.

Figure 7. Tin Isotope Clusters



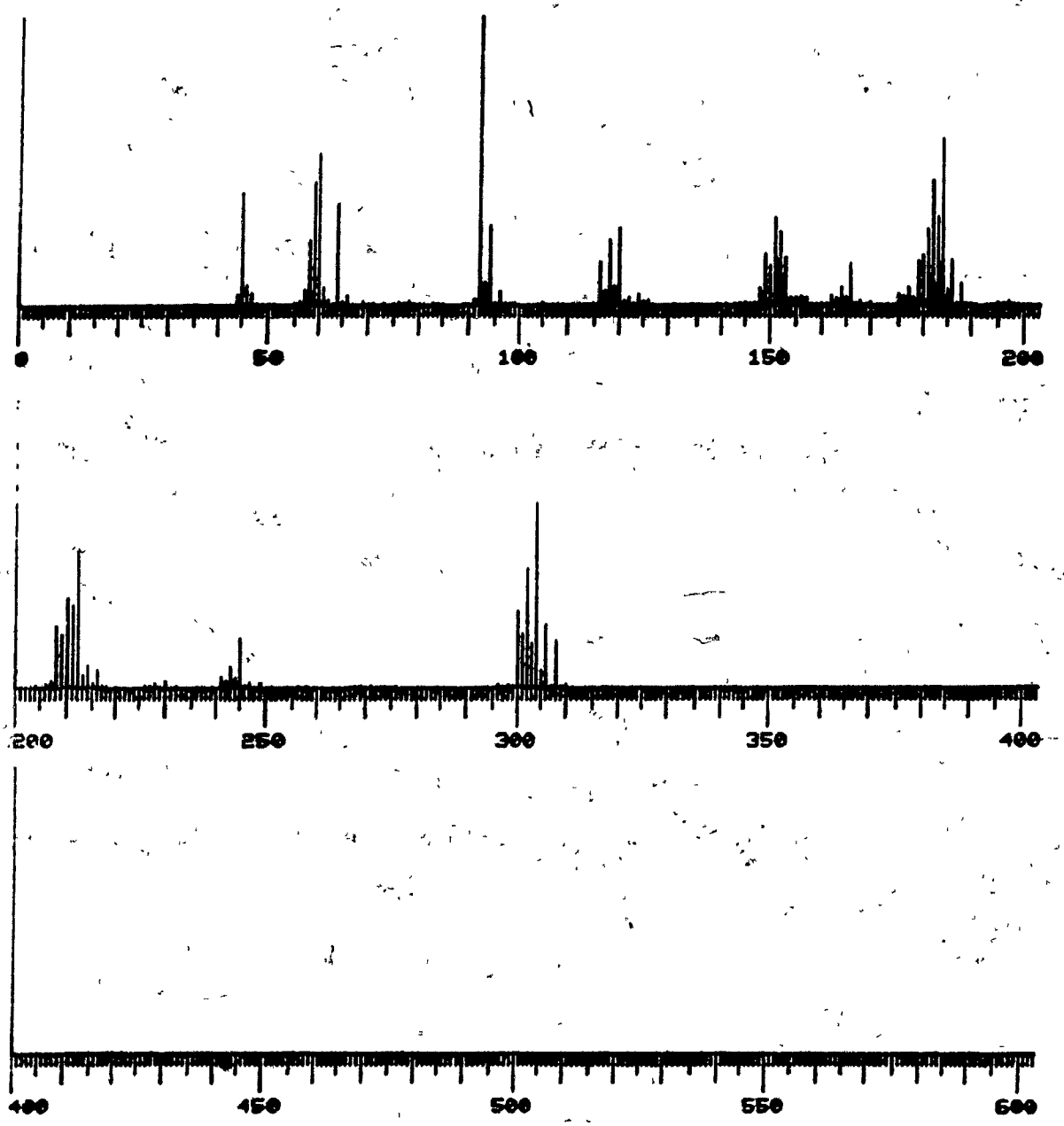
Usually, the mass spectra of monotin compounds show clusters similar to the monotin cluster presented above. The spectra of ditin species contain clusters similar to both shown above. In addition,

monotin fragments from ditin compounds are readily identified by the shape of the resultant cluster. In some instances the shape of the clusters was useful in that it discriminated between a monotin fragment and the potential for a doubly charged ditin fragment. In reporting the mass spectral data, only the two most abundant peaks from monotin compounds and the three largest peaks for ditin compounds were included. It is important to remember that the relative abundance of a single peak from a cluster may be less than some other fragment in the spectrum, however, the total of all the constituents of the same cluster may be greater. The relative abundance of a given tin containing fragment is the sum of all the components of the corresponding cluster.

For the tin derivatives studied, molecular ions were rarely detected, and then of very low intensity. Except for the tricyclohexyltin derivative, a very prominent peak was often observed at m/z = M^+ - 57. This resulted from loss of the n-butyl· group. Following this, there was often the loss of 56 (butene). Other significant clusters include those attributed to n-Bu_2SnSH^+, n-$BuHSnSH^+$, n-$BuSnH_2^+$, n-$BuSn^+$, H_2SnSH^+, $SnSH^+$ and SnH^+. The most abundant tin containing fragments were tri- and mono-substituted ions; these are believed to be more stable than the di-substituted tin containing ions.[178] This may occur as a result of loss of neutral species from various fragments[179], for instance, the loss of H_2 from H_2SnS^+ to afford SnS^+.

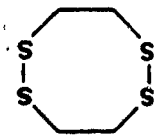
Of particular interest is the mass spectrum of 1,4,6,9-tetrathia-5-stannaspiro[4,4]nonane (**146**) (Figure 8). The cluster shapes are not quite like those usually seen for monotin compounds. This is a result of the isotopic contributions of up to four sulfur atoms per fragment. Note the peak at m/z 92, this is $C_2H_4S_2^+$; possibly having structure

Figure 8. Mass Spectrum of 1,4,6,9-Tetrathia-5-Stanna-spiro[4,4]nonane (**146**).

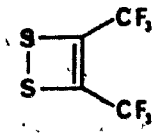


(147), a rare four-membered ring cyclic disulfide of sort. The oxidation of 1,2-ethane dithiol leads to polymerization; at best the dimeric 8-membered ring, 1,2,5,6-tetrathiacyclooctane (55), is isolated.[180] A few dithietes, unsaturated four membered ring disulfides are known; these are 3,4-bis(trifluoromethyl)-1,2-dithiete (148)[181,182] and the sterically hindered dithietes (149) and (150).[183,184]

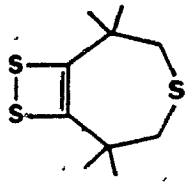
(147)



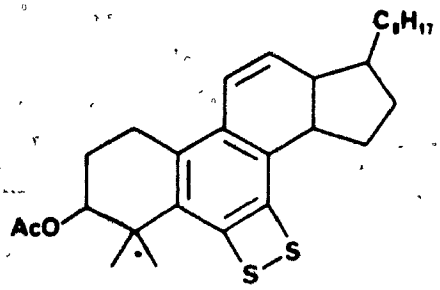
(55)



(148)



(149)



(150)

Also of interest is the peak at m/z 64; this can be attributed to S_2^+. This may result from the loss of neutral ethene from m/z 92. This peak at m/z 64 is not attributed to elemental sulfur (S_8) because while m/z 64 is common in the mass spectrum of sulfur, no other peaks usually associated with elemental sulfur are found. The common peaks in the spectrum of sulfur are m/z: 256, 224, 192, 160, 128, 96, 64, 32;

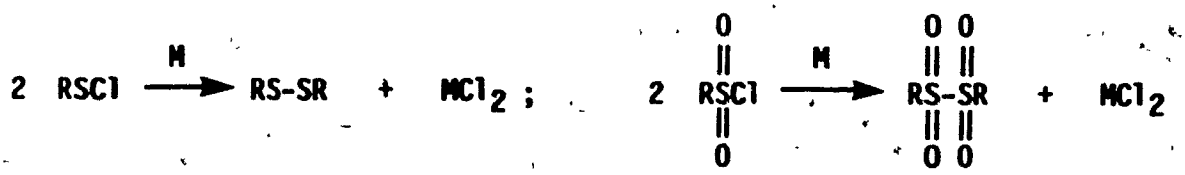
that is, multiples of the S atom up to S_8. S_2, a highly reactive intermediate of interest, has received recent attention.[185] In addition, a peak assigned to S_2^+ (m/z 92 - C_2H_4) provides credence to the four-membered ring structure (**147**) for m/z = 92.

2.5 The Preparation of vic-Disulfoxides and Thiosulfinates.

2.5.1 vic-Disulfoxides.

It is known that metals react with sulfenyl chlorides (**151**) to deliver disulfides (**6**) and with sulfonyl chlorides (**152**) to afford vic-disulfones (**153**) (Scheme 27).[186-188] With this knowledge, it was reasonable for Barnard[188] to assume that the treatment of sulfinyl chlorides (**129**) with zinc would yield vic-disulfoxides (**154**), however,

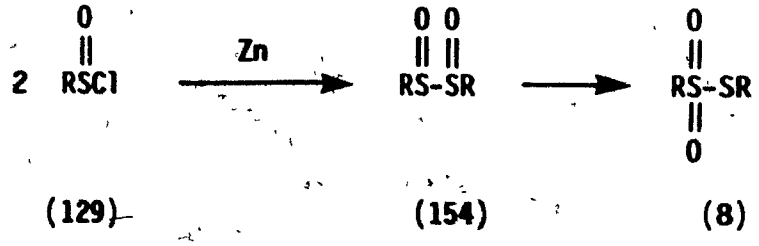
Scheme 27.



(**151**) (**6**) (**152**) (**153**)

he found the product was a thiosulfonate (**8**) (Scheme 28). He correctly reasoned that the vic-disulfoxide rearranged to the thiosulfonate.

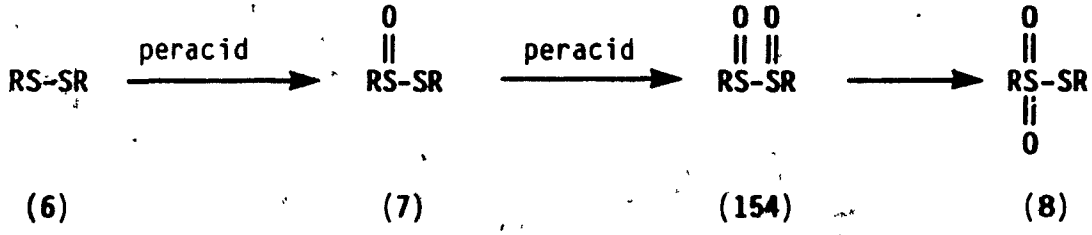
Scheme 28.



(**129**) (**154**) (**8**)

Furthermore, the oxidation of disulfides to thiosulfonates with electrophilic oxidizing reagents such as m-chloroperbenzoic acid likely occurs with rearrangement of a vic-disulfoxide. The first step in the oxidation procedure is the development of the isolable thiosulfinate (7). Oxidation can then take place at the sulfenyl sulfur or the sulfinyl sulfur. Applying the theory of hard and soft acids and bases (HSAB), the sulfenyl sulfur is expected to be softer than sulfinyl sulfur which in turn is noticeably softer than the sulfonyl sulfur.[189] The more nucleophilic nature of the sulfenyl sulfur over sulfinyl sulfur suggests vic-disulfoxide formation (Scheme 29).[190]

Scheme 29.

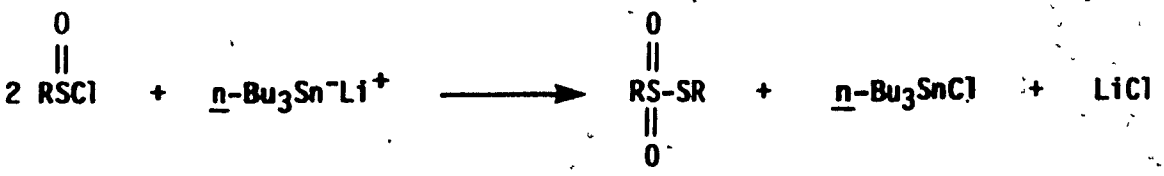


(6) (7) (154) (8)

While vic-disulfoxides are reasonable intermediates, hard evidence on this intermediacy has been lacking until recently. This is of particular interest given the relative simplicity of such a functional group; in addition, other oxo derivatives of disulfides (thiosulfinates, thiosulfonates, sulfinyl sulfones and vic-disulfones) are all isolable compounds. In the past few years, Freeman and Angeletakis have applied ^{1}H-NMR and ^{13}C-NMR studies to provide evidence for the existence of the transient vic-disulfoxides.[191,192] Product studies using ^{19}F-NMR[193] and ^{18}O labels[190] also suggest the presence of a highly unstable vic-disulfoxide.

It was of interest to provide further evidence for the intermediacy of vic-disulfoxides with the use of organotin reagents. The reaction of sulfinyl chlorides (129) with tri-n-butyltin lithium (155) provided good yields of symmetrical thiosulfonates (8) (Scheme 30); however, as we shall see, the synthesis of these thiosulfinates likely occurs via vic-disulfoxide rearrangement.

Scheme 30.



(129) (155) (8)

The required sulfinyl chlorides were prepared in excellent yields by chlorinating the respective disulfides in the presence of 2 equivalents of acetic anhydride, this preparation is based on the effective methodology described by Douglass and Norton.[194] Excess chlorine was trapped with sodium thiosulfate. The isolated yields of the thio-

Table 20. Yields of Symmetrical Thiosulfinates and the Corresponding Sulfinyl Chlorides.

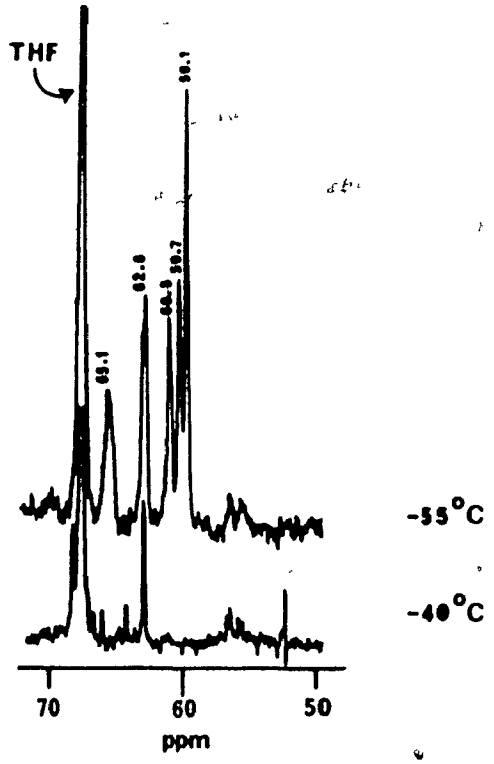
R	Sulfinyl Chloride RS(O)Cl (%)	Thiosulfonate RSO_2SR (%)
Phenylmethane	(129a), 96	(8a), 86
n-Butane	(129b), 91	(8b), 84
Benzene	(129c), 98	(8c), 75

sulfonates are presented in Table 20, benzyl phenylmethanethiosulfonate (**8a**) and phenyl benzenethiosulfonate (**8c**) were obtained as white solids, n-butyl n-butanethiosulfonate (**8b**) was isolated as a clear liquid. Physical and spectroscopic properties of each matched literature data.

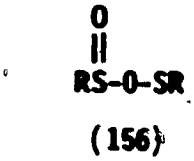
Low temperature NMR studies were carried out on the reaction of n-butanesulfinyl chloride and tri-n-butyltin lithium (-60°C). The lithium chloride was collected (-60°), the mixture was carried to the NMR instrument in a Dewar (-60°) and the ^{1}H-NMR or ^{13}C-NMR were performed at -55°C. The tin anion reagent is made commercially available as a 1 M solution in THF; presence of the THF solvent peaks swamped the proton NMR signals, thus proton NMR was of no use in this study. The carbon peaks of interest are those adjacent to sulfur; for n-butanesulfinyl chloride this peak is at 53.0 ppm, for the final product (n-butyl n-butanethiosulfonate) the peaks are at 62.6 ppm (carbon adjacent to sulfonyl sulfur) and 35.9 ppm (carbon next to sulfenyl sulfur). At -55°C the ^{13}C-NMR spectra of the reaction of n-butanesulfinyl chloride and the tin anion gave the following peaks of interest: 59.1, 59.7, 60.5, 62.6 (br), 65.1 (br) ppm.

Upon warming to -40°C, 90 min after filtration, only one peak appeared: 62.9 ppm. Repeating the experiment gave similar results except that in this run the peaks at 59.1 and 65.1 were of slightly greater intensity while those at 59.7 and 60.5 were of somewhat less relative intensity. These peaks appear to be paired, 59.1 with 65.1 and 59.7 with 60.5.

Figure 9. Low Temperature ^{13}C-NMR of the Reaction Mixture of n-Butanesulfinyl Chloride and tri-n-Butyltin Lithium

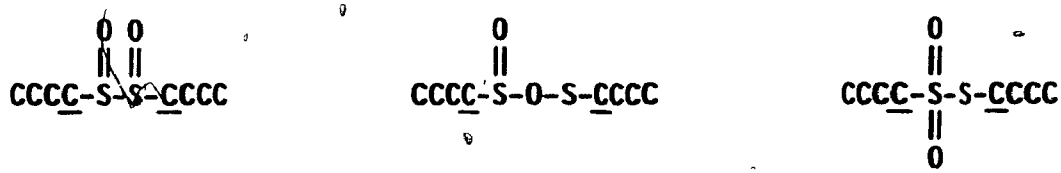


The peak at 62.9 ppm persisted and was assigned to the carbon next to the sulfonyl sulfur of n-butyl n-butanethiosulfonate (8b). The sulfoxide moiety is chiral, thus diastereomeric forms of disulfoxides may be observable by NMR. One pair of peaks may be attributed to the carbons adjacent to sulfur for RR/SS-di-n-butyl vic-disulfoxide (154a) and RS/SR-di-n-butyl vic-disulfoxide (154b). The second pair of peaks likely belong to the corresponding O,S-sulfenyl sulfinate (156). The rearrangement of vic-disulfoxides (154) to thiosulfonates (8) may proceed through this second unstable species (156).[190-192]



(156)

The ^{13}C assignments are based on the following arguments. Electron withdrawing effects are apt to be stronger for $-SO_2$ than for the -S(O)S moiety; the diastereotopic carbons from the disulfoxide should be better shielded than the carbon adjacent to the sulfonyl sulfur of the corresponding thiosulfonate. The thiosulfonate has a peak at 62.6-62.9 ppm, so the pair of disulfoxide peaks should be upfield of this value. Freeman and Angeletakis[192] have also noted this. For those cases when the R groups are equivalent, it has been noted that the carbon adjacent to a -S(O)O moiety, such as next to a sulfinate sulfur of a O,S-sulfenyl sulfinate, resonates downfield from those adjacent to a -S(O)S moiety of a disulfoxide.[191] Lastly, the carbon resonances for the diastereomers are not apt to be very different. As mentioned above, the peaks at 59.7 and 60.5 ppm appear to be paired as are those at 59.1 and 65.1 ppm. It follows from these arguments that the peaks at 59.7 and 60.5 ppm belong to the disulfoxide. The second pair of 59.1 and 65.1 ppm result from the O,S-sulfenyl sulfinate, the former peak for the carbon adjacent to the sulfenyl sulfur and the latter for the carbon next to the sulfinate ester. This is summarized below.



59.7, 60.5 | 65.1 59.1 | 62.6 35.9

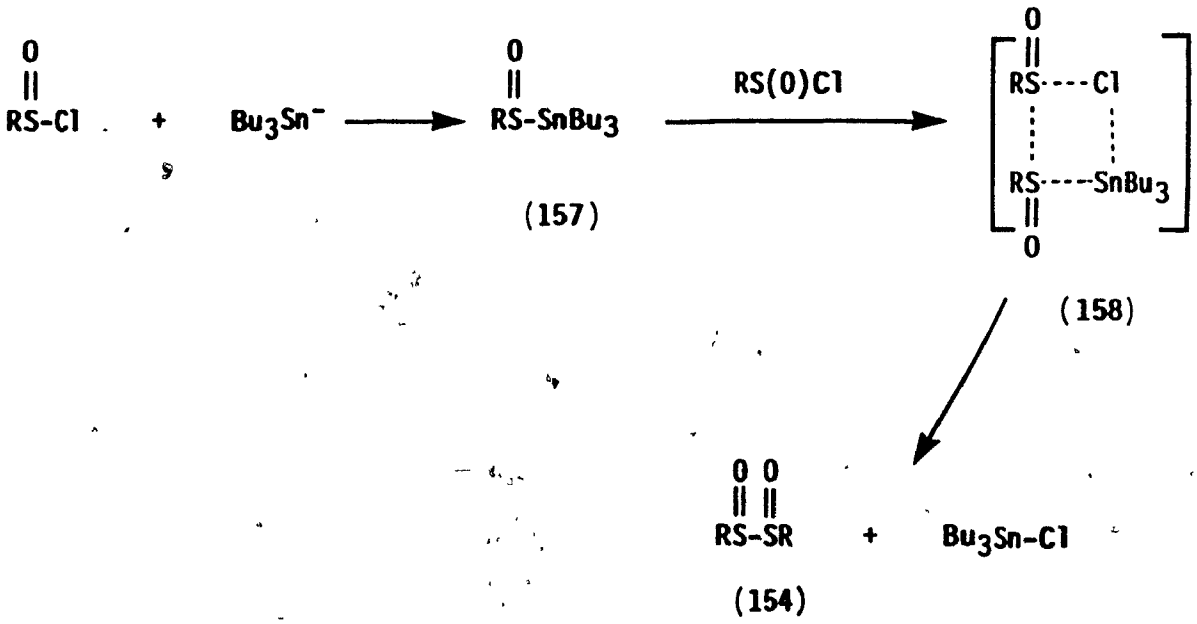
(154a), RR/SS
(154b), RS/SR | **(156)** | **(8b)**

The existence of similar intermediates leading to the formation of benzyl phenylmethanethiosulfonate **(8a)** and phenyl benzenethiosulfonate

(8c) could not be detected by low temperature NMR either because of interference with THF or, if they do indeed exist, because of the high reactivity of these intermediates. Freeman and co-workers have found the detection of these particular intermediates to be difficult.[195]

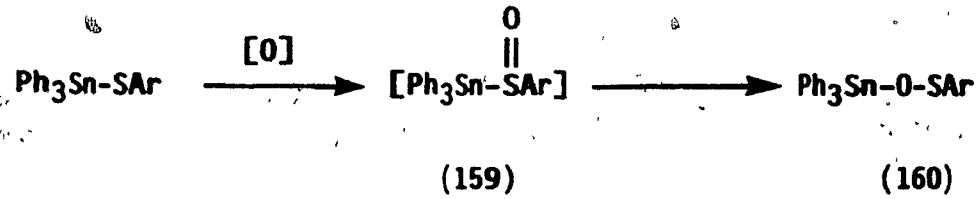
After initial attack of the tin anion on the sulfinyl chloride to form (157), the synthesis of vic-disulfoxide may be through the four centered transition state (158) (Scheme 31).

Scheme 31.



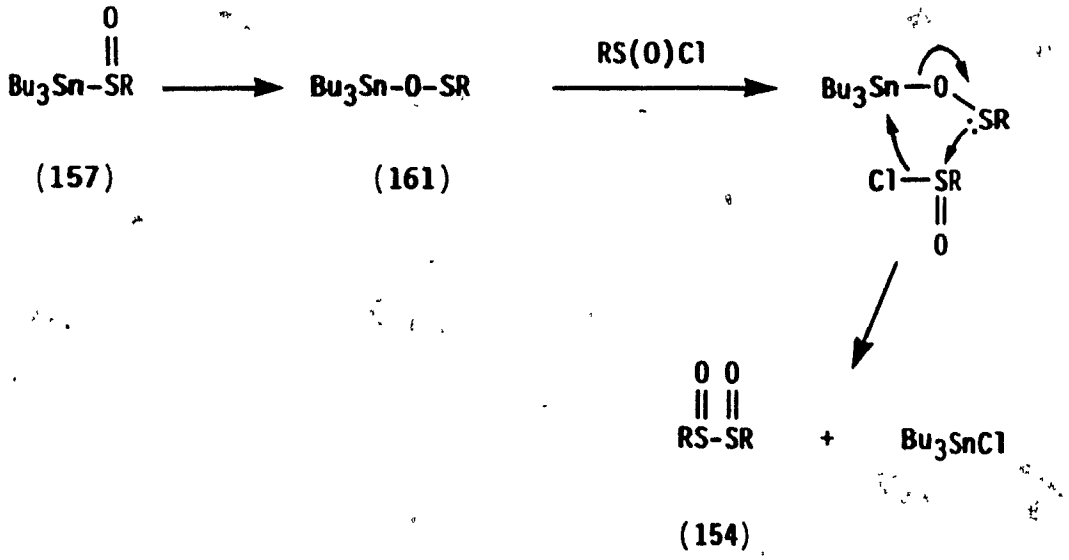
Taylor and Wardell have found that S-oxo triphenyl arylthiotin(IV) species (159) quickly rearrange to O-tin sulfenates (160) (Scheme 32).[196]

Scheme 32.



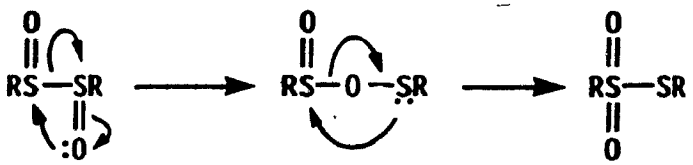
Hence, as an alternate mechanism, the sulfoxide (157) may have rearranged to the tin sulfenate (161) and then reacted as shown (Scheme 33).

Scheme 33.



Note that in considering Scheme 33 above, the oxygen, instead of sulfur, of the tin sulfenate could attack the sulfinyl chloride; if so then the O,S-sulfenyl sulfinate would be provided directly. As discussed earlier with the synthesis of disulfides from thiotins other mechanisms are possible; for instance an ionic process or five-coordinate tin.

^{13}C-NMR and mechanistic rationale indicate that vic-disulfoxides are initially formed in the reaction of sulfinyl chlorides and tin anion. The rearrangement of the vic-disulfoxide may proceed as shown below; either oxygen may attack the adjacent sulfinyl sulfur to provide the O,S-sulfenyl sulfinate (156) which in turn rearranges to the thiosulfonate (8).[197] A secondary method entails homolytic cleavage of the vic-disulfoxide to two sulfinyl radicals which may then recombine to the the O,S-sulfenyl sulfinate, this would then ultimately give the thio-



(154) (156) (8)

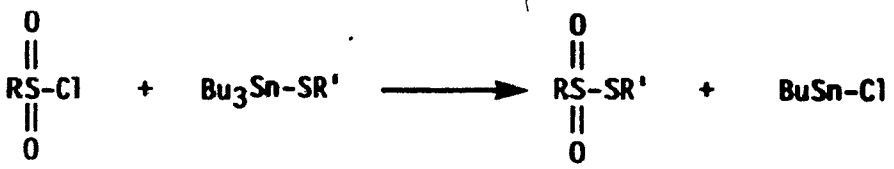
sulfonate.[190] Recent ab initio calculations support the rearrangement of vic-disulfoxides to thiosulfinates via sulfinyl radicals.[198] Homolysis of the sulfenyl sulfinate to sulfenyl and sulfonyl radicals is less likely, for if this were to occur then it is reasonable to assume that while many would recombine to thiosulfonates, some of these radicals would escape the solvent cage and recombine to form vic-disulfones (**153**) and disulfides (**6**). Disulfide formation is not observed.[193]

2.5.2 Attempted Preparation of Thiosulfonates from Thiotins and Sulfonyl Chlorides

Organotin-sulfur derivatives have been used in conjunction with sulfenyl chlorides to afford disulfides[120], and with sulfinyl chlorides to yield thiosulfinates[199] in good yield. In both cases, particularly for the preparation of the thiosulfinates, the reactions are carried out in nonpolar solvents under mild conditions.

Based on these reported results, an attempt was made to synthesize thiosulfonates (**8**) from thiotin(IV) compounds (**96**) and sulfonyl chlorides (**152**) (Scheme 34). Unfortunately the procedure (mixing of **96** and **152** in CH_2Cl_2) was unsuccessful.

Scheme 34.



(152) (96) (8)

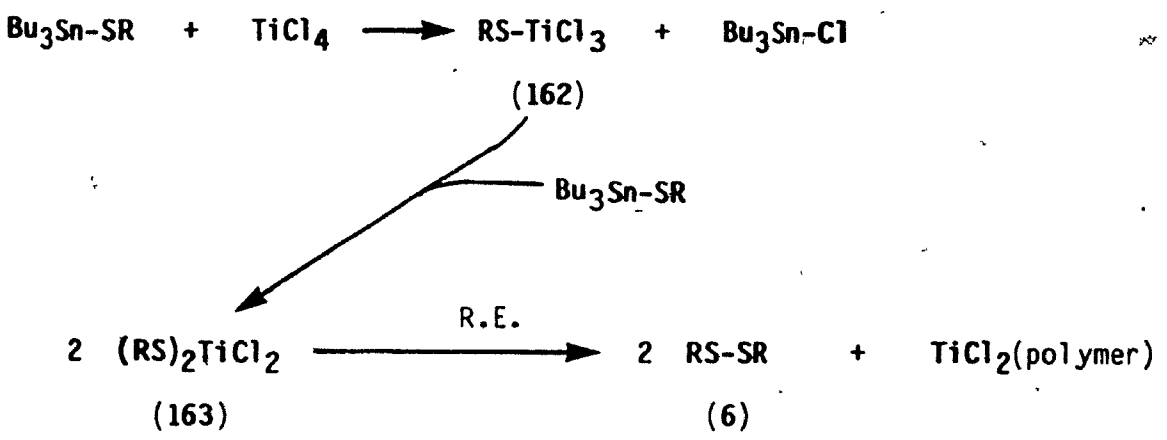
Repeating the reactions in refluxing THF for up to 20 h also did not afford any thiosulfonate, although symmetrical disulfide formation was observed. The disulfide apparently resulting from decomposition of the thiotins during work up procedures. A reason for the lack of reactivity of sulfonyl chlorides with thiotins may be that, using hard-soft (HSAB) terminology, the sulfonyl sulfur is hard, while the thiotin is a soft nucleophile; consistent with this, sulfinyl and sulfenyl sulfurs are softer electrophilic centers and are more likely to react with the soft thiotin species[189,200,201] which they readily do.[120,199]

A variety of Lewis Acids were used ($ZnCl_2$, $AlCl_3$ and $AlBr_3$) with no success. The use of $TiCl_4$ however, did yield the thiosulfonate; the proton NMR yields were at best 35-40%. A closer examination of the reaction showed that the thiosulfonate did not result from the direct attack of the thiotin reagent on the sulfonyl chloride. Initially, in less than 3 min, $TiCl_4$ provides the symmetrical disulfide from the thiotin reagent. The disulfide may have then reacted with the sulfonyl chloride, perhaps with the assistance of $TiCl_4$, to give the thiosulfonate. As a control, $TiCl_4$ was added to a mixture of dibenzyl disulfide and phenylmethanesulfonyl chloride; the corresponding thiosulfonate was detected. Adding $TiCl_4$ to tri-n-butyl phenylthiotin(IV) in an NMR tube showed that dibenzyl disulfide was formed almost instantly. These

results show that while the reaction of thiotin reagents with sulfonyl chlorides may not be useful in the preparation of thiosulfonates, $TiCl_4$ can serve as a good, mild oxidizer of thiotins toward the synthesis of symmetrical disulfides.

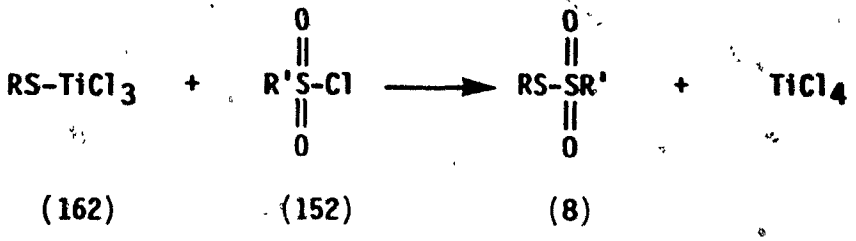
It is plausible that the thiotin reacts with $TiCl_4$ to form the intermediate (**162**). Reaction of this intermediate with a second molecule of thiotin would produce dialkylthiolatodichlorotitanium(IV) (**163**). This compound may then reductively eliminate to the disulfide and $TiCl_2$ polymers (Scheme 35).[202] Indeed, some unidentified polymeric by-product was observed in the synthesis of dibenzyl disulfide above. In addition, ^{119}Sn-NMR shows that tri-n-butyltin chloride (155.7 ppm) is formed in the reaction.

Scheme 35.



As indicated above, the thiosulfonate that was detected may result from the action of the disulfide on the sulfonyl chloride; however, there is an alternate proposal. Trichloroalkylthiolatotitanium(IV) (**162**) may react directly with sulfonyl chloride to deliver the thiosulfonate and titanium tetrachloride (Scheme 36).[202] In this mechanism there should be no appreciable symmetrical disulfide or $TiCl_2$ polymer

Scheme 36.



(162) (152) (8)

formation; both were observed in the preparation of thiosulfonates above but there is no reason to believe that both possible mechanisms are not occurring concurrently.

The isolated yield of dibenzyl disulfide formed by the action of 2 equivalents of $TiCl_4$ on tri-n-butyl benzylthiotin(IV) was 95%. Of further interest is the 93% yield of 1,2-dithiane (**74**) that resulted when 2 equivalents of $TiCl_4$ were added to μ-1,4-butyldithiohexa-n-butylditin(IV) (**109b**). This suggests that $TiCl_4$ may be fruitful in the synthesis of cyclic disulfides.

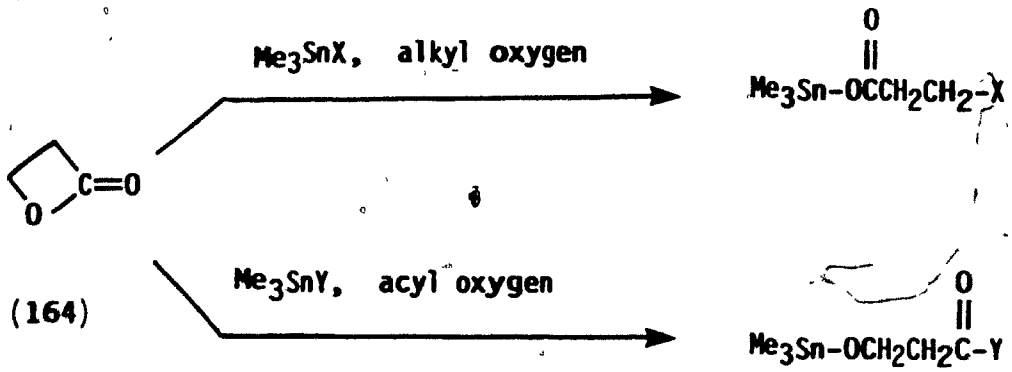
2.6 Investigation of Organotins as Sulfhydryl Protecting Groups and Attempted Synthesis of Substituted Thiophenes.

2.6.1 Preliminary Investigation.

It was of interest to see if organotin reagents might be useful as a cysteine sufhydryl protecting group. For organotin compounds to be of such use must be compatible with common amino and carboxyl protecting groups. A particularly familiar amino protecting group is the t-butyl-oxycarbonyl (t-BOC) functionallity which forms the carbamate; methyl and ethyl esters are often used to protect the carboxyl end of an amino acid.[203] While there is no evidence for the reaction of tri-alkyl alkylthiotins or trialkyltin chlorides with carbamates, these reagents

do react with esters.[204] β-Propiolactone (**164**), a four-membered size ring cyclic ester, undergoes alkyl cleavage with both thiotins and tin halides (Scheme 37).[204] Trimethyltin diethylamide and trimethyltin methoxide preferentially cleave this ester via the acyl oxygen bond.

Scheme 37.



X = SMe, Cl; Y = OMe, NEt_2

Due to large ring strain, (**164**) is known to react readily with many nucleophilic reagents.[204] An acyclic ester would probably not react with organotins as much as (**164**). To investigate this, S-tri-n-butylstannyl methylthioglycolate (**165**) was prepared. As with all thiotins,

n-Bu_3Sn-SCH_2COOMe (**165**)

n-Bu_3Sn-OMe (**166**)

tri-n-butyltin chloride was added to the thiol in the presence of triethylamine. The reaction was allowed to stir for 4 h before typical work-up procedures were carried out. Proton NMR of the crude indicated an impurity by the presence of a peak at 2.02 ppm, ^{119}Sn-NMR showed two peaks, 84.7 and 104.4 ppm with relative intensities of of ca. 9:1. The

mixture was separated by flash chromatography on silica, affording the tin-sulfur reagent (82%), with a ^{119}Sn-NMR signal at 84.9 ppm; and the impurity in question at 104.5 ppm.

This impurity proved to be tri-n-butyltin methoxide (**166**); the ^{119}Sn-NMR of an authentic sample gives a signal at 104.5 ppm and the proton NMR of each are superimposable. The authentic sample of tin methoxide was prepared by simply adding tri-n-butyltin chloride to methanol in the presence of triethylamine. Interestingly, the production of (**166**) indicates that the tin chloride or perhaps the subsequently formed thiotin gave acyl cleavage, not alkyl cleavage such has been reported for β-propiolactone (**164**).[204]

Acyl cleavage from tin chloride would also provide the corresponding acid chloride but there was no evidence of this. The acid chloride would be converted to the free acid and lost during work-up procedures.

Use of tri-n-butyltin chloride and the subsequent presence of thiotin reagents do not seem to substantially affect ester linkages. Thus, tin-sulfur derivatives may be useful as thiol protecting groups for cysteine.

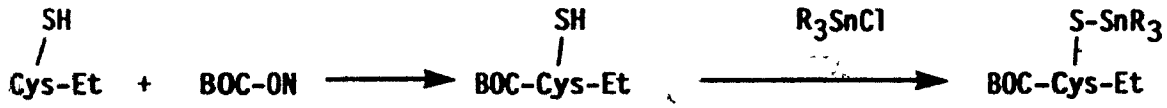
2.6.2 S-tri-n-Butylstannyl-N-Butyloxycarbonyl-L-cysteine Ethyl Ester (**167**).

Before protecting the sulfhydryl moiety of the amino acid it was necessary to have both the amino and carboxyl moieties protected. To do this, the t-butylcarbamate of cysteine ethyl ester (**168**) was prepared, by adding 2-(t-butyloxycarbonyl-oxyimino)-2-phenylacetonitrile (BOC-ON, **169**) to L-cysteine ethyl ester hydrochloride following a

published procedure.[205] The free thiol, a better nucleophile, may potentially attack (**169**), however the tendency for S to N acyl migration[206] suggests that the carbamate should be the thermodynamic product, if not necessarily the kinetic one. N-t-BOC-L-cysteine ethyl ester was prepared in 85% yield; the proton NMR and mass spectrum of the sample were consistent with the proposed structure. The viscous liquid also gave a positive result for thiols using the sodium nitroprusside test.

The fully protected amino acid (**167**) was obtained by adding tri-n-butyltin chloride to (**168**) (Scheme 38); the overall yield from cysteine ethyl ester was 77%. It was afforded as a colorless wax after quick purification on silica gel.

Scheme 38.



(**169**) (**168**) (**167**)

2.6.3 Treatment of (167) with a Variety of Amino and Carboxyl Deprotecting Agents.

S-tri-n-Butylstannyl-N-t-butyloxycarbonyl-L-cysteine ethyl ester (**167**) was treated with some common ester and carbamate cleavage reagents used for the deprotection of amino acids. The reactions were followed by ^{119}Sn-NMR and in all cases substantial cleavage of the tin-sulfur bond took place. The deprotecting conditions, which are described by Greene[203], were 3.0 M HCl for 30 min, thiophenol in CF_3COOH, trimethylsilyl iodide,[207] and KOH in D_2O/MeOH,

It is clear from Table 21 that common amino and carboxyl deprotecting agents also affect the tin-sulfur bond. During the course of peptide synthesis it is imperative that chain elongation can be carried out, that is, deprotecting either the amino or carboxyl end, without disturbing other protective groups. Organotin reagents as sulfhydryl protecting groups do not allow for this. Although (**167**) may not be usefully protected it may serve in an other way, the thiotin species could allow for the formation of functionalized cysteine residues; unsymmetrical disulfides or thiosulfinates may be formed via thiotins.

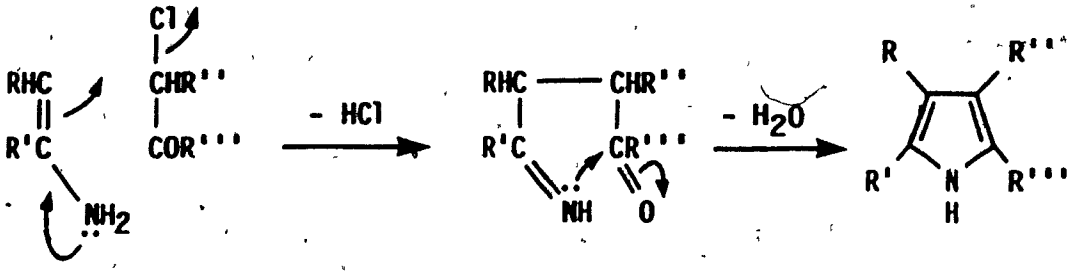
Table 21. ^{119}Sn-NMR Data for (**167**) With Various Deprotecting Reagents.

Entry	^{119}Sn-NMR ppm (relative abundance)
a) (**167**), fully protected amino acid	86.3
b) (**167**) + 3.0 M HCl, 30 min	155.7
c) n-Bu_3SnCl	155.4
d) (**167**) + 2 PhSH in CF_3COOH	73.7 (85), 86.5 (15)
e) n-Bu_3Sn-SPh	74.6
f) (**167**) + TMS-I, 6 min	84.5
g) n-Bu_3Sn-I	84.7
h) (**167**) + KOH in D_2O/MeOH	104.6 (67), 86.2 (33)
i) n-Bu_3Sn-OMe	104.5

2.6.4 Attempted Preparation of Substituted Thiophenes.

The Hantzsch pyrrole synthesis (Scheme 39) is a useful method to prepare substituted pyrroles.[208] A modification of this technique may

Scheme 39.



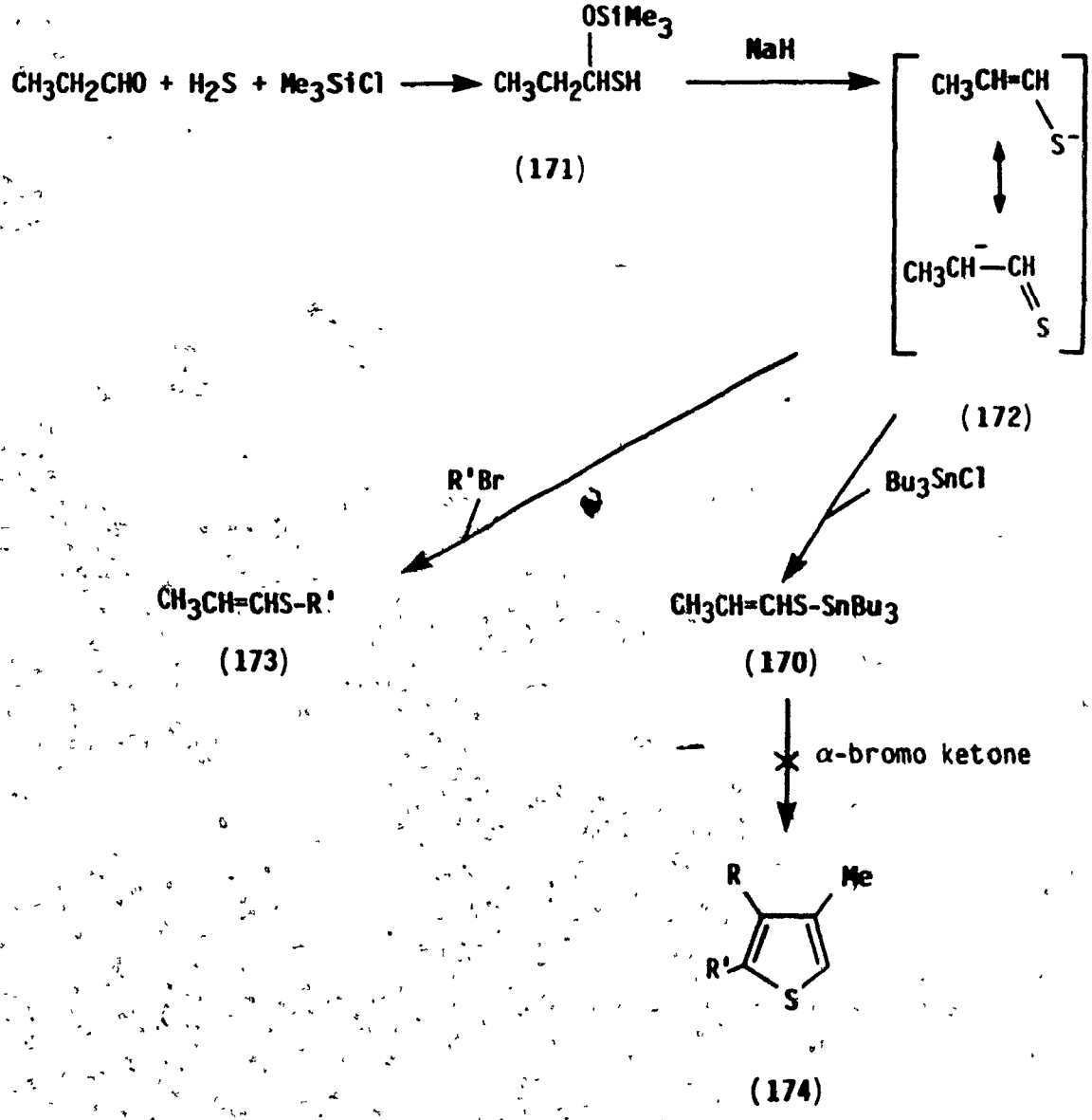
allow for the preparation of substituted thiophenes. Instead of an enamine, an enethiotin species such as (**170**) could be used. The formation of (**170**) could result from an α-siloxythiol (**171**) as depicted in Scheme 40 (next page). The highly odoriferous α-trimethylsiloxythiol was easily prepared from propanal, H_2S and trimethylsilyl chloride.[209] Thiol (**171**) was then reacted with NaH in CH_2Cl_2 to provide the enethiolate (**172**).[210] Treatment of thiols like (**172**) with alkyl halides is known to yield the respective vinyl sulfides (**173**).[210]

It was hoped that the addition of tri-n-butyltin chloride to (**172**) would yield an isolable vinylthiotin (**170**); this in turn could be reacted with α-bromo ketones to provide substituted thiophenes (**174**). Unfortunately attempts at isolating (**170**) led to decomposition, while this compound was not characterized, it may well have been formed in solution.

The presence of peaks in the aromatic region (6.5-8.0 ppm) of the proton NMR spectrum was used as the method to detect thiophene (**174**) formation. Treatment of (**170**) in situ, if actually prepared, with 3-bromo-2-butanone or α-bromoacetophenone in refluxing THF for 2 h or 24 h did not yield any thiophene (**174**). Rather, GC indicated unreacted bromo

ketone and TLC revealed many spots. The trimethylsilanol or trimethylsilanoate formed in the generation of the vinyl thiolate (172) may react with tin chloride, so the attempted preparation of (170) was repeated with 2 equivalents of tri-n-butyltin chloride. Subsequent trials with this solution of (170) were also unsuccessful.

Scheme 40.

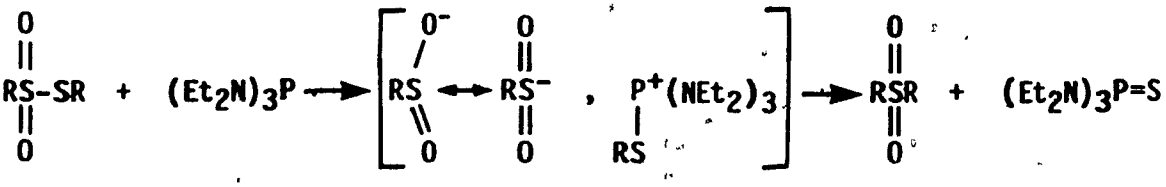


2.7 The Desulfurization of 1,2-Dithiepane 1,1-Dioxide (175).

The high yield of 1,2-dithiepane (75) via the oxidation of the pertinent tin-sulfur derivative prompted a study on the desulfurization of 1.2-dithiepane 1,1-dioxide (175), an oxidative product of the cyclic disulfide.

The reaction of acyclic thiosulfonates (8) with tris(diethylamino)-phosphine (176) affords sulfones (11).[211] The reaction takes place on the sulfenyl sulfur expelling an ambident sulfinate anion (177); this anion then undergoes S-alkylation to afford the sulfones and tris(diethylamino)phosphine sulfide (178) (Scheme 41).[211] In some instances the anion from acyclic thiosulfonates undergoes O-alkylation to yield lesser amounts of thiosulfinates (130).[211]

Scheme 41.



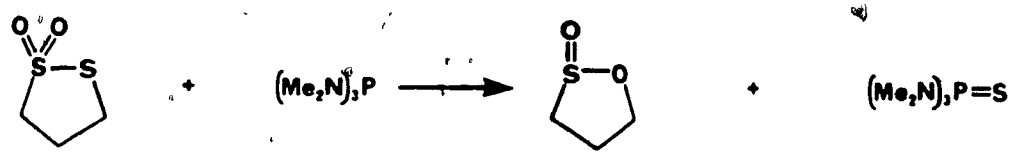
(8) (176) (177) (11) (178)

(130)

Treatment of small ring cyclic thiosulfonates with tris(diethylamino)phosphine yields primarily cyclic thiosulfinates rather than cyclic sulfones.[211,212] The addition of (176) to 1,2-dithiolane 1,1-

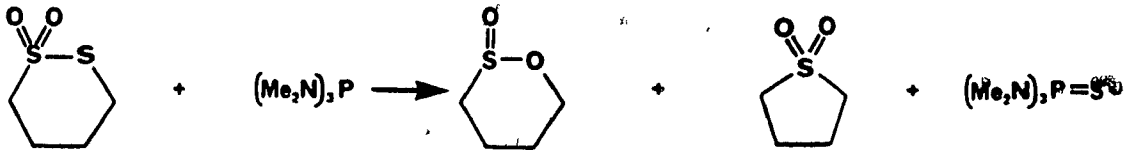
dioxide (179) results in the formation of 1,2-oxathiolane 2-oxide (180) (Scheme 42); the reaction of (176) with 1,2-dithiane 1,1-dioxide (181) affords 1,2-oxathiane 2-oxide (182) and thiolane 1,1-dioxide (183) in a ratio of 9:1 (Scheme 43).[212]

Scheme 42.



(179) (176) (180) (178)

Scheme 43.



(181) (176) (182) (183) (178)

9 : 1

Sulfinate ester formation may arise as a reflection of ring size on the course of the reaction. It was of interest to examine the desulfurization of the next higher homolog to more clearly assess this effect.

2.7.1 Synthesis of 1,2-Dithiepane 1,1-Dioxide.

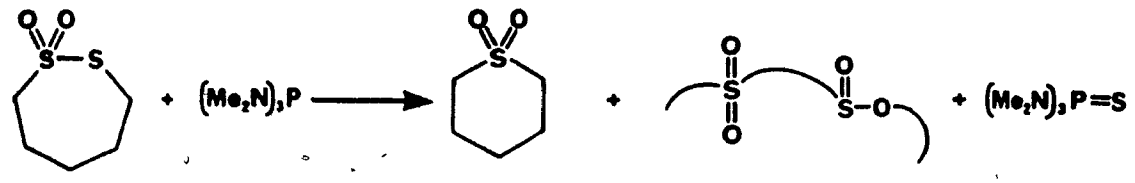
1,2-Dithiepane was oxidized with hydrogen peroxide using literature procedures[78]; the yield of the cyclic thiosulfonate was only 12% (the literature yield is 17%).[78] However, oxidation of the cyclic

disulfide with m-chloroperbenzoic acid (m-CPBA) afforded the dioxide in 33% yield. This exothermic reaction was monitored by TLC, the reaction could also be followed by color changes as described in the experimental procedures for this synthesis. Removal of the m-CBA which forms was achieved by concentrating the CH_2Cl_2 solution to precipitate the acid. The precipitate was filtered and the filtrate was concentrated again; the solution was concentrated a total of four times, the last time under a stream of nitrogen at ca. 5°C. This procedure removed most of the m-CBA. The sample was then further purified on a silica column.

2.7.2 Desulfurization of (175).

The desulfurization of 1,2-dithiepane 1,1-dioxide (**175**) was carried out in a fashion similar to the method used in the desulfurization of (**179**) and (**181**)[211], a small excess of tri(diethylamino)phosphine (**176**) was added to the dioxide (**175**) in benzene (Scheme 44). The reaction afforded 21 % of the cyclic sulfone (**184**) (thiane 1,1-dioxide) and an oily polymer (**185**). The polymer showed infrared peaks typical for sulfones (1325 vs, 1125 vs cm^{-1}) and sulfinate esters (1140 s cm^{-1}), but the bands of the latter were considerably weaker. Also isolated from the mixture was a 92 % yield of tris(diethylamino)phosphine sulfide

Scheme 44.

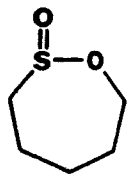


(**175**) (**176**) (**184**) (**185**) (**178**)

(178), the infrared spectrum of this compound was identical to that of an authentic sample produced by adding (176) to sulfur in toluene. The high recovery of phosphine sulfide suggests that the reaction went to near completion.

None of the 7-membered sultine (1,2-oxathiepane-2-oxide (186)) was detected by either ^{1}H-NMR or IR (1110 cm^{-1}).[213]

It appears from these data that while there was evidence of sulfinate ester formation in the polymer, most of the attack by the ambident sulfinate anion is through sulfur (S-alkylation) yielding sulfone. The



(186)

sultines formed by the aminophosphine desulfurization of (179) and (181) above seem to be governed by ring size considerations and not an inherent disposition for O-alkylation. It should be noted that 'hard-soft' considerations also favor S-alkylation.[200,201] The sulfenyl sulfur bearing carbon where alkylation takes place is more likely to be attacked by S^- than O^-.

CONCLUSIONS AND CONTRIBUTIONS TO ORIGINAL KNOWLEDGE

The development of a new general route for the preparation of cyclic disulfides was undertaken. This was performed by oxidatively coupling organotin-sulfur derivatives, specifically, μ-α,ω-alkyldithio-hexa-n-butylditin(IV) species and 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes (most of these are new compounds) with bromine or iodine. The employment of the organotin compounds provided good to excellent yields of the cyclic disulfides without the need of high dilution techniques. The effectiveness of tin-sulfur species to afford cyclic disulfides was investigated; this showed that tin derivatives yield up to tenfold greater amounts of cyclic disulfides than does simple oxidation of the dithiols without the use of tin. The increased yields were most impressive for the medium sized ring systems; that is the 8-, 9- and 10-membered ring cyclic disulfides. The combination of organotin reagents and mild dilution further increased the isolable yields of monomeric cyclic disulfides. It should be noted that 1,2-dithiolane, 1,2-dithiacycloundecane and 1,2-dithiacyclododecane, the five, eleven and twelve-membered ring cyclic disulfides, were prepared in monomeric forms but isolation led to polymerization. It was shown that what is reported in the literature as monomeric 1,2-dithiacyclododecane is in fact a dimeric species. A potential "tin effect" or "template effect" which afforded these goods yields relative to systems in which no tin is used was postulated to result primarily from auto-association and masking of the thiol moiety by tin. Good yields of symmetrical disulfides were also prepared via halogen oxidation of thiotin(IV) species.

While kinetic measurements and mixed reaction studies with I_2/Br_2 or IBr were unsuccessful, competition reactions did provide some information on the mechanism of halogen oxidation of thiotin(IV) compounds. The competition reactions which were performed with a series of trialkyl arylthiotin(IV) compounds showed an average rho (ρ) of - 0.45. This low value suggests that the reaction is likely concerted or synchronous; two possible mechanisms are thus six electron concerted or four-centered. If a four-centered mechanism is to proceed then the oxidation must be done in two steps; kinetics reveals information on the rate determining step, the other step may proceed via an ionic or other different mechanism type.

^{119}Sn-NMR were performed on all of the tin-sulfur derivatives, this extends published data on these types of compounds.

New evidence for the existence of vic-disulfoxides is presented. Although much is known about other oxygen derivatives of disulfides (thiosulfinates, thiosulfonates, sulfinyl sulfones and vic-disulfones) the same is not true for vic-disulfoxides. The reaction of sulfinyl chlorides with tri-n-butyltin lithium provided good yields of thiosulfonates, however, low temperature ^{13}C-NMR showed that the initial product of this reaction was likely a vic-disulfoxide. The unstable vic-disulfoxide may then rearrange to an O,S-sulfenyl sulfinate which in turn can rearrange to the thiosulfonate.

The combination of thiotin(IV) compounds with sulfonyl chlorides did not afford good yields of the anticipated unsymmetrical thiosulfonates; however, these studies showed that $TiCl_4$ could be useful as an oxidizer of thiotins to provide symmetrical disulfides or cyclic disulfides.

S-tri-n-Butylstannyl-N-t-butyloxycarbonyl-L-cysteine ethyl ester was prepared. While not likely of use in peptide synthesis this compound may be used to prepare cysteine residues which could be derivatized at sulfur.

The desulfurization of 1,2-dithiepane 1,1-dioxide was carried out with tris(diethylamino)phosphine. The result was 21% of the cyclic sulfone and a polymer which contained sulfone moieties and some sulfinate groups. This experiment suggests that the corresponding desulfurizations of 1,2-dithiolane 1,1-dioxide and 1,2-dithiane 1,1-dioxide which yield the respective sultines (cyclic sulfinates), does so due to ring constraints and not because of an inherent disposition to form sultines.

PROSPECTS FOR FUTURE RESEARCH

The good yields of the cyclic disulfides which were obtained from organotin-sulfur derivatives suggest that thiotin species in conjunction with sulfur chloride or sulfur monochloride could in theory provide the corresponding acyclic or cyclic trisulfides (**187**), or acyclic or cyclic tetrasulfides (**188**). Some cyclic trisulfides (GC yields) have recently been prepared in this fashion.[214] In addition, the reaction of thionyl chloride or sulfuryl chloride with the same thiotin derivatives (tri-n-butyl alkylthiotin(IV) compounds, μ-α,ω-alkyldithiohexa-n-butylditin(IV) species or 2,2-di-n-butyl-1,3,2-dithiastannacycloalkanes) could afford the oxidative products of trisulfides (acyclic or cyclic); the cyclic analogs (**189**) and (**190**), are unknown.

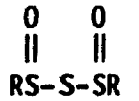
(**187**) (**188**) (**189**) (**190**)

Alternatively, bis(tri-n-butyltin) sulfide (**106**) may be added to sulfenyl chlorides, sulfinyl chlorides or sulfonyl chlorides, to provide symmetrical trisulfides (**191**) and the oxygen derivatives (**192**) and (**193**) respectively (Scheme 45). This synthesis may also be carried out with di-n-butyltin sulfide (**194**), instead of (**106**).

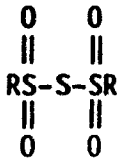
Scheme 45

$$Bu_3Sn\text{-}S\text{-}SnBu_3 \quad + \quad 2\ RS\text{-}Cl \longrightarrow RS\text{-}S\text{-}SR \quad + \quad 2\ Bu_3SnCl$$

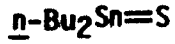
(106) (191)



(192)



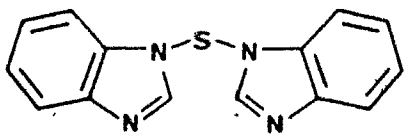
(193)



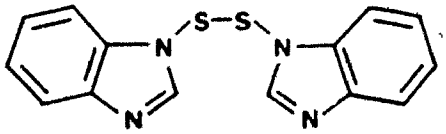
(194)

Cyclic sulfides may be provided from the reaction of the appropriate thiotin(IV) compounds with α,ω-alkane dibromides; work on this front is already in progress in our laboratory.

Sulfur transfer reagents (**195**) and (**196**)[215] may also react with tin-sulfur derivatives to afford trisulfides and tetrasulfides (acyclic or cyclic). The anticipated mild reaction conditions may provide these polysulfides in good yields.

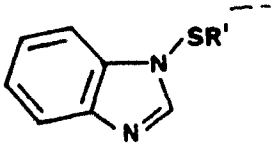


(195)

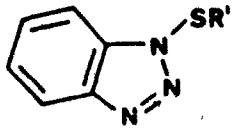


(196)

In a fashion similar to that presented above, thiotin(IV) compounds and sulfur transfer reagents such as (**197**) or (**198**) could provide for a nice preparation of unsymmetrical disulfides (**135**) (Scheme 46). While not reported in this thesis, preliminary studies on this procedure have been carried out and strong potential for this reaction is envisaged.



(197)



(198)

Scheme 46.

$R_2N\text{-}SR'$ + $Bu_3Sn\text{-}SR''$ ⟶ $R'S\text{-}SR''$ + $Bu_3Sn\text{-}NR_2$

(197,198) (96) (135)

While the formation of sulfur-sulfur bonds has been mentioned there is no reason why these studies cannot include other heteroatoms (oxygen, nitrogen, phosphorus, selenium).[155] The metal may be any of the group IVb metals or metalloids; the reaction types are many. A good deal of chemistry remains to be performed using simple coupling procedures for many of the possible combinations of heteroatoms and metals.

A small extension of the synthesis of cyclic disulfides involves the synthesis of bicyclic disulfides. The appropriate dithiols and organotin reagents followed by oxidation may afford the bicyclic disulfides in good yields.

The use of $TiCl_4$ as an oxidizer of thiotins to yield disulfides should be expanded on. This reagent may prove to be a very mild oxidizing agent with potential in elaborate syntheses where the formation of disulfides is required. Furthermore, if as proposed, a titanium-sulfur covalent bond is in fact being prepared, then this class of compound may provide a wide variety of chemistry with other

reagents to provide unsymmetrical disulfides, thiosulfinates, thiosulfonates or other sulfur containing species.[202]

As already mentioned, it would be useful to see if cysteine residues derivatized at sulfur could be prepared from S-tri-n-butylstannyl-N-t-butyloxycarbonyl-L-cysteine ethyl ester. These derivatized cysteines could be of biological interest.

Lastly, semi-empirical calculations may be carried out on many of of the compounds presented in this study. Of particular interest would be calculations on cyclic disulfides to obtain information on the stability of these systems.

CHAPTER 3

EXPERIMENTAL

3.1 General Methods

Reagents which were available from commercial sources were used directly except for the following: liquid thiols, dithiols, di-n-butyl disulfide, n-butanesulfonyl chloride, propanal and 3-bromo-2-butanone which were distilled before use; α-bromoacetophenone (phenacyl bromide) was recrystallized prior to use.

Solvents were treated as follows: hexanes and pentane were distilled over 7% by volume of concentrated sulfuric acid and passed through a column of deactivated aluminum oxide before storing over sodium; dichloromethane was distilled over phosphorus pentoxide and stored over 3 Å molecular sieves; tetrahydrofuran was distilled from the blue sodium ketyl of benzophenone; triethylamine distilled over KOH; other solvents were stored over freshly activated 3 Å sieves without any further purification. Molecular sieves were activated by heating at 200-250°C overnight and then cooled in a desiccator.[216,217]

All melting points were obtained on a Gallenkamp melting point apparatus using open ended capillaries or on a Fisher-Johns melting point apparatus using microscope cover glasses. These and boiling points are uncorrected.

Thin layer chromatography (TLC) was performed on E. Merck aluminum oxide 60 F-254 neutral (type E) and/or E. Merck silica gel 60 F-254. Both types of TLC plates were aluminum backed with a fluorescent indicator. Column chromatography was carried out on Fisher neutral

alumina Brockman activity I (80-200 mesh) or E. Merck silica gel 60 (230-400) using flash chromatography conditions.[218] Gas chromatography was accomplished on a Varian Associates (VA) model 3700 gas chromatograph equipped with a VA model 4270 printing integrator. Separations were attained using either a 2 m x 5 mm O.D. glass column containing 3% Silicone OV-17 on Chromosorb HP 80/100 or a 10 m glass capillary bonded column containing 3% Silicone OV-101.

^{1}H nuclear magnetic resonance spectra were recorded with a Varian Associates T-60, T-60a or XL-200 FT spectrometer. Data are reported in δ (ppm) units relative to internal tetramethylsilane (TMS), followed by the abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad and the relative intensities. Proton decoupled ^{13}C and ^{119}Sn NMR spectra were recorded on a VA XL-200 or a VA XL-300. The data for ^{13}C was obtained in $CDCl_3$ and is reported in ppm relative to TMS; for ^{119}Sn ca. 300 mg of sample was used, the data are reported in ppm units relative to external tetramethyltin in $CDCl_3$. Shifts downfield from the external standard are reported in positive ppm units.[174,177]

Infrared spectra were recorded on a Perkin-Elmer model 297 grating spectrometer. The data are reported in cm^{-1} units and are calibrated to the 1602 cm^{-1} band of a polystyrene reference. Raman spectra from 100 to 1000 wavenumbers were recorded on a Jobin Yvan ISA Ramanor U-1000 Raman spectrometer using the 514.5 nm (green) line of an argon laser with the polarization set to total. Single scans were taken of neat liquids and waxes in capillary tubes using the macro or microscope adapters. Solids were scanned using the microscope adapter with the sample set on uncovered glass slides. The slits were set to 300

microns, the spacing between points was 3 wavenumbers and the acquisition took 1 s per point.

Mass spectra were obtained with a DuPont Instruments 21-492B, a Hewlett Packard HP 5980A or a LKB 9000 mass spectrometer. The conditions are given, followed by the data which is reported as follows: mass/charge (m/z), relative abundance, assignment. In the case of tin containing species the two most abundant peaks of monotin clusters and the three most abundant peaks for ditin clusters are given. Molecular weight determinations were achieved with a Corona-Wescan Osmometric Molecular Weight Apparatus at 50°C in spectrograde toluene. The instrument was calibrated with benzil or sucrose octaacetate and this calibration was checked with compounds of known molecular weight such as benzyl disulfide. Low temperature molecular weight determinations were attempted in distilled CH_2Cl_2 or dry pentane at 25°C or 5°C respectively.

Ultraviolet and visible spectra were obtained on a Hewlett Packard 8451-A Diode Array Spectrophotometer or a Pye Unicam SP 800 UV Spectrophotometer. A Cantech Scientific Ltd. Stopped-Flow Apparatus interfaced with an I.B.M. personal computer was used for fast kinetic measurements.

Refractive indices were achieved with a Baush & Lomb Abbé Refractometer at 25°C. The instrument was calibrated with distilled water: 18°C, 1.3331; 25°C, 1.3325; 30°C, 1.3320.[219] The density measurement for 1,2-dithiepane (**75**) was obtained with a Sodev Vibrating Cell Densitometer which was calibrated with dichloromethane and n-hexane.

Elemental analyses were performed by Canadian Microanalytical Service inc. of Vancouver B.C.

3.2 Experimental Procedures.

Triphenylmethanethiol (Tritylthiol) (104)

Tritylthiol was prepared using a modification of the method used by Vorländer and Mittag.[124] Hydrogen sulfide was passed through a partially dissolved mixture of 6.45 g (24.8 mmol) of triphenylcarbinol and 5 drops of sulfuric acid in ca. 50 ml of acetic acid. The solution had a yellow coloration. Excess H_2S was trapped with two 2 l KOH solutions followed by a lead acetate indicating solution. Any H_2S that would have passed the two first traps would be indicated by its reaction with lead acetate to form a black lead sulfide precipitate. The addition of H_2S was ceased once this yellow color no longer persisted upon heating to 100°C. No solid remained at this point. Upon cooling, a white solid precipitated; further crystal formation was prompted with the addition of 10 ml of water. The solid was collected and recrystallized in acetone affording 6.24 g (91% yield) of fine white crystals; mp 106.5-107 °C (lit.[124,220] 107°,106-107°). ^{1}H-NMR ($CDCl_3$) δ : 3.00 (s, 1H); 7.17 (s, 15H). Further, this compound gave a positive result for detection of a thiol moiety using the sodium nitroprusside test.

Detection of Thiols and Disulfides on TLC

A nitroprusside solution was used for the detection of thiols on thin layer chromatography.[221] The reagent was prepared as follows: to 1.5 g of sodium nitroprusside in 5 ml of 2 N hydrochloric acid and 95 ml of methanol was added 10 ml of 25% ammonium hydroxide, this mixture was shaken and filtered. Developed TLC plates could then be dipped into the solution with thiol groups being visible as bright pink or red spots.

For the detection of disulfides a second spray reagent was necessary. This second solution being 2.0 g of sodium cyanide in 5 ml of water and 100 ml of methanol. Disulfides appear as pink or red spots on a yellow background when the TLC plate is dipped into the nitroprusside reagent above and then immediately placed into the cyanide solution.[221]

Each of these reagents could be kept in TLC developing jars for several months and used as required.

Dithiols

Most dithiols were available from commercial sources and were distilled before use. 1,7-heptane dithiol and 1,9-nonane dithiol were prepared from their respective dibromides by the thiouronium salt method.[128] A mixture of 20.0 g (77.5 mmol) of 1,7-dibromoheptane, 11.8 g (155.0 mmol) of thiourea, and 130 ml of 95% ethanol was refluxed for 6 h. To this was added a solution of 11.0 g (250.0 mmol) of KOH in 100 ml of water and the entire mixture was further refluxed for 2 h. The solution was acidified with dilute sulfuric acid (3 ml of concentrated acid in 20 ml of water) and then extracted twice with benzene. The benzene extracts were washed with 100 ml of water, dried over $MgSO_4$ and then evaporated at reduced pressure yielding 14.86 g of clear viscous liquid. This liquid was distilled affording 14.45 g (81% yield) of the dithiol, bp 73-75°/0.1 mm (lit.[222] 252°C). ^{1}H-NMR ($CDCl_3$) δ : 1.17-1.83 (br, 12H); 2.56 (q, 4H). 1,9-nonane dithiol was similarly prepared in 78% yield, bp 87-88° /0.1 mm (lit.[222] 284°C). ^{1}H-NMR ($CDCl_3$) δ : 1.2-1.73 (br, 14H); 2.53 (q, 4H).

tri-n-Butyl Alkylthiotin(IV) Compounds and tri-n-Butyl Phenylthiotin(IV) (96)

All of the alkyl or arylthiotin(IV) species were prepared using the same general procedure, that being a slight modification of the method used by Harpp, Aida and Chan[116] as well as Wieber and Schmidt.[114,115] The synthesis of tri-n-butyl benzylthiotin(IV) is illustrative. To 5.0 ml (42.6 mmol) of freshly distilled phenylmethanethiol and 6.25 ml (45 mmol) of distilled triethylamine in 250 ml of CCl_4 was added 14.4 g (42.6 mmol) of 96% tri-n-butyltin chloride. The white triethylamine hydrochloride salt precipitated immediately. The reaction was allowed to stir vigorously for 3-4 h. The reaction mixture was filtered, the filtrate was washed twice with 5% acetic acid, dried ($MgSO_4$), evaporated in vacuo and distilled to give tri-n-butyl benzylthiotin(IV); bp 139°C/0.3 mm in 95 % yield. In some instances the alkylthiotins were obtained as waxy solids. ^{1}H-NMR showed that these compounds were pure after they were placed under vacuum (0.1 mm to 0.4 mm) overnight hence they were used without further purification.

n-Bu,Sn-SR

tri-n-Butyl Benzylthiotin(IV) (96a)

Colorless liquid, 95% yield; bp 157°C/0.3 mm (lit.[116] 165°/0.1 mm). ^{1}H-NMR ($CDCl_3$) δ : 0.88 (t, 9H); 0.90-1.60 (br, 18H); 3.71 (s, 2H); 7.17-7.33 (br, 5H). ^{119}Sn-NMR : 70.9 ppm. Raman (neat) : 877, 844, 808, 685 (S-C), 589, 502 (Sn-C), 406, 361, 334 (Sn-S), 241. MS (EI, 70eV, 40°C) m/z : 357 (6), 355 (4) [M^+ - n-Bu·]; 323 (7), 321 (5) [M^+ - C_7H_7·]; 291 (53), 289 (54) [n-Bu_3Sn^+]; 267 (67), 265 (42) [n-Bu_2SnSH^+]; 235 (50), 233 (42) [n-Bu_2SnH^+]; 211 (20), 209 (13) [267-265 - C_4H_8]; 179

(58), 177 (100), 175 (64) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (36), 153 (56), 151 (29) [H_2SnSH^+ and $SnSH^+$]; 123 (12), 121 (43), 119 (58) [SnH^+ and SnH_3^+]; 91 (61) [$C_7H_7^+$]; 65 (11); 57 (94); 56 (51). Anal. calculated for $C_{19}H_{34}SSn$: C, 55.23; H, 8.29; S, 7.76. Found : C, 55.42; H, 8.24; S, 7.61.

tri-n-Butyl n-Butylthiotin(IV) (**96b**)

White, waxy solid, 98% yield; mp 47-54°C. ^{1}H-NMR ($CDCl_3$) δ : 0.91 (m, 12H); 1.00-1.73 (br, 22H); 2.60 (t, 2H). ^{119}Sn-NMR : 69.8 ppm. Raman (neat) : 880, 844, 811, 646 (S-C), 589, 502 (Sn-C), 382, 349 (Sn-S), 304, 208. MS (EI, 70eV, 40°C) m/z : 323 (13), 321 (10) [M^+ - n-Bu·]; 291 (15), 289 (11) [n-Bu_3Sn^+]; 267 (100), 265 (83) [n-Bu_2SnSH^+]; 235 (11), 233 (11) [n-Bu_2SnH^+]; 211 (27), 209 (16) [267-265 - C_4H_8]; 179 (61), 177 (72), 175 (38) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (38), 153 (66), 151 (18) [H_2SnSH^+ and $SnSH^+$]; 121 (48), 119 (41) [SnH^+]; 57 (60); 56 (64).

tri-n-Butyl s-Butylthiotin(IV) (**96c**)

White, waxy solid, 97% yield; mp 52-56°C. ^{1}H-NMR ($CDCl_3$) δ : 0.90 (m, 15H); 1.10-1.67 (br, 20H); 2.83 (m, 1H). ^{119}Sn-NMR : 66.2 ppm. Raman (neat) : 883, 844, 814, 733 (S-C), 592, 502 (Sn-C), 310 (Sn-S), 205. MS (EI, 70eV, 45°C) m/z : 323 (73), 321 (66), 319 (57) [M^+ - C_4H_9· and M^+ - C_4H_9· - H_2]; 293 (77), 291 (76), 289 (70) [323-319 - C_2H_6 and/or 321-319 - C_2H_4 and n-Bu_3Sn^+]; 267 (50), 265 (37) [n-Bu_2SnSH^+]; 235 (12), 233 (11) [n-Bu_2SnH^+]; 211 (34), 209 (35) [267-265 - C_4H_8]; 179 (57), 177 (74), 175 (44) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (13), 153 (35),

151 (25) [H_2SnSH^+ and $SnSH^+$]; 121 (47), 119 (52) [SnH^+]; 57 (52); 56 (100).

tri-n-Butyl t-Butylthiotin(IV) (96d)

Colorless liquid, 95% yield; bp 115°C/0.2 mm (lit.[111] 110°/0.1 mm). ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 9H); 1.03-1.73 (br), 1.45 (s, total for 1.03-1.73 and 1.45 is 27H). ^{119}Sn-NMR : 51.8 ppm. Raman (neat) : 883, 847, 817, 688 (S-C), 589, 502 (Sn-C), 391, 352 (Sn-S), 208. MS (EI, 70eV, 40°C) m/z : 323 (37), 321 (30) [$M^+ - C_4H_9\cdot$]; 293 (41), 291 (53), 289 (25) [see above]; 267 (64), 265 (38) [n-Bu_2SnSH^+]; 235 (28), 233 (19) [n-Bu_2SnH^+]; 211 (35), 209 (21), 207 (19) [n-$BuSnH_2S^+$ and n-$BuSnS^+$]; 179 (38), 177 (39), 175 (43) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (29), 153 (24), 151 (33) [H_2SnSH^+ and $SnSH^+$]; 121 (23), 119 (36) [SnH^+]; 57 (46); 56 (33); 41 (50); 29 (36); 28 (100).

tri-n-Butyl Cyclohexylthiotin(IV) (96e)

Waxy solid, 97% yield; ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.07-1.87 (br, 29H). ^{119}Sn-NMR : 63.5 ppm. Raman (neat) : 880, 847, 814, 733 (S-C), 589, 502 (Sn-C), 382, 349 (Sn-S), 304, 208. MS (EI, 70eV, 40°C) m/z : 349 (41), 347 (32) [M^+ - n-Bu·]; 293 (29), 291 (37), 289 (29) [M^+ - n-Bu· - C_4H_8 and n-Bu_3Sn^+]; 267 (41), 265 (37) [n-Bu_2SnSH^+]; 235 (11), 233 (10) [n-Bu_2SnH^+]; 211 (29), 209 (13) [n-$BuSnH_2S^+$]; 179 (40), 177 (64), 175 (39) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (43), 153 (36), 151 (29) [H_2SnSH^+ and $SnSH^+$]; 121 (34), 119 (31) [SnH^+]; 116 (38) [$C_6H_{11}SH^+$]; 83 (56) [$C_6H_{11}^+$]; 82 (65) [$C_6H_{10}^+$]; 57 (30); 56 (100); 55 (81).

tri-n-Butyl n-Decylthiotin(IV) (96f)

Colorless liquid, 94% yield; bp 180°C/0.5 mm. ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t), 0.85-1.63(br, m) total integration 48H; 2.45 (t, 2H). ^{119}Sn-NMR : 70.5 ppm. Raman (neat) : 886, 844, 814, 652 (S-C), 595, 505 (Sn-C), 454, 388, 343 (Sn-S), 175. MS (EI, 70eV, 50°C) m/z : 407 (54), 405 (41) [M^+ - n-Bu·]; 379 (5), 377 (4) [M^+ - C_6H_{13}·]; 351 (4), 349 (3) [M^+ - n-Bu· - C_4H_8 and M^+ - C_8H_{17}·]; 323 (4), 321 (3) [n-Bu_3SnS^+]; 291 (39), 289 (32) [n-Bu_3Sn^+]; 269 (28), 267 (26) [$C_8H_{21}SnS^+$]; 235 (27), 233 (34), 231 (23) [n-Bu_2SnH^+ and n-Bu_2SnH^+ - H_2]; 179 (32), 177 (31), 175 (36) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 153 (17), 151 (27) [$SnSH^+$]; 121 (35), 119 (27) [SnH^+]; 97 (17); 71 (32); 69 (33); 57 (55); 55 (42); 43 (70); 41 (61); 32 (32); 29 (37); 28 (100).

tri-n-Butyl Phenylthiotin(IV) (96g)

Colorless liquid, 93% yield; bp 157°C/0.6 mm (lit.[116] 140°/0.2 mm). ^{1}H-NMR ($CDCl_3$) δ : 0.87 (t, 9H), 1.07-1.57 (br, 18H); 7.02-7.25 (br, 3H); 7.28-7.47 (br, 2H). ^{119}Sn-NMR : 74.6 ppm. Raman (neat) : 880, 841; 697 (S-C), 589, 502 (Sn-C), 421, 385, 337 (Sn-S), 193. MS (EI, 70eV, 40°C) m/z : 343 (32), 341 (48) [M^+ - n-Bu·]; 291 (16), 289 (7) [n-Bu_3Sn^+]; 267 (44), 265 (44) [n-Bu_2SnSH^+]; 229 (41), 227 (35) [$C_6H_5SSn^+$]; 179 (33), 177 (40), 175 (25) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (24), 153 (35), 151 (18) [H_2SnSH^+ and $SnSH^+$]; 121 (21), 119 (33) [SnH^+]; 77 (34); 57 (29); 55 (28); 41 (52); 39 (27); 29 (46); 28 (100). Anal. calculated for $C_{18}H_{32}SSn$: C, 54.16; H, 8.08; S, 8.03. Found : C, 54.12; H, 8.04; S, 7.61.

tri-n-Butyl Triphenylmethylthiotin(IV) (96h)

After the usual reaction (allowed to stir for 24 h) and work-up procedures, this compound appeared as a clear, orange solution in CCl_4 in which fine white crystals had precipitated; on concentration, further crystallization occurred and this solid was collected and triturated with minimal amounts of cold hexanes. The evaporation of the solvent from the filtrate afforded a viscous, orange liquid which could not be distilled and streaked on silica or alumina. This orange liquid was non-homogeneous by ^{1}H-NMR, ^{119}Sn-NMR and MS.

Crude, orange liquid, decomposed during distillation; ^{1}H-NMR ($CDCl_3$) δ : 0.7-1.17 (br, 9H); 1.17-1.71 (br, 18H); 7.17 (m, 12.5H). ^{119}Sn-NMR : 54.7 ppm (46%); 104.9 ppm (16%); 154.6 ppm (38%). Raman (neat) : 670, 619, 592, 586 (S-C), 505 (Sn-C), 346, 334 (Sn-S), 322 (Sn-Cl). MS (EI, 70eV, 45°C) m/z : 291 (41), 289 (14) [n-Bu_3Sn^+]; 269 (91), 267 (93), 265 (72) [n-Bu_2SnCl^+ and n-Bu_2SnSH^+]; 235 (7), 233 (6) [n-Bu_2SnH^+]; 213 (42), 211 (35), 209 (12) [n-$BuSnHCl^+$ and n-$BuSnH_2S^+$]; 179 (41), 177 (88), 175 (50) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 157 (28), 155 (60), 153 (49), 151 (29) [H_2SnCl^+, $SnCl^+$, H_2SnSH^+ and $SnSH^+$]; 121 (31), 119 (47) [SnH^+]; 77 (26) [$C_6H_5^+$]; 57 (46); 56 (39); 41 (100).

White crystals; decomposed at 160-164°C turning orange. ^{1}H-NMR ($CDCl_3$) δ : 7.20 (s). A mixed melting of these crystals with dityrityl sulfide[125] showed decomposition at 159-164°C.

An authentic sample of 350 mg of bis(tri-n-butyltin) sulfide (n-$Bu_3Sn)_2S$ gave a ^{119}Sn-NMR resonance at 82.6 ppm.

Alkyl and Aryl Disulfides (6)

All of the symmetrical alkyl and aryl disulfides were prepared in the same fashion. To a vigorously stirring solution of 25.0 mmol of tri-n-butyl alkylthiotins and arylthiotins in ca. 50 ml of CH_2Cl_2 at 0°C is added dropwise 12.5 mmol of I_2 or Br_2 which had been previously dissolved in minimal amounts of CH_2Cl_2 (ca. 2 ml). The reaction was allowed to stir for 5 min before being washed with 5% sodium thiosulfate, dried ($MgSO_4$) and evaporated in vacuo. The resultant tri-n-butyltin halide and disulfide mixture was placed on aluminum oxide (ca. 40g of alumina per 1 g of mixture) and eluted with hexanes/dichloromethane 7:1. The tri-n-butyltin bromide was far more soluble in the thiosulfate wash than the tin iodide; hence the use of bromine instead of iodine as oxidant facilitated purification of the disulfide. The disulfides were identified by their ^{1}H-NMR and retention times on GC as compared to authentic samples. The isolated yields and the pertinent physical data are summarized in Table 22 below.

Attempted Preparation of Triphenylmethane Disulfide (Trityl Disulfide) (6h)

To 3.65 g of crude tri-n-butyl triphenylmethylthiotin(IV) (**96h**) in 100 ml of CH_2Cl_2 is added dropwise with vigorous stirring 0.64 g (4.0 mmol) of Br_2 which had been dissolved in 5 ml of CH_2Cl_2. After stirring for 10 min the reaction was washed with 5% sodium thiosulfate, dried $MgSO_4$ and gently concentrated in vacuo to afford a thick oil; ^{1}H-NMR of crude ($CDCl_3$) δ : 0.93 (t, 10.5H); 1.17-1.80 (br, 21H); 7.29 (s, 15H). Crystals formed with the addition of hexanes/dichloromethane 7:1 to the crude oil, these were filtered and combined with the resultant crystals

Table 22. Isolated Yields and Physical Data of Symmetrical Disulfides from the Oxidation of their Respective Thiotins.

Disulfide	% Yield[a]	GC[b] this work	GC[b] lit.	^{1}H-NMR[c]
benzyl (**6a**)	94	7.31	7.28	3.57 (s, 2H), 7.20 (s, 5H).
n-butyl (**6b**)	96	2.89	2.87	0.90 (t, 3H), 1.15-1.87 (br, 4H), 2.70 (t, 2H).
n-butyl (**6c**)	97	2.38	2.37	1.00 (t, 3H), 1.10-1.90 (br and t 5H), 2.75 (m, 1H).
t-butyl (**6d**)	89	1.77	1.76	1.30 (s).
cyclohexyl (**6e**)	94	6.20	6.18	1.07-2.25 (br, 10H) 2.73 (br, 1H).
n-decyl (**6f**)	84	11.74	11.63	0.90 (br t, 3H), 1.03-1.70 (br, 16H) 2.63 (t, 2H).
phenyl (**6g**)	91	6.06	6.03	7.27 (br s)

a) isolated yields; b) gas chromatographic retention times in min on a 10 m bonded glass capillary column containing 3% Silicone OV-101, the temperature program was set for 80°- 225° at 20°/min; c) ($CDCl_3$) δ :.

from the concentration of the filtrate. The melting point of these crude crystals was 151-157°C. Recrystallization in hexanes/dichloromethane 3:1 afforded 0.24 g (43% yield) of trityl sulfide as fine white crystals; decomposition at 161-164°C (lit.[126] mp of disulfide: 155°, of monosulfide: 165°). ^{1}H-NMR ($CDCl_3$) δ : 7.23 (s). Molecular weight determination : 497; calculated for disulfide : 551.5; for monosulfide : 519.4.

μ-α,ω-Alkyldithiohexa-n-Butylditin(IV) Compounds. (**109**)

All of the μ-α,ω-alkyldithiohexa-n-butylditin(IV) species were prepared using the same general procedure. The synthesis of μ-1,4-butyldithiohexa-n-butylditin(IV) (**109b**) is presented. To 4.0 ml (34 mmol) of 1,4-butanedithiol and 10.0 ml (72 mmol) of triethylamine in 250 ml of CCl_4 was slowly added 18.4 ml (68 mmol) of 96% tri-n-butyltin chloride. The reaction was allowed to stir vigorously for 2-5 h. The work-up conditions have been previously described for the preparation of (**96**). These dithioditins were obtained as thick liquids; they could not be distilled and streaked on alumina or silica gel. ^{1}H-NMR, ^{119}Sn-NMR and MS all showed that the dithioditins were all quite clean hence they were used without further purification. Yields in all cases approached 100%.

μ-1,3-Propyldithiohexa-n-Butylditin(IV) (**109a**)

Colorless, viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 18H); 1.07-1.80 (br, 36H); 2.63 (t, 4H). ^{119}Sn-NMR : 77.6 ppm. IR (neat) : 2970, 2930, 2860, 1465, 1380 (alkyl), 1295, 1075, 965, 875, 700, 665 (S-C). Raman (neat) : 884, 844, 594, 506 (Sn-C), 408, 344, 314 (Sn-S), 218. MS

(EI, 70 eV, 110°C) m/z : 631 (1), 629 (2), 627 (1) [$M^{+\cdot}$ - n-Bu·]; 557 (1), 555 (1), 553 (1) [M^{+} - n-Bu· - C_3H_6S]; 501 (<1), 499 (<1), 497 (<1) [557-553 - C_4H_8]; 291 (49), 289 (3) [n-Bu_3Sn^+];, 235 (46), 233 (31) [291-289 - C_4H_8]; 179 (42), 177 (52), 175 (51) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 123 (16), 121 (31), 119 (28) [SnH_3^+ and SnH^+]; 74 (17); 57 (21); 56(48); 55 (30); 43 (45); 41 (62); 39 (27); 29 (33); 28 (100).

μ-1,4-Butyldithiohexa-n-Butylditin(IV) (109b)

Colorless, viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 18H); 1.08-1.73 (br, 40H); 2.53 (t, 4H). ^{119}Sn-NMR : 77.9 ppm. IR (neat) : 2970, 2940, 2880, 2860, 1470, 1380 (alkyl), 1195, 1070, 965, 875, 720, 665 (S-C). Raman (neat) : 878, 842, 650 (S-C), 587, 500 (Sn-C), 386, 341 (Sn-S), 239, 206. MS (EI, 70 eV, 66°C) m/z : 645 (5), 643 (6), 641 (5) [M^{+} - n-Bu·]; 557 (4), 555 (4), 553 (4) [M^{+} - n-Bu· - C_4H_8S]; 501 (3), 499 (4), 497 (3) [see above]; 323 (2), 321 (2) [n-Bu_3SnS^+]; 297 (53), 295 (42) [n-$BuSnS_2C_4H_8^+$]; 291 (17), 289 (13) [see above]; 267 (6), 265 (5) [n-Bu_2SnSH^+]; 241 (11), 239 (10) [297-295 - C_4H_8]; 235 (16), 233 (12) [see above]; 179 (29), 177 (30), 175 (21) [see above]; 121 (21), 119 (15) [see above]; 89 (59); 57 (240; 56 (52); 43 (18); 41 (92); 39 (42); 29 (33); 28 (100). Anal. calculated for $C_{28}H_{62}S_2Sn_2$: C, 48.02; H, 8.92; S, 9.16. Found : C, 48.24; H, 8.89; S, 8.40.

μ-1,5-Pentyldithiohexa-n-Butylditin(IV) (109c)

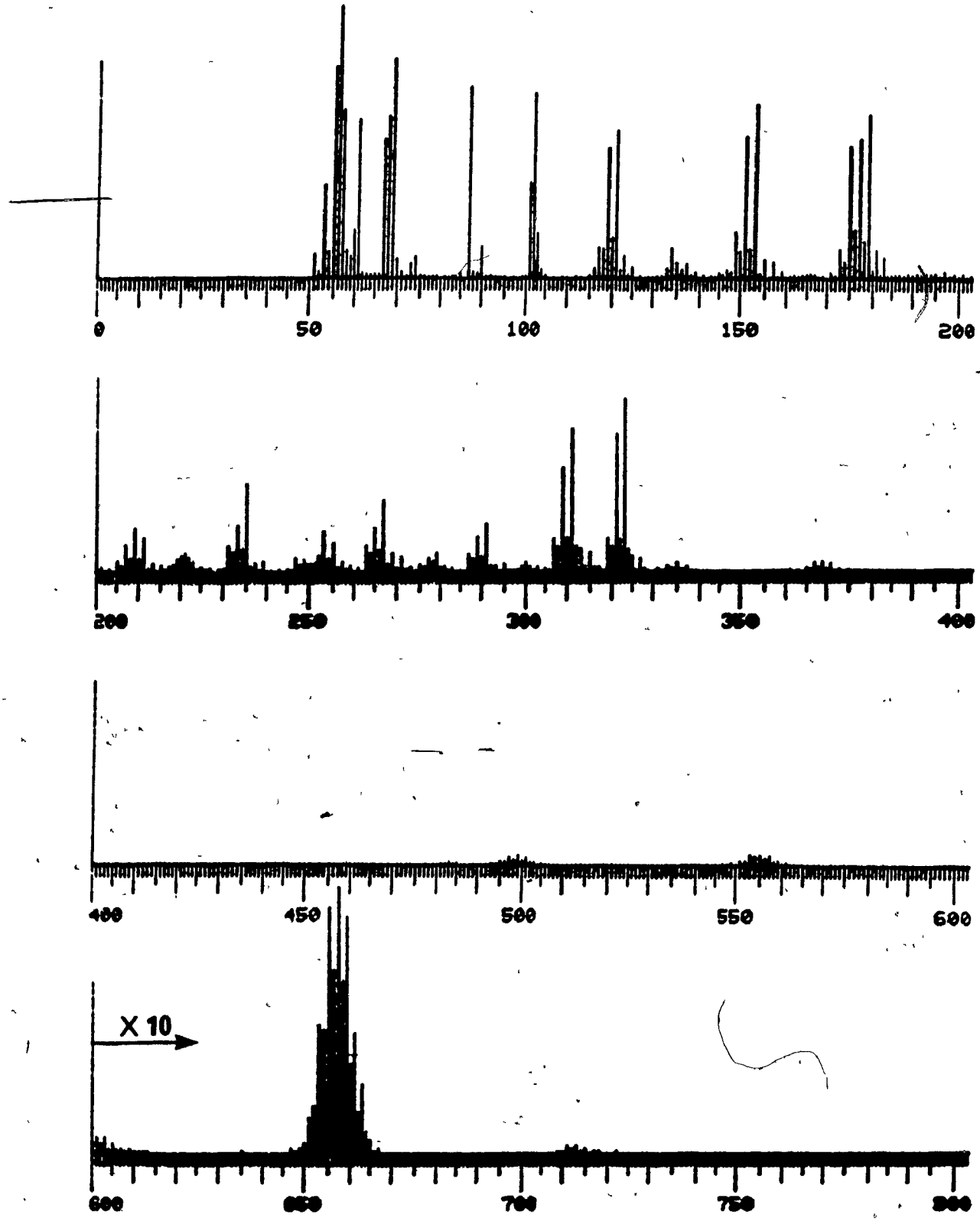
Colorless, viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 18H); 1.07-1.80 (br, 42H); 2.55 (t, 4H). ^{119}Sn-NMR : 75.5 ppm. IR (neat) : 2970, 2930, 2880, 2860, 1465, 1380 (alkyl), 1300, 1075, 960, 875, 790, 690, 665 (S-C). Raman (neat) : 880, 841, 649, (S-C), 586, 499 (Sn-C),

385, 340 (Sn-S), 238, 208. MS (EI, 70 eV, 140°C) m/z : 659 (9), 657 (11), 655 (9) [M^+ - n-Bu·]; 557 (<1), 555 (<1), 553 (<1) [M^+ - n-Bu· - $C_5H_{10}S$]; 501 (<1), 499 (<1), 497 (<1) [see above]; 323 (79), 321 (65) [see above]; 311 (73), 309 (58) [n-$BuSnS_2C_5H_{10}^+$]; 291 (18), 289 (13) [see above]; 267 (27), 265 (19) [see above]; 255 (14), 253 (17) [311-309 - C_4H_8]; 235 (33), 233 (17) [see above]; 179 (60), 177 (52), 175 (50) [see above]; 153 (64), 151 (53) [$SnSH^+$]; 121 (55), 119 (49) [see above]; 102 (69); 87 (71); 69 (81); 57 (63); 56 (100); 55 (78), (Figure 10). Anal. calculated for $C_{29}H_{64}S_2Sn_2$: C, 48.76; H, 9.03; S, 8.97. Found : C, 46.19; H, 8.29; S, 8.29.

μ-1,6-Hexyldithiohexa-n-Butylditin(IV) (**109d**)

Very viscous, colorless liquid; ^{1}H-NMR ($CDCl_3$) : 0.90 (t, 18H); 1.07-1.83 (br, 44H); 2.53 (t, 4H). ^{119}Sn-NMR : 76.6 ppm. IR (neat) : 2970, 2930, 2860, 1465, 1380 (alkyl), 1300, 1075, 960, 880, 690, 670 (S-C). Raman (neat) : 844, 646 (S-C), 586, 502 (Sn-C), 358 (Sn-S), 220. MS (EI, 70 eV, 180°C, m/z scan from 300 to 800) m/z : 673 (94), 671 (100), 669 (94) [M^+ - n-Bu·]; 557 (5), 555 (3), 553 (1) [M^+ - n-Bu· - $C_6H_{12}S$]. MS (EI, 70 eV, 255°C) m/z : 501 (15), 499 (17), 497 (12) [see above]; 325 (12), 323 (8), 321 (5) [n-$BuSnS_2C_6H_{12}^+$ and n-Bu_3SnS^+]; 291 (61), 289 (46) [see above]; 269 (17), 267 (16), 265 (9) [325-323 - C_4H_8 and n-Bu_2SnSH^+]; 235 (100), 233 (81) [see above]; 179 (69), 177 (64), 175(41) [see above], 153 (11), 151 (10) [see above]; 121 (13), 119 (9) [see above]; 57 (8), 55 (8); 41 (10).

Figure 10. Mass Spectrum of μ-1,5-Pentyldithiohexa-n-Butylditin(IV) (**109c**).



μ-1,7-Heptyldithiohexa-n-Butylditin(IV) (**109e**)

Very viscous, colorless liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 18H); 1.07-1.80 (br, 46H); 2.55 (t, 4H). ^{119}Sn-NMR : 76.5 ppm. IR (neat) : 2960, 2920, 2860, 1465, 1380 (alkyl), 1300, 1070, 960, 875, 690, 665 (S-C). Raman (neat) : 880, 838, 650 (S-C), 569, 508 (Sn-C), 342, 316 (Sn-S), 222. MS (EI, 70 eV, 220°C, m/z scan from 300 to 800) m/z : 687 (87), 685 (100), 683 (65) [M^+ - n-Bu·]. MS (EI, 70 eV, 245°C) m/z : 501 (4), 499 (5), 497 (5) [see above]; 339 (11), 337 (7) [n-$BuSnS_2C_7H_{14}^+$]; 291 (59), 289 (43) [see above]; 283 (15), 281 (10) [339-337 - C_4H_8]; 235 (100), 233 (78) [see above]; 179 (70), 177 (63), 175 (41) [see above]; 153 (13), 151 (10) [see above]; 121 (11), 119 (8) [see above]; 57 (7); 55 (9); 41 (8).

μ-1,8-Octyldithiohexa-n-Butylditin(IV) (**109f**)

Viscous, clear, slightly yellow liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 18H); 1.08-1.80 (br, 48H); 2.53 (t, 4H). ^{119}Sn-NMR : 76.6 ppm. IR (neat) : 2970, 2930, 2860, 1460, 1380 (alkyl), 1300, 1070, 960, 875, 685, 665. Raman (neat) : 876, 840, 650 (S-C), 581, 500 (Sn-C), 341, 317 (Sn-S), 219. MS (EI, 70 eV, 240°C, m/z scan from 300 to 800) m/z : 701 (91), 699 (100), 697 (73) [M^+ - n-Bu·]. MS (EI, 70 eV, 250°C) m/z : 557 (1), 555 (1), 553 (1) [M^+ - n-Bu· - $C_8H_{16}S$]; 501 (3), 499 (5), 497 (3) [see above]; 353 (13), 351 (8) [n-$BuSnS_2C_8H_{16}^+$]; 323 (7), 321 (6) [see above]; 297 (17), 295 (24) [353-351 - C_4H_8]; 291 (59), 289 (43) [see above]; 235 (100), 233 (73) [see above]; 179 (60), 177 (63), 175 (53) [see above]; 153 (16), 151 (12) [see above]; 121 (10), 119 (7) [see above]; 57 (5).

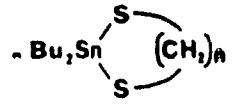
μ-1,9-Nonyldithiohexa-n-Butylditin(IV) (**109g**)

Clear, waxy solid, almost liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 18H); 1.05-1.78 (br, 50H); 2.55 (t, 4H). ^{119}Sn-NMR : 75.0 ppm. IR (neat) : 2960, 2930, 2860, 1460, 1380 (alkyl), 1300, 1075, 960, 875, 690, 665. Raman (neat) : 879, 835, 652 (S-C), 583, 502 (Sn-C), 340 (Sn-S), 220. MS (EI, 70eV, 235°C, m/z scan from 300 to 800) m/z : 715 (93), 713 (100), 711 (77) [M^+ - n-Bu·]. MS (EI, 70eV, 250°C) m/z : 557 (1), 555 (1), 553 (1) [M^+ - n-Bu· - $C_9H_{18}S$]; 501 (7), 499 (7), 497 (6) [see above]; 367 (9), 365 (6) [n-$BuSnS_2C_9H_{18}^+$]; 323 (5), 321 (4) [see above]; 311 (21), 309 (15) [367-365 - C_4H_8]; 291 (54), 289 (42) [see above]; 235 (100), 233 (82) [see above]; 179 (69), 177 (67), 175 (39) [see above]; 153 (14), 151 (11) [see above]; 121 (14), 119 (10) [see above]; 57 (9); 41 (3).

μ-1,10-Decyldithiohexa-n-Butylditin(IV) (**109h**)

Clear, waxy solid, almost liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 18H); 1.05-1.80 (br, 52H); 2.56 (t, 4H). ^{119}Sn-NMR : 75.6 ppm. IR (neat) : 2970, 2930, 2860, 1460, 1375 (alkyl), 1295, 1075, 960, 875, 690, 665. Raman (neat) : 880, 838, 652 (S-C), 580, 502 (Sn-C), 343 (Sn-S), 201. MS (EI, 70eV, 240°C, m/z scan from 300 to 800) m/z : 729 (88), 727 (100), 725 (69) [M^+ - n-Bu·]. MS (EI, 70eV, 255°C) m/z : 501 (3), 499 (4), 497 (2) [see above]; 381 (6), 379 (4) [n-$BuSnS_2C_{10}H_{20}^+$]; 325 (11), 323 (9) [381-379 - C_4H_8]; 291 (60), 289 (47) [see above]; 235 (100), 233 (79) [see above]; 179 (57), 177 (52), 175 (45) [see above]; 153 (9), 151 (7) [see above]; 121 (7), 119 (6) [see above]; 57 (4).

2,2-di-n-Butyl-1,3,2-Dithiastannacycloalkanes (110)

All of the dithiastannacycloalkyl systems were prepared with the same general procedure. The  synthesis of 2,2-di-n-butyl-1,3,2-dithiastannacyclohexane (**110a**) is presented. To a 500 ml flask equipped with a Dean-Stark reflux apparatus and condenser was added 196 ml of benzene, 2.44 g (9.80 mmol) of di-n-butyltin oxide and ca. 5 mg of para-toluenesulfonic acid. To this solution was further added dropwise at 2 ml/ min 1.06 g (9.80 mmol, dissolved in 10ml of benzene) of 1,3-propanedithiol; the concentration of the solution was 0.05 M. The mixture was refluxed with stirring for 4 h. Large, white rod shaped crystals precipitated. Concentration of the filtrate afforded more large white crystals; both batches of crystals were collected and triturated with cold benzene. The yield was 3.21 g (97%). All other entries (**110b-110h**) were isolated as thick liquids or gums by removing solvent in vacuo. Attempts to purify these compounds by chromatography on silica or alumina were unsuccessful. Vacuum distillation with an oil diffusion pump (10^{-5} mm/Hg) led to decomposition. Yields in all cases approached 100% and spectra were taken on these samples. The entire procedure was repeated for all dithiols listed in a more concentrated solution (0.20 M in benzene). In some cases mass spectrometry of the dithiastannacycloalkyls prepared in the more concentrated solution showed evidence of dimer formation. In those instances data from both mass spectra are given.

2,2-di-n-Butyl-1,3,2-Dithiastannacyclohexane (110a)

Large, white, rod like crystals, 97% yield; mp 65-67°C (lit.[223] 63-64°C). ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 6H); 1.20-1.73 (br, 12H); 1.90 (m,

2H); 2.93 (t, 4H). ^{119}Sn-NMR : 149.8 ppm. IR ($CHCl_3$ soln) : 2970, 2945, 2880, 2860 (alkyl), 1230, 1190, 1070, 700, 630 (S-C). Raman (neat) : 748, 672, 640 (S-C), 590 (Sn-C), 334, 314 (Sn-S), 238. MS (EI, 70eV, 55°C) m/z : 340 (1), 338 (1) [M^+]; 283 (18), 281 (10) [M^+ - n-Bu·]; 251 (3), 249 (2) [n-BuSnSC$_3$H$_6^+$]; 227 (4), 225 (3) [M^+ - n-Bu· - C_4H_8]; 57 (17); 56 (43) 41 (94); 39 (33); 29 (100), (Figure 11). Molecular weight determination calculated for $C_{11}H_{24}S_2Sn$: 339.1; found : 343. Anal. calculated for $C_{11}H_{24}S_2Sn$: C, 38.96; H, 7.13; S, 18.91. Found : C, 38.90; H, 7.05; S, 18.87.

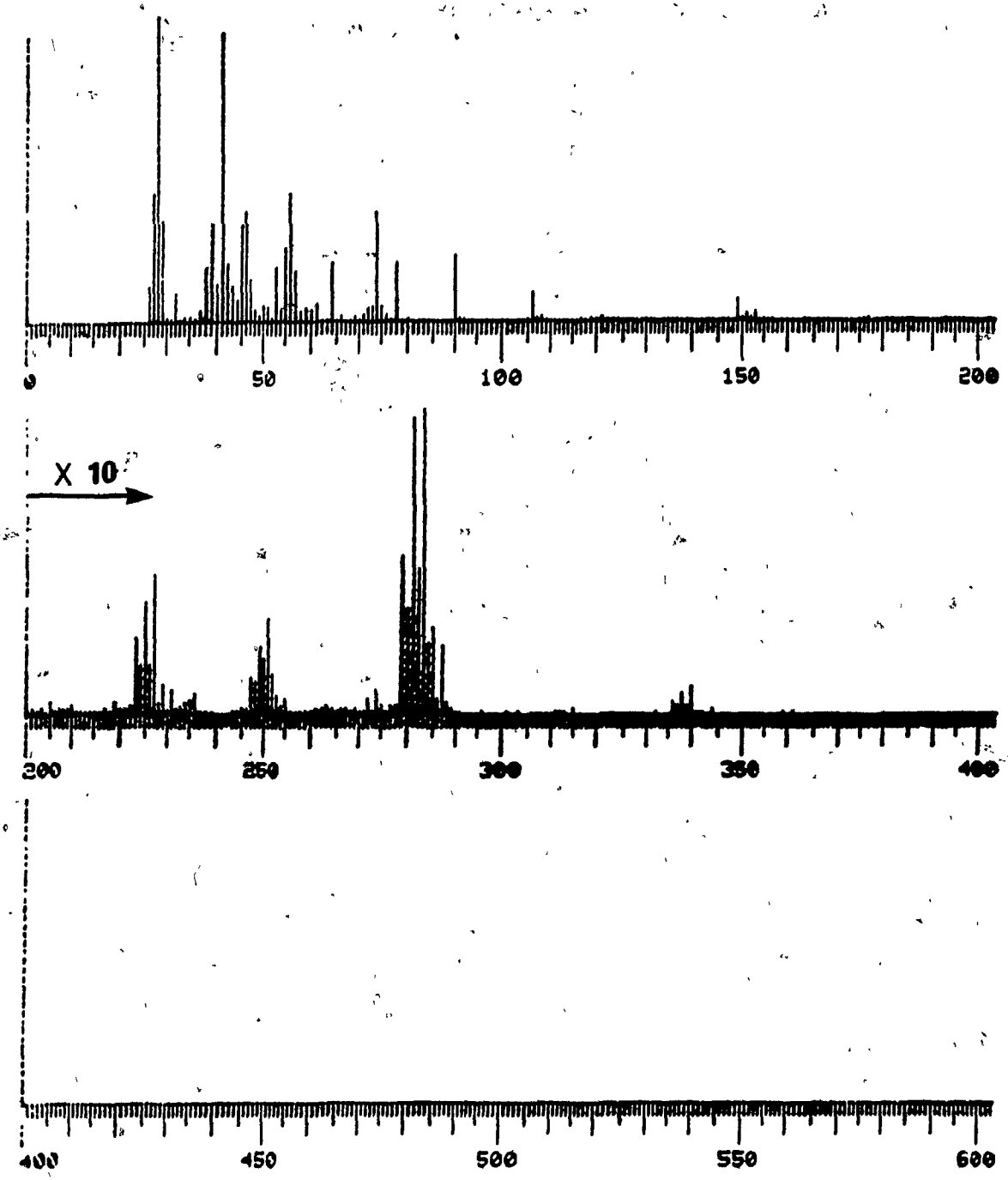
2,2-di-n-Butyl-1,3,2-Dithiastannacycloheptane (**110b**)

Opaque thick liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 6H); 1.15-1.75 (br, 12H); 1.77-2.03 (br, 4H); 2.73 (t, 4H). ^{119}Sn-NMR : 129.5 ppm. IR ($CHCl_3$ soln) : 2980, 2940, 2890, 2860, 1470, 1380 (alkyl), 1230, 1190, 1065, 725, 640 (S-C). Raman (neat) : 652 (S-C), 592, 508 (Sn-C), 346 (Sn-S), 244. MS (EI, 70eV, 40°C) m/z : 354 (1), 352 (1) [M^+]; 297 (59), 295 (40) [M^+ - n-Bu·]; 241 (7), 239 (6) [M^+ - n-Bu· - C_4H_8]; 57 (35); 56 (77); 55 (85); 41 (86); 39 (53); 29 (52); 28 (100).

2,2-di-n-Butyl-1,3,2-Dithiastannacyclooctane (**110c**)

Opaque, very viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 6H); 1.13-1.87 (br, 18H); 2.67 (t, 4H). ^{119}Sn-NMR : 127.4 ppm. IR ($CHCl_3$ soln) : 2960, 2940, 2860, 2855, 1450, 1370 (alkyl), 1225, 1170, 1070, 730, 670 (S-C). Raman (neat) : 721, 646 (S-C), 592, 508 (Sn-C), 343 (Sn-S), 244. MS (EI, 70eV, 60°C) m/z : 368 (1), 366 (<1) [M^+]; 311 (55), 309 (57) [M^+ - n-Bu·]; 255 (1), 253 (1) [M^+ - n-Bu· - C_4H_8]; 69 (78); 57 (30); 56 (68); 55 (49); 41 (86); 39 (69); 29 (43); 28 (100).

Figure 11. Mass Spectrum of 2,2-di-n-Butyl-1,3,2-Dithiastannacyclohexane (**110a**).



60°C, scan over M^+ for 0.20 M) m/z : 475 (<1), 473 (<1), 471 (<1) [n-$Bu_3Sn_2S_2^+$].

2,2-di-n-Butyl-1,3,2-Dithiastannacyclononane (**110d**)

Opaque, very viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 6H); 1.17-1.87 (br, 20H); 2.70 (t, 4H). ^{119}Sn-NMR : 127.8 ppm. IR ($CHCl_3$ soln) : 2960, 2940, 2880, 2860, 1460, 1380 (alkyl), 1225, 1180, 1075, 675 (S-C). Raman (neat) : 652 (S-C), 592, 508 (Sn-C), 343 (Sn-S), 223. MS (EI, 70eV, 75°C) m/z : 325 (38), 323 (32) [M^+ - n-Bu·]; 269 (20), 267 (24) [M^+ - n-Bu· - C_4H_8]; 83 (26); 69 (22); 57 (100); 56 (47); 55 (75); 41 (65); 39 (35); 29 (46); 28 (68).

2,2-di-n-Butyl-1,3,2-Dithiastannacyclodecane (**110e**)

Opaque, very viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 4H); 1.10-1.77 (br, 22H); 2.63 (t, 4H). ^{119}Sn-NMR : 127.5 ppm. IR ($CHCl_3$ soln) : 2980, 2940, 2880, 2860, 1470, 1380 (alkyl), 1210, 1080, 1060, 725, 665 (S-C). Raman (neat) : 722, 647 (S-C), 593, 506 (Sn-C), 341 (Sn-S). MS (EI, 70eV, 80°C) m/z : 475 (1), 473 (2), 471 (1) [n-$Bu_3Sn_2S_2^+$]; 339 (71), 337 (47) [M^+ - n-Bu·]; 283 (36), 281 (35) [M^+ - n-Bu· - C_4H_8]; 97 (55); 69 (23); 57 (52); 56 (77); 55 (100); 41 (91); 39 (72); 29 (44); 28 (81). MS (EI, 70eV, 70°C, scan over M^+ for 0.20 M) m/z : 475 (4), 473 (5), 471 (3) [see above].

2,2-di-n-Butyl-1,3,2-Dithiastannacycloundecane (**110f**)

Opaque, highly viscous oil; ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 6H); 1.10-1.75 (br, 24H); 2.70 (t, 4H). ^{119}Sn-NMR : 127.4 ppm. IR ($CHCl_3$ soln) : 2970, 2940, 2880, 2865, 1460, 1380 (alkyl), 1210,

1180, 1070, 750, 670 (S-C). Raman (neat) : 715, 647 (S-C), 592, 505 (Sn-C), 340 (Sn-S), 220. MS (EI, 70eV, 100°C) m/z : 353 (75), 351 (64) [M^+ - n-Bu·]; 297 (26), 295 (32) [M^+ - n-Bu· - C_4H_8]; 69 (69); 57 (35); 56 (61); 55 (98); 41 (90); 39 (44); 29 (61); 28 (100). MS (EI, 70 eV, 115°C, scan over M^+ for 0.20 M) m/z : 475 (1), 473 (2), 471 (1) [see above]; 419 (<1), 417 (<1), 415 (<1) [475-471 - C_4H_8].

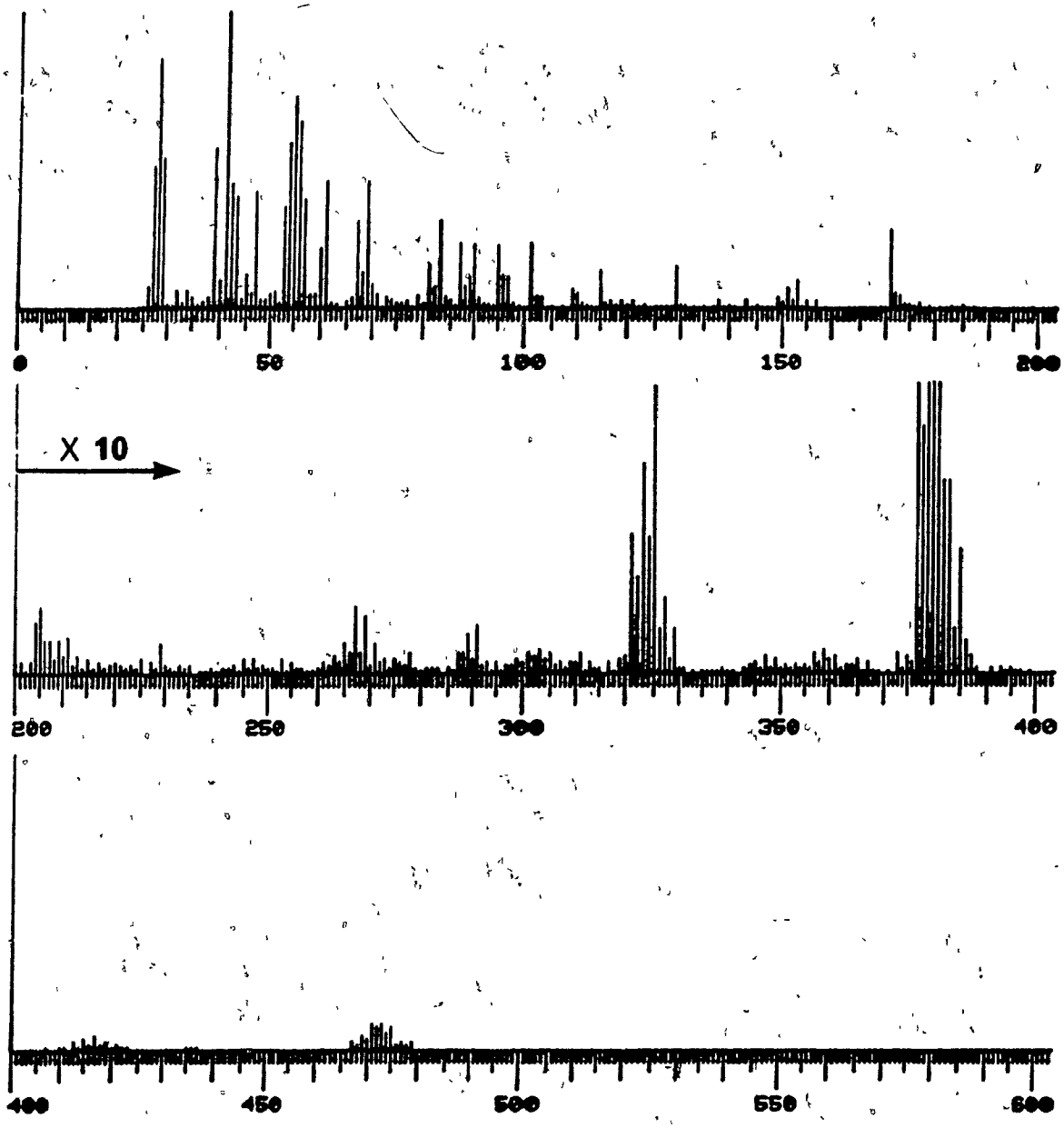
2,2-di-n-Butyl-1,3,2-Dithiastannacyclododecane (**110g**)

Opaque, highly viscous oil; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 6H); 1.13-1.77 (br, 26H); 2.63 (t, 4H). ^{119}Sn-NMR : 128.0 ppm. IR ($CHCl_3$ soln) : 2980, 2950, 2880, 2860, 1470, 1380 (alkyl), 1190, 1080, 1060, 660 (S-C). Raman (neat) : 704, 647 (S-C), 593, 506 (Sn-C), 341 (Sn-S) . MS (EI, 70eV, 130°C) m/z : 367 (43), 365 (35) [M^+ - n-Bu·]; 311 (24), 309 (11) [M^+ - n-Bu· - C_4H_8]; 83 (39); 69 (44); 57 (34); 56 (53); 55 (67); 43 (78); 41 (100); 39 (54); 29 (37); 28 (62). MS (EI, 70eV, 125°C, scan over M^+ for 0.20 M) m/z : 475 (3), 473 (3), 471 (2) [see above].

2,2-di-n-Butyl-1,3,2-Dithiastannacyclotridecane (**110h**)

Opaque, highly viscous oil; ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 6H); 1.13-1.75 (br, 28H); 2.70 (t, 4H). ^{119}Sn-NMR : 127.8 ppm. IR ($CHCl_3$ soln) : 2980, 2960, 2880, 2865, 1470, 1380 (alkyl), 1190, 1070, 650 (S-C). Raman (neat) : 703, 650 (S-C), 595, 506 (Sn-C), 340 (Sn-S), 220. MS (EI, 70eV, 130°C) m/z : 475 (1), 473 (1), 471 (1) [see above]; 381 (37), 379 (31) [M^+ - n-Bu·]; 325 (10), 323 (7) [M^+ - n-Bu· - C_4H_8]; 83 (34), 69 (44), 57 (38), 56 (64); 55 (72), 43 (39), 41 (100), 39 (55), 29 (52); 28 (85), (Figure 12). MS (EI, 70eV, 130°C, scan over M^+ for 0.20 M) m/z : 475 (2), 473 (3), 471 (2) [see above]; 419 (1), 417 (1), 415 (1).

Figure 12. Mass Spectrum of 2,2-di-n-Butyl-1,3,2-Dithiastannacyclotridecane (110h).



Preparation of Cyclic Disulfides (73)

Method A: To 5.0 mmol of ditin compounds (**109**) in 100 ml of CH_2Cl_2 (0.05 M) at 0°C was added at 2 ml/min an equimolar amount of 0.20 M Br_2 in CH_2Cl_2. This solution was allowed to stir for 5 min. The solution was washed with 5% sodium thiosulfate, dried ($MgSO_4$) and evaporated in vacuo. The resultant mixture was placed on aluminum oxide (ca. 40 g of alumina per 1 g of impure mixture) to afford the monomeric disulfide.

Method B: The procedures and work-up conditions of method A were applied with a single change, that being the oxidant which was 0.20 M I_2 in CH_2Cl_2.

Method C: To 10.0 mmol of monotin compounds (**110**) previously prepared in either 0.05 M or 0.20 M solutions) in 100 ml of CH_2Cl_2 (0.10 M) at 0°C was added at 2 ml/min an equimolar amount of 0.20 M Br_2 in CH_2Cl_2. This solution was allowed to stir for 5 minutes. The solution was washed with 5% sodium thiosulfate, dried ($MgSO_4$) and evaporated in vacuo. The mixture was placed on aluminum oxide (ca. 40 g of alumina per 1 g of impure mixture) to yield the monomeric disulfide.

Method D: The procedures (for compounds **110** previously prepared in either 0.05 M or 0.20 M solutions) and work-up conditions of method C were applied with a single change, that being the oxidant which was 0.20 M I_2 in CH_2Cl_2.

The yields and gas chromatography retention times of the cyclic disulfides are summarized in Table 23 below following the physical data for each in the series.

1,2-Dithiolane (23)

This cyclic disulfide polymerized during isolation. The proton NMR spectrum was attained by oxidizing 2,2-di-n-butyl-1,3,2-dithiastannacyclohexane (**109a**) with I_2 in $CDCl_3$ on small scale (0.214 g in 1ml $CDCl_3$, 0.6 M). 1,2-Dithiolane appeared as a yellow solution in CH_2Cl_2, $CDCl_3$ and hexane; UV (CH_2Cl_2) λ_{max} : 331 nm. ^{1}H-NMR ($CDCl_3$) δ : 2.05 (m, 2H); 2.95 (br t, 4H).

1,2-Dithiane (74)

White solid; m.p. 30-31°C (lit.[71,74] 29°, 31-31.5°). UV (CH_2Cl_2) λ_{max} : 290 nm. ^{1}H-NMR ($CDCl_3$) δ : 2.00 (br, 4H); 2.83 (br, 4H). Raman (neat) : 659 (S-C), 509 (S-S), 362, 293. MS (EI, 70eV, 40°C) m/z : 120 (78) [M^+]; 88 (99) [M^+ - S]; 87 (32) [M^+ - SH·]; 73 (9) [M^+ - CH_2SH·]; 55 (100) [$C_4H_7^+$]; 45 (76) [CHS^+]; 41 (34) [$C_3H_5^+$].

1,2-Dithiepane (75)

Clear liquid; b.p. 47°C/1.0 mm, n_D^{25} 1.5681 (lit.[74,78] 55-60°/1.7 mm, n_D^{25} 1.569, 1.570). Density : 1.14765 g/ml. UV (CH_2Cl_2) λ_{max} : 262 nm. ^{1}H-NMR ($CDCl_3$) δ : 1.97 (m, 6H); 2.83 (t, 4H). Raman (neat) : 638 (S-C), 515 (S-S), 461, 344, 275. MS (EI, 70eV, 40°C) m/z : 134 (82) [M^+]; 102 (41) [M^+ - S]; 101 (34) [M^+ - SH·]; 87 (45) [M^+ - CH_2SH·]; 69 (100) [$C_5H_9^+$]; 55 (26) [see above]; 45 (31) [see above]; 41 (72) [see above].

1,2-Dithiacyclooctane (76)

Clear liquid; n_D^{25} 1.567 (lit.[74] n_D^{25} 1.5698). ^{1}H-NMR ($CDCl_3$) δ : 1.47-1.87 (br, 8H); 2.73 (t, 4H). Raman (neat) : 701, 635 (S-C), 509

(S-S), 440, 347, 284. MS (EI, 70eV, 50°C) m/z : 148 (65) [M^+]; 116 (23) [M^+ - S]; 115 (79) [M^+ - SH·]; 101 (16) [M^+ - CH_2SH·]; 83 (78) [$C_6H_{11}^+$]; 69 (54) [see above]; 55 (100) [see above]; 45 (28) [see above]; 41 (71) [see above].

1,2-Dithiacyclononane (**77**)

Clear liquid; n_D^{25} 1.5627 (lit.[74,76] n_D^{25} 1.5642, 1.5623). ^{1}H-NMR ($CDCl_3$) δ : 1.27-1.87 (br, 10H); 2.67 (t, 4H). Raman (neat) : 702, 633 (S-C), 506, 440, 347, 281. MS (EI, 70eV, 120°C) m/z : 162 (31) [M^+]; 130 (10) [M^+ - S]; 129 (77) [M^+ - SH·]; 115 (32) [M^+ - CH_2SH·]; 101 (17) [M^+ - C_2H_4SH·]; 87 (71) [M^+ - C_3H_6SH·]; 81 (11) [$C_6H_9^+$]; 73 (10) [M^+ - C_4H_8SH·]; 69 (15) [see above]; 67 (18) [$C_5H_7^+$]; 55 (100) [see above]; 45 (16) [see above]; 41 (54) [see above].

1,2-Dithiacyclodecane (**78**)

Slightly yellow liquid; n_D^{25} 1.5407 (lit.[74] n_D^{25} 1.5461). ^{1}H-NMR ($CDCl_3$) δ : 1.23-1.93 (br, 12H); 2.70 (t, 4H). Raman (neat) : 704, 635 (S-C), 506 (S-S), 440, 347, 278. MS (EI, 70eV, 80°C) m/z : 176 (66) [M^+]; 144 (21) [M^+ - S]; 143 (56) [M^+ - SH·]; 115 (36) [M^+ - C_2H_4SH·]; 101 (62) [M^+ - C_3H_6SH·]; 87 (57) [M^+ - C_3H_6SH·]; 87 (57) [M^+ - C_4H_8SH·]; 81 (40) [see above]; 69 (65) [see above]; 67 (84) [see above]; 55 (100) [see above]; 45 (26) [see above]; 41 (64) [see above].

1,2-dithiacycloundecane (**79**)

White crystals; m.p. 31-34°C. ^{1}H-NMR ($CDCl_3$) δ : 1.23-1.48 (br, 10H); 1.50-1.90 (m, 4H); 2.71 (t, 4H). Raman (neat) : 701, 635 (S-C), 506 (S-S), 440, 344, 248. MS (EI, 70eV, 225°C) m/z : 380 (100) [M^+ of

Table 23. Isolated Yields (%) of Cyclic Disulfides Prepared by Halogen Oxidation of the Respective μ-α,ω-Alkyldithiohexa-n-Butylditin(IV) species (109) and 2,2-di-n-Butyl-1,3,2-Dithiastannacycloalkanes (110).

Disulfide	Ring Size	% Yield from 109		% Yield from 110 0.05 M ▲		% Yield from 110 0.20 M ▲	
		Br_2	I_2	Br_2	I_2	Br_2	I_2
1,2-Dithiolane (23)	5	88	92	97	97	91	93
1,2-Dithiane (74)	6	95	96	96	96	95	96
1,2-Dithiepane (75)	7	76	74	80	77	53	49
1,2-Dithiacyclooctane (76)	8	36	37	22	26	16	16
1,2-Dithiacyclononane (77)	9	39	42	36	31	18	14
1,2-Dithiacyclodecane (78)	10	59	61	45	49	20	21
1,2-Dithiacycloundecane (79)	11	(34)*	(38)*	(47)*	(40)*	(34)*	(38)*
1,2-Dithiacyclododecane (80)	12	1.5 (59)*	(61)*	(44)*	(43)*	(39)*	(37)*

▲ 2,2-di-n-Butyl-1,3,2-Dithiastannacycloalkanes (110) Prepared in Benzene Solutions of this Concentration,

* Compounds Isolated as Dimers.

dimer]; 222 (7) [$C_9H_{18}S_3^+$]; 190 (5) [M^+ of monomer or $\frac{1}{2}M^+$ of dimer]; 189 (11) [M^+ of dimer - $C_9H_{19}\cdot$]; 101 (6) [$C_5H_9S^+$]; 87 (12) [$C_4H_8SH^+$]; 83 (3) [see above]; 69 (8) [see above]; 67 (4) [see above]; 55 (18) [see above]; 45 (3) [see above]; 41 (15) [see above]. Molecular weight determination calculated for dimer $C_{18}H_{36}S_4$: 380.7; found: 398.

1,2-Dithiacyclododecane (**80**)

White crystals; m.p. 37-39°C. ^{1}H-NMR ($CDCl_3$) δ : 1.23-1.50 (br, 12H); 1.50-1.93 (m, 4H); 2.72 (t, 4H). Raman (neat) : 701, 638 (S-C), 509 (S-S), 344, 260. MS (EI, 70eV, 280°C) m/z : 408 (6) [M^+ of dimer]; 236 (2) [$C_{10}H_{20}S_3^+$]; 204 (12) [M^+ of monomer or $\frac{1}{2}M^+$ of dimer]; 171 (3) [$C_{10}H_{19}S^+$]; 115 (11) [$C_6H_{11}S^+$]; 101 (27) [see above]; 87 (38) [see above]; 83 (31) [see above]; 81 (63) [see above]; 69 (30) [see above]; 67 (77) [see above]; 55 (80) [see above]; 41 (100) [see above]. Molecular weight determination calculated for dimer $C_{20}H_{40}S_4$: 408.8; found : 418. Anal. calculated for $(C_{10}H_{20}S_2)_n$: C, 58.77; H, 9.86; S, 31.37. Found : C, 58.81; H, 9.74; S, 31.58.

Relative Yields of Cyclic Disulfides (**73**) Prepared with Thiotins Versus Prepared Without Thiotins

A standard solution of distilled CH_2Cl_2 and 2% v/v of 2,5-dimethyl thiophene was prepared and stored in a well stoppered bottle. All oxidations were done using this CH_2Cl_2 mixture, with the dimethyl thiophene serving as an internal standard for GC analyses.

To 0.05 M solutions of μ-α,ω-alkyldithiohexa-n-butylditin (IV) species (**109**) in the CH_2Cl_2 mixture was added 1 equivalent of 0.2 M bromine in CH_2Cl_2 at 2 ml/min. The reaction was done in subdued

lighting at 0°C. Once the addition of bromine was complete, 1 μl of the solution was injected in the GC (80-225°C at 20° per min on a 10 m 3% Silicone OV-101 capillary column).

The cyclic disulfides were prepared without the use of thiotin (IV) compounds as follows: to 0.05 M solutions of the respective dithiols in the CH_2Cl_2 dimethyl thiophene mixture with 2 equivalents of triethylamine was added 1 equivalent of bromine. Addition times, temperature and concentrations of reactants were similar to those already described. The reaction mixture was analysed by GC as above.

Each of the above mentioned reactions were repeated and analysed by GC. The average respective relative yields, as determined by using 2,5-dimethyl-thiophene as internal standard (retention time = 0.69-0.70 min for the conditions described), are presented thus; disulfide, relative yields: with tin / without tin., 1,2-dithiolane (**23**) : 1.8/1. 1,2-dithiane (**74**) : 1.1/1. 1,2-dithiepane (**75**) : 2.7/1. 1,2-dithiacyclooctane (**76**) : 12/1. 1,2-dithiacyclononane (**77**) : 10/1. 1,2-dithiacyclodecane (**78**) : 11/1. 1,2-dithiacycloundecane (**79**) : 8/1. 1,2-dithiacyclododecane (**80**) : 6.5/1.

Preparation of 1,2-Dithiacyclononane (77) in Various Solution Concentrations

The synthesis of the 9 membered ring disulfide (**77**) was repeated over a series of concentrations (0.50M, 0.10M, 0.05M, 0.01M and 0.005M) using two sets of conditions; these conditions being as before, with tin and without tin. The procedures were much the same as those already described, thus only a brief sketch is given. Dichloromethane solutions of corresponding concentrations of 1,7-heptanedithiol with 1.2

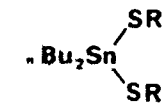
equivalents of triethylamine were oxidized with 1 equivalent of bromine. Concomitantly, similar concentrations of μ-1,7-heptyldithiohexa-n-butylditin(IV) (**109e**) were also oxidized with 1 equivalent of bromine. All ten solutions contained an equal concentration of 2,5-dimethylthiophene which was used as an internal standard for GC analyses. Deduced yields were obtained by comparing the relative GC intensity of the disulfide and the internal standard to those of disulfides that were actually isolated, these were: 0.05 M with tin, 0.005 M with tin, 0.005 without tin. The yields of (**77**) prepared with tin were: 0.50 M, 7 %; 0.10 M, 21 %; 0.05 M, 42 %; 0.01 M, 63 %; 0.005 M, 66 %. The yields of (**77**) prepared without the use of tin were: 0.50 M, no yield; 0.10 M, no yield; 0.05 M, 4 %; 0.01 M, 8 %; 0.005 M, 9 %.

Tricyclohexyl t-Butylthiotin(IV) (**142**)

Preparation of this compound was performed in a similar fashion as the synthesis of the tri-n-butyl alkylthiotins (**96**) except that tricyclohexyltin chloride was used instead of tri-n-butyltin chloride (**97**). Tricyclohexyl t-butylthiotin(IV) (**142**) was obtained as fluffy, white crystals after recrystallization in EtOH in 93% yield; mp 199-200°C. ^{1}H-NMR ($CDCl_3$) δ : 1.43 (s, 9H); 1.17-2.02 (br, 33H). ^{119}Sn-NMR : 148.7 ppm. Raman (neat) : 649 (S-C), 589, 490 (Sn-C), 424, 352, 322 (Sn-S), 193. MS (EI, 70eV, 65°C) m/z : 375 (4), 373 (3) [$M^+ - C_6H_{11}\cdot$]; 369 (1), 367 (1) [$M^+ - C_4H_8S\cdot$]; 345 (39), 343 (36); 319 (32), 317 (14) [cyclohexyl$_2$SnSH$^+$]; 293 (16), 291 (7) [$C_6H_{11}SnHSBu^+$]; 205 (18), 203 (30), 201 (28) [$C_6H_{11}SnH_2^+$ and $C_6H_{11}Sn^+$]; 181 (27), 179 (38), 177 (28), 175 (23) [$C_2H_5SnS^+$, $C_4H_9SnH_2^+$ and $C_4H_9Sn^+$]; 155 (17), 153 (8) [H_2SnS^+]; 121 (24), 119 (23)

[SnH^+]; 83 (53); 81 (27); 67 (30); 57 (21); 55 (48); 45 (26) [CHS^+]; 41 (60); 39 (32); 29 (23); 28 (100). Anal. Calculated for $C_{22}H_{42}SSn$: C, 57.78; H, 9.27; S, 7.01. Found : C, 57.69; H, 9.28; S, 7.02.

Di-n-Butyl di-n-Butylthiotin(IV) (**100a**) and di-n-Butyl Dibenzylthiotin(IV) (**100b**)

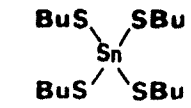
To a 250 ml round bottom flask equipped with a Dean-Stark reflux apparatus and condenser containing 

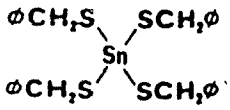
8.08 g (32.5 mmol) of di-n-butyltin oxide (**111**) and ca. 5 mg of p-toluenesulfonic acid in 150 ml of benzene was added 5.85 g (65 mmol) of distilled n-butanethiol. The reaction was refluxed while stirring for 4 h. The solvent was evaporated and the product was placed under vacuum overnight (0.1 to 0.4 mm) to afford 12.85 g (96% yield) of a thick, opaque and yellowish liquid. The product (**100a**) was used without further purification. ^{1}H-NMR ($CDCl_3$) δ : 0.92 (br t, 12H); 1.20-1.85 (br, 20H); 2.70 (t, 4H). ^{119}Sn-NMR : 127.0 ppm. Raman (neat) : 652 (S-C), 598, 511 (Sn-C), 346 (Sn-S), 241, 211. MS (EI, 70eV, 40°C) m/z : 475 (3), 473 (4), 471 (3) [n-$Bu_3Sn_2S_2^+$]; 355 (82), 353 (60) [M^+ - n-Bu·]; 323 (21), 321 (18) [M^+ - n-BuS·]; 299 (37), 297 (25) [M^+ - n-Bu· - C_4H_8]; 267 (8), 265 (7) [n-Bu_2SnSH^+ and n-BuSn(H)SBu^+]; 211 (23), 209 (41), 207 (48) [n-$BuSnH_2S^+$ and n-$BuSnS^+$]; 179 (4), 177 (7), 175 (5) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (20), 153 (40), 151 (59) [H_2SnSH^+ and $SnSH^+$]; 121 (7), 119 (5) [SnH^+]; 57 (70); 56 (58); 55 (38); 41 (77); 39 (35); 29 (57); 28 (100).

di-n-Butyl dibenzylthiotin(IV) (**100b**), prepared in a similar fashion, was a very viscous, clear and yellow liquid; it too was used without further purification. The yield of the crude compound was 98%.

^{1}H-NMR ($CDCl_3$) δ : 0.87 (t, 6H); 1.07-1.60 (br, 12H); 3.90 (s, 4H); 7.27 (br, 10H). ^{119}Sn-NMR : 125.6 ppm. Raman (neat) : 652 (S-C), 598, 511 (Sn-C), 337 (Sn-S), 244. MS (EI, 70eV, 55°C) m/z : 475 (2), 473 (3), 471 (2) [n-$Bu_3Sn_2S_2^+$]; 423 (2), 421 (1) [M^+ - n-Bu·]; 357 (2), 355 (1) [n-$Bu_2SnSC_7H_7^+$]; 267 (3), 265 (2) [n-Bu_2SnSH^+]; 211 (1), 209 (1) [n-$BuSnH_2S^+$]; 179 (1), 177 (2), 175 (1) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (2), 153 (3), 151 (2) [H_2SnSH^+ and $SnSH^+$]; 123 (10), 121 (8) [SnH_3^+]; 91 (100) [$C_7H_7^+$]; 65 (17); 57 (12); 56 (10); 45 (17); 41 (15); 39 (16); 29 (8); 28 (24).

Tetra-n-Butylthiotin(IV) (**103a**) and Tetrabenzylthiotin(IV) (**103b**)





To 2.37 g (26.3 mmol) of distilled n-butanethiol and 4 ml (28.7 mmol) of fresh triethylamine in 150 ml of CCl_4 was added dropwise 0.75 ml (6.5 mmol, slightly less than 1/4 equivalent) of $SnCl_4$. The reaction was allowed to stir for 3 h. The triethylamine hydrochloride salt was collected, the filtrate washed with 5% acetic acid, dried ($MgSO_4$), the solvent evaporated in vacuo and the product was placed under vacuum (0.1 to 0.4 mm) overnight. Tetra-n-butylthiotin(IV) (**103a**) was obtained as a yellow and very thick liquid, 2.84 g (91% yield); ^{1}H-NMR ($CDCl_3$) δ : 0.90 (br t, 12H); 1.10-1.80 (br, 16H); 2.77 (t, 8H). ^{119}Sn-NMR (215 mg or 0.05 M in $CDCl_3$) : 130.5 ppm. Raman (neat) : 643 (S-C), 355, 346 (Sn-S). MS (EI, 70ev, 90°C) m/z : 476 (2), 474 (1) [M^+]; 387 (3), 385 (3) [M^+ - n-BuS·]; 297 (3), 295 (3) [M^+ - n-BuS· - C_4H_8]; 178 (23) [$(C_4H_9S)_2^+$]; 122 (28) [178 - C_4H_8]; 90 (47) [n-$BuSH^+$]; 56 (80); 41 (100); 37 (44); 29 (33).

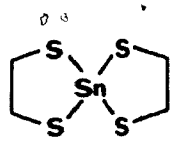
Tetrabenzylthiotin(IV) (**103b**) was similarly acquired in 88% yield

as a yellowish and highly viscous liquid; ^{1}H-NMR ($CDCl_3$) δ : 3.87 (s, 8H); 7.10-7.35 (br, 20H). ^{119}Sn-NMR (130 mg or 0.03 M in $CDCl_3$) : 139.2 ppm. Raman (neat) : 685 (S-C), 349, 340 (Sn-S). MS (EI, 70ev, 75°C) m/z : 612 (2), 610 (1) [M^{+}]; 489 (3), 487 (2) [M^{+} - $C_7H_7S\cdot$]; 246 (4) [$(C_7H_7S)_2^{+}$]; 124 (11) [$C_7H_7SH^{+}$]; 91 (100); 65 (30); 51 (21).

Di-n-Butyl Disulfide (**6b**) and Dibenzyl Disulfide (**6a**) from their Respective Di and Tetrathiotin(IV) Compounds

The disulfides were prepared by oxidizing dichloromethane solutions of the appropriate tin compounds with concentrated solutions of Br_2 in CH_2Cl_2. The reactions and workup procedures were carried out in a similar way to that which was described earlier for the synthesis of symmetrical disulfides from tri-n-butyl alkylthiotin(IV) derivatives, thus only a brief outline is given. di-n-Butyl disulfide was prepared by the addition of 1 equivalent of Br_2 to di-n-butyl di-n-butylthiotin(IV) (**100a**) or 2 equivalents of Br_2 to tetra-n-butylthiotin(IV) (**103a**), the yields of the disulfide were 94% and 80% respectively. Dibenzyl disulfide was obtained in 96% yield from di-n-butyl dibenzylthiotin(IV) (**100b**) and in 74% yield from tetrabenzylthiotin(IV) (**103b**).

1,4,6,9-Tetrathia-5-Stannaspiro[4,4]nonane (**146**)



To 1 ml (16.5 mmol) of distilled 1,2-ethanedithiol and 4.8 ml (34.4 mmol) of triethylamine in 100 ml of CCl_4 was added dropwise 0.95 ml (8.1 mmol, slightly less than 1/2 equivalent) of tin tetrachloride (**99**). The reaction was allowed to stir overnight then the mixture was filtered, the filtrate washed with 5% acetic acid and the solvent removed in vacuo to afford a white solid.

This solid was recrystallized in CH_2Cl_2; the mother liquor was collected and concentrated, the resultant solid was also recrystallized. The combined yield was 0.74 g (30%) of white needles; mp 184-185°C (lit.[118, 223] 180°, 182-183°). ^{1}H-NMR ($CDCl_3$) δ : 3.20 (s). ^{119}Sn-NMR (310 mg or 0.08 M in $CDCl_3$) : 279.2 ppm. Raman (neat) : 727, 691, 649 (S-C), 334 (Sn-S), 241, 196. MS (EI, 70eV, 145°C) m/z : 304 (63), 302 (40) [M^+]; 212 (47), 211 (29), 210 (31), 209 (18) [$C_2H_4S_2Sn^+$ and $C_2H_3S_2Sn^+$]; 184 (58), 182 (44) [S_2Sn^+]; 153 (17), 151 (31) [$SnSH^+$]; 92 (100) [$C_2H_4S_2$]; 64 (36) [S_2^+]; 60 (54) [$C_2H_4S^+$]; 59 (44) [$C_2H_3S^+$]; 45 (40) [CHS^+]; no evidence of dimer; no evidence of S_8.

Kinetic Studies

The uptake of the violet iodine color (λ_{max} 520) as it was added to tri-n-butyl phenylthiotin(IV) (**96g**) was monitored with a stopped-flow apparatus. The iodine solution was 1.57×10^{-4} M in CH_2Cl_2; the thiotin reagent concentration was 1.50×10^{-3} M in CH_2Cl_2. The procedure was carried out at ambient temperature, 22°C. The reaction was too fast for the stopped-flow apparatus; scans were taken every 0.005 s.

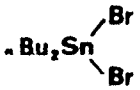
A similar experiment to the one described above was carried out with 1.57×10^{-4} M I_2 in isooctane and 1.15×10^{-3} M tricyclohexyl t-butylthiotin(IV) (**142**) also in isooctane. The temperature was ca. 22°C and the instrument scanned every 0.005 s. Once again the reaction was too fast to be measured by the stopped-flow.

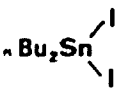
The production of 1,2-dithiolane (**23**) [UV, λ_{max} 330 nm] via the iodine oxidation of μ-1,3-propyldithiohexa-n-butylditin(IV) (**109a**) was observed with a Diode Array Spectrophotometer. The dithioditin reagent in isooctane was added to a cuvette and placed into the spectrophoto-

meter. A known amount of iodine in isooctane was then added directly into the tin-sulfur solution with Pasteur pipette; in this fashion mixing was immediate. The total time for addition of the iodine and the start of acquisitions was ca. 1 s. The final concentration of μ-1,3-propyldithiohexa-n-butylditin(IV) (**109a**) was 2.42×10^{-5} M, the final concentration of the iodine 3.33×10^{-6} M. The spectra were taken at 21°C. The full intensity of the peak at 330 nm was seen immediately. The experiment was repeated with the temperature at -20°C; once again the full amount of 1,2-dithiolane (**23**) showed immediately.

^{119}Sn-NMR of di-n-Butyltin Dibromide (**143**) and di-n-Butyltin Diiodide (**144**)

To 250 mg of di-n-butyl di-n-butylthiotin(IV) (**100a**) in 20 ml of $CCl_4/CDCl_3$ was added dropwise Br_2/CCl_4 until the red-brown bromine color persisted. To this solution was then added just enough of (**100a**) so as to get a clearing of the red-brown color. The addition of bromine was highly exothermic and care was required to prevent frothing. ^{119}Sn-NMR (131 mg or 0.03 M in $CDCl_3/CCl_4$) : 88.4 ppm.





di-n-Butyltin diiodide (**144**) was similarly prepared. The reaction was not as noticeably exothermic. ^{119}Sn-NMR (105 mg or 0.03 M in $CDCl_3/CCl_4$) : -54.6 ppm.

Three peaks were noted in the ^{119}Sn-NMR of the reaction of IBr to (**100a**), these were: 88.7 ppm, 22.1ppm, -57.7 ppm.

Each of these two compounds could be prepared in the same fashion using di-n-butyl dibenzylthiotin(IV) (**100b**).

Reaction of di-n-Butyl Dialkylthiotin(IV) with Br_2/I_2 or IBr

To di-n-butyl di-n-butylthiotin(IV) (**100a**) was added 3 different amounts of 1:1 molar Br_2/I_2 mixture in CH_2Cl_2. These amounts were : a) a total of 1 mole of oxidant per mole of (**100a**); b) a total of 1½ mole of total oxidant per mole of (**100a**); c) a small excess of 2 moles of total oxidant per mole of (**100a**). This experiment was repeated for all three sums with IBr dissolved in CH_2Cl_2. All six reactions were monitored by ^{119}Sn-NMR ($CDCl_3/CH_2Cl_2$), the results of which are given below in Table 24 (this is a duplicate of Table 16 in the discussion section).

Table 24. ^{119}Sn-NMR Data for the Reactions of di-n-Butyl Dialkylthiotin with Br_2/I_2 or IBr.

Oxidant	Total Amount of Oxidant		
	1 mole	1½ moles	XS of 2 moles
I_2/Br_2	88.5 ppm (27%)	88.4 ppm (50%)	86.4 ppm (100%)
	22.4 ppm (45%)	21.7 ppm (44%)	
	-56.7 ppm (28%)	-59.1 ppm (6%)	
IBr	89.6 ppm (25%)	88.0 ppm (43%)	88.9 ppm (100%)
	21.5 ppm (50%)	22.2 ppm (46%)	
	-58.4 ppm (25%)	-55.7 ppm (11%)	

Reaction of di-n-Butyltin Diiodide with di-n-Butyltin Dibromide

Di-n-butyltin diiodide (**144**) and di-n-butyltin dibromide (**143**) were each separately prepared by adding I_2 or Br_2 to two samples of 100 mg of di-n-butyl di-n-butylthiotin(IV) (**100a**) in 5 ml of $CDCl_3/CH_2Cl_2$. The two solutions were combined into a 10 mm NMR tube and a ^{119}Sn-NMR was taken; the acquisition took 90 min. ^{119}Sn-NMR ($CDCl_3/CH_2Cl_2$) : 88.3 ppm (26%); 23.4 ppm (51%); -57.0 ppm (23%).

Competition Reactions

tri-n-Butyl p-t-butylphenylthiotin(IV) (**96i**) [96% yield, ^{1}H-NMR ($CDCl_3$) δ : 0.87 (t, 9H); 1.00-1.87 (br, 27H); 7.23 (d of d, 4H); ^{119}Sn-NMR : 82.6 ppm], tri-n-butyl p-tolylthiotin(IV) (**96j**) [98% yield, ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.03-1.73 (br, 18H); 2.30 (s, 3H); 6.93-7.46 (d of d, 4H); ^{119}Sn-NMR : 79.7 ppm], tri-n-butyl p-fluorophenylthiotin(IV) (**96k**) [95% yield, ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.03-1.80 (br, 18H); 6.73-7.50 (br d of d, 4H); ^{119}Sn-NMR : 82.3 ppm], tri-n-butyl p-chlorophenylthiotin(IV) (**96l**) [98% yield, ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, 9H); 1.03-1.73 (br, 18H); 7.23 (d of d, 4H); ^{119}Sn-NMR : 80.7 ppm] and tri-n-butyl m-trifluoromethylphenylthiotin(IV) (**96m**) [96% yield, ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.07-1.83 (br, 18H); 7.13-7.73 (br, 4H); ^{119}Sn-NMR : 85.2 ppm] were all prepared from their respective distilled thiols and tri-n-butyltin chloride in a fashion that has been described (page 137). They, along with tri-n-butyl phenylthiotin(IV) (**96h**) were used in the competitive study. The relative GC sensitivities for the respective disulfides was determined by mixing equimolar amounts of all six arylthiotins, adding a slight excess of six equivalents of iodine and injecting this solution into the GC; it was assumed that the

yields of all disulfides would approach 100%. The GC retention times (80-225°C, 20°/min, 0.7 kg/cm^2, 10 m OV-101 capillary column) for the disulfides $(R\text{-}PhS)_2$, were : R = p-t-butyl, 10.49; R = p-methyl, 7.26; R = H, 6.52; R = p-fluoro, 6.00; R = p-chloro, 8.1; R = m-trifluoromethyl, 5.54. For clarity the arythiotins will herein be called A, B, C, D, E and F; the sequence following the sequence presented for the GC retention times of the disulfides.

The competition reactions were carried out by adding 1/2 equivalents of iodine, in CH_2Cl_2, to a vial containing 1 equivalent each of A and B in CH_2Cl_2; after quickly shaking the vial, the solution was injected into the GC. The process was repeated for a vial containing 1 equivalent each of A and C. This was also carried out for A and D, A and E, and A and F. The ratios of disulfide formed, B vs. A, C vs. A and so on was then determined. The log of these ratios was then plotted against σ; the ratio of A vs. A was taken to be 1.00, thus six points could be plotted. The entire procedure was repeated so as to be able to plot ratios against B, against C, D, E and F.

The ratios of disulfide formed were:

	A vs.	B vs.	C vs.	D vs.	E vs.	F vs.
A	1.00	.852	.787	.694	.670	.460
B	1.17	1.00	.903	.850	1.43	.560
C	1.27	1.11	1.00	.890	.939	.633
D	1.44	1.18	1.12	1.00	1.13	.780
E	1.49	.700	1.07	.890	1.00	.670
F	2.17	1.80	1.58	1.28	1.50	1.00

The determined values for ρ were: from plot vs. A, -0.53; vs. B, -0.48; vs. C, -0.45; vs. D, -0.37; vs. E, -0.40; vs. F, -0.45. The average value for ρ was -0.45.

Preparation of Sulfinyl Chlorides (**129**)

n-Butanesulfinyl chloride (**129b**) and benzenesulfinyl chloride (**129c**) were prepared in the fashion described by Douglass and Norton[194]; phenylmethanesulfinyl chloride (**129a**) was similarly prepared as follows: a mixture of 19.9 g (0.081 mol) of benzyl disulfide and 16.5 g (0.162 mol) of freshly distilled acetic anhydride was cooled to -10°C (dry ice in ethylene glycol) and chlorinated. The setup included two 1 l $Na_2S_2O_3$ solution traps to catch excess chlorine. Although the disulfide did not dissolve in the anhydride, chlorination converted it to the sulfinyl chloride and caused the mixture to liquify. With the addition of Cl_2 the mixture became orange and then cleared, before the solution was fully clear it began to turn greenish yellow indicating an excess of chlorine and addition of the gas was ceased. The solution was evaporated in vacuo (10 mm, 40°C) until boiling stopped to remove excess chlorine and acetyl chloride. The pale amber product (96%) was stable for several months when stored in the freezer; ^{1}H-NMR ($CDCl_3$) δ : 4.50 (s, 2H); 7.30 (s, 5H). IR ($CHCl_3$ soln) : 3100, 3080, 2970, 1500, 1460, 1380 (alkyl and aryl), 1150 (S-O), 910, 870, 690, 655 (S-C).

n-Butanesulfinyl chloride (**129b**) 91% yield, slightly yellow. ^{1}H-NMR ($CDCl_3$) δ : 1.00 (t, 3H); 1.27-2.17 (br, 4H); 3.47 (t, 2H). IR ($CHCl_3$ soln) : 2960, 2940, 2870, 1460, 1385 (alkyl), 1145 (S-O), 915, 700, 655 (S-C).

Benzenesulfinyl chloride (**129c**) 98% yield, amber. ^{1}H-NMR ($CDCl_3$) δ : 7.50-7.73 (br, 3H); 7.80-8.03 (br, 2H). IR ($CHCl_3$ soln) : 3080, 1580, 1445 (aryl), 1145 (S-O), 1180, 910, 865, 690, 650 (S-C).

Reaction of Sulfinyl Chlorides with tri-n-Butyltin Lithium

This reaction afforded the respective symmetrical thiosulfonates; the use of benzenesulfinyl chloride (**129c**) to prepare phenyl benzenethiosulfonate (**8c**) is presented. To 1.74 g (10.8 mmol) of benzenesulfinyl chloride (**129c**) in 10 ml of THF under nitrogen at ca. -78°C was added dropwise 5.5 ml of 1 M tri-n-butyltin lithium (**155**). The reaction warmed to -25° while stirring for 20 min. The solvent was evaporated in vacuo and the mixture was taken up in CH_2Cl_2 from which LiCl precipitated. After filtering the salt and evaporating the solvent the resultant oil was purified on 275 g of silica (hexanes/dichloromethane 3:1, using flash conditions) to yield 2.02g (75% yield) of phenyl benzenethiosulfonate (**8c**) as white crystals; mp 41-43°C (lit.[189,224] 42-43°, 45°). ^{1}H-NMR ($CDCl_3$) δ : 7.17-7.57 (br). ^{13}C-NMR ($CDCl_3$) ppm : 125.2, 127.5, 127.8, 128.8, 128.9, 129.4, 131.4, 133.7, 136.6, 142.9. IR ($CHCl_3$ soln) : 3090, 3030, 1520, 1440 (aryl), 1325 (SO_2), 1140 (SO_2), 1060, 775, 700, 660.

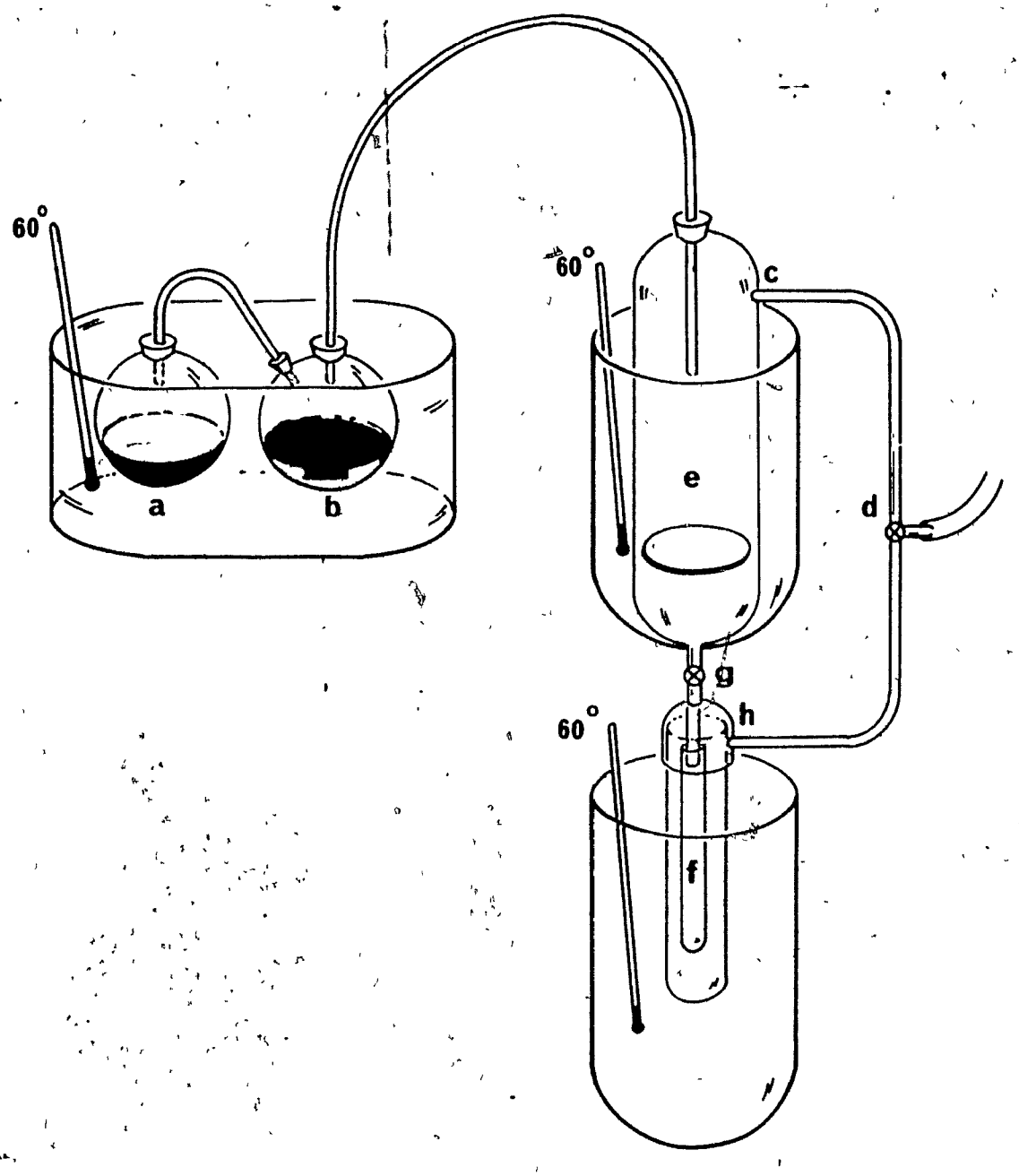
Benzyl phenylmethanethiosulfonate (**8a**) was obtained in 86% yield as white crystals; mp 102-104°C (lit.[225] 106°). ^{1}H-NMR ($CDCl_3$) δ : 4.01 (s, 2H); 4.27 (s, 2H); 7.17-7.53 (br, 10H). ^{13}C-NMR ($CDCl_3$) ppm : 41.0, 69.1, 127.4, 128.0, 128.8, 129.3, 129.5, 130.1, 130.6, 131.3, 134.4, 135.1. IR ($CHCl_3$ soln) : 3090, 2850, 1515, 1460 (alkyl and aryl), 1335 (SO_2), 1145 (SO_2), 1055, 760, 695, 650.

n-Butyl n-butanethiosulfonate (**8b**) was obtained as a clear liquid in 84% yield; ^{1}H-NMR ($CDCl_3$) δ: 0.97 (br t, 6H); 1.07-2.00 (br, 8H); 3.10 and 3.23 (pair of triplets, total 4H). ^{13}C-NMR ($CDCl_3$) ppm: 13.4, 13.5, 21.3, 21.7, 25.5, 31.6, 35.9, 62.4. IR ($CHCl_3$ soln) : 2960, 2930, 2870, 1450, 1380 (alkyl), 1335 (SO_2), 1145 (SO_2), 1040, 675.

Characterization of di-n-Butyl vic-Disulfoxide (**154**)

The apparatus depicted in Figure 13 on the next page was used to characterize di-n-butyl vic-disulfoxide (**154**). n-Butanesulfinyl chloride (**129b**), 0.715 g (5.1 mmol) in 3 ml of $CDCl_3$ (with ca. 1% TMS), was added to vessel A. To flask B was added 2.5 ml (2.7 mmol) of 1.08 M solution of tri-n-butyltin lithium (**155**) in THF. Both of these solutions were allowed to equilibrate to -60°C. The solution in flask A was then sucked into flask B by way of C with a vacuum which was controlled by a three-way stopcock D. The resultant mixture was stirred for 3-5 min before it was sucked (by way of C) into a cooled fritted funnel E. The filtrate was then collected into a cooled NMR tube F by opening stopcock G and adjusting stopcock D so as to apply suction at the adapter assembly H. Immediately after the filtration the NMR tube was then brought in a dewar to the NMR instrument; the spinning turbine and the NMR probe were previously cooled to -60°C. The reagents, fritted funnel and NMR tube were all cooled to ca. -60°C using $CHCl_3/CO_2$ slush baths. ^{13}C-NMR gave the following results which are reported in ppm: at -55°C; 59.1, 59.7, 60.5, 62.6 (br), 65.1 (br). At -40°C, 90 min after filtration; 62.9 (br). Increasing the temperature in 10-15° increments showed the presence of one narrow peak at ca. 62.9 ppm.

Figure 13. Apparatus used to Characterize di-n-Butyl vic-Disulfoxide (154).



Repeating the experiment gave similar results except that that in this run the peaks at 59.1 and 65.1 were of greater relative intensity whereas peaks 59.7 and 60.5 were of lesser relative intensity.

Attempts in obtaining ^{1}H-NMR data of this sort of experiment were unsuccessful due the presence of large resonances from the protons on THF. Similar difficulties were encountered with attempts to obtain either cold temperature ^{1}H-NMR or ^{13}C-NMR data using phenylmethanesulfinyl chloride (**129a**) and tri-n-butyltin lithium (**155**).

Benzyl n-Butanethiosulfonate and Benzyl Phenylmethanethiosulfonate

To a solution of 0.78 g (1.8 mmol) of tri-n-butyl benzylthiotin(IV) (**96a**) and 0.30 g (1.8 mmol) of n-butanesulfonyl chloride (**152b**) in 4 ml of $CHCl_3$ was added 2 equivalents of $TiCl_4$ (0.17 ml). The solution turned dark orange with the addition of the titanium tetrachloride. The reaction was allowed to stir for 15 min at room temperature. The solution was quenched by adding ca. 200 mg of sodium bicarbonate followed by a dropwise addition of distilled water. The water was added carefully so as to avoid excessive effervescence, about 1.5-2.0 ml of water was added. The mixture was filtered over celite, separated and washed once with distilled water before the solvent was removed in vacuo to afford an oil. The tri-n-butyltin derivative of the reaction was partially removed using the procedure of Leibner and Jacobus[226]; the oil which was taken up in 2-3 ml of diethyl ether and 4 ml of saturated KF, was allowed to stir for 10 min, fine white crystals of tri-n-butyltin fluoride precipitated and these were filtered. The filtrate was concentrated and placed on ca. 35 g of silica and eluted with hexanes/ dichlo-

romethane (3:1) to yield the pure thiosulfonate. Benzyl phenylmethanethiosulfonate was similarly prepared.

Benzyl n-butanethiosulfonate (**152**), 34 %. ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 3H); 1.10-2.00 (br, 4H); 3.27 (t, 2H); 3.97 (s, 2H); 7.20 (s, 5H). IR ($CHCl_3$ soln) : 3100, 2960, 2870, 1510, 1450, 1375 (alkyl and aryl), 1335 (SO_2), 1145 (SO_2), 1060, 755, 700, 660.

Benzyl phenylmethanethiosulfonate (**8c**), 39 %; white solid, mp 103.5-105°C (lit.[225] 106°). ^{1}H-NMR ($CDCl_3$) δ : 4.37 (s, 2H); 7.27-7.70 (br, 10H). IR ($CHCl_3$ soln) : 3100, 2860, 1520, 1460 (alkyl and aryl), 1335 (SO_2), 1145 (SO_2), 760, 695, 650.

Benzyl phenylmethanethiosulfonate (**8a**) from Dibenzyl Disulfide and Phenylmethanesulfonyl chloride

To 0.296 g (1.20 mmol) of dibenzyl disulfide in 4 ml of $CDCl_3$ was added 0.231 g (1.2 mmol) of phenylmethanesulfonyl chloride was added 2.4 ml of 1 M $TiCl_4$ in $CDCl_3$. The reaction was allowed to stir for 20 min at room temperature. The reaction mixture was placed into an NMR tube and a ^{119}Sn-NMR spectrum was attained: 155.7 ppm.

The reaction was repeated, quenched and worked up as above to obtain benzyl phenylmethanethiosulfonate (**8a**), 31 %; mp 104-106°C.

Oxidation of Thiotins with $TiCl_4$

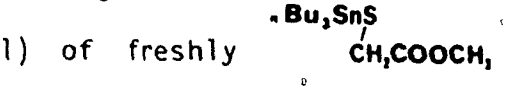
To .500 g (1.2 mmol) of tri-n-butyl benzylthiotin(IV) (**96a**) in 4 ml of $CDCl_3$ was added 2.4 ml (2.4 mmol) of 1.0 M $TiCl_4$ in $CDCl_3$. The reaction was allowed to stir for 1 min before it was quenched with Na_2CO_3. A ^{119}Sn-NMR spectrum of the reaction showed a peak at 156.2 ppm; proton NMR showed the presence of dibenzyl disulfide; the reaction

mixture was concentrated and placed on ca. 50 g of silica and eluted with hexanes/dichloromethane (3:1). The disulfide was obtained, 0.280g (95 %), GC was homogeneous, retention time 7.45 min; RT of authentic sample, 7.44 min. ^{1}H-NMR ($CDCl_3$) δ : 3.56 (s, 2H); 7.20 (s, 5H).

μ-1,4-Butyldithiohexa-n-butylditin(IV) (**109b**), .838 g (1.2 mmol) was similarly reacted with 2.4 ml (2.4 mmol) of 1.0 M $TiCl_4$ for 1 min. After typical work up procedures, 0.134 g (93 %) of the cyclic disulfide, 1,2-dithiane (**74**), was obtained; GC was homogeneous, retention time 1.39 min; RT of authentic sample, 1.36 min. ^{1}H-NMR ($CDCl_3$) δ : 2.00 (br, 4H); 2.83 (br, 4H).

S-tri-n-Butylstannyl Methylthioglycolate (**165**)

To a 250 ml round bottom flask containing 100 ml of CCl_4 was added 1.69 g (16.0 mmol) of freshly distilled methylthioglycolate, 2.30 ml (16.5 mmol) of distilled triethylamine and 4.50 ml (16.0 mmol) of 96% tri-n-butyltin chloride. The reaction mixture which had turned deep yellow was allowed to stir vigorously for 4 h. The resultant triethylamine hydrochloride salt was collected and the filtrate was washed with 5% acetic acid, dried ($MgSO_4$), evaporated in vacuo and then evacuated (0.4 mm) overnight. ^{1}H-NMR showed some impurity (ies) and ^{119}Sn-NMR showed two peaks, 84.7 ppm and 104.4 ppm with relative intensities of ca. 9:1. The mixture was purified on ca. 200 g of flash grade silica and eluted with hexanes/dichloromethane/ethanol (7:2:1) to afford a slightly yellow liquid (0.532 g) and a second fraction: 5.17 g (82%) of S-tri-n-butylstannyl methylthioglycolate (**165**) as a deep yellow liquid.



First fraction, yellowish liquid; ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.07-1.73 (br, 18H); 2.01 (s, 3H). ^{119}Sn-NMR ($CDCl_3$) : 104.5 ppm. MS (EI, 70eV, 40°C) m/z : 293 (100), 291 (60), 289 (63) [M^+ - C_2H_5· and n-Bu_3Sn^+]; 253 (34), 251 (20), 249 (19) [n-Bu_2SnOH^+]; 235 (5), 233 (8) [n-Bu_2SnH^+]; 179 (84), 177 (78), 175 (69) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 139 (20), 137 (25), 135 (30) [H_2SnOH^{+} and $SnOH^+$]; 121 (27), 119 (38) [SnH^+]; 57 (25).

Second fraction; ^{1}H-NMR ($CDCl_3$) δ : 0.93 (t, 9H); 1.10-1.83 (br, 18H); 3.27 (s, 2H); 3.70 (s, 3H). ^{119}Sn-NMR ($CDCl_3$) : 84.9 ppm. MS (EI, 70eV, 40°C) m/z : 339 (37), 337 (39), 335 (9) [M^+ - n-Bu· and M^+ - CH_3COO·]; 291 (38), 289 (13) [n-Bu_3Sn^+]; 269 (87), 267 (89), 265 (47) [M^+ - CH_3· - C_4H_8 and n-Bu_2SnSH^+]; 213 (39), 211 (15) 209 (9) [$H_3SnSCH_2COO^+$ and n-BuH_2SnS^+]; 179 (32), 177 (65), 175 (44) [n-$BuSnH_2^+$ and n-$BuSn^+$]; 155 (44), 153 (47), 151 (17) [H_2SnSH^+ and $SnSH^+$]; 121 (40), 119 (47) [SnH^+]; 57 (49); 56 (42); 47 (30); 41 (100).

The first fraction was tri-n-butyltin methoxide (**166**); see further experimental and discussions. An analysis of the amount of tri-n-butyltin methoxide (**166**) formed as a side product could be determined by using the ^{1}H-NMR signal at 2.01 ppm (OCH_3) of the crude mix. In this instance there was 11% of the tin alkoxide produced. The proton spectra of a similar reaction which was allowed to stir for 1 h showed that 7% of the tin alkoxide was generated, however ^{119}Sn-NMR showed a peak at 155.3 ppm (ca. 15% , n-Bu_3SnCl) indicating the reaction was not complete. Allowing the reaction to stir overnight yielded 14% of the tin alkoxide with no residual tri-n-butyltin chloride.

Tri-n-Butyltin Methoxide (166)

The tri-n-butyltin alkoxide was synthesized by allowing 1.0 ml (3.5 mmol) of tri-n-butyltin chloride and 0.5 ml (3.6 mmol) of triethylamine to stir in 50 ml of methanol for 4 h. The mixture was washed twice with 5% acetic acid and then with distilled water. The solution was then dried ($MgSO_4$) and evaporated in vacuo to afford an orange liquid; bp 125°C/ 0.1 mm (lit.[227] 97-97.5°/ 0.06 mm, lit.[228] 75-78°/ 0.25 mm); ^{1}H-NMR ($CDCl_3$) δ : 0.92 (t, 9H); 1.10-1.73 (br, 18H); 2.03 (s, 3H). ^{119}Sn-NMR ($CDCl_3$) : 104.5 ppm.

N-t-Butyloxycarbonyl-L-Cysteine Ethyl Ester (168)

The N-t-butyloxycarbonyl (BOC) protected amino acid was prepared in a fashion similar to that presented by Itoh, Hagiwara and Kamiya.[205] To 14.5 g (78.3 mmol) of L-cysteine ethyl ester hydrochloride (169), 11.0 ml (79.0 mmol) of triethylamine was added 17.1 g (78.3 mmol) of 2-(t-butyloxycarbonyloxyimino)-2-phenylacetonitrile (BOC-ON), these were allowed to stir in 250 ml of CH_2Cl_2 at 0°C for 8 h. The resultant triethylamine hydrochloride salt was removed by filtration and the filtrate was washed with 5% acetic acid, washed in 5% $NaHCO_3$, dried ($MgSO_4$) and evaporated in vacuo to afford 16.5 g (85%) of a viscous liquid; sodium nitroprusside test for thiols: positive. ^{1}H-NMR ($CDCl_3$) δ : 1.30 (t, 3H); 1.47 (s and m 10H); 2.87-3.10 (d of d, 2H); 4.27 (q, 2H); 4.50 (m, 1H); 5.37-5.63 (br, 1H). MS (EI, 70eV, 35°C) m/z : 193 (28) [$M^+ - C_4H_8$]; 176 (21) [$M^+ - C_4H_9O^\cdot$]; 132 (37) [$C_4H_6NO_2S^+$]; 76 (44) [$C_2H_5NSH^+$]; 74 (24) [76 - H_2 and/or t-BuOH]; 59 (45) [$C_2H_2SH^+$]; 57 (100).

S-tri-n-Butylstannyl-N-t-Butyloxycarbonyl-L-Cysteine Ethyl Ester (167)

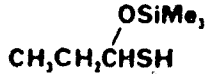
To 4.00 g (16.1) of N-BOC-L-cysteine ethyl ester (168) and 2.4 ml (17 mmol) of triethylamine in 200 ml of CCl_4 was added 4.50 ml (16.1 mmol) of 96% tri-n-butyltin chloride. The reaction was allowed to stir overnight at room temperature. The triethylamine hydrochloride salt was filtered, the filtrate was washed with 5% acetic acid, dried ($MgSO_4$), evaporated in vacuo and evacuated (0.4-0.4 mm overnight) to give a wax. This wax was placed on ca. 250 g of silica and eluted with hexanes/dichloromethane/ethanol (7:2:1) for a quick purification to again afford a colorless wax, 7.87 g (91% yield). ^{1}H-NMR ($CDCl_3$) δ : 0.90 (t, 9H); 1.10-1.73 (s and br, total 30H); 2.93-2.05 (d of d, 2H); 4.20 (q, 2H); 4.50 (m, 1H); 5.27-5.50 (br, 1H). ^{119}Sn-NMR ($CDCL_3$) : 86.3 ppm. Raman (neat) : 862, 659, 616 (S-C), 579, 505 (Sn-S), 314 (S-C), 216. MS (EI, 70eV, 40°C) m/z : 291 (25), 289 (10) [n-Bu_3Sn^+]; 269 (87), 267 (93), 265 (55) [$C_8H_{21}SnS^+$ and n-Bu_2SnS^+]; 235 (10), 233 (9) [n-Bu_2SnH^+]; 211 (47), 209 (12) [n-BuH_2SnS^+]; 179 (45), 177 (47), 175 (47) [n-BuH_2Sn^+ and n-$BuSn^+$]; 155 (34), 153 (35), 151 (13) [H_2SnSH^+ and $SnSH^+$]; 132 ($C_4H_8NO_2S^+$]; 121 (26), 119 (44) [SnH^+]; 102 (58) [$C_3H_4NOS^+$ or t-$BuOCOH^+$]; 76 (68) [$C_2H_5NSH^+$]; 74 (14) [76 - H_2 and/or t-$BuOH^+$]; 59 (54) [$C_2H_2SH^+$]; 57 (99); 41 (100)

Treatment of (167) with a Variety of Deprotecting Reagents

S-tri-n-Butylstannyl-N-t-butyloxycarbonyl-L-cysteine ethyl ester (167) was treated with some common ester and carbamate cleavage reagents for the deprotection of amino acids. After deprotection the sample was taken up in $CDCl_3$ and a ^{119}Sn-NMR was taken. The deprotecting conditions, which are described by Greene[203], were: a) 3.0 M HCl in acetic

acid for 30 min at room temperature, ^{119}Sn-NMR : 155.7 ppm; b) ca. 2 equivalents of thiophenol in trifluoroacetic acid at room temperature for 1 h, ^{119}Sn-NMR : 73.7 ppm (85%) and 86.5 ppm (15%); c) trimethylsilyl iodide in $CDCl_3$ for 6 min at room temperature, ^{119}Sn-NMR : 84.5 ppm; d) KOH in D_2O/MeOH, ^{119}Sn-NMR : 104.6 ppm (67%) and 86.2 ppm (33%).

α-Trimethylsiloxy-1-Propane Thiol (171)

This thiol was synthesized by bubbling hydrogen sulfide into a dichloromethane solution of propanal 
and trimethylsilyl chloride in a fashion analogous to that of Aida, Chan and Harpp.[209] The result was a 65% yield of a highly odoriferous and cloudy liquid; bp 46°C/ 15 mm. ^1H-NMR ($CDCl_3$) δ : 0.17 (s, 9H); 0.97 (t, 3H); 1.77 (q, 2H); 2.02 (d, 1H); 4.90 (m, 1H). MS (EI, 70eV, 150°C) m/z : 130 (16) [$M^+ - H_2S$]; 115 (27) [130 - $CH_3\cdot$]; 75 (100) [M^+ - TMSO·]; 58 (33) [$C_2H_6Si^+$]; 45 (42) [CHS^+]; 29 (55); 28 (48).

2-Methylvinylthiolate (172)

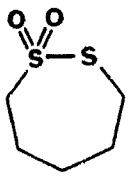
The 2-methylvinylthiolate (172) anion was prepared as needed in situ by a modification of the procedure presented by Harpp, Aida and Chan.[210] To 0.411 g (17.1 mmol) of NaH suspended in dry THF under N_2 at 0°C was slowly added 2.00 g (11.2 mmol) of α-trimethylsiloxy-1-propanethiol. The reaction which was allowed to stir for 1 h was exothermic and the solution was pale gray. Care was taken in the addition of the thiol to avoid effervescence due to the release of H_2.

S-Tri-n-Butylstannyl-2-Methylvinylthiolate (170) and Attempted Synthesis of Substituted Thiophenes

To a stirring solution of (172) prepared in situ (see above) was added 3.2 ml (11.2 mmol) of 96% tri-n-butyltin chloride. The mixture was allowed to stir for 1 h at room temperature. Attempts to workup the reaction including distillation without prior removal of the solvent were unsuccessful hence this compound (170), if produced, was used in situ for further reactions. The reaction was repeated with a small excess of 1 equivalent of triethylamine (1.7 ml) and 2 equivalents of tri-n-butyltin chloride (6.4 ml).

To a stirring solution of tri-n-butylstannyl-2-methyl-vinylthiolate (170) prepared above with one equivalent of tri-n-butyltin chloride was added one equivalent of concentrated THF solutions of 3-bromo-2-butanone or α-bromoacetophenone. The reactions were refluxed under a blanket of N_2 for 2 h and 24 h using a reflux condenser equipped with a drying tube. The solvent was removed in vacuo, the resultant oil was taken up in CH_2Cl_2, washed with water, dried ($MgSO_4$) and evaporated. ^{1}H-NMR ($CDCL_3$) of the crude product showed no resonances between 6.5 ppm and 8.0 ppm. This procedure was repeated using tri-n-butylstannyl-2-methylvinylthiolate (170) which was prepared using two equivalents of tri-n-butyltin chloride. Once again proton NMR showed no evidence of thiophene formation.

1,2-Dithiepane 1,1-Dioxide (175)



To a stirring solution of 2.78 g (20.0 mmol) of 1,2-dithiepane (75) in 50 ml of dry dichloromethane at 5-10°C was slowly added 8.62 g (40.0 mmol) of 80% m-chloroperbenzoic

acid which had been previously dissolved in 100 ml of dichloromethane. This exothermic reaction was monitored by TLC (silica, hexanes/ dichloromethane 3:1) with the Rf's being : disulfide, (.90); m-chlorobenzoic acid (.50); dioxide, (.42); impurity (perhaps polymer), (.05-.20); Upon addition of the first equivalent of m-CPBA TLC showed spots for disulfide and dioxide of approximately equal size, with further addition TLC showed the consumption of disulfide to afford the dioxide. The reaction could also be monitored by color changes; with addition of m-CPBA the solution turned brilliant pink until the first equivalent of oxidant was fully added, further addition of oxidant turned the mixture yellow and then orange, the solution cleared once the second equivalent of oxidant had been completely added. Attempts to remove any excess m-CPBA and m-CBA which formed with sodium bisulfite followed by calcium hydroxide or sodium carbonate or $MgSO_4/Na_2CO_3$ washes resulted in many spots on TLC. Thus the reaction, in CH_2Cl_2, was concentrated to precipitate out the m-CBA as fine white crystals mp 153-155°C (lit.[229] 158°). The filtrate was concentrated three more times, the last time under a stream of nitrogen at ca. 5°C. Purification was completed on ca. 75 g of silica (hexanes/dichloromethane 7:1) to afford 1.10 g (33%) of a colorless oil; UV (CH_2Cl_2) λ_{max} : 235 nm, ϵ = 56 (lit.[78] EtOH, 240, ϵ = 54). ^{1}H-NMR ($CDCl_3$) δ : 1.93-2.17 (br, 6H); 3.13-3.60 (t and br, total 4H). IR ($CHCl_3$ soln) : 2940, 2860, 1450, 1400 (alkyl), 1315 vs (SO_2), 1180, 1125 vs (SO_2), 1050, 730, 610 (lit.[75] 1310 s, 1120 s).

Desulfurization of (175)

The procedure for the desulfurization of 1,2-dithiepane 1,1-dioxide is similar to that presented by Harpp, Gleason and Ash[211,212]; to 0.32 g

(1.9 mmol) of (**175**) in 15 ml of dry benzene at ca. 5°C was added 0.50 g (2.0 mmol) of tris(diethylamino)phosphine (**176**). The reaction was allowed to stir for 10 minutes before the solvent was removed in vacuo. Purification of the resultant oil on silica (hexanes/dichloromethane 7:1) afforded three fractions: 92 % yield of tris(diethylamino)phosphine sulfide (**178**) whose IR was identical to that of a prepared authentic sample (see below); 21% yield of thiane-1,1-dioxide (six membered ring sulfone **184**), ^{1}H-NMR ($CDCl_3$) δ : 1.77-2.13 (br, 6H); 3.17 (t, 4H). IR ($CHCl_3$ soln) : 2965, 2940, 2865, 1455 (alkyl), 1305 (SO_2), 1125 (SO_2), 1055, 965, 735, 695, 655. The last fraction was an oily polymer (**185**) produced in a 74% yield; IR (neat) : 2940, 2860, 1460 (alkyl), 1325 **vs** (SO_2), 1140 **s** (SO), 1125 **s** shoulder (SO_2), 1055, 740 **vs** (S-O), 695, 670.

Tris(diethylamino)phosphine Sulfide (**178**)

To 0.34 g (1.33 mmol) of elemental sulfur in 30 ml of toluene was added 0.33 g (1.33 mmol) of tris $(Me_2N)_3P{=}S$ (diethylamino)phosphine (**176**) in 10 ml of toluene. The exothermic reaction was allowed to stir for 25 min. The solvent was evaporated and an IR was taken without any purification of the sample; IR ($CHCl_3$ soln) : 2990, 2950, 2865, 1470, 1385 (alkyl), 1210, 1190, 1020, 945, 720, 700.

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