Chapter Three

Modified Vilsmeier-Haack Reactions of $\alpha$-Methylene Ketones

3.1 Introduction

The Vilsmeier-Haack reaction\textsuperscript{1,2} of carbonyl compounds, though known to provide useful intermediates in organic synthesis is not explored to its full potential. The reaction of enolizable ketones lead to the formation of chlorovinyl iminium salts 2 which on basic hydrolysis give $\beta$-chloro substituted $\alpha,\beta$-unsaturated aldehydes 3 (Scheme 1).\textsuperscript{3,4}

Scheme 1

Acetals or ketals also under similar conditions undergo this reaction to give alkoxy substituted vinyl iminium salts which provide N,N-dimethyl aminoacroleins or $\beta$-ketoaldehydes.\textsuperscript{5,6} In a recent communication from this laboratory it has been shown
that dithioketals undergo efficient Vilsmeier-Haack reaction under mild conditions and the alkylthioiminium salts formed, on hydrolysis with cold saturated potassium carbonate solution give \( \beta \)-alkylthioethylenic aldehydes in good yields. Though it could be prepared conveniently from dithioketals, development of a one pot process for their synthesis starting from the ketones directly should be still attractive. The chlorovinyl aldehydes prepared by the Vilsmeier reaction have been shown to be useful precursors for the synthesis of \( \beta \)-alkylthioethylenic aldehydes. If the butylthio group is incorporated to the carbonyl group prior to the Vilsmeier reaction it would lead to the formation of butylthio substituted iminium salt intermediates which on basic hydrolysis should directly lead to the \( \beta \)-butylthio substituted ethylenic aldehydes on basic hydrolysis. In this chapter the reactions of carbonyl compounds with butanethiol in the presence of a Lewis acid such as boron trifluoride etherate followed by the Vilsmeier reagent prepared from \( \text{POCl}_3 \) and DMF are described. DMF itself or chloroform was used as the solvent.

3.2 Results and discussion

A variety of enolizable carbonyl compounds were allowed to react with butanethiol in the presence of a Lewis acid and was subsequently treated with Vilsmeier reagent. Substituted acetophenones, indanone, \( \alpha \)-tetralone, cyclohexanone and several aliphatic ketones were subjected to this reaction.

3.2.1 Reaction of ketones with Vilsmeier reagent in the presence of Lewis acid and thiol

The reactions of ketones were attempted with Vilsmeier reagent in the presence of butanethiol and a Lewis acid anticipating that (1) butanethiol may react with carbonyl compounds in the presence of Lewis acid to form a vinylsulfide or dithioketal
which may undergo further formylation to give β-alkylthioethylenic aldehyde. (2)

Butanethiol may add to Vilsmeier reagent to form a butylthio substituted iminium salt
which on reaction with enolizable ketones may provide vinylogous thiolesters or β-oxo

dithioacetals.

3.2.1.1 Reactions of Substituted Acetophenones, α-Tetralone and Acetyl

thiophene

The reactions of enolizable ketones where the carbonyl group is α- to an

aromatic system are described in this section. Acetophenone was allowed to react with
two equivalents butanethiol in the presence of boron trifluoride etherate in DMF and
three equivalents of POCl₃ was added subsequently to the mixture. The reaction after
usual workup with saturated potassium carbonate solution and column chromatography
gave good yields of an yellow oil which was identified to be the β-oxodithioacetal 4a
(Scheme 2). Two other products which also formed along with the β-oxodithioacetal
4a were the dithioacetal of the chlorovinyl aldehyde 5a and the dithioacetal of the
butylthioethylenic aldehyde 6a.

Scheme 2

\[
\begin{align*}
1a & \xrightarrow{\text{BuSH, BF₃OPOCl₃, DMF, Room Temp. 12h}} 4a \\
5a & + 6a
\end{align*}
\]
The formation of the β-oxodithioacetal as the major product suggests that acetophenone was not completely converted to its dithioketal when treated with Lewis acid and thiol in DMF. Therefore the thiol must have reacted with the Vilsmeier reagent which have formed subsequently. The reaction of the amide-POCl₃ adducts with thiol is known to be a method for the preparation of dialkylthioorthoamides.¹⁰,¹¹ For instance, the reaction of the DMF-POCl₃ with ethanethiol affords the diethylthioorthoamide 8 (Scheme 3).

Scheme 3

\[ \text{Scheme 3} \]

We have found that high yields of tributylthioorthoformates are formed when butanethiol was added to Vilsmeier reagent in the presence of a Lewis acid. It was also observed earlier that the reaction of butanethiol with the Vilsmeier reagent provides tributylthioorthoformate in addition to the corresponding dibutylthioorthoamide.¹⁰ Orthoformates and similar compounds which forms stabilized carbocations in the presence of a Lewis acid are known to react with electron-rich species such as silyl enol ethers. For instance, the reaction of preformed 1,2 dithienium tetrafluoroborate with silyl enol ethers proceed with high efficiency leading to the formation of the β-oxodithioacetal 11 (Scheme 4).¹²,¹³
Scheme 4

The reaction of 2-ethoxy dithianes with silyl enol ethers in the presence of Lewis acids such as ZnCl$_2$, BF$_3$Et$_2$O or TiCl$_4$ also provide the $\beta$-oxodithioacetals.$^{14}$ Though the addition of silyl enol ethers to the carbocations generated from orthoformates are very facile, the addition of simple ketones under Lewis acid catalyzed conditions to the stabilized carbocations lead to several products. Some reactions of ketones in the presence of Lewis acids with orthoformates have been attempted and found that the reaction do not lead to the formation of $\beta$-oxodithioacetals. These results are discussed in detail in chapter 5.

The formation of the dithioacetals 5 and 6 of the chlorovinyl aldehyde and the butylthioetylgenic aldehyde indicates involvement of the chlorovinyl iminium salt and the butylthiovinyl iminium salt as intermediates. Their subsequent reactions with butanethiol should lead to the corresponding dithioacetals.

Though $\beta$-oxodithioacetal 4a could be obtained in good yield from acetophenone (Scheme 2), our attempts to generalize this method for the synthesis of $\beta$-oxodithioacetals starting from ketones did not give very encouraging results. Other substituted acetophenones invariably gave mixtures of products and efforts to discover conditions that would selectively lead to the formation of any single product in general did not succeed. The reaction of $p$-methyl acetophenone gave the $\beta$-alkylthioenone 12b though in low yield. Two other products, the chlorovinyl substituted dithioacetal
5b and butylthio substituted dithioacetal 6b were also obtained in this reaction along with β-alkylthioethylenic aldehyde 13b (Scheme 5).

Scheme 5

The butylthioethylenic aldehyde 13b was obtained predominantly as the E isomer (more than 98% based on NMR). The E stereochemistry was assigned on the basis of the chemical shift of the aldehyde proton and the vinylic proton. The doublet that appears at $\delta = 9.29$ ppm ($J = 7.8$ Hz) is assigned to the aldehyde proton of the E isomer while the aldehyde proton of the Z isomer appeared at $\delta = 10.2$ ppm ($J = 7.8$ Hz). Similarly the vinylic proton of the E isomer appeared at $\delta = 6.06$ ppm ($J = 7.8$ Hz) while that of the Z isomer appeared at $\delta = 6.35$ ppm ($J = 7.8$ Hz).
Lawesson and co-workers have alkylated the vinylogous thioamide 15 with methyl iodide to get the methylthio substituted vinyl iminium salt 16 which on basic hydrolysis gave the β-methylthioethylenic aldehydes 17 as a mixture of E and Z isomers (Scheme 6). They have calculated the theoretical chemical shift of the vinylic protons of both the isomers and compared with the observed value. Thus the minor product that shows a higher δ value 7.20 ppm (calculated δ = 6.58 ppm) was assigned the Z stereochemistry. Similarly the major product that shows a lower δ value, 6.04 ppm (calculated 5.99 ppm) was assigned the E stereochemistry.

Scheme 6

The preferential formation is also justified by the theoretical calculations carried out on the the various conformers of 16 for example 16A, 16B and 16C. The heats of formation of the various possible conformations of the iminium ion 16 have been computed using semi-empirical molecular orbital method AM1. The calculated values reveal that the most stable conformation of the iminium ion is the W form 16B. Therefore the E isomer resulting from the conformation 16B must be major.
When the reaction was carried out on p-chloroacetophenone the chlorosubstituted indene 18 was the product isolated along with the chloroformylated product 19c (Scheme 7).

Scheme 7

The indene 20 must have formed by the Lewis acid catalyzed cyclization of the dithioacetal 5c derived from the chlorovinyl aldehyde 19c. When the indene 18 was refluxed in methanol in the presence of potassium hydroxide the corresponding indenone 20 could be obtained thus confirming the structure of 18.
Venugopal and Perumal have earlier observed that substituted chalcones could be converted to the respective chlorosubstituted indenes in the presence of Vilsmeier-Haack reagent. GCMS of the reaction mixture shows several other products along with these two which could not be isolated or identified. Though the chlorovinyl aldehyde was formed in the reaction the corresponding butylthioethylenic aldehyde was not obtained. However GCMS showed a peak having mass 254 which may be due to the vinylogous thiolester. When the reaction was done with p-methoxy acetophenone the dithioacetal of chlorovinyl aldehyde 5d along with the dithioacetal of butylthioethylenic aldehyde 6d was obtained. The β-butylthio substituted enaldehyde 13d was also obtained in this reaction in appreciable yield (Scheme 8). The β-alkylthioethylenic aldehyde was isolated as a mixture of E and Z isomer where the E isomer was major (90%).

The reaction with α-tetralone gave the chlorovinyl aldehyde 19e as the major product. It appears that the iminium salt derived from α-tetralone is resistant to the substitution with butanethiol. The vinyl sulfide 21 was also obtained in this reaction though the butylthio substituted enaldehyde was not formed (Scheme 9).
Scheme 8

\[
\begin{align*}
\text{1d} & \quad \overset{\text{CH}_3\text{O}}{\longrightarrow} \quad \text{13d} \\
\text{5d} & \quad \overset{\text{SBU}}{\longrightarrow} \quad \text{6d}
\end{align*}
\]

Scheme 9

\[
\begin{align*}
\text{1e} & \quad \overset{\text{Cl}}{\longrightarrow} \quad \text{19e} \\
\end{align*}
\]

Acetyl thiophene also gave three products, the β-oxodithioacetal 4f, butylthio vinyl dithioacetal 6f and chlorovinyl dithioacetal 5f (Scheme 10). Under these conditions we did not isolate any products where the thiophene ring is formylated.
Thus it seems that the reaction of aryl methyl ketones do not show much consistancy in their behaviour towards the Vilsmeier-Haack reagent under the conditions described here. While acetophenone gave the corresponding $\beta$-oxodithioacetal the only other ketone which gave similar $\beta$-oxodithioacetal was acetyl thiophene. The vinylogous thiolester was isolated only from $p$-methyl acetophenone though the reaction mixture of $p$-chloroacetophenone also showed the presence of the corresponding vinylogous thiolester in the Gas Chromatograph. It is intriguing that only $p$-chloroacetophenone gave the indene. However the dithioacetals of chlorovinyl aldehyde or butylthioethylenic aldehydes were almost always formed. Another product which usually forms is the butylthioethylenic aldehyde though this cannot be considered as a preparative method for them because the product mixture is usually complex.
3.2.1.2 Reactions of alicyclic ketones

After the investigations on the reactions of aryl methyl ketones and tetralone, the behaviour of alicyclic ketones such as cyclohexanone and cyclopentanone was examined. The Vilsmeier-Haack reaction of cyclohexanone do not provide the corresponding \( \beta \)-alkylthioethylenic aldehyde or the vinylogous thiolester under these reaction conditions. Instead the butylthio substituted pentadienaldehyde \( \text{23} \) was formed as the only product in high yield (Scheme 11).

Scheme 11

The formation of the dienaldehyde in good yields suggests that incorporation of the butylthio group do not take place prior to the first iminoalkylation. At first the reaction of the cyclohexanone with the chloromethylene iminium salt leads to the formation of the iminium salt \( \text{24} \) which rearranges to the dienamine \( \text{25} \) which on subsequent iminoalkylation provides \( \text{26} \). Addition of butanethiol to \( \text{26} \) and subsequent hydrolysis affords the pentadienaldehyde \( \text{23} \).
The pentadienaldehyde 23 forms a solid adduct with hydrazine which was identified to be 27 on the basis of spectral data.

\[
\begin{align*}
\text{BuS}- & \quad \text{Cl} \\
\text{N} & \quad \text{N} \\
\text{Cl} & \quad \text{SBu}
\end{align*}
\]

27

Cyclopentanone under similar conditions gave a complex mixture of several products which could not be separated in pure forms by column chromatography.

3.2.1.3 Reactions of aliphatic ketones

The reaction of aliphatic ketones such as acetone and ethyl methyl ketone under these conditions gave complex product mixtures which showed a number of products on the TLC. Though one major compound was obtained from ethyl methyl ketone by allowing the reaction to go on for seven days, the product could not be identified based on the available spectral data. However, vinylogous thiolester 29 could be obtained in good yield when the reaction was carried out with diethyl ketone under similar conditions (Scheme 12).

Scheme 12

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \\
\text{CH}_3 & \quad \text{H}_3\text{C} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{SBu} & \quad \text{SBu}
\end{align*}
\]
3.2.2 Reaction of ketones with Lewis acid and thiol followed by the Vilsmeier reagent

Since the reaction of ketone with Vilsmeier reagent in the presence of butanethiol and BF$_3$·Et$_2$O in DMF was initially examined as a part of the efforts to discover a one pot method for the conversion of ketones to β-oxodithioacetals or β-alkylthioethylenic aldehydes, the results show that in general the reaction do not lead to β-alkylthioethylenic aldehydes and the products obtained are either β-oxodithioacetals 4, chlorovinyl dithioacetals 5 or butylthiovinyl substituted dithioacetals 6. The butylthiovinyl substituted dithioacetals and chlorovinyl dithioacetals may prove to be important reactive intermediates in organic synthesis. The results from our experiments in DMF show that the ketones are not completely converted to dithioketals when they are allowed to react with BuSH in DMF. Therefore we chose to select a reaction condition suitable for the preparation of dithioketal as well as for carrying out the Vilsmeier-Haack reaction. Though it has been shown that TiCl$_4$ was efficient in converting ketones to dithioketals the Vilsmeier-Haack reaction in the presence of TiCl$_4$ lead to intractable mixtures of products. When BF$_3$·Et$_2$O was used as the Lewis acid it did not interfere with the Vilsmeier-Haack reaction and lead to higher yields of products with better selectivity. Therefore we thought of mixing BF$_3$·Et$_2$O in CHCl$_3$ at first to convert the ketone to dithioketal and then perform Vilsmeier-Haack reaction in the same pot. The results of these experiments are described here.

3.2.2.1 Reactions of Substituted Acetophenones, α-Tetralone and Acetyl thiophene

When acetophenone was allowed to react with one equivalent of BuSH in presence of BF$_3$·Et$_2$O in CHCl$_3$ and Vilsmeier-Haack reagent was added to it, the reaction on workup after stirring at room temperature for 12 hours gave very good
yields of β-alkylthioethylenic aldehyde 13a exclusively as the E isomer. Other substituted acetophenones also gave in good to excellent yields of β-alkylthioethylenic aldehydes 13b-d predominantly as the E isomers (Scheme 13). The E:Z ratio was determined on the basis of the ratio of the vinylic or aldehydic proton in the NMR spectra of the mixture of the two isomers. While substituted acetophenones gave the butylthioethylenic aldehyde as the only or major isolated products, p-chloroacetophenone gave some chlorosubstituted aldehyde 19c along with β-alkylthio substituted aldehyde 13c. This is probably because the conversion of p-chloroacetophenone to dithioketal was not complete in the first step of the process. p-Methyl acetophenone gave low yields of the vinylogous thiolester 12b, β-oxodithioacetals 4b, β-butylthiovinyl dithioacetals 6b and chlorovinyl dithioacetal 5b along with the β-alkylthio substituted enaldehyde 13b as is evident from the GCMS of the mixture.

![Image](image)

The β-alkylthiosubstituted enaldehyde 13f was obtained from 2-acetyl thiophene 1f under this condition in good yield (Scheme 14). This was the only product isolated from this reaction. Earlier 13f was prepared from the dithioketal of the acetyl thiophene.7

However the reaction of α-tetralone again gave only the chlorovinyl aldehyde 19e as the major product along with the vinyl sulfide 21 (Scheme 9).
3.2.2.2 Reactions of alicyclic ketones

The β-alkylthioethylenic aldehyde 30 could be prepared conveniently from cyclohexanone, though the pentadiene aldehyde 23 was also formed as a minor product. Thus when cyclohexanone was allowed to react with one equivalent of butanethiol in the presence of borontrifluoride etherate, subsequent treatment with three equivalents of Vilsmeier reagent at room temperature for twelve hours gave after usual workup and
column chromatography 70% of the enaldehyde 30 while the pentadienaldehyde 23 was isolated only in 5% yield (Scheme 15).

Scheme 15

However when the reaction was carried out with cyclopentanone the corresponding enaldehyde could not be obtained in useful yields. Instead a mixture of several products obtained which could not be separated by column chromatography.

3.2.2.3 Reactions of aliphatic ketones

Surprisingly the vinylogous thiolester 29 was the only product isolated when the reaction was carried out with diethyl ketone. Thus when 3-pentanone was allowed to react with one equivalent of butanethiol in the presence of borontrifluoride etherate, subsequent treatment with three equivalents of Vilsmeier reagent at room temperature for twelve hours gave after usual work up and column chromatography 80% of the vinylogous thiolester 29 (Scheme 12). This is in contrast with the exclusive formation of β-alkylthioethylenic aldehyde when the dithioketal of the diethyl ketone is subjected to the Vilsmeier-Haack reaction conditions.7

However acetone and ethyl methyl ketone did not lead to any major product in preparatively useful yields under these conditions.
3.2.3 Reaction of ketones with Vilsmeier reagent followed by quenching with thiol

The chlorovinyl aldehydes prepared by the Vilsmeier reaction of enolizable ketones have been shown to be useful precursors for the synthesis of β-alkylthioethylenic aldehydes.\textsuperscript{9,15} Thus Pellet and Huet\textsuperscript{9} have prepared β-alkylthioethylenic aldehydes starting from the corresponding chlorovinyl aldehyde which they have obtained from the respective carbonyl compounds. The chlorovinyl aldehydes derived from propiophenone and benzyl methyl ketone 31a (R\textsubscript{1} = Ph; R\textsubscript{2} = Me) and 31b (R\textsubscript{1} = Me; R\textsubscript{2} = Ph) on treatment with thiol in the presence of alkali afforded the respective alkyl or arylthioenaldehydes 32a (R\textsubscript{1} = Ph; R\textsubscript{2} = Me) and 32b (R\textsubscript{1} = Me; R\textsubscript{2} = Ph) (Scheme 16).

Scheme 16

![Scheme 16](image)

Similarly alkylthioethylenic aldehydes could be prepared from the chloroaldehydes derived from cyclohexanone and cycloheptanone (Scheme 17).

Scheme 17

![Scheme 17](image)
The substitution of the chlorine can also be achieved with oxygen nucleophiles. For instance, the reaction of monosodium salt of ethylene glycol with the iminium salt 2 under basic conditions lead to the formation of the β-oxoketals 35 (Scheme 18).

Scheme 18

If the chlorovinyl iminium salt intermediate 2 undergo a substitution reaction with sulfur nucleophile before being subjected to basic hydrolysis the reaction should lead to the formation of β-alkylthioethylenic aldehydes 13 in a one pot process starting from the ketones. To develop an alternative method for the synthesis of β-alkylthioethylenic aldehydes starting from the ketones directly we have also attempted quenching of the reaction mixture with butanethiol before the usual workup.

3.2.3.1 Reactions of Substituted Acetophenones, α-Tetralone and Acetyl thiophene

We have examined the reaction of the ketone with the Vilsmeier reagent and the intermediate iminium salt was allowed to react with butanethiol in the presence of a Lewis acid such as boron trifluoride etherate. Thus Vilsmeier reagent prepared from POCl₃ and DMF was added to acetophenone and boron trifluoride etherate in dry chloroform and the mixture was stirred at room temperature for 12h and quenched with two equivalents of butanethiol. The workup and column chromatography of the
mixture gave 3-butylthio-3-phenyl-1-propenal 13a in 85% yield as a mixture of E and Z isomers (95:5). Similarly other substituted acetophenones also gave the corresponding butylthioethylenic aldehydes 13b-d in good yields predominantly as E isomers (Scheme 19).

Scheme 19

\[
\begin{array}{c|c|c}
1,13 & R & E:Z ratio \\
\hline
a & H & 95:5 \\
b & CH_3 & 98:2 \\
c & Cl & 93:7 \\
d & OCH_3 & 80:20 \\
\end{array}
\]

Acetyl thiophene when subjected to similar reaction conditions gave 3-(thienyl)-3,3-bisbutylthio-1-propanal 36 as the major product along with small amount of the dithioacetal of chloroethylenic aldehyde 5f (Scheme 20).

The reaction of α-tetralone under similar conditions did not give the expected β-alkylthioethylenic aldehyde. Instead the dithioacetal of the chlorovinyl aldehyde 37 was the major product along with small amount of chlorovinyl aldehyde 19e (Scheme 21).

The investigations suggest that β-alkylthioethylenic aldehydes of substituted acetophenones can be conveniently prepared by the reaction of butanethiol with the iminium salt formed under Vilsmeier-Haack conditions.
3.2.3.2 Reactions of alicyclic ketones

When the Viisnie reaction was carried out with cyclohexanone under these conditions the corresponding $\beta$-alkylthioethylenic aldehyde 13 was not formed. Instead the butylthio substituted pentadienaldehyde 23 was formed as the only product in high
yield (Scheme 11). Apparently butane thiol is added to the iminium salt 26 formed by the double iminoalkylation of cyclohexanone.

The reaction of cyclopentanone under similar conditions gave dithioacetal of the butylthiosubstituted enaldehyde 39 and the dithioketal of the vinylogous thiolester 38. Also small amounts of dithioacetal of the chlorovinyl aldehyde 40 was isolated (Scheme 22).

Scheme 22

\[
\begin{align*}
\text{POCl}_3/\text{DMF} & \quad \rightarrow \\
\text{BF}_3/\text{Et}_2\text{O} & \quad \rightarrow \\
\text{BuSH} & \quad \rightarrow \\
\text{K}_2\text{CO}_3/\text{H}_2\text{O} & \\
\end{align*}
\]

3.2.3.3 Reactions of aliphatic ketones

Multiple iminoalkylations are frequently observed when acetone is subjected to the Vilsmeier-Haack conditions. Arnold found that the Vilsmeier reaction of acetone or its ketal or enol acetate provide the iminium salt 41 (X = OMe or Cl).
The reaction of acetone with three equivalents of Vilsmeier reagent at room temperature for 12 hours followed by addition of four equivalents of butanethiol gave the product 42 in 65% yield (Scheme 23). Formation of 42 could result from the Lewis acid catalyzed initial addition of butanethiol to the iminium salt 41 (X = Cl or S Bu) and subsequent hydrolysis.

Scheme 23

When the reaction of ethyl methyl ketone was carried out under similar conditions the major product isolated was an yellow oil which was identified as the dibutylthio acetal of the chlorovinyl aldehyde 43 (Scheme 24). $^1$H NMR shows that the product exists as a mixture of E and Z isomers which could not separated by column chromatography.

Scheme 24

The reaction of diethyl ketone gave the $\beta$-butylthio substituted $\alpha,\beta$-unsaturated ketone 29 was obtained in 60% yield. Also the GCMS of a fraction
separated by column chromatography on silicagel shows presence of a mixture of $E$ and $Z$ isomers (1:1) of the chloro substituted diene 44.

![Chemical Structure](image)

The reaction of 4-heptanone under similar reaction conditions also afforded the corresponding vinylogous thiolester 45 as the major product (Scheme 25).

**Scheme 25**

![Scheme](image)

When 2-hexanone was subjected to the Lewis acid assisted Vilsmeier reaction and subsequently treated with butane thiol before work-up with saturated potassium carbonate solution gave a mixture of two products was obtained. The major product shows two peaks in GC of the same mass fragmentation pattern which is identified as 46 which exists as a mixture of $E$ and $Z$ isomers. The butylthioethylenic aldehyde 47 was also obtained as a minor product (Scheme 26). It is interesting to note that the major product isolated in this case is derived from the reaction at the $\alpha$-methyl group while similar reaction of 2-butanone did not give any products derived from the reaction at the $\alpha$-methyl group.
Though the reaction of the benzyl methyl ketone attempted under these conditions no products other than its dithioketal could be isolated, by column chromatography of the product mixture on silicagel using hexane : ethyl acetate (95:5) as the eluent.

The iminium salt 48 derived from two sequential imino alkylation of the phenoxy propanone did not react with the butanethiol under the conditions employed here and the product isolated as an yellow crystalline solid was identified to be the \( \text{N,N-dimethyamino substituted pentadienaldehyde 50.} \)
3.2.4 Reaction of ketones with Vilsmeier reagent followed by quenching with mercaptoethanol

The reaction of ketones with Vilsmeier reagent and subsequent treatment with thiol in the presence of a Lewis acid lead to the formation of alkylthioethylenic aldehydes, vinylogous thioesters and a number of other products. Subsequently the reaction of the chlorovinyl iminium salts obtained by the imino alkylations of ketones with mercaptoethanol and ethanedithiol was examined. Though this reaction was primarily aimed at the development of a preparative method for \( \beta \)-oxo O,S-acetal and the \( \beta \)-oxodithioacetal respectively the reaction conditions could not be optimized for their formation.

When acetophenone was allowed to react with two equivalents of the Vilsmeier reagent in the presence of borontrifluoride etherate and was then treated with mercaptoethanol the reaction mixture after usual workup and column chromatography gave the chloro substituted cinnamaldehyde as the major product. The other product which was isolated was the O,S-acetal of the chlorovinyl aldehyde 51 (Scheme 28).

Other substituted acetophenones also gave only the corresponding chlorovinyl aldehydes 19 under these conditions.
The reactions of aliphatic ketone under similar conditions gave complex mixtures which could not be separated.

However reaction with cyclohexanone gave a single product as an yellow crystalline solid in high yields. This was identified as the 2-chloroethylthio substituted pentadienaldehyde 52 on the basis of spectral data (Scheme 29). The formation of the product 52 could result from the reaction of the intermediate iminium salt 22 with
mercaptoethanol. The conversion of hydroxy group to chloro group is common under Vilsmeier-Haack conditions.

Scheme 29

3.2.5 Cyclotrimerizations

When the reaction was carried out in CHCl₃, the ketone and butanethiol was allowed to react in the presence of BF₃·Et₂O and Vilsmeier reagent was added subsequently besides the formylation products cyclotrimerization products were also obtained, though in low yields. Our attempt to optimize the reaction conditions to obtain the cyclotrimerization products in higher yields were not very successful. However, when the reaction was workedup just after two hours, the reaction mixture after the removal of the solvent gave moderate yields of the cyclotrimerization products. It was noted that when the product mixture was left at room temperature for several days solid crystalline cyclotrimerization products got separated, apparently due to the cyclization of the vinyl sulfide intermediates.

The cyclotrimerization reactions of ketones under acid catalyzed conditions are not very general. However convenient preparative methods have been developed using ketals in the presence of protic acids and Lewis acids. Cyclotrimerization of ketones in the presence of alcohols are also efficient which presumably proceeds through the
formation of ketal intermediate. Cyclotrimerization of the ketones have been observed directly in the presence of solid super acid catalyst Nafion-H. 

In the present reaction it may be the vinyl sulfide that undergoes cyclotrimerization reaction. When the reaction mixture is worked up before the formylation occurs, the reaction mixture contains predominantly vinyl sulfide which undergo cyclotrimerization. Though we have further attempted the reaction in the presence POCl₃ with solvents other than DMF, such as dimethyl acetamide which will not give further formylation reactions, favourable conditions for cyclotrimerization could not be developed. Our efforts to cyclotrimerize dithioketals in the presence of Lewis acids such as boron trifluoride etherate or titanium tetrachloride also did not afford the expected products in preparatively useful yields.

When acetophenone was allowed to react with butanethiol in the presence of BF₃·Et₂O in chloroform and the subsequent addition of Vilsmeier reagent and workup after two hours gave 1,3,5-triphenyl benzene 53a (R = H) in 60% yield (Scheme 30).

Scheme 30

\[
\begin{align*}
\text{R} & = \text{H, Me} \\
1 & : \text{BF}_3 \cdot \text{Et}_2 \text{O} \\
2 & : \text{BuSH} \\
3 & : \text{POCl}_3 \cdot \text{DMF} \\
4 & : \text{K}_2 \text{CO}_3 \cdot \text{H}_2 \text{O}
\end{align*}
\]
The cyclotrimerization product of \( p \)-methyl acetophenone 53b (\( R = \text{Me} \)) and 2-acetyl naphthalene 54 also was obtained under similar reaction conditions.

![Diagram of compound 54]

3.3 Conclusions

A variety of aliphatic, aryl alkyl and cyclic ketones were subjected to Vilsmeier-Haack conditions in the presence of sulfur nucleophiles aiming at the formation of sulfur substituted iminium salt intermediates which could be further converted to potential multifunctional synthetic intermediates. Several reactions conditions were developed which involve the introduction of the sulfur nucleophiles at various stages of the reaction. Further research is necessary to establish the more general applications of the conditions developed. The various intermediates derived from the reactions described here should be explored for their synthetic applications.

3.4 Experimental

Melting points were determined on a Veego melting point apparatus and are uncorrected. Infrared spectra were measured with a Shimadzu IR-470
spectrophotometer and are given as cm⁻¹. Proton NMR spectra were recorded either on a Varian 390 (90 MHz), Jeol EX 90 (90 MHz) or a Bruker WM 300 (300 MHz) spectrometer in CDCl₃. ¹³C NMR spectra were recorded either on a Bruker WM 300 (76.49 MHz) or a Jeol GSX 400 (100.6 MHz). Chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane. Coupling constants J are given in Hz. Electron impact mass spectra were obtained on a Finnigan-Mat 312 instrument. GCMS were recorded on a Hewlett Packard 5890 Series II GC connected to a 5890 mass selective detector.

**Reaction of ketones with Vilsmeier reagent in the presence of Lewis acid and thiol**

**General Procedure**

To a solution of ketone (10 mmol) in DMF boron trifluoride etherate (1.2 ml, 10 mmol) was added followed by butanethiol (2.1 ml, 20 mmol). The mixture was stirred for 30 minutes at room temperature and then POCl₃ (2.9 ml, 30 mmol) was added slowly (over 15 minutes). The reaction mixture was stirred at room temperature for a further 12 hours. The mixture was then added to cold saturated K₂CO₃ solution (200 ml) and extracted with diethyl ether (3 x 50 ml) dried (Na₂SO₄) and evaporated. The residue was column chromatographed on silicagel using a mixture (50:1) of hexane and ethyl acetate as eluent.

3.3'-Dibutylthio-1-phenyl-propan-1-one, 4a

Isolated as yellow liquid from the reaction of acetophenone, yield 1.63 g (50%). IR (neat) ν = 2950, 2900, 1655, 1550, 1167, 1125 cm⁻¹. ¹H NMR (90 MHz) δ = 0.93 (m, 6H); 1.1 - 1.8 (m, 8H); 2.4 - 2.8 (m, 4H); 3.33 (d, J = 5 Hz, 2H); 4.8 (t, J = 5 Hz, 1H); 7.00 - 8.00 (m, 5H) ppm. ¹³C NMR δ = 13.06, 21.08, 30.09, 31.20, 31.82, 46.02, 126.50, 128.68, 129.90, 132.82, 196.20 ppm. EIMS m/z = 281, 220 (M⁺ - SBU), 178, 163, 121, 107, 105, 91, 77, 57.
3.3-Dibutylthio-1-chloro-1-phenyl-1-propene, 5a

Isolated as yellow liquid from the reaction of acetophenone, yield 0.33g (10%). IR (neat) ν = 2950, 2910, 2850, 1440 cm⁻¹. ¹H NMR (60 MHz) δ = 0.70 - 1.10 (m, 6H); 1.20 - 1.90 (m, 8H); 2.30 - 2.80 (m, 4H); 5.10 (d, J = 10Hz, 1H); 6.05 (d, J = 10Hz, 1H); 7.00 - 7.60 (m, 5H) ppm. ¹³C NMR δ = 13.728, 22.099, 31.597, 31.984, 47.071, 126.639, 128.076, 128.424, 129.089, 133.097 ppm. EIMS m/z = 240 (M + - SBu), 204, 178, 149, 122, 57.

1,3,3-Trinbutylthio-1-phenyl-1-propene, 6a

Isolated as yellow liquid from the reaction of acetophenone, yield 0.4g (12%). IR (neat) ν = 2950, 2910, 2850, 1450, 1220 cm⁻¹. ¹H NMR (60 MHz) δ = 0.70 - 1.10 (m, 6H); 1.20 - 1.90 (m, 8H); 2.30 - 2.80 (m, 4H); 5.00 (d, J = 10Hz, 1H); 5.95 (d, J = 10Hz, 1H); 7.00 - 7.60 (m, 5H) ppm. ¹³C NMR δ = 13.728, 22.099, 31.597, 31.984, 47.788, 126.639, 128.076, 128.424, 129.089, 133.097 ppm. EIMS m/z = 294 (M + - SBu), 204, 178, 149, 122, 57.

3.3-Dibutylthio-1-chloro-1-(4-methyl phenyl)-1-propene, 5b

Isolated as yellow liquid from the reaction of p-methylacetophenone, yield 0.5g (14%). IR (neat) ν = 2900, 2850, 1440 cm⁻¹. ¹H NMR (300MHz) δ = 0.85 - 0.97 (m, 6H); 1.43 - 1.50 (m, 4H); 1.60 - 1.65 (m, 4H); 2.35 (s, 3H); 2.64 - 2.69 (m, 4H); 5.03 (d, J = 10Hz, 1H); 6.16 (d, J = 10Hz, 1H); 7.12 - 7.47 (m, 4H) ppm. GCMS m/z = 253 (M + - SBu), 163, 128.

1,3,3-Trinbutylthio-1-(4-methyl phenyl)-1-propene, 6b

Isolated as yellow liquid from the reaction of p-methyl acetophenone, yield 0.40g (10%). IR (neat) ν = 2900, 2850, 1440 cm⁻¹. ¹H NMR (300 MHz) δ = 0.85 - 0.97
(m, 6H); 1.43 - 1.50 (m, 4H); 1.60 - 1.65 (m, 4H); 2.35 (s, 3H) 2.64 - 2.69 (m, 4H); 5.25 (d, J = 10Hz, 1H); 5.80(d, J = 10Hz, 1H); 7.12 - 7.47 (m, 4H) ppm.

**GCMS** m/z = 307 (M + - SbU), 253, 163.

\[ \text{3-Butylthio-1-(4-methyl phenyl)-2-propene-kone, 12b} \]

Isolated as yellow liquid from the reaction of p-methyl acetophenone, yield 0.7g (28%). IR (neat) v = 2900, 2850, 1650, 1440 cm\(^{-1}\). \(^1\)H NMR (90 MHz) \(\delta = 0.90 \text{ (t, J = 12Hz, 3H)}; 1.2 - 1.8 (m, 4H); 2.33 (s, 3H); 2.70 (t, J = 12Hz, 2H); 4.98 (d, J = 12Hz, 1H); 6.08 (d, J = 12Hz, 1H); 7.00 - 7.60 (m, 4H) ppm. GCMS m/z = 206, 193, 179, 166, 153, 148, 135, 119(100%), 108, 91.

\[ \text{3-Butylthio-3-(4-methyl phenyl)-2-propene-kone al, 13b} \]

Isolated as yellow liquid from the reaction of p-methyl acetophenone, yield 0.35g (15%) (E:Z = 98:2). IR (neat) v = 2950, 2910, 2850, 1650, 1550 cm\(^{-1}\). \(^1\)H NMR (300 MHz) E-isomer: \(\delta = 0.96 \text{ (t, J = 7.5Hz , 3H)}; 1.46 \text{ (sxt, J = 7.3Hz, 2H)}; 1.72 \text{ (qui, J = 7.3Hz, 2H)}; 2.40 \text{ (s, 3H)}; 2.86 \text{ (t, J = 7.3Hz, 2H)}; 6.06 \text{ (d, J = 7.8Hz, 1H)}; 7.20 - 7.33 (m, 4H); 9.29 (d, J = 7.8Hz, 1H) ppm; Z-isomer; \(\delta = 0.85 \text{ (t, J = 7.5Hz , 3H)}; 1.46 \text{ (sxt, J = 7.3Hz , 2H)}; 1.72 \text{ (qui, J = 7.3Hz, 2H)}; 2.40 \text{ (s, 3H)}; 2.60 \text{ (t, J = 7.3Hz, 2H)}; 6.35 \text{ (d, J = 7.8Hz, 1H)}; 7.20 - 7.33 (m, 4H); 10.25 \text{ (d, J = 7.8Hz, 1H)} ppm. \(^{13}\)C NMR \(\delta = 13.40, 21.15, 21.93, 29.54, 32.24, 122.05, 128.97, 129.15, 132.43, 140.24, 168.18, 189.56 ppm. GCMS (E -isomer) m/z = 234(M\(^+\)), 219, 177, 135, 115, GCMS (Z-isomer) m/z = 234(M\(^+\)), 219, 177, 135, 115.

\[ \text{1- Chloro-3-butylthio-5- chloro indene, 18} \]

Isolated as yellow liquid from the reaction of p-chloro acetophenone, yield 1.18g (50%). IR (neat) v = 2910, 2850, 1475, 1090 cm\(^{-1}\). \(^1\)H NMR (90MHz) \(\delta = 0.7 - \ldots\)
1.1 (m, 6H); 1.2 - 1.7 (m, 8H); 2.65 (t, J = 6Hz, 4H; 4.92 (d, J = 8Hz, 1H); 6.10 (d, J = 8Hz, 1H); 7.1 - 7.77 (m, 4H) ppm.

3-Chloro-3-(4-chlorophenyl)-2-propene, 19c
Isolated as colourless crystalline solid from the reaction of p-chloro acetophenone, yield 0.20g (10%). Mp. 91°C IR (KBr) ν = 1660, 1590, 1480, 1130 cm⁻¹. ¹H NMR (90 MHz) δ = 6.50 (d, J = 8Hz, 1H); 7.2 - 7.8 (m, 4H); 10.15 (d, J = 8Hz, 1H) ppm. EIMS m/z = 199 (M⁺ - 1), 165, 136, 101.

3,3-Dibutylthio-1-(4-methoxyphenyl)-1-propene, 13d
Isolated as yellow oil from the reaction of p-methoxyacetophenone, yield 1.17g (45%). (E:Z = 9:1) IR (neat) ν = 2950, 2910, 2820, 1645, 1590 cm⁻¹. ¹H NMR (90 MHz) E isomer δ = 0.95 (t, J = 7.2Hz, 3H); 1.30-1.90 (m, 4H); 2.95 (t, J = 7.3Hz, 2H); 3.90 (s, 3H); 6.90 (d, J = 8Hz, 2H); 7.4 (d, J = 8Hz, 2H); 9.30 (d, J = 7.8Hz, 1H) ppm; Z isomer δ = 0.90 (t, J = 7.3Hz, 3H); 1.30 - 1.90 (m, 4H); 2.55 (t, J = 7.3Hz, 2H); 3.90 (s, 3H); 6.35 (d, J = 7.2Hz, 2H); 7.4 (d, J = 8Hz, 2H); 10.25 (d, J = 7.8Hz, 1H) ppm. ¹³C NMR δ = 13.59, 22.15, 29.76, 32.53, 55.42, 113.89, 122.14, 130.99, 161.39, 168.20, 189.93 ppm. EIMS m/z = 250 (M⁺), 207, 193, 135, 94, 89.
55.33, 113.72, 124.75, 127.95, 129.42, 132.93, 160.30 ppm. GCMS m/z = 340 (M+ - Cl), 323, 269, 179, 145, 135.

1,3,3-Tributylthio-1-(4-methoxy phenyl)-1-propene, 6d
Isolated as yellow liquid from the reaction of p-methoxy acetophenone, yield 0.41g (10%). IR (neat) ν = 2900, 2850, 1600, 1495, 1450, 1240, 1170 cm⁻¹. ¹H NMR (90 MHz) δ = 0.6 - 1.1 (m, 9H); 1.2 - 1.9 (m, 12H); 2.2 - 2.75 (m, 6H); 3.8 (s, 3H); 5.23 (d, J = 10Hz, 1H); 5.80 (d, J = 10Hz, 1H); 6.85 (d, J = 7Hz, 2H); 7.3 (d, J = 7Hz, 2H) ppm. GCMS m/z = 323(M+ - SBu).

1-Chloro-2-formyl-3,4-dihydro naphthalene, 19e
Isolated as yellow liquid from the reaction of α-tetralone, yield 1.24g (65%). IR (neat) ν = 2910, 2830, 1655, 1590, 1550, 1440 cm⁻¹. ¹H NMR (90MHz) δ = 2.4 - 2.9 (m, 4H); 7.1 - 7.5 (m, 3H); 7.6 - 7.9 (m, 1H); 10.35 (s, 1H) ppm. ¹H NMR (300 MHz) δ = 2.61 - 2.66 (m, 2H); 2.82 - 2.87 (m, 2H) 7.21 - 7.36 (m, 3H) 7.84 - 7.87 (m, 1H); 10.38 (s, 1H) ppm. ¹³C NMR δ = 21.56, 27.02, 126.33, 127.09, 127.72, 131.40, 132.03, 138.98, 140.00 ppm. EIMS m/z = 192(M +), 161, 157, 129, 77.

3,4-Dibutyl thio-1-acetyl thiophene-1-propene, 4f
Isolated as yellow liquid from the reaction of acetyl thiophene, yield 1.3g (41%). IR (neat) ν = 2950, 2910, 2850, 1660, 1450, 1410 cm⁻¹. ¹H NMR (90MHz) δ = 0.6 -
1.1 (m, 6H); 1.2 - 1.8 (m, 8H); 2.3 - 2.9 (m, 4H); 3.31 (d, J = 6Hz, 2H); 4.40 (t, J = 6Hz, 1H); 6.9 - 7.6 (m, 3H) ppm.

**3,3-Dibutyl thio-1-acetyl thiophene-1-chloro-1-propene, 5f**

Isolated as yellow liquid from the reaction of acetyl thiophene, yield 0.46g (15%). IR (neat) v = 2950, 2910, 2850, 1660, 1450, 1410 cm⁻¹. ¹H NMR (90 MHz) δ = 0.6 - 1.1 (m, 9H); 1.2 - 1.8 (m, 12H) 2.3 - 2.9 (m, 6H); 5.25 (d, J = 8Hz, 1H); 6.05 (d, J = 8Hz, 1H); 6.9 - 7.3 (m, 3H) ppm.

**1,3,3-Tributyl thio-1-acetyl thiophene-2-propene, 6f**

Isolated as yellow liquid from the reaction of acetyl thiophene, yield 0.7g (19%). IR (neat) v = 2950, 2910, 2850, 1660, 1450, 1410 cm⁻¹. ¹H NMR (90MHz) δ = 0.6 - 1.1 (m, 9H); 1.2 - 1.8 (m, 12H) 2.3 - 2.9 (m, 6H); 5.25 (d, J = 8Hz, 1H) 6.05 (d, J = 8Hz, 1H); 6.9 - 7.3 (m, 3H) ppm. ¹³C NMR δ = 13.49, 13.56, 13.59, 21.90, 21.95, 30.99, 31.19, 31.74, 46.70, 124.68, 126.45, 127.35, 133.10, 140.57, 143.82 ppm. GCMS m/z = 299, 245, 189, 153, 121.

**3-Butylthiomethylene-2-chloro-1-cyclohexene carbaldehyde, 23**

Isolated as yellow liquid from the reaction of cyclohexanone, yield 1.95g (80%). IR (neat) v = 2950, 2910, 1850, 1660, 1550, 1240, 1190 cm⁻¹. ¹H NMR (90 MHz) δ = 0.9 (t, J = 6Hz, 3H); 1.2 - 2.0 (m, 6H); 2.5 - 2.8 (m, 4H); 2.95 (t, J = 6Hz, 2H); 7.4 (s, 1H); 10.3 (s, 1H) ppm. ¹³C NMR δ = 12.94, 19.87, 20.97, 23.57, 27.74, 31.89, 33.77, 127.78, 129.75, 135.66, 143.53, 189.75 ppm. EIMS m/z = 244, 122, 57.

**1-Butylthio-2-methyl pentene-3-one, 29**

Isolated as yellow liquid from the reaction of diethyl ketone, yield 1.3g (70%). IR (neat) v = 2950, 2910, 2870, 1650, 1560, 1280 cm⁻¹. ¹H NMR (90 MHz) δ =
1.00 (t, J = 6Hz, 3H); 1.15 (t, J = 6Hz, 3H); 1.3 - 1.7 (m, 4H); 1.9 (s, 3H); 2.55 (t, J = 6Hz, 2H); 2.85 (t, J = 6Hz, 2H); 7.35 (s, 1H) ppm. 13C NMR δ = 8.88, 13.18, 13.60, 21.58, 30.14, 32.63, 34.30, 132.36, 142.20, 197.71 ppm. ElMS m/z = 186, 129.

Reaction of 3-butylthio methylenic 2-chloro -1-cyclohexene carbaldehyde 24 with hydrazine hydrate : General procedure

The pentadiene aldehyde 23 2.44g (10mmol) was refluxed with hydrazine hydrate 500mg (10mmol) in methanol (50 ml) in presence of dicyclohexylamine 0.18g (1mmol) for six hours. After removing methanol under vacuum the residue was dissolved in chloroform (50 ml) and was washed with water (3x30 ml). Chloroform was evaporated off and the residue was column chromatographed on silicagel using a mixture of hexane and ethyl acetate (20 : 1).

3-Butylthiomethylene-2-chloro-1-cyclohexene carbaldehyde azine 24,

Isolated as a red solid from the reaction of 3-butylthiomethylenic 2-chloro-1-cyclohexene carbaldehyde, mp = 131°C. Yield 3.14g (85%). IR (KBr) ν = 2900, 2850, 1570, 1540 cm⁻¹. 1HNMR (300 MHz) δ = 0.95 (t, J = 6Hz, 6H); 1.45 (sxt, J = 6Hz, 2H); 1.69 (q, J = 6Hz, 2H); 1.81 (q, J = 6Hz, 2H); 2.47 (t, J = 6Hz, 2H); 2.68 (t, J = 6Hz, 2H); 2.84 (t, J = 6Hz, 2H); 6.95 (s, 2H); 8.85 (s, 2H) ppm. ElMS m/z = 484, 413, 363, 244, 181, 138, 106, 56.

Reaction of ketones with butanethiol in the presence of boron trifluoride etherate, chloroform and subsequently with the Vilsmeier reagent : General Procedure

To a solution of ketone (10 mmol) in chloroform boron trifluoride etherate (1.2 ml, 10 mmol) was added followed by butanethiol (1ml, 10 mmol). The mixture was stirred for two hours at room temperature and then the Vilsmeier reagent prepared
from POCl₃ (2.9 ml, 30 mmol) and DMF (27 ml, 0.3 mol) was added slowly (over 15 minutes). The reaction mixture was stirred at room temperature for a further 12 hours. The mixture was then added to cold saturated K₂CO₃ solution (200 ml) and extracted with diethyl ether (3 x 50 ml) dried (Na₂SO₄) and evaporated. The residue was column chromatographed on silica gel using a mixture (50:1) of hexane and ethyl acetate as eluent.

3-Butylthio-3-phenyl-1-propenal, 13a

Isolated as yellow oil from the reaction of acetophenone, yield 1.65 g (75%). IR (neat) ν = 2950, 2910, 2850, 1655, 1555 cm⁻¹. ¹H NMR (300 MHz) E-isomer; δ = 0.95 (t, J = 7.3 Hz, 3H); 1.46 (sxt, J = 7.3 Hz, 2H); 1.72 (qui, J = 7.3 Hz, 2H) 2.87 (t, J = 7.3 Hz, 2H); 6.07 (d, J = 7.8 Hz, 1H); 7.44 (s, 5H); 9.45 (d, J = 7.8 Hz, 1H) ppm. ¹³C NMR δ = 13.55, 22.06, 29.61, 32.33, 122.33, 128.39, 129.31, 130.03, 135.43, 167.89, 189.36 ppm. ElMS m/z = 220 (M⁺), 163, 112, 102, 91, 77.

3-Butylthio-3-(4-methyl phenyl)-2-propenal, 13b

Isolated as yellow oil from the reaction of 4-methyl acetophenone, yield 1.53 g (65%). (E:Z = 99:1). Spectral data described earlier.

3-Butylthio-3-(4-chloro phenyl)-2-propenal, 13c

Isolated as yellow oil from the reaction of 4-chloro acetophenone, yield 1.79 g (70%). (E:Z = 88:12). IR (neat) ν = 2950, 2910, 2850, 1655, 1550 cm⁻¹. ¹H NMR (90 MHz) E isomer; δ = 0.95 (t, J = 7.3 Hz, 3H); 1.25 - 1.90 (m, 4H); 2.85 (t, J = 7.3 Hz, 2H); 6.05 (d, J = 7.8 Hz, 1H); 7.2 - 7.6 (m, 4H); 9.20 (d, J = 7.8 Hz, 1H) ppm; Z isomer; δ = 0.90 (t, J = 7.3 Hz, 3H); 1.25 - 1.90 (m, 4H); 2.85 (t, J = 7.3 Hz, 2H); 6.20 (d, J = 7.8 Hz, 1H); 7.20 - 7.90 (m, 4H); 10.20 (d, J = 7.8 Hz, 1H) ppm. ¹³C NMR δ = 13.42, 21.98, 29.56, 32.43, 122.68, 128.67, 130.55, 133.84,
136.22, 166.36, 188.98 ppm. GCMS (E isomer) m/z = 254, 197, 155, 136, 101, 75, 57. (Z isomer) m/z = 254, 197, 155, 136, 101, 75, 57.

3-Butylthio-3-(4-methoxy phenyl)-2-propenal, 13d
Isolated as yellow oil from the reaction of 4-methoxy acetophenone, yield 1.88g (75%). (E:Z = 82:18). Spectral data described earlier.

3-Chloro-3-(4-chlorophenyl)-2-propene-1-al, 19c
Isolated as colourless crystalline solid from the reaction of 4-chloro acetophenone, yield 0.30g (15%). Spectral data described earlier.

3-Acetylthiophene-3-buty1thio-2-propene-1-al, 13f
Isolated as yellow liquid from the reaction of acetyl thiophene, yield 1.69g (75%). IR (neat) ν = 2900, 2850, 1660, 1585, 1415 cm⁻¹. ¹H NMR (60 MHz) E isomer; δ = 0.60 - 1.10 (m, 3H); 1.10 - 1.80 (m, 4H); 2.40 - 2.90 (m, 2H); 5.82 (d, J = 8Hz, 1H); 6.80 - 7.40 (m, 3H); 9.35 (d, J = 8Hz, 1H); Z isomer; δ = 0.60 - 1.10 (m, 3H); 1.11 - 1.80 (m, 4H); 2.40 - 2.90 (m, 2H); 6.22 (d, J = 8Hz, 1H); 6.80 - 7.40 (m, 3H); 9.87 (d, J = 8Hz, 1H) ppm. ElMS m/z = 226, 169, 137, 109, 97.

1-Butylthio-3,4-dihydro naphthalene, 21
Isolated as yellow liquid from the reaction of α-tetralone, yield 0.87g (40%). Spectral data described earlier.

1- Chloro-2-formyl-3,4-dihydro naphthalene, 15e
Isolated as yellow liquid from the reaction of α-tetralone, yield 0.86g (45%). Spectral data described earlier.
**1-Butylthio-2-methyl pentene-3-one, 29**

Isolated as yellow liquid from the reaction of 2-pentanone, yield 1.48g (80%). Spectral data described earlier.

**2-Butylthiocyclohexene carbaldehyde, 30**

Isolated as yellow liquid from the reaction of cyclohexanone, yield 1.50g (70%). IR (neat) \( \nu = 2910, 2850, 1660, 1570, 1450, 1250 \text{ cm}^{-1} \). \( ^1\text{H NMR (90MHz)} \) \( \delta = 0.9 \) (t, \( J = 6\text{Hz}, 8\text{H} \)); 1.4 - 1.9 (m, 8H); 2.2 - 2.6 (m, 4H); 2.8 (t, \( J = 6\text{Hz}, 2\text{H} \)); 10.3 (s, 1H) ppm. \( ^{13}\text{C NMR} \) \( \delta = 13.48, 21.30, 21.75, 22.97, 23.98, 30.67, 31.41, 31.86, 137.00, 155.88, 193.12 \) ppm. GCMS \( m/z = 198, 141, 79 \).

**3-Butylthiomethylene 2-chloro-1-cyclohexene carbaldehyde, 23**

Isolated as yellow liquid from the reaction of cyclohexanone, yield 0.11g (5%). Spectral data described earlier.

**Reaction of ketones with Vilsmeier reagent followed by quenching with thiol:**

**General procedure**

To a solution of substituted acetophenone (10 mmol) in chloroform boron trifluoride etherate (1.2 ml, 10 mmol) was added followed by the Vilsmeier reagent prepared from POCl\(_3\) (1.9 ml, 20 mmol) and DMF (15ml). The reaction mixture was stirred at room temperature for 12h and butanethiol (2.1ml, 20 mmol) was added and the mixture was stirred for another 12h. The mixture was then added to cold saturated K\(_2\)CO\(_3\) solution (200 ml) and extracted with diethyl ether (3x50ml) dried (Na\(_2\)SO\(_4\)) and evaporated. The residue was column chromatographed on silicagel using a mixture (20:1) of hexane and ethyl acetate as eluent.

**3-Butylthio-3-phenyl-1-propen, 13a**
Isolated as yellow oil from the reaction of acetophenone, yield 1.87g (85%). (E:Z = 95:5). IR (neat) ν = 2950, 2910, 2850, 1655, 1555 cm\(^{-1}\). \(^1\)H NMR (300 MHz) E-isomer; δ = 0.95 (t, J = 7.3 Hz, 3H); 1.46 (sxt, J = 7.3 Hz, 2H); 1.72 (qui, J = 7.3 Hz, 2H) 2.87 (t, J = 7.3 Hz, 2H); 6.07 (d, 1H, J = 7.8 Hz); 7.44 (s, 5H); 9.45 (d, J = 7.8 Hz, 1H) ppm; Z-isomer; δ = 0.85 (t, J = 7.5 Hz, 3H); 1.46 (sxt, J = 7.3 Hz, 2H); 1.72 (qui, J = 7.3 Hz, 2H) 2.60 (t, J = 7.3 Hz, 2H); 6.35 (d, 1H, J = 7.8 Hz); 7.44 (s, 5H); 10.05 (d, J = 7.8 Hz, 1H) ppm. \(^1\)C NMR δ = 13.55, 22.06, 29.61, 32.33, 122.33, 128.39, 129.31, 130.03, 135.43, 167.89, 189.36 ppm. EIMS m/z 220(M\(^+\)), 163, 121, 102, 91, 77.

3-Butylthio-3-(4-methylphenyl)-2-propen-1-al, 13b
Isolated as yellow oil from the reaction of p-methyl acetophenone, yield 1.88g (80%). (E:Z = 98:2). Spectral data described earlier.

3-Butylthio-3-(4-chlorophenyl)-2-propenal, 13c
Isolated as yellow oil from the reaction of p-chloro acetophenone, yield 2.04g (80%). (E:Z = 93:7). Spectral data described earlier.

3-Butylthio-3-(4-methoxy phenyl)-2-propen-1-al, 13d
Isolated as yellow oil from the reaction of p-methoxy acetophenone, yield 1.88g (75%). (E:Z = 80:20). Spectral data described earlier.

3-Thienyl-3,3-bis-(butylthio)-propan-1-al, 31
Isolated as yellow liquid from the reaction of acetyl thiophene, yield 1.89g (60%). (E:Z = 80:20). IR (neat) ν = 2950, 2900, 2850, 1715, 1660 cm\(^{-1}\). \(^1\)H NMR (90 MHz) δ = 0.08-1.10 (m, 6H); 1.4 - 1.8 (m,4H); 2.5 - 2.8 (m, 4H); 3.2 (d, J = 2Hz,2H); 6.9 - 7.5 (m,3H); 9.7 (t, J = 2Hz, 1H) ppm. \(^1\)C NMR δ = 13.63, 22.25.
3.3-Bis-(butylthio)-1-chloro-1-thienyl-prop-1-ene, 32
Isolated as dark brown liquid from the reaction of acetyl thiophene, yield 0.7g (22%).
IR (neat) ν = 2900, 1450, 1420, 1225 cm⁻¹. ¹H NMR (90 MHz) δ = 0.06 - 1.10 (m, 6H); 1.2 - 1.8 (m, 8H); 2.3 - 2.9 (m, 4H); 4.88 (d, J = 8Hz, 2H); 6.05 (d, J = 8Hz, 1H); 6.9 - 7.3 (m, 3H) ppm. ¹³C NMR δ = 13.49, 13.56, 13.59, 21.90, 21.95, 30.99, 31.19, 31.74, 46.70, 124.68, 126.45, 127.35, 133.10, 140.57, 143.82 ppm. GCMS m/z 299, 245, 189, 153, 121.

1-Chloro-3,4-dihydro-2-naphthaldehyde dibutylthioacetal, 33
Isolated as brown liquid from the reaction of α-tetralone, yield 2.5g (71%). IR (neat) ν = 2950, 2910, 2850, 1600, 1450, 1260 cm⁻¹. ¹H NMR (300 MHz) δ = 1.0 (t, 6H); 1.40 (q, 4H); 2.57 - 2.64 (m, 6H); 2.79 - 2.82 (m, 2H); 5.44 (s, 1H); 7.15 - 7.80 (m, 4H) ppm. ¹³C NMR 13.65, 22.02, 24.90, 28.13, 31.49, 31.67, 50.75, 124.97, 126.55, 126.92, 127.56, 132.50, 134.69, 136.26, 138.72 ppm. EI/MS m/z 265 (M⁺ - SBu); 191, 129, 57.

1-Chloro-2-formyl-3,4-dihydro naphthalene, 19e
Isolated as yellow liquid from the reaction of α-tetralone, yield 0.19g (10%). Spectral data described earlier.

1-Butylthiomethylene cyclopentanaldehyde dithioacetal, 38
Isolated as yellow liquid from the reaction of cyclopentanone, yield 0.81g (20%). IR (neat) ν = 2950, 2910, 2850, 1710, 1455, 1270 cm⁻¹. ¹H NMR (90MHz) δ = 0.8 - 1.1 (m, 9H); 1.2 - 1.6 (m, 12H); 1.7 - 2.0 (m, 6H) 6.0 (s, 1H) ppm. ¹³C NMR δ =

1-Butylthio cyclopentenaldehyde dithioacetal, 39
Isolated as brown liquid from the reaction of cyclopentanone, yield 0.85g (23%). IR (neat) ν = 2950, 2910, 2850, 1710, 1455, 1270 cm⁻¹. ¹H NMR (90 MHz) δ = 0.8 - 1.1 (m, 9H); 1.2 - 1.6 (m, 12H); 1.7 - 2.0 (m, 6H); 2.4 - 2.8 (m, 6H); 4.9 (s, 1H) ppm. ¹³C NMR δ = 13.43, 13.63, 13.69, 21.58, 22.24, 22.33, 30.31, 31.48, 38.78, 42.57, 46.61, 46.69, 128.53, 141.10 ppm.

1,1-Dibutylthio-2-chloro cyclopentene, 40
Isolated as yellow liquid from the reaction of cyclopentanone, yield 1.3g (46%). IR (neat) ν = 2950, 2900, 2850, 1570, 1460 cm⁻¹. ¹H NMR (90 MHz) δ = 0.75 - 1.1 (m, 6H); 1.2 - 1.9 (m, 8H); 1.95 - 2.25 (m, 2H); 2.4 - 3.0 (m, 8H); 4.95 (s, 1H) ppm. ElMS m/z = 302, 290, 248, 236, 202, 178, 122, 58.

1,5-dibutylthio-2-(1,1dibutylthiometathane)-1,4-pentadiene-3-one, 42
Isolated as yellow oil from the reaction of acetone; yield 2.90g (65%). IR (neat) ν = 2950, 2910, 2850, 1650, 1530, 1450 cm⁻¹. ¹H NMR (90 MHz) δ = 0.70 - 1.05 (m, 6H); 1.15 - 1.85 (m, 16H); 2.31 - 3.00 (m, 8H); 5.25 (s, 1H); 5.85 (d, J = 6Hz, 1H); 7.21(s, 1H); 7.22 (d, J = 4Hz, 1H) ppm. ElMS m/z = 359 ( M⁺ - SBu), 259, 203, 191, 145, 57.

3-Chloro-1,1-dibutylthio-2-methyl-2-butene, 43
Isolated as yellow oil from the reaction of 2-butanone, yield 2.10g (75%). IR (neat) ν = 2959, 2910, 2850, 1645, 1460 cm⁻¹. ¹H NMR (90 MHz) δ = 0.7 - 1.05 (m, 6H); 1.15 - 1.70 (m, 8H); 1.83 and 1.93 ( s, 1 : 3, 3H); 2.18 (s, 3H); 2.64 (t, J = 8Hz,
2H); 4.89 and 5.33 (s, 3:1, 1H); ppm. $^{13}$C NMR (major isomer) $\delta =$ 13.63, 22.36, 31.71, 32.09, 51.67, 125.24, 129.13 ppm. GCMS m/z = 280 (M+), 191; 135; 99; 57 EIMS m/z = 190 (M+ - BuSH), 134, 98, 57.

1-Butylthio-2-ethyl-1-hexene-3-one, 45
Isolated as yellow oil from the reaction of 4-heptanone, yield 1.3g (61%). IR(neat) v = 2950, 2910, 2850, 1670, 1610, 1450 cm$^{-1}$. $^{1}$H NMR (90 MHz) $\delta =$ 0.7 - 1.10 (m, 9H); 1.15 - 1.95 (m, 6H); 2.15 - 2.75 (m, 4H); 2.9 (t, J = 8Hz, 1H); 7.9 (s, 1H) ppm. GCMS m/z = 215, 157(100%), 71.

1-Butylthio-2-dibutylthiomethane-1-heptene-3-one, 46
Isolated as yellow liquid from the reaction of 2-hexanone, yield 1.2g (32%). IR (neat) v = 2950, 2910, 2850, 1670, 1610, 1455 cm$^{-1}$. $^{1}$H NMR (300 MHz) $\delta =$ 0.80 - 1.15 (m, 12H); 1.20 - 1.85 (m, 16H); 2.15 - 3.00 (m, 8H); 4.90 and 5.25 (s, 1:9, 1H); 7.25 and 7.53 (s, 9:1, 1H) ppm. GCMS m/z = 301(100%), 127, 85, 57.

2-Butylthio-2-hexene-3-carbaldehyde, 47
Isolated as yellow liquid from the reaction of 2-hexanone, yield 1.00g (50%). IR (neat) v = 2950, 2910, 2850, 1670, 1610, 1455 cm$^{-1}$. $^{1}$H NMR (90 MHz) $\delta =$ 0.80 - 1.15 (m, 12H); 1.20 - 1.85 (m, 16H); 2.15 - 3.00 (m, 8H); 9.90 (s, 1H) ppm. GCMS m/z = 200, 143(100%), 81, 67, 59.

3-chloro-5-N,N-dimethylamino-4-formyl-2-phenoxy-1,3-pentadienal, 50
Isolated as yellow crystalline solid from the reaction of phenoxy propanone, mp. = 135°C, yield = 1.50g (65%). IR (KBr) v = 3420 (br), 1690, 1588 cm$^{-1}$. $^{1}$H NMR (90 MHz) $\delta =$ 3.3 (s, 6H); 6.95 - 7.35 (m, 6H); 9.05 (s, 1H); 9.45 (s, 1H) ppm. $^{13}$C
NMR 47.60, 115.213, 122.531, 129.658, 156.673, 160.114, 184.366, 185.746 ppm. EIMS m/z = 303 (M+), 249, 186 (100%) 157, 94, 77, 43.

Reaction of ketones with Vilsmeier reagent followed by quenching with mercaptoethanol: General procedure

To a solution of substituted acetophenone (10 mmol) in chloroform boron trifluoride etherate (1.2 ml, 10 mmol) was added followed by the Vilsmeier reagent prepared from POCI₃ (1.9 ml, 20 mmol) and DMF (15 ml). The reaction mixture was stirred at room temperature for 12h and mercaptoethanol (1.4 ml, 20 mmol) was added and the mixture was stirred for another 12h. The mixture was then added to cold saturated K₂CO₃ solution (200 ml) and extracted with diethylether (3x50 ml) dried (Na₂SO₄) and evaporated. The residue was column chromatographed on silicagel using a mixture (20:1) of hexane and ethyl acetate as eluent.

O. S-acetal of chloraldehyde. 51

Isolated as yellow liquid from the reaction of acetophenone, yield 1.24 g (55%). IR (neat) ν = 2820, 1600, 1440, 1265 cm⁻¹. ¹H NMR (90 MHz) δ = 1.25 (t, J = 6 Hz, 2H); 3.15 (t, J = 6 Hz, 2H); 6.30 (d, J = 8 Hz, 1H); 6.65 (d, J = 8 Hz, 1H); 7.25-8.05 (m, 5H) ppm. GCMS m/z = 226, 191, 165, 138, 103.

3-Chloro3-phenyl-1-propen-1-ol, 19a

Isolated as yellow liquid from the reaction of acetophenone, yield 0.5 g (29%). IR ν = 2850, 1667, 1595, 1125 cm⁻¹. ¹H NMR (90 MHz) δ = 6.71 (d, J = 6 Hz, 1H); 7.3-8.1 (m, 5H); 10.25 (d, 1H) ppm. ¹³C NMR δ = 18.546, 29.703, 128.46, 128.683, 130.120, 133.316, 134.143, 138.205, 163.698 ppm. EIMS m/z = 233, 165, 131, 105, 77, 51.
3-Chloro-3-(4-methyl phenyl)-1-propenal. 19b
Isolated as yellow liquid from the reaction of 4-methyl acetophenone, yield 1.2g (67%). IR ν = 2850, 1665, 1595, 1500, 1325, 1280, 1120 cm⁻¹. 1H NMR (90 MHz) δ = 2.35 (s, 3H); 6.57 (d, J = 1Hz, 1H); 7.40 (dd, 4H) 10.15 (d, J = 1Hz, 1H) ppm.

3-Chloro-3-(4-chloro phenyl)-2-propene-1-al. 19c
Isolated as colourless crystalline solid from the reaction of 4-chloro acetophenone, yield 1.50g (75%). Spectral data described earlier.

2-Chloro-3-(1-chloro-2-ethylthio)-methylene-1-cyclohexen-1-al. 52
Isolated as yellow needle type crystals from the reaction of cyclohexanone, Mp = 89ºC, yield 1.8g (71%). IR ν = 2910, 2850, 1650, 1555, 1215 cm⁻¹. 1H NMR (90 MHz) δ = 1.65 (q, 6Hz , 2H); 2.4 (m, 4H); 3.2 (t, J=7Hz, 2H); 3.65 (t, J=7Hz, 2H); 7.1(s, 1H); 10.2 (s, 1H) ppm. 13C NMR δ = 20.326, 24.132, 28.325, 36.403, 43.067, 130.189, 131.018, 133.553, 144.030, 191.249 ppm. EIMS m/z = 249, 214, 186, 124, 91, 45.

1,3,5-Triphenyl benzene. 53a
Isolated as white crystalline solid from the reaction of acetophenone, Mp = 172ºC, Lit. Mp = 172-174ºC, yield 1.8g (58%). IR (KBr) ν = 3010, 2910, 1585, 1440, 1220 cm⁻¹. 1H NMR (90 MHz) δ = 7.3 - 7.9 (m, 18H) ppm. 13C NMR δ = 125.17, 127.34, 127.53, 128.83, 141.12, 142.33 ppm. GCMS m/z = 306, 289, 228.

1,3,5-tri(4-tolyl)benzene. 53b
Isolated as white crystalline solid from the reaction of p-methyl acetophenone, Mp = 179ºC, yield 2.26g (65%). IR (KBr) ν = 3000, 2900, 2850, 1580, 1500, 1420 cm⁻¹. 1H NMR (90 MHz) δ = 2.5 (s, 9H); 7.3 (d, J = 9Hz, 6H); 7.8 (d, J = 9Hz, 6H); 8.3
(s, 3H) ppm. $^{13}$C NMR $\delta = 21.63, 129.27, 130.26, 133.57, 133.84, 138.40, 144.13$ ppm. EIMS m/z = 315, 254, 164. GCMS m/z = 348, 91.

1,3,5-Tri(2-naphthyl) benzene. 54

Isolated as white crystalline solid from the reaction of acetyl naphthalene. Mp = 212°C, yield 2.8g (62%). IR (KBr) $\nu = 3250, 3050, 2910, 1590, 1500$ cm$^{-1}$. $^1$H NMR (90 MHz) $\delta = 7.30 - 7.69$ (m, 6H); 7.85 - 8.05 (m, 15H); 8.15 (s, 3H) ppm. $^{13}$C NMR $\delta = 125.72, 125.75, 126.13, 126.43, 127.72, 128.27, 128.62, 132.79, 133.69, 138.44, 142.46$ ppm. EIMS m/z = 244, 213, 155, 127, 77, 57.

3.5 References


