CHAPTER V

NUCLEOPHILIC ADDITION STUDIES ON α-OXOKETENE O,S-ACETALS.

V.1 INTRODUCTION

The reduction of α,β-unsaturated enones have been extensively carried out by using metal hydride complexes to afford the corresponding allyl alcohols. The substrate enones particularly i-propoxymethylene ketones of general formula 1a (scheme 1) have been known to undergo sodium borohydride reduction to give a mixture of products 2 and 3 in 68% and 21% yields respectively. The formation of 3 involves sequential 1,4-followed by 1,2-reduction. Thus the regioselective reduction of ketone alone could not be satisfactorily achieved when the alkoxy group was present in
Scheme 1

1,4-reduction
X = 0; R = Pr

1,2-reduction
X = 0; R = Pr

X = S; R = Bu

10, X = 0; R = Pr

D, X = S; R = Bu

\[ \begin{align*}
\text{OPr}^+ & \quad \text{OPr}^+ & \quad \text{SBun} \\
\text{OH} & \quad \text{OH} & \quad \text{OH}
\end{align*} \]
the enone system. However, Marshall and co-workers\textsuperscript{2,3} were the first to observe that the regioselective reduction could be achieved if the alkoxy group replaced by n-butylmercapto group 1b by reacting the corresponding hydroxy derivative with n-butylmercaptan in the presence of p-toluenesulphonic acid with continuous removal of water. The n-butylthio methylene ketone 1b thus obtained underwent exclusive 1,2-reduction with sodium borohydride in alcohol to afford the corresponding allyl alcohol 4 in 81% yield. The allyl alcohol was then hydrolysed to afford the corresponding enealdehyde which is an important intermediate in natural product synthesis.

Thus Marshall and co-workers\textsuperscript{4} successfully extended this reaction to prepare the aldehyde 6 from the corresponding n-butylthiomethylene ketone 5. Similarly the phenylthio methylene ketone 7 on reaction with lithium aluminium hydride in ether underwent 1,2-reduction followed by hydrolytic cleavage to give $\alpha,\beta$-unsaturated ketone 8 in good yield\textsuperscript{4} (scheme 2).

Similarly Marshall and co-workers\textsuperscript{5} successfully applied this new transformation in the synthesis of natural product $\beta$-valerone 11. The mercaptomethylene ketone 9 after exclusive 1,2-reduction with sodium borohydride to the corresponding allyl alcohol which was subjected to mercuric chloride assisted hydrolysis to give the corresponding ene aldehyde 10 in high yield. This was then converted into $\beta$-valerone 11 through several steps (scheme 2).
Scheme 2

1. NaBH₄ / 0.1N aq. NaOH
   MeOH, 25°C, 12 h
2. EtOH, 10% HCl, 24 h

1. NaBH₄ / MeOH
2. HgCl₂ / H₂O

1. LiAlH₄ / Et₂O
   25°C, 2 h, reflux
2. 10% HCl

1. NaBH₄ / 0.1N aq. NaOH
   MeOH, 25°C, 12 h
2. EtOH, 10% HCl, 24 h

Scheme - 2
The α-oxoketene dithioacetals 12 (scheme 3) were first reduced with sodium borohydride in methanol by Thuillier and co-workers\(^6\) to afford the corresponding allyl alcohols 13 in high yields. The allyl alcohols thus obtained when subjected to acid assisted hydrolytic cleavage a mixture of products 14, 15 and 16 were formed. Thuillier and co-workers also observed some interesting rearrangements when they reduced α-phenyloxoketene dithioacetal 17 to the corresponding alcohol 18 (scheme 3). The allyl alcohol 18 in the presence of acid underwent rearrangement involving hydrolytic cleavage either to give 21 or the sulfur stabilized carbonium ion 23 which acted as Micheal acceptor to give the adduct 20. The mechanism proposed for the formation of products 20 and 21 from 17 is depicted in scheme 4.

Myrboh, Ila and Junjappa\(^7\) in this laboratory repeated the reduction studies on α-oxoketene dithioacetals reported by Thuillier and co-workers\(^6\) using sodium borohydride in methanol to get identically high yields of the corresponding alcohols 26 (scheme 5). These alcohols were shown to undergo a facile borontrifluoride-etherate assisted methanolysis to give the corresponding eneesters 27 exclusively in high yields. Also the allyl alcohols in the presence of borontrifluoride-etherate and water underwent hydrolytic cleavage to afford the thiolesters 28 exclusively. It may be noted here that the Thuillier's group employed acids such as p-toluene sulphonyl acid and aqueous sulphuric acid and thus could not get a single product of which the ene ester 27 was
**Scheme 3**

1. **Reagents and Conditions:**
   - Reaction 12: 
     - Reagents: NaBH₄, MeOH
     - Products: R¹⁻CH⁻C=CSMe, R¹⁻CH⁻C-COSMe
   - Reaction 13: 
     - Reagents: H
   - Reaction 14: 
     - Reagents: R²⁻CH⁻C=CSMe
     - Products: R¹⁻CH⁻C-COSMe
   - Reaction 15: 
     - Reagents: R²⁻CH⁻C=CSMe
     - Products: R¹⁻CH⁻C-COSMe
   - Reaction 16: 
     - Reagents: R²⁻CH⁻C=CSMe
     - Products: R¹⁻CH⁻C-COSMe

2. **Compounds:**
   - R¹ = Me, C₆H₅
   - R² = H; R¹ = C₆H₅, C₆H₅CH₂, Me; R² = C₆H₅, CH₃
   - R¹ = R² = -(CH₂)₄-
Scheme - 4
\[
\begin{align*}
\text{R}^1 &= \text{C}_6\text{H}_5; \ 4-\text{Cl C}_6\text{H}_4; \\
&\quad \text{4-EtO C}_6\text{H}_4; \ \text{R}^2 = \text{H} \\
\text{R}^1 &= \text{C}_6\text{H}_5; \ \text{R}^2 = \text{Me, Et, n-Pr} \\
\text{R}^1 &= \text{Me}; \ \text{R}^2 = \text{H, Me, n-Bu, n-C}_5\text{H}_{11} \\
\text{R}^1 &= \text{R}^2 = -(\text{CH}_2)_3 -; -(\text{CH}_2)_4 -; \\
\end{align*}
\]

Scheme - 5
not the only product. They obtained only the thiolesters 28 as one of the mixtures along with other rearranged products. The solvolytic clean reaction to afford the eneesters 27 in exclusive trans geometry was explained through the cyclic transition state 29 which led to the stereoselective methanolysis of the mercapto group to afford 27. The reaction was found to be of general application for the synthesis of a variety of eneesters in high yields. Thus a new method was developed for the conversion of active methylene ketones to the corresponding eneesters through α-oxoketene dithioacetals. The acetophenones and higher homologs of acetophenones were conveniently converted in to corresponding trans cinnamates and β-substituted cinnamates in good yields respectively. This method was extended to the preparation of enealdehydes also. Thus the oxoketene dithioacetal 32 derived from dimethoxytetralone 31 could not only be transformed in to the corresponding ene esters 34 but also to enealdehyde 36 (scheme 6). The oxoketene dithioacetal 32 was first partially dethiomethylated with sodium borohydride in the presence of nickel chloride to afford the corresponding methylthiomethylene ketone 35. This on reduction with sodium borohydride in methanol and subsequent hydrolysis gave the corresponding enealdehyde 36 which is used in the total synthesis of antibiotic anthracyclinones.

The partial dethiomethylation of α-oxoketene dithioacetals 37 was developed in our laboratory using sodium borohydride in
Scheme 6
the presence of nickel chloride to give the corresponding methylthiomethylene ketones as a mixture of cis and trans isomers and in moderate to good yields (scheme 7). The reducing agent in this reaction was proposed to be nickel boride derived from the reaction of sodium borohydride and nickel chloride. The reduction was though selective but afforded the dethiomethylated products in moderate yields. In the case of α-oxoketene dithioacetals derived from aliphatic ketones yields were not satisfactory.

However, subsequently some important modifications were made in the reduction of α-oxoketene dithioacetals of general formula which underwent sodium borohydride reduction in the presence of acetic acid to afford the corresponding β-oxodithioacetals in high yields and no 1,2-reduction products were detected in the reaction mixture. The sodium borohydride in acetic acid reduction was originally thought of going through the formation of the corresponding borane intermediate which by regioselective 1,4-reduction to afford 41 was ruled out. However, it was demonstrated that the borane was not the intermediate reducing agent under these reaction conditions since the borane complex itself yielded only poor yield of 41 when it was used for reduction of 40. However, the mechanism of this regioselective reduction was explained on the basis of hard soft affinity inversion. Thus the protonated in the presence of acetic acid underwent initial protonation on oxygen which was stabilized by mercapto double bond with a cation residing on the carbon atom adjacent to two thiomethyl groups. The cation which is
\[ \text{NiCl}_2 \cdot 6\text{H}_2\text{O} \rightarrow \text{NaBH}_4 / \text{EtOH} \]

**Scheme - 7**

\[ R^1 = \text{C}_6\text{H}_5, 4-\text{MeC}_6\text{H}_4, 4-\text{ClC}_6\text{H}_4, 4-\text{MeOC}_6\text{H}_4, \text{Me} ; R^2 = \text{H} ; R^3 = \text{Me, Et} \]

\[ R^1 = \text{C}_6\text{H}_5, \text{Me} ; R^2 = \text{Me}, \text{Et}, \text{n-C}_3\text{H}_7, R^3 = \text{Me} \]

\[ R^1 = R^2 = -(\text{CH}_2)_3 - , -(\text{CH}_2)_4 - \]

**Scheme - 7**
a hard electrophilic centre was then proposed to be attacked by the hard hydride directly from sodium borohydride. The electrophilic hydride from sodium cyanoborohydride in acetic acid also reduces 40 in the 1,4-fashion gave the probable intermediate β-oxodithioacetals which invariably underwent elimination to afford the corresponding methylthiomethylene ketones 42 in good yields (scheme 8).

Gammill and co-workers\textsuperscript{11} had similarly used diisobutyl aluminium hydride in the presence of triethylamine to reduce the α-oxoketene dithioacetals 43 to afford the corresponding β-oxodithioacetals 44. However, they also found that when oxoketene dithioacetal 45 treated with 2 equivalent of 9-BBN over reduced product 46 was formed in 83% yield (scheme 9). The same dithioacetal 45 in catechol borane gave a mixture of β-oxodithioacetal 47 in 56% yield and the over reduction product 46 in 10% yield (scheme 9).

Gammill and co-workers\textsuperscript{12} further reported that the α-oxoketene dithioacetals undergo facile lithium aluminium hydride reduction to afford the corresponding highly diastereoselective β-hydroxy dithioacetals 49. The mechanism governing these reduction is depicted in Scheme 10. The initial 1,2-adduct 50 undergoes the formation of organo aluminium complex 51 which on subsequent intramolecular hydroalumination diastereoselectively to afford the corresponding β-hydroxy dithioacetal 49. This was the first example of open chain enones to have undergone diastereoselective reduction with lithium aluminium hydride.
\[ \text{Scheme - 8} \]

Na BH₄ / AcOH  \[ 
\begin{array}{c}
\text{R₁} \quad \text{R₂} \\
\text{SMe} \quad \text{SMe}
\end{array} \]

Na BH₃CN / AcOH  \[ 
\begin{array}{c}
\text{R₁} \quad \text{R₂} \\
\text{H} \quad \text{SMe}
\end{array} \]

\[ 41 \quad 42 \]

\[ \text{R₁} \quad \text{R₂} \\
\text{O} \quad \text{SMe} \quad \text{SMe}
\]

\[ 40 \]
Scheme 9
Scheme 10
Similarly the cyclic oxoketene dithoacetal 52 also gave the corresponding β-hydroxy dithioacetal 53 which followed the same mechanism as described above (scheme 10).

Recently the α-oxoketene O,O-acetals are reduced by borane to afford the corresponding 1,4-reduction product 56\textsuperscript{13,14}. The reduction was established when carried out in presence of D\textsubscript{2}O yielding the corresponding α-deuterated β-oxoacetal 57. The cyclciketene acetal 58 was also reduced in the presence of disiamylborane to the corresponding dihydroketone 59 in 50% yield. The β-oxodithioacetals 60 and 62 however gave β-hydroxyacetals 61 and 63 in 89% and 37% yield respectively when reduced with sodium borohydride in methanol (scheme 11).

V.2 RESULTS AND DISCUSSION

As illustrated in the preceding brief review, the alkoxyethylene ketones show lack of regioselectivity in the sodium borohydride reduction, since both 1,4- and 1,2-reduction products were formed. However, when the corresponding n-butylmercaptomethylene ketones were reduced with sodium borohydride, the corresponding 1,2-adduct allyl alcohols were found to be the sole products. Similar was the situation when the S,S-acetals were reduced with sodium borohydride. However, the α-oxoketene dithioacetals yielded 1,4-reduction products in the presence of electrophilic reducing agents like sodium cyanoborohydride, DIBAL, 9-BBN, and catechol borane or with sodium borohydride in acetic acid. The oxoketene cyclic O,O-acetals were known to be
Scheme 11

H5C6

54

\( \text{H}_3\text{B; THF} \quad \text{or} \quad \text{Thexyl borane; disiamyl borane; Catechol borane} \)

\[ \begin{align*}
55 \quad \text{Sat. NaHCO}_3 & \rightarrow 56 \\
& \quad \text{D}_2\text{O / 18 hr} \\
& \quad \text{Disiamyl borane / THF, -78 °C} \\
58 & \rightarrow 59 \quad (50\%) \\
60 & \rightarrow 61 \quad (89\%) \\
62 & \rightarrow 63 \quad (37\%)
\end{align*} \]
reduced regioselectively with borane which are known to yield the 1,4-addition products. It was therefore, considered of interest to examine the reduction pattern of the various α-oxoketene O,S-acetals which are available easily as described elsewhere in the thesis.

In the present investigation, few selected O,S-acetals have been examined with various reducing agents to study the mode of reduction of these reducing agents. Thus the α-oxoketene O,S-acetal 64a when subjected to reduction with sodium borohydride in methanol yielded a mixture of several products and the reduction therefore found to be not as clean as it was in the case of corresponding S,S-acetals. Evidently replacement of sulfur by oxygen dramatically alters the electrophilic centres in 64a towards sodium borohydride leading to a mixture of several products.

When α-oxoketene O-methyl S-methylacetal 64a was reduced using borane trimethylamine complex in dioxane the corresponding over reduced product 3-methylthio-1-phenylpropan-1-one 65 was formed in 81% yield through exclusive 1,4-reduction fashion (scheme 12). The compound 65 was found to show identical physical and chemical properties with that reported in the literature\textsuperscript{11}. The O,S-acetal 66 was similarly reduced under the described reaction conditions to give 3-methylthio-1(2'-thienyl)propan-1-one 67 in 80% yield. The structure of 67 was established from its analytical and spectral data which are described in the experimental section. However, when oxoketene O-phenyl S-methylacetal 64b
Scheme - 12

64a

\[
\text{H}_5\text{C}_6\text{C} = \text{SMe} \quad \xrightarrow{\text{BH}_3\cdot\text{NMe}_3/\text{Dioxane/100 °C}} \quad \text{H}_5\text{C}_6\text{CH}_2\text{SMe}
\]

1,4-reduction

65

66

\[
\text{C}_5\text{H}_5\text{C} = \text{SMe} \quad \xrightarrow{\text{H}_3\text{B} \cdot \text{NMe}_3/\text{Dioxane/100 °C}} \quad \text{C}_5\text{H}_5\text{CH}_2\text{SMe}
\]

67

64b

\[
\text{H}_5\text{C}_6\text{O} = \text{C}_6\text{H}_5 \quad \xrightarrow{\text{H}_3\text{B} \cdot \text{NMe}_3/\text{Dioxane/100 °C}} \quad \text{H}_5\text{C}_6\text{CH}_2\text{SMe} + 65
\]

68

69

\[
\text{O} = \text{SMe} \quad \xrightarrow{\text{H}_3\text{B} \cdot \text{NMe}_3/\text{Dioxane/100 °C}} \quad \text{C}_6\text{H}_5\text{CH}_2\text{SMe} + \text{C}_6\text{H}_5\text{CH}_2\text{SMe}
\]

69a, R = Me

69b, R = \text{C}_6\text{H}_5

70

71

\[\text{Scheme - 12}\]
was reduced under similar reaction conditions, it gave 3-methylthio-1-phenyl-2-propen-1-one 68 in 76% yield along with minor amount of 65 in 9% yield (scheme 12). It may be noted here that the phenoxy group has behaved like a leaving group in preference to the elimination of methylmercaptan. This behaviour was further evident when both O-methyl S-methyl and O-phenyl S-methylacetals were reduced under similar reaction conditions. Thus when O-methyl S-methylacetal 69a derived from tetralone was reduced under similar reaction conditions only 5% of methylthiomethylene ketone 70 was formed along with 68% of over reduction product 71. On the other hand the O-phenyl S-methylacetal 69b on reduction with borane trimethylamine complex yielded 70 in 76% yield while 71 was obtained in only 9% yield (scheme 12). Apparently the O-phenyl group has proved to be a good leaving group in these transformations. The structure of 70 and 71 were confirmed by their analytical and spectral data which were identical with those reported in the literature.

The reduction of α-oxoketene O-methyl/phenyl S-methylacetals were next examined employing sodium borohydride in ethanol. The α-oxoketene O-methyl S-methylacetal 64a gave a mixture of products after reduction with sodium borohydride in ethanol. On the other hand the oxoketene O-phenyl S-methylacetals 64b and 69b when reduced with sodium borohydride in ethanol after work-up, the corresponding S-methyl α,β-unsaturated thiocarboxylates 74 and 76 were formed in 78% and 82% yields respectively (scheme 13). Apparently, the reaction proceeded initially with 1,2-reduction followed
SMe

No BH₄

1,2-reduction

Scheme - 13
by hydrolytic cleavage and elimination of phenol to afford the 74 and 76 in high yields. The analytical and spectral data of S-methylthiocinnamate 74 and S-methyl 3,4-dihydronaphthalene-2-thiocarboxylate 76 were in accordance with the values reported in literature 7.

Interestingly, when O-methyl S-methylacetal 64a was reduced with sodium borohydride in acetic acid, the corresponding 3-methylthio-1-phenyl-2-propen-1-one 68 was formed in 88% yield. The analytical and spectral data (superimposable ir and nmr) of 68 was identical with that of reported in literature 9. Similarly O-phenyl S-methylacetal 64b also underwent reduction under the similar reaction conditions to afford the corresponding methylthiomethylene ketone 68 in 82% yield. It is interesting to note that this reduction in the presence of acetic acid provides the protons, a hard acid which preferentially protonates oxygen in preference to sulphur that contributes for their preferential elimination in both the cases to give 68. Similar was the situation when 66 and 69 were reduced under the described reaction conditions, the corresponding 79 was obtained in 76% yield and 70 in 81% (from 69a) and in 79% (from 69b) yield (scheme 14). The analytical and spectral data of 70 and 79 were in agreement with those of reported in the literature 9.

When the O,S-acetal 64a was reduced with lithium aluminium hydride, the corresponding methylcinnamate 80 (scheme 15) was formed in 76% yield through initial 1,2-reduction of 64a followed by hydrolytic cleavage. The observed hydro
Scheme 14
Scheme 15

64a

H₅C₆

SMe

H₂C₆

OMe

LiAlH₄/THF

0°C

1,2-reduction

H₅C₆

H

H

H

H

OMe

80

81

Li⁺

H₂C₆

SMe

H₂C₆

OMe

Li⁺

H₂C₆

OMe

82

64b

H₅C₆

SMe

H₂C₆

OC₆H₅

LiAlH₄/THF

0°C

1,2-reduction

H₅C₆

H

H

H₅C₆

SMe

74

Scheme 15

204
alumination in the case of dithioacetals did not follow in the case of O,S-acetals. Evidently the methylthio group in 64a is cis to the carbonyl group resulting in organometallic complex 81 co-ordinating with sulfur rather than preferred oxygen (hard-hard) because of geometrical reasons. The elimination of methyl mercaptan appears to prefer over the elimination of methanol because of the favourable equilibrium created by escaping methyl mercaptan gas. On the other hand when 64b was reduced with lithium aluminium hydride the corresponding S-methylthiocinnamate 74 was formed in 78% yield. Here the elimination of phenol is observed preferentially over the elimination methyl mercaptan. The structures 80 and 74 were established by their analytical and spectral data which were in agreement with the values reported in the literature 7.

When α-benzoylketene O-methyl S-methylacetal 64a was reduced with diisobutyl aluminium hydride in presence of triethylamine (DIBAL-NEt₃), the corresponding cinnamaldehyde 86 was formed in 58% yield (scheme 16). It appears that the unstable β-hydroxy O,S-acetal 85 was the reduction product, probably obtained through the collapse of the organo aluminium complex 84 formed through 1,2-reduction followed by hydroalumination. The hydrolytic cleavage of β-hydroxy acetal 85 afforded the cinnamaldehyde 86. The spectral data (ir and nmr) of 86 are identical with the authentic sample of cinnamaldehyde.
Scheme 16
Subsequent to the metal hydride reduction studies, a preliminary investigation on the addition of carbon nucleophile to the O,S-acetal is also been undertaken. Thus the α-benzoylketene O-methyl S-methylacetal 64a when treated with methylmagnesium iodide the S-methyl β-methylthio cinnamate 88 obtained in 62% yield (scheme 17). The known product 88\textsuperscript{16} was having the analytical and spectral data in accord with the assigned structure. Apparently, the reaction followed 1,2-addition to give the corresponding carbinol 87 which during work-up underwent hydrolytic cleavage to afford the cinnamate 88. No product derived from 1,4-addition was detected in the reaction mixture.

V.3 CONCLUSION

The behaviour of various O,S-acetals towards different reducing agents varies from those of the corresponding S,S-acetals. The reduction of O,S-acetals in the presence of sodium borohydride in ethanol was totally unsatisfactory while those reductions in the case of S,S-acetals were highly rewarding. The O,S-acetals however followed some definite pattern when they were reduced with sodium borohydride in acetic acid. The observed 1,4-reduction and elimination of OCH\textsubscript{3} or OC\textsubscript{6}H\textsubscript{5} group in preference to SCH\textsubscript{3} group was noted. The lithium aluminium hydride reduction did not follow hydroalumination and underwent only 1,2-reduction followed by hydrolysis to give the corresponding ene esters. Similarly reduction of O,S-acetal by DIBAL appears to follow 1,2-
Scheme - 17

64a + MeMgI / Et₂O $\xrightarrow{1,2\text{-addition}}$ [MeSMe]

$\xrightarrow{\text{Sat.} \text{NH}_4\text{Cl}}$

87 $\rightarrow$ 88
reduction followed by hydroalumination to afford the corresponding aldehyde.

V.4 EXPERIMENTAL

Melting points were determined on a 'Thomas Hoover' capillary melting point apparatus and are uncorrected. IR spectra were obtained on a Perkin Elmer 297 spectrophotometer, $^1$H NMR spectra on a Varian EM-390 (90MHz) spectrometer. Mass spectra were recorded on a Jeol D-300 spectrometer. Elemental analysis were performed on a Heraeus CHN-O-Rapid Elemental Analyzer.

Starting materials and Reagents

All the α-oxoketene O,S-acetals used for the present investigation were prepared according to the earlier reported procedures$^{15}$ and are described in the experimental section of chapter 3. The borane-trimethylamine complex (Ventron), sodium borohydride (Aldrich), lithium aluminium hydride (Aldrich) and diisobutyl aluminium hydride (Fluka) were purchased and used as supplied. Triethylamine was dried over KOH and distilled prior to the reaction. Diethyl ether, tetrahydrofuran and dioxane were dried over sodium wire and distilled prior to use.

General Procedures:

(A) Reduction of α-Oxoketene O,S-Acetals 64a-b, 66 and 69 with Borane-Trimethylamine Complex.
To a stirred solution of α-oxoketene O,S-acetals (0.01mol) in dry dioxane (15ml) was added borane-trimethylamine complex (0.9g, 0.012mol) and heated at 100°C with stirring for 2-3hr. (monitored by tlc). It was then cooled to room temperature, poured on to crushed ice (100g) and extracted with chloroform (2x50ml). The organic layer was washed with saturated sodium bicarbonate solution (1x50ml), water (3x100ml), dried over sodium sulphate and evaporated to give crude products which were purified by column chromatography over silica gel using hexane as eluent.

(B) Reduction of α-Oxoketene O,S-Acetals 64b and 69b with Sodium Borohydride in Ethanol.

To a solution of α-oxoketene O,S-acetals (0.01mol) in absolute ethanol (20ml) was added sodium borohydride (0.75g, 0.02mol) in one lot and refluxed on oil bath with stirring for 2-3hr. (monitored by tlc). It was then cooled to room temperature, poured on to crushed ice (100g) and extracted with chloroform (3x50ml). The organic layer was washed with saturated sodium bicarbonate solution (1x50ml), water (3x100ml), dried over sodium sulphate and evaporated to give crude products which were purified by column chromatography over silica gel using ethylacetate /hexane (2:98) as eluent.

(C) Reduction of α-Oxoketene O,S-Acetals 64a-b, 66 and 69a-b with Sodium Borohydride in Acetic acid.

To a well stirred solution of α-oxoketene O,S-acetals (0.01mol) in glacial acetic acid (25ml), sodium borohydride
(1.20g, 0.03mol) was added slowly (portion wise) (30min) at 5-10°C. The reaction mixture was further stirred at room temperature for 3hr. (monitored by tlc). The reaction mixture was poured into ice cold water (100ml), extracted with chloroform (3x100ml), dried over sodium sulphate and concentrated to give the viscous residue which on column chromatography over silica gel (hexane eluent) gave the pure methylthiomethylene ketones.

(D) Reduction of O,S-Acetals 64a and 64b with Lithium Aluminium Hydride.

To a stirred solution of lithium aluminium hydride (0.4g, 0.01mol) in THF (25ml) at 0°C under nitrogen atmosphere, O,S-acetal (0.01mol) in THF (15ml) was added dropwise. Continued the stirring at the same temperature for 1-2hr (monitored by tlc) and poured on to crushed ice (100g). It was then neutralised with 2N HCl and extracted with chloroform (2x50ml). The chloroform extract was washed with saturated sodium bicarbonate solution (1x50ml), water (2x100ml), dried (Na₂SO₄) and evaporated to give crude product. The crude product eneesters thus obtained were purified by passing through a short length silica gel column using hexane as eluent.

(E) Reduction of α-Oxoketene O-Methyl S-Methylacetal 64a with Diisobutyl Aluminium Hydride.

To a stirred solution of O,S-acetal 64a (2.20g, 0.01mol) in dry THF (25ml) at -78°C under nitrogen atmosphere, was added,
DIBAL-TEA complex [prepared by the addition of DIBAL (1.7g, 0.012mol) to a stirred solution of triethylamine (1.2g, 0.012mol) in THF (15ml), at -78°C, under nitrogen atmosphere and stirred the mixture for 30min. at the same temperature] through a syringe and continued the stirring at -78°C for 30min. Allowed the reaction mixture to come to 0°C and poured on to crushed ice (100g), drenched with 5ml Conc. HCl. It was then extracted with chloroform (2x50ml), washed with water (3x100ml), dried over sodium sulphate and evaporated. The residue was chromatographed over silica gel using hexane as eluent. The pure cinnamaldehyde 86 thus obtained in 58% yield exhibited ir and $^1$H nmr spectra identical with the authantc sample of cinnamaldehyde.

The yields of all the products obtained by the reduction of O,S-acetals on subjecting to various reducing agents following the general procedures as described above are given in the Table.

3-Methylthio-1-phenylpropan-1-one (65). Colorless viscous liquid (Table entry 1 and 4); IR (neat) 1695, 1612, 1598, 1440, 1360 cm$^{-1}$; $^1$H NMR (CCl$_4$) 2.16 (3H, s, SCH$_3$), 2.82 (2H, t, J=6Hz, CH$_2$), 3.21 (2H, t, J=6Hz, CH$_2$), 7.44-7.68 (3H, m, ArH), 7.91-8.06 (2H, m, ArH) (Anal. Calcd. for C$_{10}$H$_{12}$O$_2$: C, 66.62; H, 6.71. Found: C, 66.49; H, 6.57%).

3-Methylthio-1-(2'-thienyl)propan-1-one (67). Colorless liquid (Table entry 2); IR (neat) 1678, 1537, 1432, 1379 cm$^{-1}$; $^1$H NMR (CCl$_4$) 2.01 (3H, s, SCH$_3$), 2.78 (2H, t, J=6Hz, CH$_2$), 3.01 (2H, t, J=6Hz, CH$_2$), 7.03-7.21 (2H, m, thiienyl H),
7.54-7.75 (2H, m, thienyl H) (Anal. Calcd. for C₈H₁₀Os₂ : C, 51.58 ; H, 5.41. Found : C, 51.81 ; H, 5.66%).

3-Methylthio-1-phenyl-2-propan-1-one (68). Colorless viscous liquid (Table entry 3, 11 and 12); IR (neat) 1660, 1619, 1562, 1443, 1227 cm⁻¹ ; ¹H NMR (CDCl₃) 2.49 (3H, s, SCH₃), 6.82 (1H, d, J=18Hz, =CH), 7.42-7.71 (3H, m, ArH), 7.82-8.16 (3H, m, ArH and =CH) (Anal. Calcd. for C₁₀H₁₀Os₂ : C, 67.38 ; H, 5.66. Found : C, 67.63 ; H, 5.89%).

2-(Methylthiomethylene)-1-tetralone (70). Yellow crystals (Table entry 5, 7, 14 and 15) (CHCl₃/hex) ; m.p. 67-68°C (lit. 9 68°C) ; IR (KBr) 1653, 1590, 1547 cm⁻¹ ; ¹H NMR (CDCl₃) 2.46 (3H, s, SCH₃), 2.64-2.79 (2H, m, CH₂), 2.80-3.03 (2H, m, CH₂), 7.20-7.65 (3H, m, ArH), 7.85 (1H, s, =CH), 8.10-8.29 (1H, s, ArH) (Anal. Calcd. for C₁₂H₁₂Os : C, 70.55 ; H, 5.92. Found : C, 70.78 ; H, 6.19%).

2-(Methylthiomethyl)-1-tetralone (71). Colorless liquid (Table entry 6 and 8) ; IR (neat) 1703, 1620, 1468 cm⁻¹ ; ¹H NMR (CDCl₃) 2.18 (3H, s, SCH₃), 2.31-2.64 (4H, m, CH₂), 2.80-3.19 (3H, m, CH and CH₂), 7.01-7.47 (3H, m, ArH), 7.85-8.02 (1H, m, ArH) (Anal. Calcd. for C₁₂H₁₄Os : C, 69.86 ; H, 6.84. Found : C, 70.15 ; H, 7.01%).

S-Methylthiocinnamate (74). Colorless solid (Table entry 9 and 17) (ether/hex) ; m.p. 46-47°C (lit 48-49°C) ; IR (CCl₄) 1679, 1636, 1598, 1509, 1461 cm⁻¹ ; ¹H NMR (CCl₄) 2.40 (3H, s, SCH₃), 6.69 (1H, d, J=16Hz, =CH), 7.31-7.78 (6H, m, =CH and ArH) (Anal. Calcd. for C₁₀H₁₀Os : C, 67.38 ; H, 5.66. Found : C, 67.59 ; H, 5.91%).
S-Methyl 3, 4-dihydronaphthalene-2-thiocarboxylate (76). Colorless thick liquid (Table entry 10); IR (CCl₄) 1742, 1676, 1585, 1510, 1282 cm⁻¹; ¹H NMR (CCl₄) 2.36 (3H, s, SCH₃), 2.52-2.93 (4H, m, CH₂), 7.30 (4H, brs, ArH), 7.58 (1H, s, =CH) (Anal. Calcd. for C₁₂H₁₂OS : C, 70.55; H, 5.92. Found : C, 70.74; H, 6.09%).

3-Methylthio-1-thienyl-2-propen-1-one (79). Yellow viscous liquid (Table entry 13); IR (neat) 1652, 1575, 1439, 1286 cm⁻¹; ¹H NMR (CCl₄) 2.40 (3H, s, SCH₃), 6.73 (1H, d, J=16Hz, =CH), 7.02 (1H, t, J=3Hz, thienyl H), 7.63-7.88 (2H, m, thienyl H), 7.91 (1H, d, J=16Hz, =CH) (Anal. Calcd. for C₈H₈OS₂ : C, 63.12; H, 5.30. Found : C, 63.35; H, 5.57%).

S-Methyl β-methylthiocinnamate (88). To a stirred solution of methylmagnesium iodide (prepared by reacting magnesium 0.5g, 0.02mol and methyl iodide 1.7g, 0.012mol) in THF was added O,S-acetal 64a (2.2g, 0.01mol) at 0°C. Stirred the reaction mixture between 0-5 °C for another 2hr. It was then poured into saturated ammonium chloride solution (100ml) and extracted with chloroform (2x50ml). Washed the organic layer with water (3x100ml), dried over sodium sulphate and evaporated. The residue was chromatographed over silica gel using hexane as eluent. It was isolated as yellow viscous liquid; yield 62%; IR (CCl₄) 1709, 1620, 1457, 1372 cm⁻¹; ¹H NMR (CCl₄) 2.20 (3H, s, SCH₃), 2.49 (3H, s, CH₃), 6.48 (1H, s, =CH), 7.24-7.61 (5H, m, ArH) (Anal. Calcd. for C₁₁H₁₂OS : C, 68.71; H, 6.29. Found : C, 68.98; H, 6.55%).
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A. $\text{H}_3\text{B-NMe}_3$/Dioxane; B. $\text{NaBH}_4$/EtOH; C. $\text{NaBH}_4$/AcOH; D. $\text{LiAlH}_4$/THF; E. DIBAL-TEA/THF
REFERENCES