# SYNTHETIC STUDIES ON $\beta$-OXODITHIOACETALS

*By*

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*The work described in this thesis is original and has not been submitted for any other degree or diploma in this or any other University.*

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# PREFACE

The α-oxoketene dithioacetals are a versatile group of 3-carbon synthons with ambident 1,3- electrophilic centres thus permitting to design various methodologies for both carbocyclic and heterocyclic synthesis. Our Group's continued interest in the chemistry of these class of compounds has been centered around exploitation of the differential electrophilicity of 1,3- carbon centers for the regioselective construction of new C-H and C-C bonds involving either 1,2- or 1,4- nucleophilic additions leading to a number of synthetic routes for a wide range of organic molecules.

The work presented in this thesis has been carried out as a part of our ongoing investigations on α-oxoketene dithioacetals and their sister counterparts. The studies undertaken describes about the synthesis of β-oxodithioacetals from α-oxoketene dithioacetals and the further applications of β-oxodithioacetals through various synthetic transformations.

The first Chapter of this thesis provides a brief account on the general reactivity profile of α-oxoketene dithioacetals and some of the recently developed synthetic approaches by our group employing these class of compounds.

In the Part-A of second Chapter, the α-oxoketene dithioacetals are shown to undergo conjugate 1,4- reduction in highly regio- and chemoselective manner with sodium borohydride in acetic acid to afford the corresponding β-oxodithioacetals. The merits and demerits of this newly developed methodology has been discussed in detail. The Part-B of Chapter-II deals about successful formulation of an improved method for the synthesis of β-oxodithioacetals employing zinc in acetic acid.

An efficient route for the synthesis of biphenyls, substituted naphthalenes, phenanthraenes and other polynuclear aromatics starting from β-oxodithioacetals has been developed and the results are presented in the Chapter III.

The Chapter IV describes a new general method developed for the synthesis of 1,2-diarylethylenes, 1,4-diarylbutadienes and 1,6- diarylhexatrienes through cycloaromatization of β-oxodithioacetals derived from α-cinnamoyl ketene dithioacetals and their higher enyl analogs.

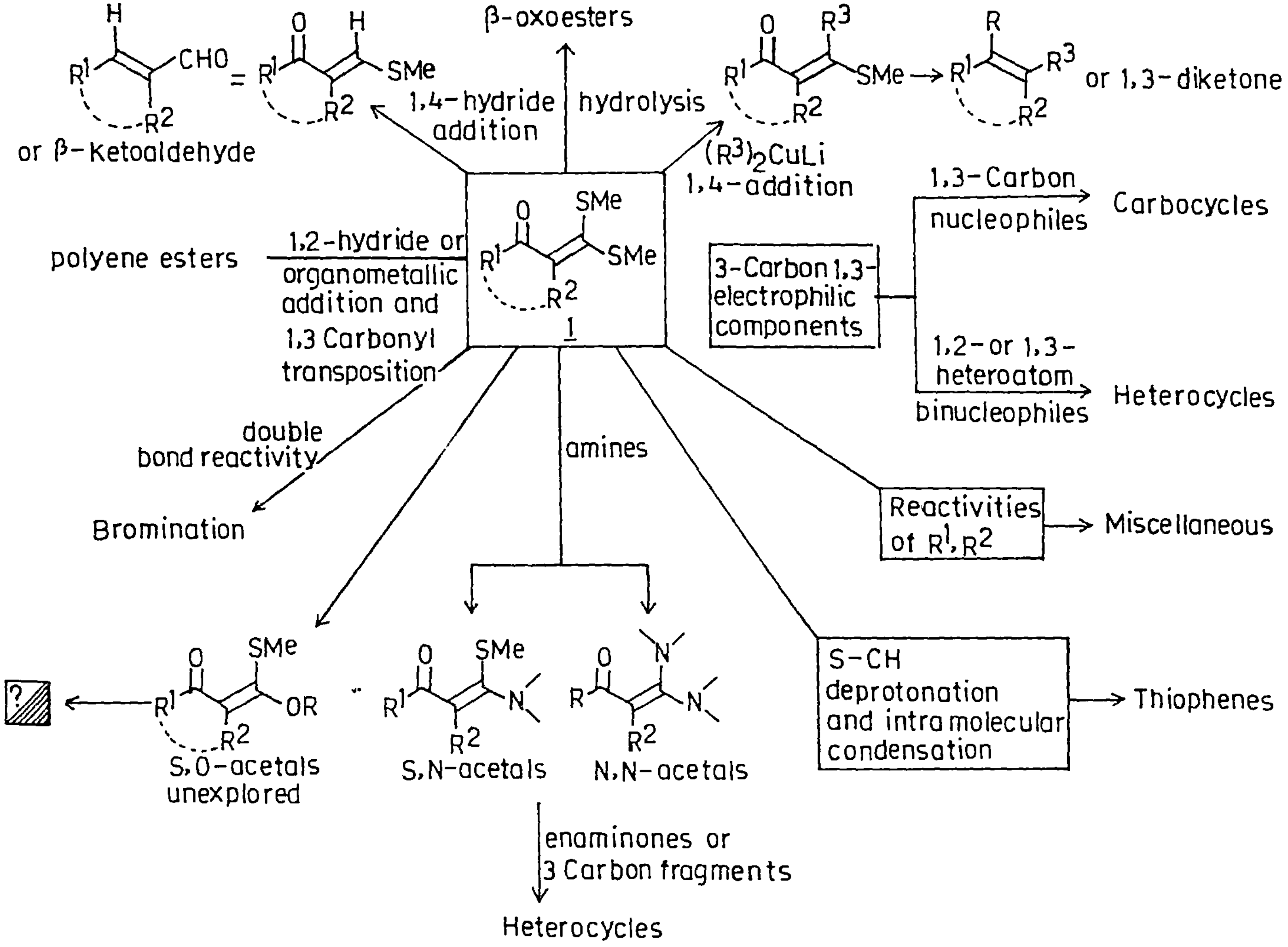
The last Chapter of this thesis describes about the selective dehydration and concomitant dehydrative dethioacetalization methods developed to manifest some important synthetic transformations utilizing the β-hydroxydithioacetals derived from β-oxodithioacetals.

# CHAPTER I

## α-OXOKETENE DITHIOACETALS AND β-OXODITHIOACETALS AS VERSATILE SYNTHONS FOR METHODOLOGY DEVELOPMENT : A GENERAL INTRODUCTION

The versatile synthon family of poalrized ketene dithioacetals have been recognised as useful building blocks in various synthetic transformations.[1] This class of compounds can be easily prepared from a wide variety of active methylene compounds and carbon disulfide in the presence of a suitable base followed by alkylation often in one pot reaction in moderate to good yields.[2-9] The oxoketene dithioacetals exhibit well defined physical properties either as crystalline solids or as distillable liquids and can be purified by conventional methods. Kelber and co-workers reported the first synthesis of α-oxoketene dithioacetals in 1910.[1,11] After the initial synthesis, for more than half a century the synthetic potential of these class of compounds remained unexplored. Later Thuillier and co-workers in 1962 synthesized oxoketene dithioacetals in higher yields using sodium amylate as base and this family of compounds emerged as very useful synthetic intermediates over the last two decades.[1]

The oxoketene dithioacetals which can be prepared by easier methods in one pot reaction in high yields exhibit greater stability than the corresponding O,O-acetals.[12] They can be further converted to the corresponding ketene dihalogenides,[13,14] N,S-[15] and N,N-[16] acetals making them more important as precursors for a large variety of functionalized acetals. The oxoketene dithioacetals have been shown to be excellent three carbon fragments, with 1,3-carbons possessing differential electrophilic properties, which is an important prerequisite in disigning methodologies for both carbocyclic and heterocyclic synthesis. They also possess considerable synthetic potential for the regioselective construction of new bonds via 1,2-nucleophilic additions to ketone carbonyl or 1,4-conjugate addition reactions to the β-carbon of the enone system. The intermediate allylic alcohols and enones can, in turn, be exploited in additional bond forming reactions.

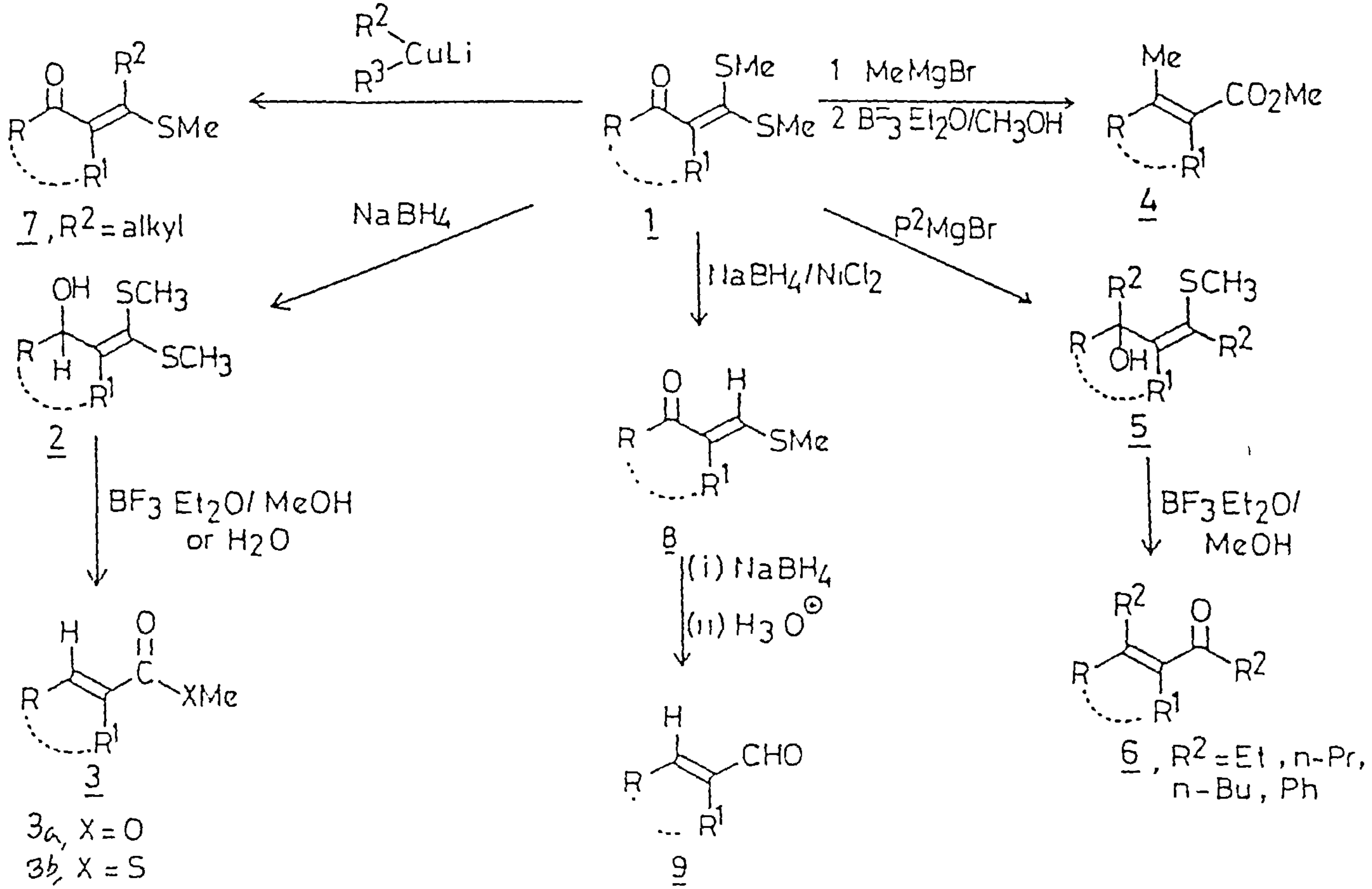

β-oxoesters
or β-Ketoaldehyde
1,4-hydride addition
hydrolysis
(R3)2CuLi 1,4-addition
or 1,3-diketone
polyene esters
1,2-hydride or organometallic addition and 1,3 Carbonyl transposition
1
3-Carbon 1,3-electrophilic components
1,3-Carbon nucleophiles
Carbocycles
1,2-or 1,3-heteroatom binucleophiles
Heterocycles
double bond reactivity
Bromination
amines
Reactivities of R1,R2
Miscellaneous
S,O-acetals unexplored
S,N-acetals
N,N-acetals
S-CH deprotonation and intra molecular condensation
Thiophenes
enaminones or 3 Carbon fragments
Heterocycles

Scheme-1

The general reactivity pattern of α-oxoketene dithioacetals 1 is outlined in the scheme 1. Hydrides and organometallic reagents add to the carbonyl carbon in a 1,2-manner but this sequence can be altered to the 1,4-path by suitably changing the reaction conditions and reagents.[17-19] Further transformations of these 1,2 or 1,4-addition products have also been investigated extensively.[17] The differential electrophilicity at 1,3-carbon of the oxoketene dithioacetals have been judiciously utilized for the synthesis of both 5- and 6- membered heterocycles by reacting with 1,2- and 1,3-heteroatom binucleophiles respectively. The 1,3-carbon binucleophiles have been similarly used in the synthesis of carbocycles. The enolate anion formed by the deprotonation (When R'=alkyl) can undergo condensation with aldehydes to give α-enoyl ketene dithioacetals.[6,20] When $R^2$ is a methyl group an allylic anion is generated in the presence of strong bases leading to rearranged products.[21] Deprotonation of the thiomethyl group followed by intramolecular Aldol type condensation to afford thiophenes is also reported.[22,23] These oxoketene dithioacetals can be easily converted to the corresponding O,S-, N,S- and N,N-acetals. The reactivity of the double bond has also been studied with electrophiles. Thus the bromination at α-position with N-bromosuccinimide has been carried out successfully.[24] In the following section some of the selected transformations reported from this laboratory are briefly summarized.

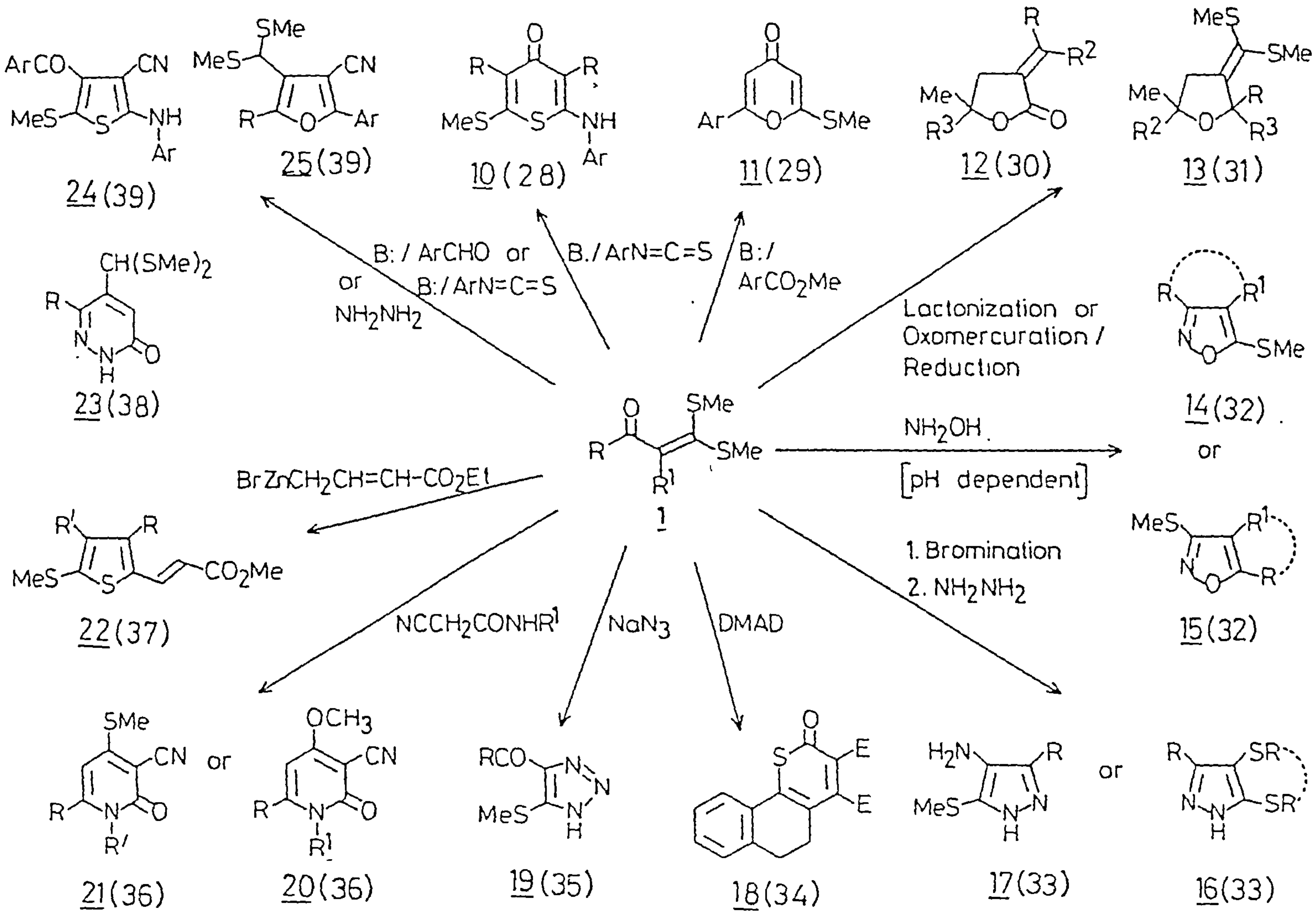
The oxoketene dithioacetals have been reported to undergo chemoselctive 1,2-reduction with $NaBH_4$ to give the corresponding carbinol acetals, 2[25,26] which were shown to undergo smooth methanolysis in the presence of borontrifluoride etherate to afford α,β-unsaturated methyl esters 3a in high yields (Scheme 2). The overall transforamtion is considered as homologation of active methylene ketones involving a 1,3-carbonyl transposition. The Grignard and organolithium reagents undergo either regioselective 1,2-addition to afford the α-hydroxyvinylsulfides.[17-19] The borontrifluoride etherate catalysed solvolysis or the hydrolysis of these carbinols yields either β-substituted α,β-unsaturated esters **4** or the corresponding ketones **6** (Scheme 2) in good yields. Dieter and co-workers have reported the chemo and stereoselective addition of organocuprates to dithioacetals 1.[18,19] Thus organocuprates are shown to undergo conjugate addition to give β-alkylthio-β-substituted α,β-unsaturated ketones **7**. The oxoketene dithioacetals were also shown to undergo nickel boride ($NaBH_4/NiCl_2$) reduction to the corresponding β-methylthioalkenylketones **8** which are further transformed to the corresponding α,β-unsaturated aldehydes 9[27] (Scheme 2).

Numerous substituted and fused five and six membered heterocyclics have been synthesised using oxoketene dithioacetals.[28,29] some of the selected transformations are shown in scheme 3. Some of the important transformations developed based on α-cinnamoyl and 5-aryl-2,4-pentadienoylketene dithioacetals are outlined in scheme 4. A general method for the synthesis of polyene esters 27[40] has been reported by 1,2-reduction of **26** followed by methanolysis



$R^2$ $R^3$ CuLi
1 MeMgBr
2 $BF_3$ $Et_2O/CH_3OH$
NaBH4
$NaBH_4/NiCl_2$
$R^2MgBr$
$BF_3$ $Et_2O$/ MeOH or $H_2O$
(i) $NaBH_4$
(ii) $H_3O^{\oplus}$
$BF_3Et_2O$/ MeOH
SMe
SMe
$SCH_3$
OH
R
$R^1$
$R^2$
Me
$CO_2Me$
CHO
XMe
1
2
3
4
5
8
9
7, $R^2$ = alkyl
3a, X = O
3b, X = S
6, $R^2$ = Et, n-Pr, n-Bu, Ph

Scheme-2

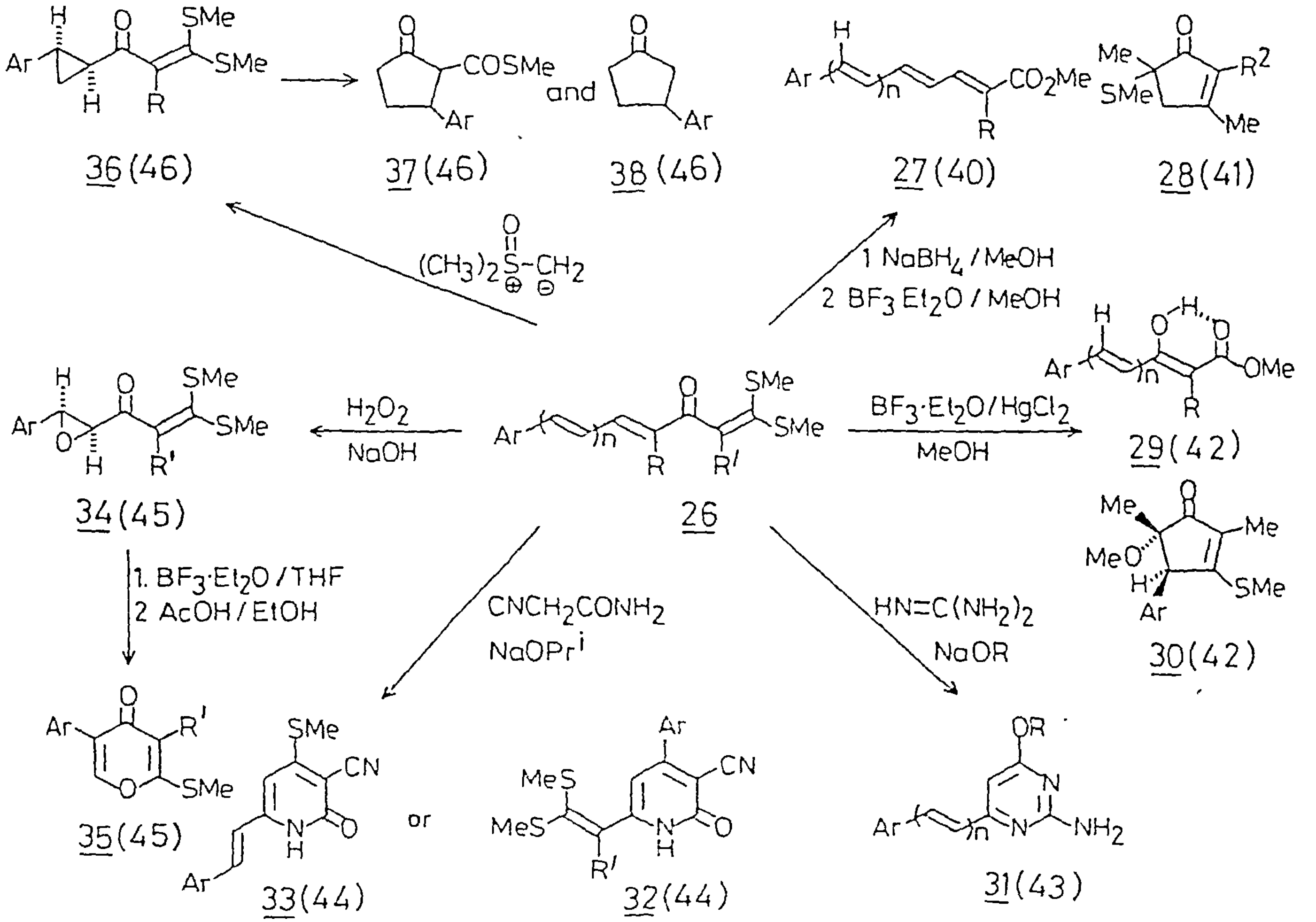


1
B: / ArCHO or B:/ArN=C=S
or NH2NH2
B./ArN=C=S
B:/ ArCO2Me
Lactonization or Oxomercuration / Reduction
NH2OH
[pH dependent]
1. Bromination
2. NH2NH2
DMAD
NaN3
NCCH2CONHR1
BrZnCH2CH=CH-CO2Et
24(39)
25(39)
10(28)
11(29)
12(30)
13(31)
14(32)
or
15(32)
23(38)
22(37)
21(36)
or
20(36)
19(35)
18(34)
17(33)
or
16(33)

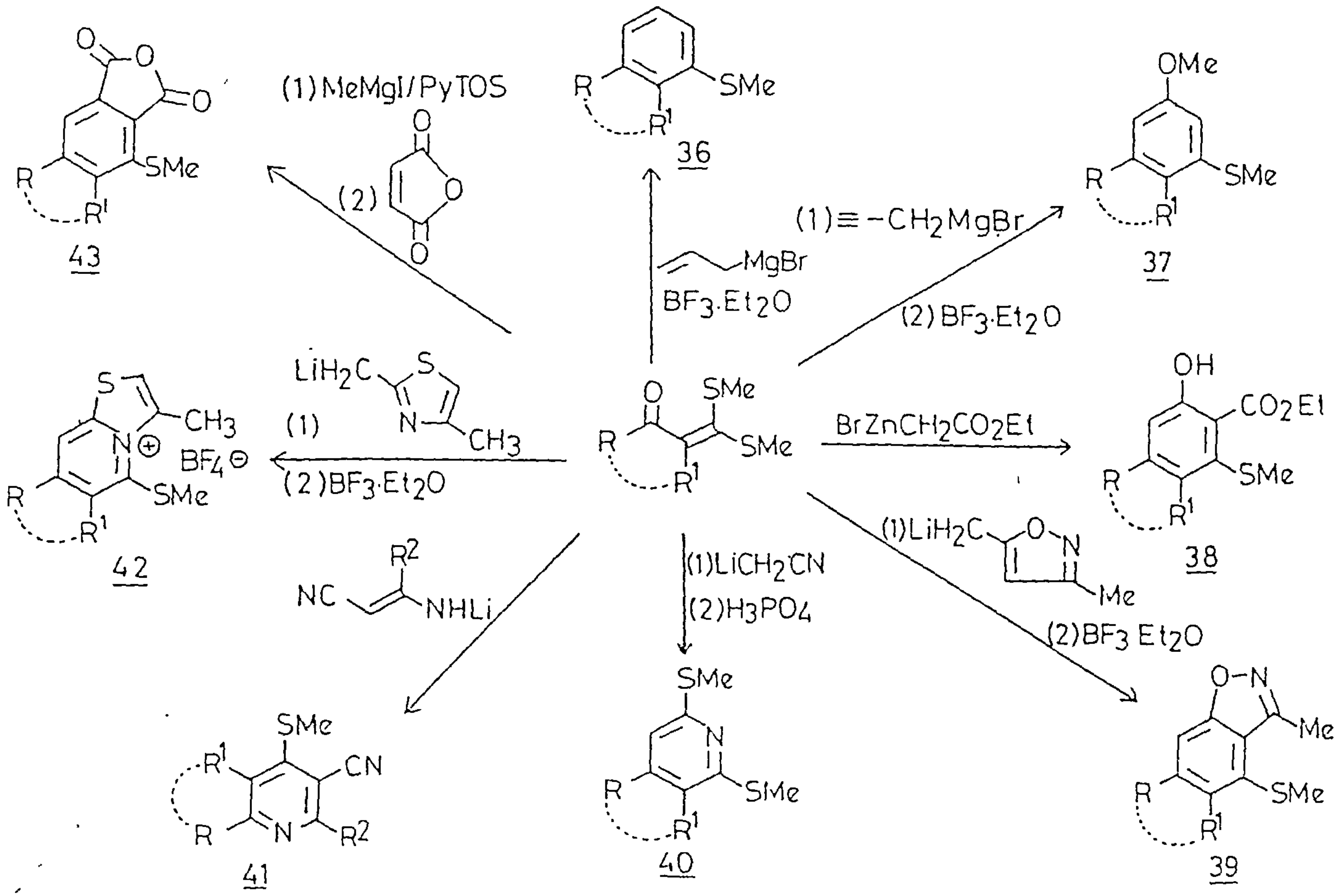
Scheme-3

in the presence of borontrifluoride etherate. In Hg(II) assisted hydrolysis the corresponding α,β-unsaturated-β-keto esters 29 are formed,[42] while in the case of 2,4-disubstituted systems (R=R'=$CH_3$) the corresponding cyclopentenones 28 and 30 are obtained under similar reaction conditions.[41,42] Synthesis of styrylpyrimidines 31, pyridones 32 and 33 were also achieved using these intermediates.[43,44] The cinnamoyl ketene dithioacetals 26 have been reported to undergo regioselective cyclopropanation and epoxidation at the styryl double bond.[45,46] These intermediates 34 and 36 were further exploited for the synthesis of pyrones 35 and cyclopentanones 37 and 38 respectively[45,46] (Scheme 4).

Aromatic annelation via α-oxoketene dithioacetals, developed from this laboratory has emerged as an area of great synthetic potential. Some of the important synthetic outcome of this aroamtic annelation methodology is depicted in scheme 5. The reaction of allylmagnesium bromide with α-oxoketene dithioacetals has been shown to undergo exclusive 1,2-addition to yield the corresponding carbinol acetals in high yields, which on $BF_3.Et_2O$ assisted cationic cyclization yield the substituted and fused benzene derivatives 6.[47] The approach is extended for the synthesis of other benzenoids 37[48] and 38[49]. The method is further shown to be extremely versatile and found general application for the synthesis of 1,2-benzisoxazoles 39,[50] pyridines 40[51] and 41,[52] thiazolopyridinium salts 42[53]. The Diels-Alder cycloadditions of vinylketene dithioacetals derived from the


36(46)
37(46)
and
38(46)
27(40)
28(41)
$(CH_3)_2\overset{O}{S}-CH_2$
1 $NaBH_4$ / MeOH
2 $BF_3 Et_2O$ / MeOH
$H_2O_2$
NaOH
$BF_3 \cdot Et_2O / HgCl_2$
MeOH
34(45)
26
29(42)
30(42)
1. $BF_3 \cdot Et_2O$ / THF
2 AcOH / EtOH
$CNCH_2CONH_2$
$NaOPr^i$
$HN=C(NH_2)_2$
NaOR
35(45)
33(44)
or
32(44)
31(43)

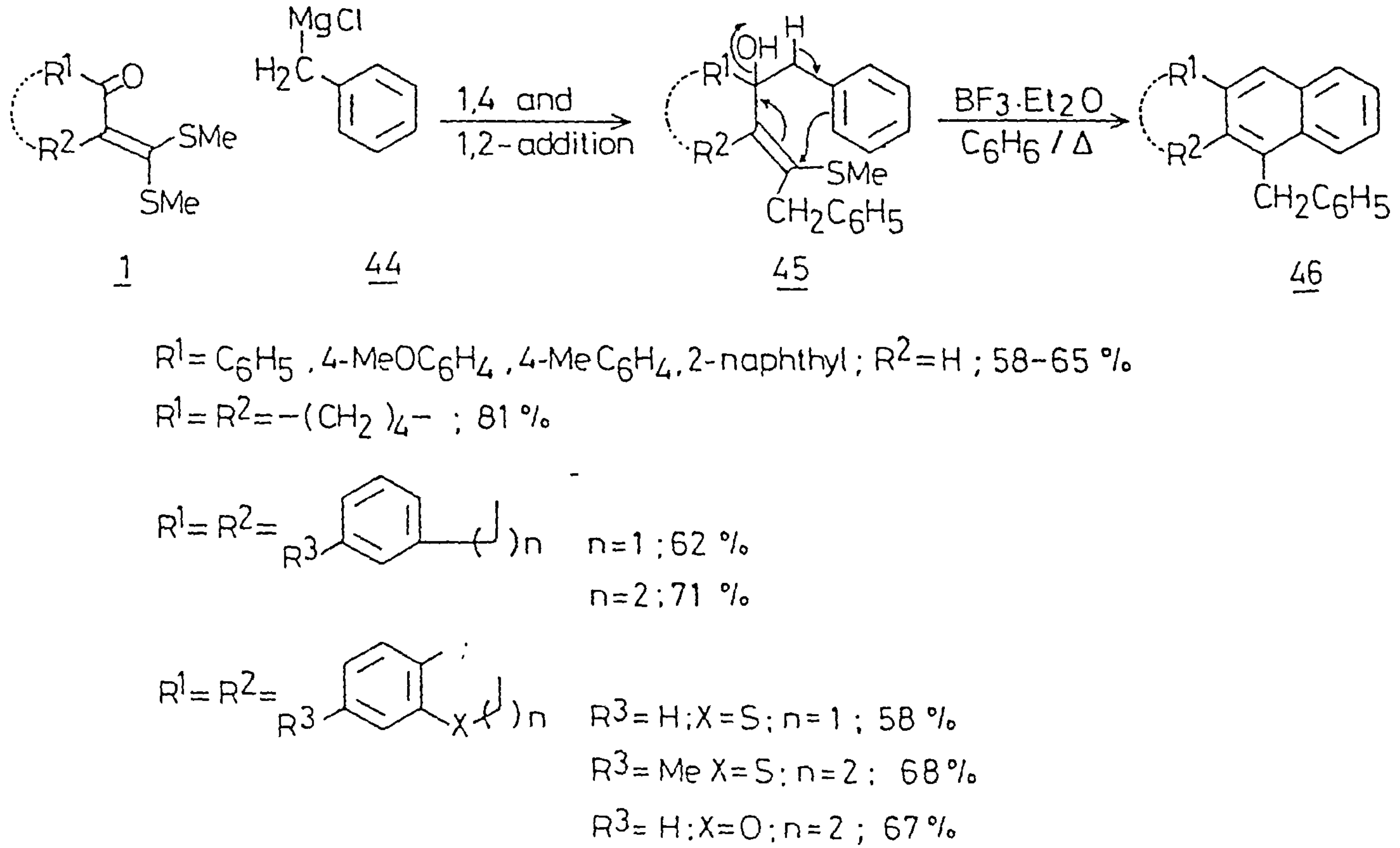
Scheme-4


(1) MeMgI/PyTOS
(2)
LiH2C
(1)
(2) BF3·Et2O
MgBr
BF3·Et2O
(1) ≡ −CH2MgBr
(2) BF3·Et2O
BrZnCH2CO2Et
(1) LiH2C
(2) BF3 Et2O
(1) LiCH2CN
(2) H3PO4
NC
NHLi
R
R1
R2
SMe
OMe
OH
CO2Et
CH3
BF4⊖
CN
Me
36
37
38
39
40
41
42
43

Scheme-5

corresponding oxoketene dithioacetals **1** with maleic anhydride afforded the phthalic anhydrides **43** in good yields.[54]

The α-oxoketene dithioacetals have been shown to be useful intermediates for synthesis of naphthalenes, phenanthrenes and other fused aromatic systems by reacting them with benzyl-, 1-naphthylmethyl- and 2-naphthylmethylmagnesium halides followed by cycloaromatization. Thus, benzylmagnesium chloride reacted with α-oxoketene dithioacetals **1** in a sequential 1,4-followed by 1,2-addition leading to the carbinolacetal **45** which on $BF_3.Et_2O$ assisted aromatic annelation afforded the corresponding naphthalenes **46** in excellent yields. The generality of this benzoannelation method[55] alongwith its merits and demerits has been extensively studied (Scheme 6). Interestingly, when these rections were extended to 1-naphthylmethylmagnesium chloride **47**, the addition took place exclusively in 1,2-fashion to yield the corresponding carbinolacetals **48** in high yields. These carbinols were smoothly cyclized in the presence of $BF_3.Et_2O$ to the corresponding phenanthrenes **49** in good yields[56] (Scheme 7). However, with α-oxoketene dithioacetals derived from cyclic ketones, **47** underwent a sequential 1,4-followed by 1,2-addition pattern thereby producing the naphthylmethyl substituted phenanthrenes. The 2-naphthylmethyl magnesium bromide addition to α-oxoketene dithioacetals **1** followed seequential 1,4- followed by 1,2-mode, behaving like benzyl Grignard additions and the resulting carbinolacetals **52** were cycloaromatized in a very facile fashion to afford the corresponding phenanthrenes **53**

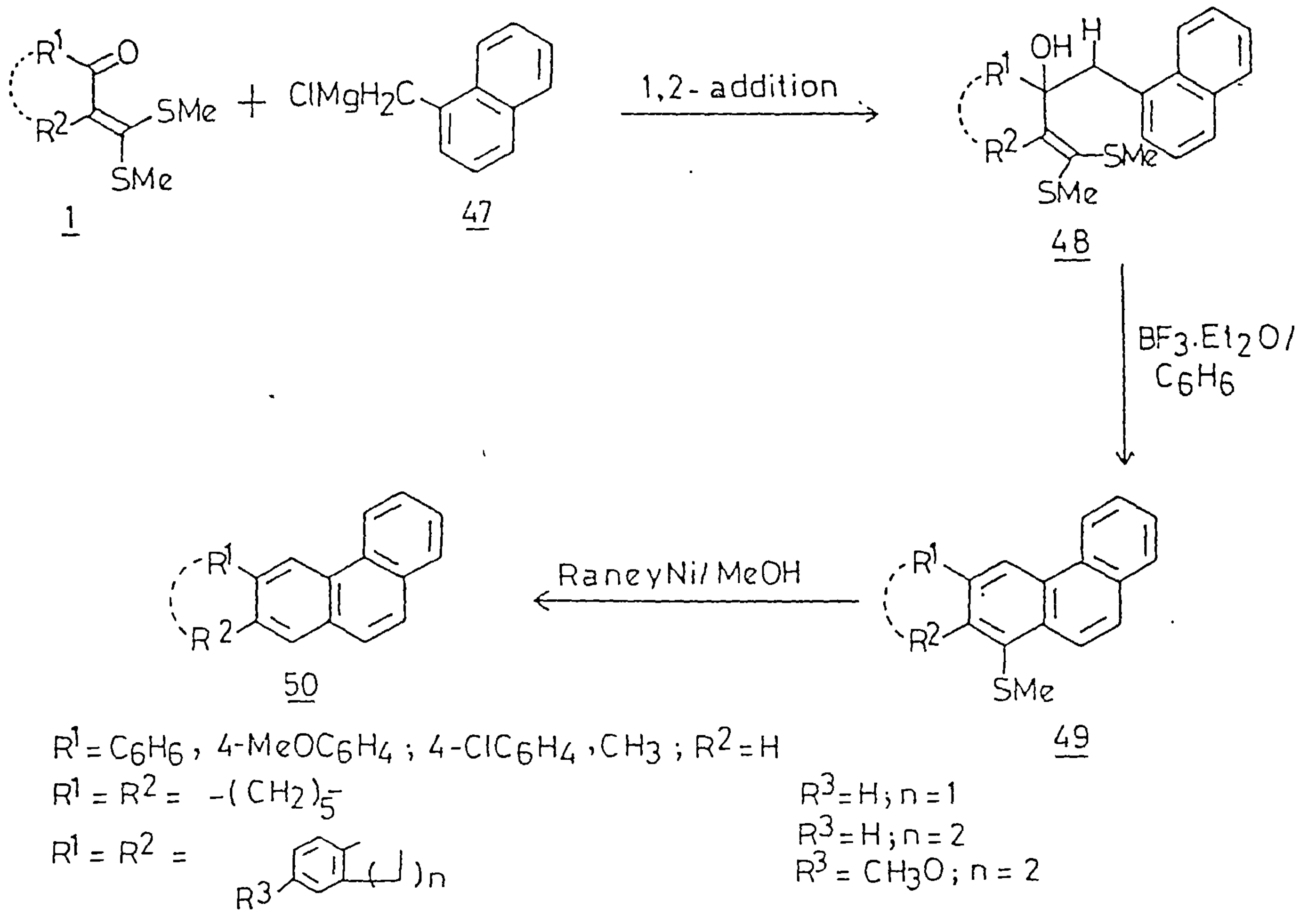


$R^1 = C_6H_5$, 4-$MeOC_6H_4$, 4-$MeC_6H_4$, 2-naphthyl; $R^2 = H$ ; 58-65 %
$R^1 = R^2 = -(CH_2)_4-$ ; 81 %

n=1 ; 62 %
n=2 ; 71 %

$R^3 = H$ ; X=S ; n=1 ; 58 %
$R^3 = Me$ X=S ; n=2 ; 68 %
$R^3 = H$ ; X=O ; n=2 ; 67 %

Scheme – 6



$R^1 = C_6H_6$, 4-$MeOC_6H_4$ ; 4-$ClC_6H_4$, $CH_3$ ; $R^2 = H$

$R^1 = R^2 = -(CH_2)_5-$

$R^1 = R^2 =$

$R^3 = H$; $n = 1$

$R^3 = H$; $n = 2$

$R^3 = CH_3O$; $n = 2$

Scheme – 7

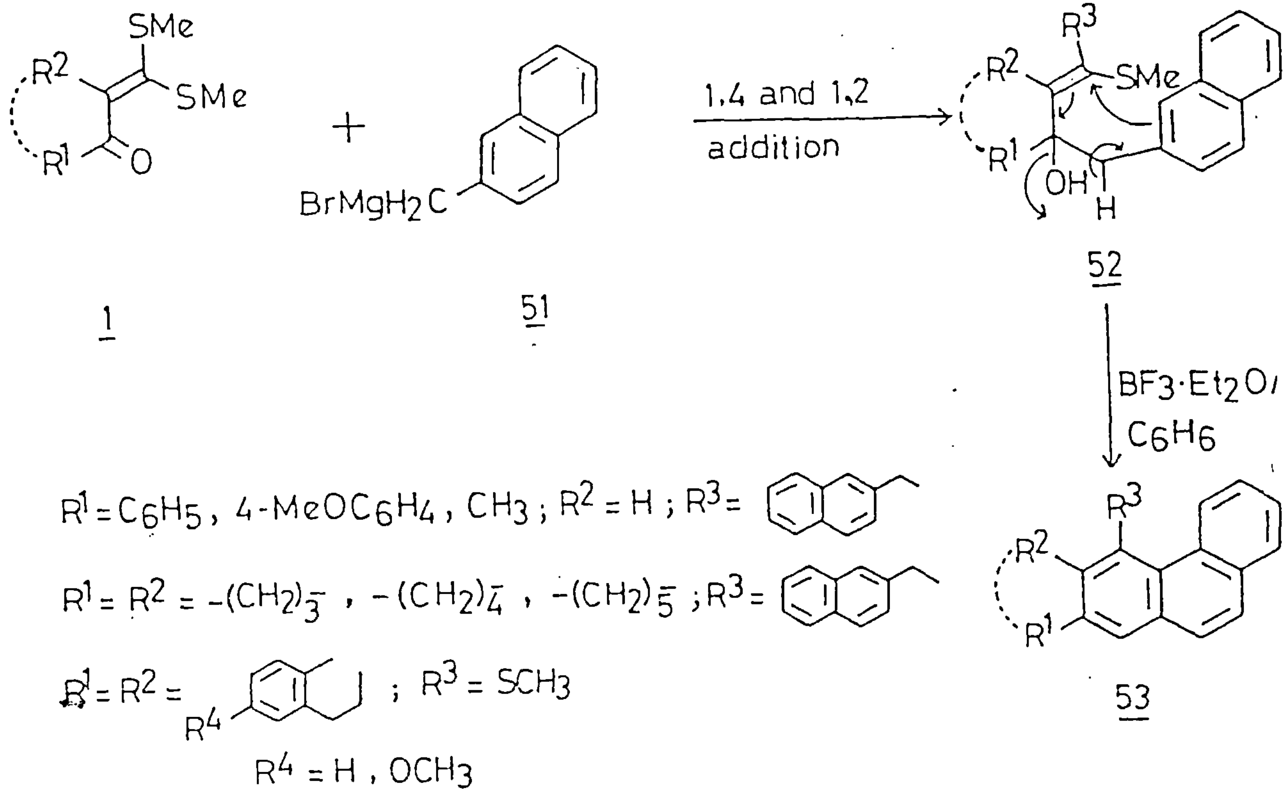
in good to excellent yields (Scheme 8). It appears that both steric and electronic factors play an important role in the different reactivity patterns of benzyl, 1-naphthylmethyl- and 2-naphthylmethylmagnesium halides with α-oxoketene dithioacetals.

A general methodology for the synthesis of quinolizinium salts with diverse structural features was formulated via oxoketene dithioacetals through their reaction with 2-picolyl lithium (Scheme 9). Thus, α-oxoketene dithioacetals 1 on reating with 2-picolyllithium 54 underwent exclusive 1,2-addition to yield the corresponding carbinolacetals 55 which on $BF_3.Et_2O$ assisted cycloaromatization provided the corresponding quinolizinium tetrafluoroborate salts 56 in very high yields[57]. The methodology developed of considerable synthetic importance due to the fact that a large number of azaallylanion could be used to construct various heteroaromatic compounds.

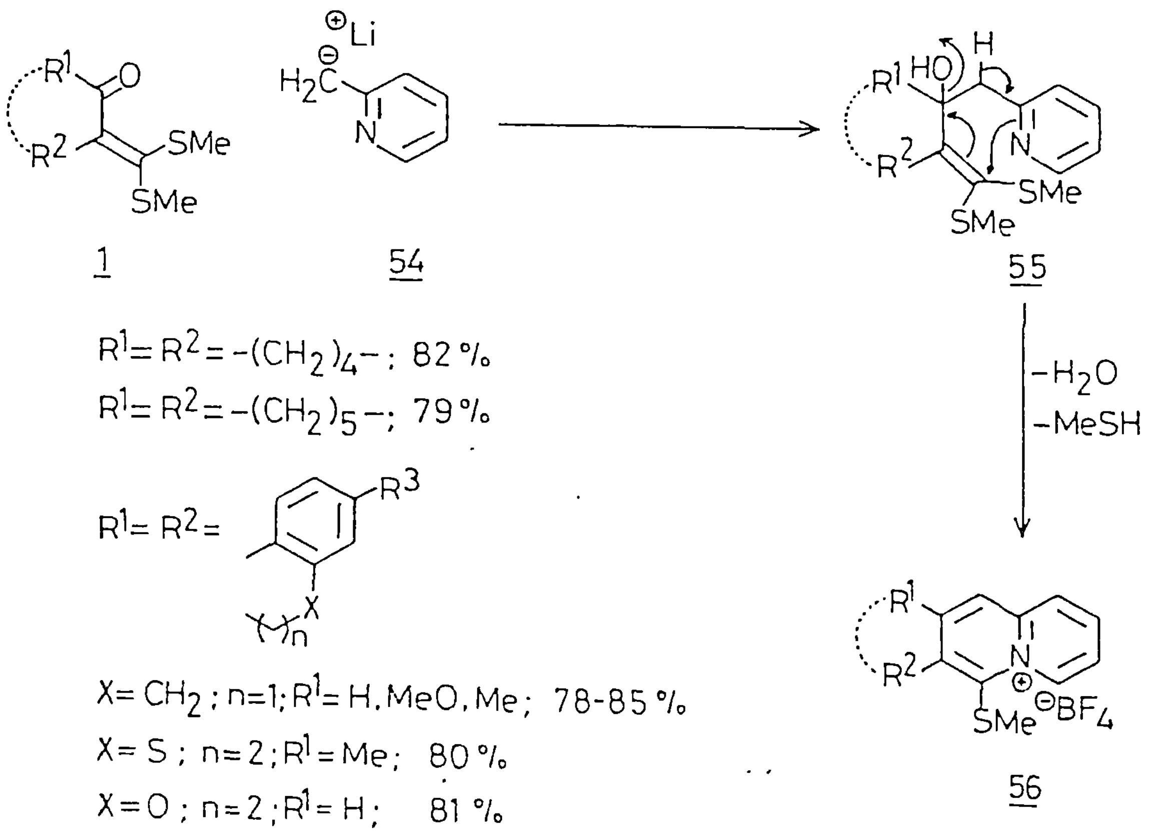
The α-oxoketene dithioacetals therefore with a wide ranging functional group variation and many easily accessible reagents and reactive intermediates manifestly hold many new synthetic possibilities leading diverse product range, including both carbocyclic and heterocyclic systems.

### Synthesis and Synthetic Utility of β-Oxodithioacetals

Our continued interest in the chemistry of α-oxoketene dithioacetals has been centred around exploitation of differential electrophilicity of 1,3-electrophilic centres of


SMe
R2
SMe
R1
O
1
BrMgH2C
51
1,4 and 1,2 addition
R3
R2
SMe
R1
OH
H
52
BF3·Et2O/ C6H6
R3
R2
R1
53
R1 = C6H5, 4-MeOC6H4, CH3 ; R2 = H ; R3 =
R1 = R2 = -(CH2)3-, -(CH2)4-, -(CH2)5- ; R3 =
R1 = R2 = ; R3 = SCH3
R4
R4 = H, OCH3

Scheme - 8



$R^1 = R^2 = -(CH_2)_4-$; 82 %

$R^1 = R^2 = -(CH_2)_5-$; 79 %

$R^1 = R^2 =$

$X = CH_2$; n=1; $R^1$ = H, MeO, Me; 78-85 %

$X = S$; n=2; $R^1$ = Me; 80 %

$X = O$; n=2; $R^1$ = H; 81 %

$R^1 = C_6H_5$, 4-Me$C_6H_4$, 4-MeO$C_6H_4$, 2-naphthyl, 2-furyl, 2-thienyl, 2-(styryl); $R^2$=H; 73-86 %

Scheme- 9

these systems for the regioselective construction of new C-H and C-C bonds involving either 1,2- or 1,4-nucleophilic additions leading to a number of new synthetic methodologies for a wide range of organic molecules.

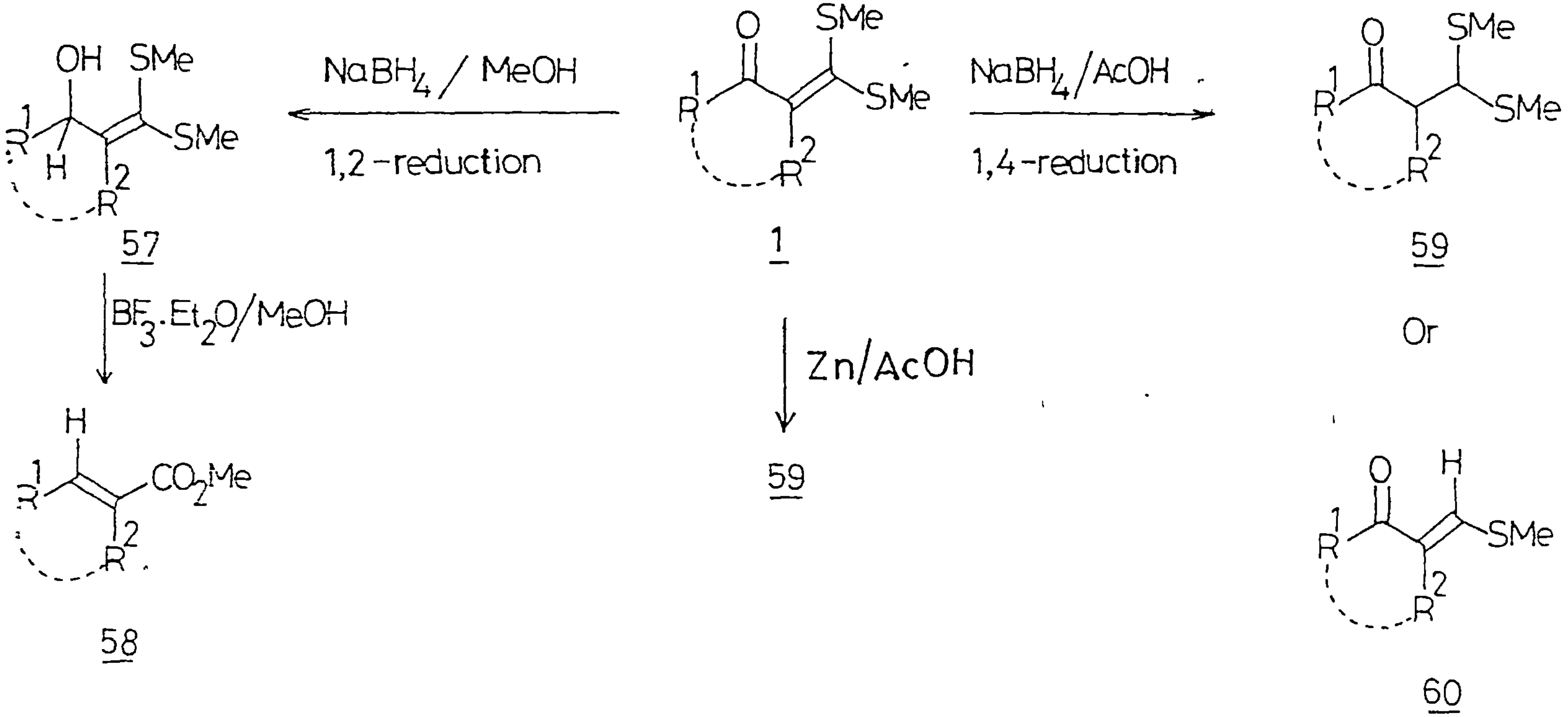
In continuation of these studies and as a part of the present research programme on β-oxodithioacetals, it was proposed to study the regioselective 1,4-conjugate reduction of 1 to their corresponding β-oxodithioacetals 59 and the further applications of 59 through various synthetic transforamtions. The following sections will provide a brief discussion on the work described in this thesis.

The reduction of α-oxoketene dithioacetals can follow different pathways depending on the nature of reducing agents and reaction conditions. Simple carbonyl group reduction affords the corresponding allyl alcohols in high yields[58]. Alternatively, the reduction can also be effected at C=C and C-S bonds or at both the carbonyl and olefinic functionalities.[59] Therefore, development of the specific procedures with effective regio control of the reduction pathways assumes considerable synthetic importance and enhances the synthetic utility of these intermediates. The α-oxoketene dithioacetals are therefore an attractive group of intermediates for the hard-soft affinity inversion studies which can be achieved either by changing the reaction conditions or by replacing one of the methylthio groups by an amino group to afford the corresponding S,N-acetals which exhibit clear 1,4-addition mode towards hard nucleophiles.

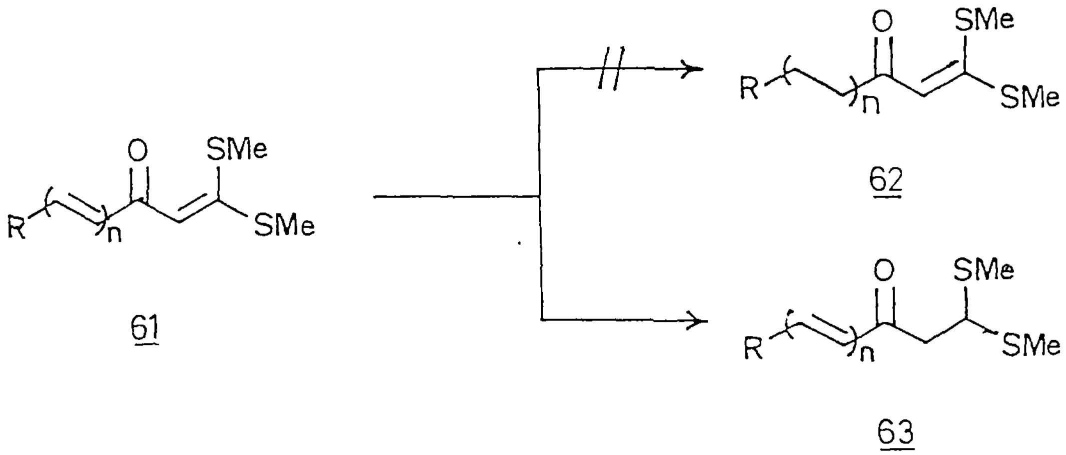
We have successfully utilized the hard-soft affinity inversion (HSAB) concept in achieving the highly regio- and chemo- selective 1,4-conjugate reduction employing sodium borohydride in the presence of a strong proton donor solvent as a medium and these results are presented in the part A of the Chapter II.

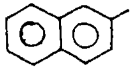
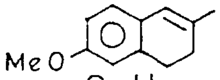
Thus, when α-oxoketene dithioacetals 1 was treated with four fold excess of sodium borohydride in large excess of acetic acid[59] as a solvent the corresponding β-oxodithioacetal was obtained in high yields. No product arising of 1,2-reduction process was observed in the reaction mixture. When less than four equivalents of $NaBH_4$ was used, the same product was obtained alongwith large amount of unaltered starting material. The other representative examples undergoing this regioselective reduction are described in the Chapter II. However, some substrates suffered elimination of thiomethyl group to afford the corresponding vinylogous thiol esters 60 in substantial yields, while some substrates yielded 60 exclusively. Steric crowding appears to enhance the elimination of MeSH group in these systems. Interestingly, the α-cinnamoyl and its higher enoyl ketene dithioacetals 61 underwent chemoselective reduction of mercapto double bond to yield the corresponding β-oxodithioacetals 62 in good yields. It is pertinent to note that the double bonds otherthan the mercapto double bond always remain intact during these reductions. This 1,4-conjugate reduction studies of α-oxoketene dithioacetals and the mechanistic interpretations alongwith the merits and demerits of this methodology have been discussed in detail.

The new method for the synthesis of β-oxodithioacetals from the corresponding α-oxoketene dithioacetals through 1,4-conjugate reduction with $NaBH_4$ in acetic acid has been successful but some limitations have been observed. The main shortcoming of this method has been that it afforded the methylthiomethyleneketones either as a side product alongwith the desired β-oxodithioacetals or as the only product. In few cases, the reduction did not proceed at all where the starting substrates were recovered unaltered. These all facts have become together as a sole constraint to the otherwise very efficient methodology. In view of the assumed synthetic potential of β-oxodithioacetals and our future proposed programme to utilize these intermediate for further important transformations, a better method for the preparation of β-oxodithioacetals has been envisaged. Therefore, an attempt in this direction has been made to evolve a general and versatile method to convert α-oxoketene dithioacetals into the β-oxodithioacetals. Thus, we have investigated the reduction of a number of oxoketene dithioacetals with zinc in acetic acid medium and observed that it could provide the β-oxodithioacetals in much improved yields without deviation in the product mixture (Scheme 10). The comparative yields of the product β-oxodithioacetals so obtained using $NaBH_4$ in acetic acid and zinc in acetic acid are described in the Part B of Chapter II. Thus, the zinc-acetic acid methodology for the transformation of α-oxoketene


NaBH4 / MeOH
1,2-reduction
NaBH4/AcOH
1,4-reduction
BF3.Et2O/MeOH
Zn/AcOH
Or
OH
SMe
SMe
R1
H
R2
O
57
58
CO2Me
1
59
59
60

Scheme 10



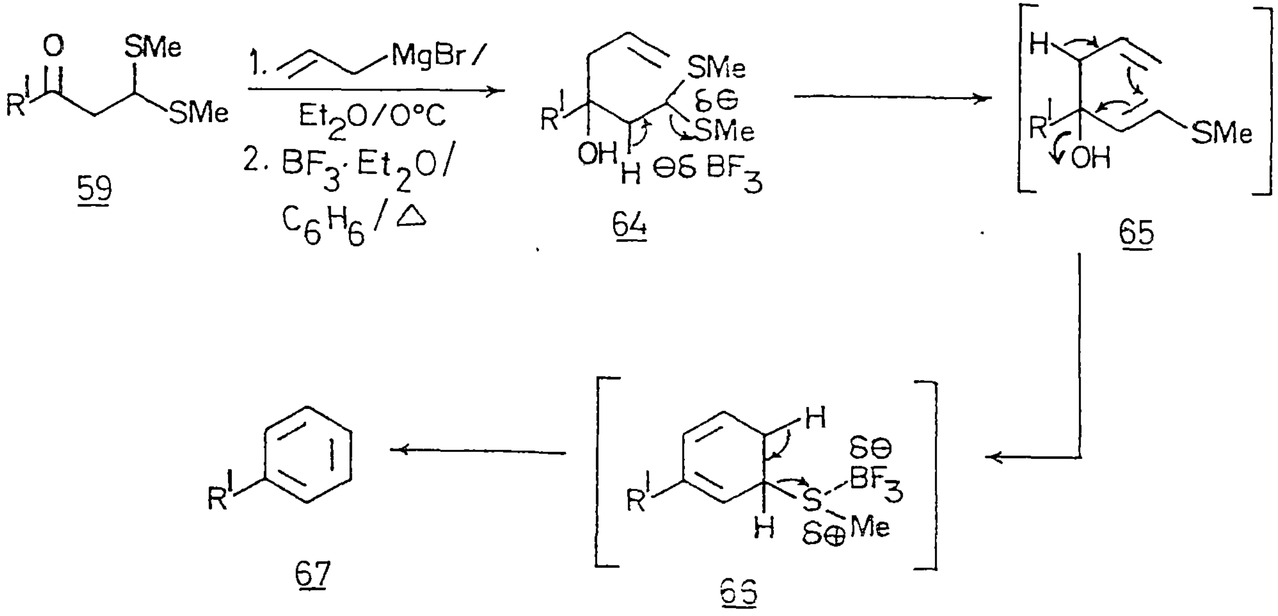
| | n | R |
|---|---|---|
| 61 - 63a, | 1 | $C_6H_5$ |
| b, | 1 | 4-MeO-$C_6H_4$ |
| c, | 1 |  |
| d, | 1 |  |
| e, | 1 |  |
| f, | 2 | $C_6H_5$ |
| g, | 2 | 4-MeO-$C_6H_4$ |
| h, | 3 | $C_6H_5$ |

Scheme—11

dithioacetals to β-oxodithioacetals has been successful in circumventing the problems and limitations associated with the reduction method using $NaBH_4$ in acetic acid.

The aromatic annelation methodology developed by our group for the construction of a variety of benzenoids and condensed aromatic via α-oxoketene dithioacetals has been found to be highly successful as described in the earlier sections in this chapter. However, the method suffers from some serious limitations. The end product aromatic so obtained always carry an undesirable substitutents in the form of either methylthio group, benzyl or naphtyl methyl group. The methylthio group may be removed relatively in more convenient way than the other observed substituents to procure the desired aromatics. It was therefore considered of interest to explore the possibilities to develop unambigous methods for the synthesis of aromatics without the observed limitations, the β-oxodithioacetals were found to be appropriate intermediates for the proposed cycloaromatization studies. The Chapter III therefore describes an account on the efficient method for the synthesis of a wide range of aromatic products starting from β-oxodithioacetals.

Thus, the β-oxodithioacetal 59 derived from 1 was reacted with allylmagnesium bromide yielding the corresponding carbinolacetal which on subsequent $BF_3.Et_2O$ assisted cycloaromatization[56] afforded the biphenyl 67 in 89% yield. The biphenyl did not carry the undesired methylthio group unlike in the case of product obtained from the



59 , 67a, $R^1 = C_6H_5$

b, $R^1 = Me$

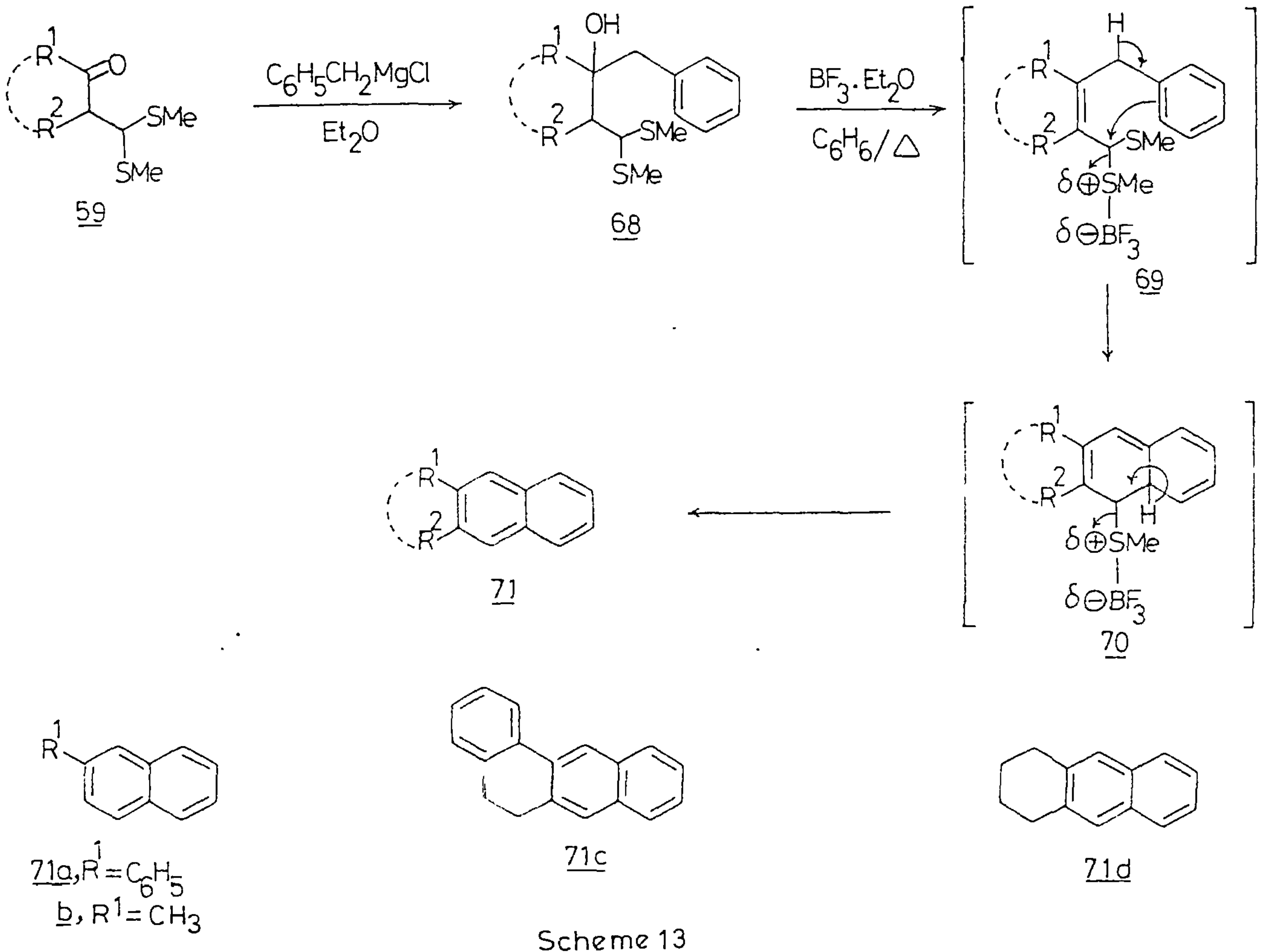
c, $R^1$ = 2-naphthyl

d, $R^1 = 4\text{-}MeOC_6H_4$

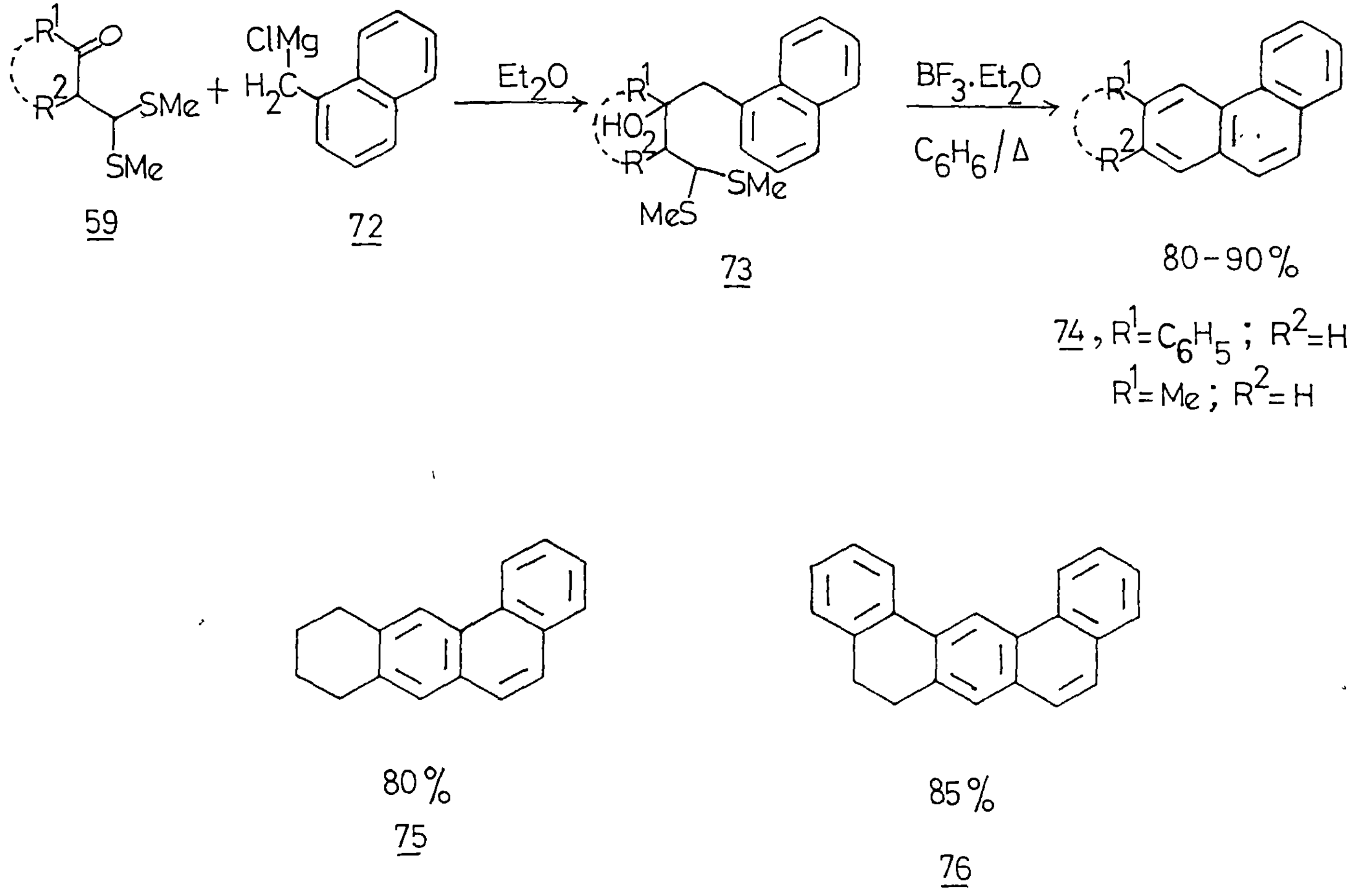
Scheme-12

corresponding oxoketene dithioacetal. The other corresponding aromatic compounds 67 were obtained in excellent yields on following the same reaction sequence. Similarly, benzylmagnesium chloride underwent facile addition to β-oxodithioacetal 59 resulting in the quantitative yield of corresponding carbinolacetal 68 which smoothly cyclized under the described conditions to afford the 2-phenyl naphthalene in high yield (Scheme 13). The same reaction has been carried out with various β-oxodithioacetals under similar reaction conditions to obtain the corresponding annelated products in good to high overall yields. All the product aromatic molecules were found to be free from the benzyl group as substituent. Therefore, the limitation of competative 1,4-addition of benzyl Grignard reagent to α-oxoketene dithioacetals ultimately resulting in the undesired benzyl group substituted naphthalene products has been completely eliminated on employing β-oxodithioacetals in place of α-oxoketene dithioacetals.

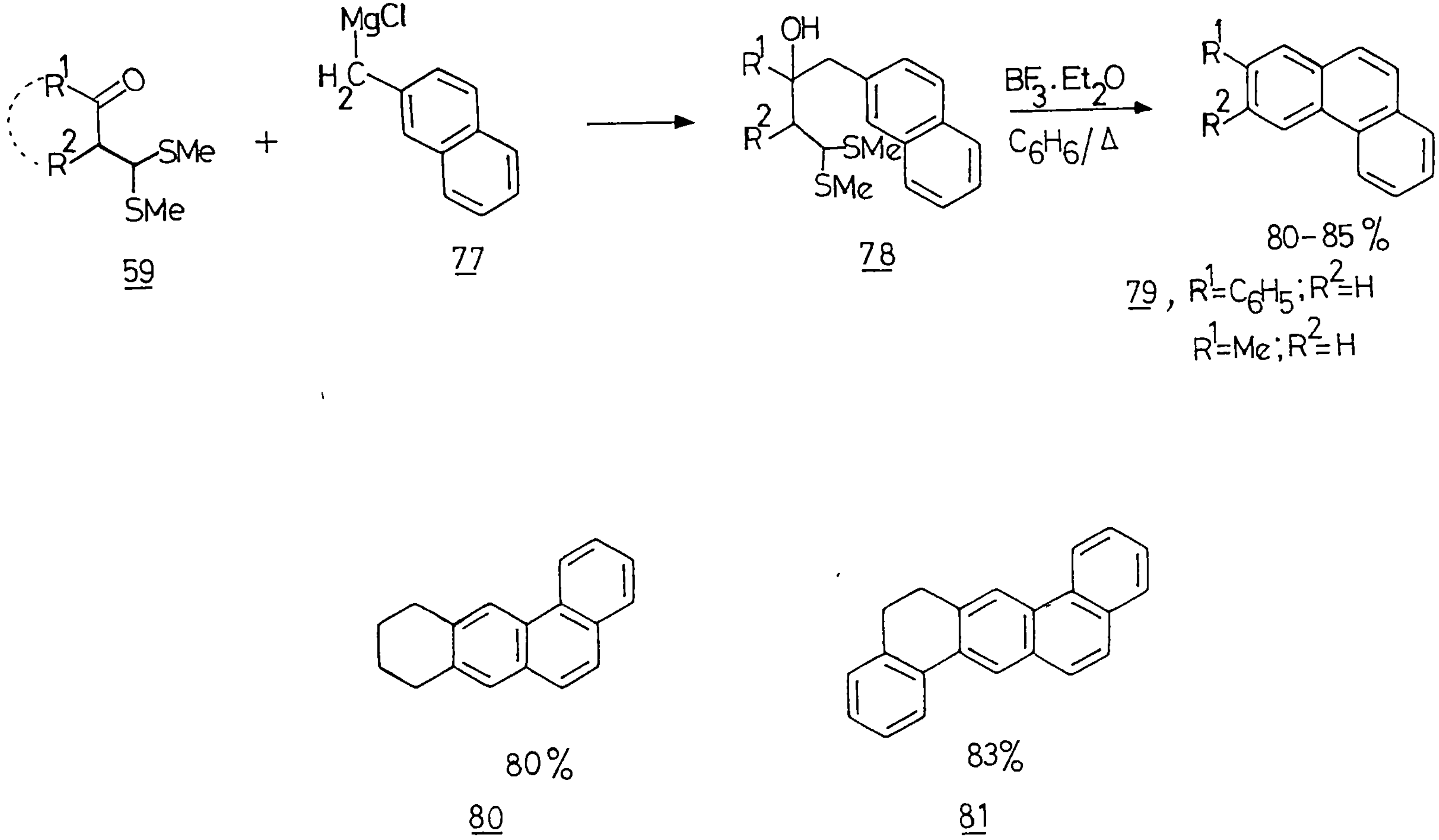
The results obtained from the reactions of 1- and 2-naphthylmethyl magnesium halides with β-oxodithioacetals also proved to be highly fruitful in achieving the synthesis of variously substituted phenathrenes 74 , 79 and condensed aromatic compounds in fairly good yields (Scheme 14 and 15). Here again, the disparities in the mode of addition of these Grignard reagents to α-oxoketene dithioacetals leading to annelated products with naphthylmethyl substitution are totally contained. The work presented in this chapter


59
$C_6H_5CH_2MgCl$
$Et_2O$
68
$BF_3.Et_2O$
$C_6H_6/\Delta$
69
70
71
71a, $R^1 = C_6H_5$
b, $R^1 = CH_3$
71c
71d
R1
R2
O
OH
SMe
H
δ⊕SMe
δ⊖BF3

Scheme 13


R1
R2
SMe
SMe
59
ClMg
H2C
72
Et2O
R1
HO
R2
SMe
MeS
73
BF3.Et2O
C6H6 / Δ
R1
R2
80-90%
74, R1=C6H5 ; R2=H
R1=Me ; R2=H
80%
75
85%
76

Scheme 14


MgCl
SMe
SMe
OH
BF3.Et2O
C6H6/Δ
80-85 %
59
77
78
79 , R1=C6H5;R2=H
R1=Me;R2=H
80%
80
83%
81

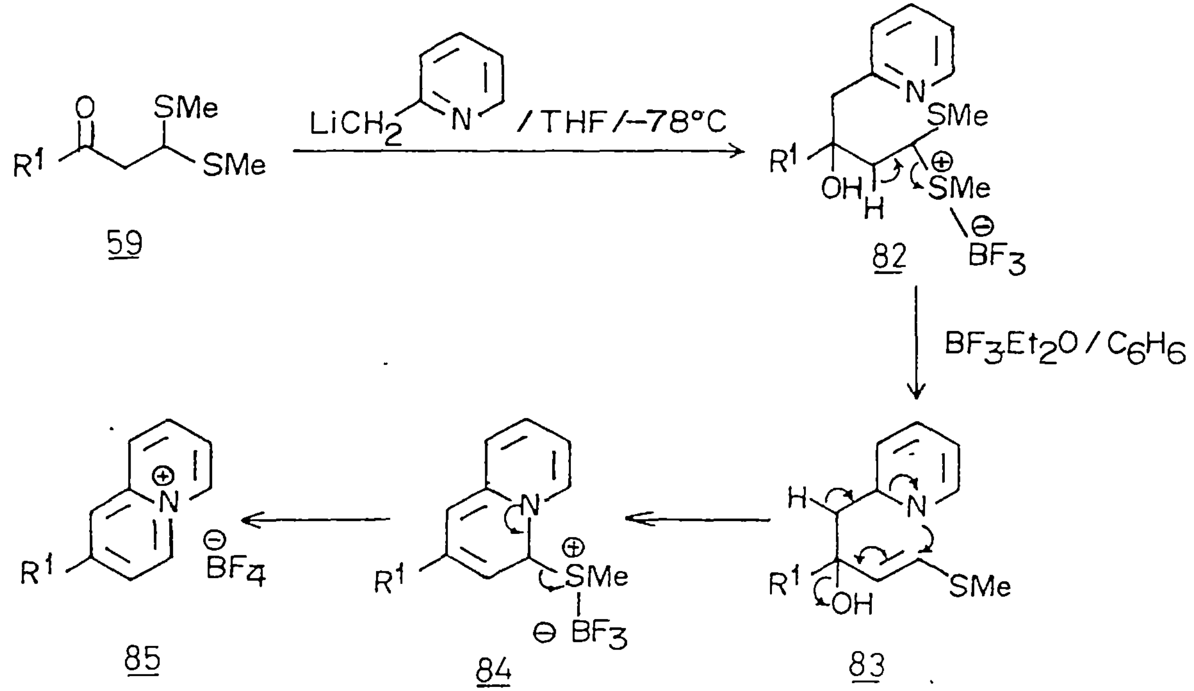
Scheme 15

therefore establishes an alternative approach for the aroamtic annelation of active methylene ketones via their β-oxodithioacetal intermediates for the synthesis of a wide range of aromatic products that stands superior to the one described earlier from our laboratory.

As an extension of this method, the β-oxodithioacetals were also reacted with 2-picolyllithium in THF at -20°C followed by $BF_3.Et_2O$ assisted cyclization whereby the sulfur free quinolizinium tetrafluoroborates 85 were obtained in good yields (Scheme 16). It is pertinent to note that the reaction of picolyllithium with α-oxoketene dithioacetals resulted in the formation of methylthio substituted quinolizinium salts. The unsuccessful desulfurization of methylthio group from those products became the main handicap of the method earlier developed by our group. In view of this drawback associated with the earlier method, the present reaction strategy using β-oxodithioacetals is therefore proved to be successful for this important heteroaromatic annelation.

The Chapter IV describes a new general method developed for the synthesis of 1,2-Diarylethylenes, 1,4-diarylbutadienes and 1,6-diarylhexatrienes through cycloaromatization of β-oxodithioactals derived from α-cinnamoylketene dithiacetals and their higher enyl analogs.[60]

In continuation of the aromatic annelation studies, our group had reported the reaction of α-cinnamoyl ketene dithioacetals with allylmagnesium halide to afford the substituted stilbenes[61] under the described reaction conditions.



59, 82 – 85a, R$^1$ = C$_6$H$_5$

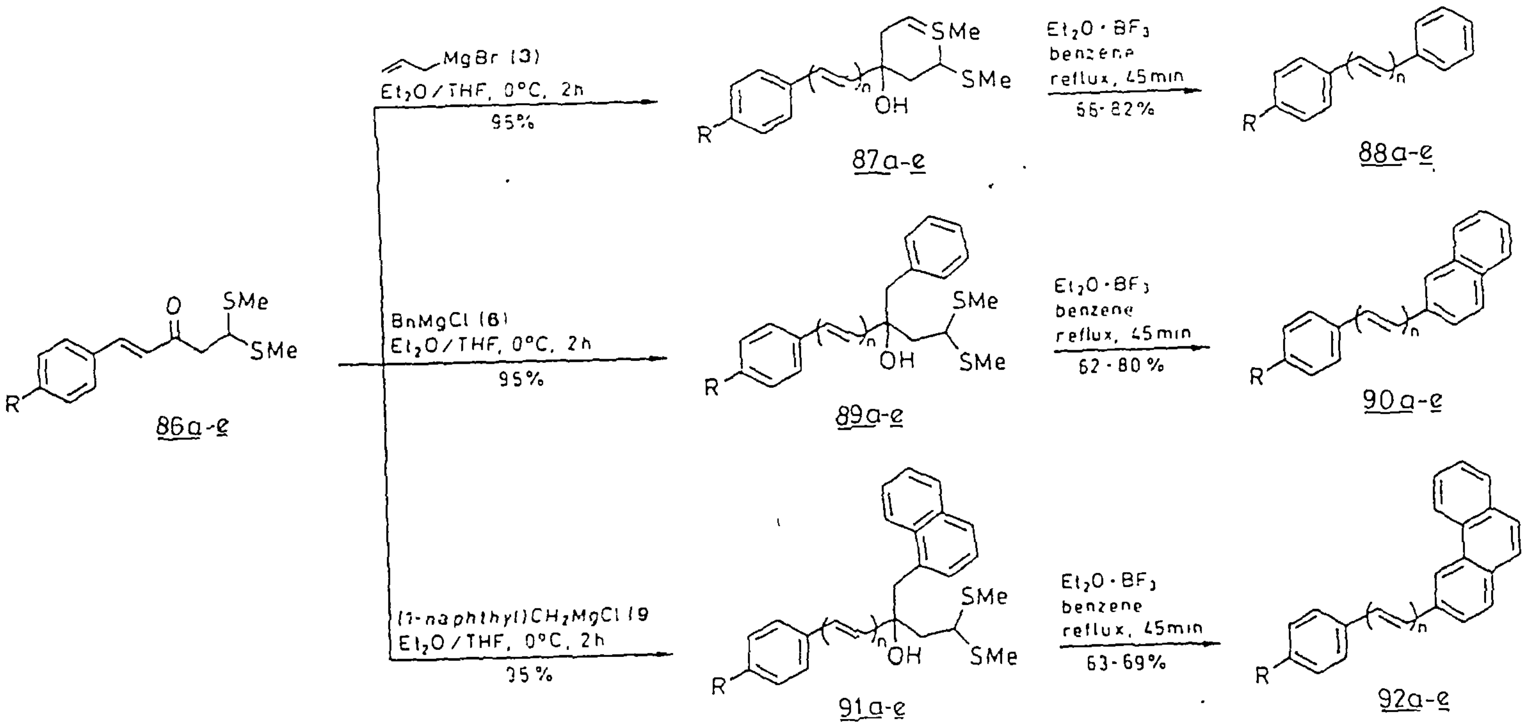
b, R$^1$ = Me

Scheme – 16

However, the reaction was not of general applications as 4-methoxy stilbene and other higher enylanalogs of stilbenes could not be prepared. This has prompted us to undertake the present study by using β-oxodithioacetals to overcome the observed limitations and thereby designing a useful general method for the synthesis of large variety of terminally substituted polyenes.

In a typical experiment, when 96 was reacted with allylmagnesium bromide, the corresponding tertiary alcohol thioacetal 86 was formed in nearly quantitative yield. This carbinol on treatment with $BF_3.Et_2O$ in refluxing benzene afforded stilbene 88 in 78% yield. Similarly, the 4-methoxy stilbene 88b which could not be prepared earlier from α-oxoketene dithioacetal was obtained in 66% yield from 86b under identical conditions (Scheme 17).

The corresponding dienyl 86c and trienyl 86e β-oxodithioacetals afforded the corresponding 1,4-diaryl butadienes 88c and 1,6-diphenyl 1,3,5-hexatrienes 88e in 78-82% overall yields by following the same reaction sequence. The methodology could be similarly extended for the synthesis of 1-aryl-2(2'-naphthyl)ethylenes 90a-b and the respective dienes 90c-d and triene 90e by reacting β-oxodithioacetals 86a-e with benzylmagnesium chloride and subsequently cyclizing the resulting tertiary alcohols under the described reaction conditions. The same strategy was found to be highly successful for the synthesis of 1-aryl-2(3'-phenanthyl)ethylenes 92a-b and their higher enylanalogs 90c-e



| 86,87,88,89,90,91,92 | R | n | | R | n |
|---|---|---|---|---|---|
| a | H | 1 | d | MeO | 2 |
| b | MeO | 1 | e | H | 3 |
| c | H | 2 | | | |

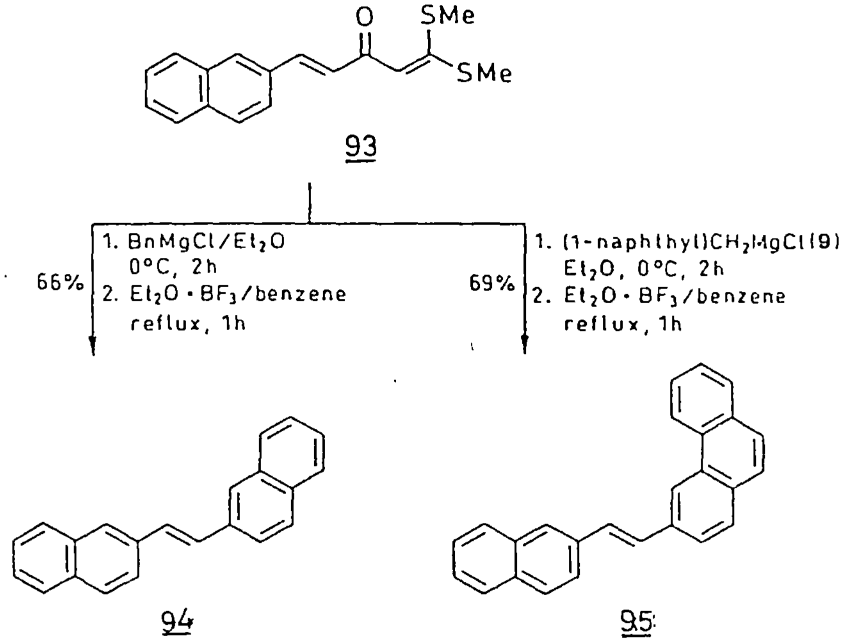
Scheme 17

by reacting 1-(napthyl)methylmagnesium chloride with 86a- e under identical conditions (Scheme 17). The 2-naphthyl derivative 93 also underwent facile cycloaromatization with benzyl magnesium chloride to yield 1,2-bis(2-naphthyl)ethylene 94 in 68% yield. The diarylethylene 95, a precursor for *hexahelicene* was similarly obtained in 64% yield by the treatment of 93 with (1-naphthyl)methylmagnesium chloride under standard conditions (Scheme 18).

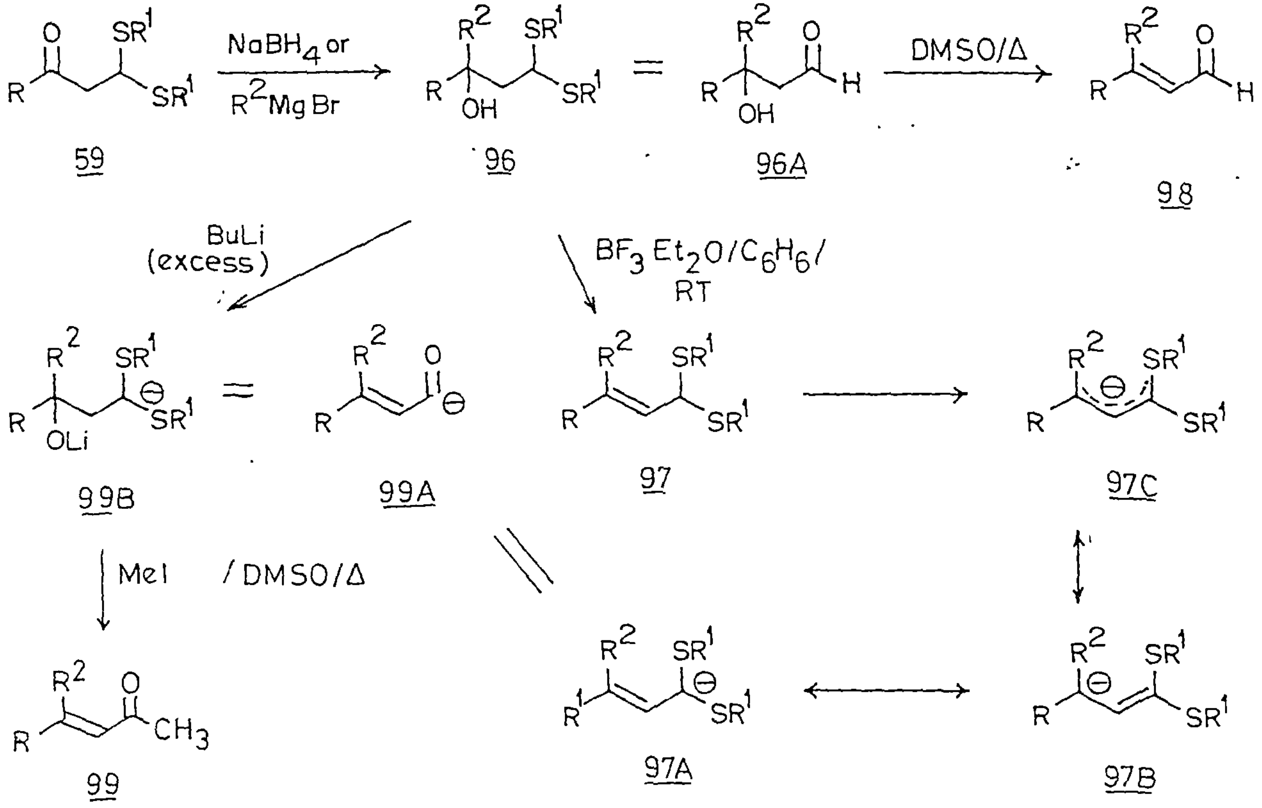
As a part of the synthetic investigations on β-oxodithioacetals, we have proposed to undertake some interesting transformations based on these intermediates and the results are presented in the last chapter.

In the present investigation, the β-oxodithioacetals 59 have been conveniently converted to the corresponding β-hydroxydithioacetals 96 either with $NaBH_4$ in ethanol or on addition of Grignard reagents (Scheme 19). These intermediates have been shown to undergo either selective dehydration to afford the corresponding enedithioacetals 97 or they can be converted to the corresponding enealdehydes 98 or enones 99 under suitable reaction conditions.

Initial studies were directed to formulate a facile dehydration procedure for the preparation of enedithioacetals 97 from β-hydroxydithioacetals. Unfortunately many attempts with various dehydrating agents failed to achieve this transformation. Interestingly, when 96 was treated with $BF_3.Et_2O$ complex in benzene at room temperature afforded 97


O
SMe
SMe
93
66%
1. BnMgCl/Et$_2$O
0°C, 2h
2. Et$_2$O · BF$_3$/benzene
reflux, 1h
69%
1. (1-naphthyl)CH$_2$MgCl (9)
Et$_2$O, 0°C, 2h
2. Et$_2$O · BF$_3$/benzene
reflux, 1h
94
95

Scheme 18


NaBH4 or
R2MgBr
DMSO/Δ
BuLi
(excess)
BF3 Et2O/C6H6/
RT
MeI
/DMSO/Δ
59
96
96A
98
99B
99A
97
97C
99
97A
97B

Scheme – 19

in moderate yields. The method was extended to some more selected examples to represent the generality of the reaction. Therefore, the β-hydroxydithioacetals 96 could be selectively dehydrated to enedithioacetals 97 without affecting the dithioacetal moiety. These product enedithioacetals are excellent precursors of allylanions for regiospecific addition studies.

Our next objective of the present investigations was to develop a facile one pot method for the concurrent dehydration and dithioacetalization of β-hydroxy dithioacetals 96 to afford ene and polyene aldehydes through a 1,3-carbonyl transposition. Our recent report[62] on the facile dethioacetalization of various dithioacetals and 1,3-dithianes on heating in DMSO under neutral conditions intrigued us to attempt the proposed transformation on β-hydroxydithioacetals under similar reaction conditions. We have indeed achieved this one pot successful operation of converting β-hydroxydithioacetals into their α,β-unsaturated aldehydes 98,on heating in DMSO at 150°C 3-5 hrs. The procedure successfully could afford the ene and polyenealdehydes from various β-hydroxydithioacetals in handsome yields.

The β-hydroxydithioacetals were next examined for their deprotonation and alkylation to produce the alkylsubstituted hydroxy dithioacetals. These ketals when subjected to DMSO thermal reaction whereby the α,β-unsaturated ketones 99 were formed in good yields.

Hence, a selective dehydration and concomitant dehydrative dethioacetalization methods have been developed to manifest some important synthetic transformations utilizing the β-hydroxydithioacetals derived from β-oxodithioacetals.

## REFRENCES

1. For review see : (a) Dieter, R.K. *Tetrahedron,* 1986, *42,* 3029; (b) Junjappa, H.; Ila, H.; Asokan, C. V. *Tetrahedron,* 1990, *46,* 5423.
2. Thuillier, A; Vialle, J.; *Bull. Soc. Chim. Fr.* 1959, 1398.
3. Chauhan, S.M.S.; Junjappa, H. *Tetrahedron,* 1976, *32,* 1779.
4. Saquet, M.; Thuillier, A. *Bull. Soc. Chim. Fr.* 1966, 1582.
5. Gompper, R.; Schmidt, R.R.; Kutter, E. *Leibigs Ann. Chem.* 1965, *37,* 684.
6. Thuillier, A.; Vialle, J. *Bull. Soc. Chim. Fr.* 1962, 2194.
7. Corey, E.J.; Chen, R.H.K. *Tetrahedron Lett.* 1973, 3817.
8. Shahak, I.; Sarson, Y. *Tetrahedron Lett.* 1973, 4207.
9. Dieter, R.K. *J. Org. Chem.* 1981, *46,* 5031.
10. Kelber, C. *Chem. Ber.* 1910, *43,* 1252.
11. Kelber, C.; Schwarz, A. *Chem. Ber.* 1912, *44,* 137.
12. McElvain, S.M. *Chem. Rev.* 1949, *45,* 453.

13. Borman, d. in *Houben-Weyl, Methoden Der Organischen Chemie B.VII/4 pp. 442*, Georqe Themie Verlag Stuttgart 1968.
14. Pohland, A.E.; Benson, W.R. *Chem. Rev.* 1966, *66*, 161.
15. Gompper, R.; Shaefer, *Chem. Ber.* 1967, *100*, 591.
16. Ref. 13, pp. 391.
17. Singh, G.; Purkayastha, M.L.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans. I.*, 1985, 1289.
18. Dieter, R.K.; silks, L.A.; Fishpaugh, J.R., Kastner, M.E. *J. Amer. Chem. Soc.* 1985, *107*, 4679.
19. Dieter, R.K.; Fishpaugh, J.R.; Silks, L.A. *Tetrahedron Lett.* 1982 *23*, 3751.
20. Myrboh, B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis* 1984, 50.
21. Apparoao, S.; Rahman, A.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1982, *23* 971.
22. Marino, J.P.; Kostuysk, J.L. *Tetrahedron Lett.* 11979, *20*, 2489.
23. Marino, J.P.; Kostusyk, J.L. *Tetrahedron lett.* 1979, *20*, 2493.
24. Singh, G.; Ila, H.; Junjappa, H. *Synthesis*, 1985, 165.
25. Saquet,M; Thuillier, A. *Bull. Soc. Chim. Fr.* 1966, 3969.
26. Myrboh, B.; Ila, H.; Junjappa, H. *J. Org. Chem.* 1983, *48* 5327.
27. Myrboh, B.; singh, L.w.; Ila, H.; Junjappa, H. *Synthesis* 1982, 307.
28. Singh, L.W. ; Ila, H.; Junjappa, H. *Synthesis* 1985, 531.
29. Singh, L.W. ; Ila, H. ; Junjappa, H. *Synthesis*1987, 873.

30. Dutta, A.; Ila, H.; Junjappa, H. *Tetrahedron* 1987, *43*, 5367.

31. Dutta, A.; Bhattacharjee, S.; Ila, H.; Junjappa, H. *Synthesis* 1988, 728.

32. Purkayastha, M.L.; Ila, H.; Junjappa, H. *Synthesis*, 1989, 20.

33. Singh, G.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans. I*, 1987, 1945.

34. Vishwakarma, J.N.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans. I* 1983, 1099.

35. Chakrasali, R.T.; Ila, H.; Junjappa, H. *Synthesis*, 1988, 453.

36. (a) Rastogi, R.R.; Ila, H.; Junjappa, H. *J. Chem. Soc. Chem. Comm.*, 1975, 645 (b) Rastogi, R.R.; Kumar, A.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans I.* 1978, 549.

37. Dutta, A.; Ila, H.; Junjappa, H..; *Synthesis*, 1988, 556.

38. Singh, L.W.; Ila, H.; Junjappa, H. *Synthesis*, 1988, 89.

39. Singh, L.W.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans. I* 1988, 2365.

40. Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis*, 1985 , 163.

41. Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1985, *26*, 1087.

42. Asokan, C.V.; Bhattacharjee, S.; Ila, H.; Junjappa, H. *Synthesis* 1988, 281.

43. Singh, L.W.; Gupta, A.K. Ila, H.; Junjappa, H.; *Synthesis* 1984, 516.

44. Singh, L.W. ; Ila, H.; Junjappa, H.; *Indian J. of Chem.* 1987, *26B*, 607.

45. Deb. B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis*, 1987, 893.

46. Deb. B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1988, *29*, 2111.

47. Singh, G.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1984 , *25* 5095

48. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1984, *25*, 5095.

49. Dutta, A.; Ila, H. Junjappa, H. *Tetrahedron Lett.* 1988, *29* 497.

50. Balu, M.P.; Pooranchand, D.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1988, *29*, 501.

51. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*1988, *29* 6633.

52. Gupta, A.K. ; Ila, H.; Junjappa, H. Unpublished Results.

53. Thomas, A.; Ila, H.; Junjappa, H. Unpublished Results.

54. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron*, 1989 *45*, 1509.

55. Balu, M.P.; Singh, G.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1986 , *27*, 117.

56. Rao, Ch. S.; Balu, M.P.; Ila, H.; Junjappa, H. *Tetrahedron*,1991, *47*, 3499.

57. Balu, M.P.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*1987, *28*, 3023.

58. Myrboh, B.; Ila, H.; Junjappa, H. *J. Org. Chem.*, 1983, *48*, 5327.

59. Rao, Ch. S.; Chakrasali, R.T.; Ila, H.; Junjappa, H. *Tetrahedron*, 1990, *46*, 2195.

60. Rao, Ch. S.; Singh, O.M.; Ila, H.; Junjappa, H. *Synthesis*, 1992, 1075.

61. Asokan, C. V.; Ila, H.; Junjappa, H. *Synthesis*, 1987, 284.

62. Rao, Ch. S.; Chandrasekharam, M.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*, 1992, *48*, 8163.

# CHAPTER II

## PART-A

## REGIO- AND CHEMOSELECTIVE CONJUGATE 1,4-REDUCTION OF α-OXOKETENE DITHIOACETALS WITH SODIUM BOROHYDRIDE IN ACETIC ACID : SYNTHESIS OF β-OXODITHIOACETALS*

### II.A.1 INTRODUCTION

The chemical and physical properties of n-(butylthio)-methylene ketones of general formula 1b have been first examined by Ireland and Marshall[1-4] either as a blocking group in the ketone methylation or as a group responsible for highly regioselective metal hydride reductions (scheme 1).

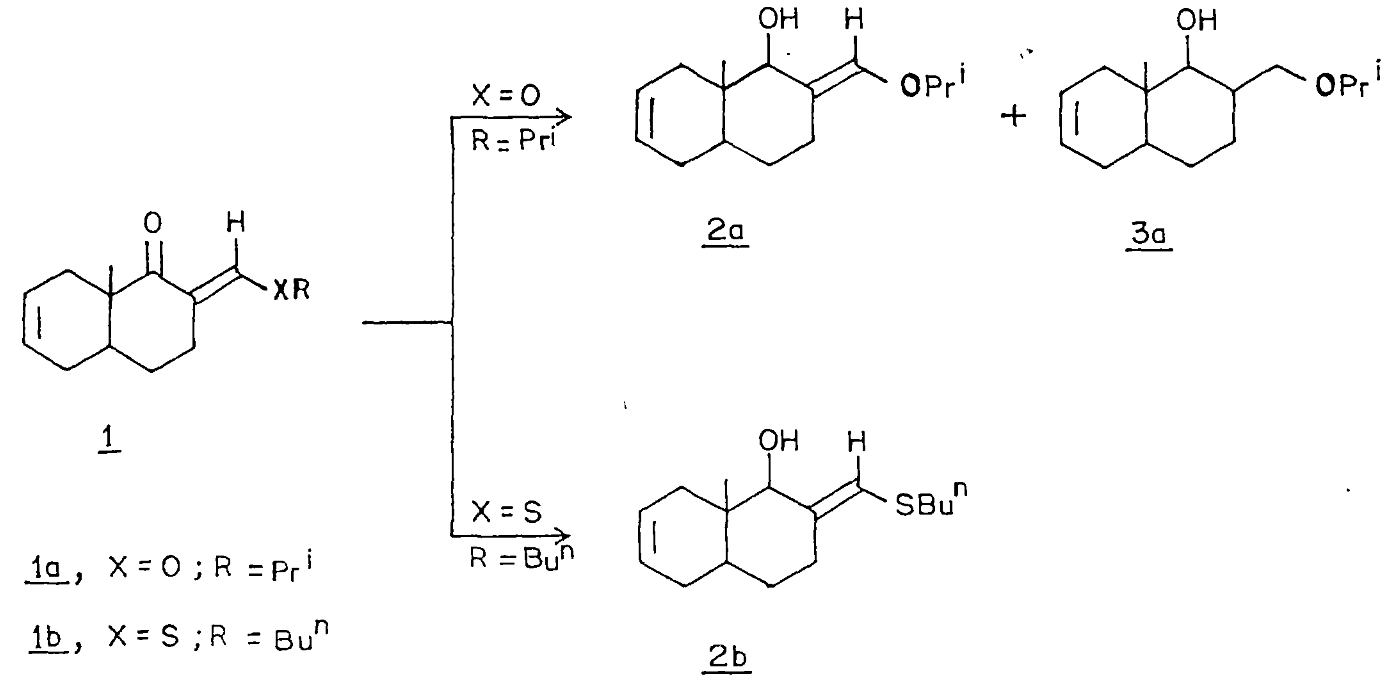
---

* Ch.Srinivasa Rao, R.T.Chakrasali, H.Ila, H.Junjappa, Tetrahedron, *46*, 2195 (1990).

They have first observed[3a] that the iso-propoxymethylene ketone 1a underwent sodium borohydride reduction in methanol to afford a mixture of two products **2a** and **3a** in 62% and 20% yields respectively. Apparently, the minor product 3a has arisen out of 1,4-reduction while and the major product **2a** formed by 1,2-reduction process. However, when n-butylthiomethylene ketone **1b** was subjected to sodium borohydride reduction in methanol, an exclusive 1,2-adduct **2b** was formed in 83% yield. The reaction mixture did not contain any 1,4-addition product. Thus, they were the first to discover that the sulfur in place of oxygen in these ketones makes the reduction process leading to highly regioselective 1,2-addition while the corresponding iso-propoxy group fails to maintain this regioselectivity[3] (Scheme 1).

The same authors extended this reduction elegantly in a sequence leading to the synthesis of β-velerone[4] containing [4,5]-decaspirodienone structural moiety (Scheme 2). Thus, the significant regioselective reduction of carbonyl function of **4** led to the corresponding carbinol 5 which on treatment with mercuric chloride underwent smooth 1,3-carbonyl transposition to afford enealdehyde 6 (Scheme 2). This was then converted to β-velerone through several steps.

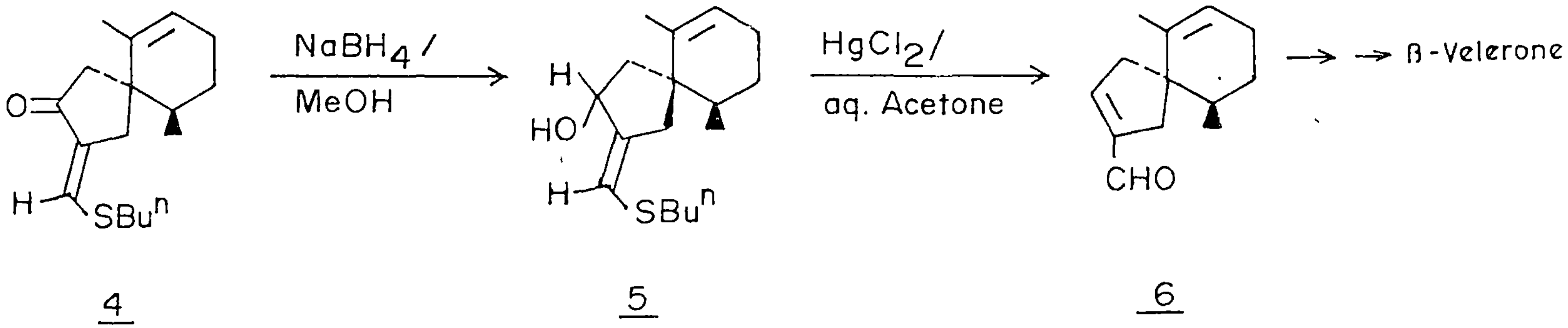
Thuillier and coworkers[5] were the first to report the sodium borohydride reduction of α-oxoketene dithoacetals 8 (Scheme 3) to afford the corresponding carbinols 9 in quantitative yields. These carbinols 9 were subsequently treated with p-



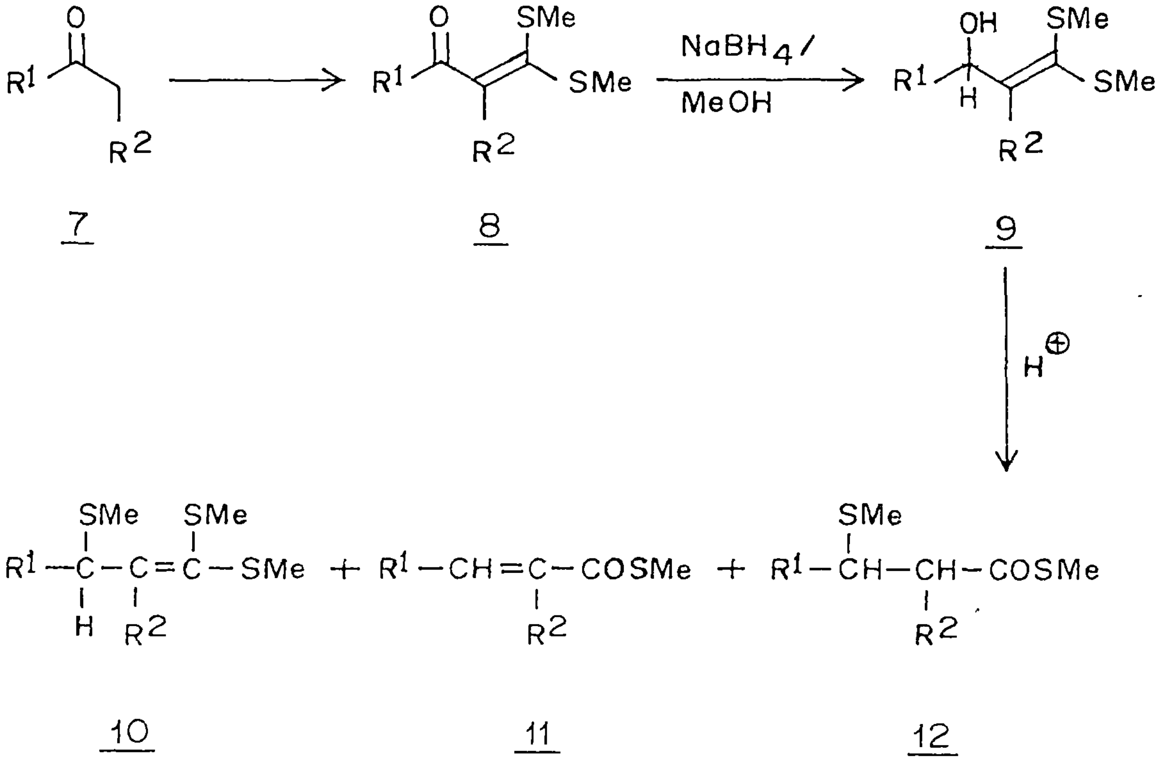
1a, X = O ; R = Pr$^i$

1b, X = S ; R = Bu$^n$

Scheme – 1



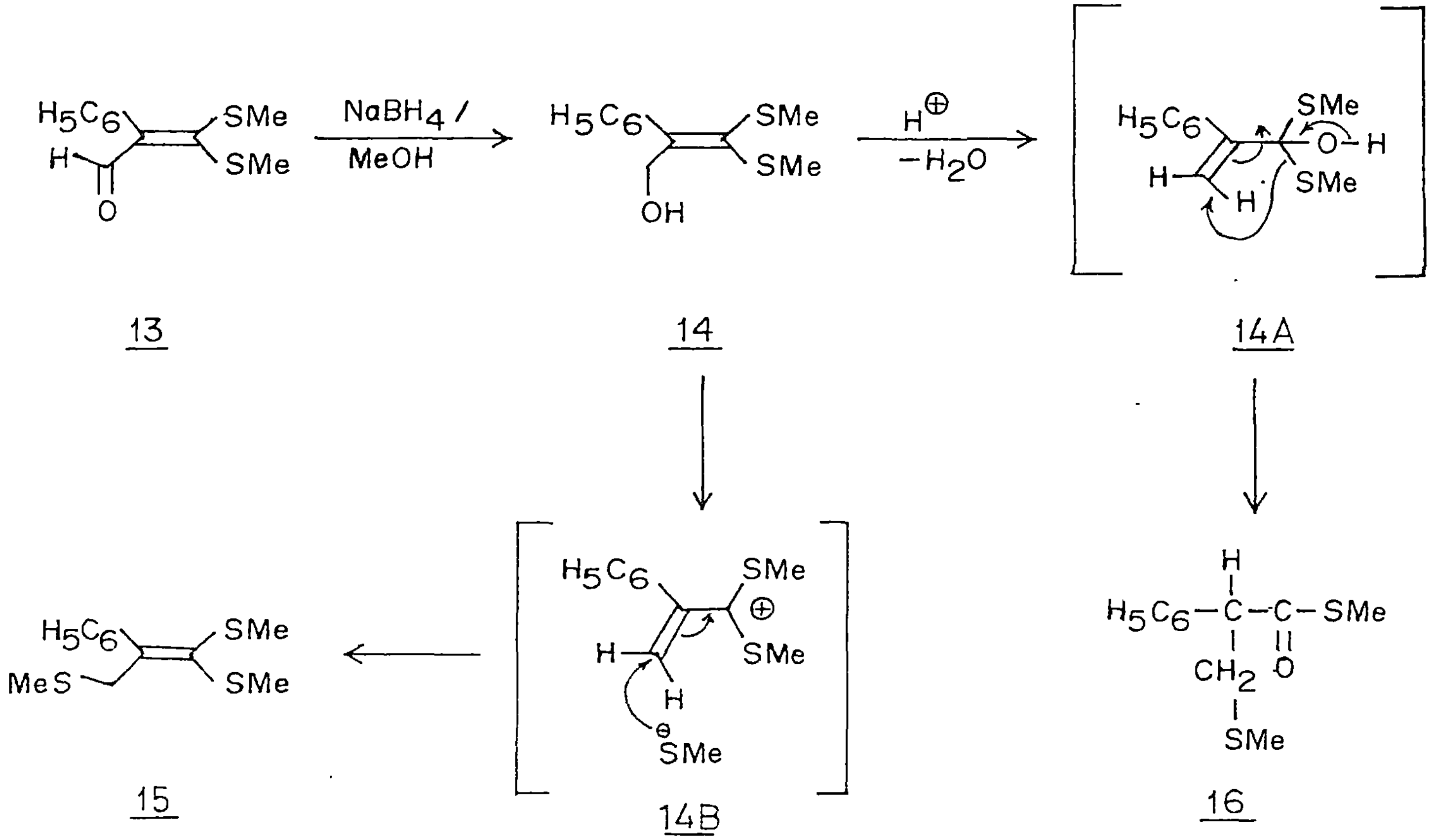
Scheme — 2



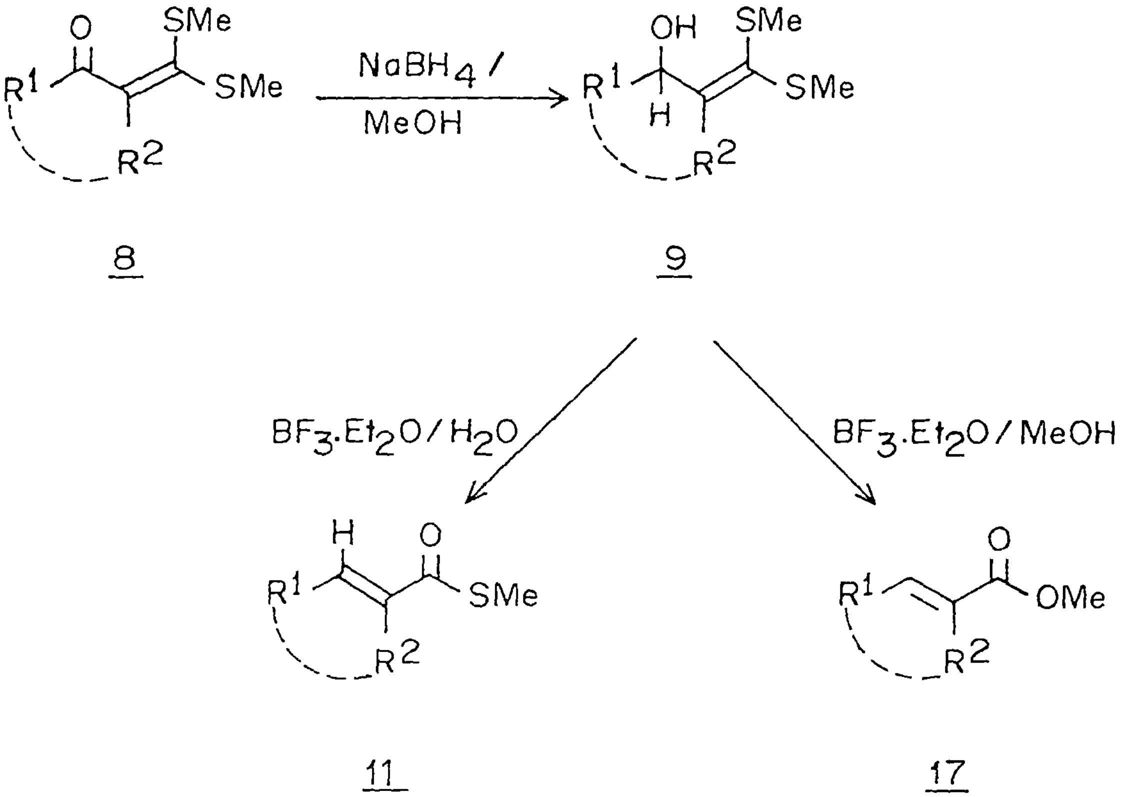
Scheme – 3

toluenesulfonic acid in refluxing benzene to afford a mixture of products 10,11 and 12. However, the thiolester 11 was obtained in very low yield. They examined various α-oxoketene dithioacetals for sodium borohydride reduction which consistently yielded 1,2-reduction products followed by interesting molecular rearrangements during the acid assisted work-up. A typical example has been shown in scheme 4.

The studies on sodium borohydride reduction of α-oxoketene dithioacetals were continued by Junjappa, Ila and Myrboh[6] with a view to develop highly stereo- and regiospecific methods for homologation of ketones. They subjected a number of α-oxoketene dithioacetals 8 for sodium borohydride reductions in methanol to afford the corresponding allylic alcohols 9 in quantitative yields (scheme 5). Interestingly, these allylic alcohols 9 underwent smooth methanolysis in the presence of $BF_3.Et_2O$ to afford the corresponding eneesters 17 in high yields. Also, the $BF_3.Et_2O$-assisted hydrolytic conditions on 9 yielded the corresponding thiolesters 11 in high yields and there were no side products detected in the reaction mixture. It is pertinent to note that the thiolester 11 could only be obtained in very low yield alongwith side products under Thuillier's hydrolytic conditions[5]. The method was generally applicable to the synthesis of α,β-unsaturated esters, aldehydes and the ketones as well. The plan involving the conversion of α-oxoketene dithioacetals to the corresponding α,β-unsaturated aldehydes is illustrated in scheme 7. However, the required methylthiomethylene ketones 18a or 18b were prepared by



Scheme — 4

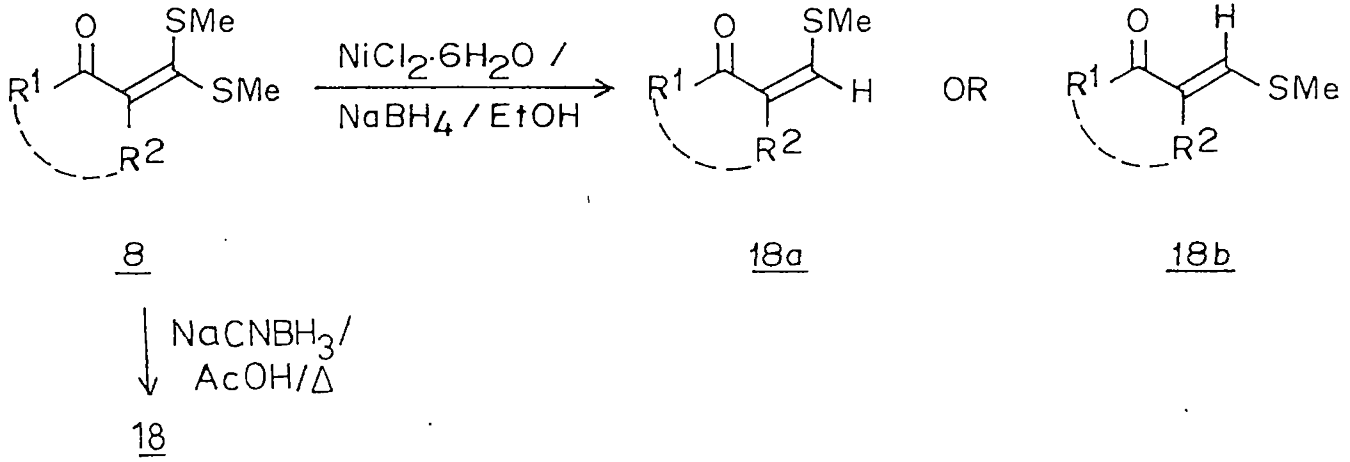

SMe
SMe
O
R1
R2
8
NaBH4 /
MeOH
OH
SMe
SMe
R1
H
R2
9
BF3.Et2O/H2O
BF3.Et2O/MeOH
H
O
R1
SMe
R2
11
O
R1
OMe
R2
17

Scheme — 5

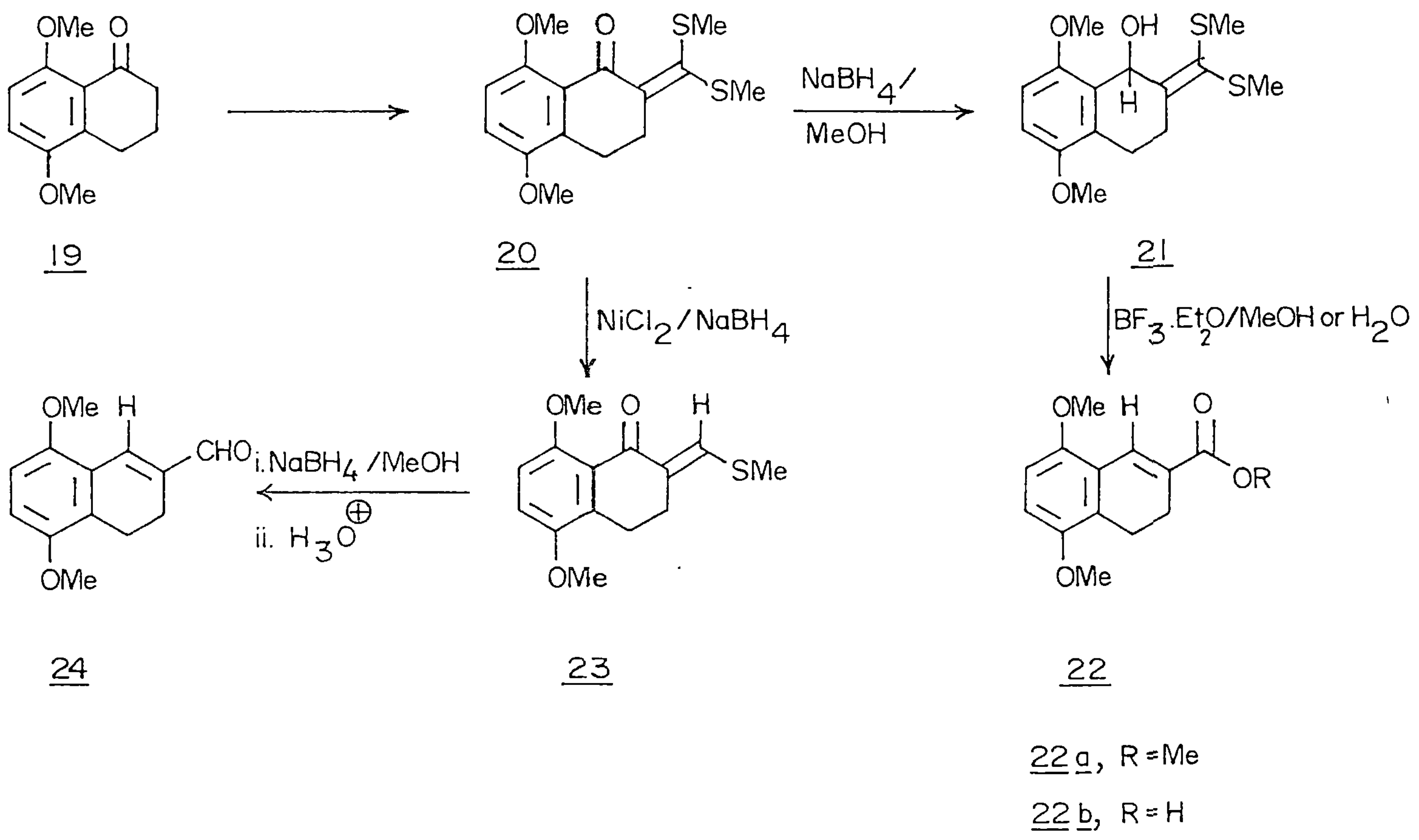
developing a new method as illustrated in scheme 6. Thus, 8 on subjecting to sodium borohydride in ethanol in the presence of nickel chloride[7], the corresponding methylthiomethylene ketones 18a or 18b were obtained in moderate to good yields. The method was fairly general though the yields for acylketene dithioacetals were not very satisfactory. The nickel boride appears to be the reducing agent in this reaction. The method also suffered from the disadvantage due to the extensive adsorption of the products to finly devided nickel boride resulting in the poor yields of the methylthiomethylene ketones. The recovery therefore, could never be achieved to get the satisfactory yields of the these ketones. However, a better method was made available for the conversion of 8 to 18 using sodium cyanoborohydride in refluxing acetic acid[8] (Scheme 6). As an example of a synthetic application of these reduction methods[6,7], the preparations of 22 and 24, which are the key intermediates in anthracyclinones synthesis, were achieved in good yields (scheme 7).

The C-S bond in α-oxoketene dithioacetals 8 has been cleaved cathodically on mercury or glassy carbon electrodes employing the tetrabutylammonium hydrogen sulfate (TBAHS) as a source of proton to afford the corresponding methylthiomethylene ketones 18 and β-ketosulphides 25 in good yields[9,10] (scheme 8).

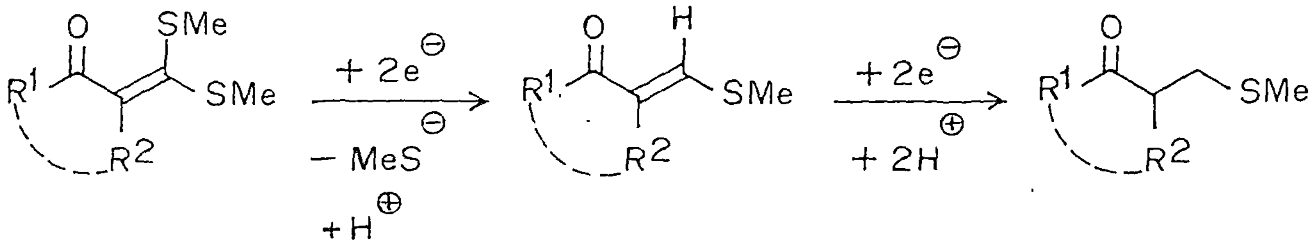
A unique regio- and stereoselective reduction of α-oxoketene dithioacetals 8 has been examined by Gammill *et al*[11-13]


SMe
SMe
$NiCl_2 \cdot 6H_2O$ /
$NaBH_4$ / EtOH
SMe
H
OR
H
SMe
O
R1
R2
8
18a
18b
$NaCNBH_3$/
AcOH/Δ
18

Scheme – 6


OMe
O
OMe
19
OMe
O
SMe
SMe
OMe
20
NaBH4/
MeOH
OMe
OH
SMe
H
SMe
OMe
21
NiCl2/NaBH4
BF3.Et2O/MeOH or H2O
OMe
H
CHO
OMe
24
i. NaBH4 /MeOH
ii. H3O⊕
OMe
O
H
SMe
OMe
23
OMe
H
O
OR
OMe
22
22a, R=Me
22b, R=H

Scheme — 7

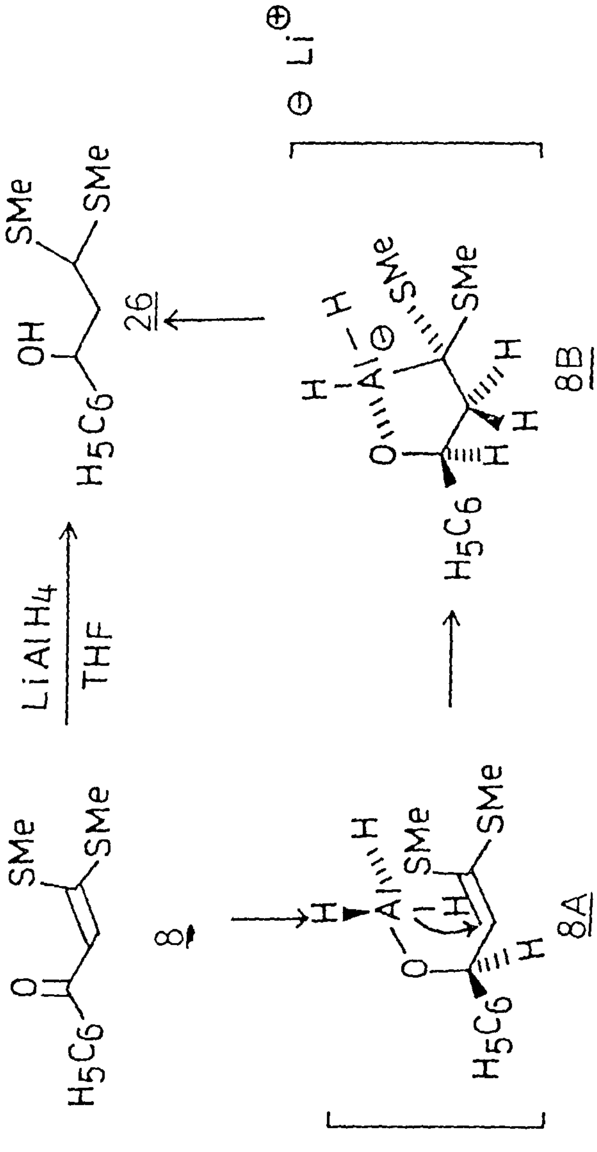


8 18 25

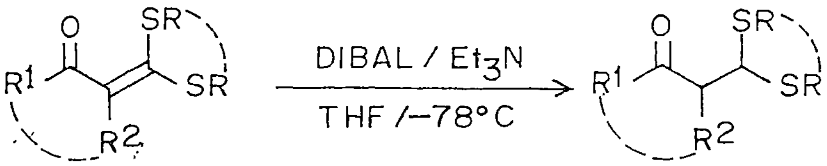
Scheme – 8

(scheme 9). They have examined the lithium aluminium hydride reductions of 8 and established that the reduction pathway proceeds in regio- and stereospecific manner demonstrating for the first time that such reductions of α,β-unsaturated ketones can infact be stereospecific. Thus α-oxoketene dithioacetal 8 was reduced with lithium aluminium hydride to give the corresponding saturated alcohol 26 in 96% yield. The regio- and stereochemistry of the reduction was explained on the basis of the structural assignments by nmr spectroscopy. The carbonyl group of the α-oxoketene dithioacetal has been shown to undergo initial regiospecific 1,2-reduction to give 8A followed by the formation of the unique organometallic intermediate 8B which facilitates intramolecular hydroalumination leading to the observed stereochemistry in the corresponding saturated alcohol 26 (scheme 9).

Subsequently, Gammill and coworkers[14] have examined the reduction of α-oxoketene dithioacetals 8 in an effort to achieve the conjugate reduction with electrophilic reducing agents. Thus, the α-oxoketene dithioacetals 8 underwent a facile 1,4-reduction with diisobutyl aluminum hydride (DIBAL) in the presence of triethylamine at -78°C to afford the corresponding β-oxodithioacetals 27 in 70-80% overall yields (Scheme 10). Also, 8 underwent a similar conjugate addition with 9-borabicyclononane (9-BBN) to afford 25 where over-reduction was observed. Similar reduction of 8 with catechol borane yielded a mixture of products 27 and 25 arising from

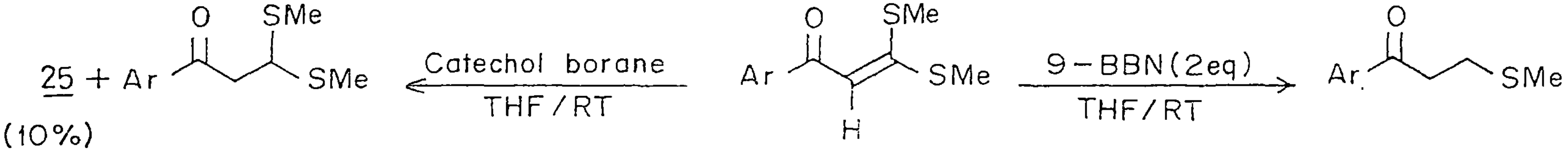

H5C6
O
SMe
SMe
8
LiAlH4
THF
H5C6
OH
SMe
SMe
26
H
Al
H
O
H
SMe
SMe
H
H5C6
H
8A
H
H
Al
O
SMe
SMe
H
H
H
H5C6
8B
Li⊕

Scheme 9



8  27

| $R^1$ | $R^2$ |
|---|---|
| $C_6H_5$ | H |
| 3−MeO−$C_6H_4$ | H |
| 2,3,4−$(MeO)_3$−$C_6H_2$ | H |
| 3−Thienyl | H |



27 (56%)

8

25 (83%)

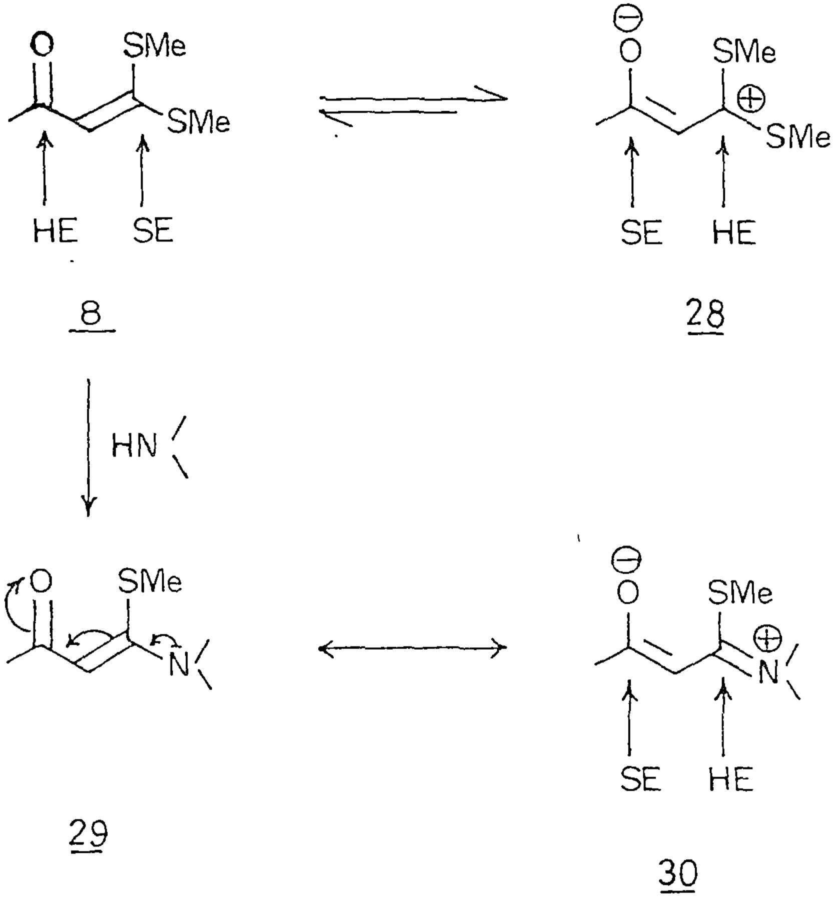
Scheme—10

conjugate addition and overreduction respectively (scheme 10).

In the preceding section, a brief review on various reduction types of α-oxoketene dithioactals has been presented. These intermediates due to the presence of sulfur atoms on the enone terminal induct high 1,2-regioselectivity towards metal hydride reductions. However, the corresponding oxygen analogs did not display 1,2-regioselectivity to the same extent which led to a mixture of products arising from both 1,2- and 1,4-reductions. The Ireland and Marshall's discovery of highly regioselective carbonyl reduction of n-butylthiomethylene ketones by sodium borohydride and the subsequent reduction studies on α-oxoketene dithioacetals by both Thuillier and our groups have amply demonstrated that the sulfur plays a significant role in directing the metal hydride reductions in an exclusive 1,2-fashion. Subsequently, Gammill and co-workers have observed interesting highly regioselective carbonyl reduction followed by intramolecular hydroalumination leading to highly stereospecific products. Apparently the 1,4-reductions preceding over the 1,2-reductions of α-oxoketene dithioacetals have not been discovered[15a-c], although some examples[14] illustrate exclusive 1,4-redutions without affecting the carbonyl group. The methods include nickel boride reductions, electrochemical reductions and the conjugate reductions using the electrophilic reducing agents such as DIBAL, 9-BBN, Catechol borane etc.. However, no method has been developed so far to achieve the exclusive 1,4-conjugate reduction of α-oxoketene dithioacetals using nucleophilic reducing agents such as sodium borohydride. The importance of converting the α-oxoketene dithioacetals into their 1,4-reduction products is to transform them from β-ketoester precursor to β-ketoaldehyde moiety. Both β-oxodithioacetals as well as methylthiomethylene ketones serve as precursors for β-ketoaldehyde functions. Hence, in the present study, an attempt in this direction has been made to evolve a method or methods to convert the α-oxoketene dithioacetals either to the corresponding β-oxodithioacetals or to methylthiomethylene ketones.

The regioselective addition patterns on α-oxoketene dithioacetals[13-15] can be rationalized on the basis of Pearsons's the Hard Soft Acid Bases (HSAB) Principle[16]. The principle states that acids show greater affinity for bases of the same class and *vice-versa*. Thus , hard acids (acceptors) tend to form strong bonds with hard bases (donors), but bind reluctantly or weakly to soft bases. The latter class of compounds interacts preferably with soft acids. Reviews of the HSAB principle in general terms as well as its application to multicentre reactions and organic chemistry have appeared[16a]. In this context, Klopman's perturbation theory[16d] is of immense utility for theoretical considerations. Thus, according to Hard Soft Acid Bases (HSAB) principle, the hard nucleophiles such as organolithium, organomagnesium reagents, lithium aluminium hydride, and sodium borohydride (in methanol) have been shown to react with α-oxoketene dithioacetals[5-16] in 1,2-manner, while the softer organocuprates, electrophilic reducing agents (DIBAL, 9-BBN, $NaBH_3CN/AcOH$ etc) and other delocalized anions undergo simple 1,4-conjugate addition or 1,4-addition elimination or sequential 1,4-conjugate addition[17] followed by 1,2-addition (in the case of delocalized Grignard reagents).

The α-oxoketene dithioacetals[15] 8 display 1,3-electrophilic centres (scheme 11) in which the electrophilicity between the two centres is delicately balanced in such a way that under neutral conditions the carbonyl carbon serves as a hard electrophilic centre (HE) and the bismethylthio carbon serves as soft electrophilic centre (SE). The exclusive regiospecific addition of hydride ion, which is a hard nucelophile from sodium borohydride, manifestly go to reduce 8 in the 1,2-fashion and no 1,4-adducts have been detected in the reaction mixture[5,6]. However, if one of the two thiomethyl groups is replaced by an amino group[18], the hard-soft centres undergo affinity inversion[19] thus making the carbonyl carbon soft-electrophilic centre (SE) and the β-carbon as hard electrophilic centre (HE) as depicted in scheme 11. Earlier Junjappa and coworkers have observed an interesting sequence of reactions of α-oxoketene dithioacetals with hydroxylamine hydrochloride under different pH range[20a]. Thus around pH 5-9, the hydroxylamine hydrochloride follows the oxime pathway followed by the intramolecular ring closure to form the 5-methylthioisoxazoles exclusively. On the otherhand, when the reaction of 8 with hydroxylamine was carried at pH 2.2, the



HE = Hard Electrophile ; SE= Soft Electrophile

Scheme-II

position of 8 equilibriates with that of 28 (scheme 11) thereby creating a carbocation on bismethylthio carbon which now becomes a hard electrophile and the enol carbon, originally the carbonyl carbon now behaves as a soft electrophile. Hence, at this pH the hydroxylamine nitrogen being a hard nucleophile attacks the hard electrophilic carbocation site followed by ring closure to afford the 3-methylthioisoxazole exclusively. It is interesting to note that the α-oxoketene dithioacetals 8 under suitable reaction conditions i.e., either in the proton-rich medium[20b] or in the presence of hard cations such as $Li^+$, $Na^+$ etc., appear to undergo affinity inversion by reverting the hard-soft electrophilic characters of 1,3-carbon centres resulting in the formation of one of the two regioisomers of isoxazoles exclusively as described above.

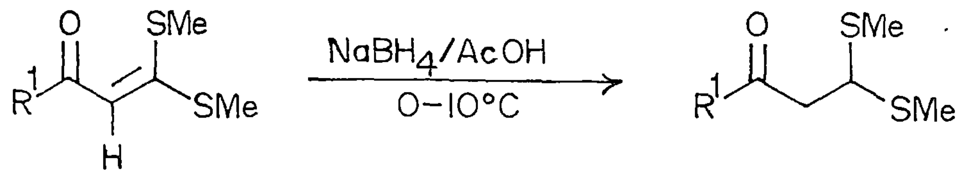
Recently, a more sophisticated interpretation of ambident reactivity of α,β-enones has been proposed in which the inversion of relative atomic coefficients occurs due to the complexation with hard cations[21]. In the uncomplexed substrate the coefficient $C_2^2$ is smaller than that of $C_4^2$ while in the complexed or protonated substrates $C_2^2$ becomes larger than $C_4^2$ resulting in the change of reactivity towards given nucleophiles. This hard-soft affinity inversion[19], if achieved under suitable reaction conditions, the softer β-carbon of the α-oxoketene dithioacetals can be converted into hard electrophilic centre thus permitting the charge-controlled attack by hard nucleophiles in the 1,4-fashion.

Also, such a charge inversion is greatly facilitated by the cation stabilizing ability of the adjacent sulfur atoms in these systems. Thus, the α-oxoketene dithioacetals 8 are an attractive group of intermediates for hard-soft affinity inversion studies where the substrates can be suitably altered either by changing the reaction conditions or by replacing one of the methylthio groups by an amino group to afford the corresponding S,N-acetals 29 which exhibit clear 1,4-regioselectivity[18] (scheme 11). The approaches in the literature so far appear to have centred to develop soft nucleophiles for the required 1,4-addition to enones while the hard nucleophiles for 1,2-addition. An alternative approach to alter the electrophilic centres within the substrate enones to achieve the desired regioselective reduction has been little attended and appears to hold bright future for developing more important regiospecific or regioselective addition reactions to enones. Our attempts in this direction have been successfully formulated for these studies on conjugate reductions of α-oxoketene dithioacetals 8 with sodium borohydride in the presence of a strong proton donor solvent so that the addition of hard hydride will go in the desired 1,4-fashion without interacting with the carbonyl carbon. Our experiments on the reduction of α-oxoketene dithioacetals 8 with sodium borohydride in acetic acid have been successfully extended to achieve the regiospecific 1,4-reduction and the results are presented in this chapter.

## II.A.2 RESULTS AND DISCUSSION

The α-oxoketene dithioacetals **8** employed in these studies were prepared according to the described literature procedures (experimental section). The hitherto unreported dithioacetals were prepared essentially by extending the procedures employed for the reported ones. The strutures of these acetals were fully confirmed by their spectral and physical properties.

When the α-oxoketene dithioacetal **8a** was treated with four-fold excess of sodium borohydride in large excess of acetic acid after work-up, the reaction mixture afforded the corresponding β-oxodithioacetal **27a** in 80% yield (scheme 12). The corresponding allyl alcohol arising from 1,2-reduction was not detected in the reaction mixture. However, when less than four equivalents of sodium borohydride was used the unreacted starting material **8a** was recovered alongwith **27a.** The β-oxodithioacetal **27a** was earlier reported by Gammill and coworkers by subjecting **8a** to an electrophilic reducing agent DIBAL in the presence of triethylamine at -78°C in 88% yield (Scheme 10). Our product was found to be identical (superimposable IR and the $^1$H NMR) with the one reported by Gammill and coworkers. Similarly **8b-g** when subjected to sodium borohydride reduction under identical conditions afforded the corresponding β-oxodithioacetals **27b-g** in 58-84% overall yields. The spectral and analytical data of **27b-d** were found to be identical with those reported in the literature. The structures of hitherto unreported β-



8 a–g        27 a–g

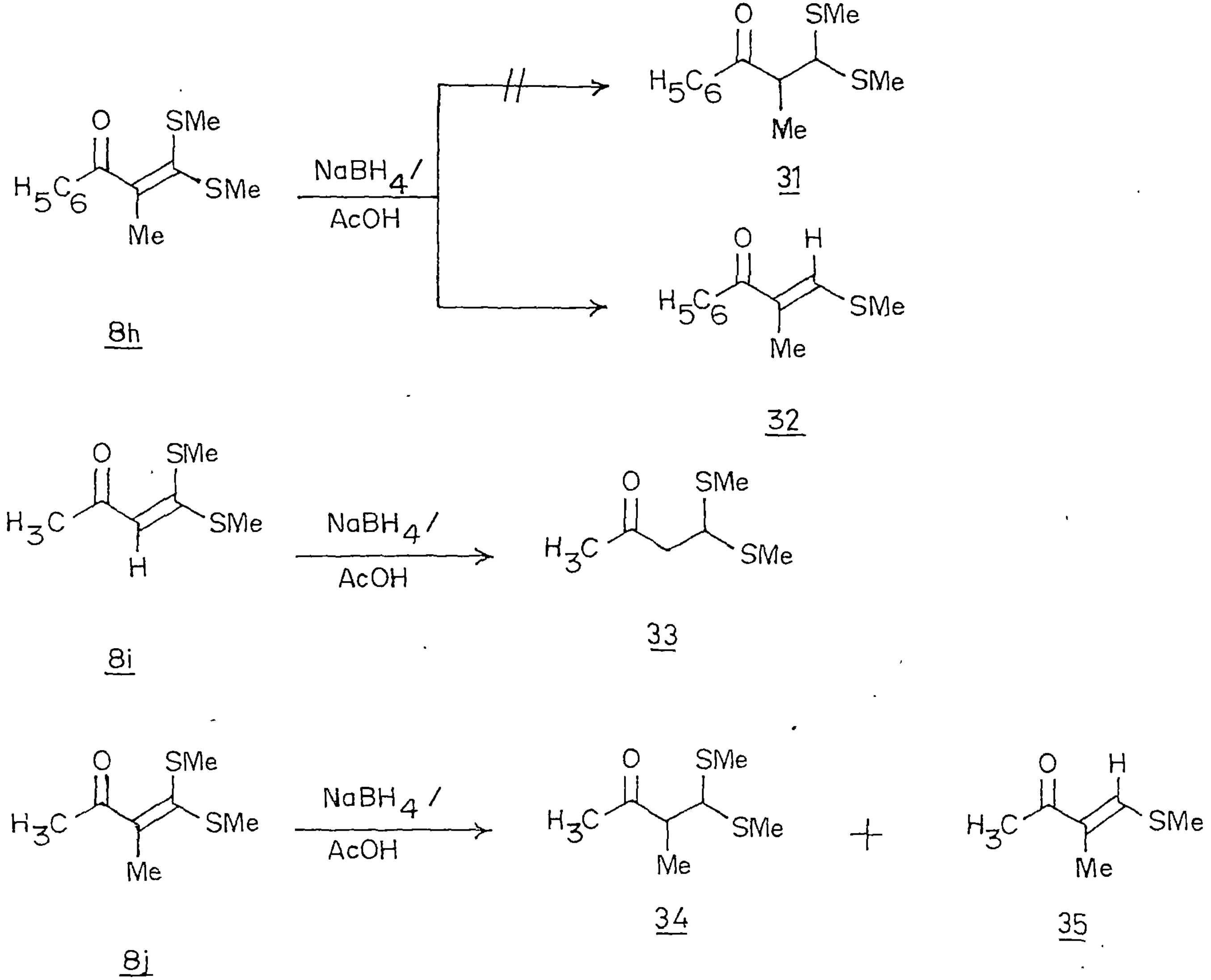
| | $R^1$ |
|---|---|
| 8a – 27a | $C_6H_5$ |
| 8b – 27b | 4–Me – $C_6H_4$ |
| 8c – 27c | 4–Cl$C_6H_4$ |
| 8d – 27d | 4–MeO – $C_6H_4$ |
| 8e – 27e | 2– furyl |
| 8f – 27f | 2 – thienyl |
| 8g – 27g | 2 – naphthyl |

Scheme–12

oxodithioacetals 27e-g were established on the basis of their spectral and analytical data (experimental). It is important to note that in none of the experiments the corresponding 1,2-adduct was detected.

Interestingly, the oxoketene dithioacetal 8h bearing α-methyl group under the described reaction conditions did not give the corresponding β-oxodithioacetal 31. The product obtained in 70% yield in this reaction was identified as 3-methylthio-2-methyl-1-phenyl-2-propen-1-one 32. Apparently, 8h has undergone initial 1,4-reduction followed by the elimination of methyl mercaptan resulting in the formation of 32 (scheme 13). The compound 32 was prepared earlier[8] in this laboratory by subjecting 8h to sodium cyanoborohydride reduction in refluxing acetic acid in good yield.

When acylketene dithioacetal 8i was reduced under the described reaction conditions, it afforded the corresponding 4,4-bis(methylthio)-2-butanone 33 in 55% yield. However, attempts to improve the yield of 33 under various reaction conditions was not successful. The structure of 33 was established by its analytical and spectral data. It was analysed for $C_6H_{12}OS_2$ and exhibited in its mass spectrum a peak at m/z 164 ($M^+$, 36% ). In its IR (neat) spectrum, the band at 1715 $cm^{-1}$ was attributed to the carbonyl group. The structure was further confirmed by its $^1H$ NMR ($CCl_4$) spectrum. The methylthio protons appeared as a singlet at δ 2.13(6H) and the signal at δ 2.19(3H) was assigned to the acylmethyl group. The doublet at δ2.89 (2H, J= 7.5Hz) was



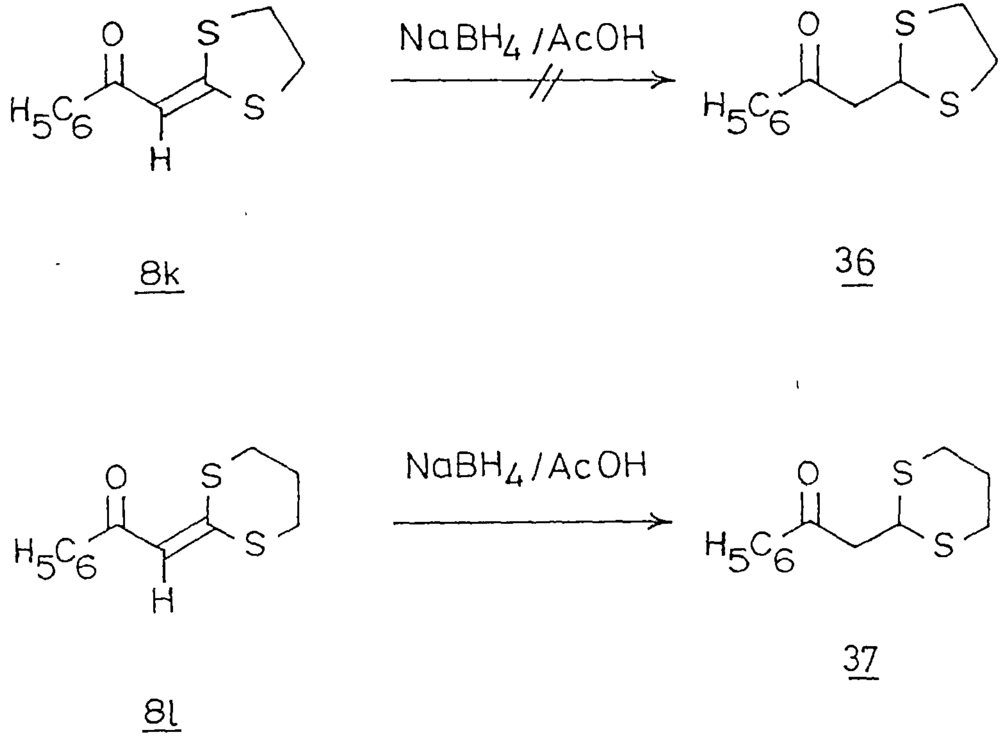
Scheme–13

assigned to the mehtylene protons and the triplet at δ 4.19 (1H, J=7.5Hz) was assigned to the proton on the bismethylthio carbon [i.e., $-CH(SMe)_2$]. Similarly, when 8j derived from ethylmethyl ketone was reduced under the described reaction conditions a mixture of 34 (30%) and 35 (59%) was obtained (Scheme 13). They were isolated in pure form and their structures were established by their analytical and spectral data (experimental section).

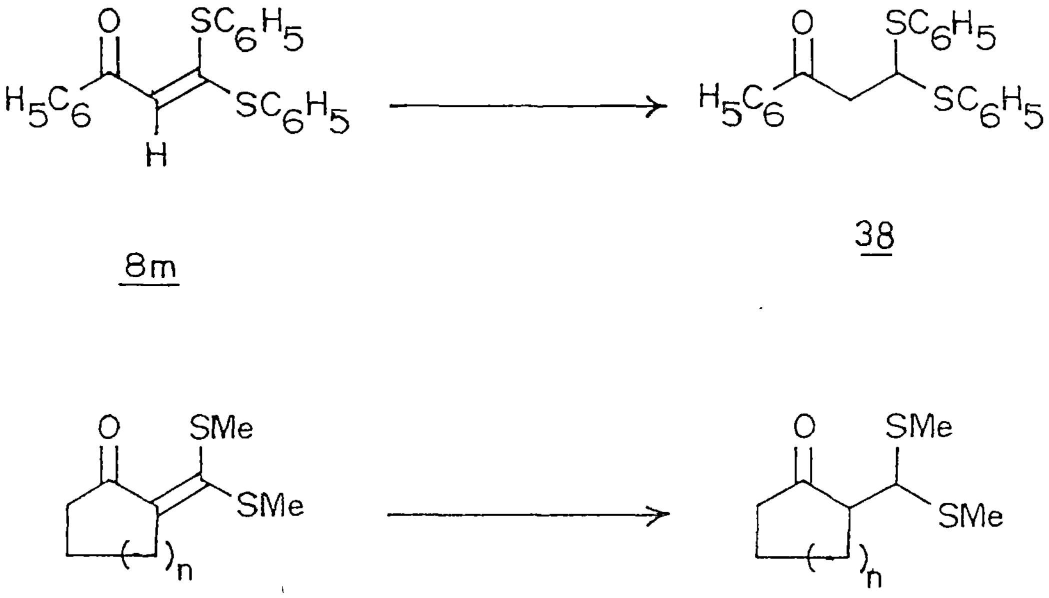
Interestingly, the cyclic 1-phenyl-2-(1,3-thiolan-2-ylidene)-ethanone 8k failed to undergo the described reduction to afford the corresponding 36 where the unreacted starting material was recovered unaltered (scheme 14). It may be noted that 8k failed in the hands of Gammill and coworkers[14] also when they subjected it for reduction with DIBAL-H. However, the corresponding dithiane 81 yielded the β-oxodithioacetal 37 in 50% yield under similar reaction conditions (Scheme 14). The structure of 37 was established on the basis of its spectral and analytical data (experimental section).

The 3,3-bis(phenylthio)-1-phenylpropen-1-one 8m underwent reduction under the described reaction conditions to afford 38 in 72% yield (scheme 15). Its structure was in accordance with its analytical and spectral data (experimental section).

The reduction studies were then extended to the cyclic oxoketene dithioacetals. When they were subjected to sodium



Scheme-14


8m

38

8n–p

39n–p

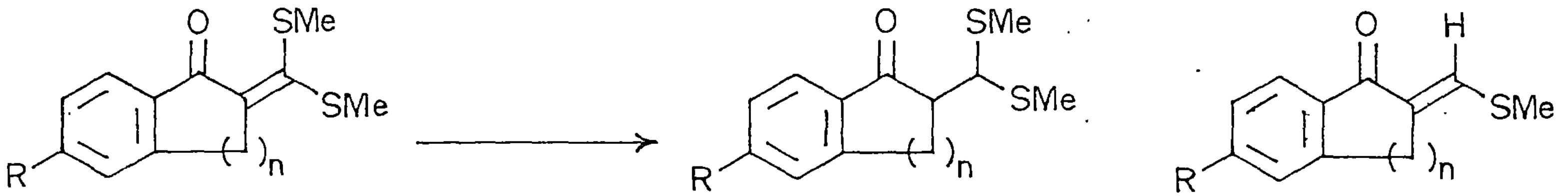
| | n | Yield,% |
|---|---|---|
| 8n–39n | 1 | 65 |
| 8o–39o | 2 | 68 |
| 8p–39p | 3 | 90 |

Scheme – 15

borohydride reduction under identical conditions, **8n-p** afforded the corresponding cyclic β-oxodithioacetals **39n-p** in 65-90% overall yields (Scheme 15). The structures of these products were in accordance with their analytical and spectral data (experimental section).

The reduction studies of α-oxoketene dithioacetals **8q-t** were next examined. The indanone mercaptal **8q** on reduction with sodium borohydride under similar reaction conditions gave exclusively the corresponding β-oxodithioacetal **40q** in 68% yield. However, the tetralone S,S-acetal **8r** under the described conditions yielded a mixture of β-oxodithioacetal **40r** (65%) and the addition-elimination product **41r** (30%). Similarly, the S,S-acetal derived from the 4-methoxytetralone **8s** afforded a mixture of the corresponding β-oxodithioacetal **40s** and the methylthiomethylene ketone **41s** in 66% and 30% yields respectively (Scheme 16). Surprisingly, the seven membered fused dithioacetal **8t** afforded exclusively the corresponding **41t** in 95% yield and no dihydro compound was detected in the reaction mixture. The compounds were separated by column chromatography using silica gel eluting with appropriate solvents (hexane + ethylacetate) . The structures of **40q-s** and **41r-t** were established on the basis of their analytical and spectral data (experimental section).

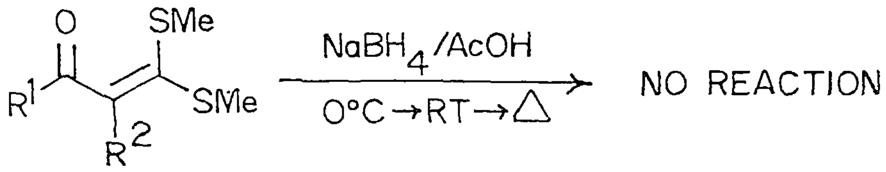
However, the oxoketene dithioacetals 8u-x failed to undergo reduction under the described conditions and the respective starting materials were recovered unaltered in all the cases (scheme 17).



8q–t 40 q,r,s 41 r,s,t

| Starting Material | R | n | Yield,% 40 | Yield,% 41 |
|---|---|---|---|---|
| 8q | H | 1 | 68 | — |
| 8r | H | 2 | 65 | 30 |
| 8s | OMe | 2 | 66 | 30 |
| 8t | H | 3 | — | 95 |

Scheme–16



8 u-x

8u, $R^1 = C_6H_5$; $R^2 = Et$

8v, $R^1 = Me$; $R^2 =$ isopropyl

8w, $R^1 = Et$; $R^2 = Me$

8x, $R^1 = Et$; $R^2 = Et$

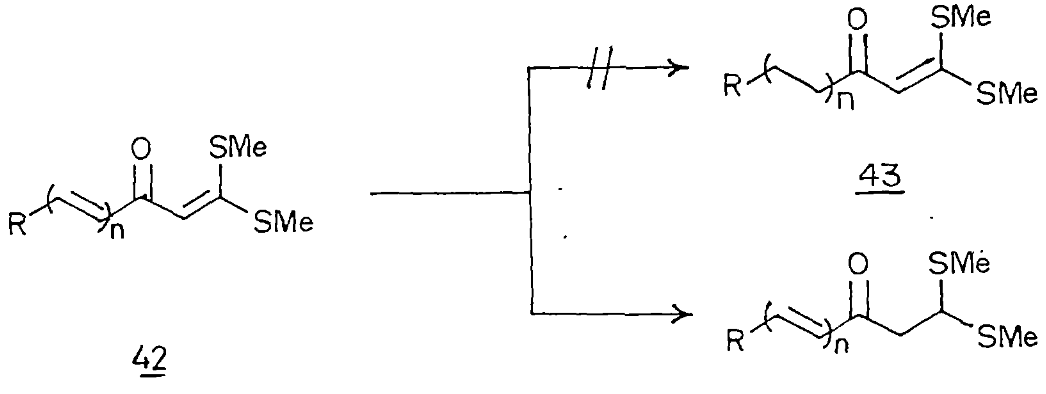
Scheme -17

We have next examined the reductions of sodium borohydride on the cinnamoyl and its higher homologous ketene dithioacetals. Thus, when these dithioacetals **42a-h** were subjected to the above reduction only the corresponding dihydro acetals **44a-h** were obtained in 70-78% overall yields (scheme 18). The structures of **44a-h** were in accordance with their analytical and spectral data. Interestingly, the olefinic bonds remained unaffected in all these reactions and hence the corresponding **43a-h** were not detected at all in the reaction mixtures. Thus, the reaction was highly chemoselective under the described reaction conditions, involving the reduction of only mercapto double bond in preference to the olefinic bonds of the substrate.

## II.A.3. MECHANISM

The results from these reductions of α-oxoketene dithioacetals with sodium borohydride in acetic acid have been rationalised according to HSAB principle in terms of 'hard soft affinity inversion' concept.

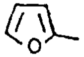
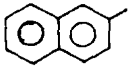
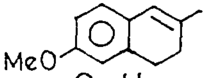
The reduction of activated double bond with sodium borohydride[22] has been observed in conjugated esters, nitroalkenes and enolacetates. A few of the α,β-unsaturated ketones have also been shown to undergo 1,4-reduction with sodium borohydride in the presence of pyridine[23]. Marshall and coworkers[24] have reported the reduction of enamine double bond with sodium borohydride in the presence of acetic acid and proposed protonation and hydride transfer mechanism for



42

43

44

| | n | R |
|---|---|---|
| 42 - 44a, | 1 | $C_6H_5$ |
| 44b, | 1 | 4-MeO-$C_6H_4$ |
| 44c, | 1 |  |
| 44d, | 1 |  |
| 44e, | 1 |  |
| 44f, | 2 | $C_6H_5$ |
| 44g, | 2 | 4-MeO-$C_6H_4$ |
| 44h, | 3 | $C_6H_5$ |

Scheme –18

the reduction. On the otherhand, in the reduction of isolated double bond with sodium borohydride which is generally carried out in the presence of one or at best five equivalents of acetic acid, the hydroboration pathway was considered plausible[25,26]. In the present studies, the reduction of oxoketene dithioacetals to the corresponding β-oxodithioacetals with sodium borohydride in the presence of large excess of acetic acid (solvent medium) should proceed by initial protonation of 8 followed by a charge controlled 1,4-hydride delivery (scheme 11) as observed in the enamine reduction under similar reaction conditions. This was supported by carrying out reduction of 8a with $NaBH_4$/AcOH under varying conditions (Table 1). Thus when 8a was treated

**Table 1 : Reduction of Oxoketene Dithioacetal 1a with Sodium Borohydride in Acetic Acid**

| Run | Substrate 8a (mmol) | $NaBH_4$ (mmol) | AcOH (mmol) | Solvent (mL) | % Yield | |
|---|---|---|---|---|---|---|
| | | | | | 27a | 8a |
| 1. | 10 | 3.70 | 3.70 | THF(5) | - | 88 |
| 2. | 10 | 5.50 | 5.50 | THF(5) | - | 90 |
| 3. | 10 | 20.00 | 20.00 | THF(13) | 10 | 75 |
| 4. | 10 | 59.00 | 760.00 | THF(130) | 70 | - |

with $NaBH_4$/AcOH in THF in the same stoichiometric ratio as reported by Hack[26] (diborane path) (run 1 and 2), no reduction was observed and unreacted 8a was recovered, whereas under Marshall's hydroboration[25] conditions (run 3), 27a was obtained only in 10% yield along with unreacted 8a. On the otherhand when 8a was treated with sodium borohydride with large excess of acetic acid, the yield of 27a was raised to 70% (run 4). It is therefore concluded that sodium borohydride/acetic acid reduction of 8 does not proceed through hydroboration and a mechanism involving protonation of oxoketene dithioacetal to give intermediate 8A followed by charge controlled hydride transfer to the β-carbon is suggested. The mechanism is similar to the reduction of simple ketene dithioacetals with organosilicon hydride in the presence of trifluoroacetic acid[27].

In conclusion, it is demonstrated that the α-oxoketene dithioacetals are an interesting group of 1,3-dielectrophilic intermediates whose electrophilicity could be inversed under suitable reaction conditions thus creating the desired affinity inversion so that the hard hydride could be used for 1,4-reduction. Hence, the concept to achieve the desired conjugate reduction of α-oxoketene dithioacetals using nucleophilic reagent ($NaBH_4$) through the substrate modification under suitable reaction conditions rather than developing a reagent with a soft hydride source is thus fully realised.

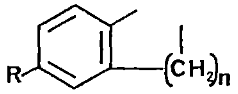
# PART B

## AN IMPROVED METHOD FOR THE SYNTHESIS OF β-OXODITHIOACETALS FROM α-OXOKETENE DITHIOACETALS WITH ZINC IN ACETIC ACID

### II.B.1. INTRODUCTION

Zinc has been extensively used for the reduction of double bonds in organic synthesis[28-30]. It is also used to reduce the α,β-unsaturated enone double bonds when the reductions were carried out in the presence of acetic acid. Thus, zinc in acetic acid medium has an advantage as a reducing agent over other metal hydride complexes described earlier that it reduces only the double bonds without affecting the carbonyl function within the molecule. Therefore, it was considered of interest that the α-oxoketene dithioacetals should be better reduced in zinc/ acetic acid medium so that the limitations and complications observed with sodium borohydride in acetic acid conditions could be contained. We have examined the reduction of a number of oxoketene dithioacetals 8 with zinc in acetic acid medium and observed that the corresponding β-oxodithioacetals were formed in much improved yields without deviation in the product mixture as observed in some cases when sodium borohydride in acetic acid medium was used (see Table 2).

Table 2 : Conjugate Reduction of α-Oxoketene dithioacetals with Zn/AcOH

| Entry | Substrate | $R^1$ | $R^2$ | Product | % yield$^a$ | % yield$^b$ |
|---|---|---|---|---|---|---|
| 1. | 8a | $C_6H_5$ | H | 27a | 94 | (80) |
| 2. | 8e | 2-furyl | H | 27e | 90 | (58) |
| 3. | 8f | 2-thienyl | H | 27f | 92 | (60) |
| 4. | 8g | 2-naphthyl | H | 27g | 89 | (69) |
| 5. | 8h | $C_6H_5$ | $CH_3$ | 31 | 64 | (-) |
| 6. | 8i | Me | H | 33 | 94 | (55) |
| 7. | 8j | Me | Me | 34 | 78 | (30) |
| 8. | 8w | Et | Me | 45 | 64 | (-) |
| 9. | 8o | $-(CH_2)_4-$ | | 39o | 88 | (68) |
| | |  | | | | |
| 10. | 8r | R=H; n=1 | | 40r | 90 | (65) |
| 11. | 8t | R=H; n=2 | | 40t | 68 | (-) |
| 12. | 42a | $H_5C_6$-CH=CH- | H | 44a | 93 | (70) |
| 13. | 42b | 4-MeO-$C_6H_4$-CH=CH- | H | 44b | 92 | (75) |
| 14. | 42d | β-naphthyl-CH=CH- | H | 44d | 91 | (78) |
| 15. | 42g | 4-MeO-$C_6H_4$-CH= CH- | H | 44g | 81 | (71) |
| 16. | 42h | $C_6H_5-(CH=CH-)_3$ | H | 44h | 82 | (69) |

[a] Zinc/AcOH reduction; [b] $NaBH_4$/AcOH reduction.

## II.B.2. RESULTS AND DISCUSSION

In a typical experiment when 8a in THF was treated with 2-5 equivalents of zinc in 8 ml of acetic acid and 1 ml of water at room temperature, the product isolated after work up, was identified as the corresponding β-oxodithioacetal 27a in 94% yield. The 27a was found to be identical in its analytical and spectral data with the one obtained from $NaBH_4$/AcOH method (Scheme 19 and Table 2). Apparently, the reduction process has yielded improved yields of 94% over 80% of $NaBH_4$/AcOH reduction process as described earlier. Similarly, 8e-g were reduced to give the corresponding 27e-g in 89-92% overall yields. The corresponding yields of $NaBH_4$/AcOH reductions are given in the Table 2 which are comparatively much lower than those obtained by this process. When the oxoketene dithioacetal 8h with α-methyl group was subjected to zinc/acetic acid the corresponding β-oxodithioacetal 31 was obtained in 64% yield, while the reduction failed to give 31 by $NaBH_4$/AcOH method. Also, the acylketene dithioacetals 8i,j were not satisfactorly reduced in $NaBH_4$/AcOH medium and yielded the corresponding 33 and 34 only in 55% and 30% yields respectively. Also 8w gave the starting material back unreacted and the β-oxodithioacetals 45not at all formed under these considtions. On the otherhand, following zinc/AcOH procedure 33,34 and 45 were obtained in 94, 78 and 64% yields respectively from 8i,j and 8w.

The cyclic ketene dithioacetals also behaved differently in the case of $NaBH_4$/AcOH medium. The dithiocetals **8o** and **8r** also yielded the corresponding β-oxodithioacetals **39o** and **40r** in 68% and 65% yields respectively. On the otherhand **8t** was reduced but underwent elimination of methylmercaptan to afford the corresponding **41t** in 95% yield. However, **8o**, **8r** and **8t** under Zn/AcOH conditions, the corresponding β-oxodithioacetals **39o**, **40r** and **40t** were obtained in 88, 90 and 68% yields. Thus, there were no side products formed in any of these reductions.

Similarly, cinnamoyl oxoketene dithioacetal **42a** was reduced under the described conditions with slight modification in the reaction procedure. Thus when **42a** was treated with 10ml equivalents of zinc in 10 ml of acetic acid and 2 ml of water at 10°C the corresponding β-oxodithioacetal **44a** was formed in 93% yield. However, when excess zinc was employed, reduction of the double bond in conjugation with the phenyl group was observed. Similarly the other enoylketene dithioacetals **42b**, **42d** and **42g,h** were reduced in 81-92% overall yields.

In conclusion, it may be stated that the α-oxoketene dithioacetals could be transformed to β-oxodithioacetals in much improved yields using zinc/AcOH medium. Also, the problems and limitations observed in $NaBH_4$/AcOH medium have been fully contained and therefore, the method appears to be superior to the method of $NaBH_4$ - acetic acid reduction.

## EXPERIMENTAL SECTION

### General:

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The IR spectra were obtained on a Perkin Elmer 297 Spectrophotometer. $^1H$ NMR spectra were recorded on Varian EM-390, 90MHz spectrometer and are reported in δ units downfield from $Me_4Si$. The coupling constants are given in Hertz(Hz). Mass spectra were obtained on a Jeol D-300 spectrometer. T.l.c. (silica gel, ACME'S) was used for monitoring the reactions.

### Chemicals and Reagents

Commercially available $NaBH_4$ (Aldrich) was used for these reductions and all the necessary precautions were taken while handling as the exposure of the reagent leads to erratic results. Glacial acetic acid (Merck) was used as such. THF was intially deperoxidised and then dried by keeping over sodium wire followed by distillation. Commercially supplied zinc dust (Merck, AR Grade) was activated with 1,2-dibromoethane according to Vogel's procedure[43].

### Starting Materials:

The commercial samples of acetophenone, 4-methyl-acetophenone, 4-chloroacetophenone , 4-methoxyacetophenone, acetone, cyclopentanone, cyclohexanone and cycloheptanone were purified by distillation under reduced pressure before use. 1-Tetralone, b.p. 140-150°C (10 mm)[31], 1-indanone, m.p. 39-40°C[32], propiophenone, b.p. 105-110°C (8 mm)[33], were prepared according to the reported procedures. The following aldehydes were used for the preparation of cinnamoylketene dithioacetals and their higher analogs. Commercially available benzaldehyde, 4-methoxybenaldehyde, furfural and cinnamaldehyde were made acid free by distillation before use. 2-Naphthaldehyde[43] 4-methoxycinnamaldehyde, dienealdehyde, trienealdehyde and 3,4-dihydro 2-naphthaldehyde[44] were prepared according to the reported procedures.

The oxoketene dithioacetals 8a-x required for the present investigation were prepared according to the earlier reported procedures[39-41]. The following oxoketene dithioacetals; 3,3-bis(methylthio)-1-phenyl-2-propen-1-one 8a, m.p. 93°C[34]; 3,3-bis(methylthio)-1-(4-chlorophenyl)-2-propen-1-one 8c, m.p. 109-10°C[34], 3,3-bis(methylthio)-1-(4-methoxyphenyl)-2-propen-1-one 8d m.p.100°C[34], 2-[bis(methylthio)methylene]-cyclohexanone 8o b.p. 118°C (1 mm)[35], 2-[bis(methylthio)-methylene]-1-indanone 8q m.p. 70-71°C[36]; 2-[bis(methylthio)methylene]-1-tetralone 8r m.p. 58°C[37]; 2-[bis(methylthio)methylene]-6-methoxy-1-tetralone 8s m.p. 78°C[38]; 3,3-bis(methylthio)-2-methyl-1-phenyl-2-propen-1-one 8h b.p. 168- 170°C (13 mm)[39], were prepared according to general proceudre described in the following section.

**General method for the preparation of Oxoketene Dithioacetals using Sodium-t-butoxide**

A mixture of the ketone (0.5 mol) and carbon disulphide (0.5 mol) in dry benzene (100 ml) was added dropwise to an ice cooled and well stirred suspension of sodium-t-butoxide (1.0 mol) and the reaction mixture was stirred for 4-5 hr.

Methyliodide (1.1 mol) was then gradually added with cooling and the reaction mixture was further stirred for 6 hr and then refluxed for 1 hr, cooled and poured into ice cooled water. The benzene layer was separated and the aqueous phase was extracted with benzene (200 ml), the combined benzene extracts were washed with water (200 ml), dried ($Na_2SO_4$) and evaporated to give the crude dithioacetals 1 which were further purified either by crystallization or by distillation under reduced pressure.

**Preparation of 3,3-Bis(phenylthio)-1-phenyl-propen-2-one(8m):** To a well stirred solution of thiophenol (100 mmol) and aqueous 10% sodium hydroxide solution, 3,3-dichloracrylophenone (10 mmol) was added and heated the contents at 80°C for 8 hr (monitored by tlc). The reaction mixture was then poured into ice cold water followed by neutralization with dil. HCl. It was extracted with ether (2x75 ml) and the combined ether extracts were washed with water (2x100 ml), dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure to give a viscous oil. The coloumn chromatography over silica gel afforded the pure 3,3-Bis(phenylthio)-1-phenyl-propen-2-one in 62% yield as pale yellow solid.(m.p. 129-130°C) 62% yield.

**Condensation of α-Acylketene Dithioacetals with Aldehydes: General Procedure for the Preparation of α-Cinnamoyl ketene dithioacetals and their higher homologs.**

To a cooled and stirred solution of sodium ethoxide in ethanol, prepared by dissolving sodium ( 6 mmol) in ethanol

(10 ml), a solution of the α-acylketene dithioacetals (3 mmol) and the aldehyde (3 mmol) in minimum quantity of ethanol (10 ml) was added dropwise over a period of 5 minutes. The reaction mixture was brought to room temperature over a period of 30 minutes and further stirred at room temperature for 4-5 hrs. The mixture was diluted with water (4x25 ml), filtered and dried. The cinnamoyl ketene dithioactals **40,41** and their higher analogs **42a-h** were prepared according to reported procedures.[40,41]

## PREPARATION OF β-OXODITHIOACETALS

### Method A : General Procedure for Reduction of α-Oxoketene Dithioacetals with Sodium Borohydride in Acetic Acid:

To a well stirred solution of α-oxoketene dithioacetal (10 mmol) in glacial acetic acid (60 mL), sodium borohydride (40 mmol) was added slowly (portion wise) (30 min.) at 5-10°C. The reaction mixture was further stirred at room temperature for 3 hr (monitored by t.l.c.) and then poured into ice-cold water (100 mL) followed by extraction with chloroform (3x50 mL). The combined organic layer was washed with water (3x100 mL), dried over sodium sulfate and concentrated to give a viscous residues, which on column chromatography over silica gel (hexane as eluent) gave pure β-oxodithioacetals and/or β-methylthioalkenyl ketones (from **8h** and **8t**). In the case of ketene dithioacetals **8j**, **8r** and **8s**, column chromatography of reaction mixtures (elution with hexane) gave first the corresponding β-oxodithioacetals **34,40r**, **40s** followed by the respective **35,41r,41s**.

In the case of ketene dithioacetal 81, reduction was carried out with excess of $NaBH_4$ (60 mmol) for prolonged time (12 h).

**Reduction of 8a with Sodium Borohydride/Acetic Acid in Tetrahydrofuran (for mechanistic studies, see Table 1):**

All reductions of 8a shown in Table 1 were carried out under identical conditions as described by Hack[26] (run 1 and 2) and Marshall[25] (run 3) for hydroboration of olefin and for reduction of 3-N-pyrrolidylcholestadiene-3,5 to 3-β-N-pyrrolidylcholesten-5[24] (run 4).

The reaction mixtures were worked up by pouring into ice cold water (100 ml) and extracting with $CHCl_3$ (2x50 mL). The organic layers were dried ($Na_2SO_4$) and evaporated to give residues which were column chromatographed over silica gel using hexane as eluent to give either 8a or 27a (Table 1).

**Method B : General Procedure for Reduction of α-Oxoketene Dithioacetals with Zinc/Acetic Acid:**

To a well stirred mixture of Zn dust (25 mmol), acetic acid (8 ml) and water (1 ml) was added a solution of oxoketene dithioacetals 8 (10 mml) in THF (15 ml). The contents were stirred further at room temperature for 3-5 hr (monitored by tlc). It was then filtered and washed with chloroform (50 ml). The filtrate was poured into ice-cold aqueous 5% $NaHCO_3$ solution. The aqueous layer was extracted with $CHCl_3$ (2x25 ml) and the combined organic extracts were washed with water (2x50 ml), dried ($N_2SO_4$) and evaporated to give residues of β-oxodithioacetals. The column chromatography over silica gel afforded the products in very pure form. The yields of the β-oxodithioacetals obtained by this procedure are given in Table 2. The spectral and analytical data of those products which were not formed by $NaBH_4$/AcOH reduction (Method A) are described separately.

All the known β-oxodithioacetals and β-methylthioalkenyl ketones were characterized by comparison of their melting points, NMR, IR spectra with those of reported data and of authentic samples. Their spectral and analytical data are given below:

**3,3-Bis(methylthio)-1-phenyl-1-propanone (27a):** viscous liquid (lit.[14]); IR (neat) 1695,1600,1585 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.07 (s, 6H, $SCH_3$); 3.30 (d, J = 7.5Hz, 2H, $CH_2CH(SCH_3)_2$); 4.40 (t, J = 7.5Hz, 1H, $CH_2CH(SCH_3)_2$); 7.20-7.56 (m, 3H, ArH); 7.79-8.00 (m, 2H, ArH); m/z 226 ($M^+$, 16%), 179 ($M^+$ -47, 44%). (Anal. Calcd. for $C_{11}H_{14}OS_2$ : C, 58.37; H, 6.24. Found : C, 58.24; H, 6.37%).

**3,3-Bis(methylthio)-1-(4-methylphenyl)-1-propanone (27b):** white crystalline solid; m.p. 46-48°C; IR (KBr) 1674, 1602, 1399 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.15 (s, 6H, $SCH_3$); 2.39 (s, 3H, $CH_3$); 3.61 (d, J = 7Hz, 2H,-$CH_2$-); 4.24 [t, J = 7Hz, 1H, -$CH(SCH_3)_2$], 7.28 (d, J = 9Hz, 2H, ArH); 7.88 (d, J = 9Hz, 2H, ArH). m/z 240 ($M^+$, 9%), 193 (17), 119(100). (Anal. Calcd. for $C_{12}H_{16}OS_2$ : C, 59.95; H, 6.71. Found : C, 60.06; H, 6.63%).

**3,3-Bis(methylthio)-1-(4-chlorophenyl)-1-propanone (27c):** colourless crystalline solid (hexane); m.p.78-79°C; IR (KBr) 1680, 1582, 1562 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.20 (s, 6H, $SCH_3$); 3.41 (d, J = 7.5Hz, 2H, $CH_2CH$); 4.31 (t, J = 7.5Hz, 1H, $CH_2CH$); 7.49 (d, J = 8Hz, ArH); 7.93 (d, 2H, J = 8Hz, ArH). m/z 262, 260 ($M^+$, 1%, 3%), 215, 213 (3,38). (Anal. Calcd. for $C_{11}H_{13}ClOS_2$ : C, 50.66; H, 5.02. Found : C, 50.89; H, 4.83%).

**3,3-Bis(methylthio)-1-(4-methoxyphenyl)-1-propanone (27d):** m.p. 58-59°C; IR (KBr) 1678, 1598, 1573, 1510 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.12 (s, 6H, $SCH_3$); 3.31 (d, J = 7.5Hz, 2H, $CH_2CH(SCH_3)_2$) ; 3.80 (s, 3H, $OCH_3$); 4.30 (t, J = 7.5Hz, 1H, $CH_2CH(SCH_3)_2$); 6.90 (d, J = 9Hz, 2H, ArH); 7.90 (d, J = 9Hz, 2H, ArH). m/z 209 ($M^+$ -47, 41%), 256(8), 241(1), 209(8). (Anal. Calcd. for $C_{12}H_{16}O_2S_2$ : C, 56.21; H, 6.29. Found: 56.33; H, 6.18%).

**3,3-Bis(methylthio)-1-(2-furyl)-1-propanone (27e):** colourless crystalline solid (hexane); m.p.42-43°C; IR (KBr) 1695, 1575, 1470 $cm^{-1}$; $^1H$ NMR ($CCl_4$) : 2.12 (s, 6H, $SCH_3$); 3.14 (d, J = 7.5Hz, 1H, $CH_2CH$); 4.27 (t, J = 7.5Hz, 1H, $CH_2CH$); 6.51 (dd, J = 4, 1.5Hz, 1H, H-4' furyl); 7.19 (brd, J = 4Hz, 1H, H-3' furyl);7.59 (brs, 1H, H-5' furyl). (Anal.Calcd. for $C_9H_{12}O_2S_2$: C, 49.97; H, 5.59.Found : C, 49.23;H, 5.81%).

**3,3-Bis(methylthio)-1-(2-thienyl)-1-propanone (27f)** : viscous oil; IR (neat) 1668, 1415 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.10 (s, 6H, $SCH_3$); 3.20 (d, J = 7Hz, 2H, $CH_2CH$); 4.24 (t, J = 7Hz, 1H,

$CH_2CH$); 7.09-7.14 (m, 1H, thienyl); 7.62-7.76 (m, 2H, thienyl). m/z 232 ($M^+$, 10%), 185(24), 111(100). (Anal. Calcd. for $C_9H_{12}OS_3$ : C, 46.51;H, 5.21. Found : C, 46.79; H, 5.48%).

**3,3-Bis(methylthio)-1-(2-naphthyl)-1-propanone (27g)** : colourless crystalline solid (hexane); m.p.72-73°C; IR (KBr) 1668, 1620, 1590 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.24 (s, 6H, $SCH_3$); 3.61 (d, J = 7.5Hz, 2H, $CH_2CH$); 4.50 (t, J = 7.5Hz, 1H, $CH_2CH$); 7.61-7.72 (m, 2H, ArH); 7.90-8.20 (m, 4H, ArH); 8.51 (s, 1H, ArH). m/z 276 ($M^+$, 12%), 156 (100). (Anal. Calcd. for $C_{15}H_{16}OS_2$: C, 65.18; H, 5.84. Found :C, 64.98; H, 6.05%).

**4,4-Bis(methylthio)-2-butanone (33)** : viscous oil; IR (neat) 1715, 1510, 1420 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.13 (s, 6H, $SCH_3$); 2.19 (s, 3H, $CH_3$); 2.89 (d, J = 7.5Hz, 2H, $CH_2CH$); 4.19 (t, J = 7.5Hz, 1H, $CH_2CH$). m/z 164($M^+$, 36%), 117(100). (Anal. Calcd. for $C_6H_{12}OS_2$: C, 43.86;H, 7.37. Found : C, 43.61; H, 7.12%).

**4,4-Bis(methylthio)-3-methyl-2-butanone (34)** : viscous oil; IR (neat) 1725, 1543 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1.49 (d, J = 7.5, 3H, $-CHCH_3$); 2.18 (s, 6H, $SCH_3$); 2.48-2.67 (m, merged with $CH_3$, 1H, $CH_3CH-$); 2.67 (s, 3H, $CH_3CO$); 4.38 [d, J = 7.5Hz, 1H, $(CH_3S)_2CH$]. (Anal. Calcd. for $C_7H_{14}OS_2$: C, 47.15; H, 7.91. Found : C, 46.87; H,8.19%).

**1-Phenyl-2-(1,3-dithian-2-yl)ethanone (37)** : yellow solid; m.p. 58-59°C (lit.[14] m.p. 59-61°C ); IR(KBr) 2972, 2958, 1694, 1600, 1583, 1449 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1 .65-2.14 (m, 2H, $-CH_2-$), 2.53-3.05 (m, 4H, $-CH_2$); 3.22 (d, J = 7.5Hz, 2H, $CH_2-$); 4.62 (t, J = 7.5Hz, 1H, $CH(SCH_3)_2$); 7.18 (m, 3H, ArH); 8.11 (m, 2H, ArH). (Anal. Calcd. for $C_{12}H_{14}OS_2$: C, 60.47; H, 5.88; Found: C, 60.11; H, 5.71%).

**3,3-Bis(phenylthio)-1-phenyl-1-propanone (38)** : Colourless viscous oil; 72%; IR ($CCl_4$) 1700, 1659, 1540, 1500, 1365, 900 $cm^{-1}$; $^1H$ NMR ($CCl_4$); 3.31 (d, J = 6Hz, 2H, $-CH_2$); 5.18 [t, J=6Hz, 1H, $CH(SCH_3)_2$], 7.04-7.69 (m, 13H, ArH); 7.80-8.02 (m, 2H, ArH). (Anal. calcd. for $C_{21}H_{18}OS_2$ : C, 71.96; H, 5.17 ; Found: C, 72.08; H, 5.04%).

**2-[Bis(methylthio)methyl]cyclopent-1-one (39n)** : viscous oil; IR (neat) 1740,1630, 1532 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.67-2.10 [m, 4H$(CH_2)_2$]; 2.11 (s, 6H, $SCH_3$); 2.29-2.59 (m, 3H, $CH_2$ and COCH); 4.10 [(d, J = 5Hz, 1H, $CH(SCH_3)_2$]. m/z 190 ($M^+$, 26%), 143(95). (Anal.Calcd. for $C_8H_{14}OS_2$: C, 50.49; H, 7.41. Found : C, 50.22; H,7.66%).

**2-[Bis(methylthio)methyl]cyclohex-1-one (39o)** : viscous oil; IR (neat) 1710, 1543 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.59-1.90 [m, 6H, $(CH_2)_3$]; 2.12 (s, 6H, $SCH_3$); 2.16-2.31 (m, 2H, $CH_2$); 2.43-2.70 (m, 1H, COCH); 4.09 [d, J = 7.5Hz, 1H, $CH(SCH_3)_2$]. m/z 204 ($M^+$, 38%), 157(100). (Anal. Calcd. for $C_9H_{16}OS_2$: C, 52.90; H, 47.89. Found : C, 53.16; H, 8.17%).

**2-[Bis(methylthio)methyl]cyclohept-1-one (39p)** : viscous oil; IR(neat) 1708, 1452 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.12-1.92 [m, 8H,$(CH_2)_4$]; 2.31 (s, 6H, $SCH_3$); 2.16-2.31 (m,2H, $CH_2$); 2.43-2.70 (m, 1H, COCH); 4.09 [d, J = 7.5Hz, 1H, $CH(SCH_3)_2$]. m/z

218 ($M^+$, 25%), 171(100). (Anal. Calcd. for $C_{10}H_{18}OS_2$ : C, 55.00; H, 8.31. Found : C, 54.73; H,8.59%).

**2-[Bis(methylthio)methyl]-indan-1-one (40q)** : m.p.44-45°C (lit.[14] m.p.45-47°C); IR (KBr) 1718, 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.15 (s, 3H, $SCH_3$); 2.25 (s, 3H, $SCH_3$); 2.54 -2.79 [m, 1H,-CH-CH($SCH_3$)$_2$]; 3.29 (brs, 2H, -$CH_2$-); 4.33 [m, 1H, -CH($SCH_3$)$_2$)]; 7.37 -7.90 (m, 4H, ArH). m/z 191 ($M^+$, 100%), 192 (81). (Anal. Calcd. for $C_{12}H_{14}OS_2$: C, 60.47; H, 5.92. Found : C, 60.56; H, 6.06%).

**2-[Bis(methylthio)methyl]-1-tetralone (40r)** : viscous oil; IR (neat) 1685, 1598, 1480 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.10 (s, 6H, $SCH_3$); 2.10-2.32 (m, 2H, $CH_2$); 2.55-3.00 (m, 3H, $CH_2$ and COCH); 4.43 [d, J =4Hz, 1H, CH($SCH_3$)$_2$]; 7.03-7.40 (m, 3H, ArH); 7.84-7.98 (m, 1H, ArH). m/z 252 ($M^+$, 35%), 205 (100). (Anal. Calcd. for $C_{13}H_{16}OS_2$ : C, 61.86; H, 6.39. Found : C, 62.15; H, 6.11%).

**2-[Bis(methylthio)methyl]-6-methoxy-1-tetralone (40s)** : viscous oil; IR (neat) 1680, 1600, 1595 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.20 (s, 6H, $SCH_3$); 2.20-2.41 (m, 2H, $CH_2$); 2.80-3.01 (m, 3H, $CH_2$ and COCH); 3.80 (s, 3H, $OCH_3$); 4.60 [d, J = 5Hz, 1H, -CH($SCH_3$)$_2$]; 6.88-6.95 (m, 2H, ArH); 8.09 (d, J = 9Hz, 1H, ArH). (Anal. Calcd. for $C_{14}H_{18}O_2S_2$: C, 59.54; H, 6.42. Found : C, 59.40; H, 6.34%).

**1,1-Bis(methylthio)-5-phenyl-4-penten-3-one (44a)** : viscous oil; IR (neat) 1685, 1660, 1605 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.14 (s, 6H, $SCH_3$); 3.01 (d, J = 7.5Hz, 1H, $CH_2$CH); 4.22 (t, J =

7.5Hz, 1H, $CH_2CH$); 6.71 (d, J = 15Hz, 1H, olefinic); 7.28-7.61 (m, 6H, ArH and olefinic). (Anal. Calcd. for $C_{13}H_{16}OS_2$ : C,61.90; H, 6.35. Found : C, 62.12; H, 6.14%).

**1,1-Bis(methylthio)-5-(4-methoxyphenyl)-4-penten-3-one (44b):** white crystalline solid (hexane); m.p.44-45°C; IR (KBr) 1685, 1658, 1598 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.14 (s, 6H, $SCH_3$); 2.99 (d, J = 7.5Hz, 2H, $CH_2CH$); 3.79 (s, 3H, $OCH_3$); 4.20 (t, J = 7.5Hz, 1H, $CH_2CH$); 6.53 (d, J =15Hz, 1H, olefinic); 6.85 (d, J = 9Hz, 2H, ArH); 7.38-7.68 (m, 3H, ArH and olefinic). (Anal. Calcd. for $C_{14}H_{18}O_2S_2$ : C,59.57; H, 6.38. Found : C, 59.76; H, 6.49%).

**5,5-Bis(methylthio)-1-(2-furyl)pent-1-ene-3-one (44c) :** yellow viscous liquid; 71%; IR (neat) 2950, 1639, 1570 $cm^{-1}$; 2.12 (s, 6H, $SCH_3$); 2.91 (d, J = 7.5Hz, 2H, $CH_2$); 4.19 (t, J = 7.5Hz, 1H, $-CH(SCH_3)_2$); 6.44-6.53 (m, 1H, H-5'furyl); 6.67 (d, J = 16Hz, 1H, olefinic), 6.69 -6.75 (m, 1H, H-4 furyl); 7.38 (d, J = 16Hz, 1H, olefinic); 7.49-7.58 (m, 1H, H-6 furyl). (Anal. Calcd. for $C_{11}H_{14}O_2S_2$ : C, 54.51; H, 5.82; Found : 54.63; H, 5.93%).

**5,5-Bis(methylthio)-1-(2'-naphthyl)-pent-1,4-diene-3-one (44d) :** colourless solid; 69-70°C; 74-75%; IR(KBr) 1705, 1620, 1380,1110 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.22 (s, 6H, $SCH_3$); 3.19 (d, J = 6Hz, 2H, $CH_2$); 4.33 (t, J = 6Hz, 1H, $CH(SCH_3)_2$); 7.00 (d, J = 15Hz, 1H, olefinic); 7.60-8.23 (m, 8H, ArH). (Anal. Calcd. for $C_{17}H_{18}OS_2$ : C, 6.75; H, 5.99. Found : C, 6.81; H, 6.04%).

**5,5-Bis(methylthio)-1[2(6-methoxy-3,4-dihydronaphtyl)] -pent-1,4-diene-3-one (44e)** : yellow viscous oil; 69%; IR(neat) 2948,1684,1600 cm$^{-1}$; $^{1}$H NMR ($CCl_4$) 2.01 (s, 6H, $SCH_3$); 2.32 (d, J = 6Hz, 2H, $-CH_2$); 2.56-2.94 (m, 4H,$-CH_2-$); 3.62 (s, 3H, $OCH_5$); 4.18 [t, J=6Hz, 1H, $-CH(SCH_3)_3$], 6.05 (d, J =16Hz, 1H, =CH); 6.38-6.70 (m, 3H, ArH); 6.89 (d, J=7.5Hz, 1H, olefinic); 7.26 (d, J = 16Hz, 1H, olefinic). (Anal. Calcd. for $C_{18}H_{22}O_2S_2$ : C, 63.54; H, 6.83. Found : C, 63.41; H, 6.91%).

**1,1-Bis(methylthio)-7-phenyl-4,6-heptadien-3-one (44f)** : white crystalline solid (hexane); m.p.85-86°C; IR (KBr) 1679, 1615, 1599 cm$^{-1}$; $^{1}$H NMR ($CDCl_3$) 2.26 (s, 6H, $SCH_3$); 3.09 (d, J = 7.5Hz, 2H, $CH_2CH$); 4.31 (t, J =7.5Hz, 1H, $CH_2CH$); 6.02 (d, J = 15Hz, 1H, olefinic); 6.98-7.49 (m, 8H, ArH and olefinic). (Anal. Calcd. for $C_{15}H_{18}OS_2$: C, 64.75; H, 6.47. Found : C, 64.87; H, 6.36%).

**1,1-Bis(methylthio)-7-(4-methoxyphenyl)-4,6-heptadien-3-one (44g)**: white crystalline solid; m.p. 98-99°C; IR (KBr) 1672, 1618, 1600 cm$^{-1}$; $^{1}$H NMP ($CDCl_3$) 2.24 (s, 6H, $SCH_3$); 3.07 (d, J = 7.5 Hz, 1H, $CH_2$); 3.68 (s, 3H, $OCH_3$); 4.19 (t, J = 7.5Hz, 1H, $CH(SCH_3)_2$); 6.09 (d, J = 15Hz, 1H, olefinic); 6.48 (dd, J = 15, 2Hz, 1H, olefinic); 6.61 (dd, J = 9Hz, 3H, olefinic and ArH); 7.09 (d, J = 9Hz, 2H, ArH); 7.72 (brs, 1H, olefinic). (Anal. Calcd. for $C_{16}H_{20}O_2S_2$ : C,62.30; H, 6.53. Found : C, 62.33; H, 6.59%).

**1,1-Bis(methylthio)-9-phenyl-4,6,8-nonatrien-3-one (44h)** : pale yellow solid; m.p. 105°C; 60%; IR (KBr) 1682, 1598, 1370, 1018 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 2.16 (s, 6H, $SCH_3$); 2.89 (d, J = 6Hz, 2H, $CH_2$); 4.20 [t, J = 6Hz, $CH(SCH_3)_2$] 6.19 (d, J = 16Hz, 1H, olefinic); 6.51 (dd, J = 16, 1.5Hz, 1H, olefinic); 6.70-6.89 (m, 2H, olefinic); 7.18-7.60 (m, 7H, olefinic and ArH). (Anal. Calcd. for $C_{17}H_{20}OS_2$: C, 67.06; H, 6.62. Found: C, 66.93; H, 6.53%).

**Z-3-Methylthio-2-methyl-1-phenyl-2-propen-1-one (32)** : viscous oil; IR (neat) 1638, 1572, 1441 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 1.89 (s, 3H, $SCH_3$); 2.28 (s, 3H, $CH_3$); 6.98 (s, 1H, olefinic); 7.21-7.98 (m, 5H, ArH). (Anal.Calcd. for $C_{11}H_{12}OS$ : C, 68.64;H, 6.24. Found : C, 68.39; H, 6.41%).

**E-4-Methylthio-3-methyl-3-buten-1-one (35)** : viscous oil; IR (neat) 1660, 1570, 1430 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 1.89 (s,3H, $SCH_3$); 2.48 (s, 3H, $CH_3$); 7.38 (brs, 1H, olefinic). (Anal. Calcd. for $C_6H_{10}OS$: C, 55.38; H, 7.69. Found : C, 55.17; H, 7.82%).

**E-2-(Methylthiomethylene)-1-tetralone (41r)** : pale yellow solid; 65%; m.p. 68-69°C (lit.[6] m.p. 69°C); IR (KBr) 1660,1602,1340 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 2.43 (s, 3H, $SCH_3$); 2.79 [q, 4H, $(CH_2)_2$]; 7.00-7.40 (m, 3H, ArH); 7.51 (s, 1H, olefinic); 7.90-8.05 (m, 1H, ArH). (Anal. Calcd. for $C_{12}H_{12}OS$: C, 70.48; H, 5.87. Found : C, 70.72; H, 5.91%).

**E-2-(Methylthiomethylene)-6-methoxytetralone (41s)** : m.p.92-93°C; IR (KBr) 1642, 1600, 1555 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 2.50 (s, 3H, $SCH_3$); 2.63-3.05 [m, 4H, $(CH_2)$]; 3.82 (s, 3H, $OCH_3$);

6.70-6.95 (m, 2H, ArH); 7.70 (s, 1H, olefinic); 8.10 (d, J =9Hz, 1H, ArH). (Anal. Calcd. for $C_{13}H_{14}O_2S$ : C, 66.64; H, 6.02. Found: C, 66.73; H, 5.88%).

**E-2-(Methylthiomethylene)benzosuberone (41t)** : yellow solid 75%; m.p. 74-75°C; IR (KBr) 1620,1618,1548,1250 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1.95 (q, 2H, $(CH_2)_3$; 2.39 (t, J= 6Hz, 1H, $CH_2$); 2.49 (s, 3H, $SCH_3$); 2.78 (t, J = 6Hz, 2H, $CH_2$); 6.90-7.31 (m, 3H, =CH, ArH); 2.78-7.68 (m, 2H, ArH). (Anal. Calcd. for $C_{13}H_{14}OS$ : C, 71.49; H, 6.45. Found : C, 71.33; H, 6.53%).

**3,3-Bis(methylthio)-2-methyl-1-phenyl-1-propanone (31):** (Method B);pale yellow oil; 64%; IR ($CCl_4$) 2980, 1758, 1445 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.41 (d, J = 6Hz, 3H, $CH_3$); 2.11 (s, 6H, $SCH_3$); 2.69 [brs, 1H, CH(CO)], 4.01 (q, J = 6Hz, 1H, $CH(SCH_3)_2$), 7.06-7.62 (m, 3H, ArH); 7.79-8.19 (m, 2H, ArH). (Anal. Cald. for $C_{12}H_{16}OS_2$ : C, 59.97; H, 6.66. Found : C, 60.08; H, 6.72%).

**2-[Bis(methylthio)methyl]-1- benzsuberone (40t):** (Method B); yellow viscous oil; IR ($CCl_4$) 1682, 1608, 1522 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.98 (q, 2H, $CH_2$); 2.29 (t, J = 6Hz, 2H, $CH_2$); 2.38 (s, 6H, $SCH_3$); 2.54-3.02 (m, 3H, -CH(CO), $CH_2$); 4.45 (d, J = 4 Hz, 1H, CH $(SMe)_2$); 7.05-7.42 (m, 3H, ArH); 7.79-7.88 (m, 1H, ArH). (Anal. Calcd. for $C_{14}H_{18}OS_2$ : C, 62.38; H, 6.76. Found : C, 62.49; H, 6.81%).

**5,5-Bis(methylthio)-4-methyl-3-pentanone (45):** (Method B); colourless viscous oil; IR (neat) 1738,1640,1562 $cm^{-1}$;$^1H$ NMR ($CCl_4$) 1.38 (d, J = 6Hz, 3H, $CH_3(CH_2)$; 1.42 (t, J = 6Hz, 2H,

$-CH_2(CH_3)$; 1.48 (d, J = 7.5 Hz, $-CH-CH_3$); 2.13 (s, 6H, $SCH_3$); 2.39-2.54 [m, 1H, $CH(CH_3)$]; 4.34 (d, 1H, J = 7.5Hz, $-CH(SCH_3)_2$). (Anal. Calcd. for $C_8H_{16}OS_2$: C, 49.97; H, 8.33. Found : C, 49.71; H, 7.99%).

## REFERENCES AND NOTES

1. (a) Ireland, R.E. Marshall, J.A. *J.Am.Chem.Soc.,* 1959, *81*, 6336; (b) Church, R.F., Ireland, R.E., Marshal, J.A. *Tetrahedron Lett*, 1961 *34*; *ibid*, 1961 493.
2. Ireland, R.E., Marshall, J.A., *J. Org. Chem.,* 1962 *27*, 1615 and references cited therein; *ibid*, 1962, *27*, 1620, 1622.
3. (a)Church, R.F., Ireland, R.E., Marshall, J.A., *J. Org. Chem*, 1962 *27*, 1118; (b) See also, Bernstein, P.R. *Tetrahedron Lett.*, 1979, 1015.
4. Marshall, J.A., Johnson, P.C., *J. Org. Chem.* 1970, *35*, 193.
5. Saquet, M., Thuillier A. *Bull. Soc. Chim. Fr.,* 1966, 3969-3977.
6. Myrboh, B., Ila, H., Junjappa, H. *J. Org. Chem.,* 1983, *48*, 5327-5332 and references cited therein.
7. Myrboh, B., Singh, L.W., Ila, H., Junjappa, H. *Synthesïs,* 1982, 307-309.
8. Rao, Ch.S; Chakrasali, R.T.; Ila, H.; Junjappa, H. *Tetrahedron*, 1990. *46*, 2195.

9. Ruettinger, H.-H., Rudorf, W.-D., Matsehiner, *J. Prakt, Chem.* 1979, *321* , 443.

10. Schultz-von Itter.; Stickhan, E., *Tetrahedron,* 1987, *43,* 2475.

11. Gammill, R.B., Gold, P.M., Mizsak, S.A. *J. Am. Chem. Soc.,* 1980, *102*, 3095-3100.

12. Gammill, R.B., Bell, L. T., Nash, S.A., *J. Org. Chem.,* 1984, *49,* 3039 (1984).

13. Gammill, R.B., Nash, S.A., Bell, L. T., Watt, W., Mizsak, S.A., Scahill. T. A., Sobieray, D., *Tetrahedron Lett.,* 1990 *31*, 5301, 5303.

14. Gammill, R.B., Sobieray, D.M., Gold, P.M. *J. Org. Chem.,* 1981, *46,* 3555-3558.

15. For more details on the reactivity profile of α-oxoketene dithioacetals - see (a) Dieters R.K., *Tetrahedron* 1986, *43,* 3029; (b) Junjappa, H.; Ila, H.; Asokan, C.V. *Tetrahedron* 1990, *46,* 5324; (c) Paderes, G.D., Metivier, P.; Jorgensen, W.L.*J.Org.Chem.* 1991, *56,* 4718.

16. The 1,2 and conjugate reduction of α,β-unsaturated carbonyl compounds has been discussed in terms of HSAB principle; see (a) HO, T-L. *Chem. Rev.,* 1975, *75,* 1-20 ; and references cited therein; (b) Bottin, J., Eisenstein, O., Minot, C., Anh, N.J. *Tetrahedron lett.,* 1972, 3015-3018; (d) Klopman, G. *J.Am.Chem.Soc.* 1968, *90,* 223-234.

17. The bulkier localized Grignard reagents also exhibit their preference for 1,4-addition probably due to steric reasons.

18. Balu, M.P.; Bhat, L.N.; Ila, H.; Junjappa, H. *Ind. J. Chem.* 1991, *30B*, 245.

19. For a review on 'Hard Soft Affinity Inversion' see : Fuji K. *Nucleophilicity, Advances in Chemistry,* Series 215; Harris, J.M., McManus, S.P., Eds, American Chemical Society, Washington, Chapt. 15, p. 219-231.

20. (a) Purkayastha, M.L., Ila, H., Junjappa, H. *Synthesis,* 1989, 20-24; (b) Lane, C.F. *Synthesis,* 1975, 135-146; (c) Hutchins, R.O, Kandasamy, D. *J. Org. Chem.,* 1975, *40,* 2530-2533.

21. (a) Sauvetre, R., Roux-Schmitt, M-C., Seyden-Penne, J. *Tetrahedron,* 1978, *34,* 2135-2140; (b) Lefour, J-M., Loupy, A. *Tetrahedron,* 1978, *34,* 2597-2605; (c) Kyriakakou, G., Roux-Schmitt, M.C., Seyden-Penne, J. *Tetrahedron,* 1975, *31,* 1883-1888; (d) Schultz, A.G., Yee, Y.K. *J. Org. Chem.,* 1976, *41,* 4044-4045.

22. (a) Kadin, S.B. *J. Org. Chem.,* 1966, *31,* 620-622; (b) Salomon, R.G. Sachinvala N.D., Raychaudhuri, S.R., and Miller, D.B. *J. Am. Chem. Soc.,* 1984, *106,* 2211-2213; (c) Sinhababu, A.K., Borchardt, R.T., *Tetrahedron Lett.,* 1983, *24,* 227-230; (d) Shechter, H., Ley, D.E., Roberson Jr. E.B. *J. Am. Chem. Soc.* 1956, *78,* 4984-4991; (e) Dauben, W.G., and Easthan, J.F. *J. Am. Chem. Soc.* 1951, *73,* 4463-4464; (f) Dauben, W.G., Michaeli, R.A., Eastham, J.F. *J. Am. Chem. Soc.* 1952, *74,* 3852-3855.

23. (a) Kupfer, D. *Tetrahedron,* 1961, *15*, 193-196; (b) Jackson W.R., Zurquiyah, A. *J. Chem. Soc.* 1965, 5280-5287; (c) Iqbal, K., Jackson, W.R. *J. Chem. Soc.(C),* 1968, 616-620; (c) Johnson, M.R., Rickborn, B. *J. Org. Chem.,* 1970, *35*, 1041-1045.
24. Marshall, J.A., Johnson, W.S. *J. Org. Chem.,* 1963, *28*, 421- 423.
25. Marshall, J.A., Johnson, W.S. *J. Org. Chem.,* 1963, *28*, 595-596.
26. Hach , V. *Synthesis,* 1974, 340-342.
27. Carey, F.A., Neegaard, J.R. *J. Org. Chem.,* 1971, *36*, 2731-2735.
28. Corey, E.J., Crouse, D. *J.Org.Chem,* 1968, *33*, 298.
29. Suryawanshi, S.N., Mukhopadhyay, A., Dhami, T.S., Bhakuni, D.S. *Ind.J.Chem.* 1990, *29B*, 1001.
30. Pfaltz, A., Anwar, S., *Tetrahedron Lett.,* 1984, *25*, 2977
31. Olsen, C.E.; Bader, A.D. *Organic Synthesis Coll. Vol. 4* 1963, 898.
32. Koo, J. *J. Am. Chem. Soc.* 1953, *75*, 1891.
33. Noller, C.R.; Adams, R. *J. Am. Chem. Soc.* 1924, *46*, 1889.
34. Thuillier, A.; Vialle, J. *Bull. Soc. Chim. Fr.* 1959, 1398.
35. Thuillier, A.; Vialle, J. *Bull. Soc. Chim. Fr.* 1962, 2194.
36. Apparao, S.; Datta, A.; Ila, H.; Junjappa, H. *J. Chem. Soc. Perkin Trans. I,* 1984, 921.
37. Chauhan, S.M.S.; Junjappa, H. *Tetrahedron,* 1976, *32*, 1779.

38. Shahak, I.l Sarson, I. *Tett. Lett.* 1973, 4207.

39. Chauhan, S.M.S. and Junjappa, H., *Tetrahedron*, 1976, *32*, 1779-1787.

40. Thuillier, A., and Vialle, J. *Bull. Soc. Chim. Fr.*, 1962 2182-2186, 2187.

41. Maignan, J., Vialle, J. *Bull. Soc. Chim. Fr.*, 1973, 2388-2392.

42. Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis*, 1985, 163. (1984).

43. Vogel's Text Book of Practical Organic Chemistry, Ed. IV; 1978, Longman Group Limited, London.

# CHAPTER III

## CYCLOAROMATIZATION OF β-OXODITHIOACETALS WITH BENZYL-, 1-(NAPHTHYLMETHYL) AND 2-(NAPHTHYLMETHYL) MAGNESIUM HALIDES : SYNTHESIS OF CONDENSED POLYNUCLEAR AROMATIC HYDROCARBONS*

### INTRODUCTION .

Construction of benzene derivatives and other condensed aromatics from the open chain precursors is one of the important synthetic operations[1]. There have been several attempts in the past to achieve the synthesis of aromatics from their alicyclic counterparts[2]. Such a synthetic strategy has been widely employed for the construction of

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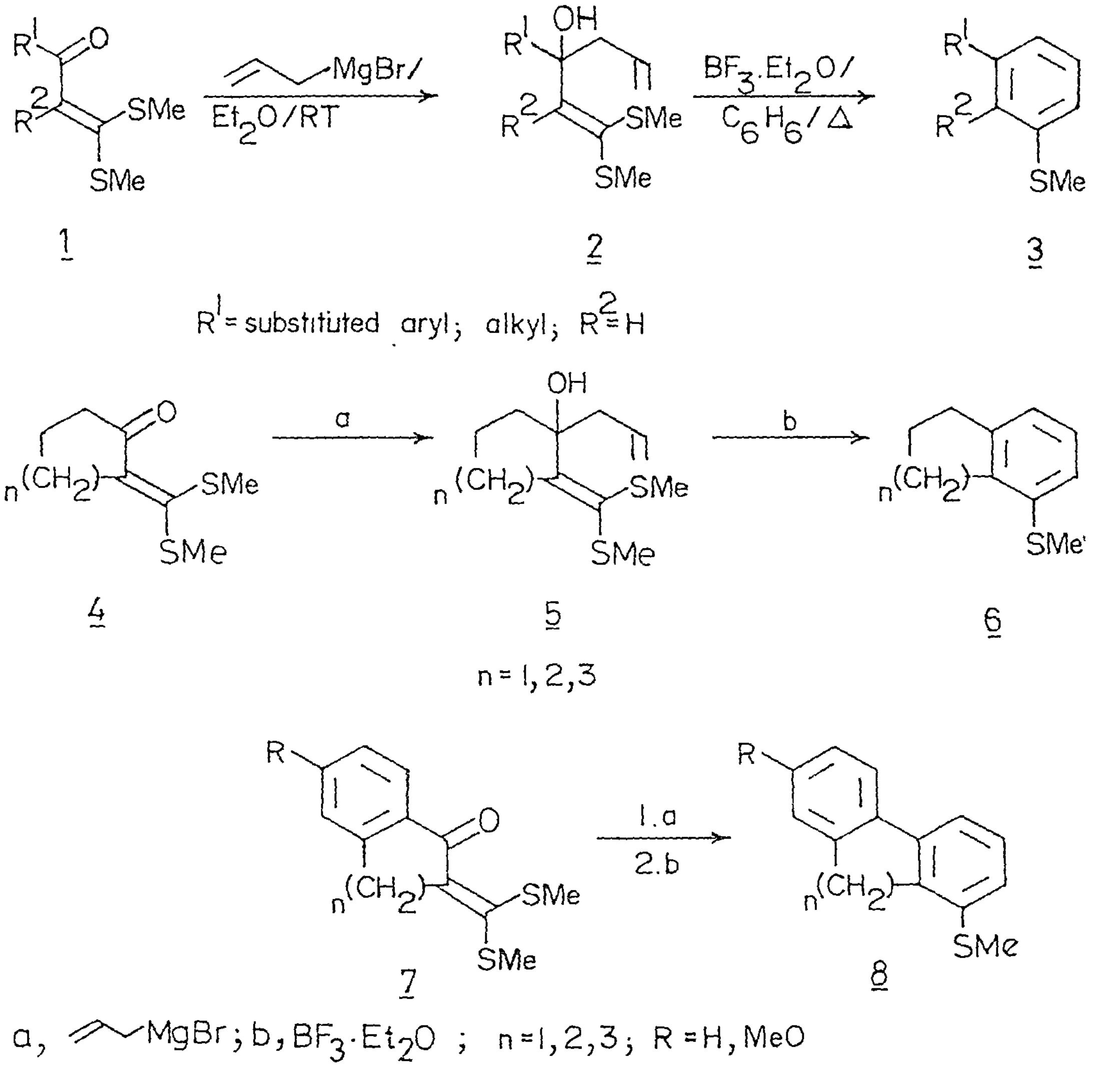
*Rao, Ch.S.; Balu, M.P.; Ila, H.; Junjappa, H. *Tetrahedron,* 1990, *47,* 3499.

heterocyclic compounds. However, the synthesis of benzene derivatives and other condensed aromatics following such a strategy was less attended by the chemists as they were preoccupied for development of electrophilic substitution chemistry of the preconstructed aromatic molecules. This situation prevailed due to the easy availability of these hydrocarbons from the fossil sources. With an increasing large scale utilization of these natural hydrocarbons, their availability in the future has become uncertain and thus warrant appropriate chemical strategies to make these compounds available from the open chain precursors which may originate from the renewable sources. Besides, for the synthesis of multisubstituted benzenoids, a sequential multistep substitution reactions are employed resulting in overall poor yields at the end products. Also, the restrictions imposed by electrophilic substitution interms of *ortho* and *para* mixtures further reduce the chances of acquiring improved yields of the end products.

Attempts have therefore been made to construct multifunctional benzenoids from the open chain precursors with appropriate substituents so that these substituents become part of the product aromatic ring[2]. Such a strategy also has an advantage in preparing the multisubstituted benzenoids in improved yields. The most commonly employed synthetic strategy involves the condensations of 1,3-carbonyl compounds with appropriate 3-carbon fragments[3]. A number of approaches have been developed on the basis of this strategy for the synthesis of benzene derivatives and their condensed aromatics[4,5].

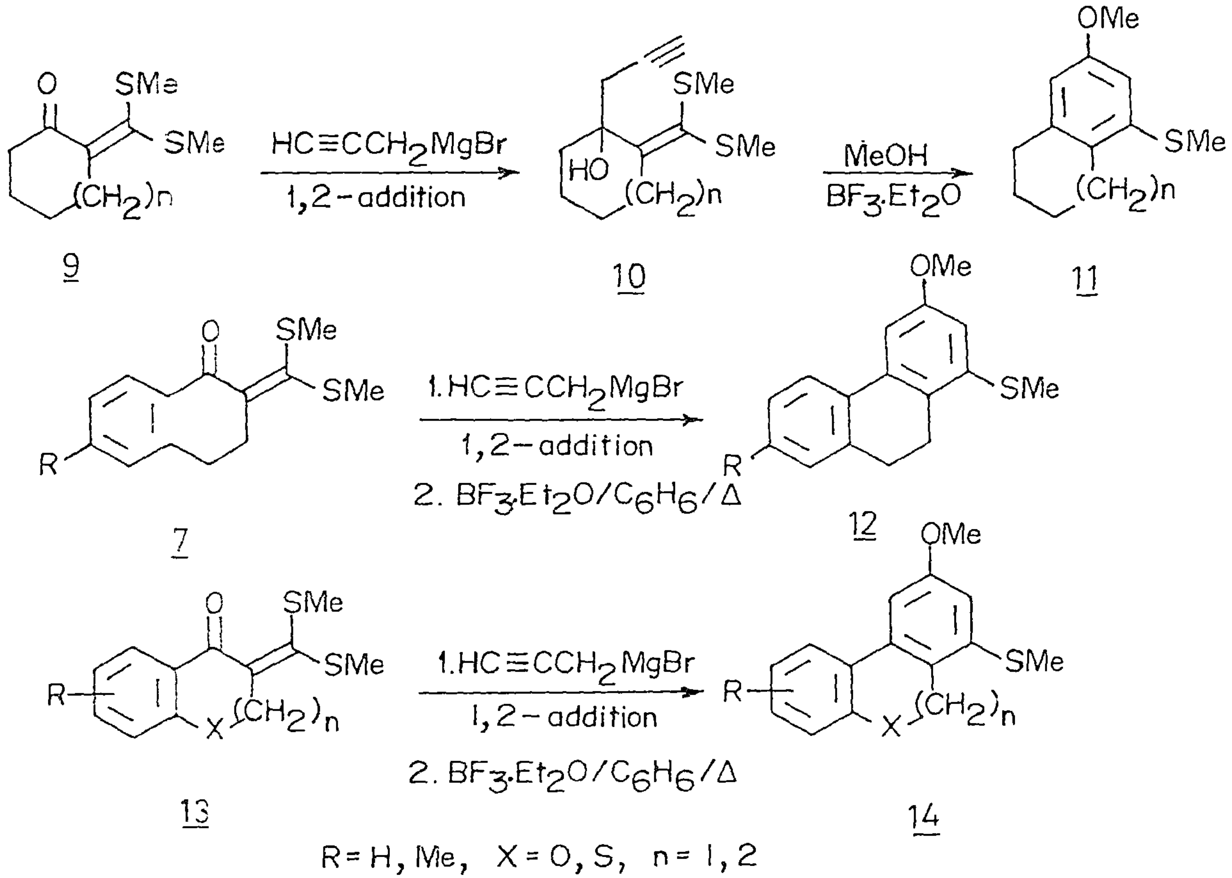
As a part of the program to develop a new approach for the synthesis of benzenoids and our interest in the chemistry and synthetic applications[6] of α-oxoketene dithioacetals 1, we discovered that the allylmagnesium bromide undergoes facile 1,2-addition with 1 yielding the corresponding carbinolacetal 2 in near quantitative yields. These carbinolacetals 2 underwent smooth cycloaromatization[7] in the presence of $BF_3.Et_2O$ in refluxing benzene to afford the corresponding benzene derivatives 3 in good to excellent yields. The methylthio substituted aromatics on desulphurisation with *Raney Nickel* afforded the corresponding sulphur free benzenoids. The method was of general applications to a variety of α-oxoketene dithioacetals derived from a wide range of active methylene ketones (scheme 1).

Similarly, when the α-oxoketene dithioacetals 9 reacted with propargyl magnesium bromide afforded the corresponding carbinols 10 in excellent yields. These carbinols 10 underwent intramolecular ring closure in the presence of $BF_3.Et_2O$ with nucleophilic solvent participation (methanol) to afford the corresponding methoxy substituted aromatics 11. The methodology has been successfully extended to many α-oxoketene dithioacetals for the synthesis of the corresponding methoxy substituted aromatic systems[8] (scheme 2).



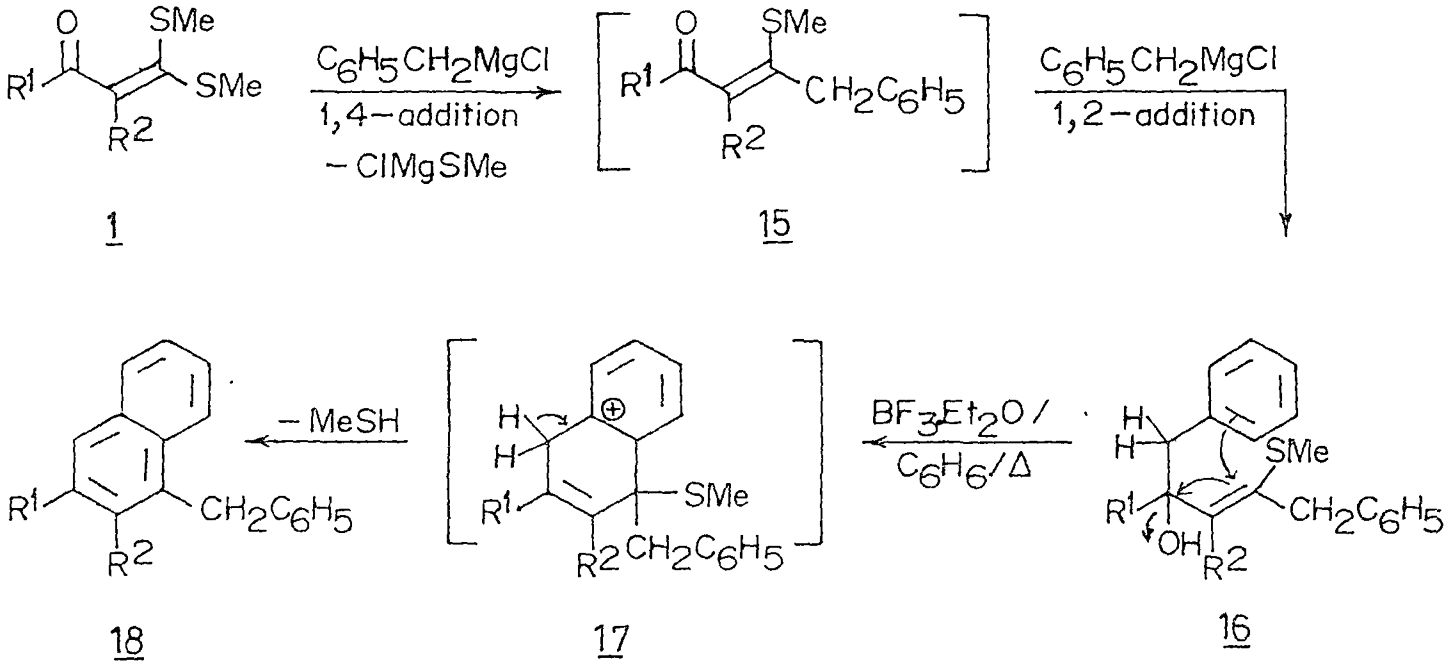
1
2
3
CH2=CHCH2MgBr/
Et2O/RT
BF3.Et2O/
C6H6/Δ
R1 = substituted aryl; alkyl; R2=H
4
5
6
a
b
n = 1, 2, 3
7
8
1. a
2. b
a, CH2=CHCH2MgBr; b, BF3·Et2O ; n=1,2,3; R = H, MeO

Scheme-1


O
SMe
SMe
(CH2)n
9
HC≡CCH2MgBr
1,2-addition
SMe
SMe
HO
(CH2)n
10
MeOH
BF3·Et2O
OMe
SMe
(CH2)n
11
O
SMe
SMe
R
7
1. HC≡CCH2MgBr
1,2-addition
2. BF3·Et2O/C6H6/Δ
OMe
SMe
R
12
O
SMe
SMe
R
X
(CH2)n
13
1. HC≡CCH2MgBr
1,2-addition
2. BF3·Et2O/C6H6/Δ
OMe
SMe
R
X
(CH2)n
14
R = H, Me, X = O, S, n = 1, 2

Scheme-2

This strategy was extended to the reaction of benzylmagneisum chloride with 1 so that the carbinolacetals thus obtained could be cyclized under the described reaction conditions to afford the corresponding napththalenes and other condensed aromatics.[9] The carbinolacetal was considered to undergo ring closure through the participation of the aromatic ring to afford the annelated product. However, when benzyl magnesium chloride was reacted with 1, only 32% yield of benzyl substituted naphthalene 18 (scheme 3) was obtained. Apparently, the benzylmagnesium chloride underwent the initial 1,4-addition to give the corresponding 15 which now competes with 1 to react with benzyl Grignard reagent in 1,2-fashion to afford the corresponding carbinol 16. It was apparent that two equivalents of benzyl magnesium chloride were used for each mole of 1. Because of the observed sequential 1,4- followed by 1,2-addition the annelated product was obtained in overall low yield. However when the the three fold excess of benzylmagnesium chloride was used to react with 1, the yield of 18 was increased to 82% with no trace of starting material in the reaction mixture. However, when the benzyl Grignard reagent was decreased to half equivalent to that of 1, most of the starting dithioacetal was recovered back unaltered alongwith the 1,4- followed by 1,2-addition product 18. This reaction was extended to a number of α-oxoketene dithioacetals which uniformly yielded the benzyl substituted aromatics without any exception (Scheme 3). An interesting deviation was observed when α-methylnaphthylmagnesium chloride 19 and β-methylnaphthyl

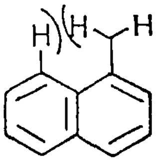


$R^1 = C_6H_5$, $4\text{-}MeOC_6H_4$, $4\text{-}MeC_6H_4$, B-naphthyl, $R^2 = H$

Scheme-3

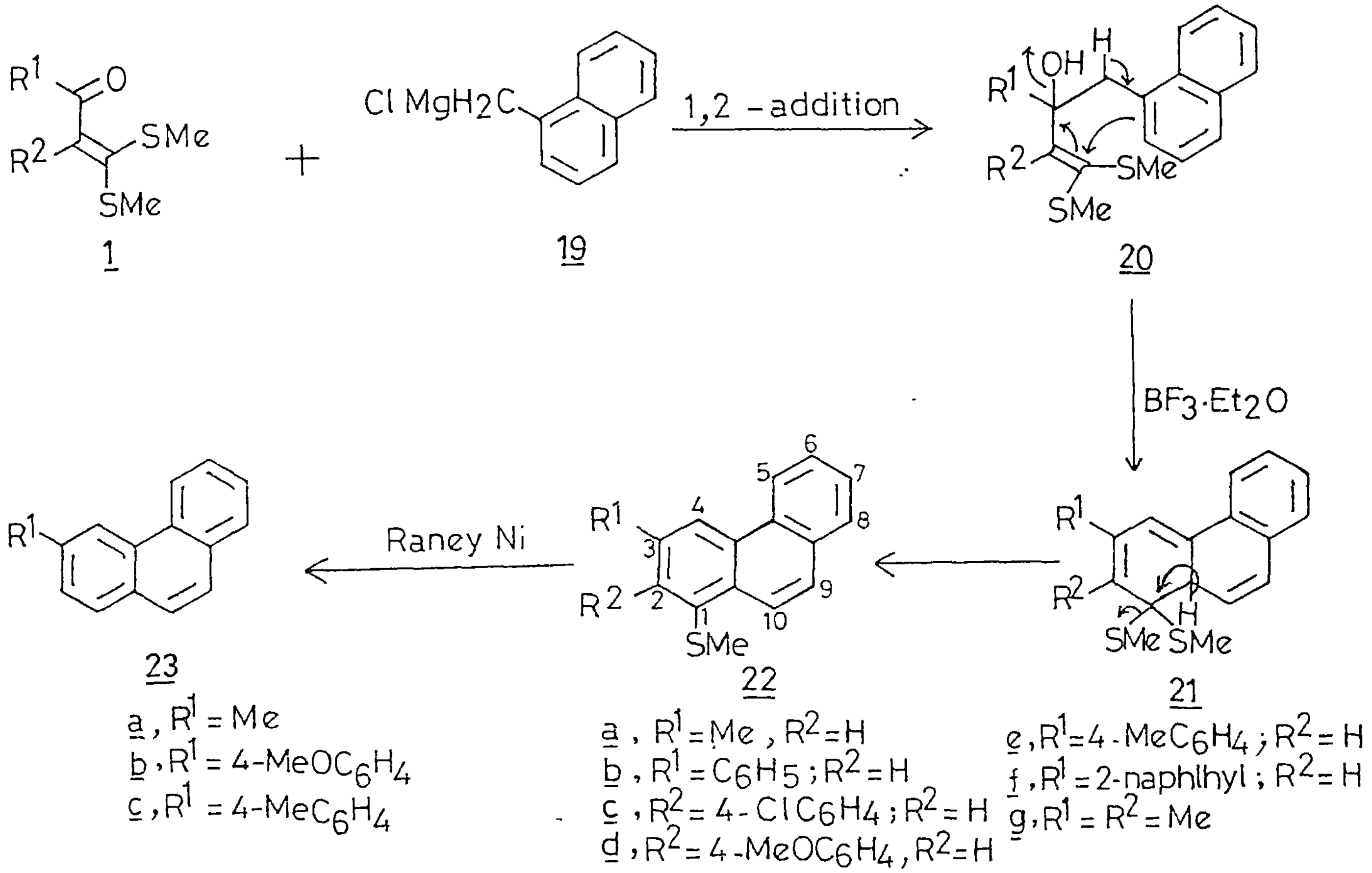
magnesium bromide **24** were reacted with the α-oxoketene dithioacetals[10]. In principle, 1-(naphthylmethyl) magnesium chloride due to *peri-interaction* may suffer liberal delocalization of the negative charge over the ring and consequently may undergo charge controlled 1,2-addition[11] to **1** (Scheme 4). On the otherhand, the corresponding 2-(naphthylmethyl)magnesium bromide **24** might simply follow sequential 1,4-followed by 1,2-addition to **1** in the absence of steric inhibition for the charge delocalization[11] (Scheme 5). Thre have been some theoretical studies on these interactions. In their solvolytic studies, Dewar and Sampson[12] have shown that the methylene group in the 1-(naphthylmethyl) cation cannot be coplanar with the ring without one of its hydrogen atoms overlapping too closely with the peri-hydrogen (Structure A).

Structure A

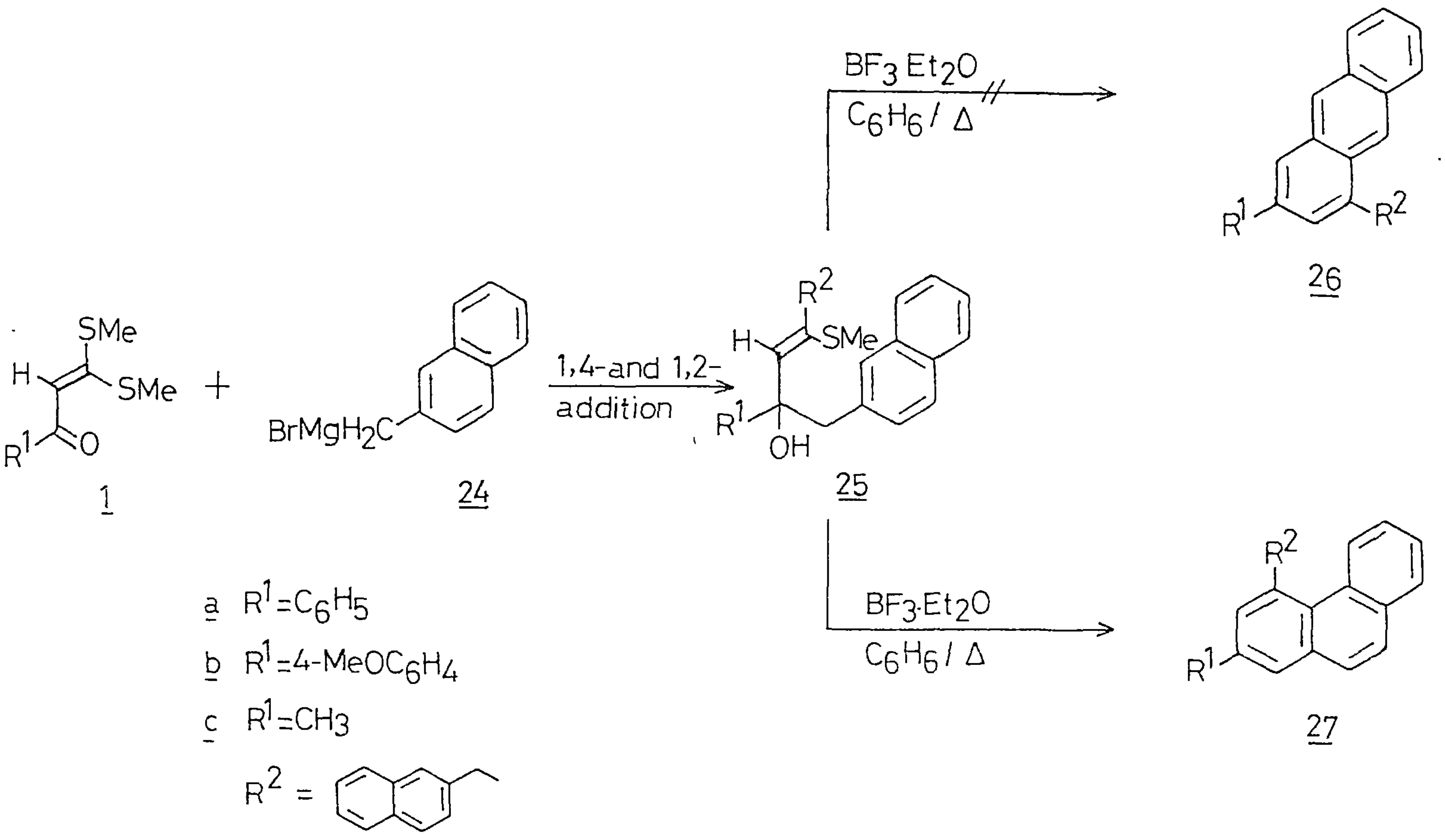


The strain energy in these systems was calculated to be around 2.3 k.cal/mole, which is enough to hinder the electronic interactions between the ring and the methyl cation. However, in another study, Kronzer and Sandel[13] have investigated the structural features of 1- and 2-(naphthylmethyl)anions by $^1H$ NMR spectra and concluded that the methylene carbon is $sp^2$ hybridized and consequently the methylene hydrogens lie in or near the plane of ring. But the regioselectivity of these anions towards ambident electrophiles has not been investigated. Dewar argues that the strain energy of 2.3 k.cal/mol calculated for naphthylmethyl and related systems using PMO method is correct, while the other methods of calculations which do not distinguish between α-naphthyl and β-naphthyl type systems are in error[12]. In view of these findings, our experiments of α-(naphthylmethyl)magnesium chloride and β-(methylnaphthyl)magnesium bromide should reveal interesting regioselectivity when they are reacted with the α-oxoketene dithioacetals. Thus, 1-(naphthylmethyl)magnesium chloride 19 when reacted with 1 gave the intermediate carbinol acetal 20 which on subsequent cycloaromatization yielded the corresponding phenanthrene 22 while retaining the thiomethyl group intact (Scheme 4). Apparently, the *peri-interaction* in 19 with the ring is playing an important role in inhibiting the charge delocalization and permitting charge-controlled 1,2-addition only. This is further exemplified when the β-(naphthylmethyl) Grignard reagent 24 was reacted with 1 the product phenanthrene 27 carried the corresponding methylnaphthyl side chain instead of the $-SCH_3$ group. Apparently in the absence of *peri-interaction* the anion freely delocalizes in the ring and undergoes the preferred orbital controlled 1,4-addition to yield the products observed (Scheme 5). Also, it is interesting to note that the cycloaromatization did not proceed to yield the anthracenes 26.

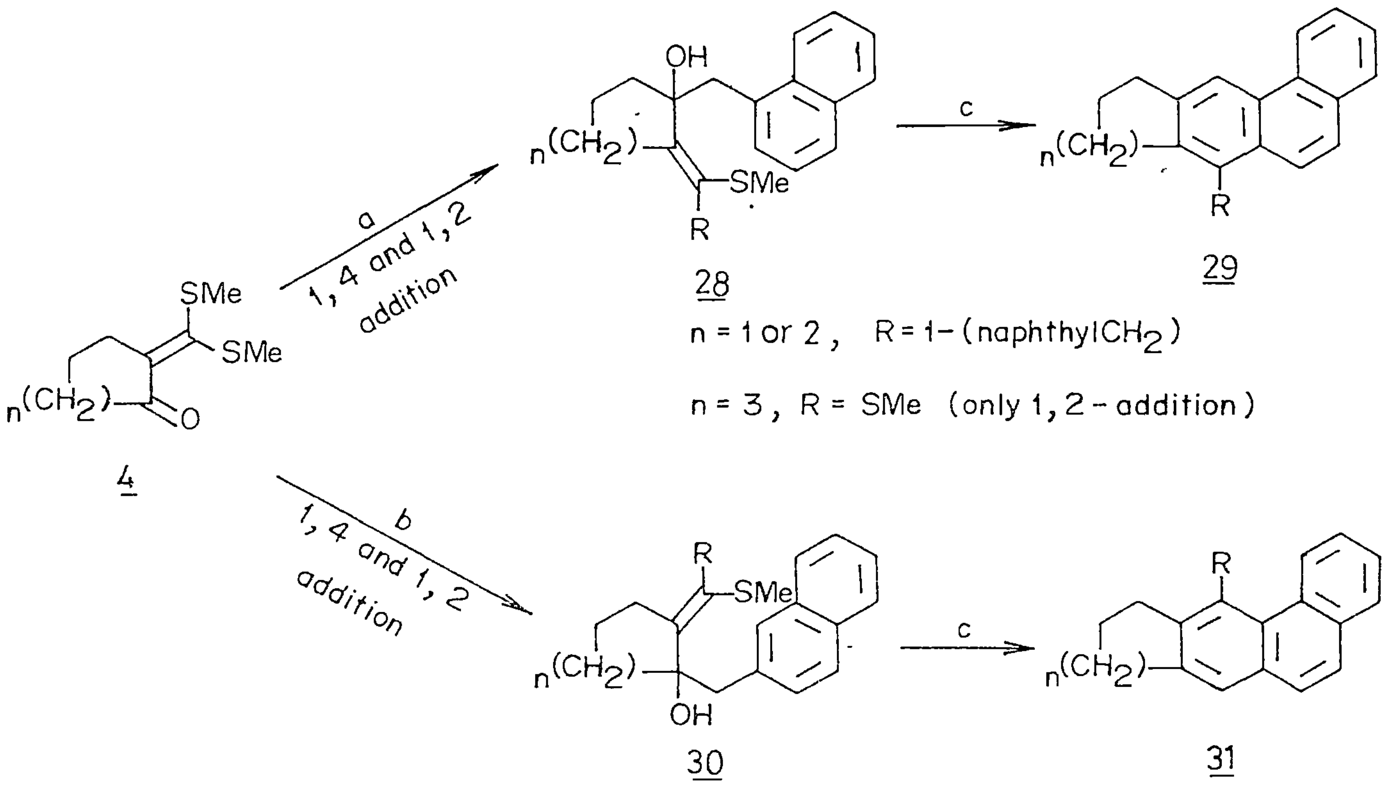
However, when 19 and 24 reacted with the cyclic oxoketene dithioacetals 4 yielded the products arising exclusively from


1
19
1,2 -addition
20
$BF_3 \cdot Et_2O$
21
22
Raney Ni
23
ClMgH2C
OH
H
SMe
R1
R2
1
2
3
4
5
6
7
8
9
10
a, $R^1$ = Me
b, $R^1$ = 4-$MeOC_6H_4$
c, $R^1$ = 4-$MeC_6H_4$
a, $R^1$ = Me, $R^2$ = H
b, $R^1$ = $C_6H_5$; $R^2$ = H
c, $R^2$ = 4-$ClC_6H_4$; $R^2$ = H
d, $R^2$ = 4-$MeOC_6H_4$, $R^2$ = H
e, $R^1$ = 4-$MeC_6H_4$; $R^2$ = H
f, $R^1$ = 2-naphlhyl; $R^2$ = H
g, $R^1$ = $R^2$ = Me

Scheme 4


SMe
H
SMe
R1
O
1
+
BrMgH2C
24
1,4-and 1,2-
addition
R2
H
SMe
R1
OH
25
BF3 Et2O
C6H6 / Δ
R1
R2
26
BF3·Et2O
C6H6 / Δ
R2
R1
27
a R1=C6H5
b R1=4-MeOC6H4
c R1=CH3
R2 =

Scheme 5



n = 1 or 2 , R = 1-(naphthylCH$_2$)

n = 3 , R = SMe (only 1,2-addition)

n = 1,2,3 R = 2-(naphthyCH$_2$)

a, 1-(naphthylCH$_2$)MgCl / Et$_2$O / RT , b, 2-(naphtylCH$_2$)MgBr / Et$_2$O / RT

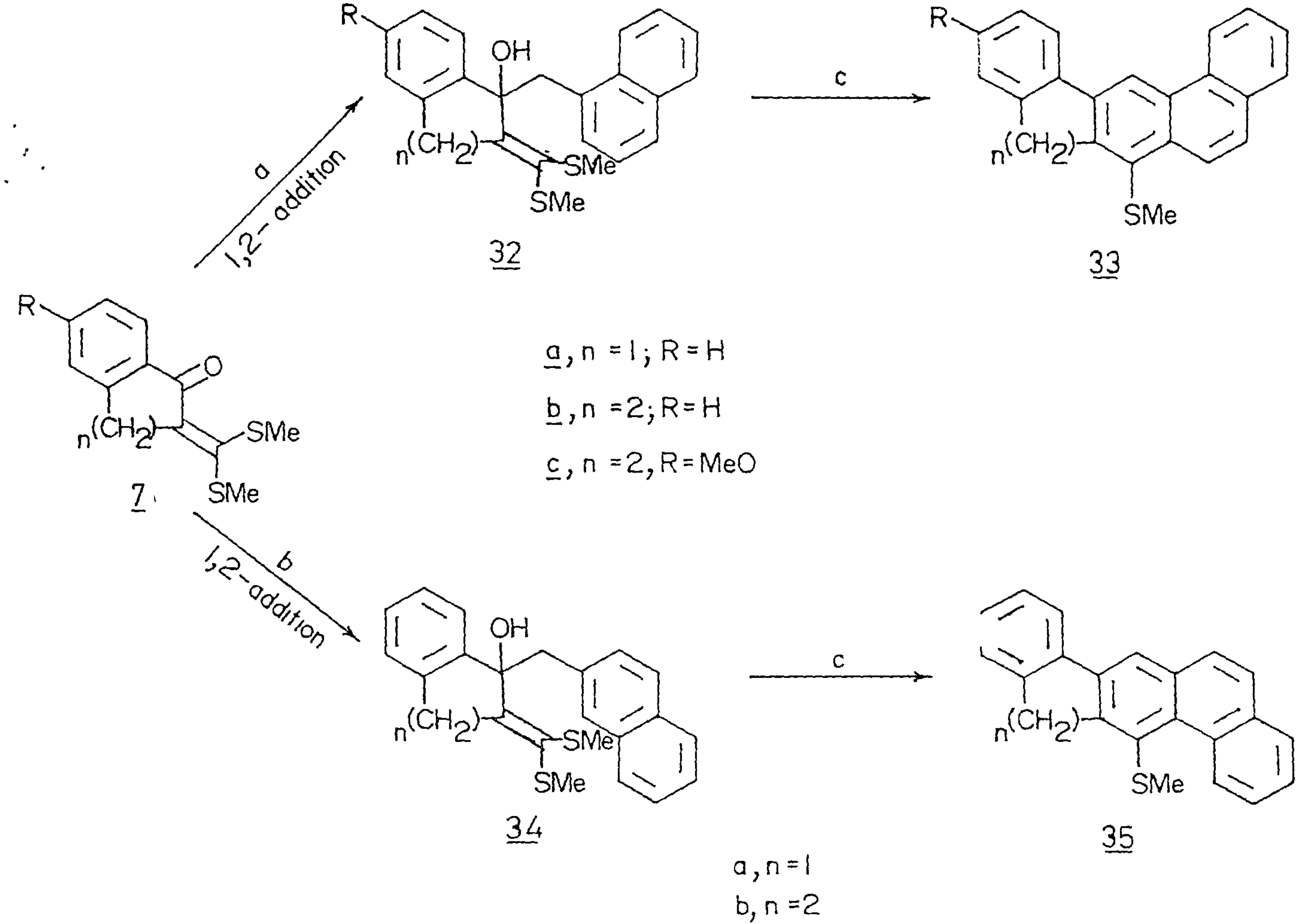
c, BF$_3$Et$_2$O / C$_6$H$_6$ /

Scheme – 6

1,4-followed by 1,2-additions, **29** and **31** respectively (Scheme 6). It is pertinent to note that the 1,2-selectivity of **19** failed in the case of cyclic oxoketenedithioacetals. This observation was again reversed when both **19** and **24** reacted with the oxoketene dithioacetals derived from Indanone and tetralone (Scheme 7). Thus, **19** reacted with **7** to give exclusively initial 1,2-adducts **32** followed by cyclization to afford **33**. No product from 1,4-addition was detected in the reaction mixture. Similarly interesting reversal was observed when **24** reacted with **7**, the product **35** confirmed that the addition underwent exclusively in 1,2-fashion (Scheme 7). It appears that the 1,2-versus 1,4-addition mode not only dependent on the anions **19** and **24** but also on the substrates though the factors associated with its deviation cannot be immediately answered.

## RESULTS AND DISCUSSION

The reaction of benzylmagnesium chloride with α-oxoketene dithioacetals **1** has resulted in the 1,4-followed by 1,2-addition sequence leading to the benzyl substituted product aromatics. This became a serious limitation of our method since it is more difficult to remove the benzyl group than the methylthio group. Similarly the reaction of α- and β-naphthylmethyl magnesium halides did not follow consistent pattern of additions to α-oxoketene dithioacetals though in some cases α-methylnaphthyl magnesium chloride did yield the desired aromatics with the retention of methylthio group. On the otherhand, in majority of the reactions the β-

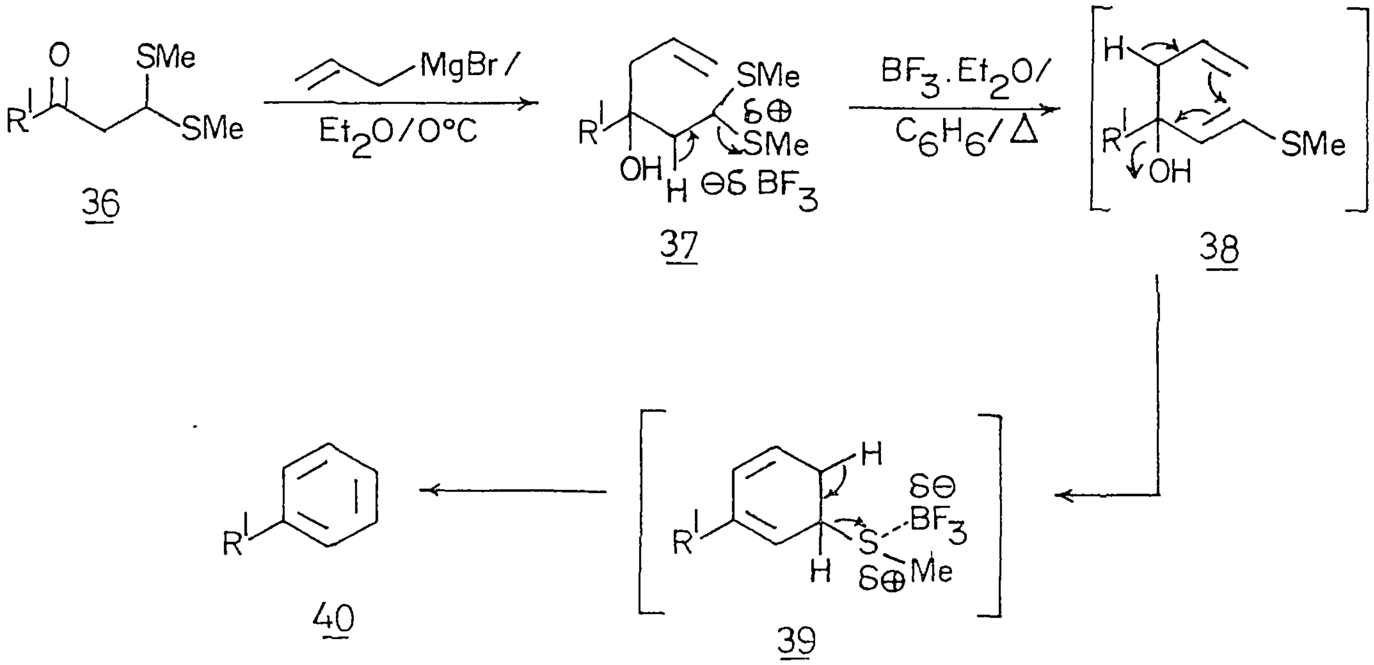


a, 1-(naphthyl $CH_2$) MgCl/$Et_2O$/RT; b, 2-(naphthyl $CH_2$) MgBr/$Et_2O$/RT; c, $BF_3.Et_2O/C_6H_6/\Delta$

Scheme-7

(methylnaphthyl)magnesium bromide with 1 gave invariably the methylnaphthyl substituted aromatics with a few exceptions. It was therefore considered of interest to further explore the possibilities to develop unambiguous methods of synthesis of these aromatics. These results are presented in this chapter.

It may be noted that an efficient method of regioselective reduction[14] of mercapto double bond of α-oxoketene dithioacetals 1 has been developed as described in the Chapter II. Apart from the method of $NaBH_4/AcOH$, the prodcedure involving Zinc and acetic acid for the reduction of mercapto double bond if 1 has been highlighted as the best high yielding method. We therefore considered the product β-oxodithioacetals 36 may prove to be useful intermediates for the construction of aromatics without the observed limitations as discussed in the preceding section. Thus the β-oxodithioacetal 36a derived from 1a was reacted with allylmagnesium bromide to afford the corresponding carbinol 37a which subsequently was treated with $BF_3.Et_2O$ in refluxing benzene to afford the corresponding biphenyl 40a in 89% yield (Scheme 8). The biphenyl did not carry any undesired substituents and it was found to be identical with that of the reported one [15a] (superimposable IR and NMR). The present method therefore stands superior to the one developed earlier[10] in this laboratory because of the fact that it directly provides the aromatic products without the substituents which are to be removed later. The other β-oxodithioacetals 36b–d similarly yielded, under the described



36 , 40a, $R^1 = C_6H_5$

b, $R^1$ = Me

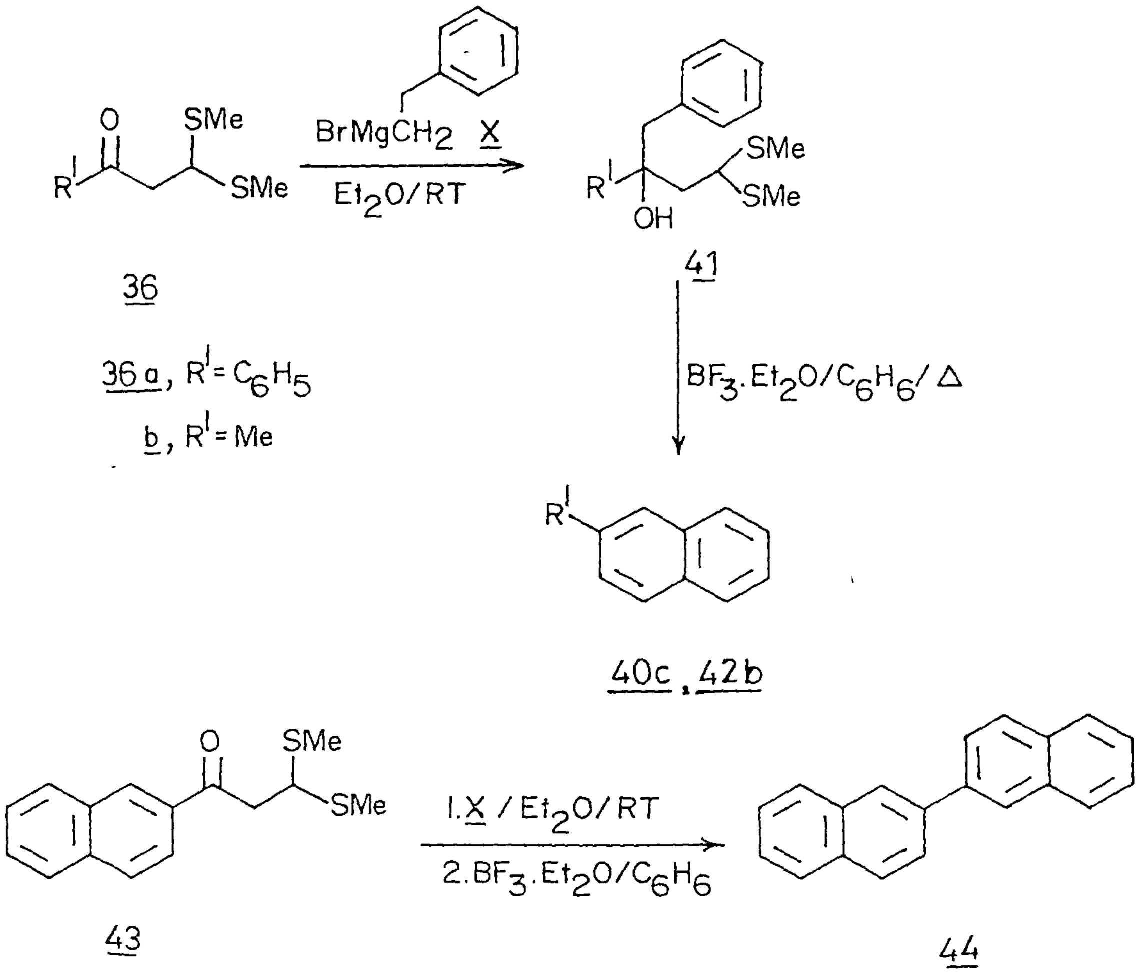
c, $R^1$ = 2-naphthyl

d, $R^1 = 4-MeOC_6H_4$

Scheme-8

reaction conditions, the corresponding aromatic compounds **40b-d** in excellent yields (Scheme 8). All the product thus obtained were characterized on the basis of their spectral and analytical data and on comparison with the known compounds in the literature[15]

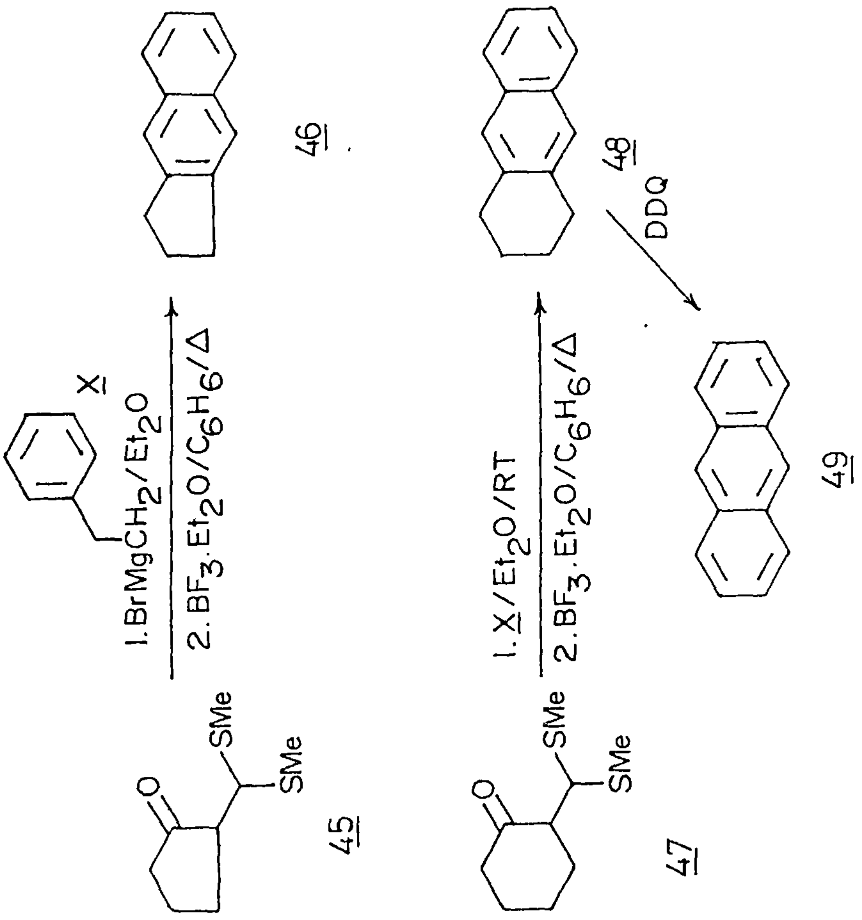
The interesting extension of this reaction has been found when the β-oxodithioacetals were reacted with the benzylmagnesium chloride to obtain the naphthalene products in high yields (Scheme 9). Thus when **36a** was reacted with benzylmagnesium chloride the corresponding carbinol **41a** was obtained in quantitative yield which on $BF_2Et_2O$ catalyzed cyclization afforded the corresponding 2-phenylnaphthalene **40c** in 90% yield. The spectral and analytical properties of **40c** was in accordance with the assigned structure and identical with that of reported in the literature[16]. Apparently, the limitation of 1,4-addition of benzyl Grignard reagent with α-oxoketene dithioacetals is totally eliminated thus making this method superior for the benzoannelation protocols. The β-acyldithioacetal **36b** similarly afforded the β-methylnaphthalene **42b** in 90% yield. The compound was confirmed by comparing the physical and spectral data with the reported one in the literature[17]. The 2,2'-binaphthyl **44** was obtained in 92% yield by treating the corresponding β-oxodithioacetal **43** with benzylmagnesium chloride under the described conditions. The structure of **44** was established by comparing the physical and spectral properties with that reported in the literature[18] (Scheme 9).


SMe
SMe
O
R$^1$
BrMgCH$_2$ X
Et$_2$O/RT
SMe
SMe
R$^1$
OH
36
41
36a, R$^1$ = C$_6$H$_5$
b, R$^1$ = Me
BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
R$^1$
40c, 42b
O
SMe
SMe
1. X / Et$_2$O/RT
2. BF$_3$.Et$_2$O/C$_6$H$_6$
43
44

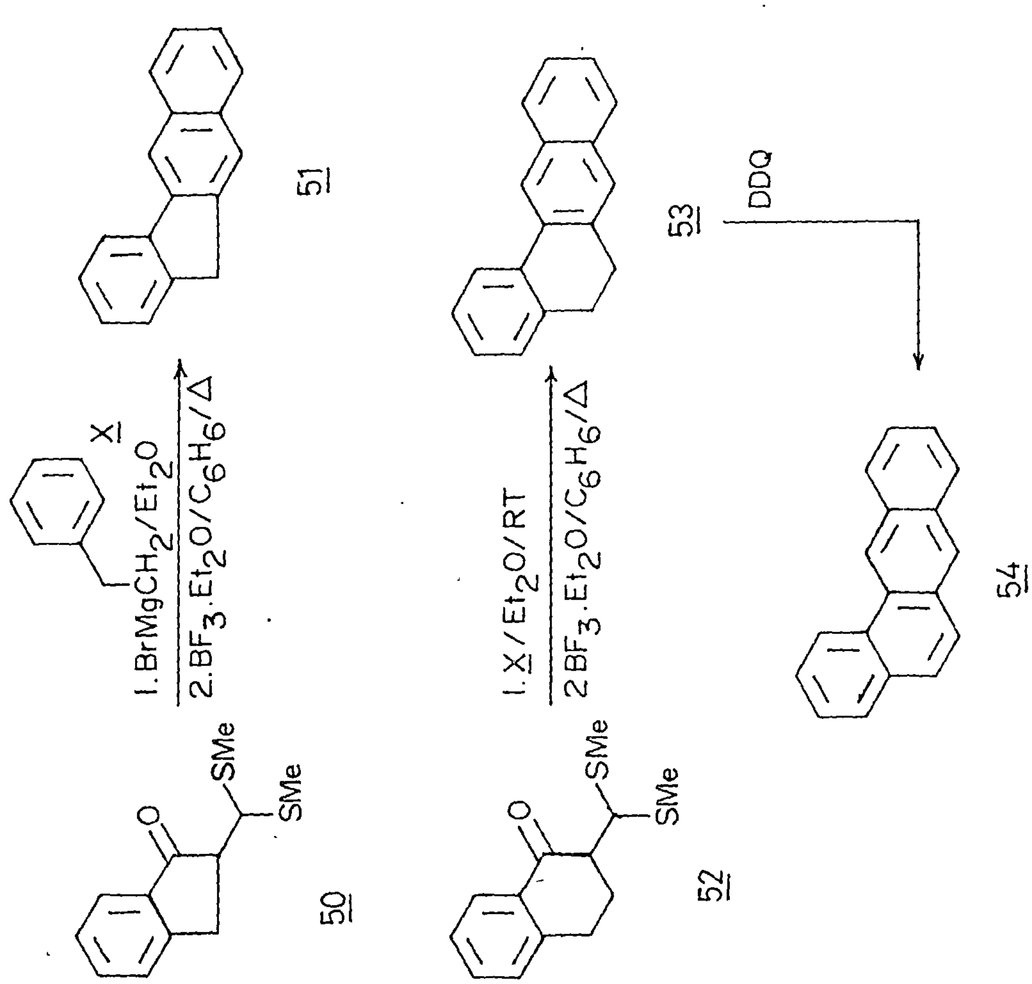
Scheme-9

The cyclic β-oxodithioacetal **45** similarly reacted with benzylmagnesium chloride followed by subsequent Lewis acid cycloaromatization to afford the corresponding linearly annelated benz[f]indan **46** in 95% yield (Scheme 10). Similarly, the 1,2,3,4-tetrahydroanthracene **48** could be obtained in 89% yield from **33** by following similar reaction sequence with benzyl Grignard reagent under the identical conditions (Scheme 10). Both **46** and **48** were characterized on the basis of their spectral and analytical data and found to be identical with the reported data[19,20] (experimental section). When **48** was dehydrogenated in the presence of DDQ the corresponding anthrancene **49** was obtained in 64% yield (Scheme 10).

The method was equally facile with the β-oxodithioacetals derived from indanone **50** and tetralone **52**. Thus when **50** was reacted with benzyl Grignard reagent and on subsequent cyclization afforded the corresponding 11H-Benzo[*b*]-fluorene **51** in 80% yield (Scheme 11). Its analytical and spectral properties were in agreement with those reported in the literature[15e]. Similarly when the β-oxodithioacetal **52** derived from tetralone was subjected to benzyl Grignard reaction followed by cyclization afforded the corresponding 5,6-dihydrobenzanthrancene **53** in 92% yield. The dehydrogenation of **53** with DDQ gave the corresponding 5,6-benzanthracene **54** in good yield (Scheme 11). The structures of these aromatic products were fully characterized[21] with the help of their spectral and analytical data (experimental section).


SMe
SMe
45
X
1. BrMgCH$_2$/Et$_2$O
2. BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
46
SMe
SMe
47
1. X/Et$_2$O/RT
2. BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
48
DDQ
49

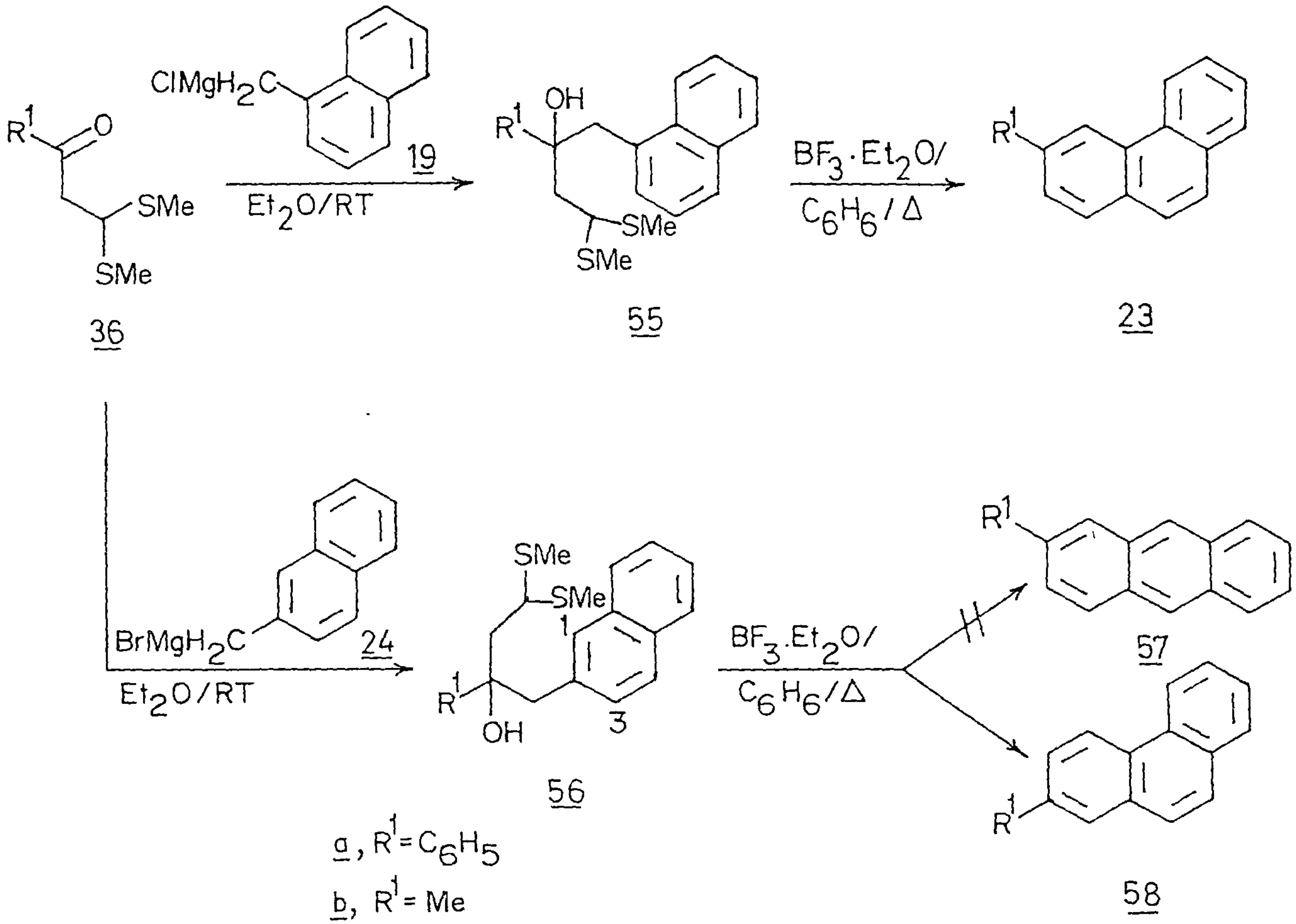
Scheme-10


SMe
SMe
O
50
X
1. BrMgCH$_2$/Et$_2$O
2. BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
51
SMe
SMe
O
52
1. X / Et$_2$O/RT
2 BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
53
DDQ
54

Scheme-11

We have next examined the reactions of α- and β-naphthylmethyl Grignards **19** and **24** with various β-oxodithioacetals so as to synthesize the polynuclear aromatic hydrocarbons through cycloaromatization procedure.

Thus the β-oxodithioacetal **36a** when reacted with 1-(naphthylmethyl)magnesium chloride **19** gave the corresponding carbinol **55a** in quantitative yield which on subsequent $BF_3.Et_2O$ assisted cycloaromatization smoothly afforded the corresponding 3-phenylphenanthrene **23a** in 89% yield (Scheme 12). Its analytical and spectral properties were in agreement with those reported in the literature[22]. Similarly the 3-methylphenanthrene[15f] **23b** was obtained in 82% yield when **19** was reacted with **36b** under the described reaction conditions. The reaction of 2-(naphthylmethyl)magnesium bromide **24** with **36a** yielded the corresponding 2-phenylphenanthrene **58a** in 95% yield. The analytical and spectral properties were in agreement with those reported in the literature[22]. Similarly, the corresponding 2-methylphenanthrene **58b** was obtained in 88% yield when **24** was reacted with **36b**. The structure of **58b** was confirmed by its analytical and spectral data and found to be identical with the reported data in the literature[15] (Scheme 11). It is pertinent to note that the reactions of β-oxodithioacetals **36a,b** with β-naphthylmethyl bromide following cycloaromatization did not give the corresponding linearly annelated aromatics **57a,b** as expected. However the reactions invariably afforded the phenanthrenes **58a,b**. This is due to the participation of the 1,2-double bond of the naphthalene



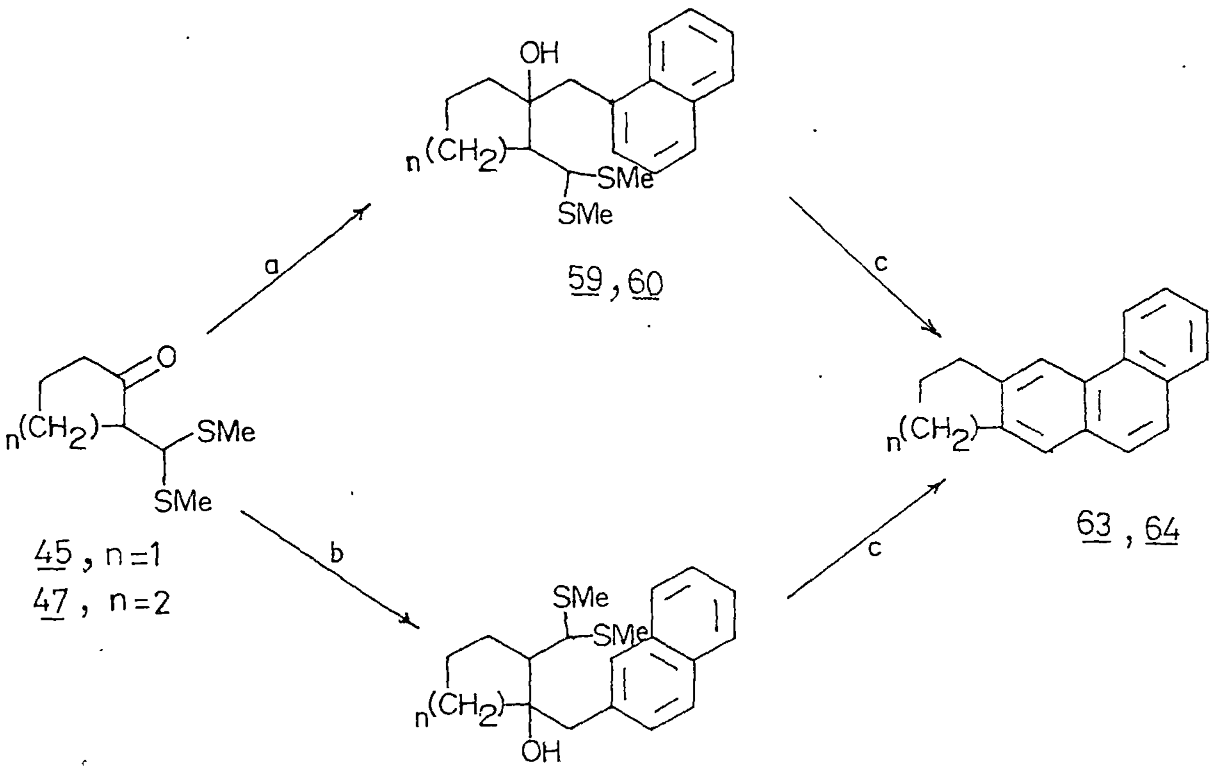
ClMgH₂C
19
Et₂O/RT
BF₃·Et₂O/
C₆H₆/Δ
R¹
O
SMe
SMe
OH
36
55
23
BrMgH₂C
24
Et₂O/RT
1
3
BF₃.Et₂O/
C₆H₆/Δ
56
57
58
a, R¹=C₆H₅
b, R¹= Me

Scheme-12

ring rather than the 2,3-olefin during cycloaromatization. Apparently, the 1,2- bond may acquire more double bond character than the 2,3- bond in the naphthalene ring during the resonance stabilization.

We have next investigated the α- and β-naphthylmethyl Grignard reactions on the cyclic β-oxodithioacetals **45,47**. Thus when **45a** reacted with **19**, the corresponding 3,4-cyclopentanophenanthrene **63** was obtained in 86% yield. Interestingly the same product was also obtained by reacting **24** with **45** under the described conditions in almost identical yields (Scheme 13). Similarly the tetrahydrobenzanthracene **64** was obtained from **47** following both the routes in 68% and 72% yields respectively as shown in scheme 13. Thus it is evident that 2-naphthylmethylmagnesium bromide **24**, which afforded the naphthylmethyl substituted benzanthracene **31** with the corresponding oxoketene dithioacetal (Scheme 6), is now conveniently used to prepare the unsubstituted tetrahydrobenzanthracene **64** in high yield (Scheme 12).

Similarly, 8H-Indeno[2,1-*b*]phenanthrene **65** was obtained by reacting **19** with the β-oxodithioacetal derived from indanone **50** in very high yield under the similar reaction conditions (Scheme 14). Its structure was established from its spectral and analytical data. When **52** was reacted with **19** the corresponding dihydrobenzanthracene **66** was obtained in 85% yield. The structure of **66** was established by its analytical and spectral data. The dehydrogenation of **66** with DDQ afforded the corresponding debenzanthrancene **67** in 78% yield.



59, 60

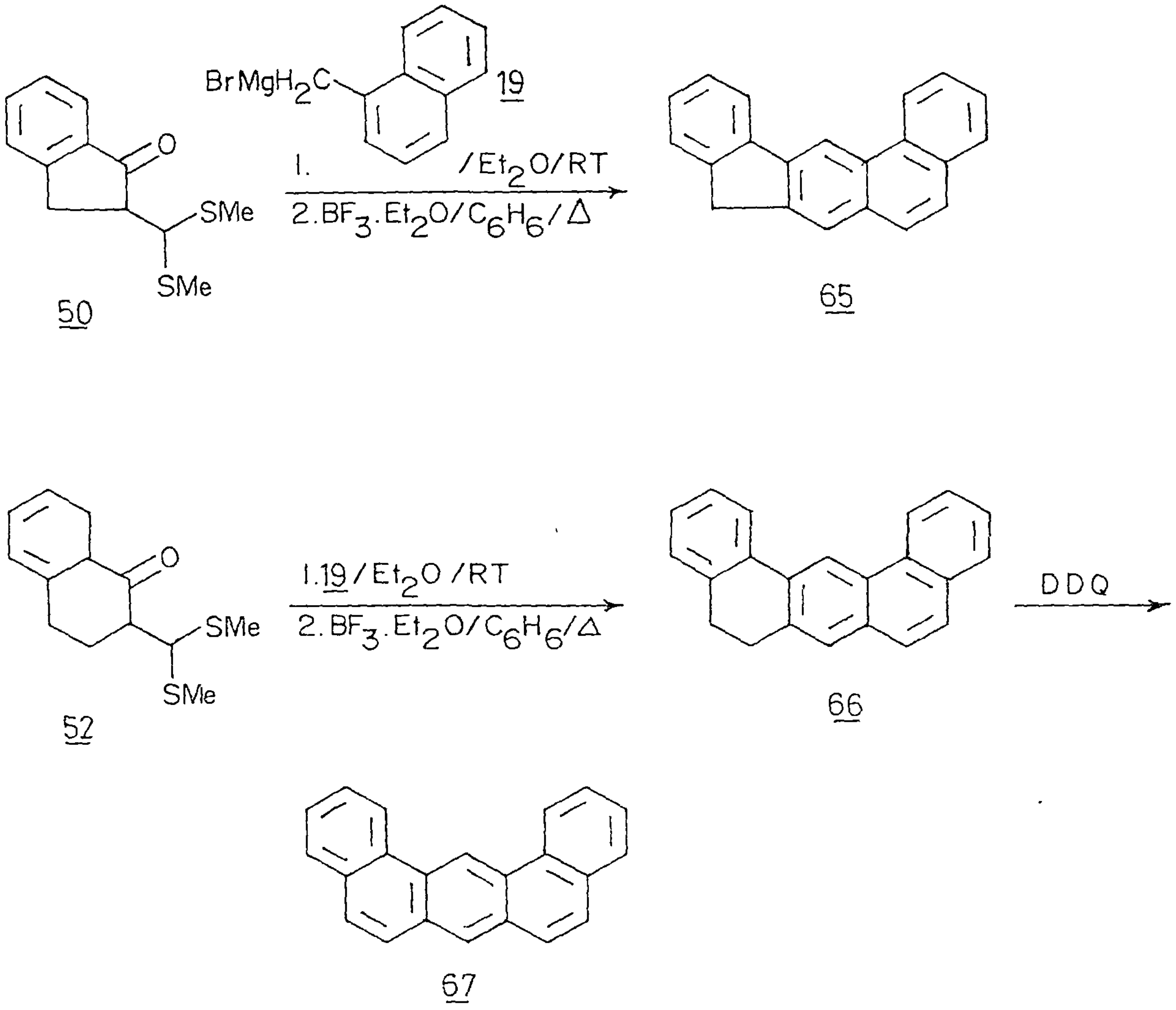
45, n=1
47, n=2

63, 64

61, 62

a, 1(naphthylmethyl)MgCl/Et$_2$O; b, 2-(naphthylmethyl)MgBr/Et$_2$O; c, BF$_3$.Et$_2$O/C$_6$H$_6$/Δ

Scheme-13


BrMgH$_2$C
19
1. /Et$_2$O/RT
2. BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
SMe
SMe
50
65
1. 19/Et$_2$O/RT
2. BF$_3$.Et$_2$O/C$_6$H$_6$/Δ
52
66
DDQ
67

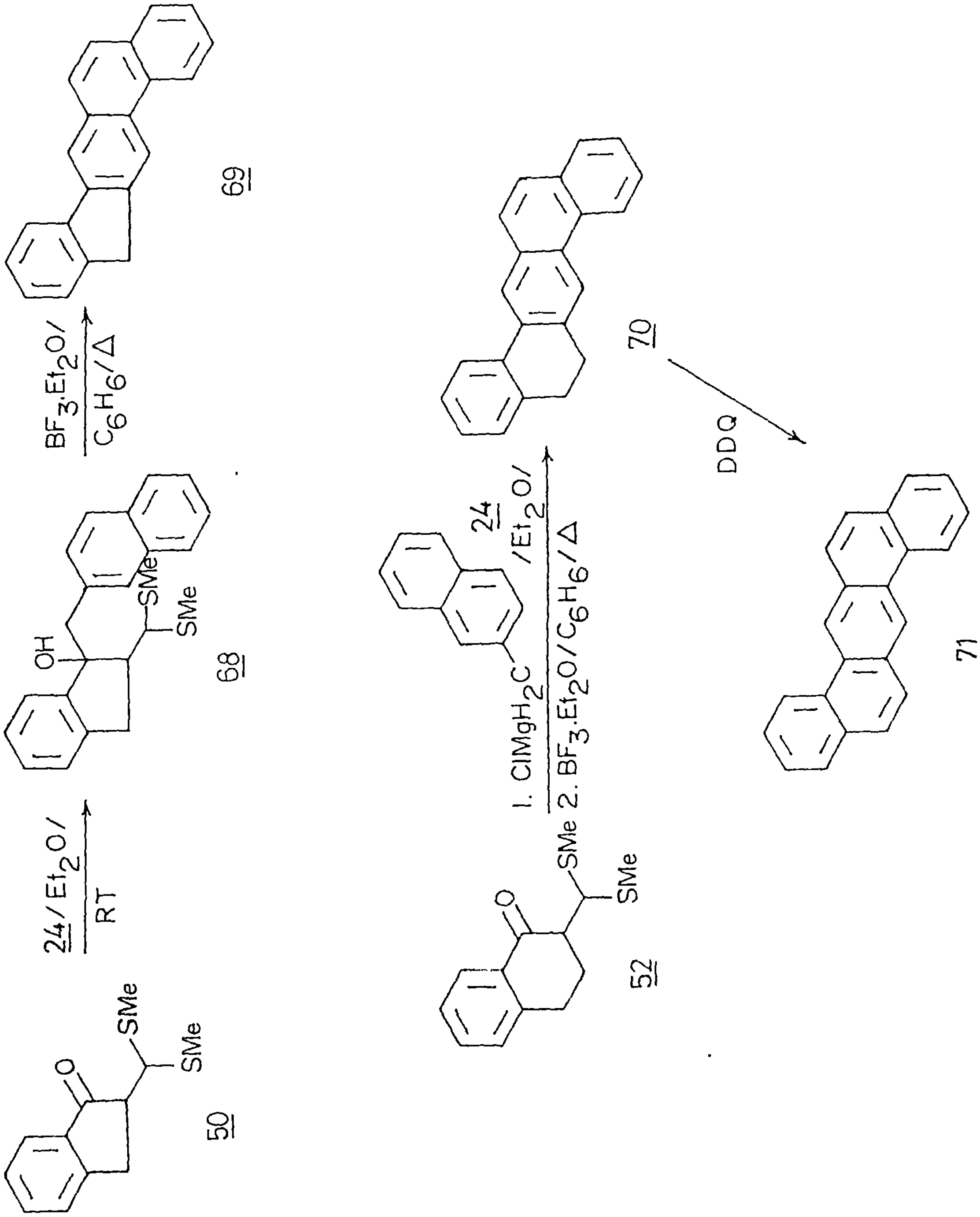
Scheme — 14

It was identical in its spectral and analytical properties with the authentic sample[15g,22] (Scheme 14).
The 2-(naphthylmethyl)magnesium bromide **24** similarly reacted with **50** to afford the corresponding 12H-indeno[1,2-*b*]phenanthrene **69** in 75% yield. The structure of **69** was established on the basis of its spectral and analytical data. Similarly **24** was reacted with **52** to afford the corresponding dihydrodibenzanthracene **70** in 68% yield, which on subsequent dehydrogenation with DDQ gave the dibenzanthracene **71**. The analytical and spectral data of **71** in total agreement with the reported in the literature[15h].

From these examples it is evident that the present method of aromatic annelation using β-oxodithioacetals with various allyl anions including those derived from arylmethyl and naphthylmethylmagnesium halides react regiospecifically by first undergoing addition with carbonyl function followed by $BF_3.Et_2O$ assisted cyclizations in one pot reaction to afford the corresponding benzenoids, naphthalenes, phenanthrenes and benzanthracenes in excellent yields. Therefore the method is established as superior to the one described in our earlier report.

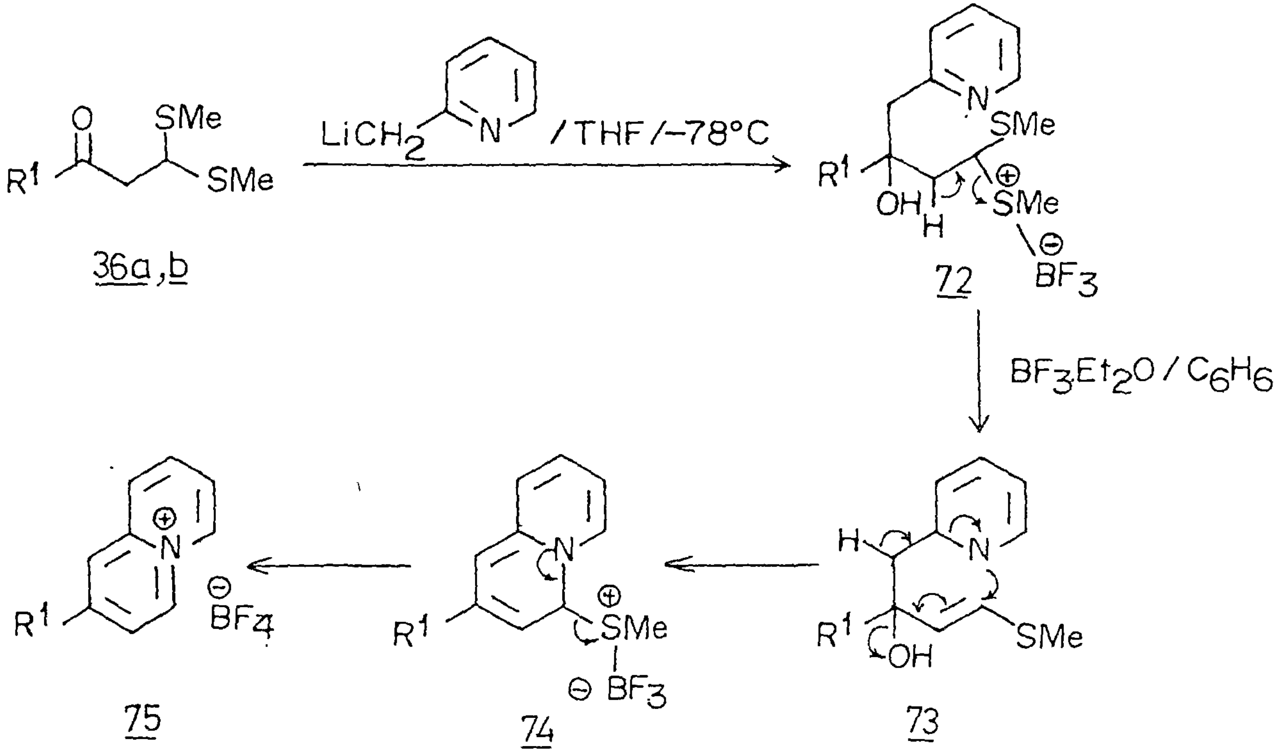
### Cycloaromatization of β-oxodithioacetals with 2-picolyllithium : Synthesis of sulfur free quinolizinium compounds.

As an application of the work described above it was considered of interest to react 2-picolyllithium with β-oxodithioactals so as to prepare sulfur free quinolizinium


50
SMe
SMe
24/Et2O/
RT
68
OH
SMe
SMe
BF3.Et2O/
C6H6/Δ
69
52
SMe
SMe
1. ClMgH2C
24
/Et2O/
2. BF3.Et2O/C6H6/Δ
70
DDQ
71

Scheme–15

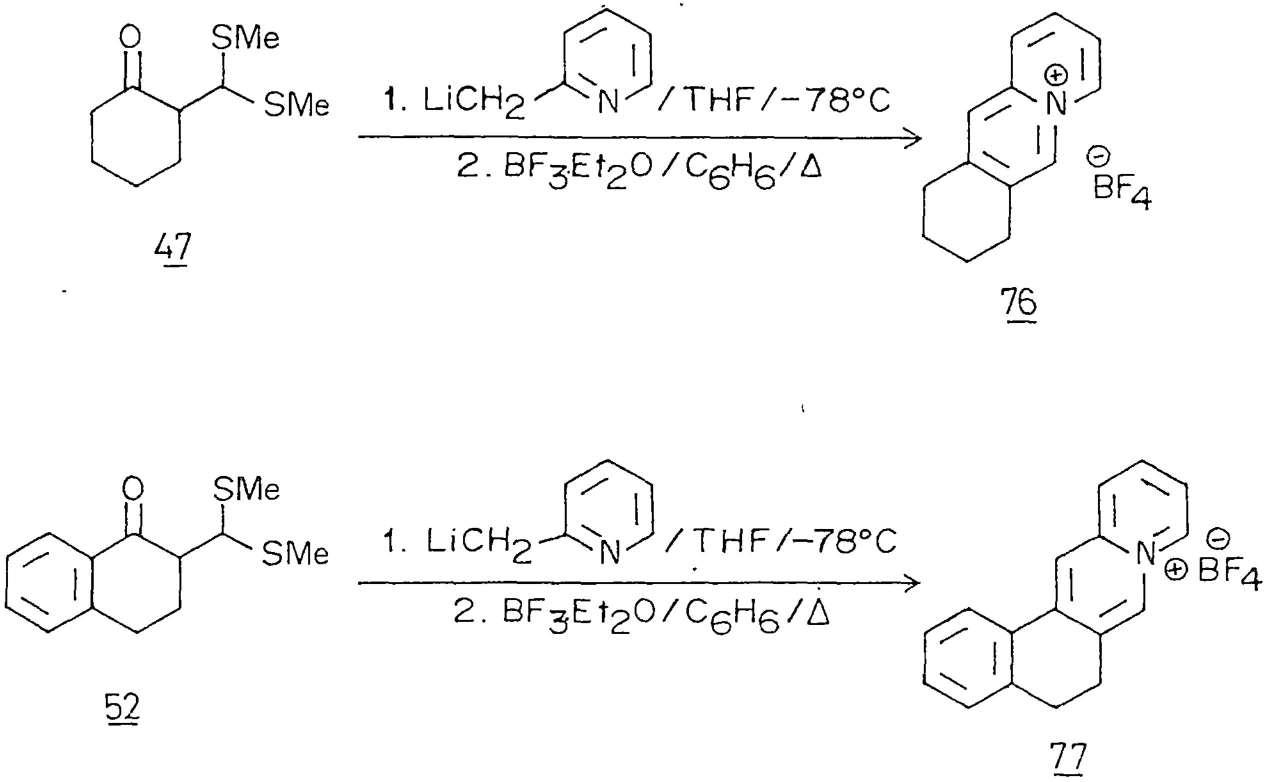
tetrafluoroborates. It is pertinent to note here that the reaction of 2-picolyllithium with oxoketene dithioacetals invariably yielded the methylthiosubstituted quinolizinium salts and desulphurization failed under different conditions[23]. The quinolozinium frame work containing compounds are mainly naturally occuring and known well for their useful biological activities. In order to prepare the sulfur free quinolizinium salts, the β-oxodithioactals could be used as appropriate intermediates. As expected, the reaction of 2-picolylithium with β-oxodithioacetals has provided the sulfur free quanilizinium salts from the initial carbinol formations followed by cycloaromatization with $BF_3.Et_2O$ in refluxing benzene as shown in schemes 16 and 17. Thus, when β-oxodithioacetals **36a** was reacted with 2-picolyllithium at -78°C the carbinol acetal **72a** was obtained in quantitative yield. Subsequent $BF_3.Et_2O$ assisted cyclization yielded the sulfur free 2-phenyl quinolizinium tetraflùoroborate **75a** in 91% yield. Its spectral and analytical data was in full agreement with the assigned structure. Similarly 2-methyl quinolizinium salt **75b** was obtained in 81% yield from the corresponding β-oxodithioacetal **36b** under similar reaction conditions (Scheme 16). When the reaction was extended to the cyclic β-oxodithioacetals **47** and **52** under identical reac tion conditions afforded **76** and **77** in 84% and 88% yields respectively. The spectral and analytical data of these compounds **76** and **77** are described in the experimental section.



a, $R^1 = C_6H_5$

b, $R^1 = Me$

Scheme–16



Scheme−17

## EXPERIMENTAL SECTION

**General:** Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. $^1H$ NMR spectra were measured at 90 MHz on a Varian EM-390 spectrometer in $CDCl_3$ or $CCl_4$ using TMS as internal standard. Mass spectra were obtained on a Jeol JMS-D-300 spectrometer. Elemental analysis were carried out on a Heraeus CHN-O-RAPID instrument.

Grignard grade magnesium turnings (SISCO) were used for all the Grignard reaction, which were carried out under an atmosphere of oxygen free dry nitrogen gas. Benzylchloride and 1-chloromethylnaphthalene were purchased (Aldrich) and used as supplied. 2-Bromomethylnaphthalene was prepared by reported procedure.[24] Borontrifluoride etherate was distilled (125-26°C) before use. Tlc (slica gel Acme's) was used for monitoring the reactions.

2-Picoline and n-butyl bromide were purchased (Aldrich) and distilled prior to use. Lithiun ingot (Aldrich) were cut into smaller pieces and washed with dry ether twice before use. n-Butyllithium was prepared according to the reported procedure.

All the starting α-oxoketene dithioacetals and β-oxodithioacetals were prepared according to the earlier reported procedures and the general procedures described in Chapter II.

## General Procedure for the Reaction of β-Oxodithioacetals with Allyl-, Benzyl-, 1-(Naphthylmethyl)- and 2-(Naphthylmethyl)-magnesium halides

The reaction of oxoketene dithioacetals **1a** with benzylmagnesium chloride is representative. To a ice-cooled solution (0-5°C) of benzylmagnesium chloride [0.03 mol, *prepared from magnesium turnings (1.0g) and benzyl chloride* (3.80g, 0.03 mol)] in dry ether (60 ml), **36a** (3.40g, 0.015 mol) in dry benzene (25 ml) was added dropwise (2-3 min.) under $N_2$ atmosphere. The reaction mixture was further stirred for 45 min. and the temperature was raised to room temperature. It was then decomposed by pouring over satd. aqueous $NH_4Cl$ solution (50 ml), extracted with ether (2x50 ml) and the combined ether extracts were washed with water (50 ml), dried ($Na_2SO_4$) and evaporated to give the crude carbinol **41a** which was used as such for cycloaromatization step. The reaction of oxoketene dithioacetals and β-oxodithioacetals with allyl, 1-(naphthylmethyl)-and 2-(naphthylmethyl)magnesium halides were carried out in the similar manner and all the crude carbinols were subjected to cycloaromatization step without further purification.

## General Procedure for $BF_3.Et_2O$ Cycloaromatization of Carbinols

Cycloaromatization of carbinol **41a** is representative. To a solution of crude allylic carbinol **41a** (0.015 mol), obtained from the reaction of **36a** with benzylmagnesium chloride, in dry benzene (50 ml), borontrifluoride etherate (2 ml) was added and the reaction mixture was refluxed for 45 min. It was then cooled, poured into satd. $NaHCO_3$ solution (50 ml), extracted with chloroform (2x100 ml), washed with water (50 ml), dried ($Na_2SO_4$) and evaporated to give a viscous residue which on column chromatography over silica gel (hexane as eluent) afforded analytically pure **42a**. The analytical and spectral data of cycloaromatized products are given below.

**1,1'-Biphenyl (40a)** : was isolated as colourless cystals (hexane); 89%; m.p. 68-71°C (lit.[15a] m.p. 71°C); IR(KBr) 1609, 1410, 918 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.98-7.33 (m, 4H, ArH); 7.34-7.51 (m, 6H, ArH). (Found : C, 93.74; H, 5.64. Calcd. for $C_{12}H_{10}$: C, 93.89; H, 6.41%); m/z 204($M^+$, 100%).

**Toluene (40b)** : was isolated as colourless oil; 76%; IR (neat) 2956, 1600, 1541, 1430 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.39 (s, 3H, $CH_3$); 7.08-7.31 (m, 5H, ArH). (Found: C, 89.94; H, 6.93. Calcd. for $C_7H_8$: C, 90.18 ; H, 7.01%).

**2-Phenylnaphthalene (40c)** : was isolated as colourless solid (90%); m.p. 100- 101°C (lit.[16],103°C); IR (KBr) 1598, 1490 $cm^{-1}$; $^1H$ NMR ($CCl_4$ 7.12-7.49 (m, 5H, ArH); 7.52-8.03 (m, 7H, ArH). (Found : C, 94.18; H, 5.71; Calcd. for $C_{16}H_{12}$ : C, 94.07; H,5.92%); m/z 204 ($M^+$,100%).

**1-(4-Methoxy)-1'-biphenyl (40d)** : isolated as colourless solid; m.p. 71°C (lit.[15b] m.p. 73°C); 82%; IR (KBr) 2997, 1601, 1580, 1444 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.51 (s, 3H, $OCH_3$); 5.94-6.00 (m, 2H, ArH); 6.11-6.80 (m, 4H, ArH); 7.00-7.28 (m, 3H, ArH). (Found: C, 90.01; H, 7.10; Calcd. for $C_{13}H_{12}$: C, 90.11; H, 6.92%).

**2-Methylnaphthalene (42b):** colourless crystals; 90%; m.p.36-37°C (lit.[17] 37°C);Ir (KBr) 1599, 819, 805, 745 cm$^{-1}$; $^1$H NMR ($CCl_4$) 2.40 (s, 3H, $CH_3$); 7.19-7.83 (m, 7H, ArH). (Found : C, 92.65; H, 6.87. Calcd. for $C_{11}H_{10}$ : C, 92.91; H, 7.09%).

**2,2'-Binaphthyl (44)** : colourless crystals; (92%); m.p.185-186°C (lit.[15a,18] 187°C); IR (KBr) 1616, 1408, 900, 864, 825, 743 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 7.40-7.72 (m, 4H, ArH); 7.80-8.11 (m, 8H, ArH); 8.11-8.51 (m, 2H, ArH). (Found : C, 94.71; H, 5.29. Calcd. for $C_{20}H_{14}$: C, 94.45; H, 5.55%).

**Benz[*f*]indan (46)** : colourless crystals; 95%; m.p. 82-83°C (lit.[19,20] 84-85°C); IR (KBr) 1604, 1629 cm$^{-1}$; $^1$H NMR ($CDCl_3$) 1.98-2.44 (m, 2H, $CH_2$); 2.91-3.31 (m, 4H, $CH_2$); 7.09- 7.56 (m, 4H, ArH); 7.71-7.85 (m, 2H, ArH). (Found : C, 92.72; H, 7.12. Calcd. for $C_{13}H_{12}$ : C, 92.80; H, 7.19%); m/z 168 ($M^+$, 100%).

**1,2,3,4-Tetrahydroanthracene (48)** : colourless crystals; 89%; m.p. 92-93°C (lit.[19,20] 92-94°C); IR (KBr) 1613, 1595 cm$^{-1}$; $^1$H NMR 1.69-2.01 (m, 4H, $CH_2$); 2.94 (brs, 4H, $CH_2$); 7.38-7.50 (m, 2H, ArH); 7.60 (brs, 2H, ArH); 7.69-7.88 (m, 2H, ArH). (Found : C, 92.12; H, 7.52. Calcd. for $C_{14}H_{14}$: C, 92.25; H, 7.74%); m/z 182 ($M^+$, 100%).

**Anthracene (49)** : colourless crystals; 64%; m.p. 215-216°C (lit.[15d] 218°C); IR (KBr) 1619, 1560, 1449 cm$^{-1}$; 7.31-7.69 (m, 4H, ArH); 7.81-8.18 (m, 4H, ArH); 8.41 (s, 2H, ArH).

(Found : C, 94.45; H, 5.78. Calcd. for $C_{14}H_{10}$ : C, 94.34; H, 5.61%).

**11*H*-Benzo[*b*]fluorene (51)** : colourless crystals; 80%; m.p. 206-207°C (lit.[15e] 209°C); IR (KBr) 1619, 1568, 883,726 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.63 (s, 2H, $CH_2$); 7.44-7.78 (m, 5H, ArH); 7.90-8.19 (m, 3H, ArH); 8.31-8.49 (m, 2H, ArH). (Found : C, 94.68; H, 5.81 Calcd. for $C_{17}H_{12}$: C, 94.41; H, 5.59%).

**5,6-Dihydrobenz[*a*]anthracene (53)** : colourless crystals; 92%; m.p.92-93°C; IR (KBr) 1510, 890, 808, 768, 740 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.91 (brs, 4H, $CH_2$); 7.19-7.50 (m, 5H, ArH); 7.63 (s, 1H, H-7); 7.58-8.11 (m, 3H, ArH); 8.19 (s, 1H, H-12). (Found : C, 94.11; H, 5.89. Calcd. for $C_{18}H_{14}$: c, 93.87; H, 6.13%); m/z 230 ($M^+$, 50%).

**1,2-Benzanthracene (54)** : colourless crystals (88%); m.p. 158-159°C; (lit.[21] 161-162°C); IR (KBr) 1619, 1581 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.19-8.22 (m, 10H, ArH); 8.61-8.91 (m, 2H, ArH). (Found : C, 94.88; H,5.52. Calcd. for $C_{18}H_{12}$ : C, 94.70; H, 5.30%).

**3-Phenylphenanthrene (23a)** : colourless crystals; 89%; m.p.71-72°C (lit[22] 73°C); IR (KBr) 1613, 816, 757, 743 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.19-8.95 (m, 11H, ArH); 8.12 (d, J = 2.5Hz, 1H, H-4); 8.59-8.76 (m, 2H, ArH); (Found : C, 94.20; H, 5.76. Calcd. for $C_{20}H_{14}$ :C, 94.45; H, 5.55%).

**3-Methylphenanthrene (23b)** : colourless crystals; 82%; m.p.62-63°C (lit.[15f] 64°C); IR (KBr) 1599,819, 805,745 $cm^{-1}$; $^1H$ NMR 2.78 (s, 3H, $SCH_3$); 7.56-7.81 (m, 4H, ArH); 7.91-8.11

(m, 3H, ArH); 8.66-8.90 (m, 2H, ArH). (Found : C, 93.84; H, 6.50. Calcd. for $C_{20}H_{14}$ : C, 94.45; H, 5.54%).

**2-Phenylphenanthrene (58a)** : was obtained as colourless crystals; 95%; m.p.196-197°C (lit.[22], 198°C); IR (KBr) 1461, 891, 815, 757, 742, 712 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.18-8.97 (m, 11H, ArH); 8.14 (d, J = 2.5Hz, 1H, H-1); 8.60-8.70 (m, 2H, ArH); (Found : C, 94.36; H, 5.28. Calcd. for $C_{20}H_{14}$: C, 94.45; H, 5.55%).

**2-Methylphenanthrene (58b)** : colourless crystals; 88%; m.p.56-57°C (lit.[22] 57-58°C); IR (KBr) 1600, 820, 804, 745 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.68 (s, 3H, $CH_3$); 7.40-8.11 (m, 7H, ArH); 8.02-8.75 (m, 2H, ArH). (Found : C, 93.81; H, 6.48. Calcd. for $C_{15}H_{12}$ : C, 93.70, H, 6.29%).

**9,10-Dihydro-*8H*-cyclopenta[*b*]phenanthrene (63)** : colourless crystals; 86%; m.p.133-134°C; IR (KBr) 1593, 811, 772, 747 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.25 (quint, J = 8Hz, 2H, $CH_2$); 3.09-3.40 (two overlapping t, 4H, $CH_2$); 7.45-7.98 (m, 6H, ArH); 8.51-8.75 (m, 2H, ArH). (Found : C, 93.79; H, 6.68. Calcd. for $C_{17}H_{14}$ : C, 93.54; H, 6.46%); m/z 218 ($M^+$, 100%).

**8,9,10,11-Tetrahydrobenz[*a*]anthracene (64)** : colourless crystals; 72%; m.p.121-122°C; IR (KBr) 1600, 887, 747 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.74-2.19 (m, 4H, $CH_2$); 2.92 (brt, 2H, $CH_2$); 3.19 (brt, 2H, $CH_2$); 7.61-7.92 (m, 6H, ArH); 8.26-8.72 (m, 2H, ArH). (Found: C, 93.27; H, 7.20. Calcd. for $C_{18}H_{16}$ : C, 93.06; H, 6.94%).

**8H-Indeno[2,1-*b*]phenanthrene (65)** : colourless crystals; 82%;

m.p. 101-102°C; IR (KBr) 1590, 809, 801, 734 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 4.02 (s, 2H, $CH_2$); 7.21-8.05 (m, 10H, ArH); 8.75 (brd, J =8Hz, 1H, ArH); 9.01 (s, 1H, H-13). (Found : C, 94.83; H, 5.54. Calcd. for $C_{21}H_{14}$ :C, 94.70; H, 5.30%).

**5,6-Dihydrodibenz[*a,j*]anthracene (66)** : colourless crystals; 85% ; m.p.134-135°C; IR (KBr) 1597, 882, 764, 740 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.00 (brs, 4H, $CH_2$); 7.18-8.00 (m, 9H, ArH); 8.09 (brd, J = 8Hz, 1H, ArH); 8.64 (brd, J = 8Hz, 1H, ArH); 9.11 (s, 1H, H-14); (Found : C, 94.47; H, 5.91. Calcd. for $C_{22}H_{16}$ : C, 94.25; H, 5.75%).

**Dibenz[*a,j*]anthracene (67)** : colourless cyrstals (78%); m.p. 195-196°C; (lit[15g] 198°C); IR (KBr) 1613, 1581 $cm^{-1}$; $^1$ H NMR (DMSO-$d_6$) 7.64-8.22 (m, 10H, ArH); 9.15-9.20 (m, 2H, ArH); 9.48 (s, 2H, ArH). (Found: C, 94.87; H, 5.02; $C_{22}H_{14}$ requires C, 94.93; H, 5.07%).

***12H*-Indeno[1,2-*b*]phenanthrene (69)** : colourless crystals; 75%; m.p. 132-133°C; IR (KBr) 1612,874,811;743 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.82 (s, 2H, $CH_2$); 7.10 (d, J= 8Hz, 2H, ArH); 7.50-8.22 (m, 9H, ArH); 8.90 (brs,1H,ArH). (Found: C, 94.48; H, 5.07. Calcd. for $C_{22}H_{14}$: C,94.70; H, 5.30%).

**5,6-Dihydrobenz[*a,h*]anthracene (70)** : colourless crystals; 68%; m.p. 189-190°C; IR(KBr) 1603, 1433, 887, 775, 761, 732 $cm^{-1}$; $^1H$ NMR 2.72-3.31 (m, 4H, $CH_2$); 7.23-8.12 (m, 9H, ArH); 8.28 (m, 1H, ArH); 8.63 (brs, 1H, ArH); 8.76 (brd, 1H, ArH). (Found: C, 94.48; H, 5.91. Calcd. for $C_{22}H_{16}$: C, 94.25; H, 5.75%) ; m/z 280 ($M^+$, 100%).

Dibenz[*a,h*]anthracene (71) : colourless crystals; 78% m.p. 264-265°C (lit.[15h,22], 269°C); IR (KBr) 1610, 1503 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.31-8.00 (m, 10H, ArH); 8.75-8.93 (m, 2H, ArH); 9.10 (s, 2H, ArH). Found : C, 95.17; H, 5.23. Calcd. for $C_{22}H_{14}$: C, 94.93; H, 5.07%).

**General Procedure for the reaction of 2-Picolyllithium with β- oxodithioacetals:**

A solution of β-oxodithioacetal (10 mmol) in dry THF (25 ml) was added to a solution of 2-picolylithium [15 mmol, prepared at -20°C, 2-picoline (1.39 gm, 15 mmol) and n-Butyllithium (15 mmol)] in 25 ml of THF at -78°C under $N_2$ atmosphere. The reaction mixture was further stirred at the same temperature for 45 min and allowed to attain the ambident temperature in another hour. When the reaction was complete, it was worked up by pouring into aqueous $NH_4Cl$ solution (50 ml), extracted with ether (2x50ml) and the combined extract was washed with water (2x50 ml), dried ($Na_2SO_4$) and evaporated tos give the crude carbinols in quantitative yields. These carbinols were found to be very unstable and thus were used as such in the cycloaromatization step.

**General Procedure for the cycloaromatization of carbinol-dithioacetals : Synthesis of substituted and fused quinolizinium tetrafluroborates 75a-b,76-77.**

To a solution of crude carbinol dithioacetal (ca. 10 mmol) obtained from the above reation in dry benzene (50 ml), $BF_3.Et_2O$ (3 ml) was added and the reaction mixture was refluxed with stirring for 45 min. It was then cooled and the benzene layer was removed by decantation. The remaining residue was dissolved in a minimum amount of acetone, neutralized with saturated $NaHCO_3$ solution and the solid separated was collected by filtration, washed with water (3x50 ml) and diethyl ether (2x10 ml). Analytically pure products were obtained by recrystallization from glacial acetic acid.

**2-Phenylquinolizinium tetrafluoroborate (75a)** : Isolated as pale yellow solid (AcOH); 91%; m.p. 161°C; IR(KBr) 1611, 1598,1018-1120 (br) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.62-7.90 (m, 3H, ArH); 8.11-8.30 (m, 3H, ArH); 8.35-8.55 (m, 2H, H-8 and H-3); 8.60 (d, J = 7Hz, 1H, H-9); 8.86 (s, 1H, H-1); 9.38 (d, J=7Hz, 1 H, H-6). (Found : C, 61.48; H, 4.12; N, 4.77; Calcd. for $C_{15}H_{12}NBF_4$: C, 61.16; H, 3.98; N, 4.48%) .

**2-Methylquinolizinium tetrafluoroborate (75b)**: isolated as pale yellow solid (AcOH); 81%; mp. 139-140°C; IR (KBr) 1608, 1564, 1018-1120 (br) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.01 (s, 3H, $CH_3$); 8.38-8.61 (m, 4H, ArH); 9.11 (d, J = 7Hz, 1H); 9.43 (d, J = 7Hz, 1H, H-6). (Found : C, 52.47; H, 4.63; N, 6.36; Calcd. for $C_{10}H_{10}NBF_4$ :C, 52.17; H, 4.32; N, 6.08%).

**7,8,9,10-Tetrahydrobenz[b]quinolizinium tetrafluroborate (76)** was isolated as light yellow solid (EtOAc-hexane); 84%; mp. 118°C; IR (KBr) 1610 , 1554, 1022-1150 (br) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1.92 (m, 4H, $CH_2$-); 3.10 (t, J = 7Hz, 2H, -$CH_2$-) ; 3.21 (t, J = 7Hz, 2H, -$CH_2$-); 7.98-8.32 (m, 4H, ArH); 9.48 (d, J = 7Hz, 1H, H-4); 10.01 (d, J = 7Hz, 1H, H-6). (Found:

C, 54.18; H, 4.09; N, 3.11; Calcd. for $C_{13}H_{14}NBF_4$; C, 53.99; H, 3.94; N, 2.99%).

**5,6-Dihydro-naphtho[1,2-b]quinolizinium tetrafluoroborate (77):** was isolated as yellow solid (AcOH); 88% mp. 171°C; IR (KBr); 1624, 1601, 1572, 990-1200 (br) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.06 (t, J = 8Hz, 2H,$CH_2$-); 3.53 (t, J = 2H, -$CH_2$-); 7.48-7.61 (m, 3H, ArH); 9.20 (s, 1H, ArH); 8.31-8.58 (m, 2H, ArH); 9.20 (s, 1H, ArH); 10.05 (d, J = 7Hz, 1H, ArH). (Found : C, 63.39; H, 4.76; N, 4.10; Calcd for $C_{17}H_{16}NBF_4$ : C, 63.75; H, 5.00; N, 4.38%)

## REFERENCES

1. (a) Review: Bambfield, P.; Gordon, P.F. *Chem. Soc. Rev.* 1984 *13*, 441-488; (b) Chemistry of carbon compounds, Part IIIb , Elsevier, Ansterdam, 1956, 1273.
2. (a) Smith, A.B.; Kilenyi, S.N. *Tetrahedron lett.* 1985, *26*, 4419; (b) Sivavec, T.M.; Katz. T.J. *Tetrahedron Lett.* 1985, *26*, 2159; (c) Dieter, R.K.; Lin, Y.J. *Tetrahedron Lett.* 1985, *26*, 39; (d) Kelly, T.R.; Lin,H. *J.Am.Chem.Soc.* 1985 , *107*, 4998; (e) Wulff, W.D.; Kaesler, R.W.; Peterson G.A.; Tang, C. *J.Chem.Soc.* 1985, *107*, 1060; (f) Freskas, J.N.; Swenton, J.S. *J. Chem.Soc.Chem.Comm.* 1985, 658; (g) Sivavec, T.M.; Katz, T.J. *J.Am.Chem.Soc.* 1985, *107*, 737 ; (h) Boger, D.L.; Mullican, M.D. *J.Org.Chem.* 1984, *49*, 4033; (i) Gee , S.K.; Danheiser, R.L. *J.Org.Chem.*, 1984 *49*, 1672.
3. Seebach, D. *Angew.Chem.Int.Ed.Engl.* 1988, *27*,1624.

4. (a) Tius, M. A. *Tetrahedron Lett.* 1981, *22*, 3335; (b) Tius, M.A.; Ali, S. *J.Org.Chem.*, 1982, *47*, 3163; (c) Tius, M.A.; Savariar, S. *Synthesis*, 1983, 467; (d) Tius, M.A.; Thurkauf, A.; Truesdell, J.W. *Tetrahedron Lett* 1982, *23*, 2819; (e) Tius, M.A.; Thurkauf, A. *J.Org.Chem.* 1983, *48*, 3839.
5. (a) Chen, T.S.; Canonne, P.; Leitch, L.C. *Synthesis*, 1973, 621; (b) Canonne, P.; Leitch, L.C.; *Can.J.Chem.* 1967 , *45*, 1761; (c) Woinska-Mocydlarz, J.; Canonne,P.; Leitch, L.C. *Synthesis* 1974, 566.
6. (a) Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron*, 1990, *46*, 5423; (b) Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron lett.* 1988, *29*, 6633-6636; (c) Gupta, A.K.; Ila, H. Junjappa, H. *Tetrahedron* 1990, *46*, 2561-2572; (d) *ibid* 1990, *46* 4 295-4302.

7. Singh, G.; Ila, H.; Junjappa, H.*Tetrahedron Lett. 1984, 25* 5095-5098.
8. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1987, *28*, 1459.
9. Balu, M.P.; Singh, G.;Ila, H.; Junjappa, H. *Tetrahedon Lett. 1986, 27*, 117-120.
10. Rao, Ch.S.; Balu, M.P.; Ila, H.; Junjappa, H. *Tetrahedron,* 199 1, *47*, 3499.
11. (a) Klopman, G.*J. am. Chem.Soc. 1968, 90*, 223-234; (b) Lefour, J-M.; Loupy, A.*Tetrahedron 1978, 34*, 2597-2605; (c) Sauvetre, R.; Rouxschmitt M-C.; Seyden-Penne, J. *Tetrahedron 1978, 34*, 2135-2140 and references therein.

12. (a) Dewar, M.J.s.in "The Molecular Orbital Theory of Organic Chemistry"; McGraw Hill Book Co., New York; 1969; p.305-306 and references therein (b) Dewar, M.J.S; Sampson, R.J. *J.Chem.Soc.* ***1956,*** 2789-2797; ***1957,*** 2946-2952; 2952-2954.

13. Kronzer, F.J.; Sandel V.R.*J. Am. Chem. Soc. 94*, 1974, 5730-5759.

14. Rao, C.S; Chakrasali, R.T.; Ila, H.; Junjappa, H. *Tetrahedron* ***1990,*** *46*, 2195-2204.

15. "CRC Hand Book ofData on Organic Compounds"; Weast, R.c.; Astle, M.J., Ed., CRC Press Inc., ***1985,*** (a) Vol.1, p.289; (b) Vol.1, 299; (c) Vol.1, p.872; (d) Vol.1, p.94; (e) Vol.1, p.208; (f) Vol. 2, p. 43; (g) Vol.1, p.152; (h) Vol. 1, p.545.

16. Hey, D.H.; Lawton, S.E. *J.chem.Soc.* ***1940,*** 374-383.

17. Durand, P.; Parello, J.; Buu-Hoi, N.P. *Bull. Soc. Chem. France* ***1963.*** 2438-2441.

18. McKillop, a.;Elsom, L.F.; Taylor, E.C.*Tetrahedron* ***1970,*** *26* 4041-4050.

19. Tius, M.A.; Gomez-Galeno, J. *Tetrahedron Lett.* ***1986,*** *27,* 2571-2574.

20. Carpino, L.A.; Lin, Y-Z. *J.Org. Chem.* ***1990,*** *55*, 247-250.

21. Martin, R.H., *Tetrahedron* ***1964*** *20*, 897-902; 1073-1090.

22. Dickerman, S.C; Zimmerman, I. *J.Org. Chem.* ***1974,*** *39,* 3429-3430. 23. Balu, M.P.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*, **1987**, *28*, 3023-3026.

24. Chapman, N.B.; Williams, J.F.A. *J.Chem.Soc.* 1952, 5044.

# CHAPTER IV

## A NEW GENERAL ROUTE TO 1,2-DIARYLETHYLENES, 1,4-DIARYLBUTADIENES AND 1,6-DIARYLHEXATRIENES THROUGH CYCLOAROMATIZATION OF β-OXODITHIOACETALS*.

### INTRODUCTION

Synthetic methods for the preparation of symmetrical as well as unsymmetrical stilbenes have been generally developed by more than one approach involving dimerization, oxidation-reduction process, elimination from diaryl compounds, coupling of aromatic compounds with styrenes and other allenes, condensation of nucleophiles with electrophilic arylmethyl compounds and Wittig reaction starting with benzyl halides.[1-7] Most of these methods involve both the aryl

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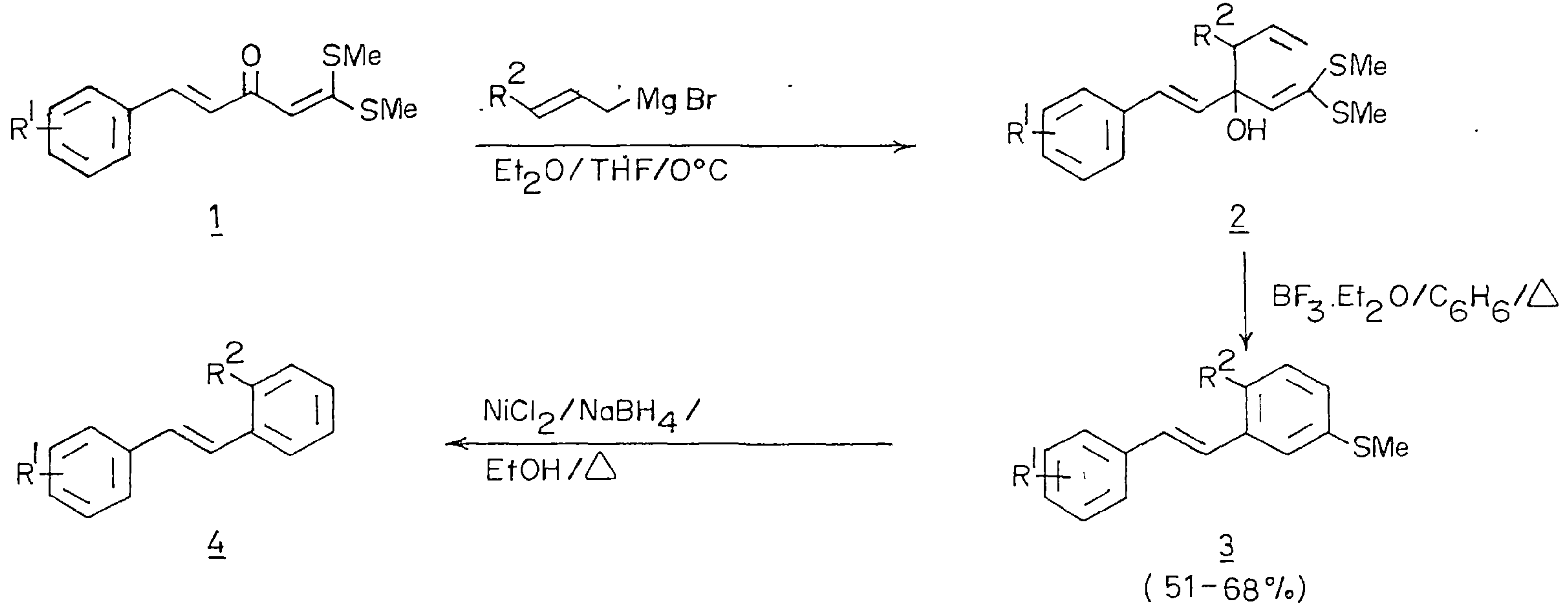
* Rao, Ch.S.; Singh, O.M.; Ila, H.; Junjappa, H *Synthesis*, 1992, 1075.

fragments being preconstructed[1] and some of the methods may not suit for the synthesis of unsymmetrical stilbenes. For the synthesis of 1,4-diaryl dienes,[8] the synthetic approaches are still rare and again all the available methods utilize the starting materials possessing preconstructed aryl fragments. Similar is the situation for the synthesis of 1,6-diarylhexatrienes.[9] Such compounds generally have been prepared by applying Wittig or Wittig-Horner type of reactions. However, the synthesis of stilbenes involving direct construction of one or both aromatic rings from acyclic precursors is not known in the literature.[10]

Junjappa and his coworkers[11] have recently reported a new general method for the synthesis of stilbenes involving construction of one of the aromatic rings by reacting the cinnamoylketene dithioacetals 1 with allylmagnesium bromide or substituted allylmagnesium halides followed by cationic cyclization of resulting carbinolacetals 2 with $BF_3.Et_2O$ complex. Thus when 1,1-bis(methylthio)- 5-phenylpenta-1,4-diene-3-one 1a was reacted with allylmagnesium bromide, the corresponding carbinolacetal 2a was obtained in quantitative yield. Subsequently, 2a was directly treated with $BF_3.Et_2O$ complex in refluxing benzene to afford the desired 3-methylthio stilbene 3a in 67% yield. It was further converted to stilbene 4a on desulphurization using sodium borohydride and nickel(II) chloride.[12] It was the first method for the synthesis of stilbenes through cycloaromatization of acyclic precursors derived from easily accessible active methylene



<u>1</u>,<u>4</u> $R^1$ = H, 4-Me, 4-Cl, m-MeO, O-Cl, 2,6-$Cl_2$, 3,4-$Cl_2$; $R^2$ = H
$R^1$ = H, 4-Me, 4-Cl; $R^2$ = Me
$R^1$ = H, 4-Me, 4-Cl; $R^2$ = H,Me

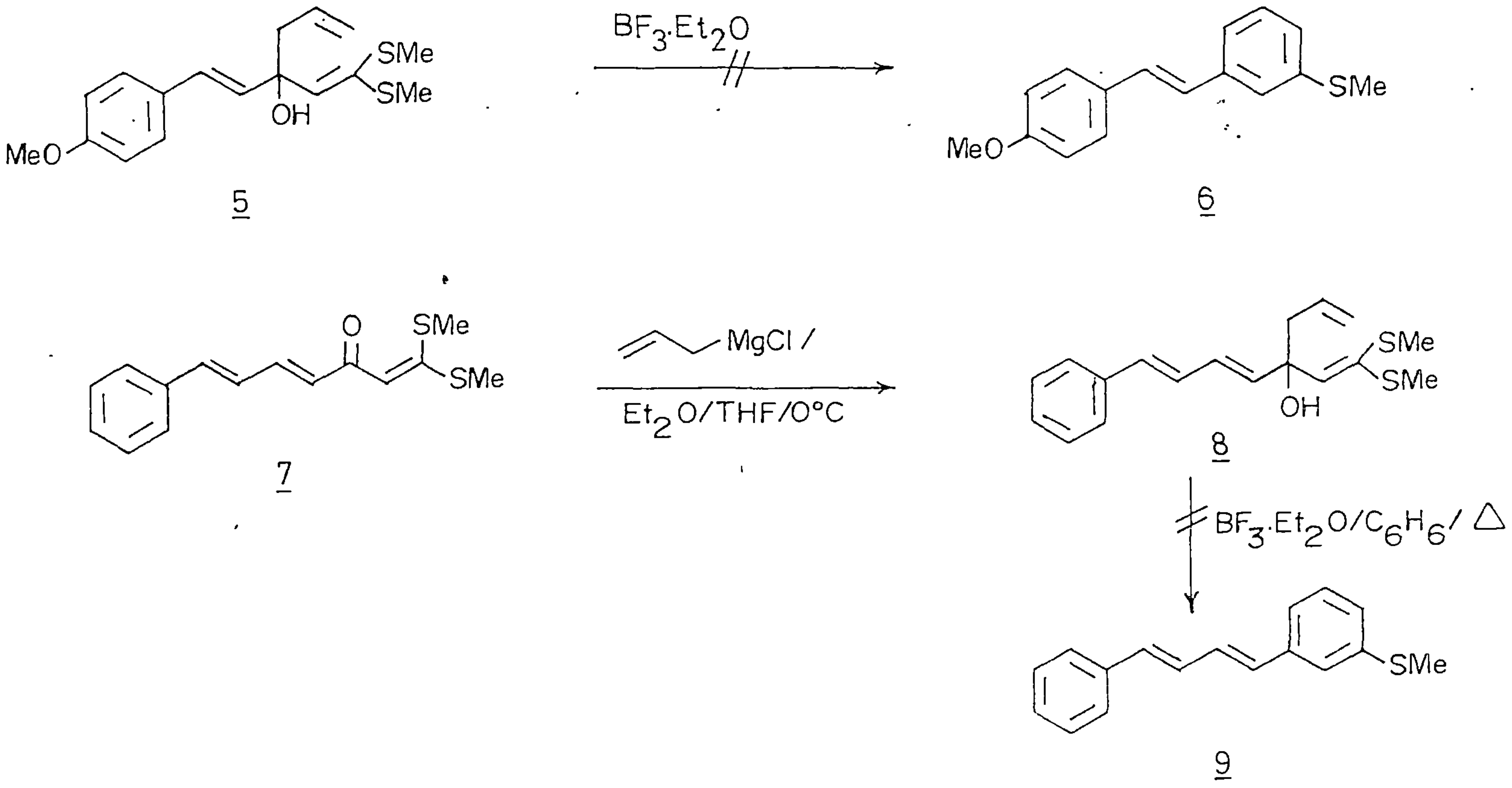
Scheme - I

ketones. A number of symmetrical as well as unsymmetrical stilbenes were prepared by this method in good to high yields. The stilbenes thus obtained were shown to possess *trans* configuration (Scheme 1).

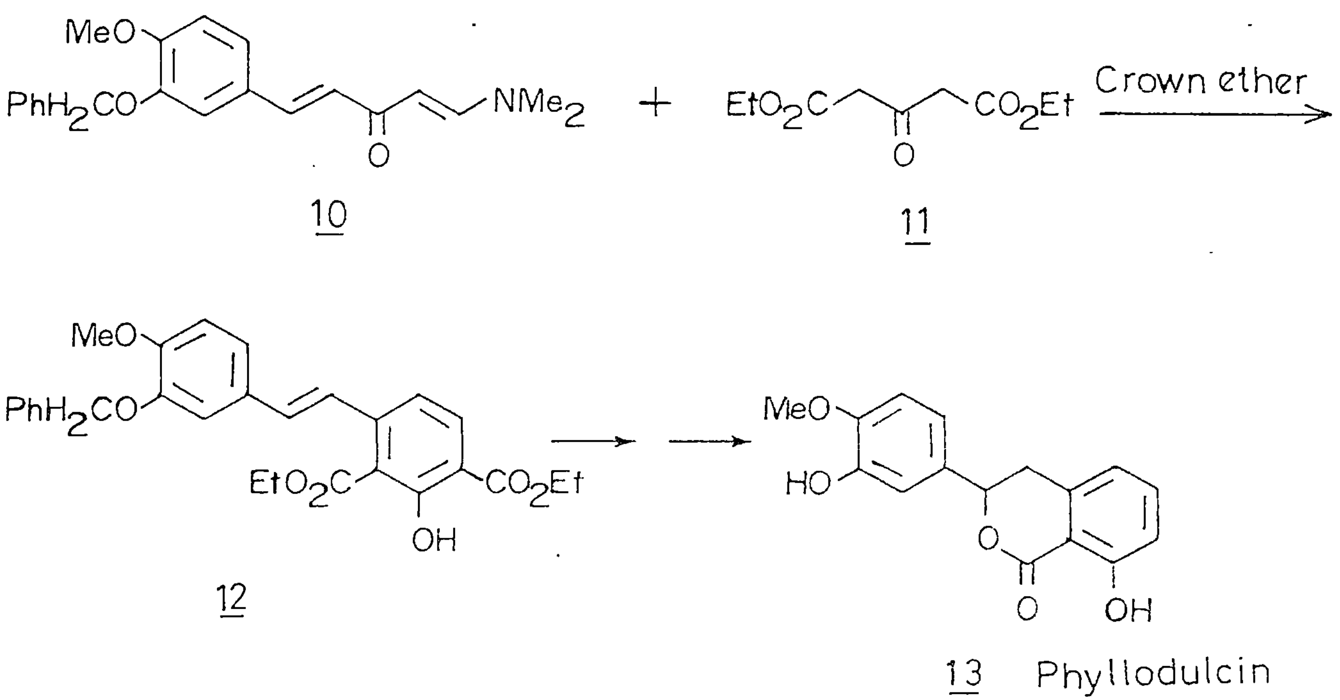
The present method was however not successful for the synthesis of 4-methoxystilbene. Thus, when 4-methoxycinnamoylketene dithioacetal was reacted with allylmagnesium bromide, the corresponding hydroxy dithioacetal 5, although obtained in high yield failed to undergo cycloaromatization with $BF_3.Et_2O$ under varying conditions. The reaction mixture ended up in an intractable tar and therefore the corresponding stilbene 6 could not be prepared by this procedure[11]. Similarly dieneylketene dithioacetal 7 reacted smoothly with allylmagnesium bromide, however the resulting carbinolacetal 8 with $BF_3.Et_2O$ failed to undergo cycloaromatization to afford the desired 1,4-diphenyl butadiene 9 under varying reaction condition (Scheme 2). Thus this method was only applicable to a limited extent for the synthesis of stilbenes though its advantages for the synthesis of unsymmetrical stilbenes were fairly evident.

The only important method for the synthsis of unsymmetrical stilbenes 12 (Scheme 3) involves the condensation of enaminone 10 with acetone dicarboxylate(3-oxoglutarate) 11 in the presence of crown ether as base. Subsequently 12 on further elaboration afforded phyllodulcin 13.[10]

Recently, Paventi and Hay[8] have reported a facile method for the synthesis of unsymmetrical butadienes 16 through the


MeO
OH
SMe
SMe
5
BF$_3$.Et$_2$O
MeO
SMe
6
O
SMe
SMe
7
MgCl /
Et$_2$O/THF/0°C
OH
SMe
SMe
8
BF$_3$.Et$_2$O/C$_6$H$_6$/ △
SMe
9

Scheme–2

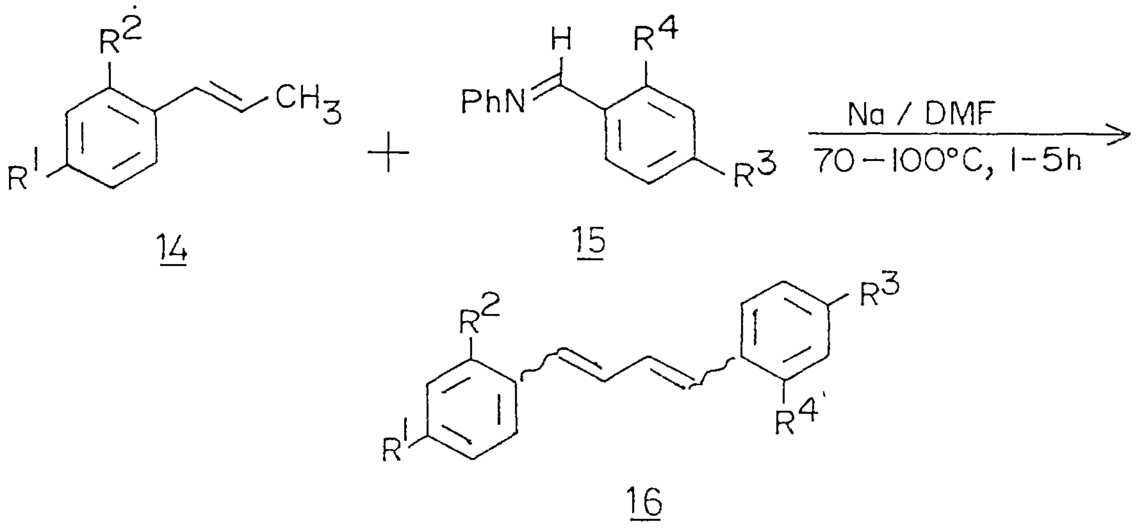

MeO
PhH2CO
NMe2
O
10
+
EtO2C
CO2Et
O
11
Crown ether
MeO
PhH2CO
EtO2C
CO2Et
OH
12
MeO
HO
O
O
OH
13 Phyllodulcin

Scheme-3

condensation of methyl aryl ethylene 14 with 15 in the presence of sodium metal or potassium *tert*-butoxide in dimethyl formamide (Scheme 4). Effenberger and Scholsser[13] have formulated a novel Wittig approach for the synthesis of polyenyl compounds of the general formula 20 and 22 as shown in Scheme 5. The trienyl dialdehyde 17 on condensation with the Wittig reagent 18 in the presence of butyllithium yielded a mixture of monocondensation product 19 (53%) and dicondensation product 20 (9%). The aldehyde 19 on further condensation with the Wittig reagent 21 in the presence of butyllithium gave the corresponding diaryldecapentene 22 in 72% yield (Scheme 5).

It is apparent from the literature that methods for the synthesis of dieneyl-, trienyl- and other polyenyl diaryl compounds are not many and always not necessarily suitable for products carrying unsymmetric aryl groups.

As an extension of our earlier report on the synthesis of stilbenes[11] and keeping in view the limitations experienced by its failure to afford the 4-methoxy substituted stilbenes and diarylbutadienes, it was considered to examine the cycloaromatization of cinnamoyl β-oxodithioacetals and their higher homologs so as to explore the possibilities to develop an improved method of stilbenes, dienes and trienes etc.. These results are presented in this chapter.

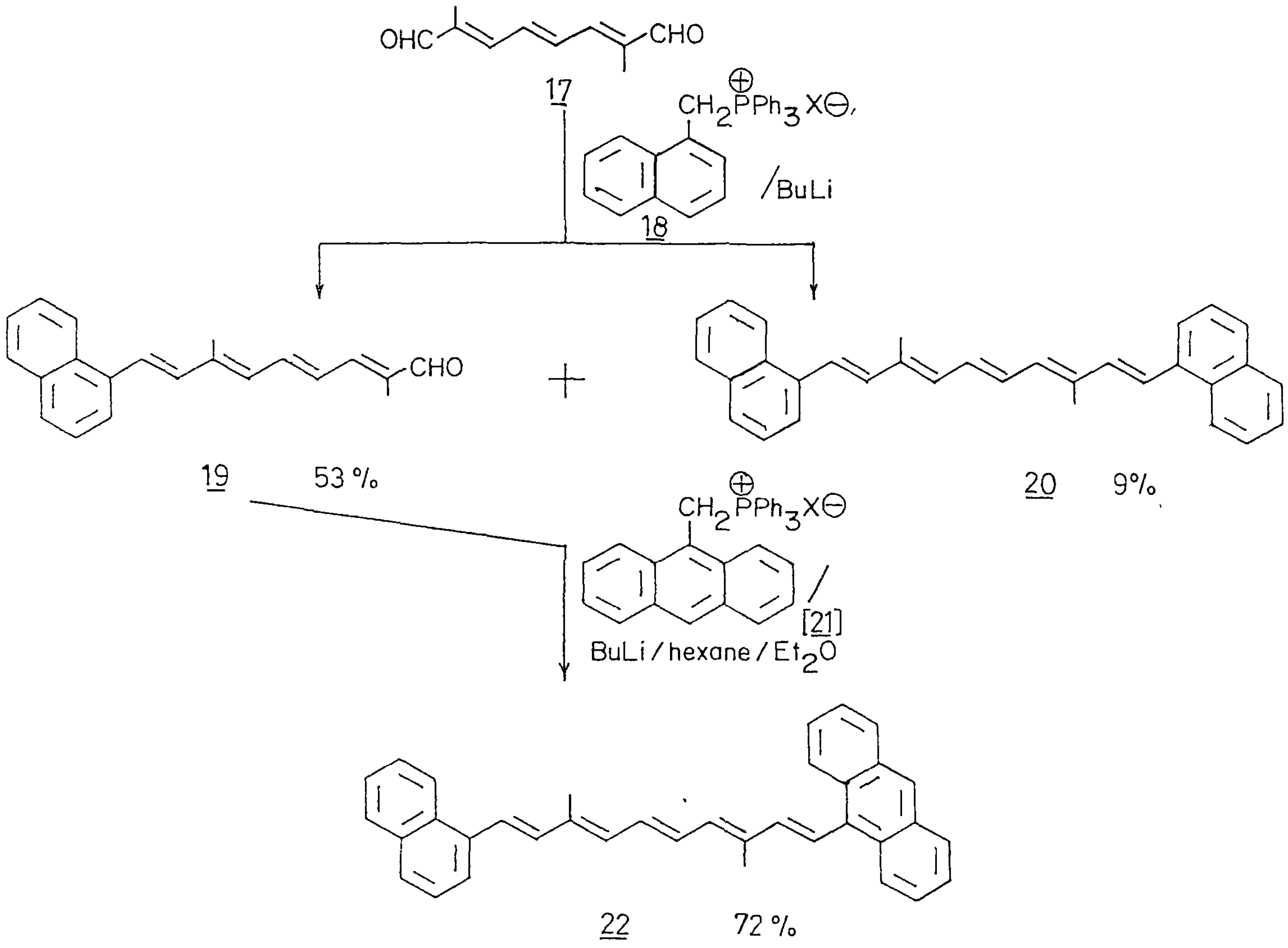


$R^1$ = H, MeO, $R^2$ = H, 2–($CH_3CH=CH$)$C_6H_4OCH_2O$

$R^3$ = H, MeO, 4–($PhN=CH$)$C_6H_4O$ $CH_2O$

$R^4$ = H, 2–($PhCH=CH$)$_2$ $C_6H_4OCH_2O$

Scheme – 4


OHC
CHO
17
$CH_2\overset{\oplus}{P}Ph_3X^{\ominus}$,
/BuLi
18
CHO
19
53 %
+
20
9%
$CH_2\overset{\oplus}{P}Ph_3X^{\ominus}$
/
[21]
BuLi / hexane / $Et_2O$
22
72 %

Scheme-5

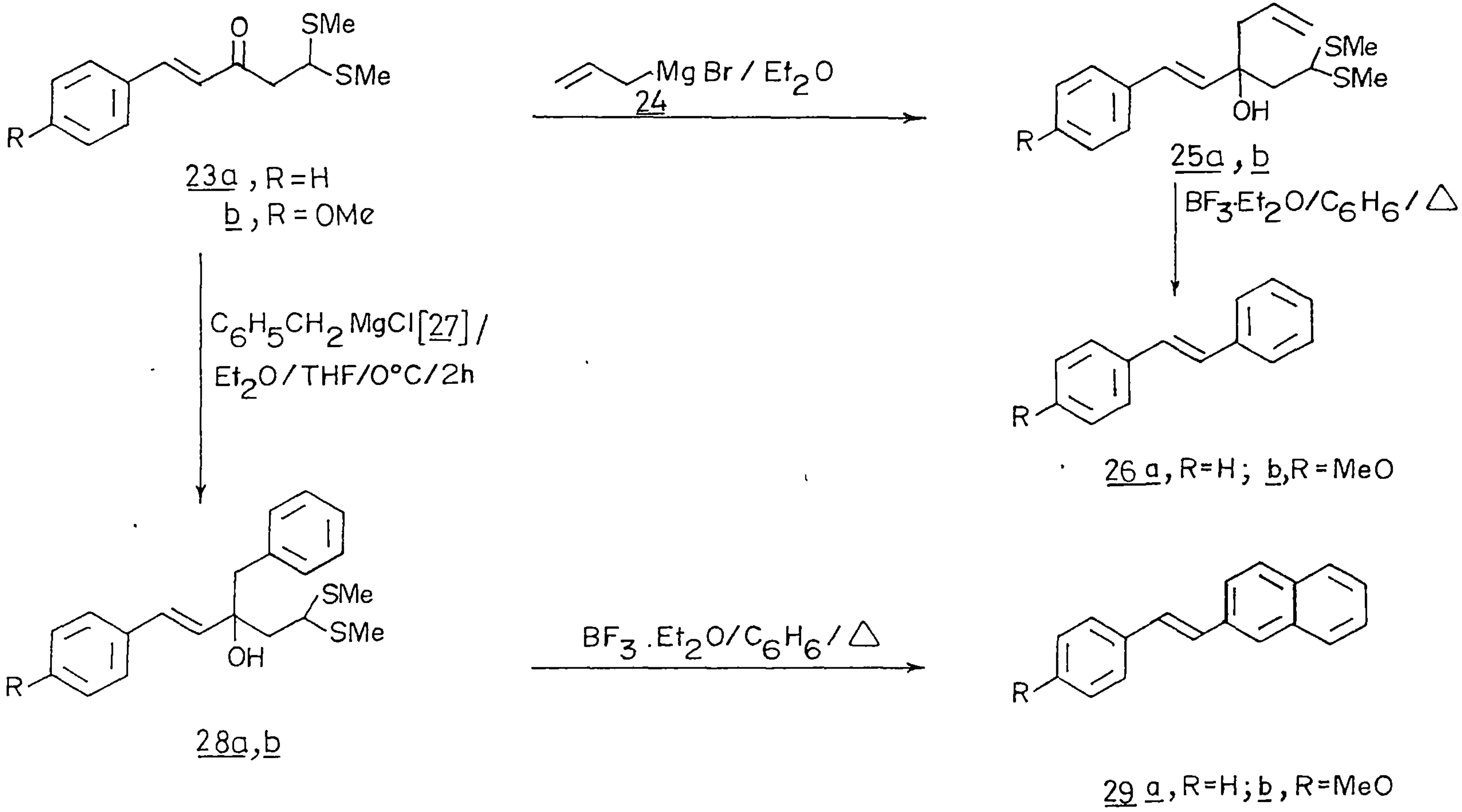
## RESULTS AND DISCUSSION

In Chapter II of this investigation, we have described an efficient method for the chemoselective reduction of the cinnamoylketene dithioacetals to the corresponding β-oxodithioacetals using sodium borohydride in acetic acid or zinc in acetic acid. It was therefore considered appropriate to utilize these important intermediates for the synthesis of stilbenes and other polyenyl diaryl compounds through the method of aromatic annelation as described earlier. Thus, when **23a** was reacted with allylmagnesium bromide (**24**) the corresponding carbinolacetal **25a** was obtained in quantitative yield. The **25a** was used directly without further purification for the subsequent $BF_3.Et_2O$ assisted cycloaromatization in refluxing benzene to afford the corresponding *trans*- stilbene **26a** in 78% yield. It may be noted here that the *trans*- stilbene was obtained only in 68% yield by our earlier method starting from the cinnamoylketene dithioacetal **1a** under similar reaction conditions (Scheme 1). Also the earlier procedure requires the desulphurization of the methylthio substituted stilbene **3a** so as to get the sulphur free *trans* - stilbene **4a**, while the present method directly affords **26a**. We have next examined the reaction of 4-methoxycinnamoyl β-oxodithioacetal **23b**, since the corresponding oxoketene dithioacetal failed to afford the corresponding stilbene through the described aromatic annelation process (Scheme 2). Thus, when **23b** on reaction with allylmagnesium bromide yielded the corresponding carbinolacetal **25b** quantitatively which on treatment with

$BF_3.Et_2O$ in refluxing benzene afforded the corresponding 4-methoxystilbene[2a] 26b in 66% yield (Scheme 6). Thus the present method is apparently superior to the earlier method developed from our laboratory.

The methodology could be similarly extrapolated for the construction of naphthalene ring over the ethylene bond by reacting 23a-b with benzylmagnesium chloride 27 and subsequently cyclizing the resulting carbinols 28a-b under the described reaction conditions (Scheme 6). Thus when 23a was reacted with 27 the corresponding carbinolacetal 28a was obtained in quantitative yield which underwent smooth cationic aromatic annelation in $BF_3.Et_2O/\ C_6H_6$ to afford the 1-phenyl-2-(2'-naphthyl)ethylene 29a in 80% yield (Scheme 6). Under the similar reaction conditions, 23b afforded the 1-(4'-methoxyphenyl)-2-(2'-naphthyl)ethylene 29b in 68% yield (Scheme 6). The structural assignments for 29a-b were made on the basis of their spectral and analytical data and on comparison with those reported in the literature.[14]

The approach was equally successful for the synthesis of 3-phenanthryl-2-phenyl ethylenes 32a-b from the reactions of 1-naphthylmethyl magnesium chloride 30 and 23a-b under the described conditions. Thus, when the β-oxodithioacetal 23a was reacted with 30 the corresponding carbinolacetal 31a was obtained in quantitative yield. It underwent smooth cyclization with $BF_3.Et_2O$ in benzene to afford 1-phenanthryl-2-phenyl-ethylene 32a in 69% yield. The spectral and analytical data of 32a was in agreement with the assigned

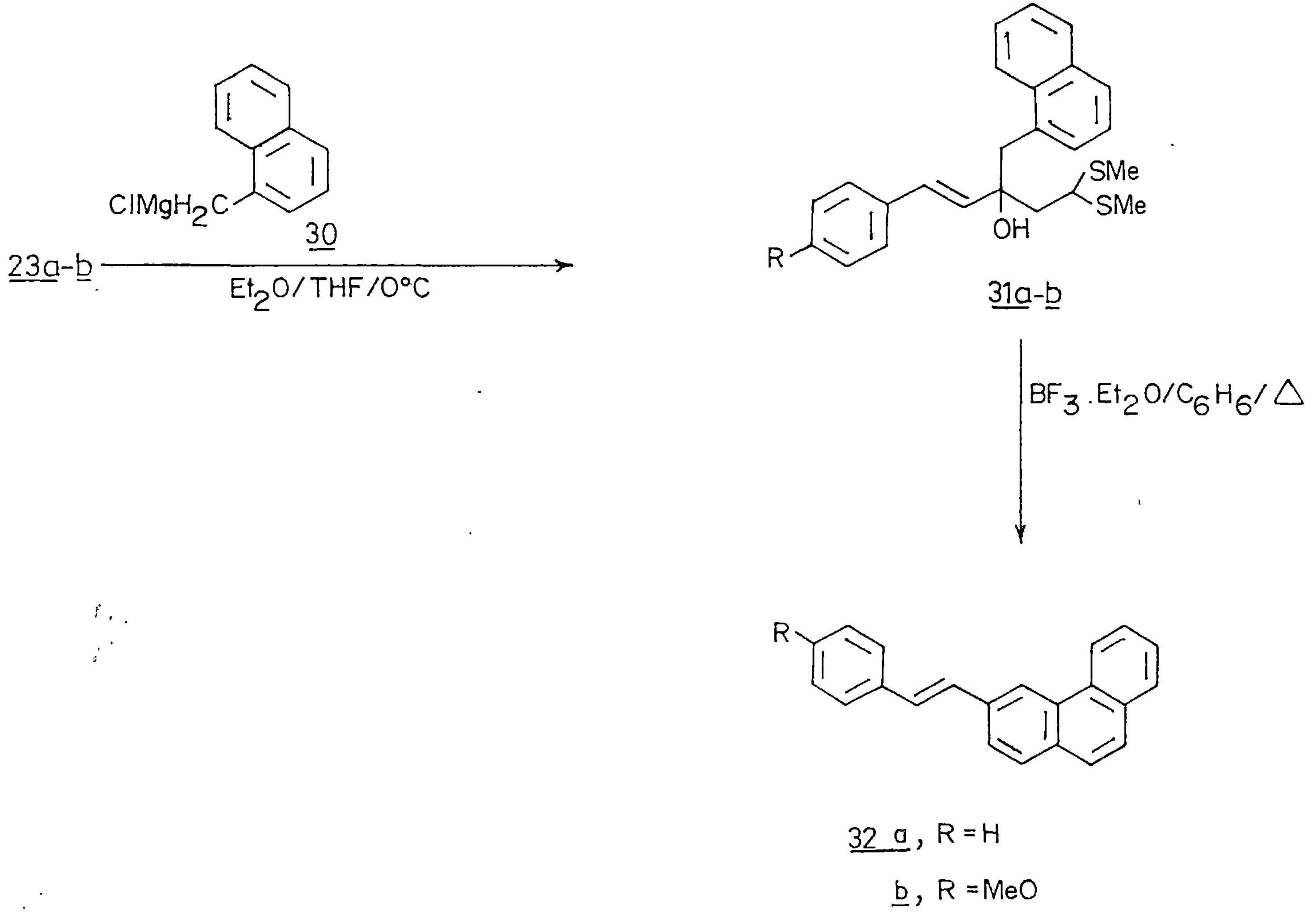

O
SMe
SMe
R
23a, R=H
b, R=OMe
MgBr / Et2O
24
SMe
SMe
OH
R
25a, b
BF3·Et2O/C6H6/△
C6H5CH2MgCl[27]/
Et2O/THF/0°C/2h
R
26 a, R=H; b, R=MeO
SMe
SMe
OH
R
28a, b
BF3.Et2O/C6H6/△
R
29 a, R=H; b, R=MeO

Scheme -6

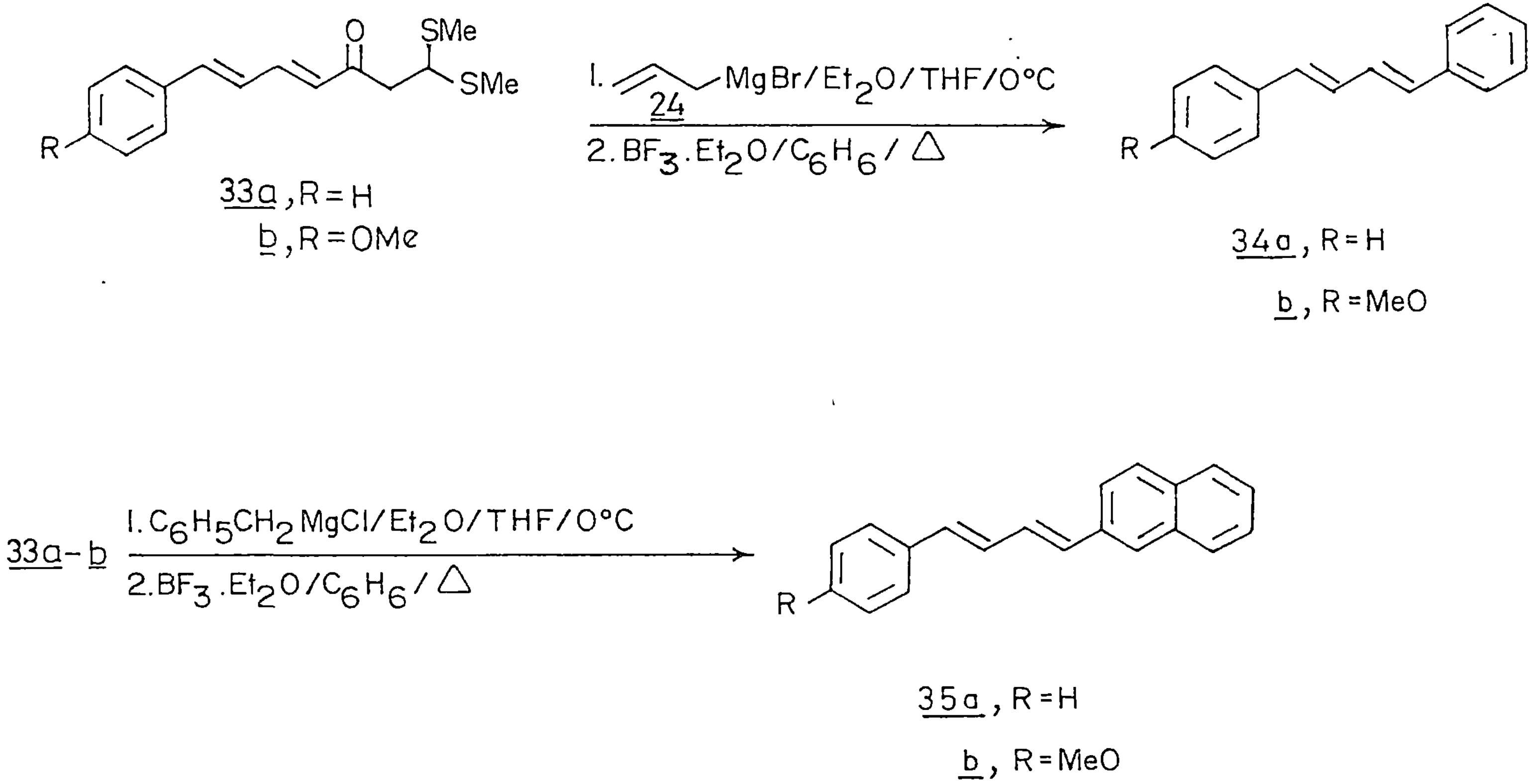
structure and also found to be identical with the reported sample[15] (Scheme 7). Similarly, following the same reaction sequence 23b afforded the corresponding methoxy substituted product 32b in 65% yield. The structure of the compound was found to be identical with the aunthentic compound [16] (superimposable IR) (Scheme 7).

The 1,4-diaryldienes 34a-b were similarly prepared by reacting the corresponding dienyl β-oxodithioacetals 33a-b following the described reaction sequence. Thus, 33a on treatment with allylmagnesium bromide 24 yielded the corresponding carbinolacetal which on subsequent cycloaromatization afforded 1,4-diphenyl 1,3-butadiene 34a in 82% yield (Scheme 8). The compound was identical with the aunthentic sample[17](mixed melting point 152°C, superimposable IR) and both the double bonds were assigned to E,E-geometry. Similarly the 1-(4-methoxyphenyl)- 4- phenyl-1,3-butadiene 34b was obtained in 78% yield from the reaction of 33b with 24 followed by its acid assisted cyclization. The structural assignments were made on the basis of its physical, analytical and spectral data[18] (Experimental Section) (Scheme 8).

The dienyl β-oxodithioacetals 33a-b were also reacted with benzylmagnesium chloride 27 to construct the naphthalene ring on the diene terminal carbon atom. Thus, 33a when reacted with 27 and following its subsequent aromatic annelation afforded 1-(2'-naphthyl)- 4-phenyl 1,3-butadine 35a in 72% yield. The structure of 35a was confirmed on the basis of its


23a-b
ClMgH2C
30
Et2O/THF/0°C
R
SMe
SMe
OH
31a-b
BF3.Et2O/C6H6/Δ
R
32 a, R = H
b, R = MeO

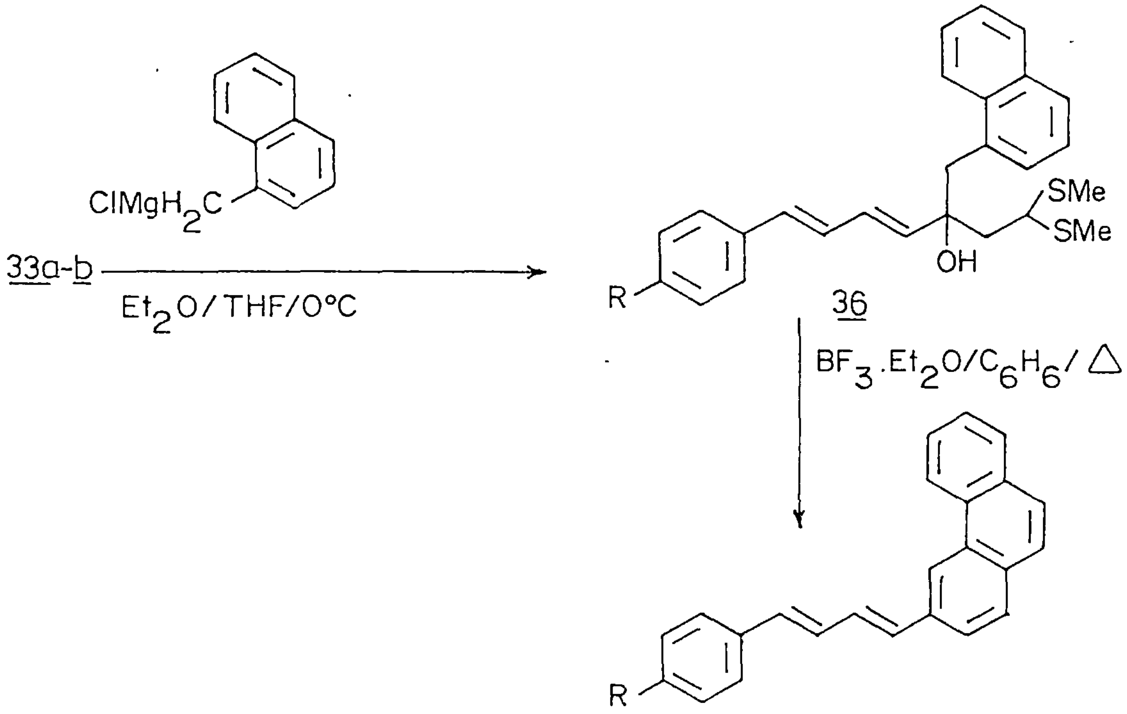
Scheme – 7


O
SMe
SMe
R
33a, R = H
b, R = OMe
1. 24 MgBr/Et2O/THF/0°C
2. BF3.Et2O/C6H6/ △
R
34a, R = H
b, R = MeO
33a-b
1. C6H5CH2MgCl/Et2O/THF/0°C
2. BF3.Et2O/C6H6/ △
R
35a, R = H
b, R = MeO

Scheme – 8

analytical and spectral data and by comparing with the literature data.[19] The reported method of preparing the same compound involves the condensation of 2-methylnapthalene with cinnamaldehyde in the presence of a base followed by dehydration as a cis : trans mixture (51%). The present method therefore seems to be better as it provides exclusively the trans isomer with an improved yield. Similarly the 1-(2'-naphthyl)-4-(4'-methoxyphenyl)- 1,3 -butadiene **35b** was obtained in 77% yield from the reaction of **33b** with **27** following the same reaction sequence (Scheme 8). The spectral and physical properties were found to be identical with that of the reported compound.[20] Here again the present method affords the trans isomer exclusively.

The efficacy of our method was further demonstrated by creating a phenanthrene ring on the terminal carbon of the diene. Thus, **33a** when reacted with α-naphthylmagnesium chloride **30** followed by the cyclization of the resulting carbinol **36a** to afford the corresponding 1-(phenanthryl)-, 4-phenyl 1,3-butadiene **37a** in 69% yield (Scheme 9). This compound[9] was prepared earlier by condensing 2-methylphenanthrene with cinnamaldehyde in the presence of a base to afford a mixture of cis : trans dienes in moderate yields. The product **37a** was found to possess all trans geometry and its structure was established on the basis of its spectral and analytical data. Similarly 1-(3-phenanthryl)-4-(4'-methoxyphenyl)-1,3-butadiene **37b** was obtained in 65% yield (Scheme 9). The compound was found to



33, 36, 37a, R=H

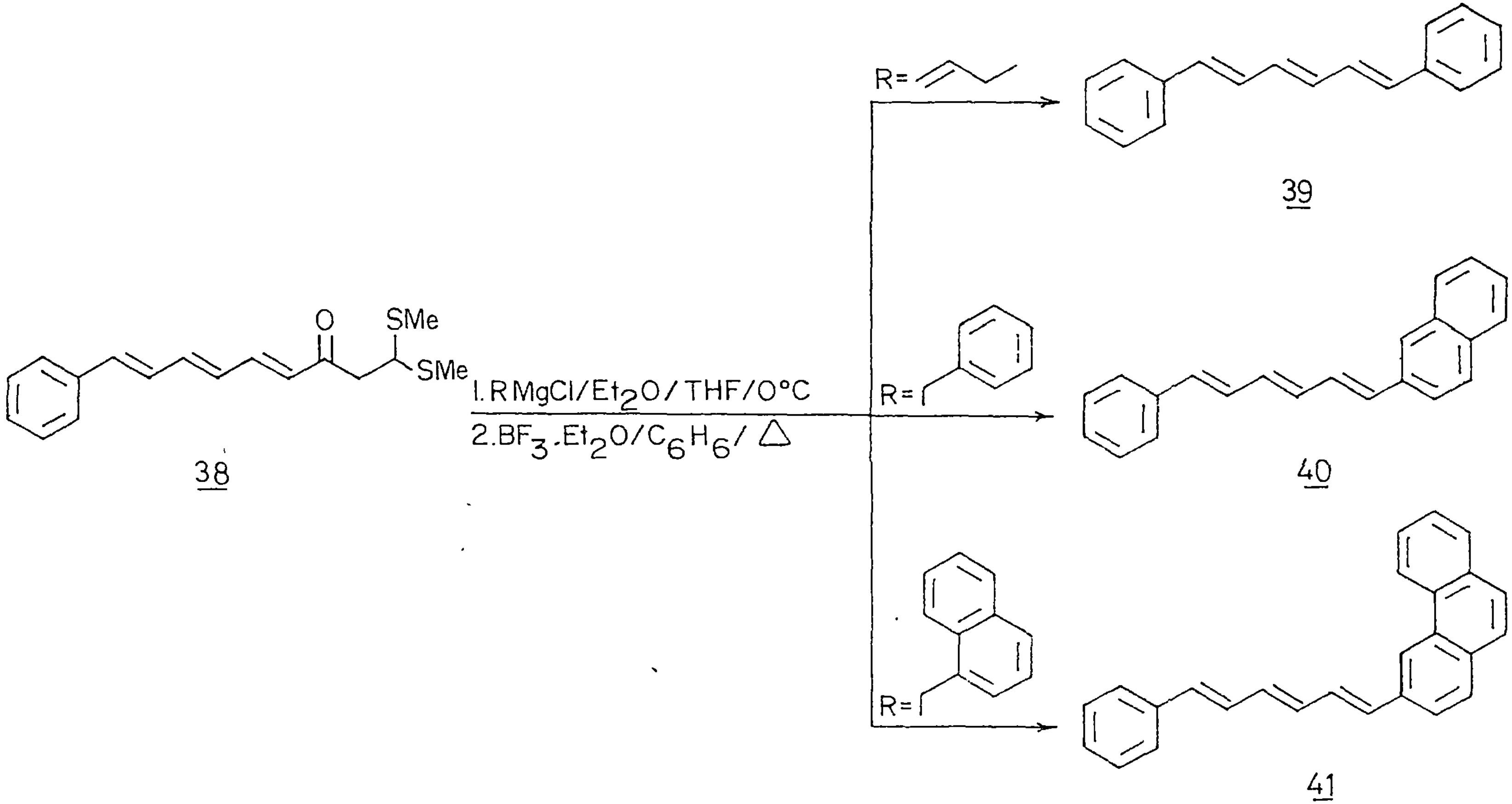
b, R=MeO

Scheme—9

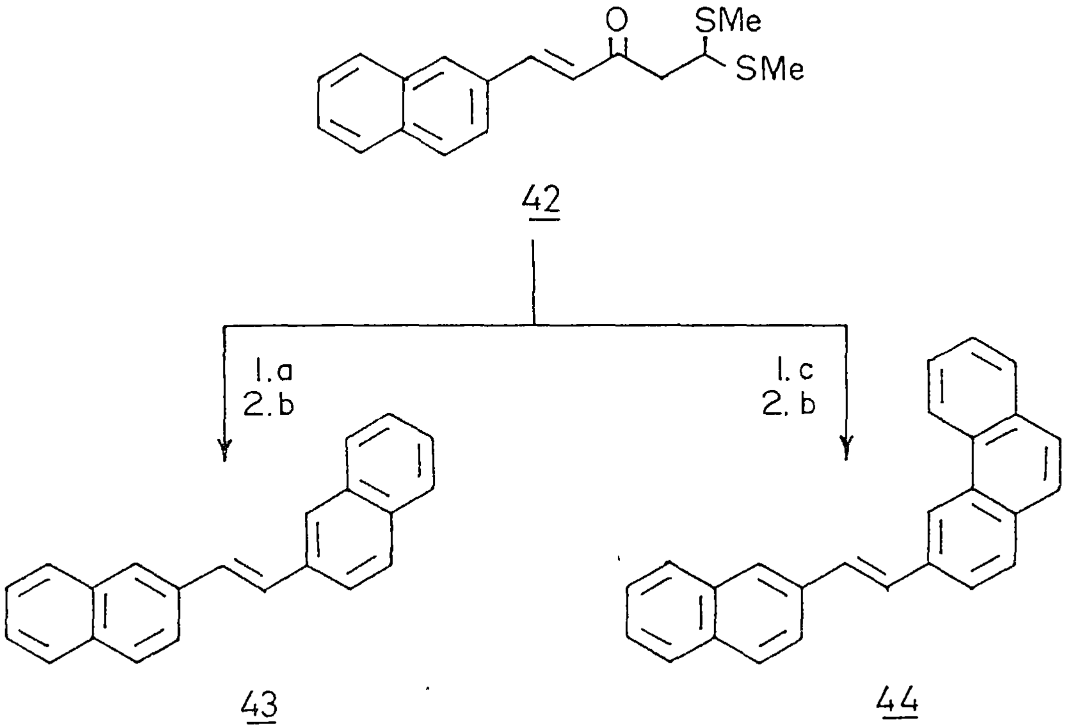
be identical with the reported trans isomer[9] (mixed melting point and superimposable IR).

The trienyl β-oxodithioacetal 38 was then examined for its utility for the synthesis of 1,6-diaryl trienyl products following the present methodology. Thus, 38 on reacting with the allylmagnesium bromide followed by its subsequent cycloaromatization in the presence of $BF_3.Et_2O$ resulted in the formation of 1,6-diphenyl 1,3,5-hexatriene 39 in 81% yield (Scheme 10). The structure of this compound was established on the basis of its spectral and analytical data and on further comparison with the reported one in the literature.[21] Similarly when 38 reacted with benzylmagnesium chloride and after cyclization afforded 1-(2'-naphthyl)-6-phenyl-1,3,5-hexatriene 40 in 62% yield. The reaction 38 with α-naphthylmethylmagnesium chloride under similar reaction conditions resulted in the formation of 1-(2'-phenanthryl)-6-phenyl-1,3,5-hexatriene 41 in 63% yield. Both 40 and 41 were reported earlier and they were observed to be identical in their spectral and analytical data.[9] Also they were shown to contain all the double bonds in E - geometry.

The 2-naphthyl derivative 42 also underwent facile reaction with benzylmagnesium chloride followed by cycloaromatization to yield 2,2'-(binaphthyl) ethylene 43 in 68% yield. It was compared with the authentic sample reported in the literature[22] and they found to be identical (Scheme 11). The reaction of 42 with 1-naphthylmethylmagnesium chloride under similar reaction conditions afforded 1-(β-naphthyl)-3-



Scheme –10



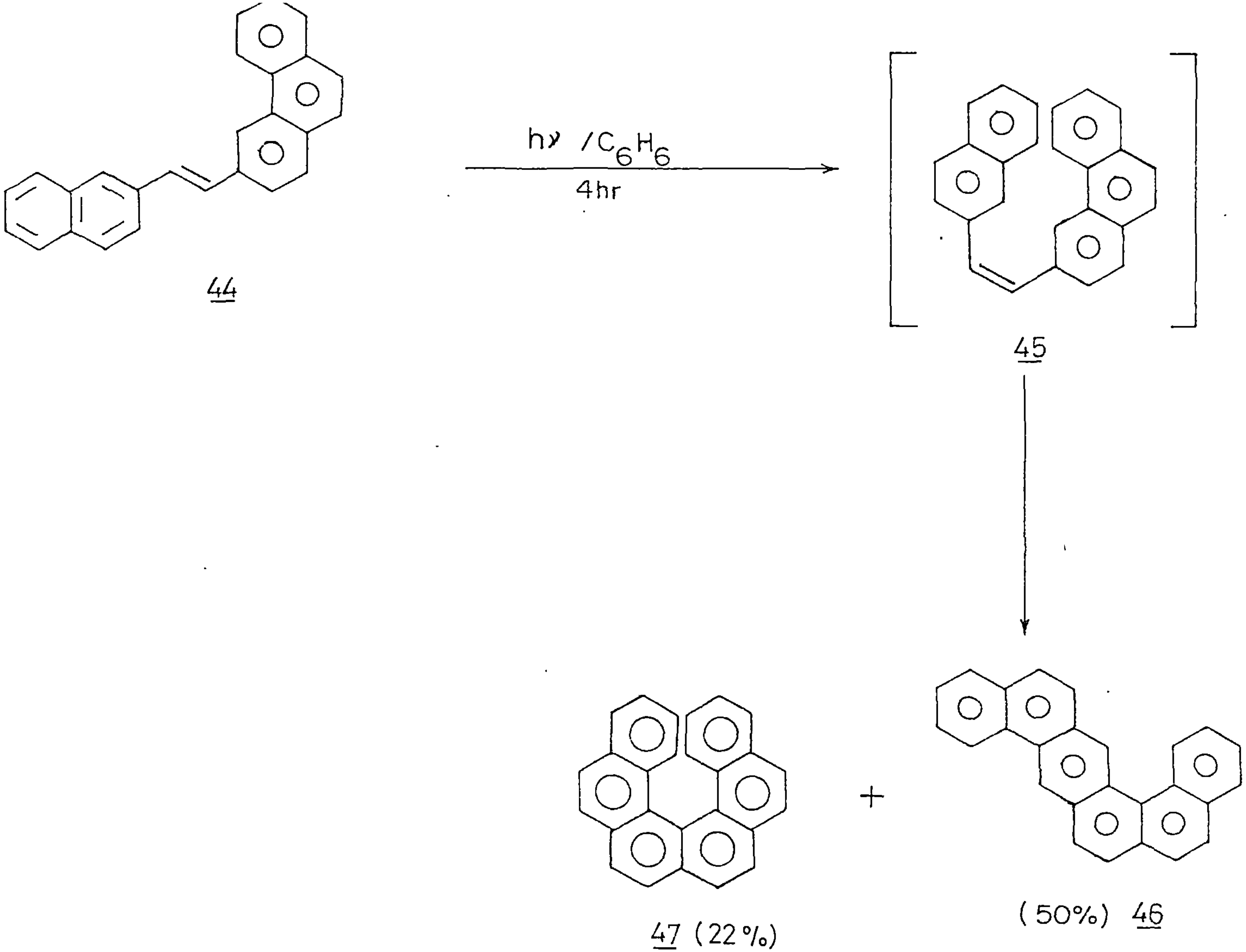
a, $C_6H_5CH_2MgCl/Et_2O/THF/0°C$, b, $BF_3.Et_2O/C_6H_6/$

c, 1-( naphthyl $CH_2$) $MgCl/Et_2O/THF/0°C$

Scheme-11

phenanthryl ethylene **44** in 69% yield. The structure of this compound was established on the basis of its spectral and analytical data and on comparison with that reported in the literature.[23] The compound **43** is a precursor for hexahelicene **47** (Scheme 12) and hence this method provides an easy access for the synthesis of **44** which is otherwise prepared in very low yields by earlier methods.

In summary, a new efficient synthesis of 1,2-diarylethylenes, 1,4-diarylbutadienes and 1,6-diaryl 1,3,5- hexatrienes has been formulated. The overall strategy of creating an aromatic ring through its acyclic precursors yielding otherwise inaccessible diaryl ethylenes has been successfully realised. The method is equally efficient for the synthesis of diphenyl, phenyl- naphthyl, phenyl-phenanthryl, dinaphthyl and naphthyl-phenanthryl substituted olefins. Since the yields are generally high and the starting materials are easily available, the present approach should be a method of choice for the synthesis of these compounds. Many of these olefins are useful substrates for photocyclization to condensed aromatics **24-26** and in the Diels' Alder reactions.[24-26] The 1,6-diphenyl hexatrienes are useful molecular probes in the study of membrane fluidity[27]. Particularly interesting is the preparation of **44** which on photoinduced isomerization affords the hexahelicene **47**.[23] In view of the limited methods available in the literature for the synthesis of this important hexahelicene precursor and also the fact that the earlier methods are low yielding, our present method gains paramount importance. Development of



Scheme-12

methodologies for the synthesis of stilbenes and other related diarylsubstituted olefines is still an important area of research as many of them are naturally occuring or possessing useful biological activities.[2a,10,28-33] They also known to be important intermediates for the synthesis of drugs, dyes, agrochemicals and various heterocyclic compounds.[2b,5]

## EXPERIMENTAL SECTION:

### General

Melting points were determined on a Thomas Hoover capillary melting points apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. $^1H$ NMR spectra were measured at 90 MHz on a Varian EM-390 spectrometer in $CDCl_3$ or $CCl_4$ and the chemical shift values are reported in $\delta$ units downfield from $Me_4Si$. Mass spectra were obtained on a Jeol-D-300 spectrometer. Elemental analysis were carried out on a Heraeus CHN-O-RAPID instrument.

### CHEMICALS AND REAGENTS

Grignard grade magnesium turnings (SISCO) were used for all the Grignard reactions. Allyl bromide, benzyl chloride and chloromethylnaphthalene (Aldrich) were purchased and used as supplied. Borontrifluoride etherate was distilled (125-126°C) before use. Diethylether, THF and benzene (acid-treated) were dried according to the procedures described in

Vogel Practical Book of Organic Chemistry. Tlc (Silica gel, Acme's) was used for monitoring the reaction progress.

STARTING MATERIALS

All the β-oxodithioacetals required for the present investigation were prepared from their corresponding α-cinnamoyl ketene dithioacetals and their higher eneyl analogs following the procedures described in the Chapter II.

**Synthesis of 1,2-Diarylethylenes 26,29,43,44, 1,4-Diaryl-1,3-butadienes 34,35,37 and 1,6-Diaryl-1,3,5-hexatriene 39,40,41 : General Procedure.**

To a well stirred and cooled (0°C) suspension of allyl/benzyl/1-(naphthylmethyl)magnesium halide, [prepared from allyl bromide (1.90g, 16mmol), benzyl chloride (1.98g, 16mmol) or 1-(naphthylmethyl) chloride (2.3g, 16mmol) and Mg turnings (1.2g, 0.52 atom)] in dry ether (40mL), a solution of β-oxodithioacetals23,33,38,42 (8mmol) in dry THF (30mL)was added and the mixture was further stirred at 0°C for 1hr.It was then poured into saturated aqueous $NH_4Cl$ (300mL), extracted with ether (3x30mL), dried ($Na_2SO_4$)and evaporated *in vacuo* to crude carbinols nearly quantitative yields which are used as such for cyclization without further purification.

**General Procedure for $BF_3.Et_2O$ Cycloaromatization of Carbinols**

To a solution of crude carbinol, obtained as above, in dry benzene (60mL), $BF_3.Et_2O$ (10mL), was added and the reaction mixture was refluxed for 45min. After cooling, it was poured into $H_2O$ (300mL), dried ($Na_2SO_4$) and evaporated to give corresponding crude olefins which were further purified by passing through silica gel column using hexane as eluent. The spectral and analytical data of the products obtained are given below.

**E-Stilbene (26a):** Colourless crystals; m.p. 123-124°C (hexane) (lit.[2a]. m.p. 124-125°C); 78%; IR (KBr) 1598, 1496, 1460, 950 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.79-7.75 (m, 12H, =CH and ArH). (Anal. Calcd. for $C_{14}H_{12}$ : C, 93.29; H, 6.71. Found : C, 93.46; H, 6.92%).

**4-Methoxystilbene (26b):** Colourless solid; m.p. 134°C (hexane) (lit.[2a] m.p. 136°C); 66%; IR (KBr) 1612, 1520, 1280, 959 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.88 (s, 3H, $OCH_3$), 6.72-7.12 (m, 4H, =CH, ArH); 7.30-7.80 (m, 7H, ArH). (Anal. Calcd. for $C_{15}H_{14}O$ : C, 85.68; H, 6.71. Found : C, 85.91; H, 6.89%).

**1-Phenyl-2-(2'-naphthyl)ethylene (29a)** : Colourless solid; m.p. 147°C (lit.[14] mp. 148°C); 80%; IR (KBr) 1598, 1494, 1448, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.21-7.70 (m, 10H, =CH and ArH), 7.72-8.08 (m, 4H, ArH). (Anal. Calcd. for $C_{18}H_{14}$ : C; 93.87; H, 6.12. Found : C, 93.19; H, 6.37%).

**1-(4'-Methoxyphenyl)-2-(2'-naphthyl)ethylene (29b):** Colorless crystals; m.p. 177-178°C (lit.[14] m.p. 178- 179°C); 68%; IR (KBr) 2990, 1604, 1405, 1024 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.42 (s, 3H, $OCH_3$); 7.35-7.85 (m, 12H, =CH, and ArH); 8.18-8.30 (m, 4H, ArH). (Anal. Calcd. for $C_9H_{16}O$ : C, 93.40; H, 6.60. Found : C, 93.59 ; H, 6.79%).

**1-(3'-Phenanthryl)-2-phenyl-ethylene (32a):** Colourless solid; m.p. 151-152°C (hexane) (lit.[15] m.p. 153°C); 69%; IR (KBr) 1606, 1441, 991 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 7.02 (s, 1H, =CH); 7.24-8.11 (m, 13H, =CH and ArH); 8.62-8.89 (m, 2H, ArH). (Anal. Calcd. for $C_{22}H_{16}$ : C, 94.24; H, 5.75. Found : C, 94.46; H, 5.98%).

**1-(4'-Methoxyphenyl)-2-(3'-phenanthryl)ethylene (32b):** Colourless solid; m.p. 195-196°C (lit.[16] mp. 197°C); 65%; IR (KBr) 2997, 1601, 1400, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.61 (s, 3H, $OCH_3$); 7.31-7.58 (m, 8H, =CH and ArH); 7.59-8.20 (m, 5H, ArH); 8.68-8.90 (m, 2H, ArH). (Anal. Calcd. for $C_{23}H_{18}O$ : C, 93.84; H, 6.16. Found : C, 93.98; H, 6.32%).

**1,4-Diphenyl-1,3-butadiene (34a)** : Pale yellow solid: m.p. 151-152°C (hexane) (lit.[17] m.p. 153°C) 82% IR (KBr) 1502, 1460, 1000 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.41-7.00 (m, 4H, =CH); 7.11-7.62 (m, 10H, ArH). (Anal. Calcd. for $C_{16}H_{14}$ : C, 93.16; H, 6.84. Found : C, 93.34; H, 6.97%).

**1-(4'-Methoxyphenyl)-4-phenyl-1,3-butadiene (34b)** : Pale yellow solid; m.p. 160°C (lit.[18] m.p. 161°C); 78%; IR (KBr) 2996, 1510, 1415, 1015 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.88 (s, 3H, $OCH_3$); 6.55-7.44 (m, 6H, =CH and ArH), 7.30-7.63 (m, 7H, ArH). (Anal. Calcd. for $C_{17}H_{16}O$ : C, 86.40; H, 6.82. Found : C, 86.61; H, 6.91%).

**1-(2'-Napthyl)-4-phenyl-1,3-butadiene (35a):** Colourless solid; m.p. 170-171°C (lit.[19] m.p. 172°C); 72%; IR (KBr) 3000, 1601, 1441 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 6.81-7.12 (m, 4H, =CH); 7.16-7.61 (m, 7H, ArH); 7.68-8.05 (m, 5H, ArH). (Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found : C, 93.89; H, 6.46%).

**1-(2'-Naphthyl)-4-(4'-methoxyphenyl)-1,3-butadiene (35b):** Colourless solid, m.p. 164-165°C (lit.[20] mp. 167°C); 71%; IR (KBr) 2988, 1596, 1410 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 3.51 (s, 3H, OCH$_3$); 6.65 -6.81 (m, 5H, =CH and ArH); 7.12-7.40 (m, 5H, ArH) 7.71-8.11 (m, 5H, ArH). (Anal. Calcd. for $C_{21}H_{18}O$ : C, 93.29; H, 6.70. Found : C, 93.41; H, 6.83%).

**1-(3'-Phenanthryl)-4-phenyl-1,3-butadiene (37a):** Colourless solid; m.p. 146- 147°C (lit.[9] m.p. 148°C; 69%; IR(KBr) 2991,1588, 1404 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 6.67-6.90 (m, 5H, =CH and ArH); 7.12-7.94 (m, 10H, ArH); 8.40-8.99 (m, 3H, ArH). (Anal. Calcd. for $C_{24}H_{18}$ : C, 94.07; H, 5.92. Found : C, 94.21; H, 6.03%).

**1-(4'-Methoxyphenyl)-4-(3'-phenanthryl)-1,3-butadiene (37b):** Colourless crystals; m.p. 195°C (lit.[9] m.p. 197°C); 68%; IR (KBr) 3005, 1605, 1410 cm$^{-1}$; $^1$H NMR (CDCl$_3$) 3.56 (s, 3H, OCH$_3$); 6.84-7.18 (m, 5H, =CH and ArH), 7.20-8.12 (m, 12H, ArH); 8.21-9.01 (m, 3H, ArH); (Anal. Calcd. for $C_{25}H_{20}O$ : C, 93.98; H, 6.42. Found: C, 93.98, H; 6.42%).

**1,6-Diphenyl-1,3,5-hexatriene (39):** Colourless crystals, m.p. 200-201°C (lit.[21] m.p. 200-202°C); 81%; IR (KBr) 2980, 1600, 1415 cm$^{-1}$; $^1$ H NMR (CDCl$_3$) 6.48-7.00 (m, 4H, =CH); 7.04-7.76

(m, 12H, ArH). (Anal. Calcd. for $C_{18}H_{16}$ : C, 93.05; H, 6.94. Found : C, 93.20; H, 7.01%).

**1-(2'-Naphthyl)-6-phenyl-1,3,5-hexatriene (40)** : Colourless solid; m.p. 152-153°C (lit.[9] m.p. 154°C); 62%; IR (KBr) 2988, 1602, 1460 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.51-6.99 (m, 4H, =CH); 7.01-7.81 (m, 10H, =CH and ArH), 7.83-8.01 (m, 4H, ArH). (Anal. Calcd. for $C_{22}H_{18}$: C, 93.57; H, 6.42. Found: C, 93.69; H, 6.60%).

**1-(3'-Phenanthryl)-6-phenyl-1,3,5-hexatriene (41)**: Colourless solid; m.p. 250-252°C (lit.[9] m.p. 254°C); 63%; IR (KBr) 1601, 1511 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.98-7.11 (m, 11H, =CH and ArH) 7.48-7.61 (m, 6H, ArH), 7.62-8.05 (m, 2H, ArH), 8.89-8.94 (m, 1H, ArH). (Anal. Calcd. for $C_{26}H_{20}$ : C, 93.93; H, 6.06. Found : C, 94.02, H, 6.21%).

**2,2'-(Binaphthyl)ethylene (43)**: Colourless solid; m.p. 257-258°C (lit.[22] m.p. 258°C); 66%; IR (KBr) 1612, 1604, 1480 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.51 (brd, 1H, =CH); 7.01-7.54 (m, 13H, =CH and ArH); 7.55-7.79 (m, 2H, ArH). (Anal. Calcd. for $C_{22}H_{16}$ : C, 94.24; H, 5.75. Found : C, 94.41; H, 5.84%).

**1-(2'-Naphthyl)-2-phenyl-ethylene (44)**; White crystals; m.p. 273°C (lit.[23] m.p. 275°C); 69%; IR (KBr) 1616, 1600, 1498 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.52-6.54 (m, 11H, =CH and ArH); 7.04-7.83 (m, 6H, ArH), 8.81 (m, 1H, ArH). (Anal. Calcd. for $C_{26}H_{18}$; C, 94.81; H, 5.71. Found : C, 95.08; H, 5.96).

## REFERENCES AND NOTES

1. Harper, S.H., "Chemistry of Carbon Compounds", Vol. 3, E.H. Rodd , Ed., Elsevier Publishing Corp., New York, 1956, Chapter 18.
2. For reviews on the synthesis of Stilbenes, see: (a) Wheeler, O.H., Battle de Pabon, H.N., *J.Org. Chem.* ,1965, *30*, 1473. (b) Becker, K.B., *Synthesis*, 1983, 341.
3. Corey, E.J., Hopkins, P.B. *Tetrahedron Lett.*, 1982, *23* 1979.
4. Chamchaang, W., Chantarasiri, N., Shaona, S., Thebtaranonth, C., Thebtaranoth, Y., *Tetrahedron* , 1984, *40*, 1727.
5. Banerjee, A.K., Sulbarande Currasco, M.C., Frydrych-Honge, C.S., Motherwell, W.B., *J. Chem. Soc. Chem. Comm.* ,1986, 1803.
6. Yeung, L.L.; Yip, Y.C., Luh, T., *J. Chem. Soc. Chem. Commun.*, 1987, 981.
7. Choudhary, B.M., Sharma, M.R., *Tetrahedron Lett.*,1990, *31*, 1495.
8. For recent literature on synthesis of stilbenes and 1,4-diarylbutadienes : Paventi, M.; Hay, A.S. *Synthesis* 1990, 878 and references therein.
9. Mikhailov, B.M.; Tersarkisyan, G.S. *Izv. Akad. Nauk, SSSR Octd. Khim. Nauk.* 1960, 1267; *Chem. Abstr.* , 1961, *55*, 543a.

10. Takeuchi, N., Ochi, K., Murase, M., Tominaga, S. *J. Chem. Soc. Chem. Commun.* 1980, 593.

11. Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis*, 1987, 284.

12. Truce, W.E.; Perry, F.M. *J.Org. Chem.*, 1960, *30*, 1316.

13. Effenberger, F., Scholsser, H. *Synthesis*, 1990, 1085.

14. Siegrist, A.E.; Liechti, P.; Mayer, H.R.; Weber, K. *Helv. Chim. Acta.*, 1969, *52*, 2521.

15. Laarhoven, W.H. Cuppen, JH. J.H.M.; Nivard, R.J.F. *Tetrahedron*,1970,*26*, 1069.

16. De Jong, M.H.; Laarhoven, W.H. *Red. Trav. Chim. Payas. Bans*, 1973, *92*(5), 673 ; *Chem. Abstr.*, 1973, *79*, 17903.

17. McDonald, R.N.; Campbell, T.W. *J. Org. Chem.* , 1959, *24* 1969 .

18. Guesten, H.; Salzwedel, M. *Tetrahedron*, 1967, *23* 173 (Ger.).

19. Hayward, R.J.; Leznoff, C.C. *Tetra hedron*,, 1971, 2085.

20. S. Iraelasvili, *Proc. Int. Cong. Pure Appl. Chem.* (London), 1947, *2*, 138; *Chem. Abstr.*, 1975 , 45631.

21. CRC Handbook of Data on Organic Compounds; Weast, R.C.; Astle,M.J.; Ed.; *C.R.C. Press Inc.* : 1985, Vol 1, p. 726.

22. Spatz, S.M. *J. Org. Chem.* 1961, *26*, 4160.

23. Laarhoven, W.H.; Cuppen, TH. J.H.M., Nivard, R.J.F. Tetrahedron ,1970, 26, 4865.

24. Martin, R.H.; Flammang-Bartrieux, M; Cosyn, J.P.; Gelbcke, M. *Tetrahedron Lett.* 1968 , 3507.

25. Bogaert-Verhoogen, D.; Martin, R.H. *Tetrahedron Lett.*, 1967, 3045.

26. Carruthers, W. *J. Chem.. Soc. C,* 1967, 1525 and references therein.

27. Beck, A.; Heissler, B.; Duportail, G. *Tetrahedron* , *47* 1991, 1459.

28. Askawa, Y., *Bull. Chem. Soc. Japan,* , 1970, *43*, 575.

29. Maria, Z-S, Gyorgio, S., *Harba. Hung.*, 1966, *5*, 91; Chem. Abstr. 1968, 68, 43090.

30. Gupta, D., Singh, J. *Phytochemistry,*, 1990, *29*, 1945.

31. Rowe, J.W., Bower, C.L. and Wagner, E.R., *Phytochemistry,* , 1969, *8*, 235.

32. Miquel, J.F., *Tetrahedron,* 1960, *8*, 205.

33. Cardone, M.L., Fernandez, M.I.; Garcia, M.B., Pedro, J.R., *Tetrahedron,* 1986, *42*, 2725 and references therein.

# CHAPTER V

## A FACILE ONE POT THERMAL DEHYDRATION AND DETHIOACETALIZATION OF β-HYDROXYDITHIOACETALS WITH DIMETHYL SULPHOXIDE : SYNTHESIS OF α,β-UNSATURATED ALDEHYDES.

### V.1.INTRODUCTION

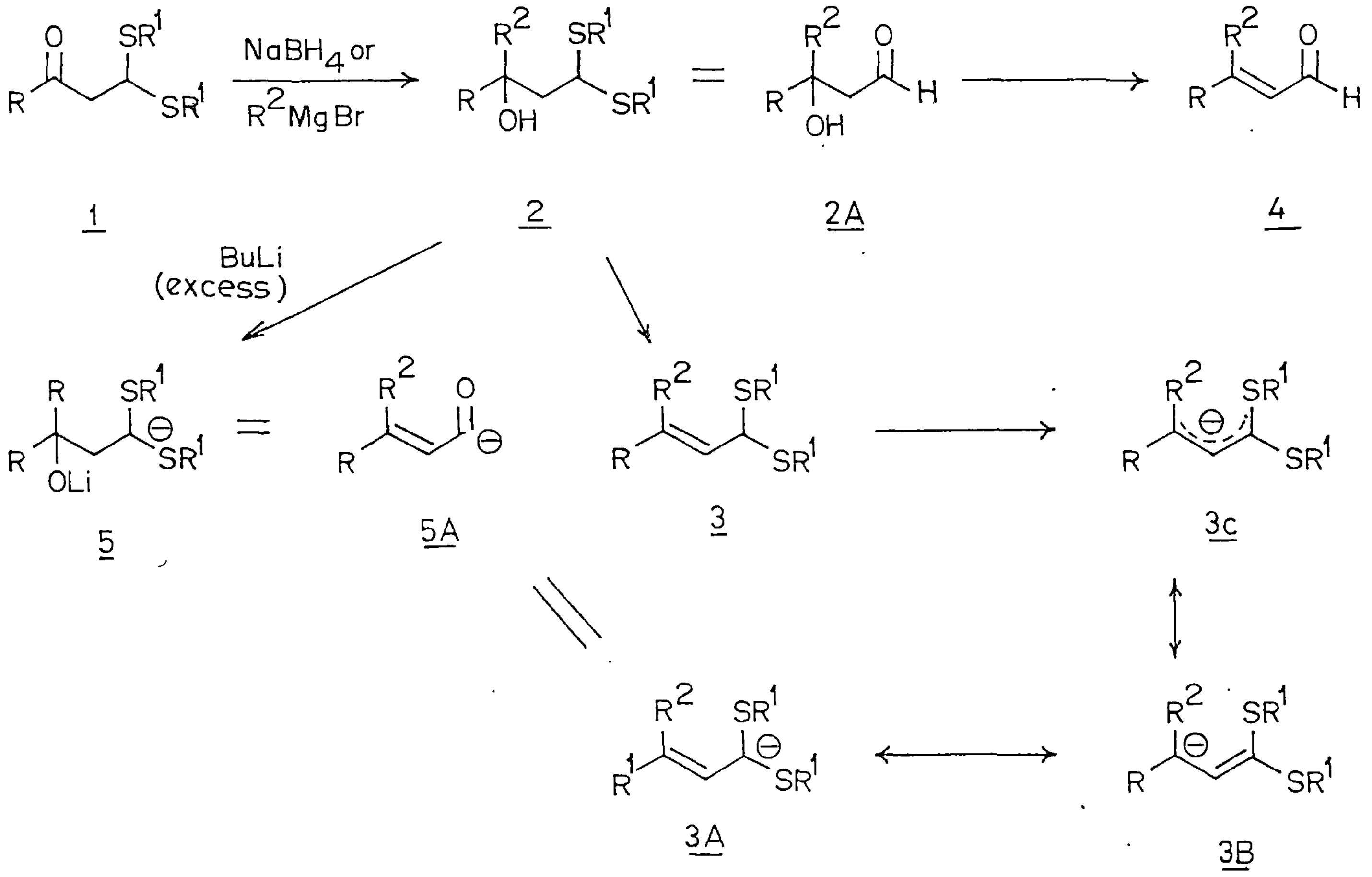
In the preceding chapter II, we have described an efficient and new general method for the reduction of mercapto double bond of α-oxoketene dithioacetals by using zinc in acetic acid to afford β-oxodithioaceatls in much improved yields than our earlier reported method employing sodium borohydride in acetic acid. These β-oxodithioacetals 1 are of considerable interest since on metal hydride reduction or addition of carbanions 1 could afford the corresponding β-hydroxydithioacetals 2 in quantitative yields (scheme 1).

The β-hydroxy dithioacetals 2 are precursors of the corresponding β-hydroxyaldehydes 2A, enealdehydes 4, enedithioacetals 3 as well as the dianions 5. The dianion 5 is an acyl anion equivalent **5A** which can undergo a facile reaction with a variety of electrophiles as described in dithiane chemistry developed by Seebach and coworkers[1]. The hydroxydithioacetal 2 could also undergo dehydration under some specific reaction conditions to afford the corresponding enedithioacetal 3 which is again a potential precursor of the allylanions[2] 3A-C (Scheme 1).

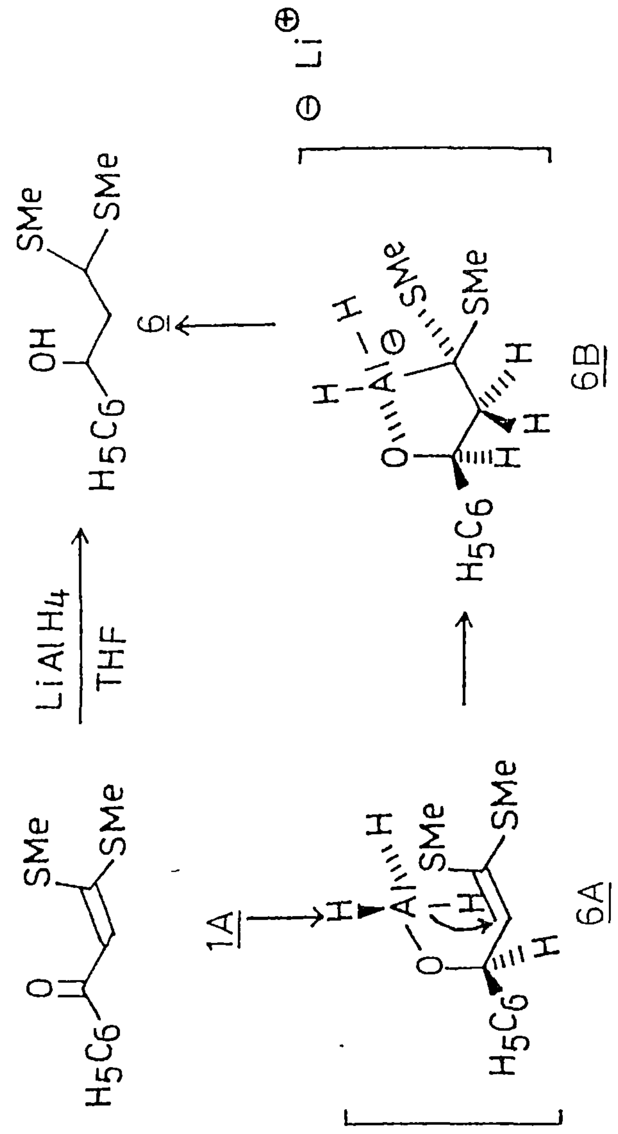
It was therefore decided to examine these possibilities with β-oxodithioacetals which are easily accessible from α-oxoketene dithioacetals by the methods described in the preceding chapter. Before the actual work is presented, the earlier status with regard to the β-hydroxydithioacetals and their chemistry described in the literature will be briefly discussed so that the present work can be evaluated for its merits as a method of preparative importance.

Gammill and coworkers[3] were the first to observe the lithium aluminium hydride reduction of α-oxoketene dithioacetals 1A to 6 in high yields. The hydroxydithioacetals 6 were obtained in diastereospecific manner since the initial 1,2-reduction product **6A** which underwent intramolecular hydroalumination through a cyclic transition state **6B** to afford 6 (Scheme 2).

Subsequently, Davey and coworkers[5] prepared a series of β-hydroxy cyclic acetals 9 from the reaction of 1,3-dithiane anion 7 with appropriate epoxides 8. These acetals 9 were



Scheme –1


H5C6
O
SMe
SMe
LiAlH4
THF
H5C6
OH
SMe
SMe
6
1A
H
Al
H
H
O
SMe
SMe
H5C6
H
6A
H
Al
H
O
SMe
SMe
H5C6
H
H
H
6B
⊖ Li⊕

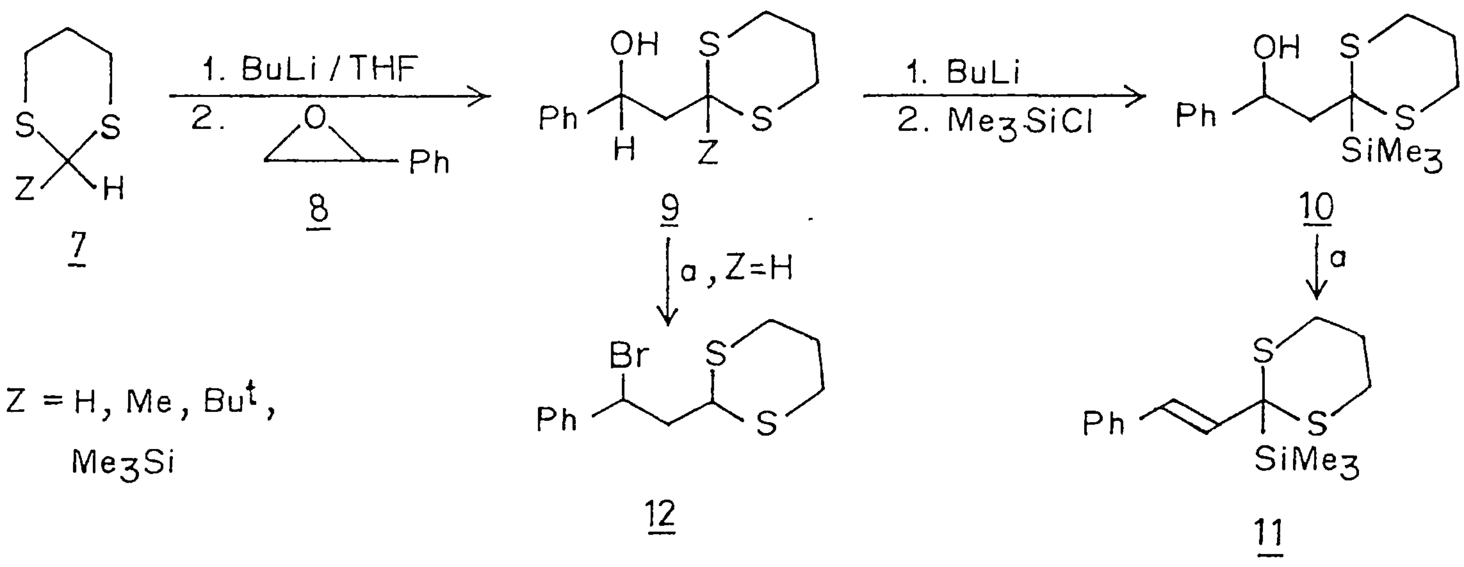
Scheme 2

subsequently deprotonated to generate the sulphur stabilized anions which were reacted with various electrophiles (Scheme 3).

In a similar sequence of reactions, Tarnchompoo *et al*[5] had described the *insitu* preparation of β-hydroxy dithioacetals **14** from the reaction of **13** with 1,3-dithiane **7** in the presence of n-butyllithium (Scheme 4). They have generated the dianion **16** from **14** using one more equivalent of base followed by the addition of ketone **15** which on subsequent intramolecular cyclization afforded the dithiane derivative of furanone **19**. The dethioacetalization of **19** ultimately gave the furanone **20** (Scheme 4).

The diethoxy epoxides **21** were also cleaved by dithiane anion followed by the addition of acetic anhydride to afford the corresponding β-acetoxyacetal derivatives[6] **22** (Scheme 5). These acetals were hydrolysed to the acetoxyaldehyde derivatives **23** which were further transformed to the γ-diethoxyenealdehydes **24**. It is interesting to note that in the presence of mercuric oxide only the thioacetal was cleaved while the oxyacetal functionality remained intact (Scheme 5).

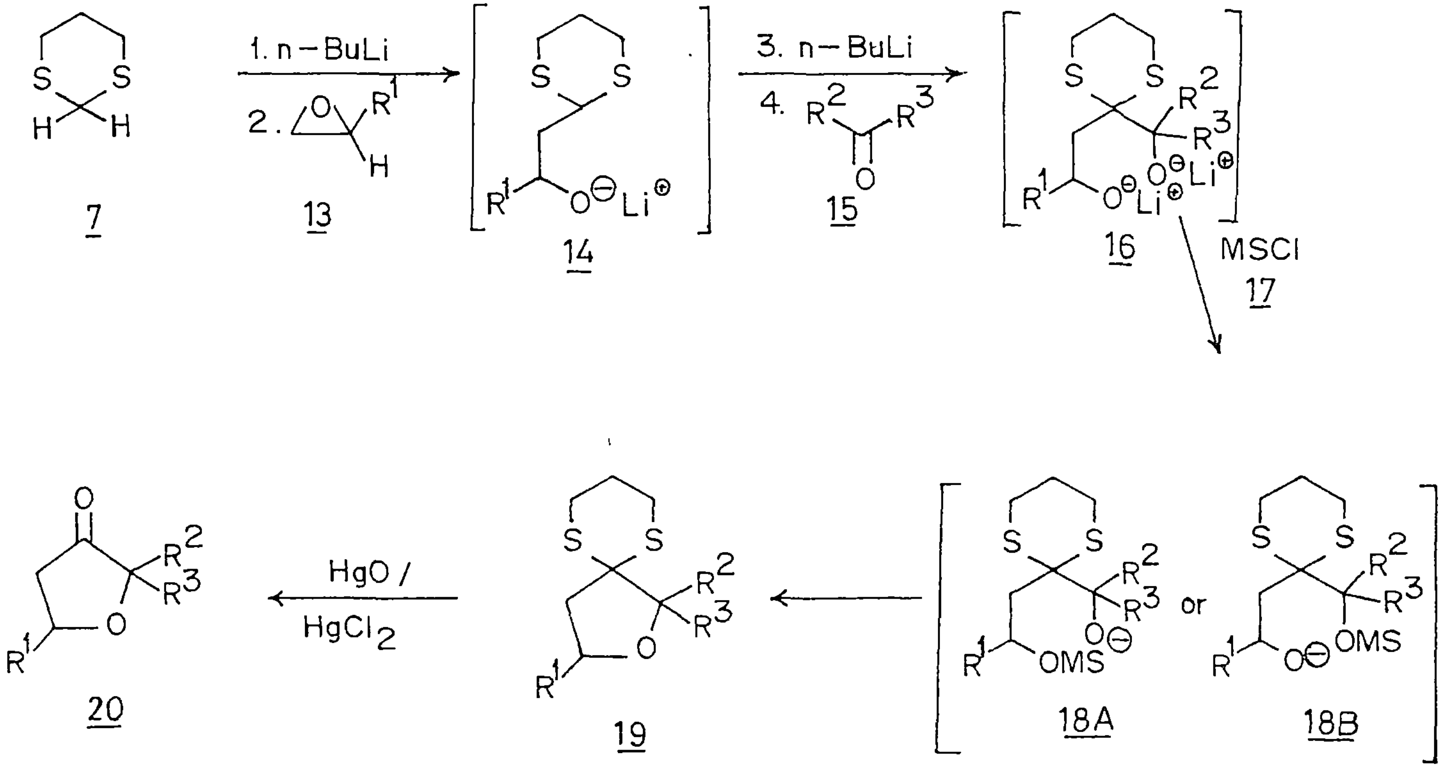
The above cited examples on the synthesis of β-hydroxyacetals apparently prove that there are only few methods available for the preparation of these intermediates. The most effective procedure appears to be that of cleavage of epoxides by the anions derived from dithianes.



Z = H, Me, Bu$^t$,
Me$_3$Si

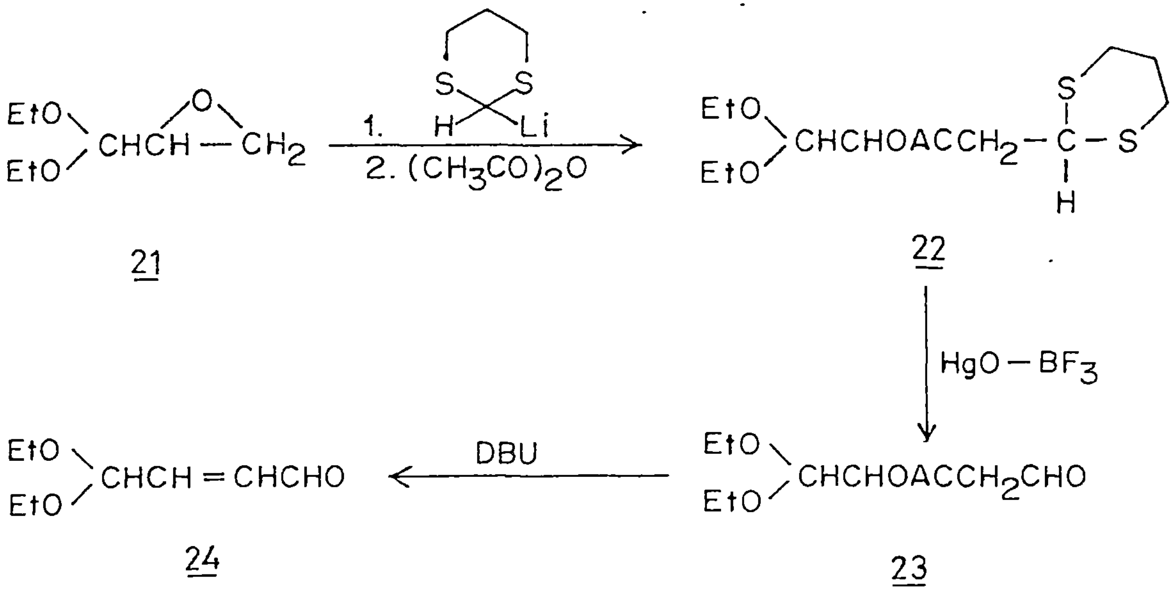
a, $Ph_3P / CBr_4$

Scheme 3



$R^1$ = H, Me, Ph ; $R^2$ = Me, Ph ; 4-MeO$C_6H_4$ ; $R^3$ = H, Me

Scheme – 4


EtO
EtO
CHCH — CH2
O
21
1. H Li S S
2. (CH3CO)2O
EtO
EtO
CHCHOACCH2 — C — S
S
H
22
HgO — BF3
EtO
EtO
CHCHOACCH2CHO
23
DBU
EtO
EtO
CHCH = CHCHO
24

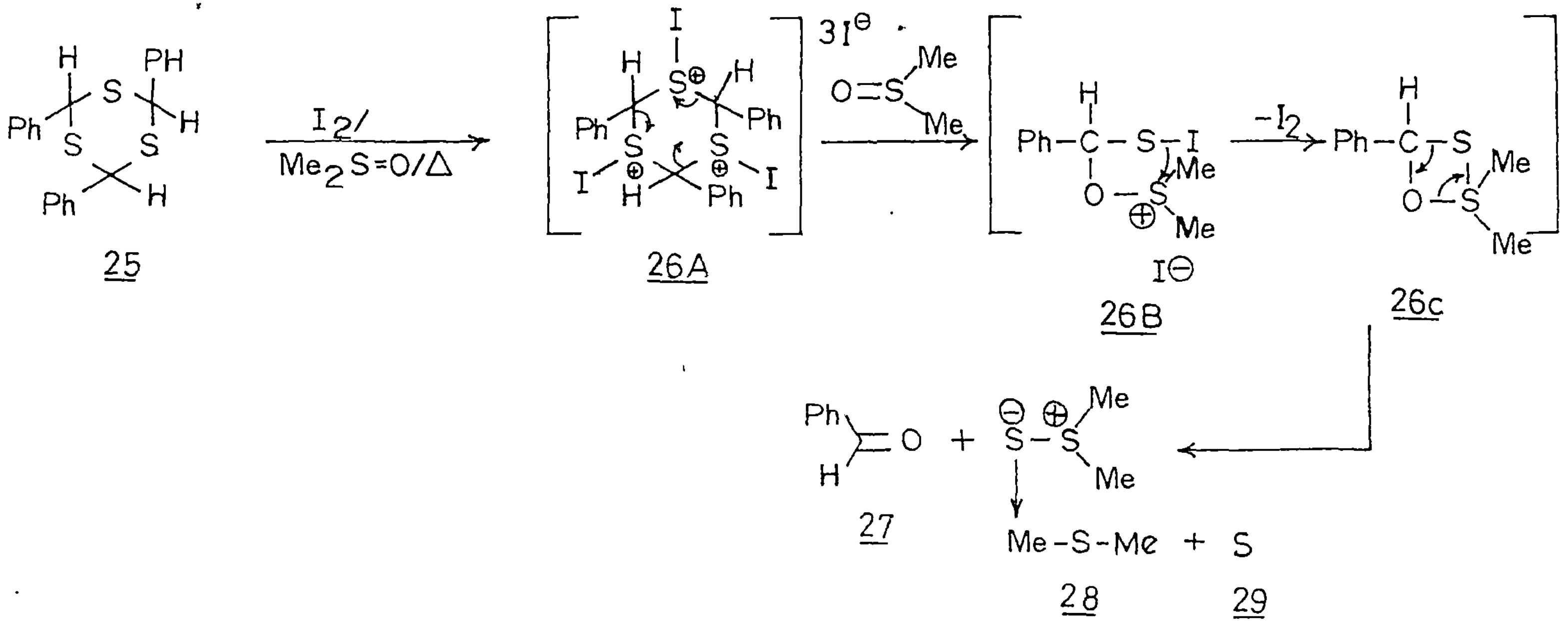
Scheme – 5

**Dethioacetalization Methods involving DMSO :**

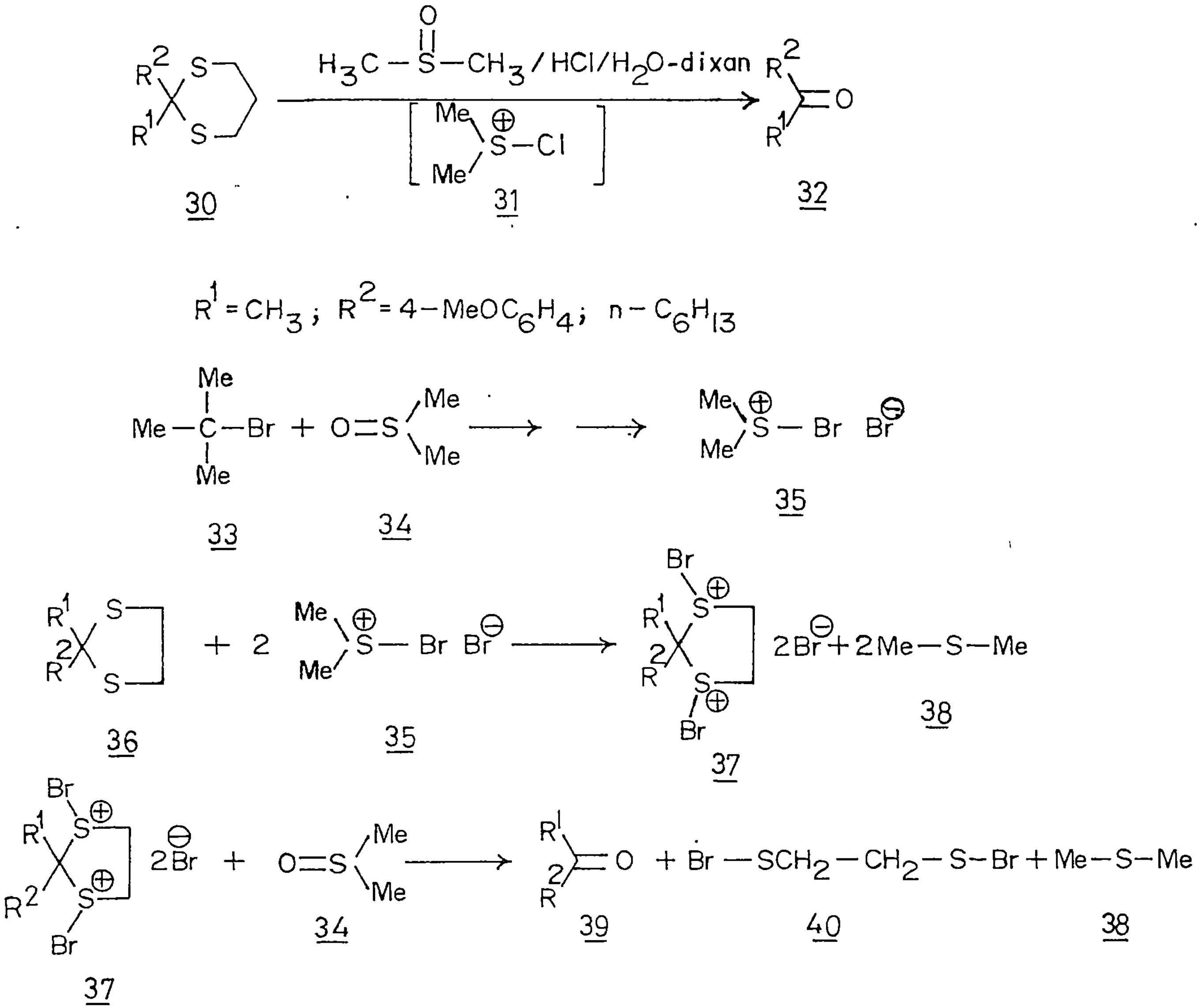
Since we are interested in examining the dehydration and the clevage of β-hydroxydithioacetals, the literature methods on the clevage of thioacetals are briefly illustrated in the following section. The thioacetals and thioketals are generally resistant to the acid hydrolysis and yield under these conditions the corresponding thiolesters. There have been several methods described in the literature on the use of transition metals to cleave the thioacetal and ketal linkages to the corresponding aldehydes and ketones.[24] However, dimethyl sulphoxide has been used variously in the presence of catalysts to achieve the cleavage of acetals and ketals and only those methods are described here.

Thus, Ramarao and coworkers[7] employed dimethyl sulphoxide in the presence of iodine to cleave the trithianes 25 to afford the corresponding aldehydes 27 (Scheme 6). They explained the mechanism involving the intermediacy of 26A which opened up on reacting with dimethyl sulphoxide to the aldehyde 27 alongwith atomic sulfur and dimethyl sulphide as depicted in Scheme 6.

Similarly the ketals 30 were cleaved to the corresponding ketones 32 on heating in dimethyl sulphoxide in the presence of hydrochloric acid in dioxane[8] (Scheme 7). Olah and coworkers[9] employed a novel approach to cleave the ketals 36 to the corresponding ketones 39 as formulated in Scheme 7. Thus, the dimethylsulphonium bromide 35 was formed on reacting tert-butyl bromide 33 with dimethyl sulphoxide which



Scheme — 6


H3C—S(O)—CH3/HCl/H2O-dixan
Me2S⊕—Cl
30
31
32
R1 = CH3; R2 = 4-MeOC6H4; n-C6H13
Me3C—Br + O=SMe2
33
34
Me2S⊕—Br Br⊖
35
36
35
37
2Br⊖ + 2Me—S—Me
38
37
2Br⊖
34
39
40
38
Br—SCH2—CH2—S—Br + Me—S—Me

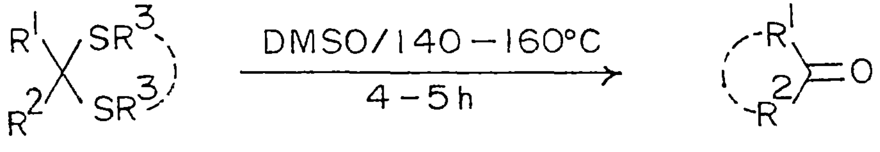
Scheme.— 7

on reaction with cyclic ketal 36 yielded the corresponding sulphonium bromide 37. The 37 ultimately underwent thioketal ring opening on reaction with one more molecule of dimethylsulphoxide to afford the corresponding ketones 39 in high yields (Scheme 7).

Interestingly, in our laboratory we have recently observed that the cleavage of the acetals and ketals by dimethyl sulphoxide[10] under thermal conditions need not necessarily associated by any catalysts. Thus, the acetals or ketals 41 on merely heating with dry dimethyl sulphoxide at 140-150°C afforded aldehydes or ketones 42 in high yields as shown in Scheme 8.

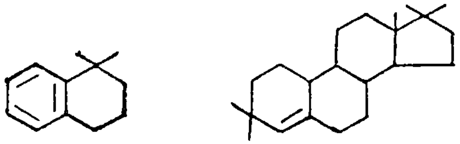
## III. Related Literature Methods of the Synthesis of Ene- and Polyenealdehydes.

Development of methods for polyenealdehydes is an important synthetic transformation since there are many natural products that contain polyenealdehyde functionality. Akiyama and coworkers[11] developed an efficient method for the synthesis of dienealdehydes 48 through the sequence of reaction described in Scheme 9. The acetylacetylene 43 underwent Michael addition with butanethiol to afford the corresponding products 44. The condensation of 44 with aldehydes 45 in the presence of a base afforded 46. They were either reduced with lithium aluminium hydride or reacted with organolithium compounds to afford the corresponding carbinols 47 which were finally dethioacetylated to the dienealdehydes

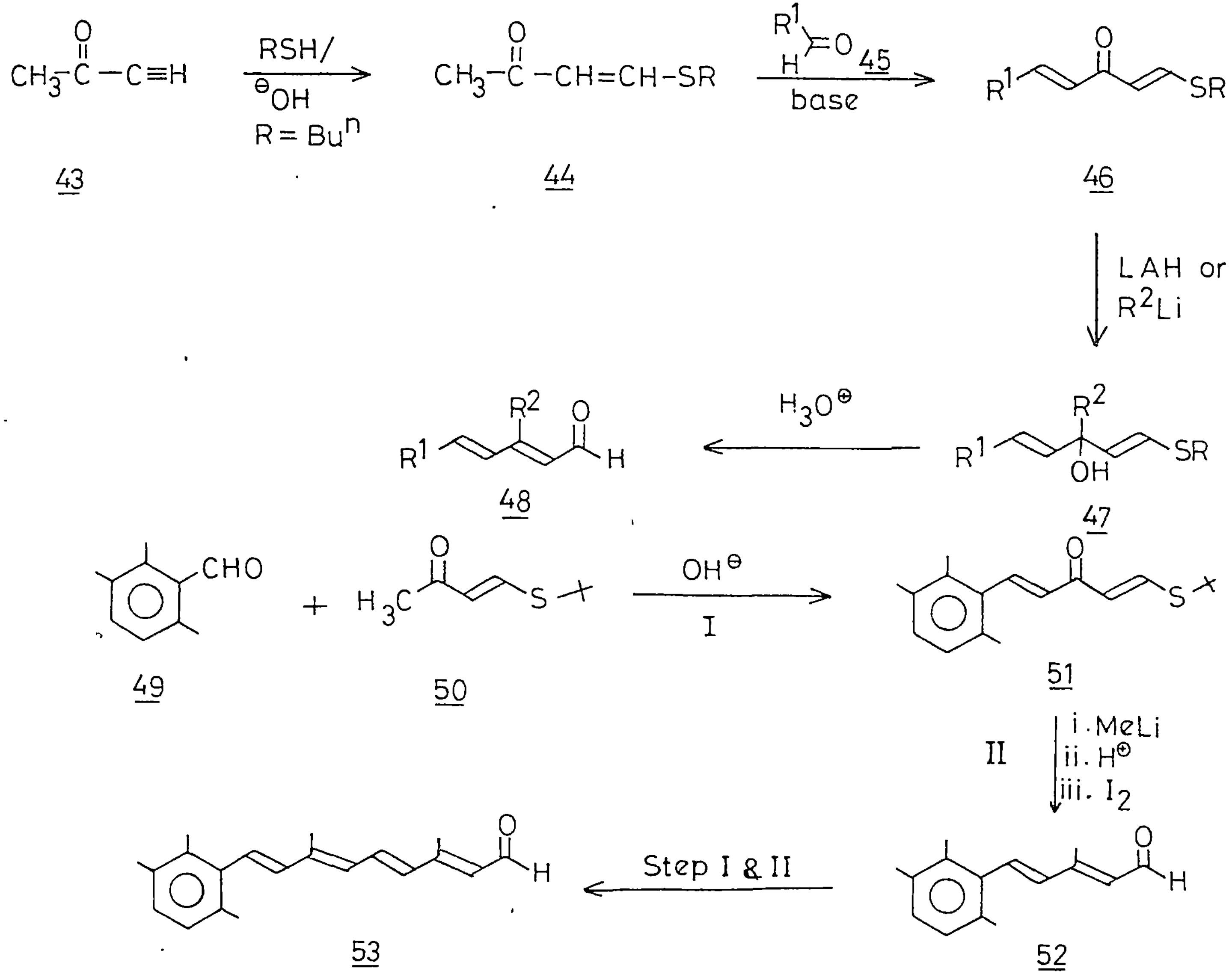


41 42

$R^1 = C_6H_5$; $C_6H_5-CH=CH-$; Et; $Me(CH_2)_2-$; $Me(CH_2)_{10}$; $R^2 = H$; Me, Et

$R^1 = R^2 = -(CH_2)_5-$;  66–94%

Scheme 8



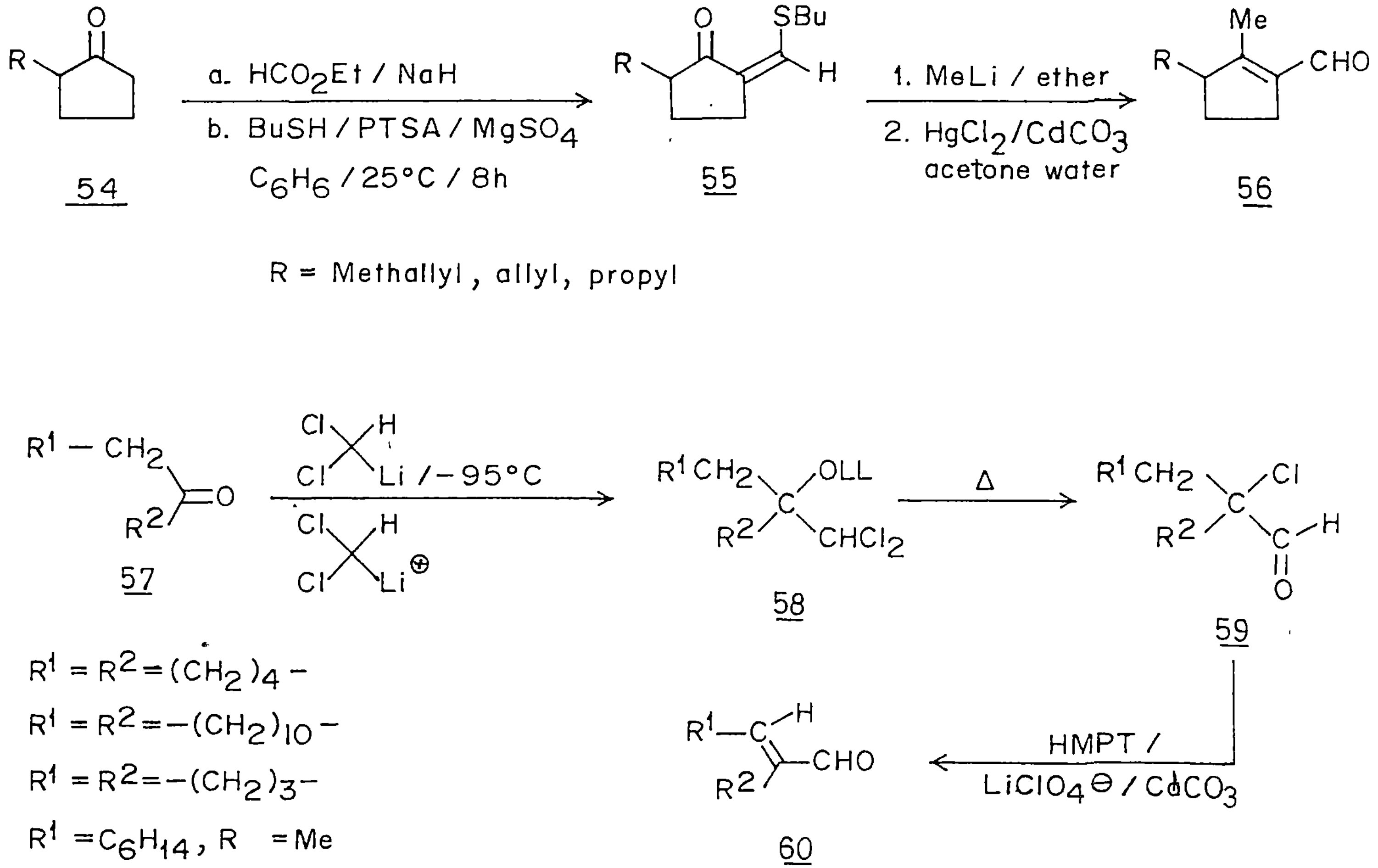
Precursor for Isorenieratene **Scheme 9**

48 in good yields. The transformation from 46 to 48 involves 1,3-carbonyl transposition. The same strategy was extended for the synthesis of natural product precursor Isorenieratene 53. Thus, trimethylbenzaldehyde 49 was condensed with 50 to give the corresponding derivative 51 which on the addition of methyllithium followed by hydrolytic carbonyl transposition afforded the corresponding dienaldehyde 52. The 52 on repetition of the reaction sequence described above yielded the corresponding product 53.

Marshall and coworkers[12] were the first to observe that the butylthiomethylene ketones undergo exclusive 1,2-reduction or addition in difference to the corresponding oxygen analogs to afford the corresponding 1,2-adducts. These adducts on hydrolytic cleavage in the presence of mercury salts afforded the corresponding enealdehydes in excellent yields. Similarly Bernstein and coworkers[13] extended these studies for the synthesis of 56 starting from 54 through the Marshall's intermediate 55 (Scheme 10).

Taguchi and associates[14] achieved the synthesis of enealdehyde 60 by reacting lithiomethylene chloride with ketone 57 to yield the corresponding adduct 58 which on heating gave the corresponding chloraldehyde 59. This on treatment with lithium perchlorate in the presence of cadmium carbonate in HMPT afforded the corresponding enealdehyde 60 (Scheme 10).

Similarly, Duhamal and coworkers developed an efficient method for enealdehydes. Thus the lithio derivatives of



54 55 56

R = Methallyl, allyl, propyl

57 58 59 60

$R^1 = R^2 = (CH_2)_4-$

$R^1 = R^2 = -(CH_2)_{10}-$

$R^1 = R^2 = -(CH_2)_3-$

$R^1 = C_6H_{14}$, R = Me

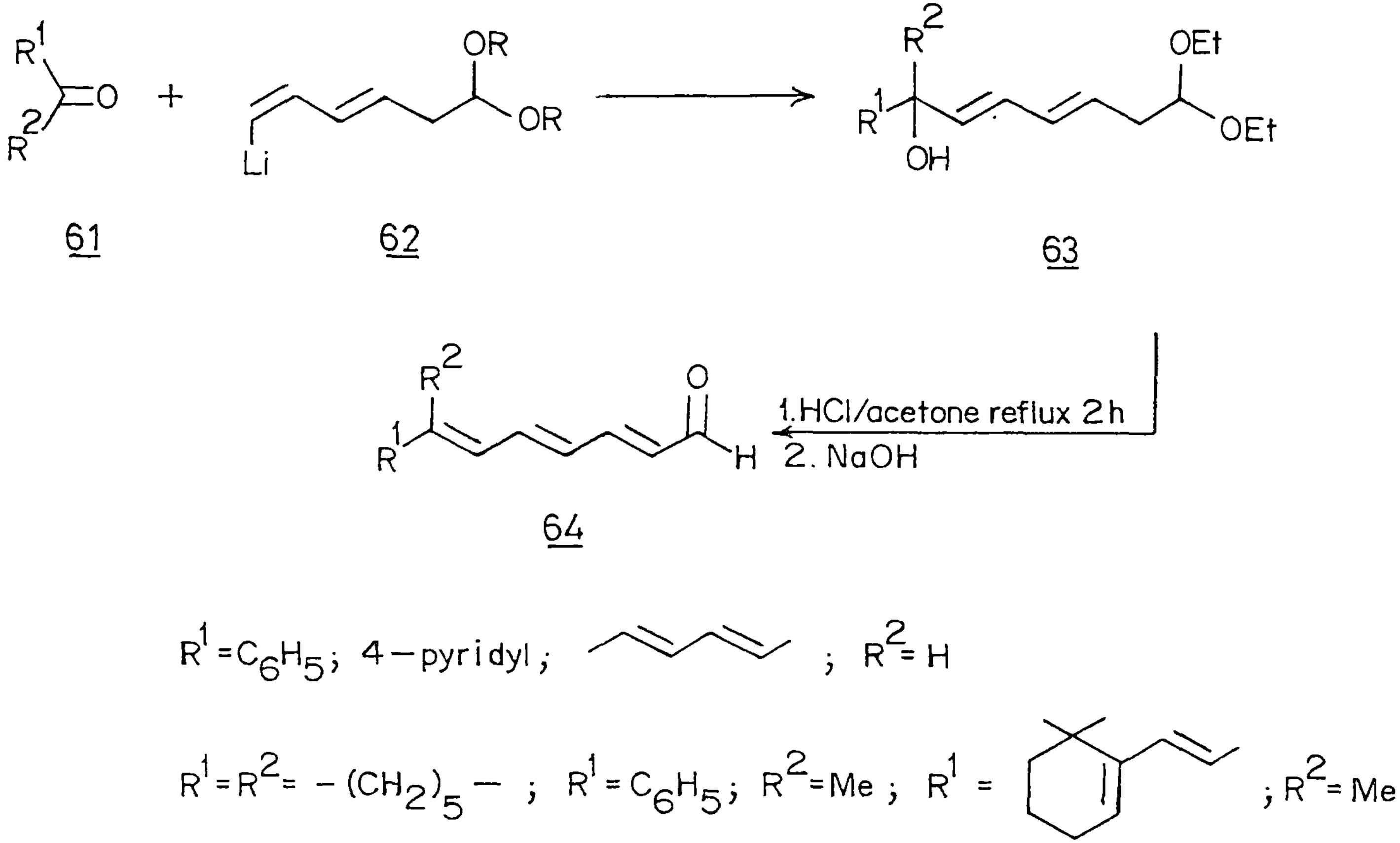
Scheme-10

hexadiene acetals 62 were added to ketones 61 to give the corresponding hydroxy O,O-acetals 63 which were cleaved by sequential acid and base assisted elimination and hydrolysis to afford the trienealdehyde 64 (Scheme 11).

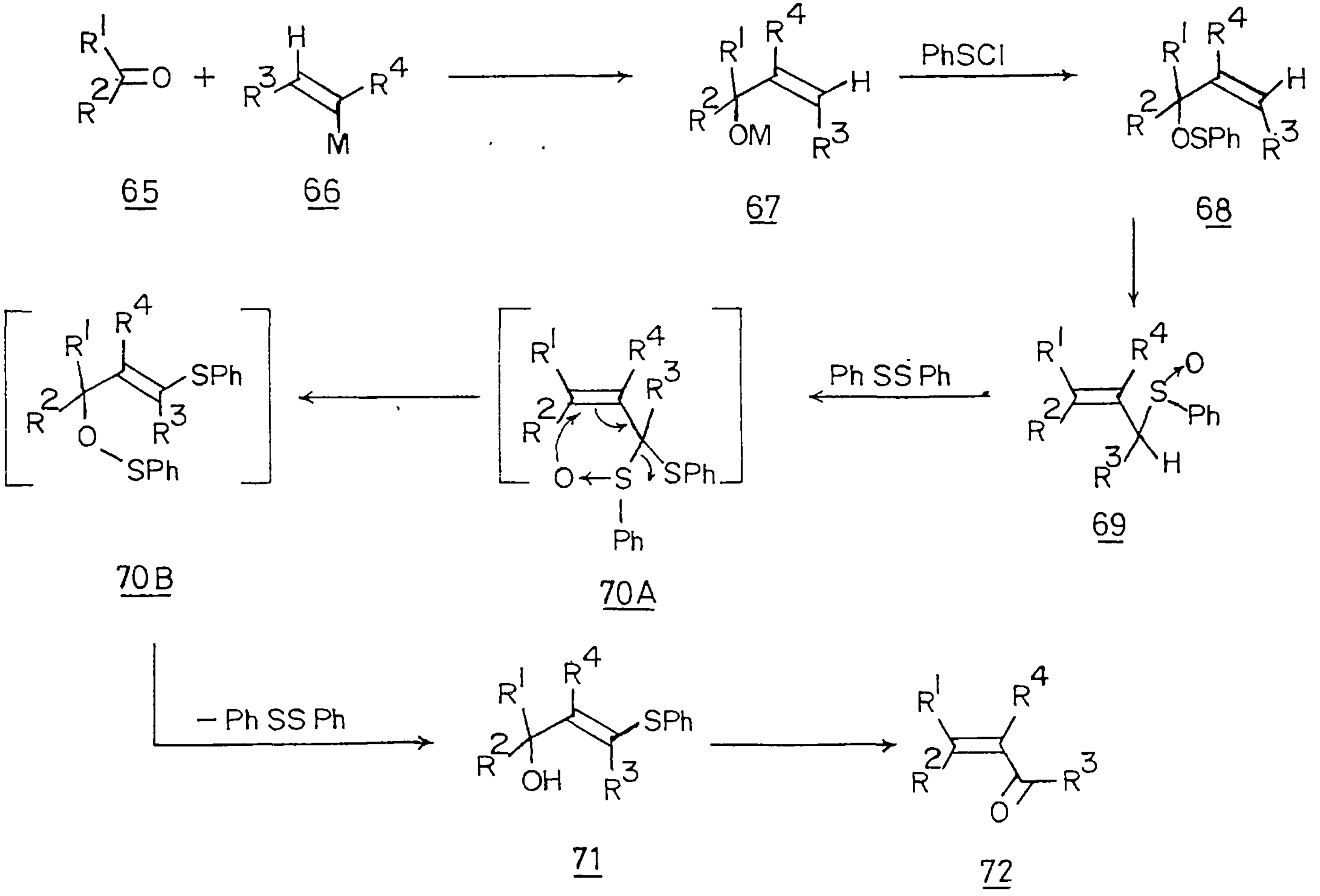
Trost and his associates[16] developed an interesting sequence of 1,3-carbonyl transposition for the synthesis of enealdehydes and enones. Thus, the anion 66 on addition to ketone 65 gave the corresponding allylalcohol 67 which on reaction with phenylsulphenyl chloride followed by rearrangement to afford the corresponding sulphoxide 69. The latter on treatment with diphenyldisulphide rearranged to give 70B which ultimately cleaved to afford the corresponding phenylthiomethylene carbinols 71. The subsequent hydrolytic cleavage of 71 through 1,3-carbonyl transposition afforded the corresponding enones 72 in good yields (Scheme 12).

## RESULTS AND DISCUSSION

An excellent method for the reduction of α-oxoketene dithioacetals to the corresponding β-oxodithioacetals has been developed as described in Chapter II. These β-oxodithioacetals have also been shown to be attractive 1,3-dielectrophilic precursors for the construction of aromatic rings by reacting them with various allylanions followed by acid assisted cycloaromatization. The method was shown to be highly efficient for the construction of sulphur free benzenoids and condensed aromatics. These results have been described in the Chapter III and IV of the present


61
62
63
64
R1
R2
O
OR
OR
Li
OEt
OEt
OH
H
1.HCl/acetone reflux 2h
2. NaOH
R1 = C6H5; 4-pyridyl; ; R2 = H
R1 = R2 = -(CH2)5- ; R1 = C6H5; R2 = Me ; R1 = ; R2 = Me

Scheme-11

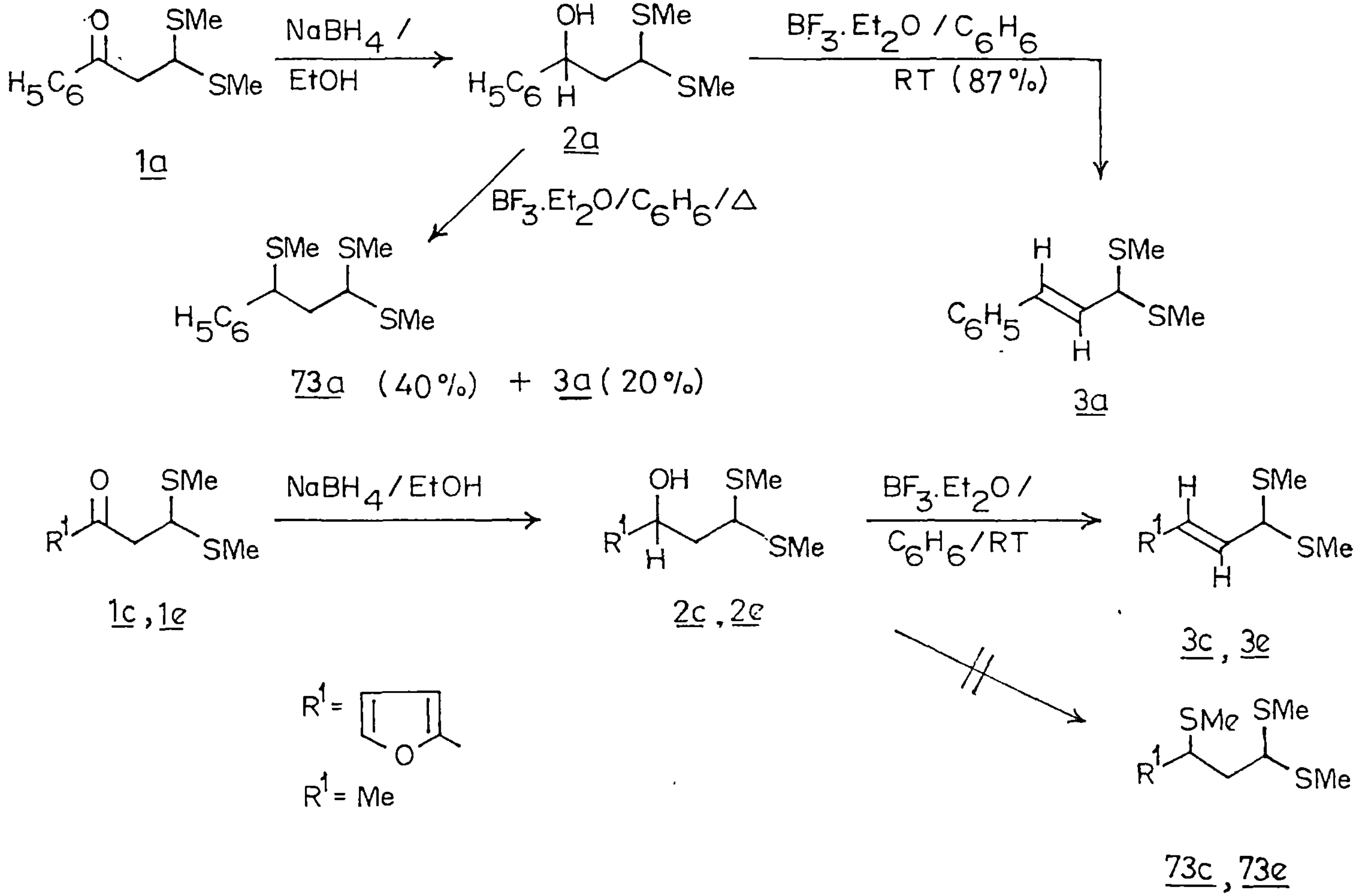


Scheme –12

investigation. It was further considered of interest since these β-oxodithioacetals could be important intermediates for transforming them to the corresponding β-ketoaldehydes under appropriate reaction conditions. In the present investigation they have been conveniently reduced by subjecting them to sodium borohydride in ethanol to afford the corresponding β-hydroxydithioacetals. These intermediates have been shown to undergo either selective dehydration to afford the corresponding enedithioacetals or they can be converted to the corresponding enealdehydes or enones under suitable reaction conditions involving concomitant dehydration and dethioacetalization. These successful experimental results have been described in the present chapter.

**Attempted Dehydrative Studies of β-Hydroxydithioacetals.**

The β-oxodithioacetals 1 were reduced with sodium borohydride in ethanol to afford the β-hydroxydithioacetals 2 in quantitative yields (scheme 13). In one case, 2a was isolated and characterized while in the subsequent experiments the hydroxy compounds were carried to the next step *in situ* so that the overall transformation was reduced to one pot protocol. The structure of β-hydroxydithioacetals 2a was established on comparison with the reported analytical and spectral data[3]. Several experiments were conducted to study the mode of dehydration without cleaving the dithioacetal functionality to get the corresponding enedithioacetals 3. However, the attempts to dehydrate 2a to enedithioacetal 3a using many dehydrating agents such as iodine in benzene,

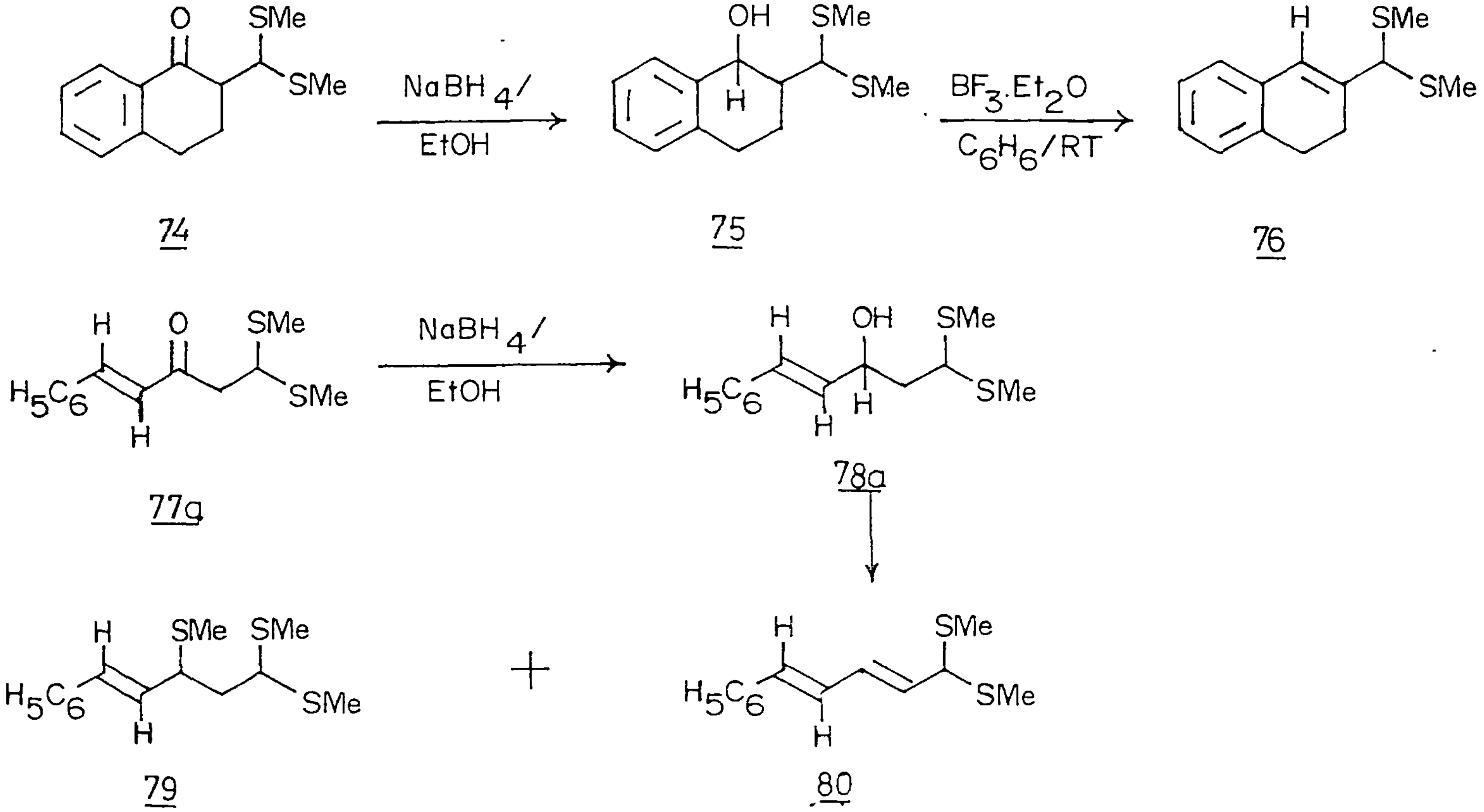

NaBH4 / EtOH
BF3.Et2O / C6H6 RT (87%)
BF3.Et2O/C6H6/Δ
1a
2a
3a
73a (40%) + 3a (20%)
NaBH4/EtOH
BF3.Et2O / C6H6/RT
1c, 1e
2c, 2e
3c, 3e
73c, 73e
R1 =
R1 = Me

Scheme–13

p-toluenesulphonic acid, pyridinium tosylate,acetic anhydride, potassium bisulphite, $POCl_3$/ DMF, pyridine etc. yielded only unsatisfactory results. Recently Posner *et al*[17] have reported an efficient method for the regioselective and controlled dehydration of tertiary alcohols under very mild conditions employing $BF_3.Et_2O$. This has prompted us to examine the dehydration of β-hydroxydithioacetals using $BF_3.Et_2O$. Interestingly, when 2a was treated with borontriflouride etherate complex in refluxing benzene it afforded a mixture of 3a and 73a in 20% and 63% yields respectively (Scheme 13). The structure of 3a was established on the basis of its spectral and analytical data. It showed in its infra red spectrum strong bands at 2900, 1605 and 1440 $cm^{-1}$. In its $^1H$ NMR spectrum in $CCl_4$, the signal at δ 2.21 (6 protons ) was assigned to the two methylthio group protons and the doublet at δ 4.32 for 1H with J=9Hz was assigned to the hydrogen attached to the bismethylthio carbon atom. The double doublet at δ 6.20 with J=12Hz, J=9Hz, was assigned to the α-vinylic proton while the doublet at δ 6.62 corresponds to the other vinylic proton. The aromatic protons (5H) appeared as a multiplet between δ 7.26-7.64. Similarly, the structure of hitherto unreported 73a was characterized on the basis of its spectral and analytical data (experimental section).

However, in an effort to avoid the formation of 73a alongwith the desired 3a, the $BF_3.Et_2O$ assisted reaction was carried out at room temperature instead of heating could result in the exclusive formation of only the desired enedithioacetal 3a. Thus, it was possible to achieve selective dehydration of 2a to afford the enedithioacetal 3a in 89% yield. Similarly 3c and 3e were obtained in 51% and 54% yields respectively. The dithioacetal moiety under these conditions was found to be unaffected and remained intact thereby permitting the procedure to effect only dehydration. As already discussed in the preceding section, in view of the nonavailablity of methods in the literature for the selective dehydration in the presence of an acetal or ketal group, the present method thus attains much synthetic importance. The procedure was successful in affording the 2,2-bis(methylthio)methyl 3,4-tetrahydronaphthalene 76 from the reaction of corresponding β-hydroxydithioacetal derived from tetralone 75 with $BF_3.Et_2O$ at room temperature under controlled conditions. The structure was assigned on the basis of its spectral and analytical data. The styryl hydroxydithioacetal 78a however afforded a mixture of enedithioacetal 80 and the corresponding trimethylthio compound 79 under identical conditions in 40% and 25% yields respectively (Scheme 14).

Therefore, it is evident from the above examples that the β-hydroxydithioacetals could be transformed selectively to the corresponding enedithioacetals retaining the dithioacetal protecting group. The methodology is of considerable importance since the product enedithioacetals are excellent precursors of allylanions for regiospecific addition studies.


NaBH4/
EtOH
BF3.Et2O
C6H6/RT
NaBH4/
EtOH
74
75
76
77a
78a
79
80
SMe
OH
H5C6

Scheme—14

## Concurrent Dehydration and Dethioacetalization of β-Hydroxydithioacetals to α,β-Unsaturated Aldehydes :

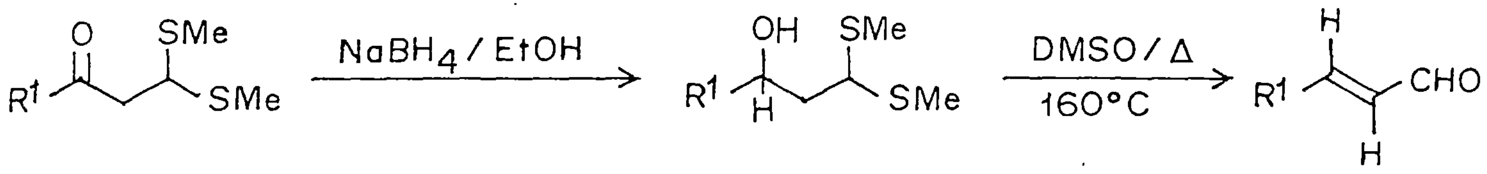
Subsequent to our above described dehydration studies, we were intrigued to examine the β-hydroxydithioacetals 2 could be transformed into the corresponding enealdehydes directly in one pot reaction under suitable reaction conditions since many possibilities exist to achieve this transformation. Recently, we have observed in this laboratory a facile cleavage of the dithioacetal protecting groups using neutral dimethyl sulphoxide under thermal conditions to afford the corresponding aldehydes or ketones in high yields[10]. We therefore proposed to extend this interesting dethioacetalization methodology so as to achieve a single pot conversion of β-hydroxydithioacetals to the corresponding enealdehydes thus simultaneously effecting both dehydration and cleavage of the dithioacetal group. We have indeed achieved this one pot successful operation of converting β-hydroxydithioacetals directly into their corresponding α,β-unsaturated aldehydes. The results from these experiments are presented here.

Thus, β-hydroxydithioacetal 2a on heating with four-fold excess of dimethyl sulphoxide at 150°C afforded the corresponding cinnamaldehyde 4a in 90% yield. The struture of the product was in full agreement with the aunthetic sample of cinnamaldehyde and the geometry has been shown to be in exclusive *trans* form. The reaction was found to be very clean without any side products. The procedure successfully afforded the enealdehydes 4b-e in 64-92% overall yields from the corresponding β-hydroxydithioacetals 2b-e under similar reaction conditions. All these enealdehydes 4b-e which are known in the literature and found to be in full confirmity with their spectral and analytical data as described in experimental section (Scheme 15).

It was observed that any deviation from the described reaction conditions would result in unsatisfactory results. Thus, when 2a was heated in DMSO at 110°C rather than at 150°C, it ended up in a mixture of products comprising of 3a and 73a in 41% and 34% yields respectively.

The cyclic β-hydroxydithioacetal 82 also underwent the described transformation smoothly to afford the corresponding cyclohexene carboxaldehyde 83 in 65% yield (Scheme 15). Its structure was confirmed by its spectral and analytical data and found to be in full agreement with the reported values. Similarly, the 3,4-dihydronaphthalene-2-carboxaldehyde 84 was obtained in 63% yield under identical reaction condition from the corresponding hydroxydithioacetal 75 (Scheme 16).

The 1,1-bis(methylthio)-3-hydroxy-5-phenyl-4-pentene 78a derived from 77a also underwent the desired transformation to afford the corresponding dienealdehyde 85a in 86% yield (scheme 16). Apparently, since the reaction conditions are neutral, the described transformation is providing attractive yields of enealdehydes without leading to undesirable tar and other side products. The structure of 85a was established



1a,e 2a,e 4a-e

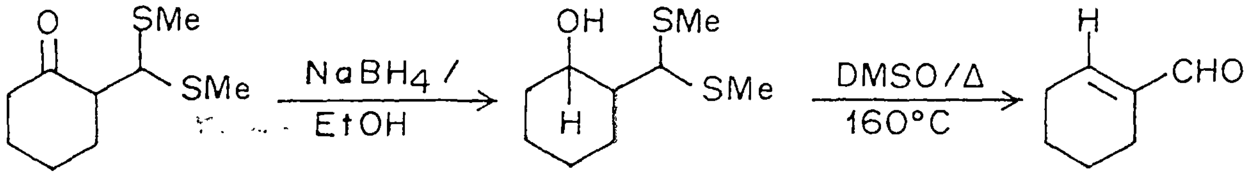
1,2a, 4a, $R^1 = C_6H_5$

1,2b, 4b, $R^1 = 4\text{-}MeOC_6H_4$

1,2c, 4c, $R^1 = 2\text{-}$Furyl

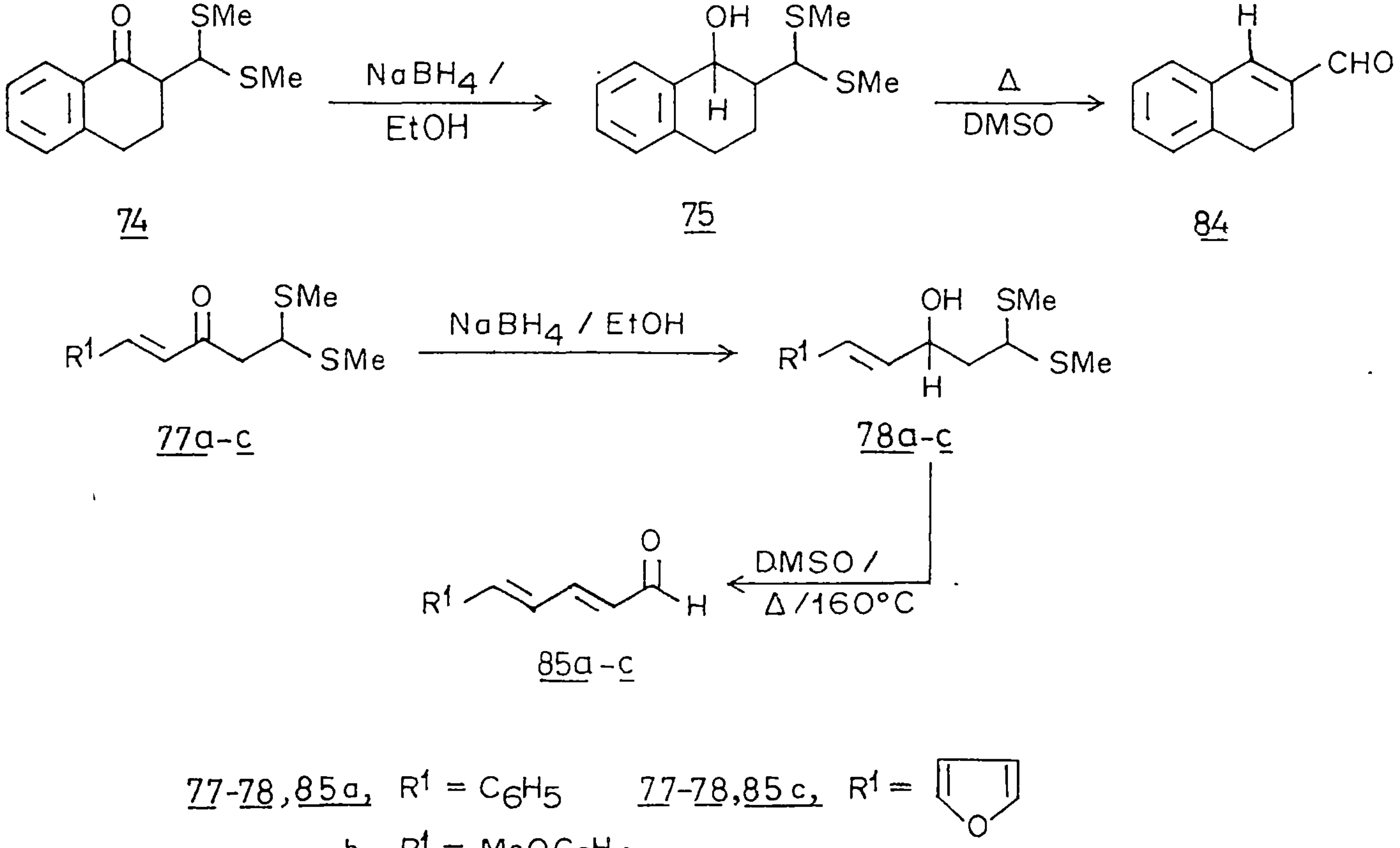
4d, $R^1 = 2\text{-}$Thienyl

4e, $R^1 = Me$



81 82 83

Scheme –15

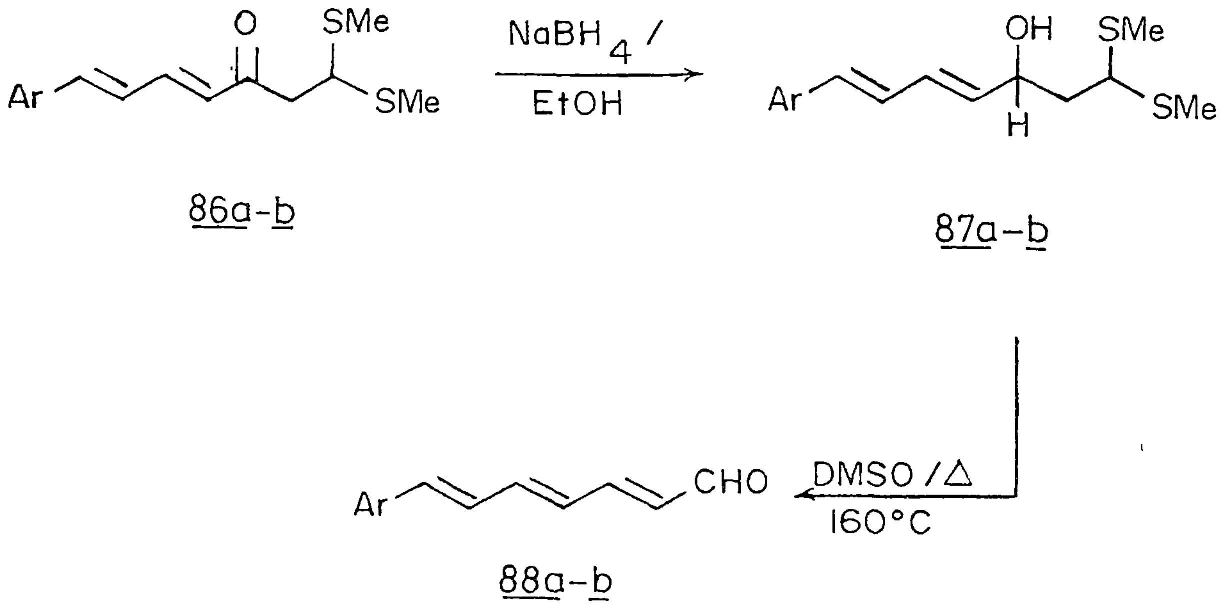

O
SMe
SMe
NaBH4 /
EtOH
OH
SMe
H
SMe
Δ
DMSO
H
CHO
74
75
84
O
SMe
R1
SMe
NaBH4 / EtOH
OH
SMe
R1
H
SMe
77a-c
78a-c
O
DMSO /
Δ /160°C
R1
H
85a-c
77-78,85a, R1 = C6H5
b, R1 = MeOC6H4
77-78,85c, R1 =
O

Scheme — 16

from its spectral and analytical data and by comparison with the reported data in literature (experimental Section). The dienealdehyde **85b** and **85c** were obtained in 89% and 81% yields respectively following the same procedure from the corresponding β-hydroxydithioacetals **78b** and **78c**. Their analytical and spectral data were found to be in agreement with the reported values in the literature. Again it should be noted that **85c** with furan ring, which is acid sensitive could be obtained in 89% yield due to the fact that the overall transformation was performed under neutral conditions (scheme 16).

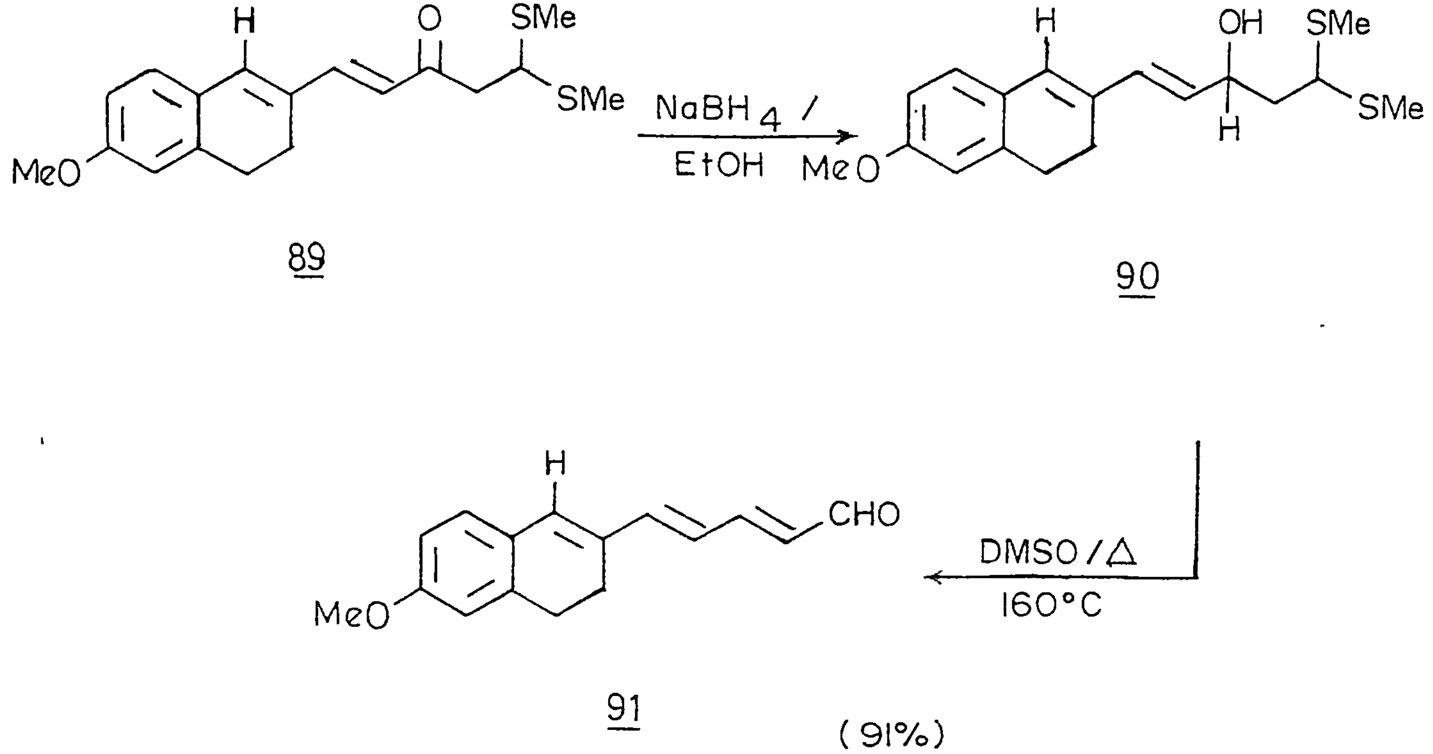
This became further evident when the reaction was extended to the synthesis of trienealdehydes. Thus, **87a** and **87b** on heating with DMSO at 150°C smoothly underwent the described transformation to afford the corresponding trienealdehydes **88a** and **88b** in 72% and 81% respectively (Scheme 17). Both these trienealdehydes were found to be identical with those reported in the literature (Experimental section). The cyclic trienealdehyde **91** was also obtained in 91% yield from the corresponding hydroxyacetal **90** as described in Scheme 18. The reported data of **91** were identical with the product obtained through this transformation (Experimental Section).

Subsequently, we have decided to study this transformation using hydroxydithioacetals obtained from the addition of methyl and phenyl Grignard reagents to the β-oxodithioacetals. Thus, the β-hydroxydithioacetal **92a**, derived from the addition of methylmagnesium iodide to the



86, 87, 88 a, Ar = $C_6H_5$
b, Ar = 4−MeO $C_6H_4$

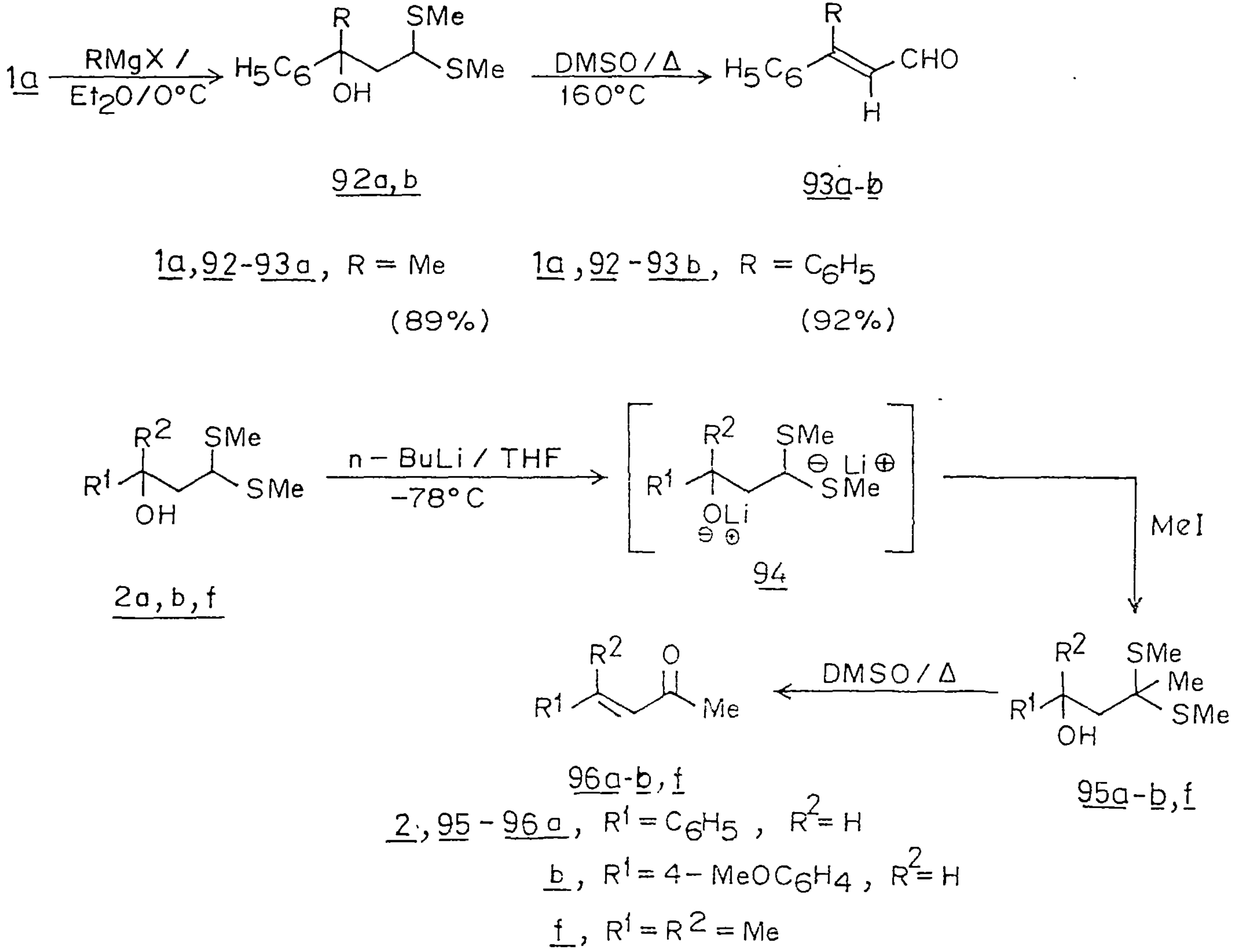
Scheme — 17


H
O
SMe
SMe
MeO
89
NaBH4 /
EtOH
H
OH
SMe
SMe
H
MeO
90
DMSO / Δ
160°C
H
CHO
MeO
91
(91%)

Scheme –18

corresponding β-oxodithioacetal 1a, which on heating with DMSO under similar reaction conditons afforded the β-methylcinnamaldehyde 93a in 89% yield. Similarly, the β-hydroxydithioacetal 92b afforded the corresponding β-phenyl substituted cinnamaldehyde 93b in 92% yield (scheme 19). The structure of these products were established by comparing their spectral and analytical data with those reported in the literature.

The homologation of the aldehydes to the corresponding α,β-unsaturated aldehydes is an important synthetic operation.[18,19] These aldehydes form an important group of useful organic molecules in perfumes and other naturally occuring organic compounds. There are numerous methods described in the literature for the transformation of aldehydes into their corresponding α,β-unsaturated aldehydes and their polyenealdehyde analogs.[11,19-20] Many of these methods employ drastic reaction conditions which often affect the overall yeilds of the product enealdehydes.[1,24] Particularly, the polyenealdehydes which are sensitive to the drastic reaction conditions and thus require careful and mild conditions for their efficient synthesis. Various methods described in the literature for enealdehydes and their limitations cannot be described here since they have been already discussed in many comprehensive reviews in recent years.[20-23] It may be noted that the method described here for the synthesis of enealdehydes and polyenealdehydes is perhaps the most appropriate in terms of its employed reaction conditions, particularly for the synthesis of



1a, 92-93a, R = Me (89%)  1a, 92-93b, R = $C_6H_5$ (92%)

2, 95-96a, $R^1 = C_6H_5$, $R^2 = H$

b, $R^1 = 4-MeOC_6H_4$, $R^2 = H$

f, $R^1 = R^2 = Me$

Scheme — 19

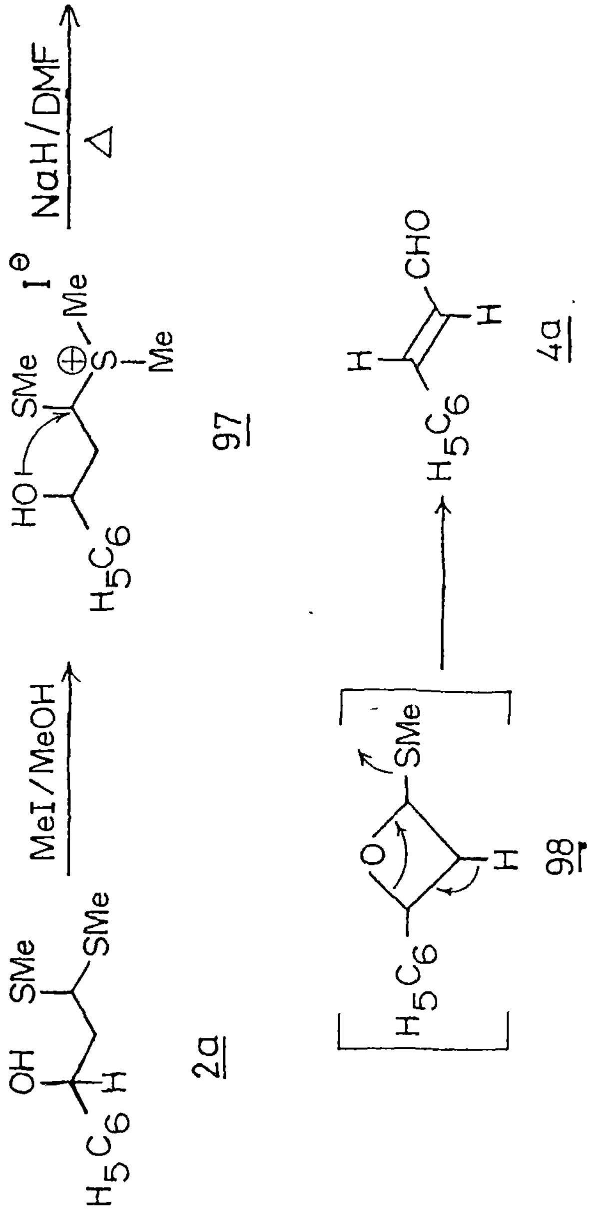
polyenealdehydes. It is therefore, expected that the present approach would be the method of choice for the homologation of aldehydes into enealdehydes. The other applications of this method to many natural aldehydes is being currently investigated since the structural diversity in the products obtained from this method amply demonstrate the success of this methodology.

The β-hydroxydithioacetals were next examined for their deprotonation and alkylation studies in order to prepare the alkylsubstituted hydroxydithioacetals which under the described reaction conditions should afford the α,β-unsaturated ketones. Thus, when **2a** was treated with an excess of n-butyllithium yielded the dianion **94** which on subsequent alkylation *in situ* afforded the corresponding β-hydroxydithioketal **95a** in quantitative yield. This ketal **95a** when heated in DMSO at 150°C resulted in the corresponding enone **96a** in 81% yield. The structure of **96a** was confirmed from its spectral and analytical data and also by comparing with the reported values in literature. Similarly, the enones **96b** and **96f** were obtained following the reaction sequence depicted in Scheme 19. Their structures were established on the basis of their spectral and analytical data (Experimental Section). Apparently, the masked aldehyde functionality can be easily converted to the keto function. Thus, the versatile β-hydroxydithioacetals can also be used as useful precursors to the corresponding β-hydroxyketals and their conversion to the corresponding enones. However, when higher alkyl halides were used for alkylation to afford the corresponding ketals under the described reaction conditions, the results were unsatisfactory.

Alternatively, another approach for the transformation of β-hydroxydithioacetals to enealdehydes under mild reaction conditions was successfully attempted. Thus, β-hydroxydithioacetal **2a** was quarternized with methyl iodide in methanol to afford the corresponding sulphonium iodide **97** in quantitative yield. This sulphonium salt when reacted with sodium hydride in DMSO at 60°C yielded the cinnamaldehyde **4a** in 92% yield. The reaction was very clean and the overall transformation was thus achieved under very mild conditions. It appears that the oxetane **98** may be the probable intermediate which spontaneously cleaves to the respective enealdehydes. However, extensive studies on this transformation are underway.

Thus the combination of this method and the described method earlier should serve as useful procedure for making enealdehydes and polyenealdehydes.

In conclusion, we have developed a facile high yield procedure for the transformation of β-hydroxydithioacetals to ene- and polyenealdehydes as well as enones by their one pot thermal dehydration and dethioacetalization with dimethyl sulphoxide. The usual methods for ene- and polene aldehydes involve multistep reaction sequences and drastic reaction conditions for the dethioacetalization[24]. Dimethyl sulphoxide, which has been shown to be a useful reagent for



Scheme —20

dehydration of alcohols [25] and hydrolysis of 1,3-dithianes and dithioacetals[10] could also successfully effect the concurrent dehydrative dethioacetalization of β-hydroxydithioacetals as described in the present investigation.

## EXPERIMENTAL SECTION

Melting points were recorded on a 'Thomas Hoover' capillary melting point apparataus and are uncorrected. IR spectra were obtained on a Perkin Elmer-297 spectrophotometer. The $^1H$ NMR spectra were recorded on a Varian EM-390 (90MHz) spectrometer using TMS as internal standard and chemical shifts are expressed in δ (ppm) units downfield from TMS. Elemental analysis were performed on a Heraeus CHN-O-Rapid elemental Analyzer.

Commercially available AR grade DMSO was dried by refluxing over calcium hydride followed by distillation under reduced pressure (b.p. 83°C/17mm).[25b] The pH of DMSO was determined by Systronics Digital pH meter-335 prior to use and found to be neutral. All the strating β-oxodithioacetals were prepared according to the procedures described in chapter II.

### General Procedures

### (a) Reduction of β-Oxodithioacetals by $NaBH_4$/EtOH : Synthesis of β-Hydroxydithioacetals :

The reduction procedure of 1a to 2a is representative. To a well stirred solution of 1a (10mmol) in absolute ethanol

(30mmL), $NaBH_4$ (20mmol) was added and the contents were refluxed for 2h., monitored by TLC. The ethanol was evaporated and the residue was poured over a saturated $NH_4Cl$ solution (50mL). It was extracted with $CHCl_3$ (2x25mL), washed with water (3x50mL), dried over $Na_2SO_4$ and concentrated to give 2a in quantitative yield. The column chromatography of the crude carbinol on silica gel using EtOAc-hexane (97:3) afforded 2a in very pure form. The spectral and analytical data is given below.

**α-[2,2-Bis(methylthio)ethyl]benzenemethanol (2a)** : pale yellow viscous liquid[3]; 96%; IR (neat) 3450,1600, 1503,1435, $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.82-2.19 (m, 8H, $CH_2$ and $SCH_3$); 3.16(brs, 1H, OH, exchangeable with $D_2O$); 3.72 [dd, J = 6.5, 8.5 Hz, 1H , $CH(SCH_3)_2$ ]; 4.88 [dd, J =4.5, 8.5Hz, 1H, CH(OH)]; 7.28 (s, 5H, ArH). (Anal. Calcd. for $C_{11}H_{16}OS_2$ : C, 57.85; H, 7.06. Found C, 57.98; H, 6.92%).

Similarly the oter β-hydroxydithioacetals were obtained in nearly quantitative yields from their corresponding β-oxodithioacetals and they were used as such for the next steps without any further purification.

### (b) Addition of Grignard Reagents to β-Oxodithioacetals : Synthesis of β-Methyl/Phenyl β-Hydroxydithioacetals.

To an ice cooled solution of methyl/phenyl magnesium halides [30mmol, prepared from Mg turnings (1g) and MeI/PhBr (30mmol)] in dry ether (50mL) was added 1a-b,f (15mmol) in dry benzene (25mL) dropwise under $N_2$ atmosphere. The reaction mixture further stirred for 45min. and then allowed to reach room temperature. It wsa decomposed by pouring over sat. $NH_4Cl$ solution, extracted with ether (2x50mL), washed and dried over $Na_2SO_4$. Evaporation of the solvent afforded the carbnolacetals **92a-b** and **92f** and they were used directly for the next reaction.

### (c) Alkylation of β-Hydroxydithioacetals : Synthesis of β-Hydroxydithioketals

To a stirred solution of respective β-hydroxydithioacetals [**2a -b** and **2f**; 10 mmol] in THF (15mL) at -78°C under $N_2$ was added n-BuLi (25mmol) in THF (10mL) over a period of 5min. . It was stirred for 30min. at the same temperature and then was added MeI (30mmol) in THF (5mL). It was stirred further for 15 min. at -78°C and then allowed to attain room temperature. It was poured over sat. $NH_4Cl$ solution extracted with ether, and washed, dried and evaporated to afford the β-hydroxythioketals **95a-b,95f**. They were used as such without further purification.

### General Procedure for $BF_3.Et_2O$ Assisted Dehydration of β-Hydroxydithioacetals.

To a well stirred solution of β-oxodithioacetals **2a,2c,2e,75** and **78a** (10mmol) in dry benzene (20mL) under $N_2$ atmosphere $BF_3.Et_2O$ (2mL) was added and the reaction mixture was stirred for 3h. at room temperature (monitored by TLC). It was poured into ice cold water, benzene layer was separated and the aqueous layer was extracted with benzene (2x25mL). The combined extracts were washed with 5% $NaHCO_3$ solution (2x25mL), water (2x100mL), dried ($Na_2SO_4$) and evaporated under reduced pressure. The crude products were chromatographed over silica gel using hexane as eluent to obtain the pure products. The analytical and spectral data of the compounds are given below.

**3,3-Bis(methylthio)-1-phenyl-1-propene (3a)** : yellow viscous liquid; 89%; IR (neat) 2940, 1442,$cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.21 (s, 6H, $SCH_3$); 4.32 [d, J = 9Hz, 1H, $CH(SCH_3)_2$]; 6.20 (dd, J = 9, 15Hz, 1H, =CH); 6.62 ( d, J = 15Hz, 1H, =CH); 7.26-7.64 (m, 5H, ArH). (Anal. Calcd. for $C_{11}H_{14}S_2$ : C, 62.80; H, 6.70. Found : C, 63.01; H, 6.93%).

**1,3,3-Tri(methylthio)-1-phenylpropane (73a)** : colourless viscous oil; 63%; IR (neat) 2941, 1560, 1445 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 1.99 (s, 3H, $SCH_3$); 2.03 (s, 6H, $SCH_3$); 2.05-2.15 (m, 2H, $CH_2$); 3.52 (t, J = 9Hz, 1H, CH); 4.01 [ t, J =9Hz, 1H, CH $(SCH_3)_2$]; 7.20-7.48 (m, 5H, ArH). (Anal. Calcd. for $C_{12}H_{18}S_3$: C, 55.76; H, 7.01. Found : C, 63.84; H, 7.36%).

**3,3-Bis(methylthio)-1-(2'-furyl)-1-propene (3c)** : pale yellow oil; 51%; IR (neat) 2962, 1608, 1583, 1310$cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.09 (s, 6H, $SCH_3$); 4.28 [d, J= 7.5Hz, 1H, $CH(SCH_3)_2$]; 6.39-6.44 (m, 1H, furyl); 6.68 (dd, J = 1.5, 12Hz, 1H, =CH); 6.89 (dist.dd, J = 1.5, 12Hz, 1H, =CH); 7.01 ( d, J = 3.5Hz, 1H, furyl); 7.56 (brs, 1H, furyl). (Anal. Calcd. for $C_9H_{12}OS_2$ : C, 54.38; H, 6.19. Found : C, 54.45; H, 6.09%).

**4,4-Bis(methylthio)-2-butene (3e)** : colourless oil; 54%; IR (neat) 2951, 1600, 1480cm$^{-1}$; $^1$HNMR ($CCl_4$) 1.98 (d, J = 9Hz, 3H, $CH_3$); 2.09 ( s, 6H, $SCH_3$); 4.11 [d, J= 4Hz, 1H, $CH(SCH_3)_2$]; 6.10 (dd, J = 4, 9Hz, 1H, =CH); 6.88 (d, J = 4Hz, 1H, =CH). (Anal. Calcd. for $C_6H_{12}S_2$ : C, 51.96; H, 4.99. Found : C, 52.09; H, 5.18%).

**2,2-Bis(methylthio)methyl-3,4-dihydronaphthalene (76):** yellow viscous liquid; 83%; IR (neat) 2910, 1505, 1446, 1226 cm$^{-1}$; $^1$H NMR ($CCl_4$) 2.02 (s, 6H, $SCH_3$); 2.31 (t, J = 6Hz, 2H, $CH_2$); 2.76 (t, J =6Hz, 2H, $CH_2$); 4.18 [s,, 1H, $CH(SCH_3)_2$]; 6.34 ( s, 1H, =CH); 6.89-7.26 (m, 5H, ArH). (Anal. Calcd. for $C_{13}H_{16}S_2$: C, 66.05; H, 6.82. Found : C, 66.17; H, 6.94%).

**5,5-Bis(methylthio)-1-phenyl-1,3-pentadiene (80)** : yellow viscous oil; 40%; IR (neat) 2920, 1580, 1470 cm$^{-1}$; $^1$H NMR ($CCl_4$) 2.08 (s, 6H, $SCH_3$); 4.28 [d, J = 9Hz, 1H, $CH(SCH_3)_2$]; 5.98 (dd, J = 6, 15Hz, 2H, =CH); 6.29 ( dd, J = 9,15Hz, 1H, =CH); 6 .49 (d, J = 15Hz, 1H, =CH); 7.11- 7.43 (m, 5H, ArH). (Anal. Calcd. for $C_{13}H_{16}S_2$ : C, 66.05; H, 6.82. Found : C, 66.26; H, 6.97%).

**3,5,5-Tri(methylthio)-1-phenyl-1-pentene (79)** : yellow viscous liquid; 34%; IR (neat) 2954, 1548, 1449cm$^{-1}$; $^1$H NMR ($CCl_4$) 1.98 (s, 3H, $SCH_3$); 2.00-2.03 (m, 8H, $CH_2$ and $SCH_3$); 3.58 (t, J= 9Hz, 1H, CH); 3.81 [ t, J= 9Hz, 1H, $CH(SCH_3)_2$]; 6.02 (dd, J= 9, 15Hz, 1H, =CH); 6.51 (d, J = 15Hz, 1H, =CH-ArH); 7.21-7.60 (m, 5H, ArH). (Anal. Calcd. for $C_{13}H_{20}S_3$: C, 52.94; H, 6.28. Found : C, 51.12; H, 6.14%).

**Dimethyl Sulphoxide Induced Thermal Dehydrative Dethioacetalization of β-Hydroxydithioacetals : Synthesis of Ene- , Polyenealdehydes and Enones.**

A solution of β-hydroxydithioacetal 3a (2.28g, 10mmol) and DMSO (3.90g, 50mmol, freshly distilled over calcium hydride) was heated at 150°C for 3-5h.. It was cooled to room temperature and then poured over saturated $NH_4Cl$ solution and extracted with ether (2x50mL). The combined extracts were washed with water (2x50mL), dried over $Na_2SO_4$ and evaporated to afford the crude product 5a. It was purified by passing through a silica gel column using EtOAc- hexane (2:98) as eluent. The spectral and analytical data of the products obtained from the DMSO assisted thermal dehydrative dethioacetalization of β-hydroxydithioacetals are described below.

**E-Cinnamaldehyde (4a)** : pale yellow liquid [26a]; 90%; IR (neat) 3060, 3020, 2750, 1680, 1630, 1570 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 6.60 (dd, J = 6,15Hz, 1H, = CH); 6.80-7.41 (m, 6H, =CH and ArH); 9.70 (d, J = 9Hz, 1H, -CHO). (Anal. Calcd. for $C_9H_8O$ : C, 88.46; H, 6.59. Found : C, 89.07; H, 6.63%).

**4-Methoxy cinnamaldehyde (4b):** white crystals ; m.p. 58-59°C, (lit.[27] mp. 61°C) ; 95%, IR (KBr) 2990, 1700, 1622, 1525, 1275, 1145 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.82 (s, 3H, $OCH_3$); 6.58(dd, J = 4.5,9Hz, 1H,=CH); 6.90 (d, J = 9Hz, 2H, ArH); 7.24-7.65 (m, 3H, =CH and ArH); 9.70 (d, J = 9Hz, 1H, -CHO). (Anal. Calcd. for $C_{10}H_{10}O_2$ : C, 74.05; H, 6.21. Found : C, 74.38; H, 6.39%).

**3-(2'-Furyl)propen-2-al (4c)** : colourless solid; m.p. 49-50°C (lit.[26b,28] m.p. 52°C); 82%; IR ($CCl_4$) 2840, 1680, 1645, 147 0, 1380, 1135 cm$^{-1}$; $^1$ H NMR ($CDCl_3$); 6.46 (dd, J = 1.8,3.5Hz, 1H); 6.53 (dd, J = 7.9,15.8Hz, 1H; 6.70 (d, J = 3.5, 1H); 7.17 (d, J = 15.8Hz, 1H); 7.49 (d, J = 1.4Hz, 1H); 9.53 (d, J = 7.9Hz, 1 H). (Anal. Calcd. for $C_7H_6O_2$: C, 68.84; H, 4.94. Found : C, 69.18; H, 4.69%).

**3-(2-Thienyl)propen-2-al (4d)** : yellow viscous liquid [26c,29]; 80%; IR ($CCl_4$) 2820,2720,1682,1615,1520,1420 cm$^{-1}$; $^1$H NMR ($CCl_4$) : 6.42 (dd, J = 9Hz,3Hz, 1H, =CH); 7.00-7.18 (m, 1H, H-4); 7.22-7.58 (m, 2H,H-3); 7.68 (s, 1H, H-5); 9.65 (d, J= 9Hz,1H,-CHO). (Anal. Calcd. for $C_7H_6OS$: C, 60.84; H, 4.37. Found : C, 61.22; H, 4.01%).

***trans* 2-Butenal (4e)** : colourless liquid [16d]; 63%; IR (neat) 2943,2862,2709,1706,1644 cm$^{-1}$; $^1$H NMR ($CCl_4$) : 2.08 (d, J = 6Hz, 3H, $CH_3$); 6.06 (dd, J = 6,9Hz, 1H, =CH); 6.90 (dd, J = 6,9Hz, 1H, =CH); 9.51 (d, J = 9Hz, 1H, -CHO). (Anal. Calcd. for $C_4H_6O$ : C, 68.55; H, 8.61. Found : C, 68.49; H, 8.72%).

**1-Cyclohexen-1-carboxaldehyde (83)**[26e,30] : colourless liquid; 65%; IR (neat) 3014, 2918, 2826, 2710, 1728, 1651, 1438 cm$^{-1}$; $^1$H NMR ($CCl_4$); 1.41-2.72 (m, 8H, $-CH_2-$); 5.71 (brs, 1H, =CH); 9.63 (brs, 1H, -CHO). (Anal. Calcd. for $C_7H_{10}O$ : C, 75.70; H, 9.49. Found : C, 74.91; H, 9.03%).

**3,4-Dihydronaphthalen-2-carboxoaldehyde (84)**[31] : viscous liquid, 63%; IR ($CCl_4$) 2.50 (m, 2H, $-CH_2-$); 2.88 (m, 2H, -

$CH_2$-); 7.12-7.40 (m, 5H, =CH, ArH); 9.78 (s, 1H, CHO). (Anal. Calcd. for $C_{11}H_{10}O$; C, 83.51 ; H, 6. 37. Found : C, 83.89; H, 6.12%).

**5-Phenyl-2,4-pentadien-1-al (85a)** : yellow solid; 86%; m.p. 40°C (lit.[26f] m.p. 42°C); IR (KBr) 2995 , 1710, 1640, 1300, 1115 $cm^{-1}$; $^1H$ NMR ($CDCl_3$); 6.00 (dd, J = 3 ,9Hz, 1H, =CH ); 6.80-7.19 (m, 2H, =CH); 7.12-7.44 (m, 6H, =CH, ArH); 9.58 (d, J = 9Hz,1H,-CHO). (Anal. Calcd. for $C_{11}H_{10}O$, C, 83.51; H, 6.37. Found : C, 84.06; H, 6.21%).

**5-(4'-Methoxyphenyl)-2,4-pentadien-1-al (85b)** : 89%; m.p. 77-79°C; (lit.[27] m.p. 80°C); IR (KBr) 2840, 1648 $cm^{-1}$; $^1H$ NMR ($CDCl_3$); 3.41 (s, 3H, $OCH_3$); 6.12 (dd, J = 8,16Hz, 1H, =CH ) 6.80 (m, 5H, ArH); 7.32 (dd, J = 2,8Hz, 2H, ArH); 9.61 (d, J = 8Hz, 1H, CHO). (Anal. Calcd. for $C_{12}H_{12}O_2$; C, 76.56; H, 6.42. Found : C, 77.01; H, 6.31%).

**5-(2'-Furyl)pent-2,4-dien-1-al (85c)** : white crystals, 89%; m.p. 63-64°C (lit.[32] m.p. 65-66°C ); IR (neat) 1700, 1560, 1270, 1110 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.32 (dd, 1.5,6Hz, 1H, =CH); 6.59-6.74 (m, 3H, =CH and furyl); 6.92-7.13 (m, 1H, furyl); 7.22-7.59 (m, 2H, =CH); 7.63-7.85 (m, 1H, furyl); 9.81 (d, J = 6Hz, 1H, -CHO). (Anal. Calcd. for $C_9H_8O_2$ : C, 72.95; H, 5.44. Found : C, 73.23; H, 5.61%).

**7-Phenyl-2,4,6-heptatrien-1-al (88a)** : yellow solid; 72% m.p. 110-112°C (lit.[33] m.p. 115°C); IR (KBr) 2832, 1700, 1560, 1270, 1112 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.15-6.58 (dd, J = 3, 7.5 Hz, 1H, =CH); 6.94-7.85; (m, 10H, =CH and ArH); 9.61 (d, J = 7.5Hz, 1H, CHO). (Anal. Calcd. for $C_{13}H_{12}O$ : C, 84.74; H, 6.56. Found : C, 84.91; H, 6.66%).

**7-(4'-Methoxyphenyl)-2,4,6- hepta-trien-1-al (88b)** : brown solid; 81%; m.p. 135°C (lit.[34] m.p. 138°C); IR (neat) 3070, 1695, 1600, 1230, 1180 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 3.78 (s, 3H, $OCH_3$); 6.16 (dd, J = 1.5,6Hz, 1H, =CH), 6.48-7.01 (m, 7H, =CH, ArH); 7.42 (d, J = 9Hz, 2H, ArH); 9.60 (d, J = 6Hz, 1H, CHO). (Anal. Calcd. for $C_{14}H_{14}O_2$ : C, 78.47; H, 6.58. Found : C, 78.53; H, 6.69%).

**5-(6'-Methoxy-3,4-dihydronaphthyl)-2,4-pentadiene-1-al (91)** : yellow crystals; 91%; m.p. 108°C; IR (KBr) 3090, 1700, 1610, 1222, 1120 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.28-2.56 (m, 2H, $-CH_2-$); 2.71-2.98 (m, 2H,$-CH_2$); 3.80 (s, 3H, $OCH_3$); 6.16 (dd, J =1.5,4.5Hz, 1H, =CH); 6.61-6.90 (m, 5H, =CH, ArH); 7.09-7.48 (m, 2H, ArH); 9.62 (d, J = 4.5 Hz, 1 H, -CHO). (Anal. Calcd. for $C_{16}H_{16}O_2$ : C, 79.97; H, 6.71. Found : C, 80.09, H, 6.58%).

**E-3-Phenyl-2-buten-1-al (93a)** : pale yellow solid; 89%; m.p.90-91°C (lit.[35] m.p. 95°C); IR (KBr) 3095, 1680, 1235, 1160 $cm^{-1}$; $^1H$ NMR ($CCl_4$) 2.55 (s, 3H, $CH_3$), 6.38 (d, J = 6Hz, 1H, =CH); 7.25-7.68 (m, 5H, ArH); 10.28 (d, J=6Hz, 1H, -CHO). (Anal. Calcd. for $C_{10}H_{10}O$ : C, 82.15; H, 6.89. Found : C, 83.28; H, 6.93%).

**3,3-Diphenyl-2-propen-1-al (93b)** : pale yellow crystals; 92%; m.p. 40°C (lit.[26g] m.p. 44°C); IR (KBr) 1680, 1610, 1460, 1380 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 6.51 (d, J = 6Hz, 1H, =CH); 7.12-

7.60 (m, 10H, ArH); 9.60 (d, J = 6Hz, 1H, -CHO). (Anal. Calcd. for $C_{15}H_{12}O$ : C, 87.34; H, 5.81. Found : C, 87. 21; H, 5.78%).

**4-Phenyl-3-butene-2-one (96a)** : 81%; m.p. 39-40°C (lit.[26h] m.p. 42°C); IR (KBr) 3032, 2953, 1691, 1674, 1611, 1490 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 2.41 (s, 3H, $CH_3$); 6.73 (d, J = 9.5Hz, 1H, =CH); 7.54 (m, 6H, =CH, ArH). (Anal. Calcd. for $C_{10}H_{10}O$; C, 82.15; H, 6.89. Found : C, 82.31; H, 6.93%).

**4-(4'-Methoxyphenyl)-3-butene-2-one (96b)**; 86%; m.p. 69-70°C; (lit.[26i]m.p. 73°C); IR (KBr) 3030, 2940, 1700, 1670, 1610, 1520, 1470, 1430 $cm^{-1}$; $^1H$ NMR ($CDCl_3$); 2.31 (s, 3H, $CH_3$); 3.84 (s, 3H, $OCH_3$); 6.61 (d, J = 3Hz, 1H, =CH); 6.93 (d, J = 9Hz, 2H, ArH); 7.29-7.59 (m, 3H, =CH, ArH).(Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86; C, 75.09; H, 6.99%).

**4-Methyl-3-pentene-2-one (96f)**[26j] : colourless viscous liquid; 79%; IR (neat) 2983, 2921, 1692, 1621, 1440 $cm^{-1}$; $^1H$ NMR ($CCl_4$); 1.78 (d, J = 6Hz, 3H, $CH_3$); 1.98 (s, 3H, $CH_3$); 2.08 (s, 3H, $CH_3$); 6.02 (q, J = 6Hz, 1H, =CH). (Anal. Calcd. for $C_6H_{10}O$: C, 73 .42; H, 10.27. Found : C, 73.61; H, 10.18%).

**A Typical Procedure for the Preparation of Enealdehydes from β-Hydroxydithioacetals by Method -B .**

Methyl iodide (10.5mmol) was added to a solution of 2a (10mmol) in methanol (20mL) at room temperature and stirred for 1h.. It was refluxed for 2h. and allowed to attain room temperature and left overnight whereby a white solid

separates out. it was filtered and washed with methanol (10mL) and ether (15mL) and dried in a dessicator. The sulphonium salt was heated in DMSO in the presence of NaH (20mmol) for 3h. . It was brought to room temperature, poured onto crushed ice and extracted with ether (2x25mL). The combined extracts were washed with water, dried ($Na_2SO_4$) and concentrated to give a viscous yellow oil. It wsa passed through a silica gel column using EtOAc: hexane (2:98) as eluent to afford analytical pure 4a in 92% yield.
Its spectral and analytical data were identical with that of *trans* - cinnamaldehyde 4a obtained from DMSO method.

## REFERENCES AND NOTES

1. (a) Seebach, D. *Synthesis* 1969, 17; (b) Seebach, D. *Angew Chem. Int. Ed. Engl.* 1969, *8* 639; (c) Corey, E.J.; Seebach, D. *Angew Chem. Int. Ed. Engl.* 1965, *4*, 1075, 1077.
2. (a) Murphy, W.S.; Wattanasin, S. *J.C.S. Perkin Trans. I* 1980, 2678; (b) Murphy, W.S.; Wattansin,S. *Tetrahedron Lett.* 1979, 1827; (c) Fang, J-M; Liao, L-F; Hong, B-C. *J. Org. Chem.* 1986, 51, 2820-2829; (d) Fang J-M; Hong, B-C *J. Org. Chem.* 1987, *52*, 3161-3165; (e) Fang J-M; Chen, M-Y *Tetrahedron Lett* 1988, *29*, 5939; (f) Fang,J-M.; Chen, M-Y; Yang, W-J; *Tetrahedron Lett.* 1988, *29*, 5937; (g) Fang, J-M; Hong,B-C.; Liao, L-F.; *J. Org. Chem* 1987, *52*, 855; (h) Kozikavski, A.P.; Chen,Y-Y.; *J.Org. Chem.* 1980, *45*, 2236.

3. Gammill, R.B.; Gold, P.M.; Mizsak, S.A. *J.Am. Chem. Soc.* 1980, *102*,3095.

4. Davey, A.E.; Parrons, A.F.; Taylor, R-J.*J. Chem. Soc. Perkin Trans 1* 1989, 1853.

5. Tarnchompoo, B.; Thebtaranonth, Y.; *Tetrahedron Lett.* 1984, *25*, 5567.

6. Vedejs, E.; Fuchs, P.L. *J. Org. Chem.* 1971, 36, 366.

7. Chattopadhyaya, J.B.; Ramarao, A.V. *Tetrahderon Lett.* 1973, 3735.

8. Prato, M.; Quintily, V.; Scorrano, G.; Sturaro, A. *Synthesis*, 1982, 679.

9. Olah, G.A.; Mehrotra, A.K.; Narang, S.C. *Synthesis* 1982, 151.

10. Rao, Ch. S.; Chandrasekharam, M.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1992, 8163.

11. Akiyama, S.; Nakatsuji, S.; Hamamura, T.; Kataoka, M.; Nakagawa, M. *Tetrahedron Lett.* 1979 , 2813 and ref.4 cited therein.

12. Church, R.F.; Ireland, R.E.; Marshall, J. *J. Org. Chem.* 1962, *27*, 1118.

13. Bernstein, P.R. *Tetrahedron Lett.* 1979, 1015.

14. Taguchi, H.; Tanaka, S.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* , 1973, 2465.

15. (a) Duhamal, L.; Ramondee, G . Ple. *Tetrahedron Lett.* 1989, *30*, 7377; (b) Duhamal, L.; Duhamal, P.; Lecoune, J.P. *Tetrahedron* , 1987, *43*, 4349..

16. Trost, B.M.; Stanton, J.L. *J. Am. Chem. Soc.* 1975, *97*, 4018.

17. Posner, G.H.; Shulman-Roskes, E.M.; Chang, H.O.; Carry, J-C.; Greene, J.V.; Clark, A.B.; Dai, H.; Anjeh, T.E.N. *Tetrahedron Lett.*, 1991, *32*, 6489.

18. For leading references on the homologations of aldehydes into α,β-unsaturated carbonyl compounds.
(a) Deshong, P.; Leginus, J.M.; *J. Org. Chem.* 1984, *49*, 3421 and ref. 1 and 2 cited therein. (b) Gaudemar, M.; Bellassoud, M.; *Tetrahedron Lett* ., 1990, *31*, 349. (c) Bellassoud, M.; Gaudemar, M. *Tetrahedron Lett.* , 1988, *29*, 4551 and ref. 1-7. (d) Olestein, R.; Stephenson, E .F.M.; *Aust. J. Chem.*, 1979, *32*, 681 and ref. 12- 25.

19. For a discussion of various approaches ; see:
(a) Corey, E.J.; Enders, D.; Bock, M.G.*Tetrahedron Lett.*, 1976, 7. (b) Dauben, W.G.; Michno, D .M. *J. Org. Chem.*, 1979, *42*, 682. (c) Pauling, H.; *Chimia* ,1973, *27*, 383.

20. Brettle, R.; *Comprehensive Organic Chemistry* Stoddart, J.F.; (ed.) Pergamon Press, Oxoford, 1979, *Vol.1*, 979.

21. Martin, S.F. *Synethesis* ,1979, 633.

22. Reiff,H.;in "*Newer methods Prep. Org. Chem.*" 1979, *6*, 48.

23. Neilson, A.T.; Houlshan, W.J. *Org. React.*, 1968, *16*, 1.

24. (a) Grobel; B.T.; Seebach, D. *Synthesis* 1977, 357; (b) Greene, T.W. *Protective Groups in Organic Synthesis*, John Wiley and Sons, New York 1981, pp. 129-138, 311-314.

25. (a) Traynelis, V.J.; Hergenrather, W.L., Hanson, H.T. and Volicent, J.A. *J. Org. Chem.* 1964, *29*, 123-129; (b) Traynelis, V.J. Hergenrother, W.L.; Livingston, J.R.; Valicenti, J.A. *J. Org. Chem.* 1962, *27*, 2377; (c) Gilles, B.T.; Beck, P.E., *J. Org. Chem.* 1963, *28*, 1388; (d) Vlad,

P.F.; Ungur, N.D. *Synthesis* 1983, 216; (e) Patro, B.; Ila, H.; Junjappa, H. *Tetrahedron Lett* 1992, *33*, 809-812.

26. "*CRC Atlas of Spectral Data and Physical Constants for Organic Compounds*" Ed., Grasselli, G.; William, M. S.; Ritchey, M. (a) Vol.3, p.59.; (b) Vol.4, p.298; (c) Vol.4, p.631; (d) Vol.2, p.627; (e) Vol.3 p.135; (f) Vol.2, p.6; (g) Vol.3, p.60; (h) Vol.2, p.637; (i) Vol.2, p.636; (j) Vol.4, p.54.
27. Reddy, M.P.; Krishna Rao, G.S. *Synthesis*,1980, 815.
28. Deshong, P.; Liginus, J.M. *J. Org. Chem.* 1984 , *49*, 3421.
29. (a) Kossmehl,G.; Bohn,B. *Chem. Ber.* ,1974, *107*(8), 2791. (b) Quinion, Lozach, N. *Buli. Soc. Chim. Fr.*, 1963, 1171.
30. (a) Corey, E.J.; Borger, D.L. *Tetrahedron Lett.*, 1978, *9*, 13; (b) Roussean, G.; Le Perches, P.; Conia, J.M. *Synthesis*, 1978, 67.
31. Bhattacharjee, S.; Mandal, A.N.; Roy, S.R.; Chatterjee, A. *Tetrahedron Lett.*, 1984, *25*, 3007.
32. (a) Crabbe, P.; Depres, J.-P.; *J. Chem. Soc. Perkin. Trans. I* , 1980, 2081. (b) Lipp, M.; Dallacker, F. *Chem. Ber.*, 1957, *90*, 1730.
33. Whitlock, H. W. Jr.; Reich, C.; Woessner, W.D.; *J. Am. Chem. Soc.* , 1971, *93*, 2483.
34. Makin, S.M.; Eramakova, Q.A.; Shavrygina, O.A.; Pleshkova, A.P.; Vozlesluti, V.N. *Zh. Org. Chim.*, 1979, *15*, 1852 (Russ.).
35. Julia, M.; Surzur, J.A. *Bull. Soc. Chim. Fr.*, 1956, 1615.