SYNTHETIC STUDIES ON ß-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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1. Highlights of Organic Chemistry
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C O N T E N T S

P R E F A C E

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 poly-nuclear 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.

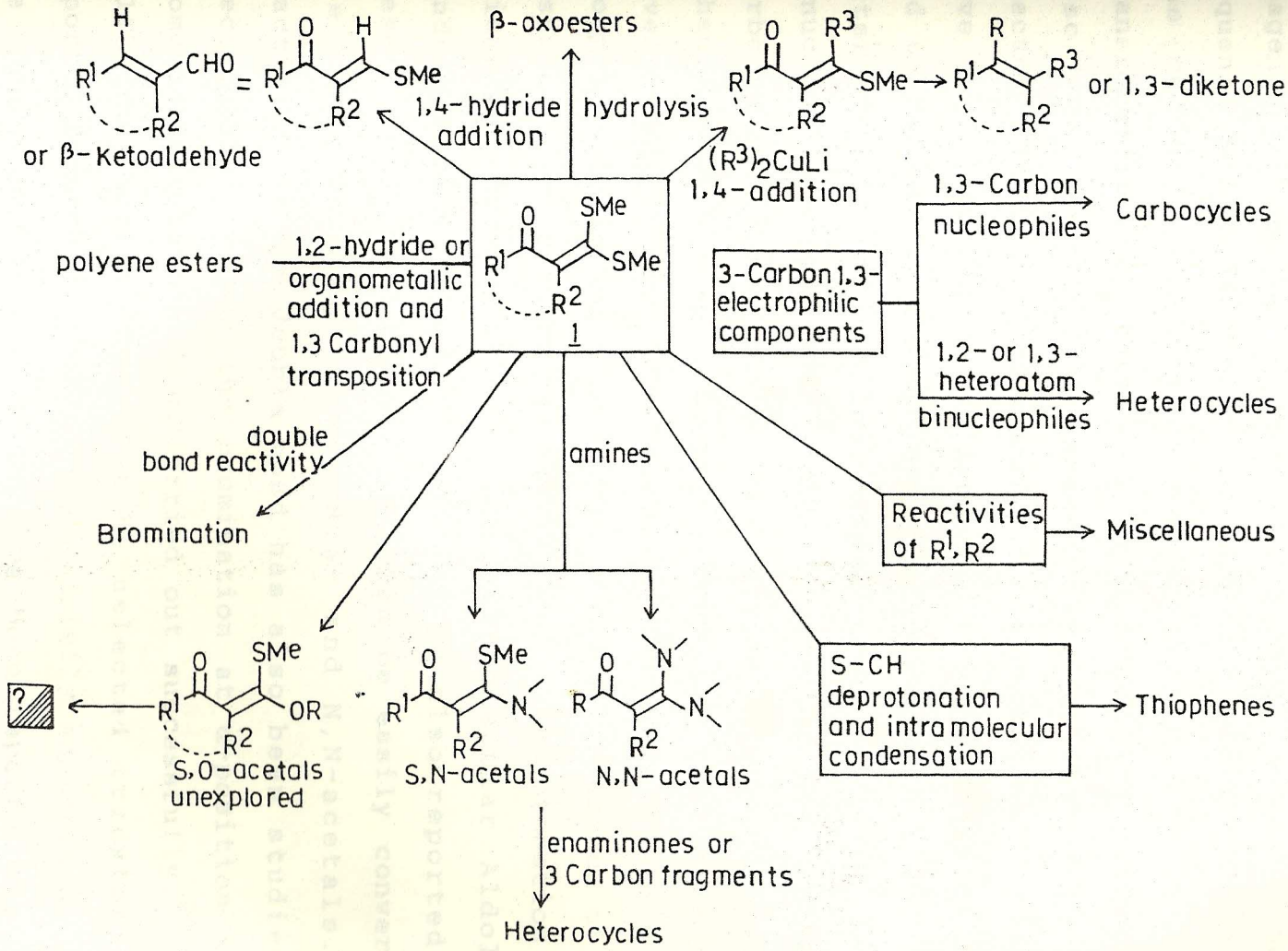
CHAPTER I

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
1,3-Carbon nucleophiles
Carbocycles
3-Carbon 1,3-electrophilic components
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

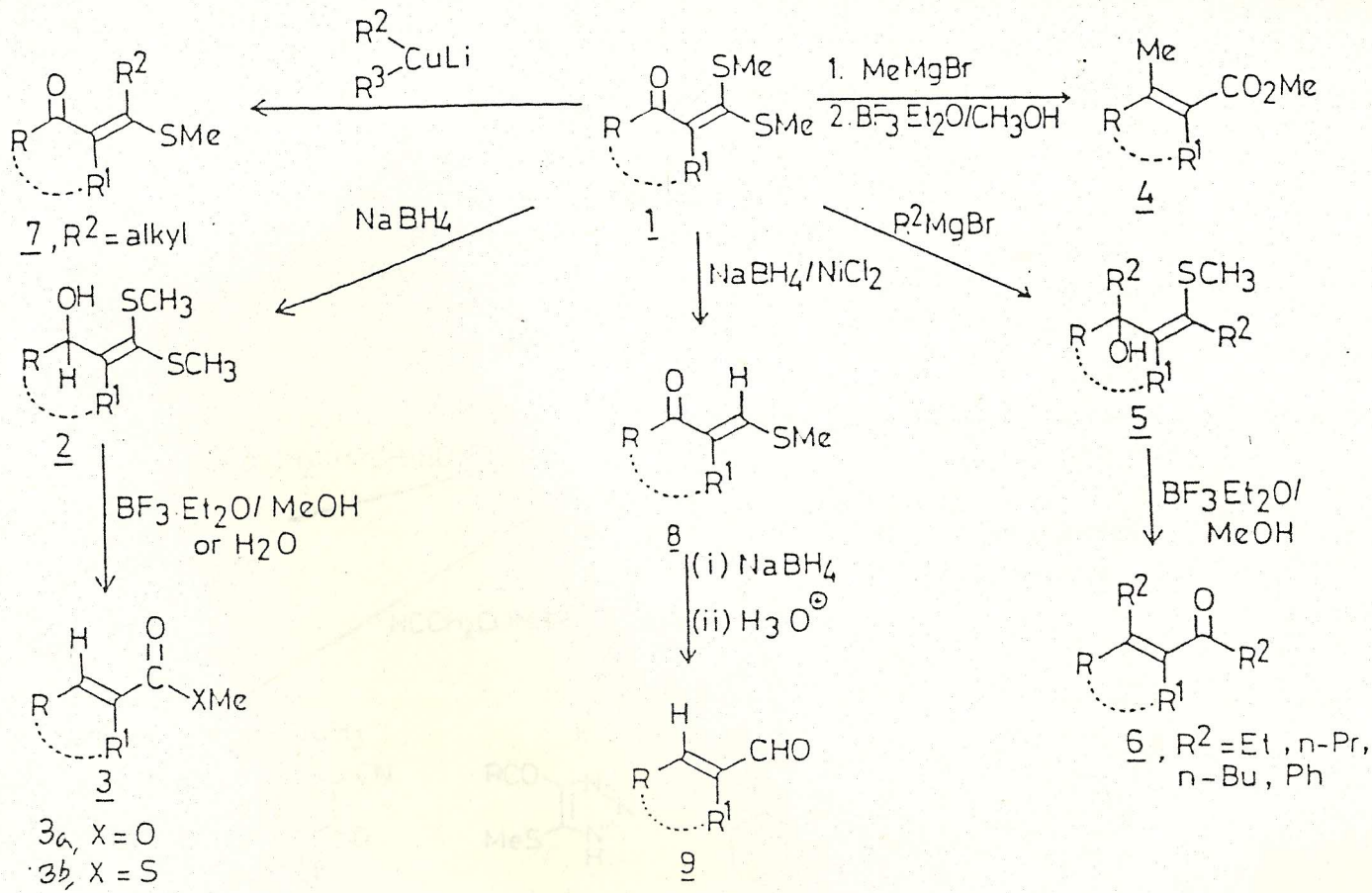
Scheme-1

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 t he selected transformations reported from this laboratory are briefly summarized.

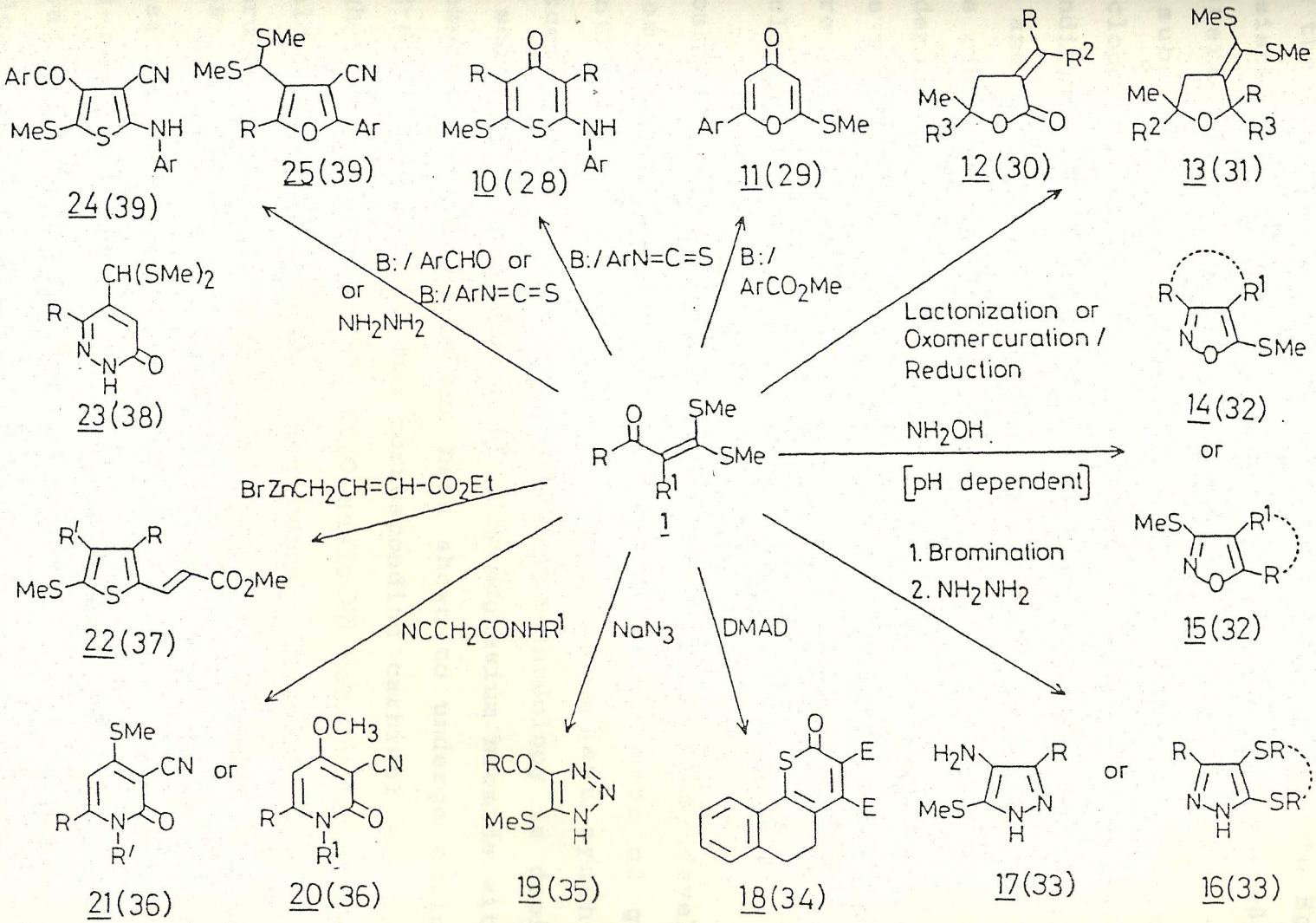
The oxoketene dithioacetals have been reported to undergo chemoselctive 1,2-reduction with $NaBH_4$ to give the

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


R2
R3CuLi
1. MeMgBr
2. BF3 Et2O/CH3OH
NaBH4
NaBH4/NiCl2
R2MgBr
BF3 Et2O/ MeOH
or H2O
BF3 Et2O/
MeOH
(i) NaBH4
(ii) H3O⊕
7, R2 = alkyl
1
4
2
5
8
9
3
6, R2 = Et, n-Pr,
n-Bu, Ph
3a, X = O
3b, X = S

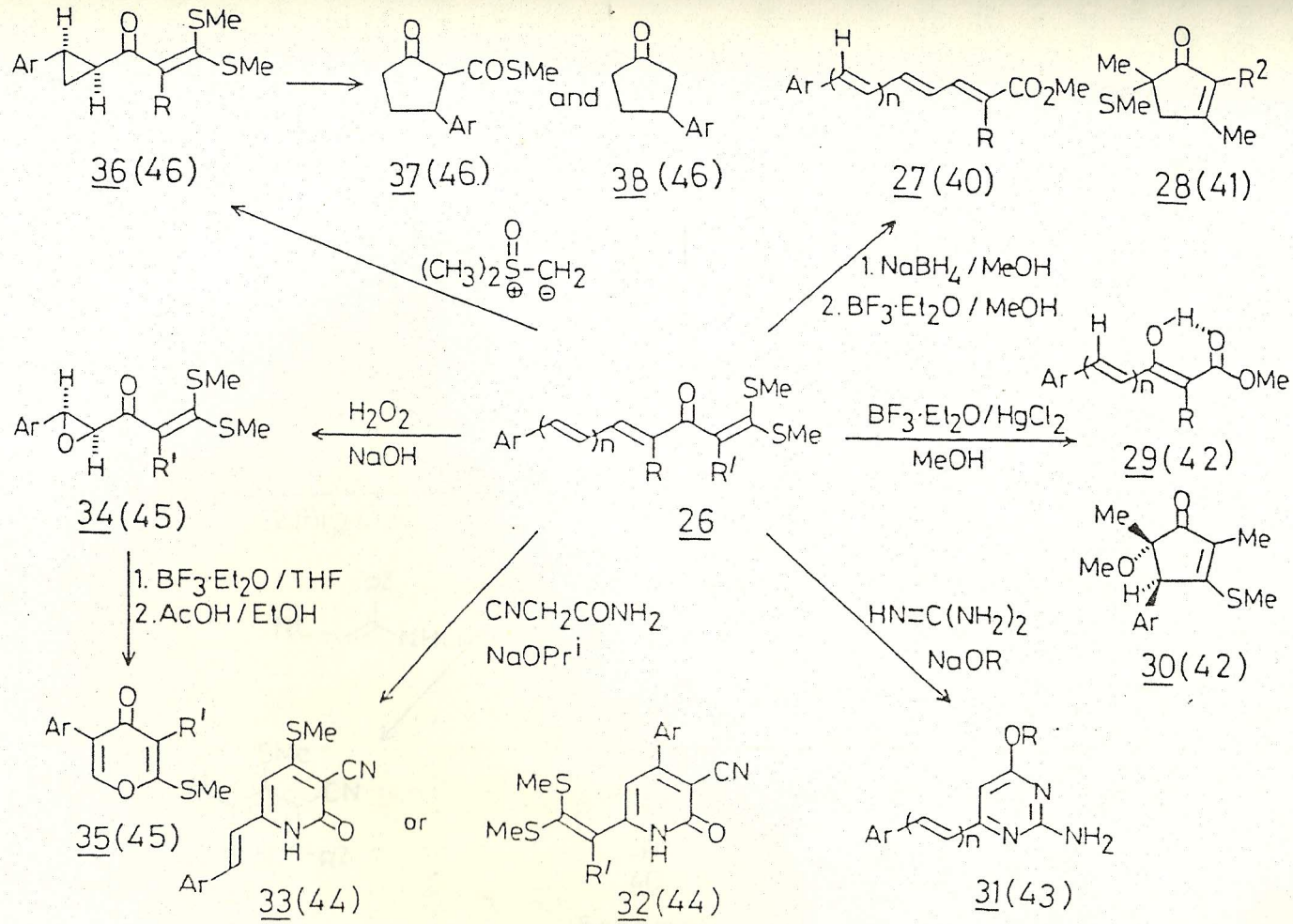
Scheme-2


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

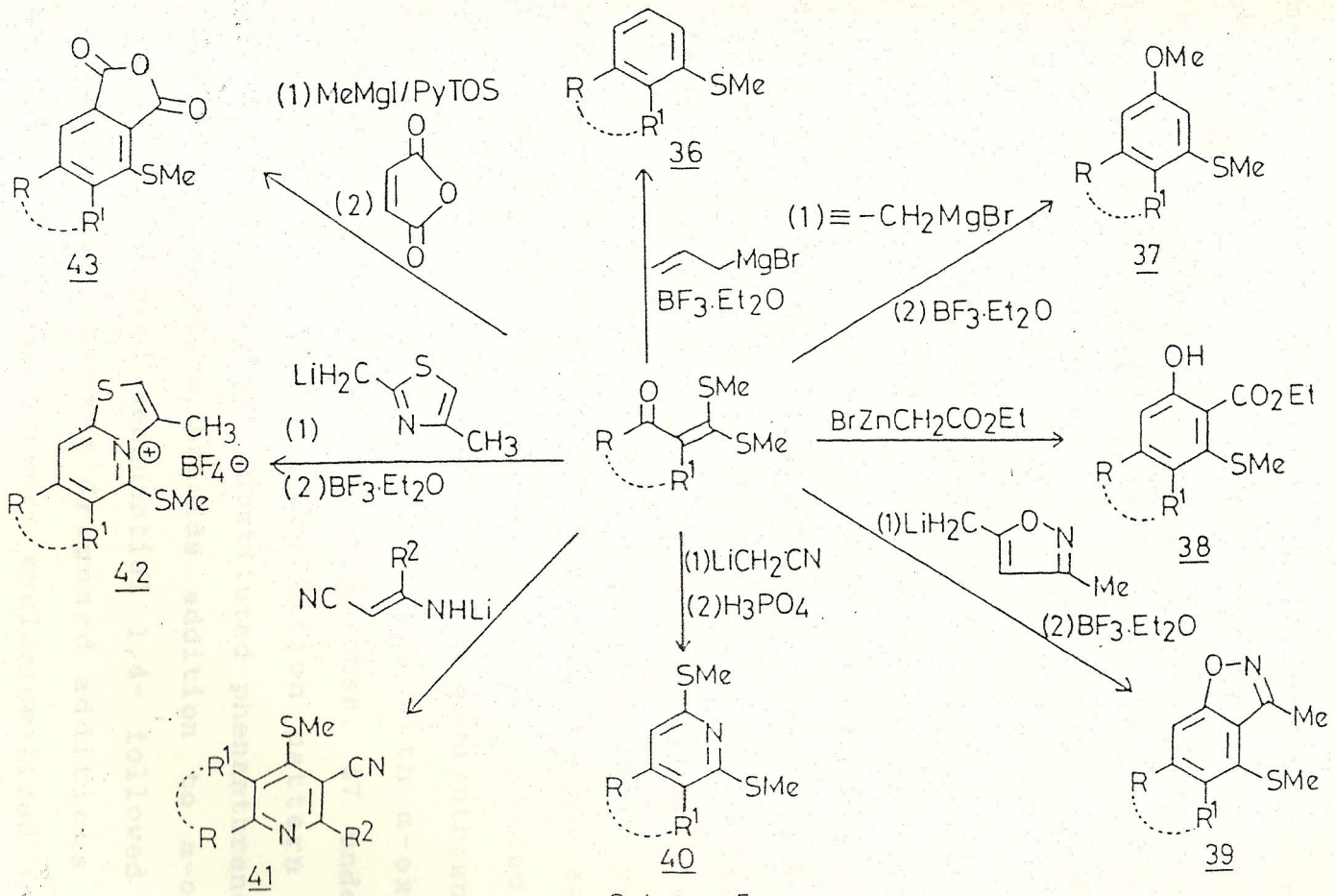
Scheme-3

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)
1. NaBH4 / MeOH
2. BF3·Et2O / MeOH
H2O2
NaOH
BF3·Et2O/HgCl2
MeOH
29 (42)
34 (45)
26
1. BF3·Et2O / THF
2. AcOH / EtOH
CNCH2CONH2
NaOPri
HN=C(NH2)2
NaOR
30 (42)
35 (45)
or
33 (44)
32 (44)
31 (43)

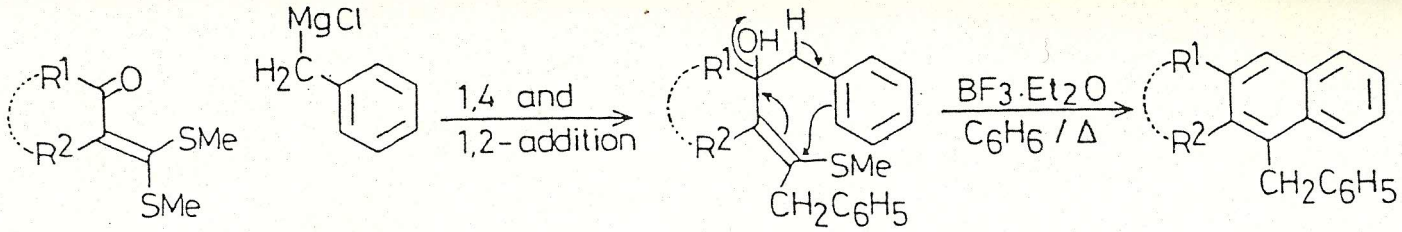
Scheme-4


(1) MeMgI/PyTOS
(2)
MgBr
BF3·Et2O
(1) ≡ −CH2MgBr
(2) BF3·Et2O
BrZnCH2CO2Et
(1)
(2)BF3·Et2O
(1)LiCH2CN
(2)H3PO4
(1)LiH2C
(2)BF3·Et2O
43
36
37
42
38
41
40
39

Scheme-5

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

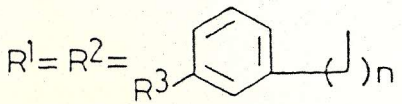
The α-oxoketene dithioacetals have been shown to be useful intermediates for synthesis of naphthalenes, phenanthrenes and other fused aromatic systems by reacting them with benzyl-, 1-naphthylmethyl- and 2-naphthylmethylmagnesium halides followed by cycloaromatization. Thus, benzylmagnesium chloride 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



1 44 45 46

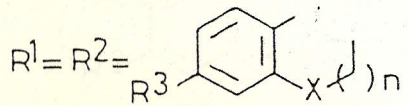
$R^1 = C_6H_5$, 4-$MeOC_6H_4$, 4-MeC_6H_4, 2-naphthyl ; $R^2 = H$; 58–65 %

$R^1 = R^2 = -(CH_2)_4-$; 81 %



n = 1 ; 62 %

n = 2 ; 71 %

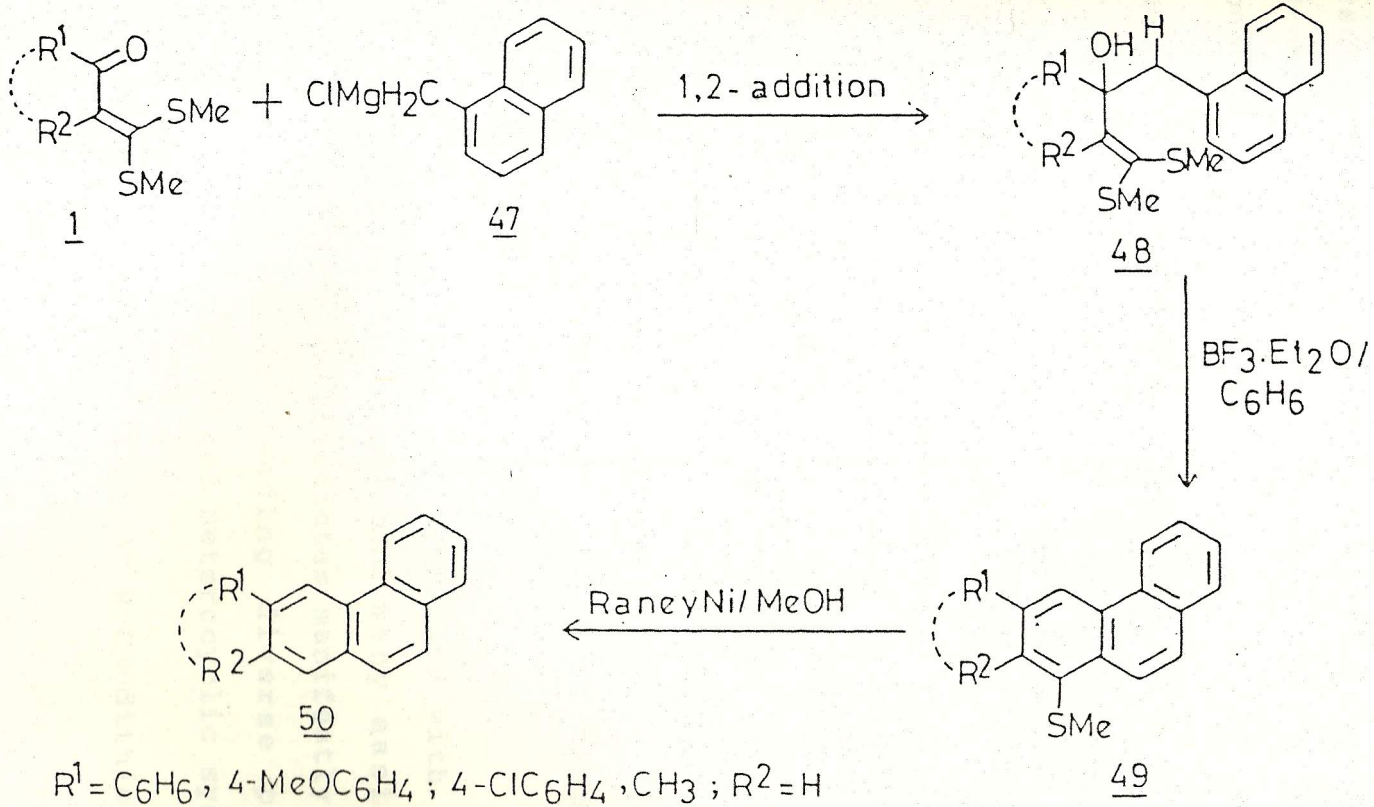


R^3 = H ; X = S ; n = 1 ; 58 %

R^3 = Me X = S ; n = 2 ; 68 %

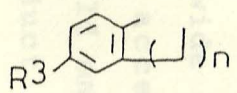
R^3 = H ; X = O ; n = 2 ; 67 %

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

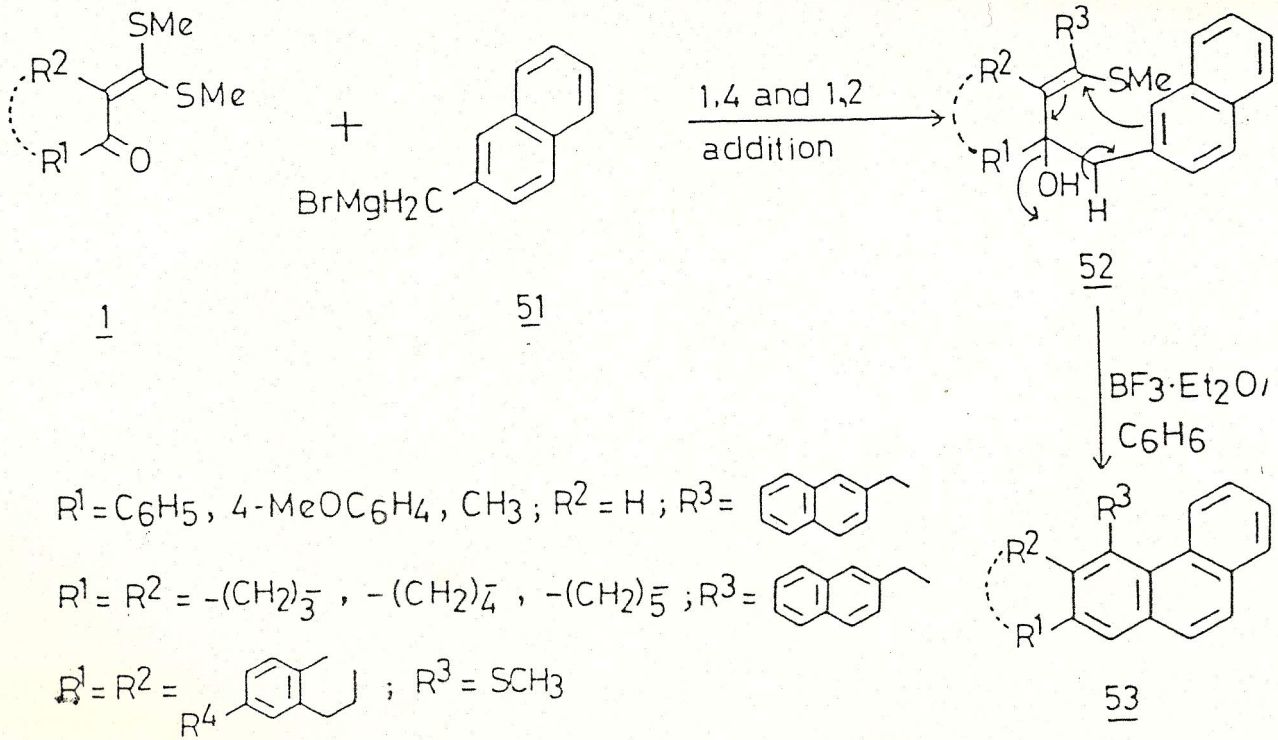
in good to excellent yields (Scheme 8). It appears that both steric and electronic factors play an important role in the different reactivity patterns of benzyl, 1-naphthylmethyl- and 2-naphthylmethylmagnesium halides with α-oxoketene dithioacetals.

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



1 51

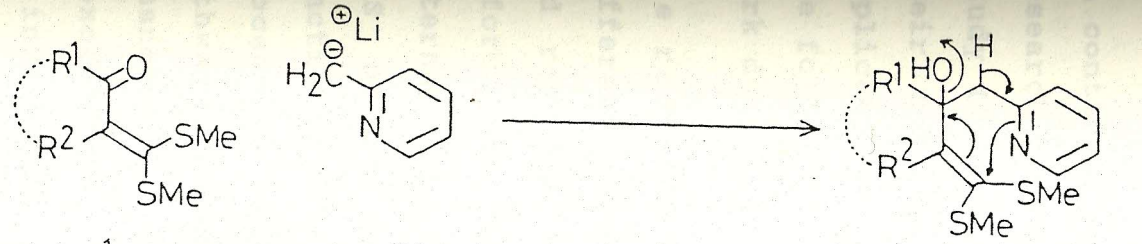
$R^1 = C_6H_5$, 4-$MeOC_6H_4$, CH_3 ; $R^2 = H$; $R^3 =$

$R^1 = R^2 = -(CH_2)_3^-$, $-(CH_2)_4^-$, $-(CH_2)_5^-$; $R^3 =$

$R^1 = R^2 =$; $R^3 = SCH_3$

$R^4 = H$, OCH_3

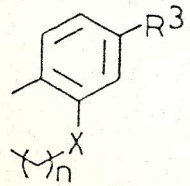
Scheme - 8



1 54 55

$R^1 = R^2 = -(CH_2)_4-$; 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-MeC_6H_4 , 4-$MeOC_6H_4$, 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.

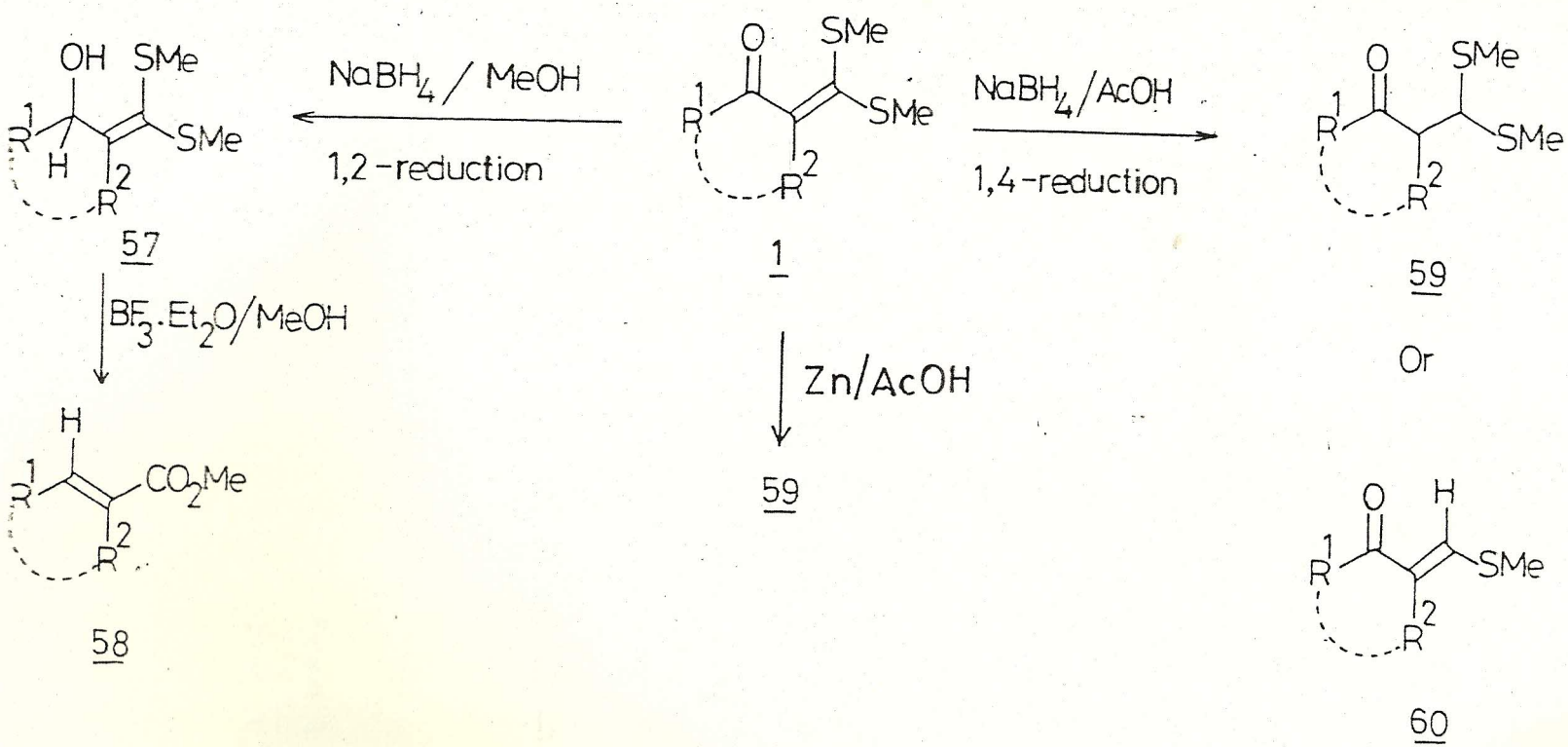
The reduction of α-oxoketene dithioacetals can follow different pathways depending on the nature of reducing agents and reaction conditions. Simple carbonyl group reduction affords the corresponding allyl alcohols in high yields[58]. Alternatively, the reduction can also be effected at C=C and C-S bonds 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.

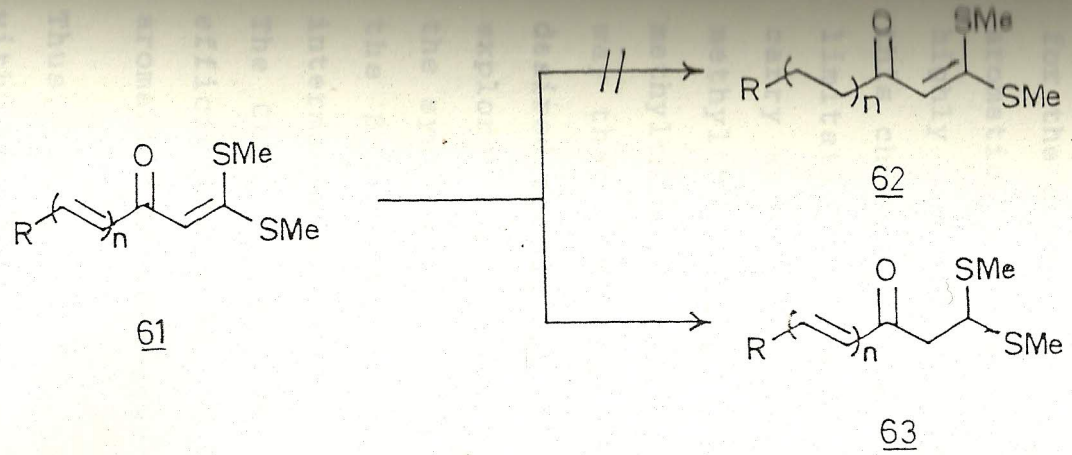
Thus, when α-oxoketene dithioacetals 1 was treated with four fold excess of sodium borohydride in large excess of acetic acid[59] as a solvent the corresponding β-oxodithioacetal was obtained in high yields. No product arising of 1,2-reduction process was observed in the reaction mixture. When less than 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

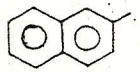
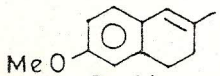
alongwith the merits and demerits of this methodology have been discussed in detail.

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


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

Scheme 10



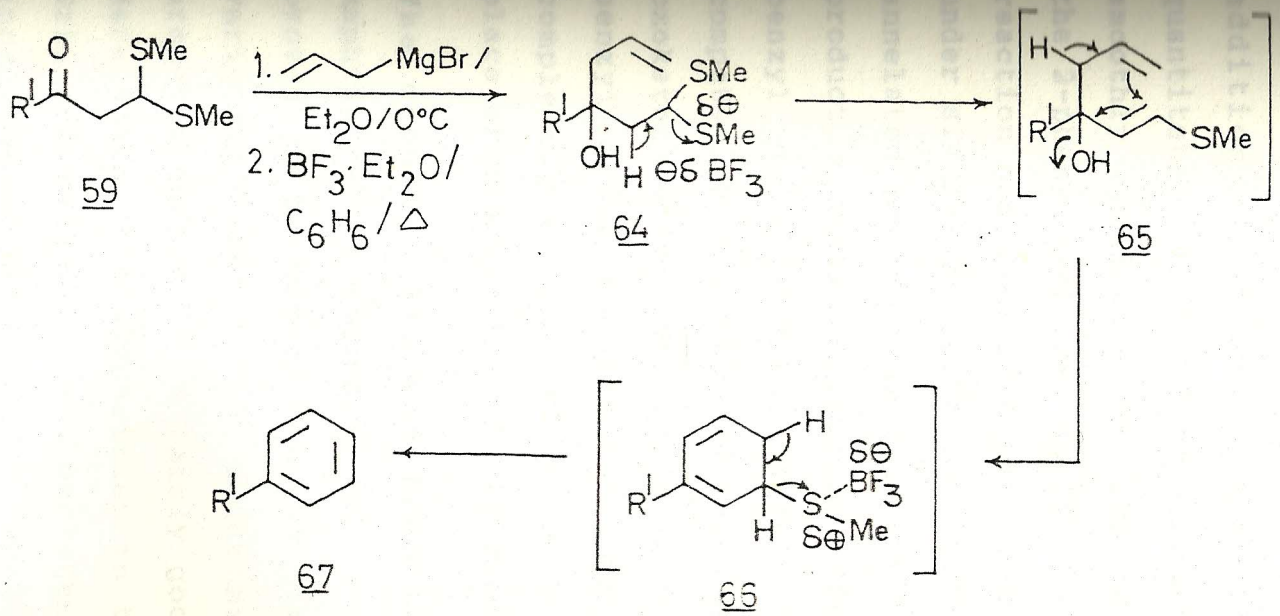
	n	R
61 -63a,	1	C_6H_5
b,	1	4-MeO-C_6H_4
c,	1	
d,	1	
e,	1	
f,	2	C_6H_5
g,	2	4-MeO-C_6H_4
h,	3	C_6H_5

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

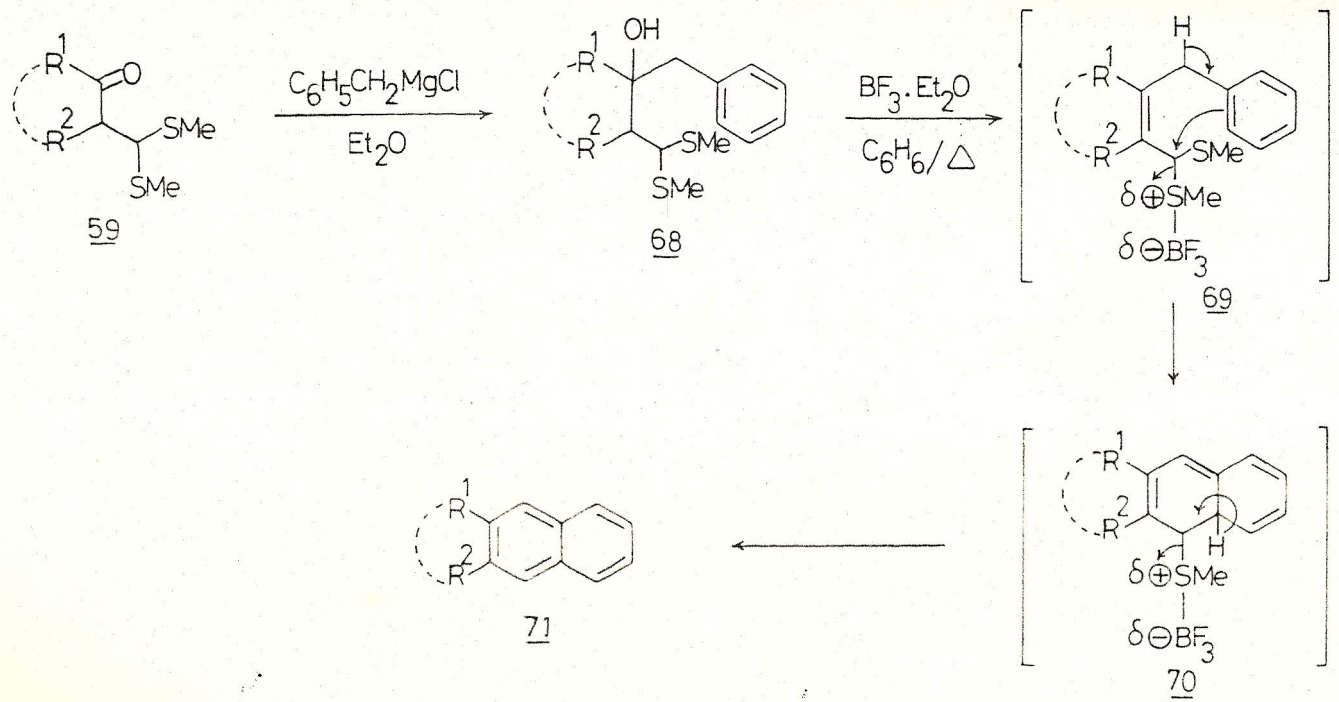
c, R^1 = 2-naphthyl

d, $R^1 = 4\text{-MeO}C_6H_4$

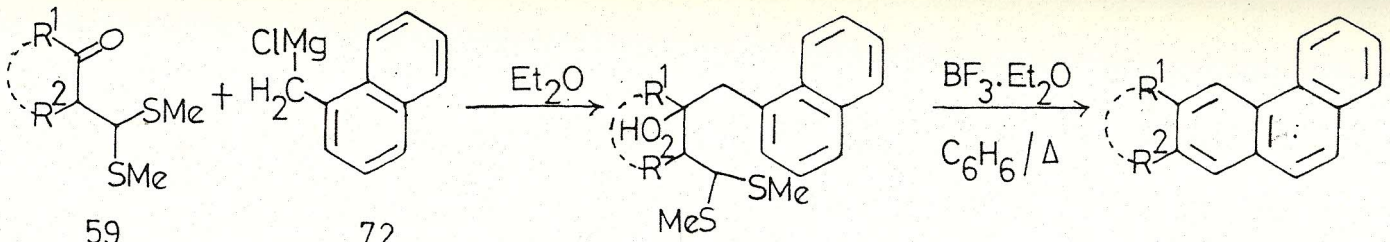
Scheme - 12

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


R1
O
R2
SMe
SMe
59
C6H5CH2MgCl
Et2O
OH
68
BF3.Et2O
C6H6/△
H
69
δ⊕SMe
δ⊖BF3
70
71
71a, R1 = C6H5
b, R1 = CH3
71c
71d

Scheme 13

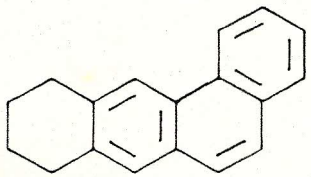


59 72 73

80-90 %

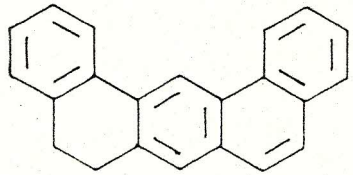
74, $R^1 = C_6H_5$; $R^2 = H$

$R^1 = Me$; $R^2 = H$



80 %

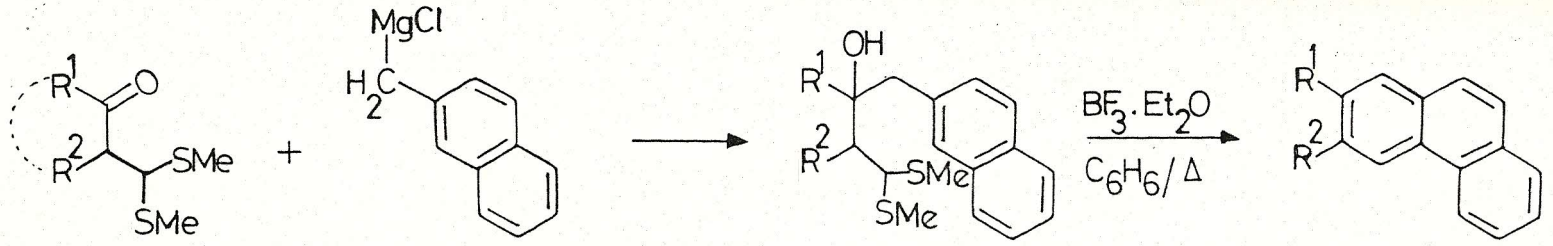
75



85 %

76

Scheme 14

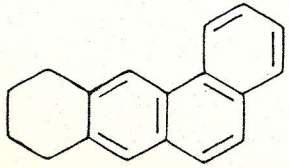


59 77 78

80–85 %

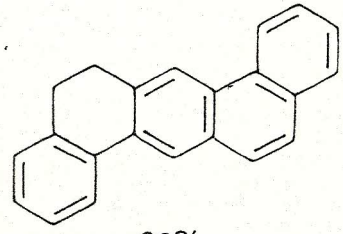
79, $R^1=C_6H_5$; $R^2=H$

$R^1=Me$; $R^2=H$



80 %

80



83%

81

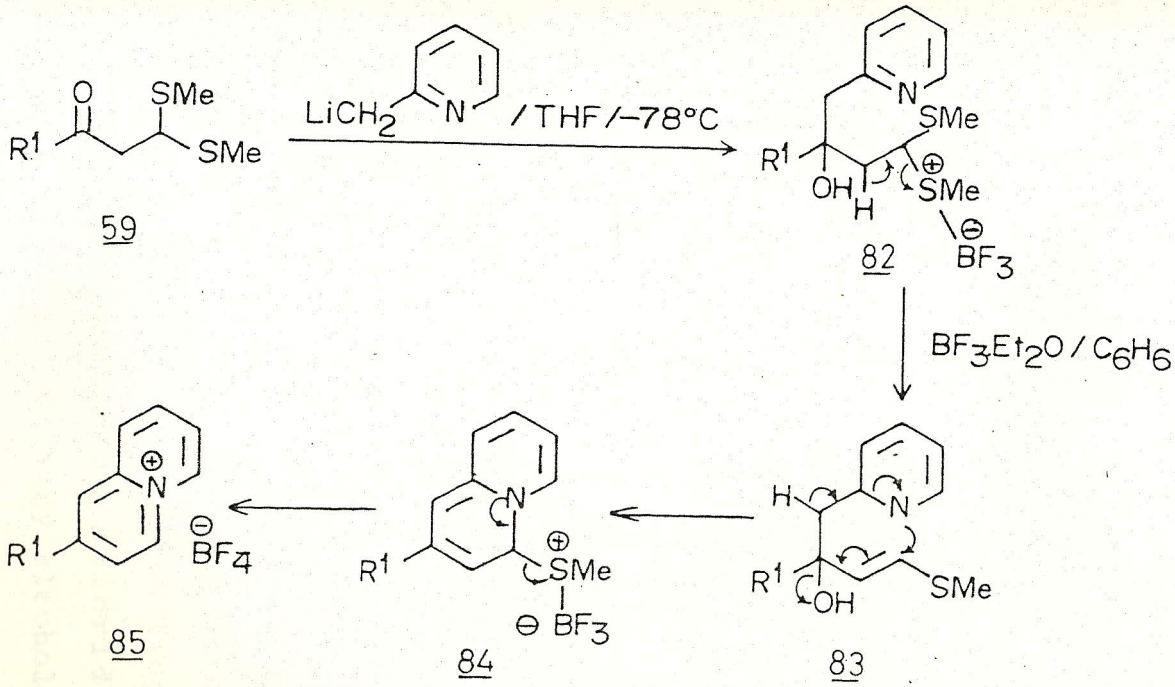
Scheme 15

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_6H_5

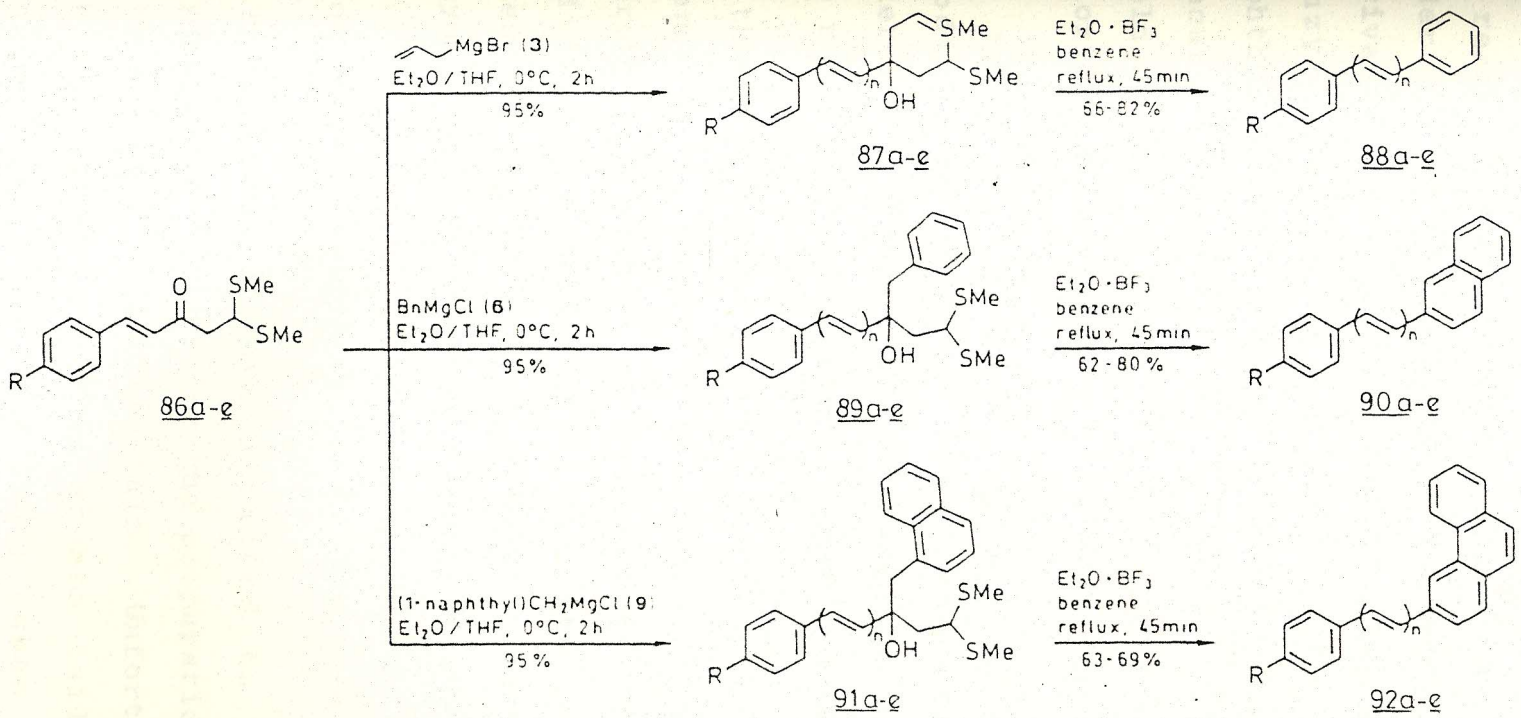
b, R^1 = Me

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			

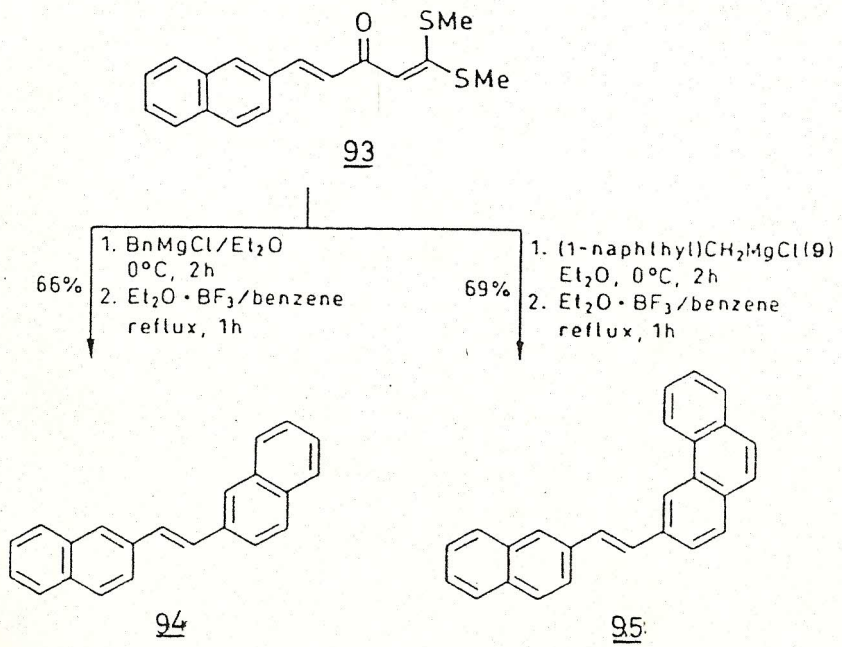
Scheme 17

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).

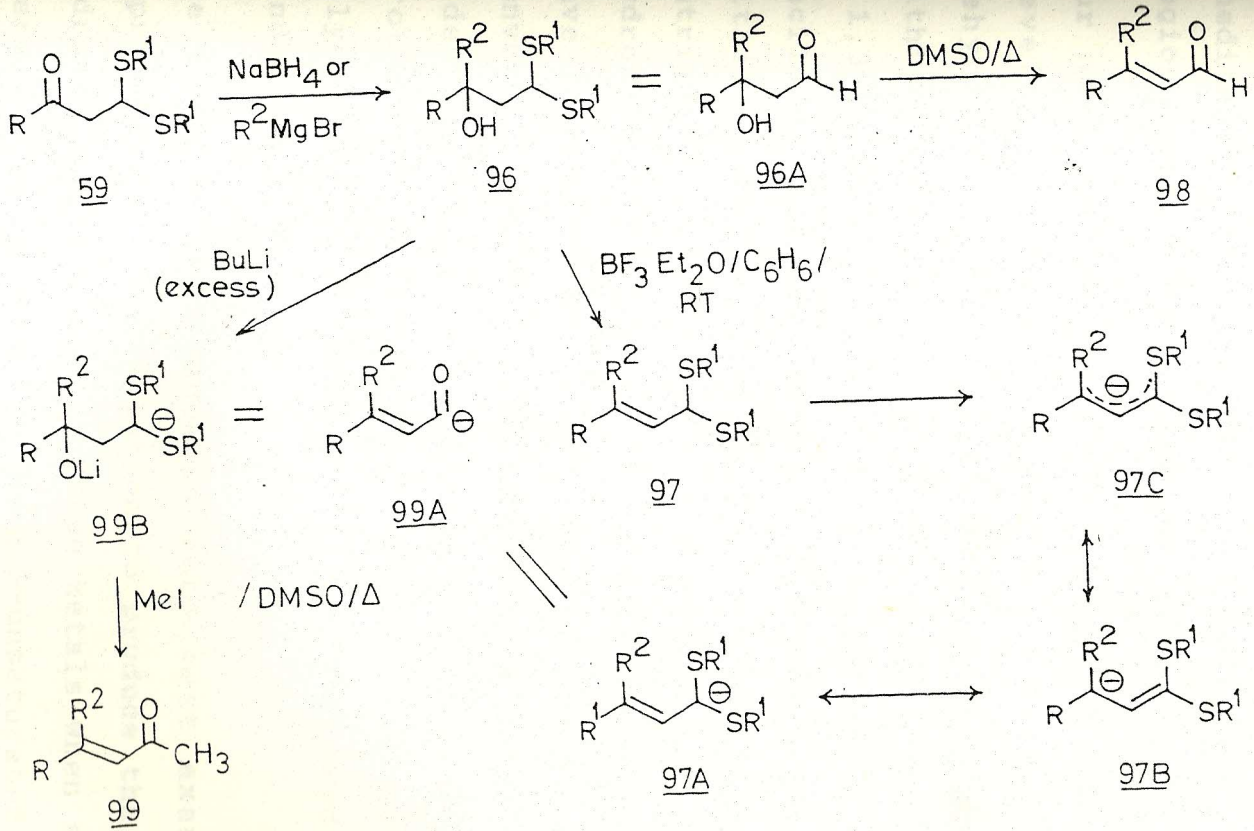
As a part of the synthetic investigations on β-oxodithioacetals, we have proposed to undertake some interesting transformations based on these intermediates and the results are presented in the last chapter.

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
1. BnMgCl/Et2O
0°C, 2h
2. Et2O · BF3/benzene
reflux, 1h
66%
1. (1-naphthyl)CH2MgCl(9)
Et2O, 0°C, 2h
2. Et2O · BF3/benzene
reflux, 1h
69%
94
95

Scheme 18



59 96 96A 98

99B 99A 97 97C

97A 97B 99

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.

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