SYNTHETIC AND MECHANISTIC STUDIES ON POLARIZED KETENE DITHIOACETALS

ABSTRACT

By

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A THESIS

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IN

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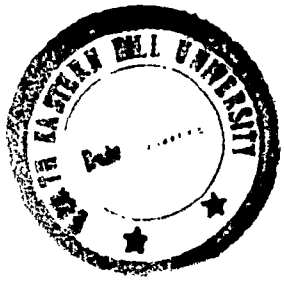
To



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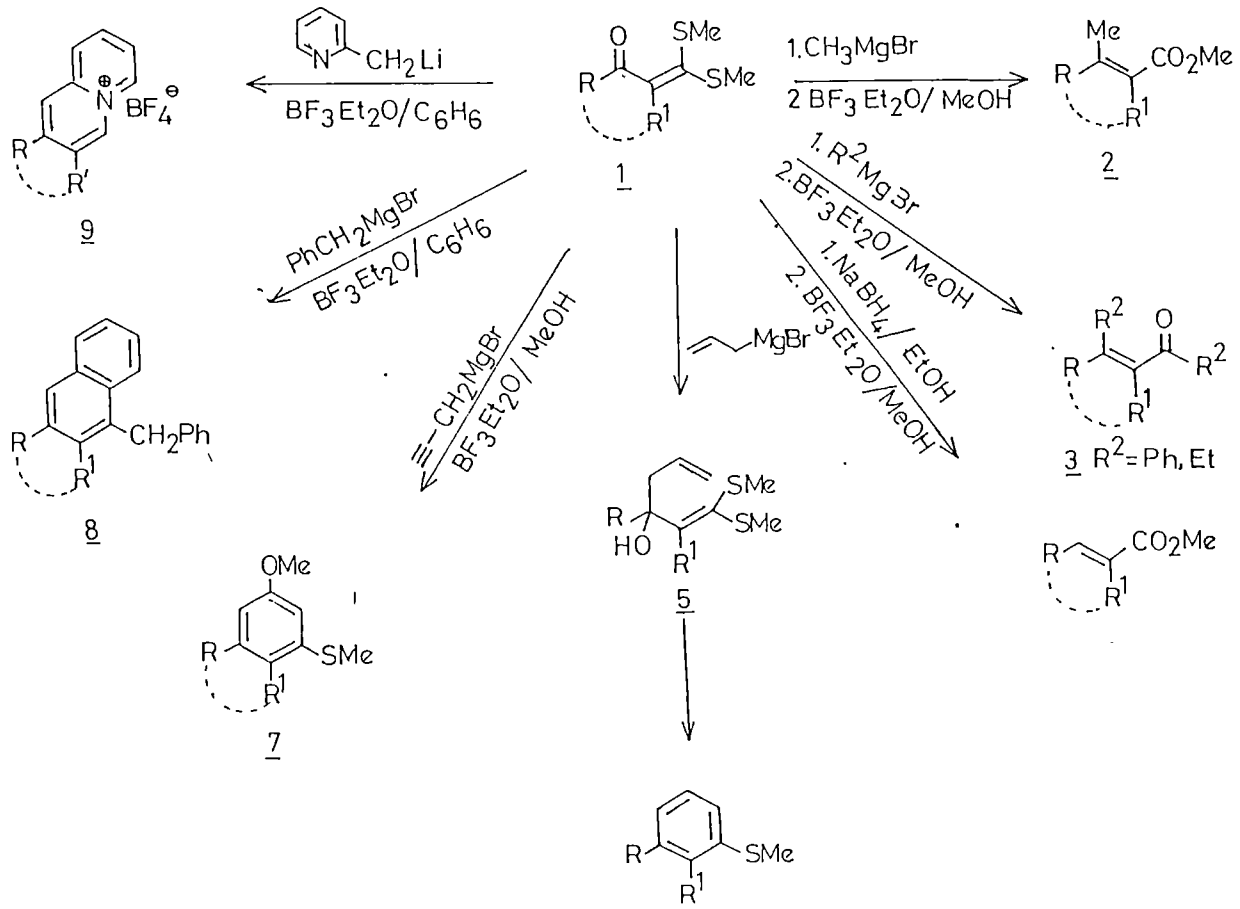
1988

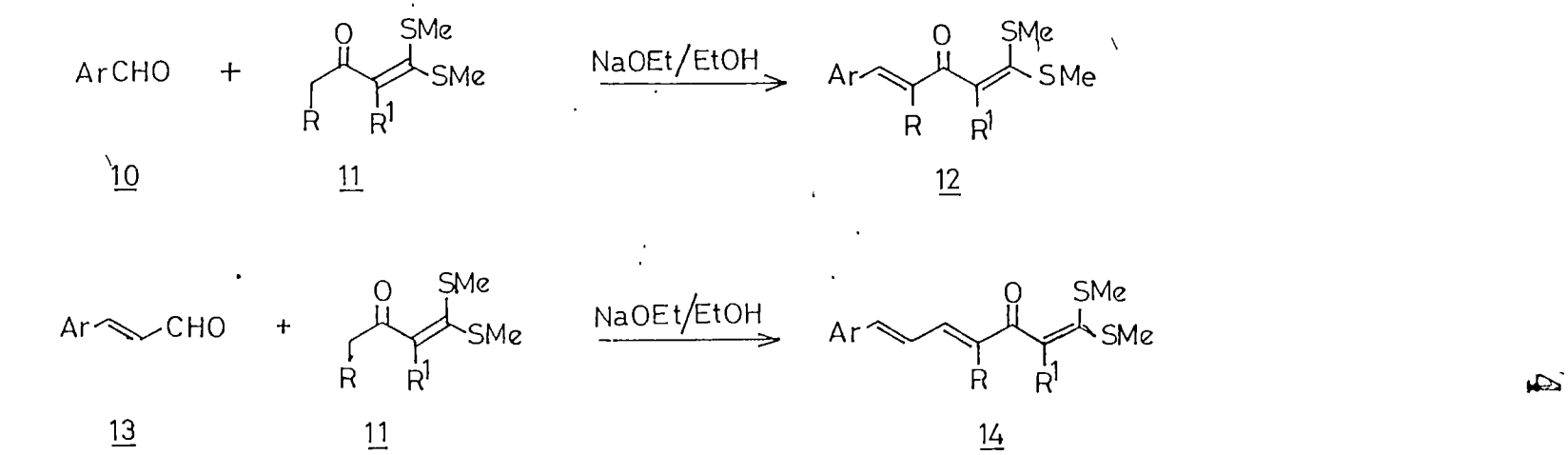
Thesis.

The synthesis of α-oxoketene dithioacetals of the general formula 1 were first reported in 1910, by Kelber and co-workers[1]. A number of these compounds have been subsequently prepared by reacting active methylene ketones with carbon disulphide, in the presence of suitable base followed by alkylation. Many experimental variations of this method have been developed[2-4] in order to improve the yields of dithioacetals 1 evolving the overall process to a one pot transformation. It is therefore now possible to prepare large structural variants of 1 from widely occuring active methylene ketones. The α-oxoketene dithioacetals posses 1,3-electrophilic centers with differing electrophilicity thus making them excellent class of 3-carbon synthons. Their 1,3-electrophilic reactivity has been extensively exploited for the regioselective construction of new 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. For example, the dithioacetal 1 have been shown to undergo exclusive 1,2-reduction with sodium borohydride followed by boron trifluoride etherate assisted methanolysis to afford highly stereoselective eneesters 4 (Scheme 1)[5]. This method is of particular interest since it provides a convenient transformation of easily available active methylene ketones to corresponding eneesters via α-oxoketene dithioacetals. Similarly methyl magnesium iodide is also shown to add to ketene dithioacetal 1 in a 1,2 fashion, while the bulkier Grignard reagents undergo a sequential 1,4-addition followed by a 1,2-addition, resulting in the formation of regioselectively substituted α,β-unsaturated esters (2) and ketones (3) respectively[6]. The allyl magnesium bromide undergoes exclusive 1,2 addition and the resultant carbinol acetals 5 underwent smooth aromatization with a new C-C-bond formation to yield the corresponding


CH2Li
BF3Et2O/C6H6
BF4
R
R'
9
O
SMe
SMe
R
R1
1
1.CH3MgBr
2 BF3 Et2O/ MeOH
Me
CO2Me
R
R1
2
1. R2MgBr
2.BF3Et2O/ MeOH
PhCH2MgBr
BF3Et2O/ C6H6
1.NaBH4/ EtOH
2.BF3Et2O/MeOH
CH2MgBr
BF3Et2O/ MeOH
MgBr
R2
O
R2
R
R1
3 R2=Ph, Et
CH2Ph
R
R1
8
OMe
SMe
R
R1
7
SMe
SMe
R
HO
R1
5
CO2Me
R
R1
SMe
R
R1
6

Scheme 1

benzenoids 6[7]. Similarly propargyl magnesium bromide underwent 1,2-addition followed by ring closure to the corresponding methoxy benzenoids 7[8], with the participation of the solvent methanol. The reaction of the S,S-acetal 1 with benzyl magnesium bromide however underwent sequential 1,4 and 1,2-addition followed by ring closure to the corresponding naphthalene derivatives 8[9]. The reaction of 1 with 2-picolyl-lithium has also been shown to involve only 1,2 addition and their ring closure in the presence of boron trifluoride etherate in benzene gave the quinolizinium salts 9[10]. These representative transformations manifest immense synthetic potential of 1 to construct aromatic as well as heteroaromatic ring systems and their further application in this area is still an ongoing research activity in this laboratory. In continuation of these studies and as a part of the research programme on polarized ketene dithioacetals, it was proposed to study further applications of these synthons for the synthesis of conjugated polyene esters and products arising thereof. Thus the α-oxoketene dithioacetals of the general formula 11 (Scheme 2) were condensed with aromatic aldehydes 10 or 13 to give the corresponding cinnamoyl ketene dithioacetals 12 or the homologus 5-aryl 2,4-pentadienoyl ketene dithioacetals (14). However, the aliphatic aldehydes could not be condensed as described above and an alternative approach was therefore developed. Thus the acyl ketene dithioacetals 11 were first reacted with N,N-dimethylformamide diethylacetal 15 to obtain the enaminoketones 16 which underwent 1,4-addition with various alkyl magnesium halides to afford the corresponding alkenoyl ketene dithioacetals 17 in good yields[11]. The above intermediates 12 and 14 were shown to undergo *methanolysis in the presence of boron trifluoride etherate and mercuric* chloride to yield the γ,δ-unsaturated β-ketoesters 18 which are

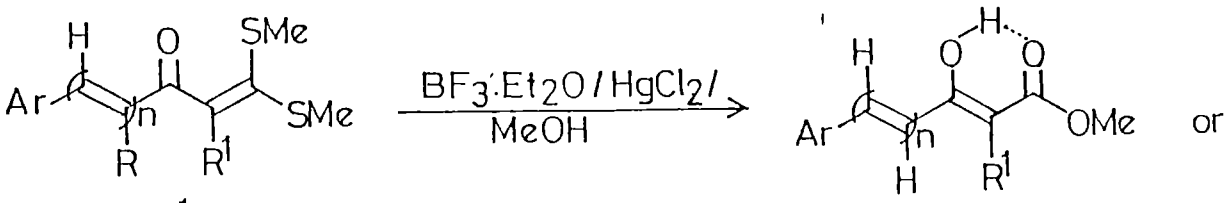

ArCHO
NaOEt/EtOH
10
11
12
13
14
$(CH_3)_2N-CH(OEt)_2$
Δ
R^2MgBr
11,12,14,16,17 a R = R¹ = H
b R = H ; R¹ = Me
c R = R¹ = Me
R^2 = Me, Et, i-Pr, n-Pr.

Scheme 2

potential precursors in various synthetic transformations[12]. The cinnamoyl ketene dithioacetals 12c having substituents at the 2 and 4 positions underwent boron trifluoride etherate assisted Nazarov cyclization to give substituted cyclopentenone 19[12]. The generality of this cyclopentenone synthesis and the structural requirement for such ring closure have been discussed in detail in Chapter II of the thesis.

The cinnamoyl ketene dithioacetals were shown to undergo 1,2-reduction with sodium borohydride followed by methanolysis to afford the corresponding methyl 5-aryl-2,4-pentadienoates in good yields[13]. In the present work, this methodology has been extended to the synthesis of methyl 7-aryl-2,4,6-heptatrienoates[14]. Thus the dithioacetals 14 (Scheme 4) obtained by condensation of 11 and cinnamaldehyde underwent 1,2-reduction with sodium borohydride followed by methanolysis to give the corresponding methyl 7-aryl-2,4,6-heptatrienoates 20 in good yields. Though a substitution at 2-position (14b) did not affect the formation of trieneester, the 2,4-disubstitution in both 12 and 14 (12c and 14c) changed the reaction pattern resulting in the formation of rearranged 2-aryl or styryl cyclopentenones 21[15] (Scheme 4). The detailed explanation for the formation of cyclopentenones and the conformational profiles of their open chain precursors have been discussed in the Chapter III of the thesis.

The cinnamoyl ketene dithioacetals 12 underwent 1,4-addition with alkyl and aryl grignard reagents resulting in the formation of corresponding δ -substituted β -ketoesters 22 in high yields after subsequent methanolysis of the Michael adduct. However allyl magnesium bromide exhibited preference for 1,2-addition to give the corresponding styryl

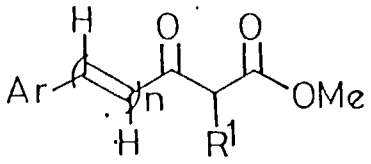


12 , R^1 = H , Me; n = 1

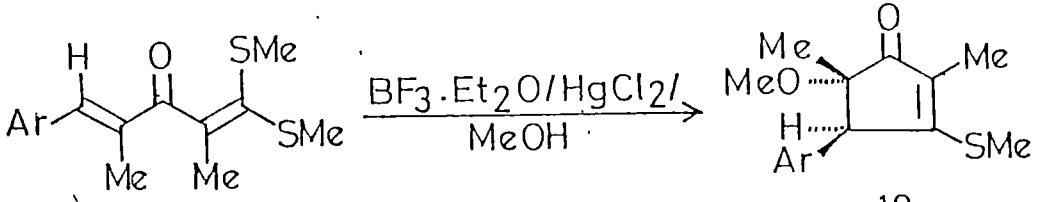
14 , R^1 = H; n = 2

or

18 A



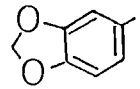
18 B



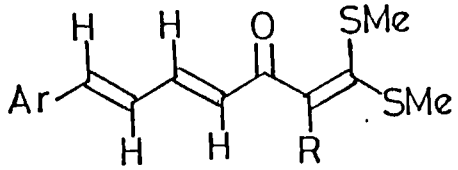
12 c

19

Ar = C_6H_5; 4-$CH_3C_6H_4$; 4-$CH_3OC_6H_4$; 3-$CH_3OC_6H_4$; 3,4$(CH_3O)_2C_6H_4$; p.Cl C_6H_4;

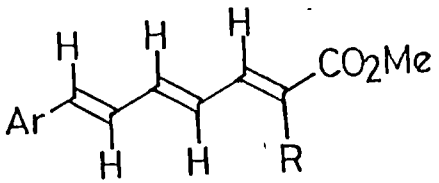


Scheme 3

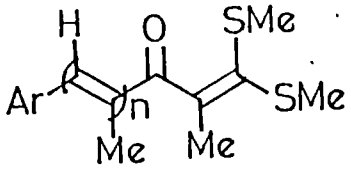


14 a , R = H
b , R = Me

1. $NaBH_4$ / MeOH
2. $BF_3.Et_2O$/MeOH

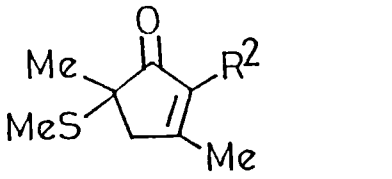


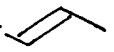
20 a , R = H
b , R = Me

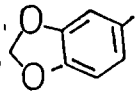


12 c , n = 1
14 c , n = 2

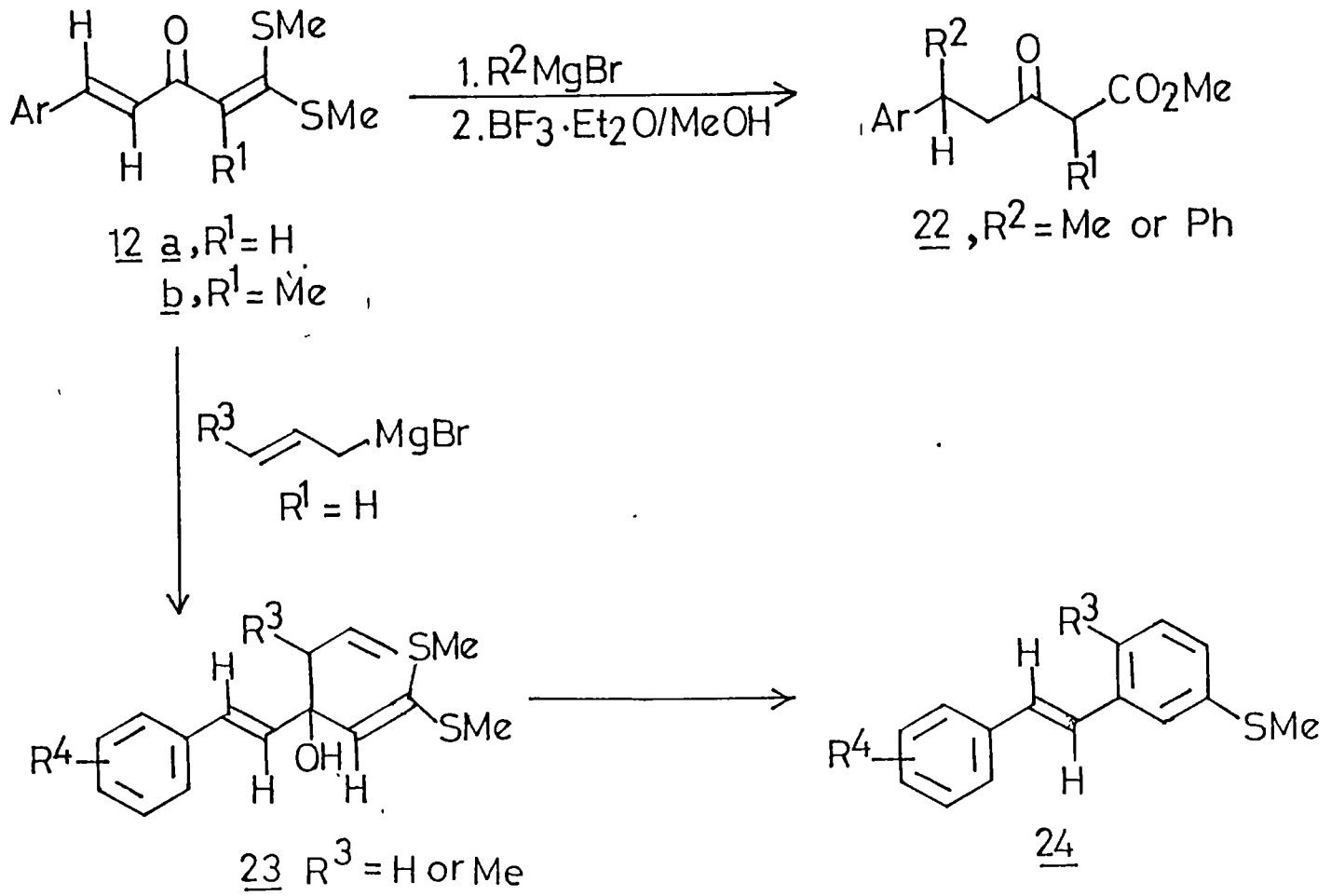
1. $NaBH_4$ / MeOH
2. $BF_3.Et_2O$/MeOH



21 a , R^2 = Ar
b , R^2 = Ar 

20-21; Ar = p MeC_6H_4 ; 4-$MeOC_6H_4$; C_6H_5 ; 

Scheme -4

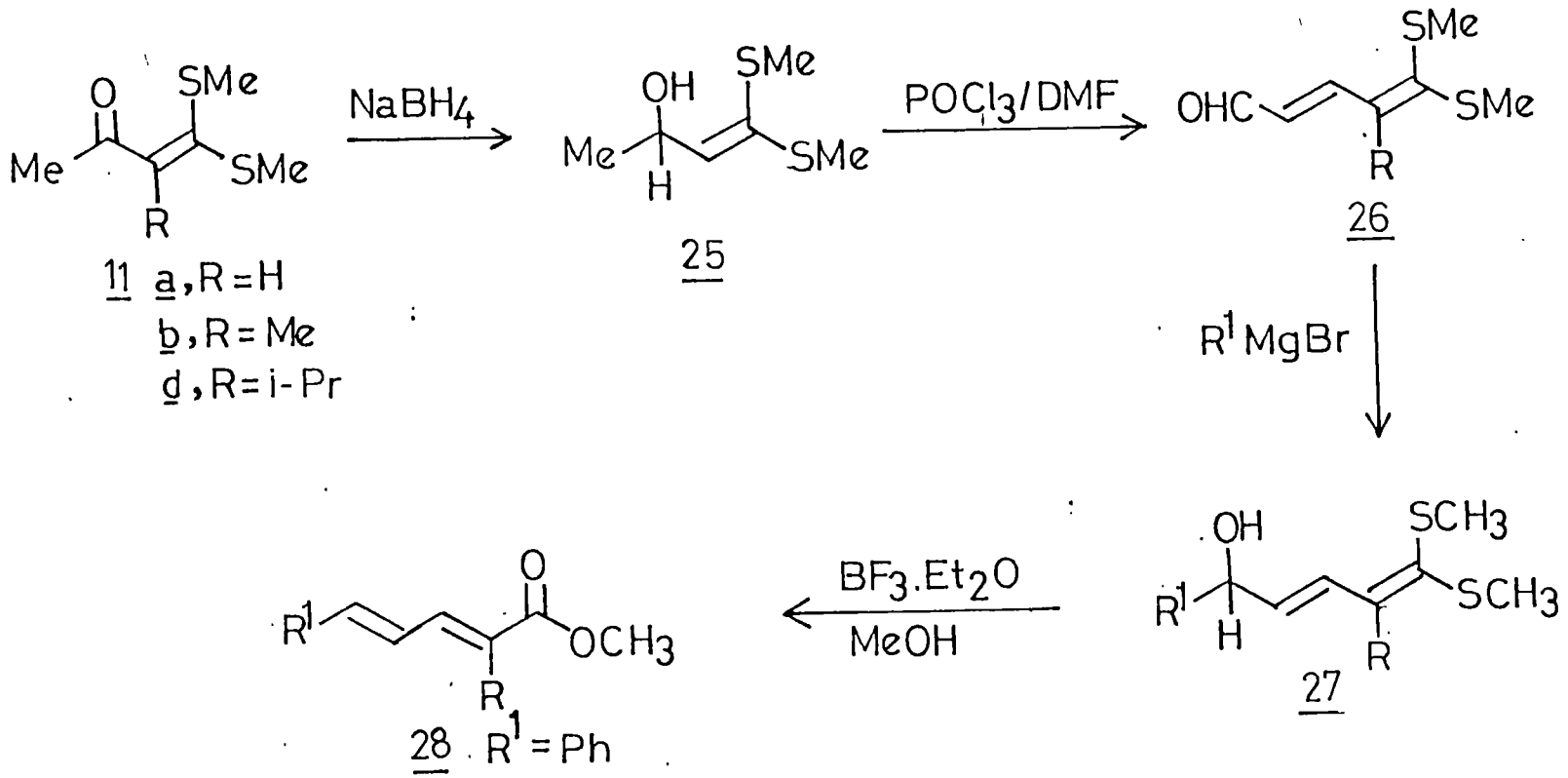


23, 24; R = H; 4-Me; 4-Cl; 3-MeO; 2,4-Cl_2; 3,4-Cl_2.

Scheme-5

carbinol acetals 23 which underwent cycloaromatization to yield the corresponding stilbenes 24 (Scheme 5). The generality of this new stilbene synthesis[16] has been investigated and described in the Chapter IV of the thesis.

The α-oxoketene dithioacetals were shown to undergo 1,3-carbonyl transposition involving sodium borohydride reduction or nucleophilic addition followed by solvolysis (Scheme 1). It was considered of interest to utilize these versatile synthons for the study of 1,5 to 1,11 alternatively sequential carbonyl transpositions. The α-oxoketene dithioacetals of the general formula 11 underwent 1,2-reduction with sodium borohydride to give the carbinol acetal 25 which under Vilsmeier-Haack reaction conditions gave the dienealdehyde 26. The aldehyde 26 underwent smooth 1,2 addition with phenyl magnesium bromide to give the corresponding dienealcohol 27 followed by methanolysis to yield the corresponding dieneesters 28 through 1,5-carbonyl transpositions. Thus a new method for the synthesis of dieneesters 28 through 1,5-carbonyl transposition starting from oxoketene dithioacetal 11 (Scheme 6) is developed. The method is further extended for synthesis of homolo - gous polyenealdehydes 28 and 30 through the sequence of reactions described in Scheme 7. These aldehydes were in turn condensed with various active methylene ketones to yield the corresponding polyeneketones 31, 34, 37 (Scheme 8) which are suitable precursors for 1,7; 1,9 and 1,11 carbonyl transpositions respectively. Thus the heptatrienones 31 (n=1) after sodium borohydride reduction or methyl magnesium iodide addition yielded the corresponding trienol acetals 32 which underwent smooth 1,7 carbonyl transposition to give the corresponding trieneesters



11 a, R = H
b, R = Me
d, R = i-Pr

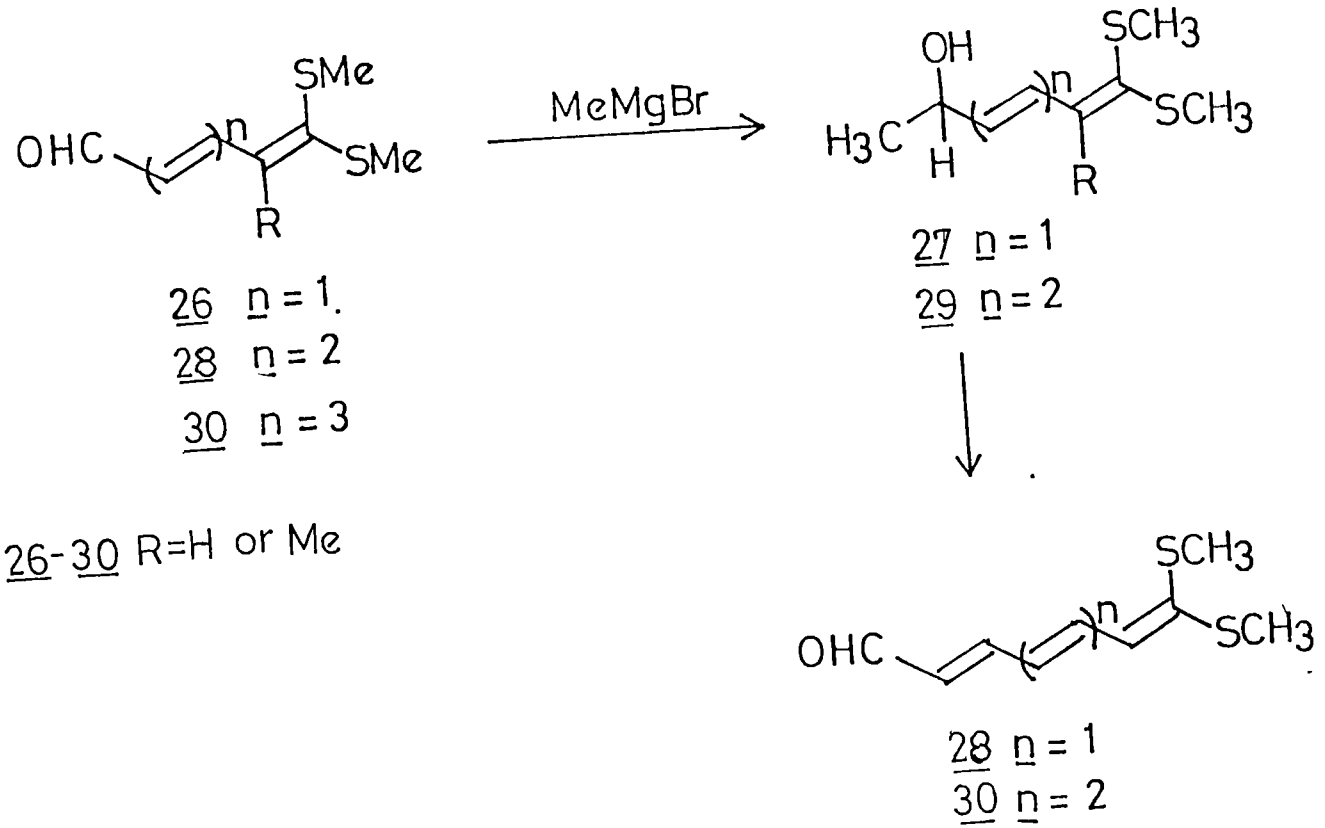
25

26

27

28 R^1 = Ph

Scheme-6



26 n = 1
28 n = 2
30 n = 3

26-30 R=H or Me

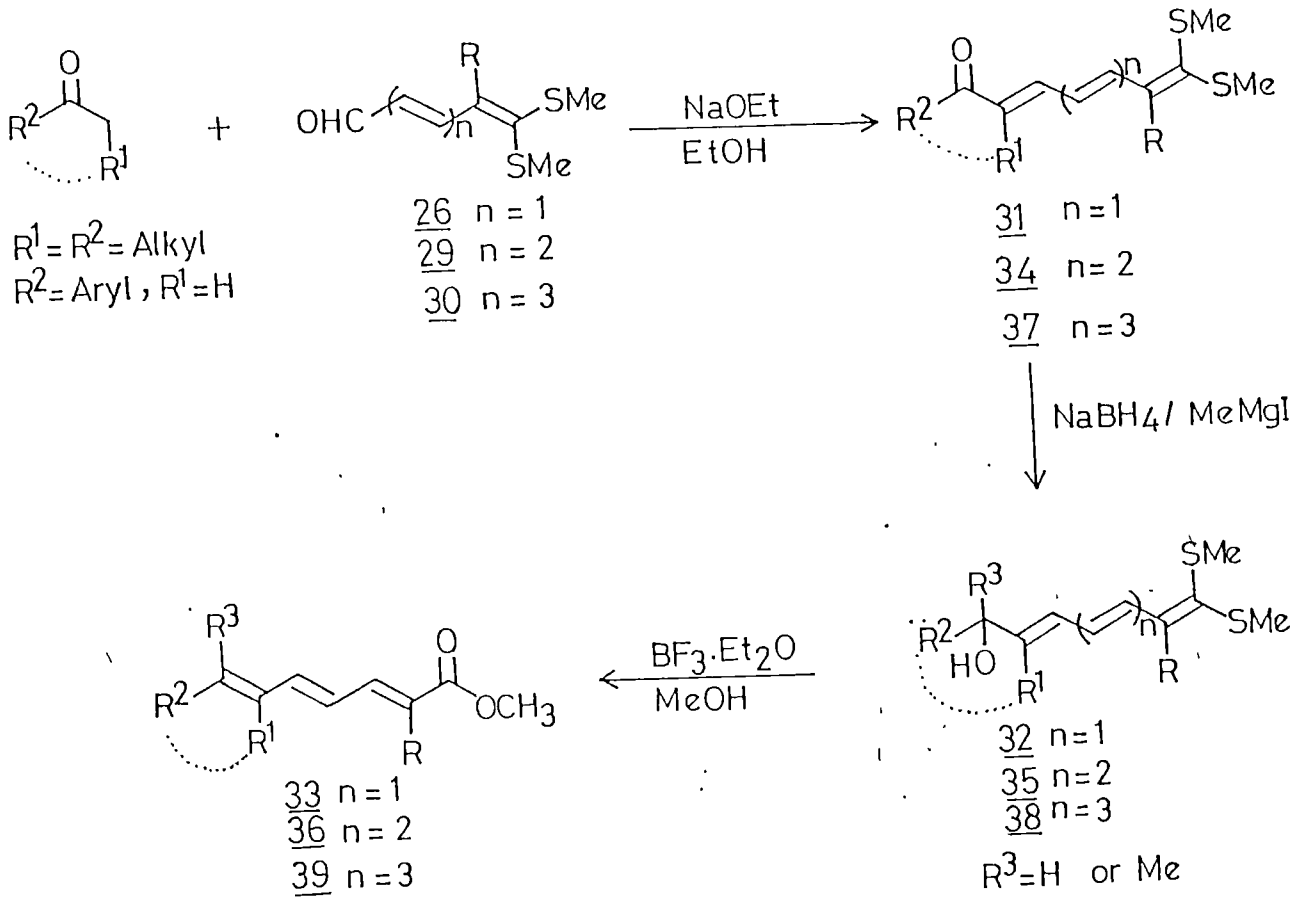
27 n = 1
29 n = 2

28 n = 1
30 n = 2

Scheme-7

33 in good yield. Similarly tetraenyl ketones 34 (n=2) (Scheme 8) were shown to undergo the described reaction sequence (Scheme 8) to give the corresponding tetraeneesters 36 (n=2) in good yields. The overall process involves an unprecedented 1,9-carbonyl transposition. When 37 (n=3) was subjected to sodium borohydried reduction the corresponding enolacetals 38 were formed, which underwent methanolysis involving an unprecedented 1,11-carbonyl transposition to yield the corresponding pentaeneesters 39 in good yield (Scheme 8).

The generality of this new method involving unprecedented alternatively sequential carbonyl transposition to yield highly stereospecific all trans polyenesesters have been described in detail in the Chapter V of the thesis.



30-39, R^2 = Aryl ; R^1 = H

$R^2 = R^1$ =

R^2 = ; R^1 = H

$R^2 = R^1$ =

Scheme-8

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Professor H. Junjappa
Department of Chemistry

This is to certify that the work described in this thesis has been carried out by Mr. C.V. Asokan under my supervision. He has satisfactorily completed the pre-Ph.D. courses prescribed and the minimum period of two years of investigational work for the award of Ph.D. degree in Chemistry.

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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This is to certify that Mr. C.V. Asokan, a Ph.D student of the Department of Chemistry has satisfactorily completed the following courses as a part of his Ph.D. course programme.

Course No.	Title
1. Chem - 668	Electrochemistry
2. Chem - 630	Biosynthesis and Natural Product Chemistry
3. Chem - 631	Medicinal Chemistry
4. SPS - 602	German Language

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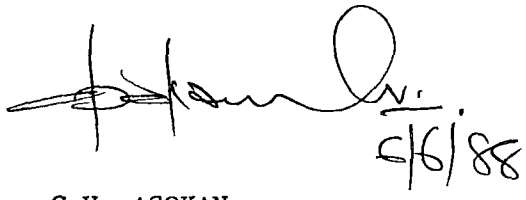


C.V. ASOKAN

C O N T E N T S

PREFACE

Polarized ketene dithioacetals, which can be easily prepared from a wide variety of active methylene compounds have been extensively explored in this laboratory for the development of new synthetic methods for a variety of heterocyclic and carbocyclic compounds. The work described in this thesis has been carried out as a part of this ongoing research programme and highlights new transformations of oxoketene dithioacetals.

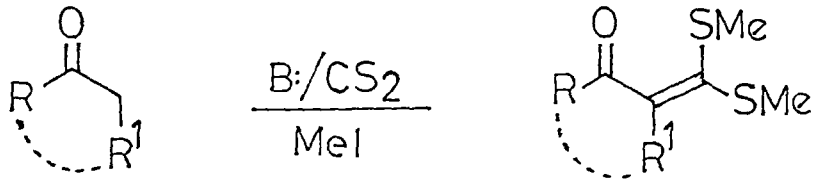
The first chapter gives an account of some of the recent transformations of oxoketene dithioacetals reported from this laboratory. The second chapter deals with the solvolytic studies on cinnamoyl- and 4-aryl-2,4-pentadienoyl ketene dithioacetals leading to a new method for γ, δ-unsaturated β-ketoesters and substituted cyclopentenones. In the third chapter of the thesis, 1,2-reduction of cinnamoyl- and 5-aryl-2,4-pentadienoyl ketene dithioacetals with sodium borohydride and further solvolytic studies of the resulting carbinol acetals leading to 7-aryl-2,4,6-heptatrienoates and substituted cyclopentenones have been described. A new synthesis of unsymmetrical stilbenes *via* cycloaromatization has been described in the fourth chapter. Studies on the addition of phenyl and methyl grignard reagents to cinnamoyl and 5-arylpentadienoyl ketene dithioacetals have also been presented in the same chapter.

The fifth chapter of the thesis deals with 1,5- to 1,11- alternatively sequential carbonyl transpositions *via* oxoketene dithioacetals. Synthesis of several bis(methylthio) polyene aldehydes and polyenyl ketones as well as the studies on the transposition of their carbonyl functionalities have been discussed in detail.

CHAPTER I

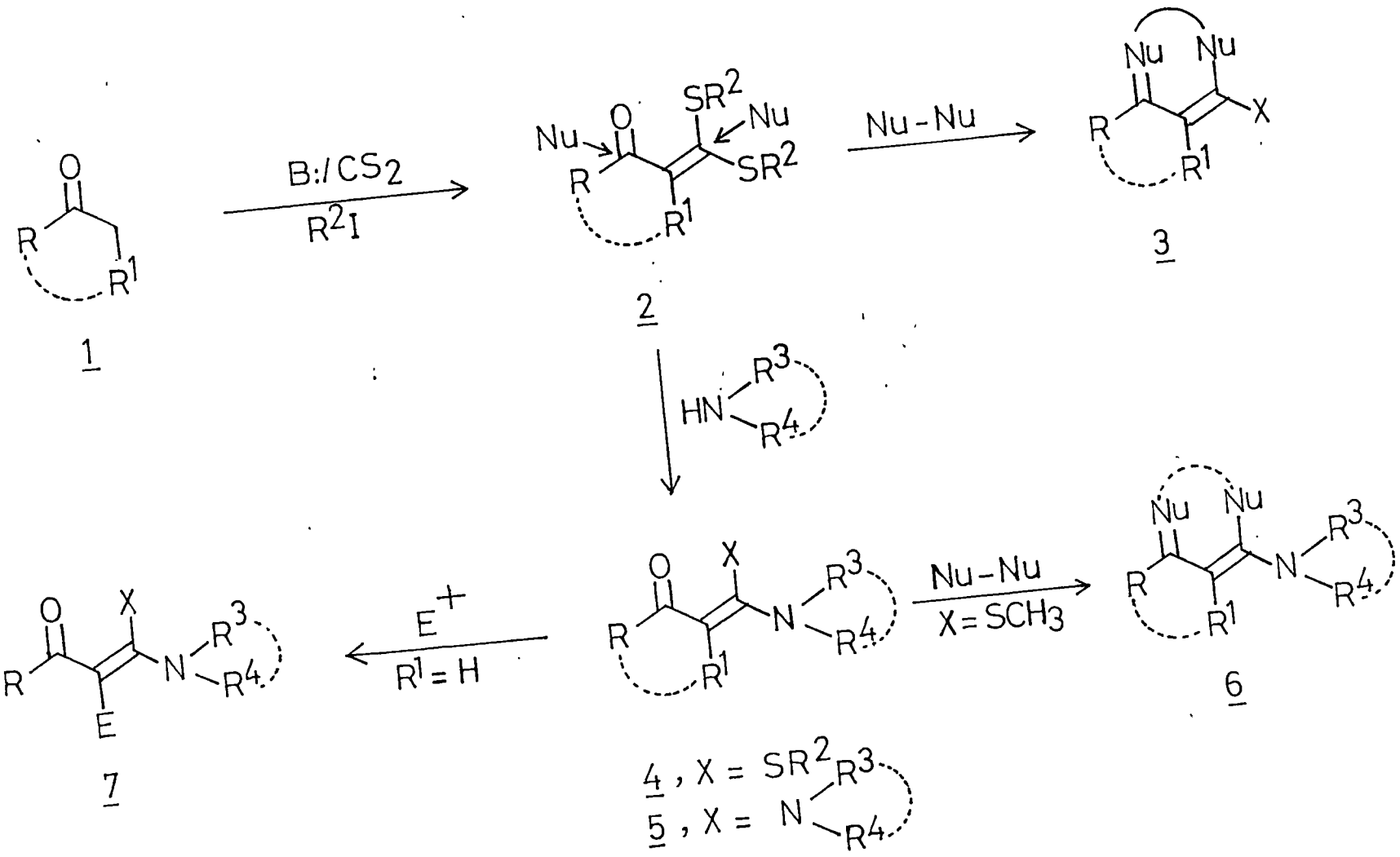
INTRODUCTION

The α -oxoketene dithioacetals[1] 2 are among the simplest synthetic intermediates, which can be prepared[5-13] by treating any active methylene compound of the general formula 1 with two equivalents of base and carbon disulphide followed by alkylation. The first synthesis of 2 from acetophenone was reported by Kelber and co-workers in 1910[2-4].



However the method was not of synthetic importance and the chemistry of these compounds remained dormant until Thuillier and co-workers prepared these compounds in high yields often in one pot reaction by reacting the active methylene ketones with carbon disulphide in the presence of sodium amylate followed by alkylation[5-8]. Subsequently these reaction conditions have been greatly improved using different bases otherwise maintaining the same conditions[9-13]. A large number of α-oxoketene dithioacetals have now been reported and their chemistry has been reviewed[14].

The dithioacetals 2 execute well defined physical properties and can be purified by conventional purification methods. They are stable at room temperature and can withstand mild acidic and alkaline conditions. The corresponding α-oxoketene O,O-acetals have generally been prepared by reacting ketene O,O-acetals with alkyl or aryl acid chloride in the presence of anhydrous aluminium chloride[15,16]. These compounds are extremely moisture sensitive and undergo hydrolysis under mild conditions. Therefore the α-oxoketene dithioacetals which can be prepared by easier methods in one pot reaction in high yields, should make them synthetically useful class of compounds. They exhibit greater stability than the corresponding O,O-acetals. They can further be converted to the corresponding ketene dihalogenides[17,18], S,N[19] and N,N[20] acetals making them more important as precursors for a large variety of functionalized acetals. Any organic molecule with two replaceable hydrogen atoms by base can be converted into the corresponding dithioacetals involving the choice of a wide variety of organic structural framework.



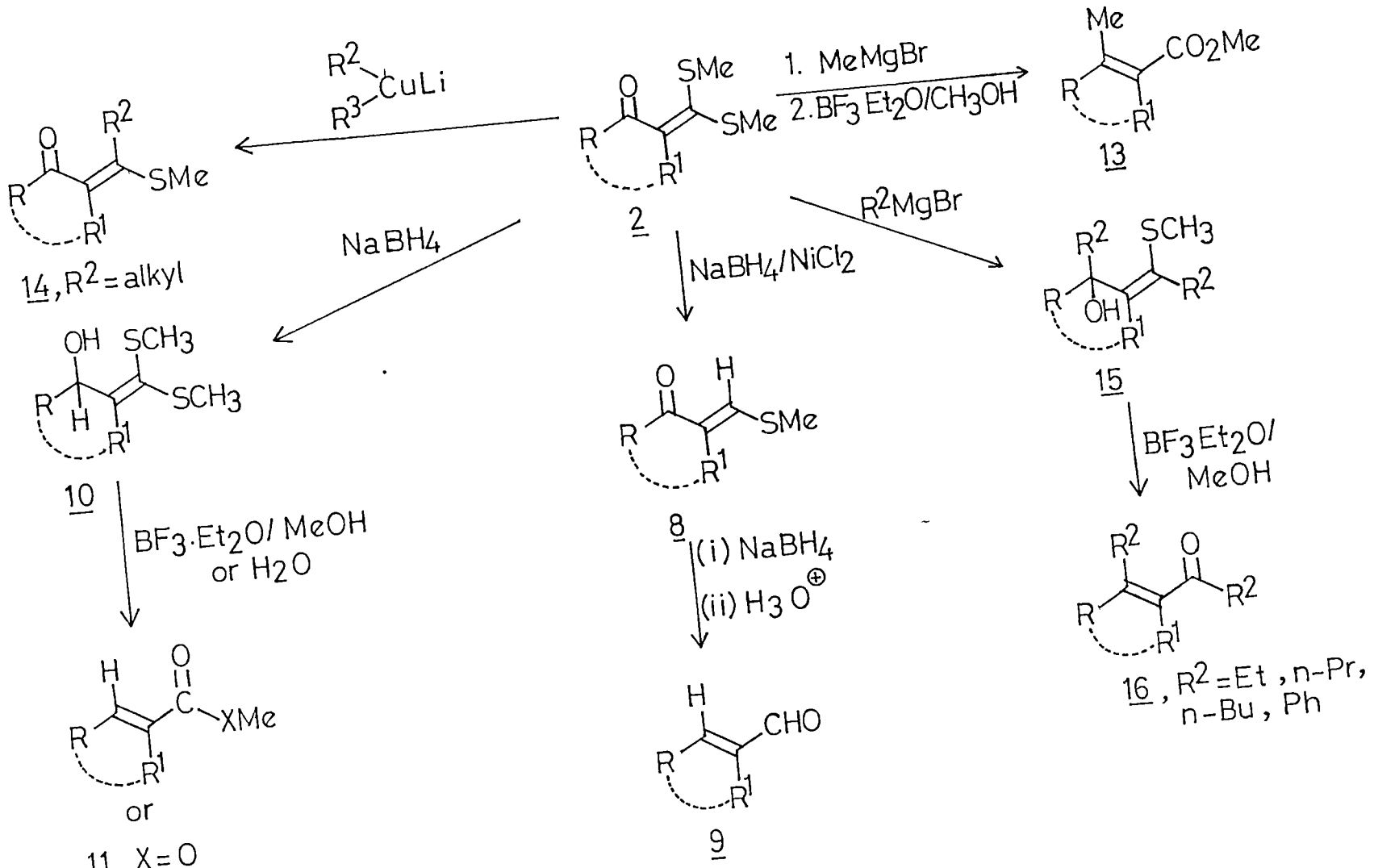
Scheme 1

The α-oxoketene dithioacetals have been shown to be excellent 3-carbon fragments possessing 1,3-electrophilic centers with differing electrophilic properties, suitable for synthetic exploitation. These S,S-acetals and α-oxoketene S,N and N,N-acetals have been extensively used in this laboratory for developing a number of new synthetic methods, for both heterocyclic and carbocyclic systems[21-51]. For example, new general synthesis of alkoxypyrimidine[21,22,13,30,31,32], aminopyrimidines[33,46], 2H-pyridones[24,27,34,36,34], alkoxy and aminopyrazoles[23,31,47], isoxazoles[35], thiazoles[40,41], pyrazolopyrones[25], imidazoles[41,42,48], quinoxaline[41], and aminopyrones[50] have been developed.

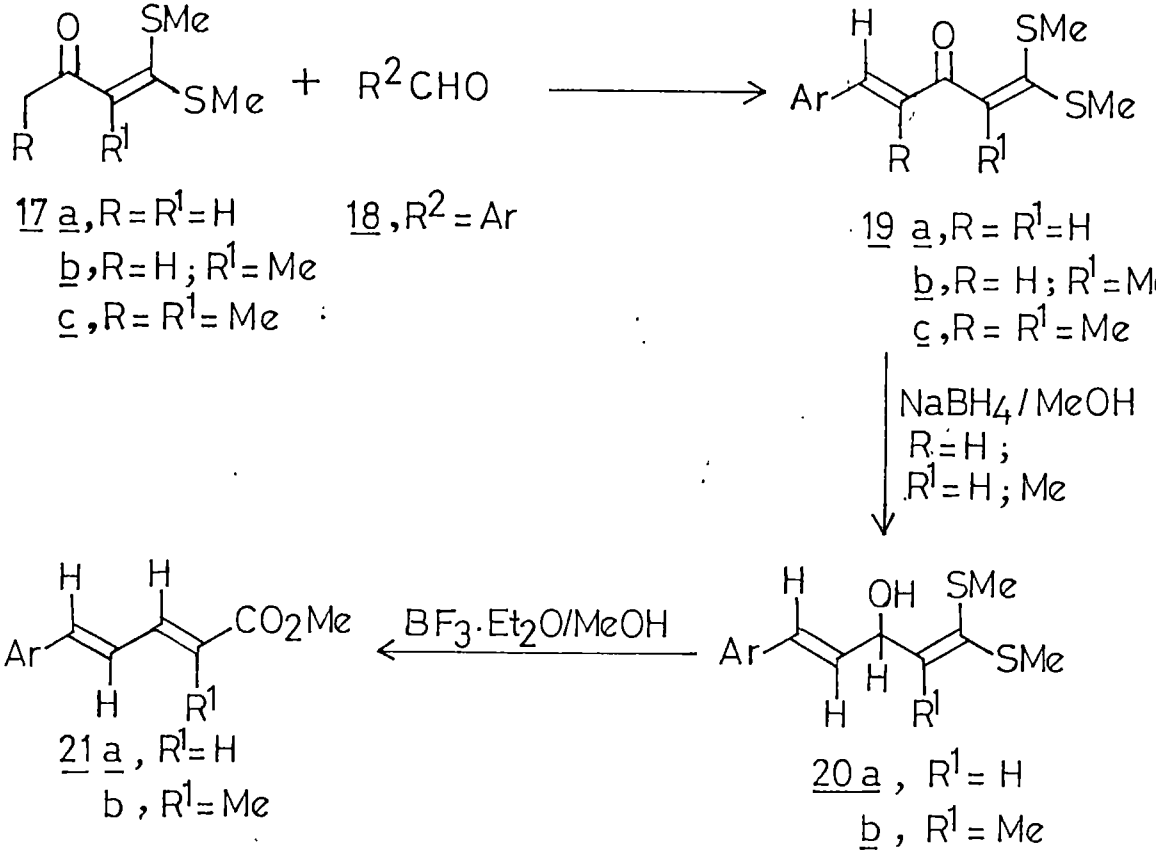
The carbonyl group of α-oxoketene dithioacetals have been reported to undergo sodium borohydride reduction to give the corresponding carbinol acetals 10[52] (Scheme 2) by Thuillier and co-workers in 1966. These carbinol acetals on subsequent acid catalyzed treatment gave a number of rearranged products. The 1,2-reduction of α-oxoketene dithioacetals was reinvestigated in this laboratory when the resultant carbinol acetals 10 obtained as above were shown to undergo smooth methanolysis in the presence of boron trifluoride etherate to afford highly regio and stereoselective α,β-unsaturated methyl esters 11 in high yields[53]. The method was therefore of preparative importance since the product mixture on methanolysis was obtained as a single compound in high yields. Under controlled $BF_3.Et_2O$ catalyzed hydrolysis, 10 could also afford the corresponding thiol ene-esters 12 in high yields. The overall transformation is considered as a homologation of active methylene ketones at the α-carbon involving a 1,3-carbonyl transposition. Thus a new general regio- and stereoselective method was developed for the synthesis of α,β-unsaturated esters.

The 1,3-carbonyl transposition was further extended in this laboratory for the synthesis of diene esters[55]. Thus the α-oxoketene dithioacetals 17a-c derived from aliphatic ketones were condensed with benzaldehydes[54] to give the cinnamoyl ketene dithioacetals 19, which on borohydride reduction and solvolysis afforded the corresponding 7-aryl 2,4-pentadienoates 21 in high yields (Scheme 3)[55]. The α-oxoketene dithioacetals were also shown to undergo nickel boride ($NaBH_4/NiCl_2$) reduction to give the corresponding β-methylthioalkenyl ketones 8, which are masked β-ketoaldehydes[56]. The borohydride reduction of these intermediates and subsequent hydrolysis yielded the corresponding α,β-unsaturated aldehydes 9 (Scheme 2).

The Grignard and organolithium reagents undergo either regioselective 1,2-addition to afford the α-hydroxy ketene dithioacetals or a sequential 1,4 and 1,2 addition to afford the β-hydroxyvinylsulphides 15. The boron trifluoride etherate catalyzed solvolysis or the hydrolysis of these carbinols yield either β-substituted α,β-unsaturated esters 13 or the corresponding ketones 16 (Scheme 2)[57] in good yields. Generally the bulkier grignard reagents undergo initial 1,4 followed by 1,2-addition, while the methyl magnesiumiodide gave exclusively 1,2-addition. Dieter and co-workers have exploited the potentiality of α-oxoketene dithioacetals 2 as substrates for chemo- and stereoselective construction of new C-C bonds using organocuprate reagents[58,59]. They have examined the addition of a series of organocuprate reagents and studied the effect of these reagents on the product distribution and stereoselectivity. The compounds thus obtained were also subjected to 1,2-reduction with sodium borohydride followed by hydrolysis to afford the corresponding α,β-unsaturated ketones.


R2
R3CuLi
SMe
SMe
1. MeMgBr
2.BF3 Et2O/CH3OH
Me
CO2Me
2
13
14, R2 = alkyl
NaBH4
NaBH4/NiCl2
R2MgBr
SCH3
OH
10
8
15
BF3·Et2O/ MeOH
or H2O
(i) NaBH4
(ii) H3O⊕
BF3Et2O/
MeOH
XMe
CHO
or
9
16, R2 = Et, n-Pr,
n-Bu, Ph
11, X = O
12, X = S

Scheme-2



17 a, R = R1 = H
b, R = H ; R1 = Me
c, R = R1 = Me

18, R2 = Ar

19 a, R = R1 = H
b, R = H ; R1 = Me
c, R = R1 = Me

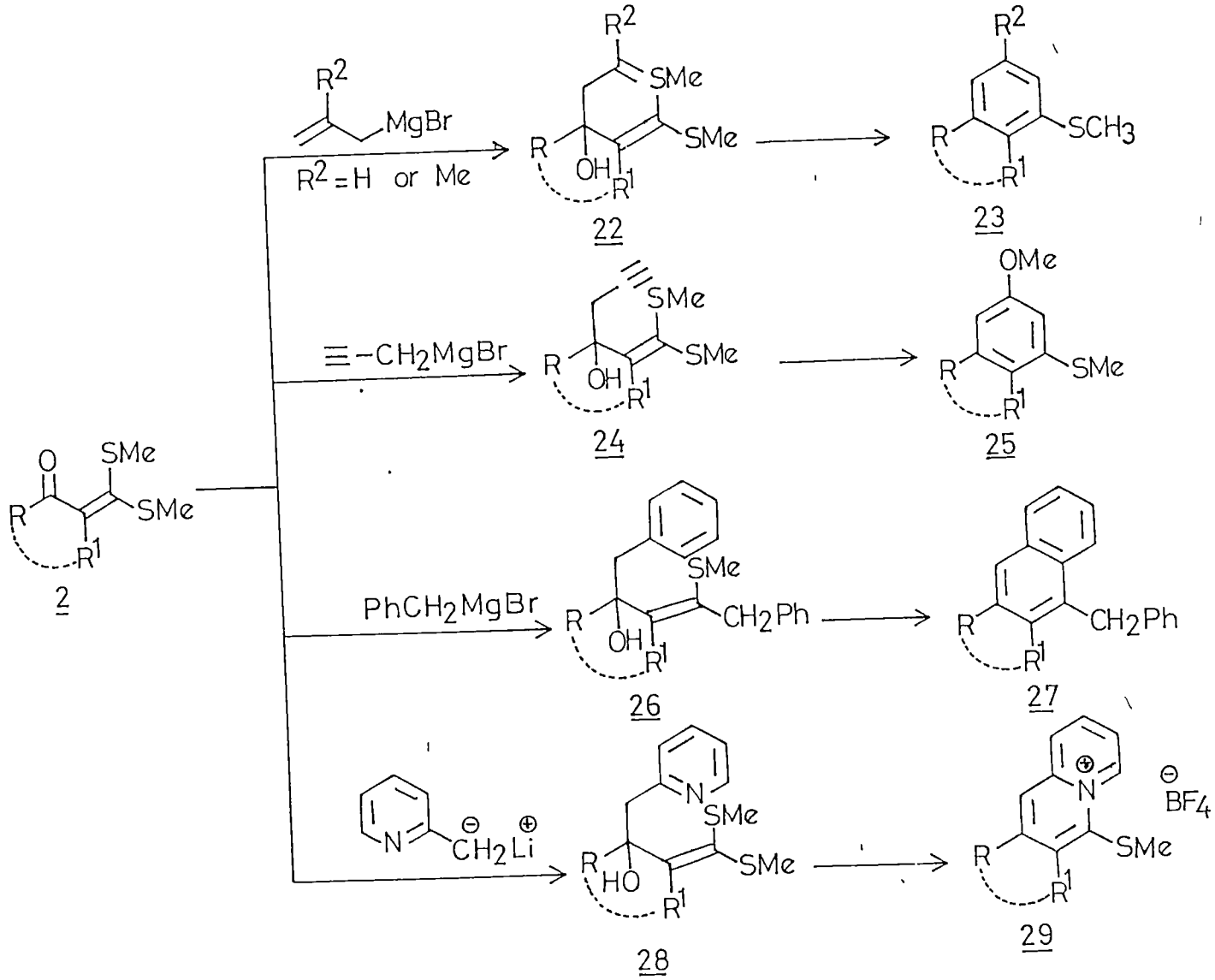
20 a, R1 = H
b, R1 = Me

21 a, R1 = H
b, R1 = Me

Scheme-3

A new general method for aromatic annelation was developed by Singh, Ila and Junjappa by reacting the α-oxoketene dithioacetals with allyl magnesium halide to give the corresponding allyl carbinolacetals 22, which underwent benzoannelation on treatment with boron trifluoride etherate in benzene to yield the corresponding aromatic systems 23[60]. The method is further shown to be extremely versatile and found general applications for the synthesis of benzenoids[61,62], napthalenes[63], phenanthrenes, quinolizinium salts[64a] benzisoxazoles[64b] etc. From the examples described in Scheme 4, it is apparent that the method is of considerable synthetic potential and holds prospects for further studies for many novel aromatic and heteroaromatic systems.

It was proposed to undertake in the present studies, various transformations of α-cinnamoyl ketene dithioacetals 19 and α-(5-Aryl 2,4-pentadienoyl) ketene dithioacetals 31[65] (Scheme 5). In the second chapter, these α-oxoketene dithioacetals 19a, 19b and 31a, 31b are shown to undergo mercuric chloride catalyzed methanolysis to give the corresponding γ,δ-unsaturated β-keto esters 32[66]. When these studies were extended to 2,4-disubstituted S,S-acetals 19c, the expected β-keto esters were not obtained and the products isolated were characterized as 2,5-dimethyl-5-methoxy-3-methylthio-4-aryl cyclopentenones 33[66]. The generality of the method and the factors governing the steric and electronic properties of the acetals 19c leading to the cyclopentenones 33 have been investigated and discussed in the second chapter. The same chapter also describes a method for the synthesis of α-alkenoyl ketene dithioacetals 35, starting from α-oxoketene dithioacetals 17 derived from aliphatic ketones[67]. The dithioacetals 17 were first condensed

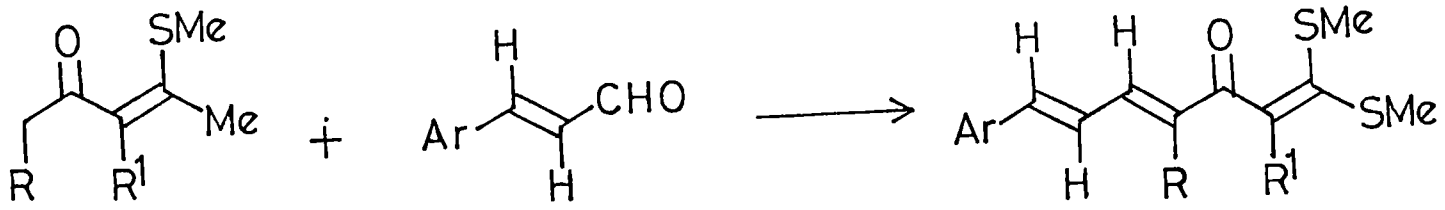

R2
MgBr
R2 = H or Me
SMe
SMe
R
OH
R1
22
SCH3
23
≡–CH2MgBr
24
OMe
25
PhCH2MgBr
CH2Ph
26
27
CH2Li
28
BF4
29
O
2

Scheme-4

with N,N-dimethylformamide diethylacetal to give the enaminoketones 34 and were shown to undergo chemoselective 1,4-addition with grignard reagents to give the corresponding α'-substituted propionoyl ketene dithioacetals 35 in good yields.

The reductive 1,3-carbonyl transposition has been further exploited for the synthesis of methyl 7-aryl 2,4,6-heptatrienoates[65]. Thus the α-oxoketene dithioacetals 31a and 31b obtained from cinnamaldehydes and 17a and 17b respectively, underwent smooth 1,2-reduction with sodium borohydride followed by methanolysis to yield the corresponding heptatrienoates 36 (Scheme 8). However when 4-H in 19b or 31b is replaced by methyl group the corresponding carbinol acetals obtained by sodium borohydride reduction also underwent cyclization to give the corresponding cyclopentenones 37a and 37b[68]. The stereoelectronic factors leading either to the corresponding cyclopentenones or the triene esters have been discussed in chapter III.

In chapter IV, the reaction of allylmagnesium bromide with α-oxoketene dithioacetals and then subsequent transformations are described. The initial product carbinol acetals 39 underwent boron trifluoride ether assisted cycloaromatization to yield the corresponding trans stilbenes 40 in high yields (Scheme 9)[69]. The approach of stilbene synthesis involving the construction of one of the aromatic rings from open chain precursors is unprecedented and provides synthetic advantages to construct unsymmetrically substituted stilbenes. The scope and limitations of this new general method has been discussed. Alternatively the dithioacetals 19 and 31 were also shown to undergo conjugate addition with alkyl and aryl grignard reagents and subsequent methanolysis gave



17 a, R = R^1 = H

b, R = H, R^2 = Me

c, R = R^1 = Me

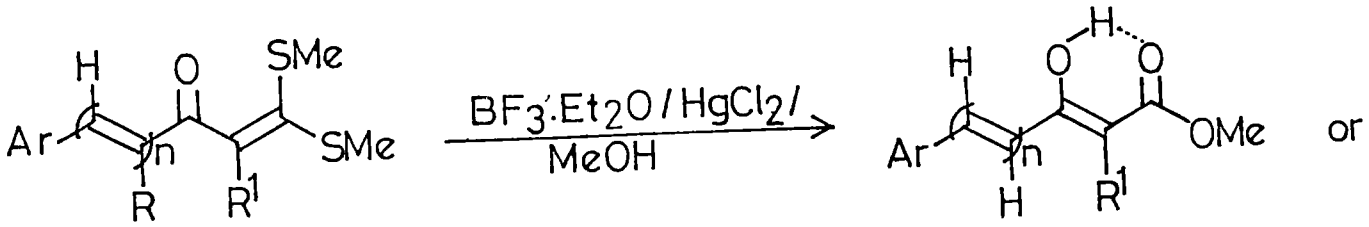
30

31 a, R = R^1 = H

b, R = H, R = Me

c, R = R = Me

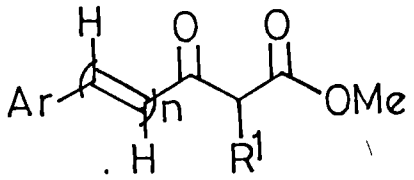
Scheme-5



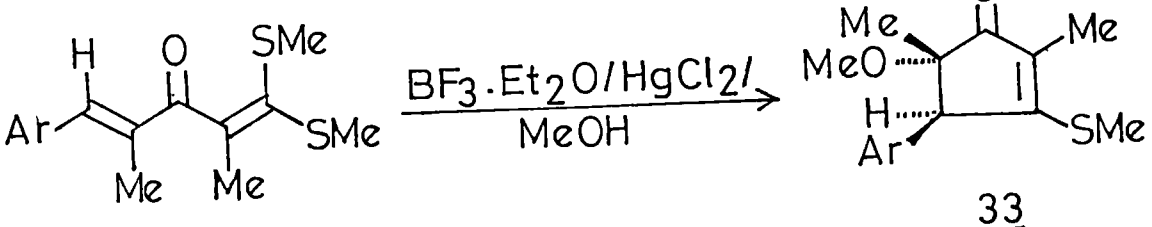
19 , R^1 = H , Me; n = 1

31 , R^1 = H; n = 2

32 A

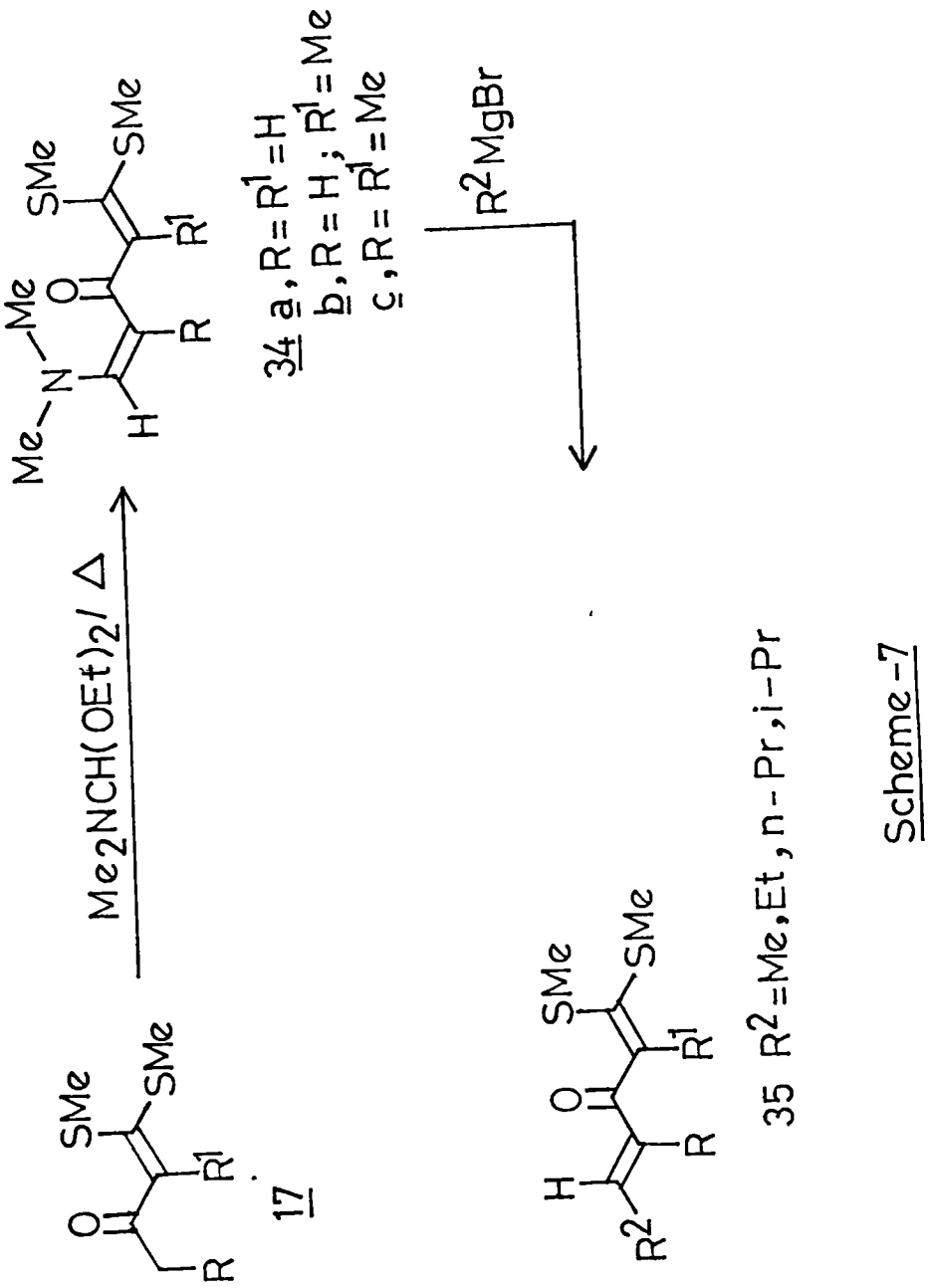


32B

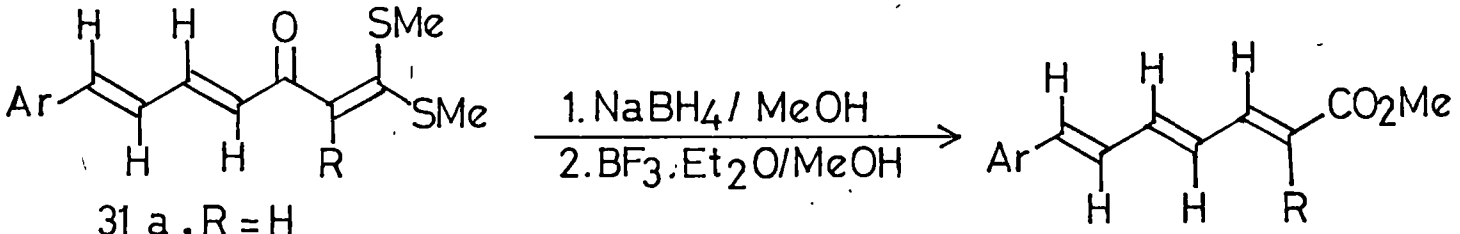


33

Scheme-6

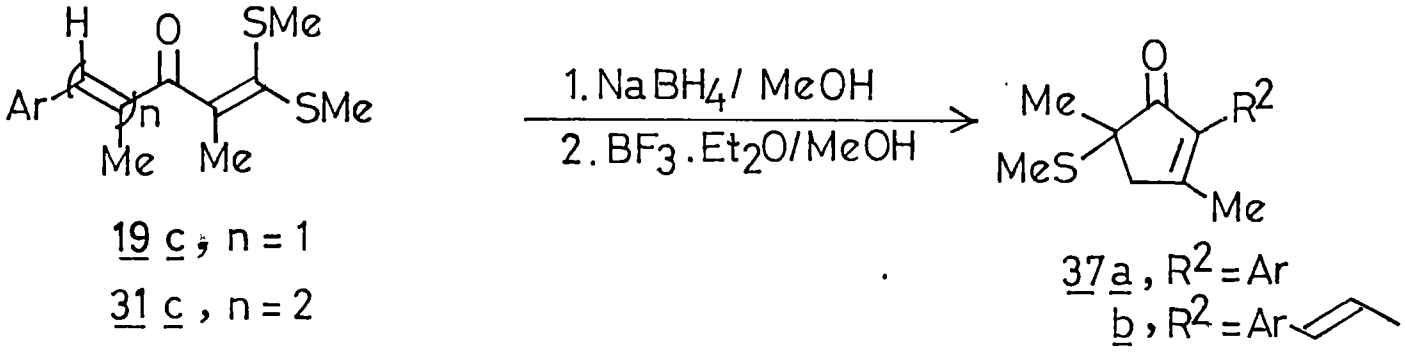

Me2NCH(OEt)2/ Δ
R2MgBr
34 a, R=R1=H
b, R=H; R1=Me
c, R=R1=Me
17
35 R2=Me, Et, n-Pr, i-Pr

Scheme-7



31 a, R = H
b, R = Me

36 a, R = H
b, R = Me



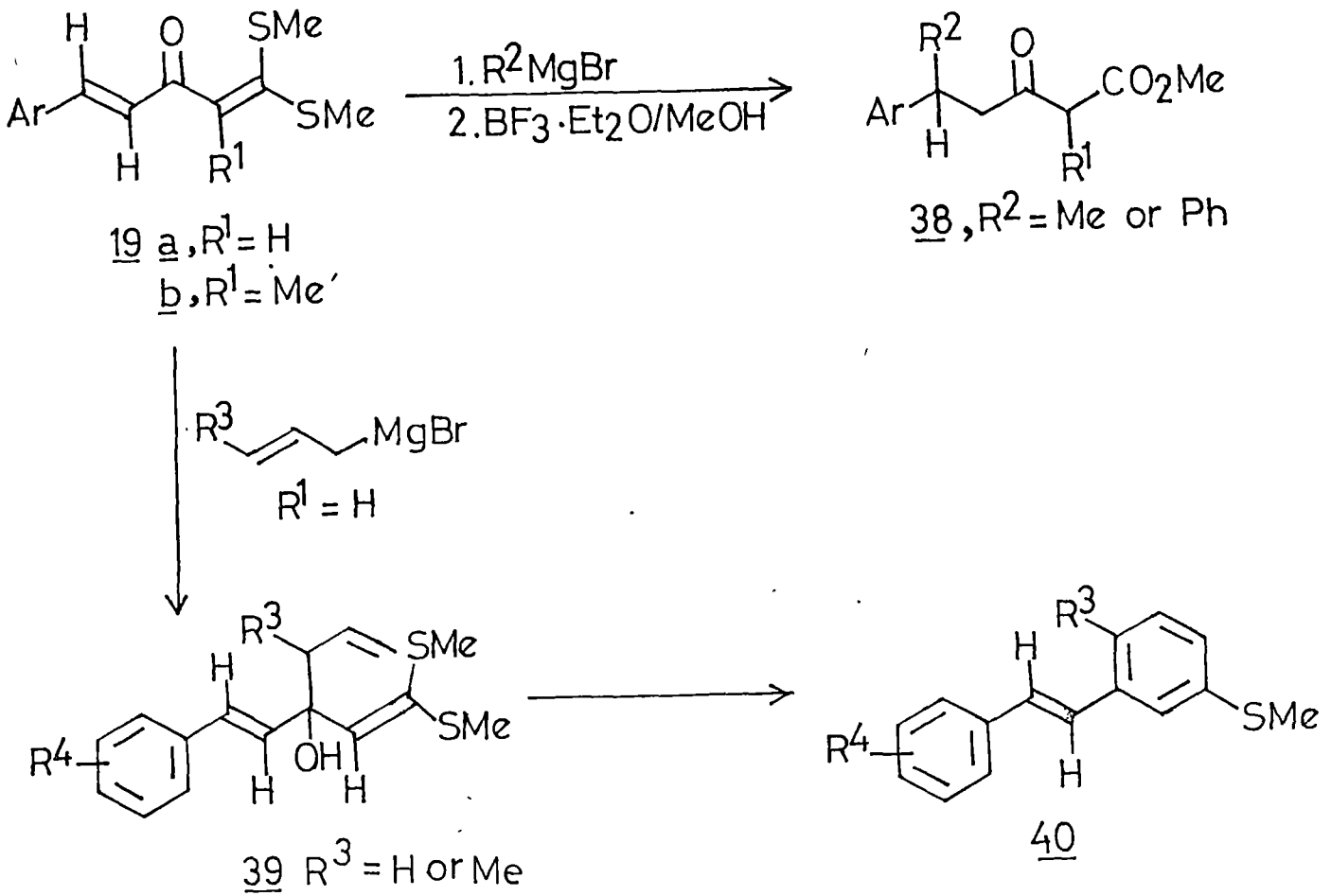
19 c, n = 1

31 c, n = 2

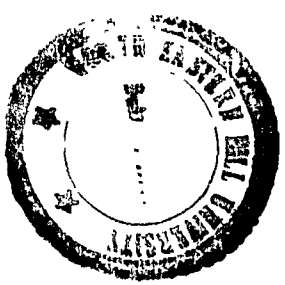
37 a, R^2 = Ar

b, R^2 = Ar

Scheme-8



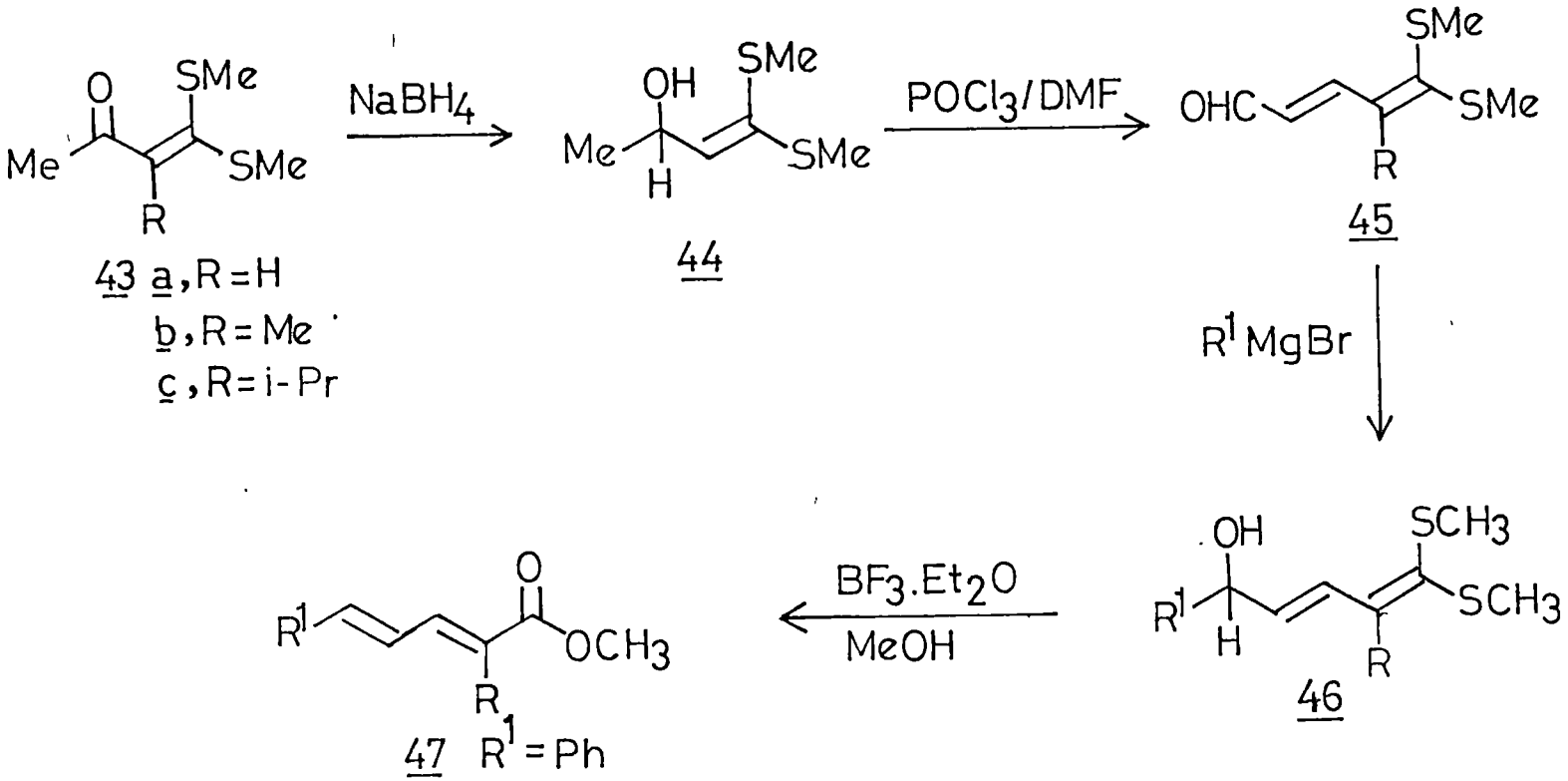
Scheme-9



the ζ-disubstituted β-keto esters in high yields. Thus the importance of these acetals, which can be used in many synthetic transformations have been discussed.

The 1,3-carbonyl transposition of α-oxoketene dithioacetals involving sodium borohydride reduction and solvolysis or hydrolysis to give the corresponding ene esters has been shown to be of general application while the methodology for higher carbonyl transposition involving 'n' carbon atoms, where 'n' could be any odd number, have little been studied. Only 1,2 to 1,4-carbonyl transpositions have been extensively investigated as a part of strategy in many synthetic programmes. However the corresponding 1,5 to 1,7 carbonyl transpositions are sporadic and the examples are confined only to intramolecular hydride transfer between keto-enol functionalities[70]. Despite abundance of carbonyl group in organic molecules methodologies with wider synthetic applications involving sequential carbonyl transpositions have been totally neglected. An attempt for the first time has been made in the present investigation to formulate and develop a methodology for alternatively sequential carbonyl transpositions as an effective tool for the construction for polyene esters, aldehydes and ketones.

A molecule with a carbonyl group separated from a bis(methylthio) functionality by conjugated double bonds could be designed and created as described in chapter V which are suitable synthons for the study of various envisaged carbonyl transposition reactions. Thus the compound 41 is an excellent candidate for the study of 1,5 carbonyl transpositions under described condition to yield the corresponding polyene esters (R^1=SMe), aldehydes (R^1=H) or the ketones (R^1=alkyl or aryl).



43 a, R = H
b, R = Me
c, R = i-Pr

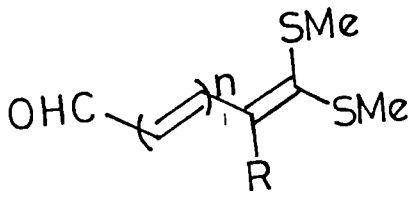
44

45

46

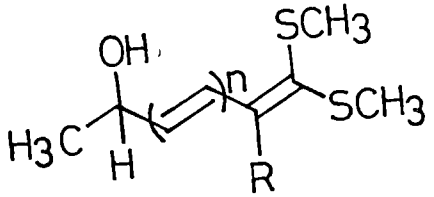
47 R^1 = Ph

Scheme-10

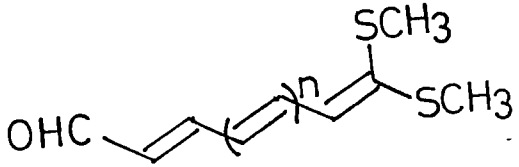


45 n = 1
48 n = 2
49 n = 3

MeMgBr

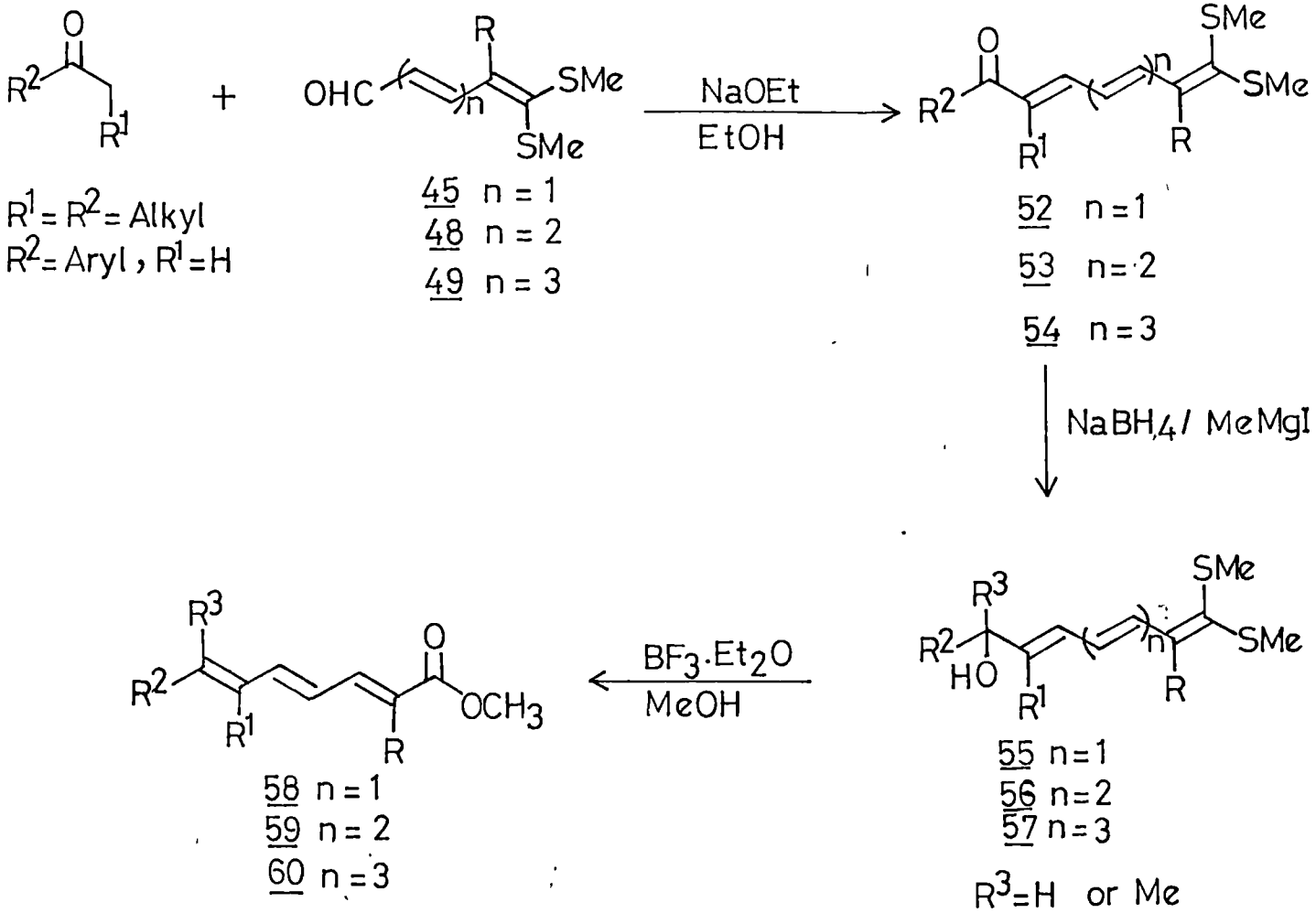


50 n = 1
51 n = 2



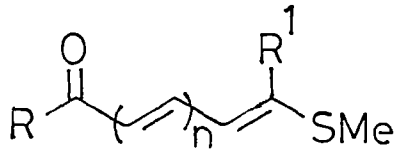
48 n = 1
49 n = 2

Scheme-11


R2
R1
O
+
OHC
R
SMe
SMe
n
NaOEt
EtOH
45 n = 1
48 n = 2
49 n = 3
R1 = R2 = Alkyl
R2 = Aryl , R1 = H
52 n = 1
53 n = 2
54 n = 3
NaBH4 / MeMgI
R3
HO
55 n = 1
56 n = 2
57 n = 3
R3 = H or Me
BF3.Et2O
MeOH
OCH3
58 n = 1
59 n = 2
60 n = 3

Scheme-12

Similarly with the increase of one more double bond the molecule becomes qualified for 1,7 carbonyl transposition under similar reaction conditions, to the corresponding trienoates.



41 n=1 R=H, Alkyl, Aryl
R^1=H, SMe, Alkyl

42 n=2

Similarly the concept can be extended to 1,9; 1,11; 1,13; and 1,15 carbonyl transpositions by separating the carbonyl and mercapto functionality by appropriate number of double bonds. Importance of the methodology has been highlighted, since there are no methods reported in the literature for such transformations. The present methodology which spans from 1,3 to 1,11 carbonyl transpositions (Scheme 10, 11 and 12) has been discussed with its scope and merits for the polyene synthesis with ester as the terminal functionality.

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CHAPTER II

SOLVOLYTIC STUDIES OF CINNAMOYL AND 5-ARYLPENTADIENOYL KETENE DITHIOACETALS: FORMATION OF METHYL 5-ARYL 3-OXO-4-PENTENOATES AND NOVEL SUBSTITUTED CYCLOPENTENONES*

II.1 INTRODUCTION

The α-oxoketene dithioacetals have been known to be more stable under hydrolytic conditions than the corresponding O,O-acetals. This property has been used to the advantage in chemical synthesis involving α-oxoketene dithioacetals. In fact, ketene S,S-acetals in general require special reaction conditions to ensure the complete hydrolysis to the corresponding sulphur free compounds. Many reagents

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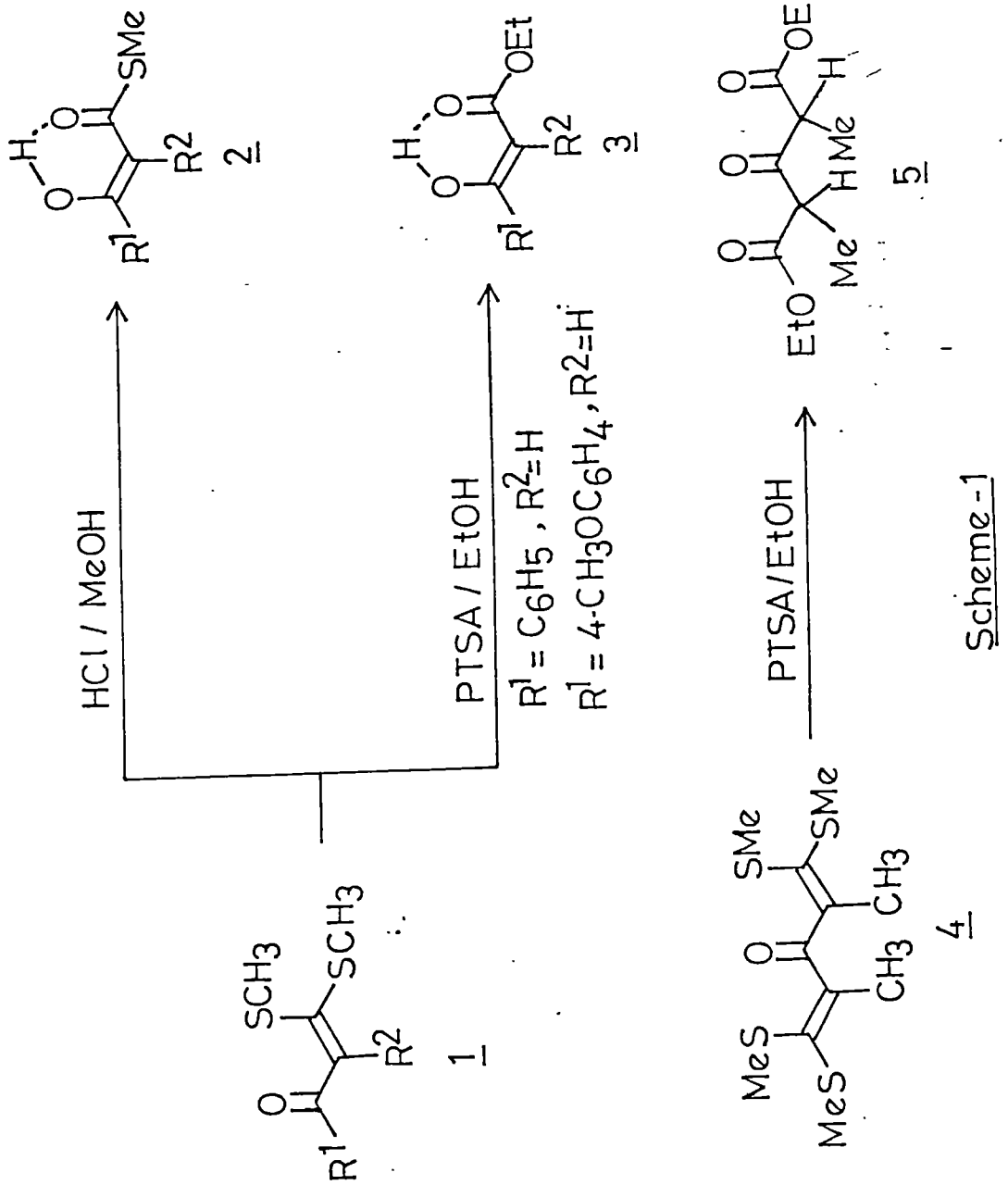
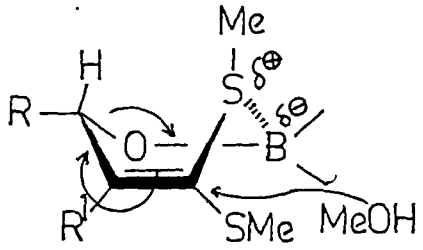
* C.V. Asokan, S. Bhattacharji, H. Ila and H. Junjappa, Synthesis, 0000(1988).
C.V.Asokan, M.P. Balu, H. Ila and H. Junjappa, Synthesis, 0000 (1988).

have been therefore developed with varying degrees of success to effect these transformations. The methods using different reagents have been recently reviewed by Seebach and Grobel[1]. However most of these studies are confined to acetals and hemiacetals of aldehydes and ketones and in some cases, to unactivated ketene S,S-acetals. The α-oxoketene dithioacetals should in principle undergo solvolysis and hydrolysis more easily than the corresponding unactivated acetals due to the presence of α-electron withdrawing group. The oxoketene S,S-acetals, however, under normal reaction conditions, such as in the presence of mineral acids and water or in the presence of alkaline conditions generally undergo partial hydrolysis to the corresponding β-keto thiolesters 2. Thus there are a few methods that have been found successful application for the hydrolysis of α-oxoketene dithioacetals to the corresponding β-ketoesters. The only report on complete solvolysis of few dithioacetals 1 and 4 was by Shahak and co-workers[2]. They found that in the presence of PTSA and ethanol, 1 underwent complete solvolysis to give the corresponding β-keto esters 3 in high yields. Similarly 4 also underwent solvolysis under similar conditions to give the corresponding diester 5. Myrboh, Ila and Junjappa observed that the carbinol acetals 6 derived from 1 when subjected to solvolysis under Shahak's conditions, the corresponding sulphur free esters were not obtained and the rearrangement of methyl mercaptan occured, probably due to the incepient carbonium ion generated by the elimination of allylic hydroxyl group, yielding the thiol esters 7[3]. This difficulty was overcome by subjecting 6 to methanolysis in the presence of boron trifluoride etherate, when the corresponding ene-esters were obtained


HCl / MeOH
PTSA / EtOH
$R^1 = C_6H_5$, R^2=H
R^1 = 4-$CH_3OC_6H_4$, R^2=H
PTSA/EtOH
1
2
3
4
5

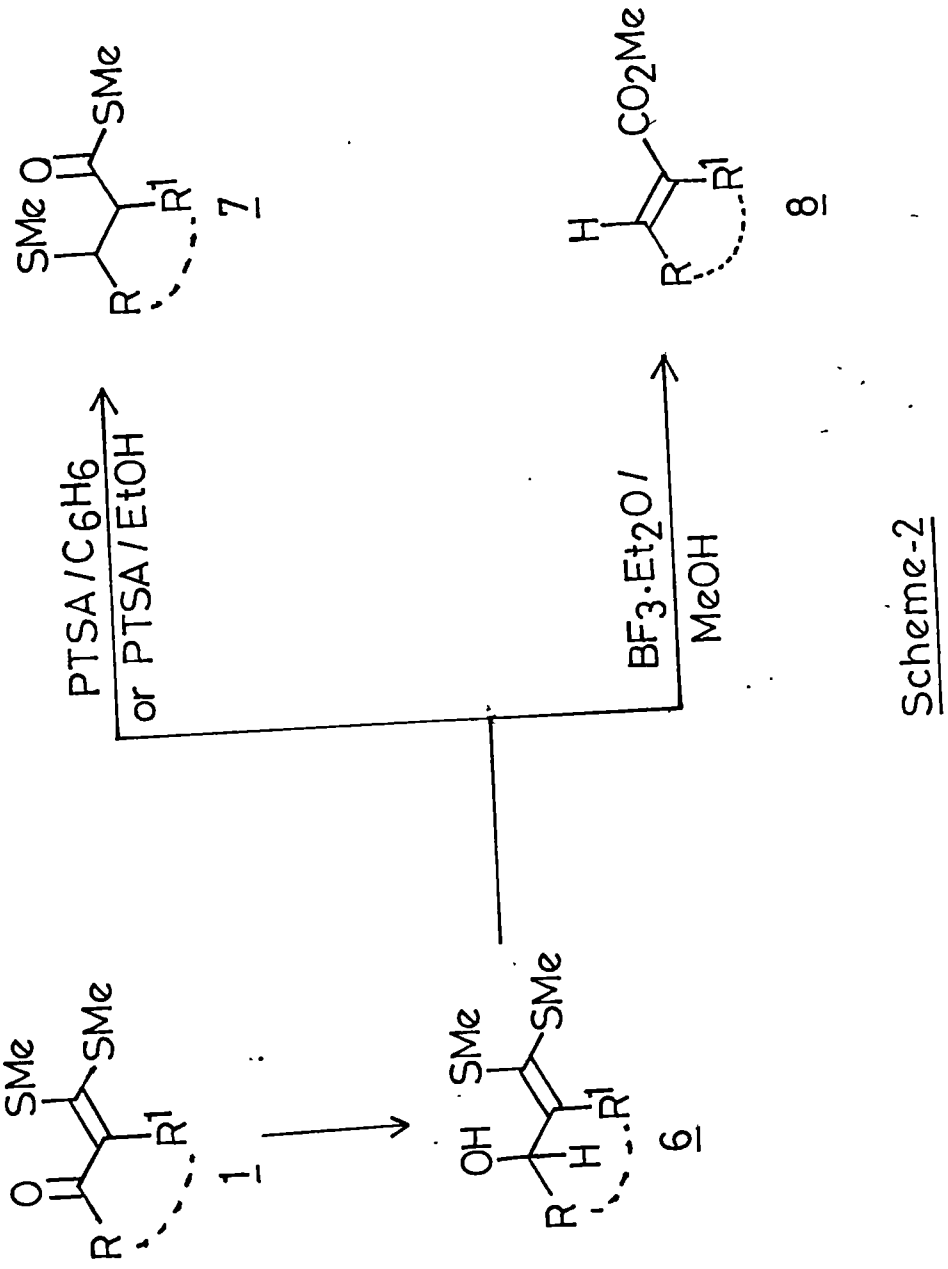
Scheme-1

in high yields. This method was found to be stereospecific, since E geometry was consistently observed in all the ene-esters obtained. It was therefore proposed that the boron trifluoride etherate and allylic hydroxyl group form a six membered twist boat transition state (6A) which subsequently collapses to the observed geometry, with the participation of the solvent alcohol. In the

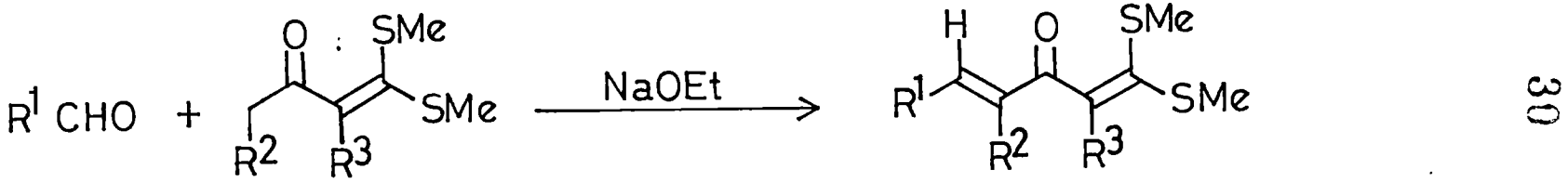


6A

present investigation, a number of α -cinnamoyl ketene dithioacetals 11, 12 and 13 and 5-Arylpentadienoyl ketene dithioacetal 14 were prepared to study their behaviour under solvolytic conditions. These dithioacetals are easily obtained in good yields by facile base catalyzed condensation of the corresponding acyl ketene dithioacetals 10a-c with substituted benzaldehydes and cinnamaldehyde respectively[5] (Scheme 3). However, it is apparent from the table 1, that all the aldehydes employed were aromatic and the corresponding aliphatic compounds could not be satisfactorily prepared by condensation of aliphatic aldehydes with 10 due to the problems associated with self condensation of aliphatic aldehydes. But these compounds 17 were required to draw generalisation in the envisaged solvolytic studies (Scheme 4). An alternative route was therefore developed for their synthesis involving a condensation with N,N-dimethylformamide diethylacetal and subsequent chemoselective 1,4-addition of grignard reagents derived from aliphatic halides.


SMe
SMe
O
R
R1
1
OH
SMe
SMe
H
R
R1
6
PTSA / C6H6
or PTSA / EtOH
BF3.Et2O /
MeOH
SMe O
SMe
R
R1
7
H
CO2Me
R
R1
8

Scheme-2



9

10 a, $R^2 = R^3 = H$

b $R^2 = H$, $R^3 = Me$

c $R^2 = R^3 = Me$

11 $R^2 = R^3 = H$, $R^1 = Ar$

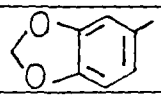
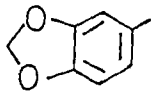
12 $R^2 = H$, $R^3 = Me$, $R^1 = Ar$

13 $R^2 = R^3 = Me$, $R^1 = Ar$

14 $R^2 = R^3 = H$, $R^1 = C_6H_5CH=CH$

Scheme-3

Table 1

		R^1	R^2	R^3
11	a	C_6H_5	H	H
	b	3-MeC_6H_4	H	H
	c	4-ClC_6H_4	H	H
	d	4-$MeOC_6H_4$	H	H
	e	3,4-$(MeO)_2C_6H_3$	H	H
	f	3,4,5-$(MeO)_3C_6H_3$	H	H
	g		H	H
12	a	C_6H_5	H	Me
	b	4-ClC_6H_4	H	Me
	c	4-$MeOC_6H_4$	H	Me
13	a	C_6H_5	Me	Me
	b	4-MeC_6H_4	Me	Me
	c	4-ClC_6H_4	Me	Me
	d	4-$MeOC_6H_4$	Me	Me
	e	3-$MeOC_6H_4$	Me	Me
	f	3,4-$(MeO)_2C_6H_3$	Me	Me
	g	3,4,5-$(MeO)_3.C_6H_2$	Me	Me
	h		Me	Me
14		C_6H_5-CH=CH-	H	H

II.2 RESULTS AND DISCUSSION

A few selected ketene dithioacetals (11a-g, 12a-c, 13a-h and 14a) required in the present investigation were prepared according to the known procedures[5] by condensation of acyl ketene dithioacetals 10a-c with benzaldehydes and cinnamaldehyde (Table 1). The structures of all known dithioacetals (11a-d, 11g, 12a-c and 14) were confirmed by comparison of their spectral and analytical data with those of authentic samples. The hitherto unknown oxoketene dithioacetals 11e, 11f and 13a-h were also prepared essentially by extending the described method and were characterized by their spectral and analytical data (experimental).

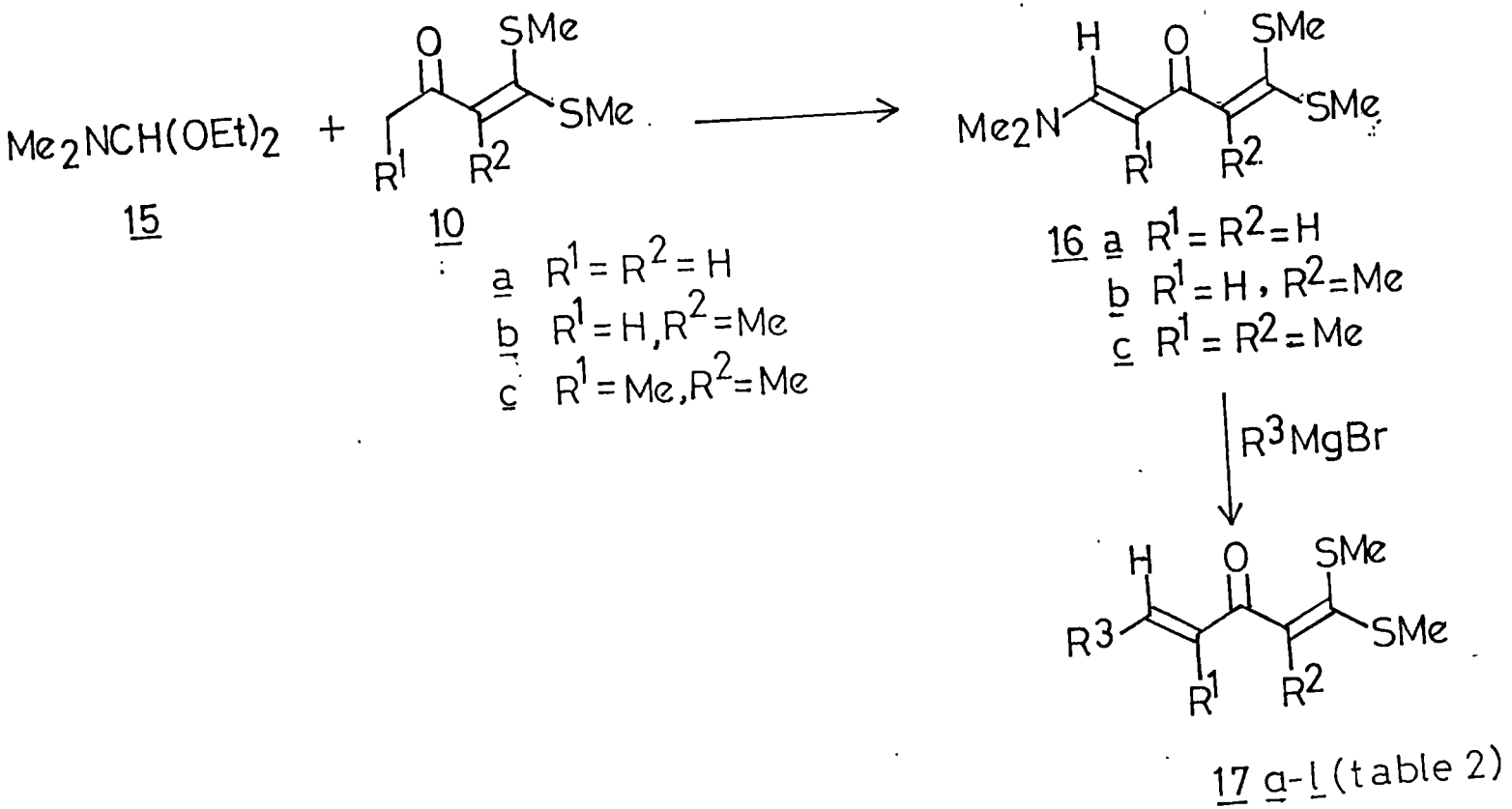
II.2.1 A Novel Route to 5-Alkyl-1,1-bis(methylthio) 1,4-pentadiene-3-ones

When the acyl ketene dithioacetals 10a was heated at 110°C with N,N-dimethylformamide diethylacetal in a steel bomb for 3 hr, column chromatography of the reaction mixture afforded a crystalline solid (92%), which was characterized as 1,1-bis(methylthio)-5-(N,N-dimethylamino)-3-oxo-penta-1,4-diene (16a) on the basis of its spectral and analytical data. Thus 16a was analyzed for $C_9H_{15}NOS_2$ and exhibited molecular ion peak at m/z 217 (29%) in its mass spectrum. Its i.r. spectrum (KBr) displayed characteristic bands at 1630 cm^{-1} and 1641 cm^{-1} due to the carbonyl group and the olefinic double bonds respectively. Further structural proof for 16a was obtained from its ^1H n.m.r.($CDCl_3$) spectrum which showed three singlets at δ 2.34 (3H), δ 2.35(3H) and δ 2.90(6H) due to two methylthio groups and dimethylamino groups respectively. The absorption due to three olefinic protons appeared at δ 5.81(s,1H,H-2); 4.86(d,1H,J=12Hz) and δ 7.26(d,1H,J=12Hz,H-5) respectively. The corresponding

2-methylpentadiene 16b and 2,4-dimethylpentadiene 16c were also obtained by the condensation of the respective acyl ketene dithioacetals 10b and 10c with N,N-dimethylformamide diethylacetal 15. The enaminoketone 16a was reacted with methylmagnesium iodide and the product thus obtained after work-up and column chromatography in 91% yield was characterized as 1,1-bis(methylthio)-3-oxo 1,4-hexadiene 17a on the basis of its spectral and analytical data. It showed molecular ion peak at m/z 188 (32%) and was analyzed for $C_8H_{12}OS_2$. The i.r. spectrum (neat) of 17a exhibited characteristic absorptions due to α , β-unsaturated carbonyl group at 1652 cm^{-1} and double bonds at 1600 cm^{-1}. The ^1H n.m.r. spectrum of 17a displayed signals at δ 1.85(dd,3H,J=7Hz,1.5Hz,CH_3); 2.39(s,3H,SCH_3); 2.42 (s,3H,SCH_3); 5.98(s,1H,H-2); 6.06(dq,1H,J=15Hz,1.5Hz,H-4); 6.61(dq,1H,J=15Hz,7Hz,H-5). Similarly, several bis(methylthio) dienones 17a-l (Table 2) were prepared from 16a-c employing various alkyl grignard reagents in 78-92% overall yields. The spectral and analytical data of all these compounds which are in agreement with the assigned structures, have been described in the experimental section.

II.2.2 Solvolytic Studies

In the present investigation, the pentadienones 11a-g and 12a-c were subjected to different solvolytic conditions such as PTSA in ethanol, BF_3 etherate in methanol etc, however no clear cut products were obtained under these conditions. When 11a was refluxed in methanol in the presence of boron trifluoride etherate and mercuric chloride, the product isolated after work-up was identified as methyl 5-phenyl-3-oxo-4-pentenoate 18a obtained in 70% yield.

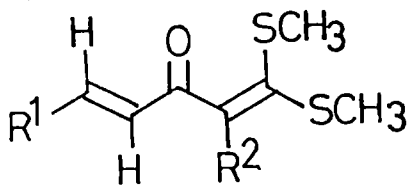

Me2NCH(OEt)2
15
+
O
SMe
SMe
R1
R2
10
a R1 = R2 = H
b R1 = H, R2 = Me
c R1 = Me, R2 = Me
H
O
SMe
Me2N
SMe
R1
R2
16 a R1 = R2 = H
b R1 = H, R2 = Me
c R1 = R2 = Me
R3MgBr
H
O
SMe
R3
SMe
R1
R2
17 a-l (table 2)

Scheme-4

Table-2

17	R^1	R^2	R^3
a	H	H	Me
b	H	H	Et
c	H	H	n-Pr
d	H	H	i-Pr
e	H	Me	Me
f	H	Me	Et
g	H	Me	n-Pr
h	H	Me	i-Pr
i	Me	Me	Me
j	Me	Me	Et
k	Me	Me	n-Pr
l	Me	Me	i-Pr

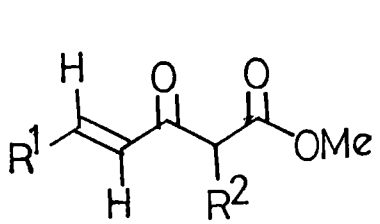
The compound was analyzed for $C_{12}H_{12}O_3$ and showed molecular ion peak at m/z 204 (M^+,65%). It exhibited bands in its i.r. spectrum at 1632 cm^{-1}, and 1532 cm^{-1} which was assigned to the ester carbonyl group and the double bond in the enol form of the compound. The structure was further confirmed from its ^1H n.m.r. spectrum (CCl_4), which showed the presence of both keto and the enol form (1:4 ratio) in the solution. Thus the signal at δ 3.42(s,0.4H) was assigned to the mobile methylene group between two carbonyl functions while the absorption due to methoxy protons appeared at δ 3.6(s, 3H). The singlet at δ 5.04(0.8H) was assigned to the olefinic proton at C-2 of the enol form. One of the styryl protons in the enol form was present at δ 6.31(d,0.8H,J=15Hz) while the aromatic and other styryl proton signals appeared as complex multiplet between δ 6.70-7.68. The enolic OH was found at δ 11.90 exchangeable with D_2O (0.8H). Similarly 11b-g and 12a-c underwent solvolysis under the described conditions to afford γ, δ-unsaturated-β-ketoesters 18b-g and the corresponding 2-methyl derivatives 19a-c in 65-85% overall yields (Table 3). The compounds were characterized by their analytical and spectral data which are described in the experimental section. When the solvolytic studies were extended to 1,1-bis(methylthio) 3-oxo-5-alkyl-1,4-pentadienes 17 under identical conditions, the corresponding 5-alkylpentadienoates were not obtained. The method was therefore found to be limited to the synthesis of 5-aryl 3-oxopentenoates only. Similarly methanolysis of the α-(5-phenyl-2,4-pentadienoyl) ketene dithioacetal 14 yielded the corresponding methyl 7-phenyl 3-oxo-4,6 heptadienoate 20 though in low yield.



11, 12, 14

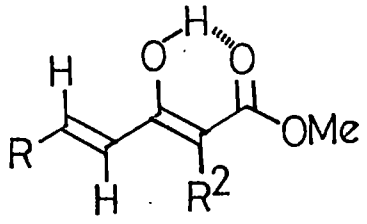
$BF_3 Et_2O / HgCl_2 / MeOH$

65 - 85%



A

+

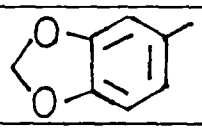


B

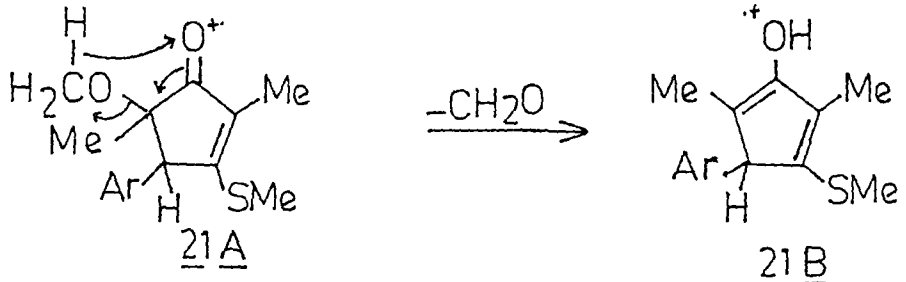
18 a-g (table 3)
19 a c
20

Scheme-5

Table 3

	R^1	R^2
11,18 a	C_6H_5	H
b	4-MeC_6H_4	H
c	4-ClC_6H_4	H
d	4-$MeOC_6H_4$	H
e	3,4$(MeO)_2C_6H_3$	H
f	3,4,5$(MeO)_3C_6H_2$	H
g		H
12,19 a	C_6H_5	Me
b	4-ClC_6H_4	Me
c	4-$MeOC_6H_4$	Me
14,20	C_6H_5-CH=CH-	H

The dithioacetals 13a-g obtained by condensation of α-propionyl-α-methyl ketene dithioacetals and benzaldehydes were next examined under solvolytic conditions. When 13a was subjected to methanolysis, the expected methyl, 2-4,dimethyl-5-aryl-3-oxo 4-pentenoate 22a was not detected. The product, obtained as colourless crystals (m.p. 52°C), in 73% yield, was characterized as 2,5-dimethyl-5-methoxy 3-methylthio-4-phenyl-2-cyclopentene-1-one 21a on the basis of spectral and analytical data. Thus it was analyzed for $C_{15}H_{18}O_2S$. The mass spectrum of the compound 21a showed weak molecular ion peak at m/z 262 (4%) and the base peak at 232 (100%). Evidently the base peak at M^+-30 is due to the ion 21B formed by the elimination of formaldehyde through McLafferty rearrangement involving transfer of γ-hydrogen[6] (Scheme 7). The i.r. spectrum of 21a showed

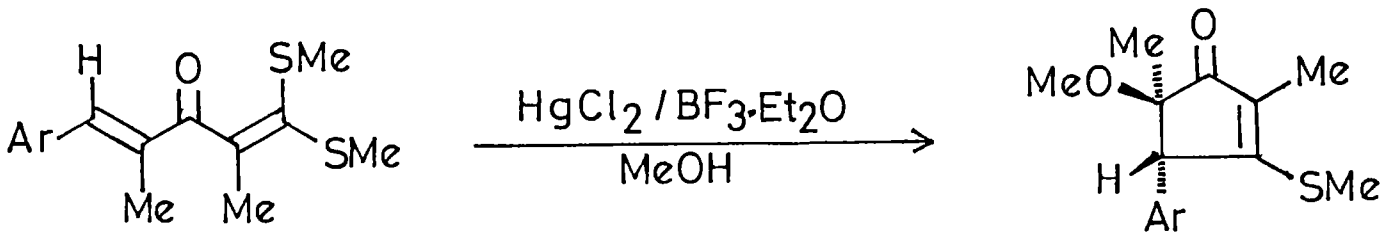


21A 21B

Scheme-7

characteristic band at 1674 cm^{-1} due to cyclopentenone carbonyl group. The relative stereochemistry at C-4 and C-5 atoms and position of substituents were confirmed from its ^1H n.mr. and ^{13}C n.m.r. spectra. Thus the signals due to 5-methyl, 3-methylthio and 5-methoxy groups appeared as three singlets at δ 0.71(3H), δ 2.02(3H) and δ 3.81(3H) respectively. The absorption due to 2-methyl group was present as sharp doublet (J=2.5Hz) at δ 1.82

due to allylic coupling with benzylic H-4 proton, which was present as quartet at δ 4.0(1H,J=2.5Hz). The aryl multiplet integrating for 5-protons appeared at δ 7.00-7.40. The higher field chemical shift of 5-methyl group (δ 0.71) is apparently due to shielding by phenyl group thus showing the cis stereochemical relationship between the two groups. The structure of 21a was further supported by its ^{13}C n.m.r.spectrum which exhibited peaks at δ 8.72(5-$\underline{C}H_3$); 13.49(2-$\underline{C}H_3$); 18.14(S$\underline{C}H_3$); 51.74(O$\underline{C}H_3$); 57.94($\underline{C}$-4); 82.71($\underline{C}$-5); 127.58, 128.86($\underline{C}$-H aromatic); 133.10($\underline{C}$-2); 137.77($\underline{C}$-1' aromatic); 171.79($\underline{C}$-3) and 204.0($\underline{C}$=O). The method was found to be general, when 13b-g gave the corresponding cyclopentenones 21b-g in 55-73% overall yields. In all the cases the stereochemical features at C-4 and C-5 were having E-configuration as in 21a. Thus the mechanism governing the cyclopentenone formation should have rigid reaction coordinates leading to the same stereochemical features in all the cases. Evidently the transformation from 13 to 21 is going through the boron trifluoride etherate catalyzed Nazarov type cyclization[7] to give cyclopentenyl cation 24, which is attacked by the solvent methanol at C-5 position from the rear side of the phenyl group due to steric reasons, thus leading to the observed stereochemistry at C-4 and C-5. Subsequent elimination of methyl-mercapto group gives the products cyclopentanones 21 (Scheme 8). Apparently, the presence of methyl groups at 2 and 4-positions of 13a is responsible for forcing the carbonium ion 23B to a twisted non-planar 2-Z, 3-Z configuration 23A, thus creating favourable geometries for cyclization to the cyclopentene ring. Shoppe and Cooke[8] have reported a similar acid catalyzed cyclization of



13 a-h

21

13, 21 a, Ar = C_6H_5

b, Ar = 4-MeC_6H_4

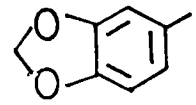
c, Ar = 4-ClC_6H_4

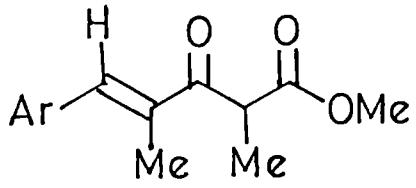
d, Ar = 4-$MeOC_6H_4$

e, Ar = 3-$MeOC_6H_4$

f, Ar = 3,4-$(MeO)_2C_6H_3$

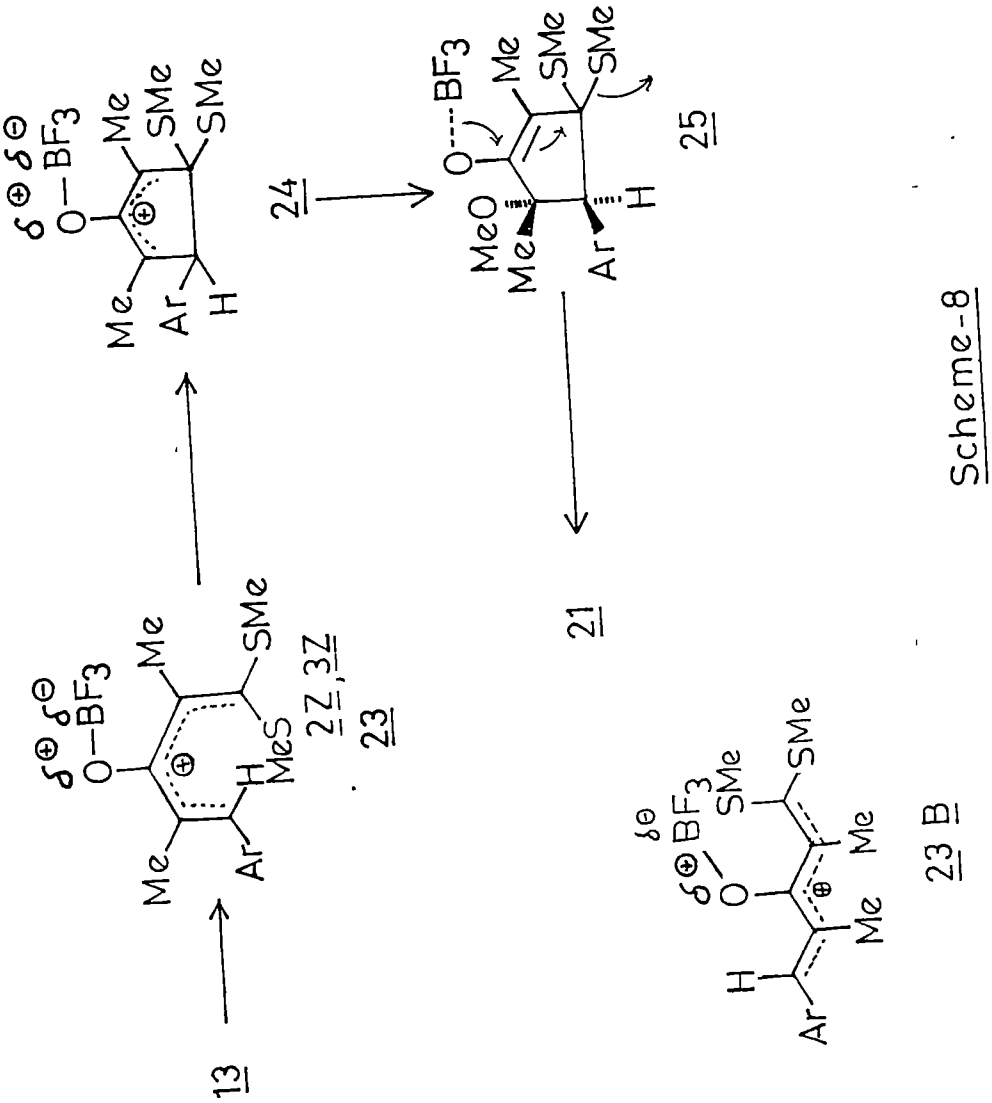
g, Ar = 3,4,5-$(MeO)_3C_6H_2$

h, Ar = 



22

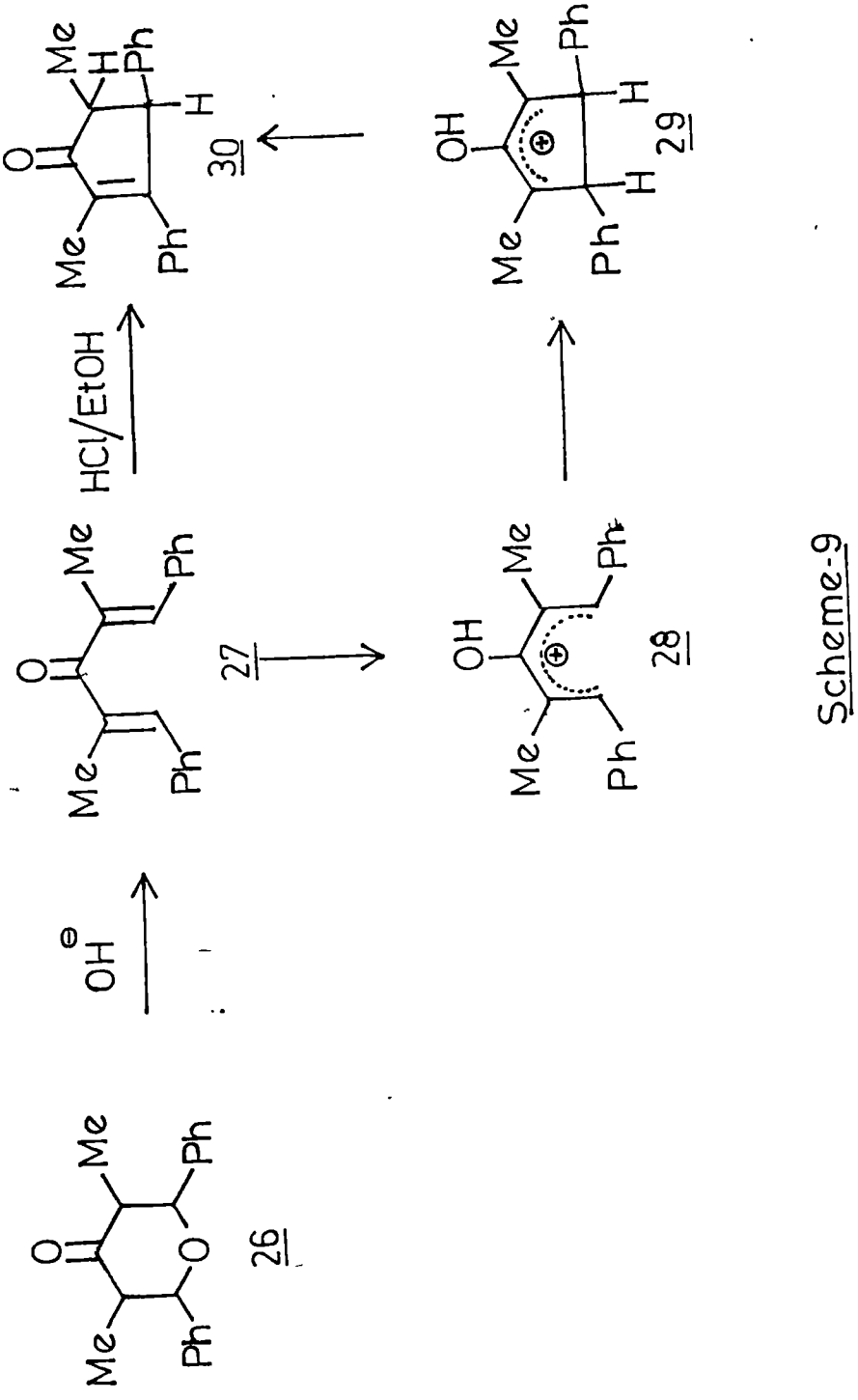
Scheme-6



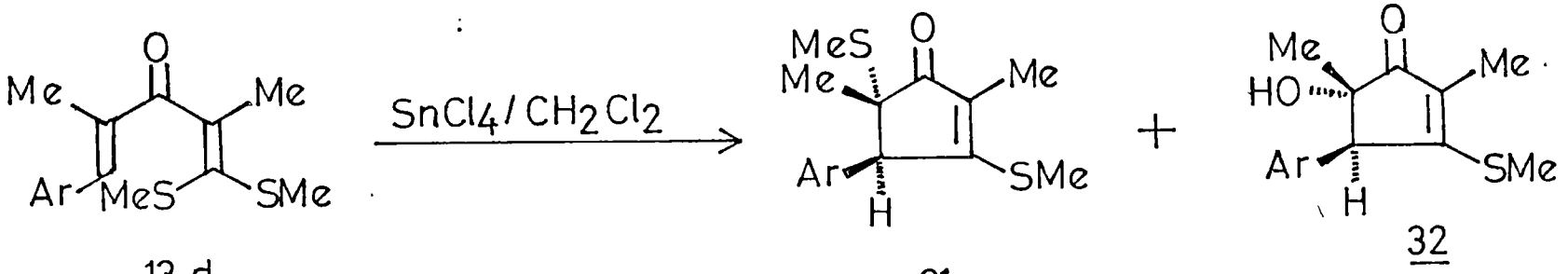
Scheme-8

2,4-dimethyl 1,5-diphenyl-penta-1,4-dien-3-ones (27) (Scheme 9). They have suggested a conrotatory thermal ground state electrocyclization of the pentadienyl cation 28 to a cyclopentenyl cation 29 followed by loss of proton and ketonization to give the cyclopentenones 30 (Scheme 8).

Incidently, the Nazarov cyclization was attempted with 13d in the presence of anhydrous tin(IV) chloride in dichloromethane. After work-up of the reaction mixture , two products (TLC) were obtained which were separated by column chromatography and characterized as 2,5-dimethyl 3,5-bis(methylthio)-4-(4-methoxyphenyl)-2-cyclopentene-1-one 31 (30%) 2,5-dimethyl-5-hydroxy-3-methylthio-4-(4-methoxyphenyl)-2-cyclopentene-1-one 32 (50%). The structure of 31 and the stereochemistry at C-4 and C-5 were confirmed by spectral and analytical data. The compound was analyzed for $C_{15}H_{20}O_2S_2$ and showed the molecular ion peak in its mass spectrum at m/z 296. The i.r. spectrum showed characteristic cyclopentenone carbonyl frequency at 1690 cm^{-1}. The structure of the compound was further confirmed by its ^1H n.m.r. spectrum (CCl_4). The singlet at δ 0.80 (3H) was assigned to the 5-methyl protons while the sharp doublet at δ 1.91(3H,J=2.5Hz) was due to the 3-methyl proton which is coupled with benzylic proton at C-4, which appeared as a quartet at δ 3.91(J=2.5Hz). The singlets at δ 2.12(3H) and δ 2.15(3H) were assigned to the protons of methylthio groups at C-5 and C-3 respectively. The methoxy proton signal appeared as singlet at δ 3.8(3H) along with the aromatic multiplet between δ 6.62-7.45(4H). The structure and stereochemistry of the compound 32 was also confirmed by spectral and analytical data and are described in the experimental section.



Scheme-9



13 d

31

32

Ar = 4-$CH_3OC_6H_4$

Scheme-10

Apparently, the SMe migration must have occured intramolecularly from the rear side of the aryl group. Similarly the compound 32 must have arisen during work-up, when the hydroxyl group has attacked the carbocation from the rear side of the aryl group.

Our literature survey has revealed that, though the γ,δ-unsaturated β-ketoesters are highly valued synthetic intermediates in a number of transformations, their methods of preparation described until recently were not generally applicable and suffered from low yields or used difficultly accessable starting materials[9]. These reagents are also called Nazarov reagents particularly useful in Robinson annelation of cycloalkanones[10-13], or the corresponding enamines[14,15], in the Mannich reaction[16] and in the Diels-Alder reactions of enolacetals[17,18]. Nakata and co-workers have used the 2-methyl substituted pentenoate 19a for the synthesis of (±)-Oudemansin, which is an antibiotic with strong antifungal activities[19]. The most general method for the synthesis of these intermediates involve condensation of either dianions[20] or Wittig reagents[9] derived from acetoacetic esters with appropriate carbonyl compounds[21-23]. The present method is a simple route for these compounds employing easily accessible α-oxoketene dithioacetals with a latent β-keto-ester functionality as starting material.

II.3 CONCLUSION

In conclusion it may be summarised: (1) a method of preparative importance for the synthesis of alkenoyl ketene dithioacetals 17 was formulated from the easily available ketones via the α-oxoketene dithioacetals (10).

(2) Solvolytic studies of the cinnamoyl ketene dithioacetals 11, 12 and 13 have been undertaken through which new synthetic methods for the preparation of γ, δ-unsaturated-β-ketoesters 18 and 19 and novel substituted cyclopentenones 21 have been developed.

II.4 EXPERIMENTAL

Melting points were determined on a Thomas Hoover (capillary method) apparatus and are uncorrected. The i.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer and the frequencies are reported in cm^{-1}. The ^1H n.m.r. spectra were recorded on a Varian EM-390, 90 MHz spectrometer using TMS as internal standard and the chemical shifts are expressed as δ (ppm). The mass spectra were recorded on a Jeol-D 300 Mass Spectrometer.

Starting Materials

The commercial samples of acetone, ethylmethylketone, diethylketone, benzaldehyde, 4-tolualdehyde, 4-chlorobenzaldehyde, anisaldehyde, 3-methoxybenzaldehyde, 3,4-dimethoxybenzaldehyde, 3,4,5-trimethoxybenzaldehyde, piperanal, cinnamaldehyde, N,N-dimethylformamide diethylacetal, methyl iodide, ethyl iodide, n-propyl bromide and isopropyl bromide were available commercially and were purified before use.

The previously reported ketene S,S-acetals i.e. 4,4-bis(methylthio)-3-buten-2-one 10a, m.p. 66-67°C[5], 4,4-bis(methylthio)-3-methyl-3-butene-2-one 10b, b.p. 68°C (0.1 mm)[5] and 1,1-bis(methylthio), 3-methyl-1-pentene-3-one (10c)[2,24,25] were prepared as given below.

General method for the preparation of α -oxoketene dithioacetals (10a-c) using sodium t-butoxide: A mixture of ketone (0.2 mol) and carbon disulphide (0.2 mol) was added dropwise to an ice cold and well stirred suspension of sodium t-butoxide (0.4 mol) in dry benzene (100 ml) and the reaction mixture was allowed to stir at room temperature for 5-6 hrs. Methyl iodide (0.4 mol) was then gradually added with stirring and external cooling (exothermic reaction) and the reaction mixture was allowed to stand for 6-10 hr at room temperature with occasional shaking and poured over ice water (200 ml). The benzene layer was separated and the aqueous portion was extracted with benzene (3x50 ml), the combined extracts were washed with water (3x100 ml), dried (Na_2SO_4) and concentrated to give crude dithioacetals 10, which were further purified either by crystallization or by distillation under reduced pressure.

5-Aryl,1- bis(methylthio) 1,4-pentadiene-3-ones 11a-g, 12a-c, 13a-h and 1,1-Bis(methylthio)-7-phenyl-1,4,6-heptatriene-3-ones 14; General Procedure [5]: Sodium (0.6mol) was dissolved with cooling in 30 ml of 95% ethanol. A solution of α -oxoketene dithioacetal (0.03 mol)

and benzaldehyde or cinnamaldehyde (0.03 mol) in 25 ml of 95% ethanol was added dropwise to the sodium ethoxide solution and the reaction mixture was stirred at room temperature for 4-5 hrs. It was then diluted with cold water (200 ml), the solid separated was filtered, washed with water (3x25 ml) and dried. In the cases where the product is liquid (13a-e,13h), the reaction mixture after dilution with water was extracted with chloroform (3x50 ml), washed with water (4x50 ml) dried (Na_2SO_4) evaporated to give crude products which were further column chromatographed (ethylacetate:hexane, 1:20 eluent).

1,1-Bis(methylthio)-5-(3,4-dimethoxyphenyl)-1,4-pentadiene-3-one (11e) was obtained as yellow crystalline solid (methanol); m.p. 130-131°C; yield 85%; i.r.(KBr): ν_{max} = 1650, 1610 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.30(s,3H,SCH_3); 2.38(s,3H,SCH_3); 3.81[s,6H,$(OCH_3)_2$]; 6.43(s, 1H,H-2); 6.76(s,$2H_{styryl}$); 6.91-7.30(m,$3H_{arom}$). (Found: C,58.31; H,6.07. Calc. for $C_{15}H_{18}O_3S_2$ (310.4): C,58.06; H,5.81%).

1,1-Bis(methylthio)-5-(3,4,5-trimethoxyphenyl)-1,4-pentadiene-3-one (11f) was obtained as yellow crystalline solid (methanol); m.p. 142-143°C; yield (86%); i.r.(KBr): ν_{max} = 1635, 1605, 1590 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.57(s,6H,SCH_3); 3.92(s,9H,OCH_3); 6.33(s,1H,=CH, H-2); 6.80(d,1H,J=16Hz,H-4); 6.86(s,$2H_{arom}$); 6.57(d,1H,J=16Hz,H-5). (Found: C,56.78H, 5.67. Calc. for $C_{16}H_{20}O_4S_2$ (340.4): C,56.44; H,5.92%).

1,1-Bis(methylthio)-2,4-dimethyl-5-phenyl-1,4-pentadiene-3-one (13a) was isolated as yellow liquid; yield 78%; i.r.(neat): ν_{max} = 1640, 1620 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.13(s,3H,J=2.5Hz,CH_3); 2.16(s,3H,-CH_3); 2.17(s,3H,-SCH_3); 2.32(s,3H,-SCH_3): 7.20-7.50(m,$6H_{arom}$+H-5 $_{olefinic}$).

(Found: C,64.79; H,6.26. Calc. for $C_{15}H_{18}OS_2$(278.4): C,64.94; H,6.18%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(4-methylphenyl)-1,4-pentadiene-3-one (13b) was isolated as yellow liquid; yield 81%; i.r.(neat): ν_{max} = 1640, 1620 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.12(m,6H,CH_3); 2.13 (s,3H,SCH_3); 2.32(s,3H,CH_3); 2.33(s,3H,SCH_3); 6.91-7.45(m,$5H_{arom+olefin}$). (Found: C,66.15; H,6.42. Calc. for $C_{16}H_{20}OS_2$(292.4): C,65.94; H,6.57%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(4-chlorophenyl)-1,4-pentadiene-3-one (13c) was isolated as yellow liquid; yield 85%;i.r. (neat): ν_{max} = 1640, 1618, 1580 cm^{-1}; ^1H n.m.r.(CCl_4): 2.09(d,3H,J=2.5Hz, CH_3); 2.10(s,3H,CH_3); 2.11(s,3H,SCH_3); 2.28(s,3H,SCH_3); 7.10(q, 1H,J=2.5Hz,H-5); 7.32(s,$4H_{arom}$). (Found: C,58.08; H,5.38. Calc. for $C_{15}H_{16}OClS_2$(311.85): C,57.76; H,5.13%). m/z 312(M^+,17.5%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(4-methoxyphenyl)-1,4-pentadiene 3-ones (13d) was isolated as yellow liquid; yield 90%; i.r.(neat): ν_{max}= 1640, 1620 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.09(d,3H,J=2.5Hz,CH_3); 2.10(s,3H,CH_3); 2.11(s,3H,SCH_3); 2.29(s,3H,SCH_3); 3.81(s,3H,OCH_3); 6.78-7.45(m,$5H_{arom}$+H-5). (Found: C,62.42; H,6.46. Calc. for $C_{16}H_{20}O_2S_2$(380.4): C,62.30; H,6.54%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(3-methoxyphenyl)-1,4-pentadiene-3-one (13e) was isolated as yellow liquid; yield 91%; i.r.(neat): ν_{max}= 1650, 1640, 1595 cm^{-1}; ^1H n.m.r. (CCl_4): δ 2.08(d,3H,J=2.5Hz, CH_3): 2.10(s,3H,CH_3); 2.11(s,3H,SCH_3); 2.29(s,3H,SCH_3); 3.78(s,3H,OCH_3); 6.65-7.40(m,$5H_{arom}$ H-5). (Found: C,62.15; H,6.62. Calc. for $C_{16}H_{20}O_2S_2$(308.4): C,62.30; H,6.54%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(3,4-dimethoxyphenyl)-1,4-pentadiene-3-one (13f) was isolated as yellow crystalline solid (methanol); m.p. 52°C; yield 85%; i.r.(KBR): ν_{max}= 1640, 1615, 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.08(d,3H,J=2.5Hz,CH_3); 2.11(s,3H, CH_3): 2.12(s,3H,SCH_3); 2.31(s,3H,SCH_3); 3.86(s,6H,OCH_3); 6.75-7.45 (m,$4H_{arom}$+H-5). (Found: C,60.41; H,6.34. Calc. for $C_{17}H_{22}O_3S_2$(338.4): C,60.32; H,6.55%). m/z 338(M^+,21%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(3,4,5-trimethoxyphenyl)-1,4-pentadiene-3-one (13g) was isolated as yellow crystalline solid (methanol); m.p. 62-63°C; yield 91%; i.r.(KBr): ν_{max}= 1645, 1578 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.08(d,3H,J=2.5Hz,CH_3); 2.10(s,3H,CH_3); 2.11(s, 3H,SCH_3); 2.31(s,3H,SCH_3); 3.74(s,3H,OCH_3); 3.81(s,6H,OCH_3); 6.45 (q,1H,J=2.5Hz,H-5); 6.95(m,$2H_{arom}$). (Found: C,58.71; H,6.48. Calc. for $C_{18}H_{24}O_4S_2$(368.49): C,58.67; H,6.56%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(3,4-methylenedioxyphenyl)-1,4-pentadiene-3-one (13h) was isolated as yellow liquid; yield 87%; i.r.(neat): ν_{max} = 1638, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.06 (d, 3H,J=2.5Hz,CH_3); 2.09(s,3H,CH_3); 2.10(s,3H,SCH_3); 2.28(s,3H,SCH_3); 5.94(s,2H,-CH_2-); 6.67-7.38(m,$4H_{arom}$+H-5). (Found: C,59.71; H,5.69. Calc. for $C_{17}H_{18}O_3S_2$(322.42): C,59.60; H,5.61%). m/z 322(M^+).

1,1-Bis(methylthio)-5-(dimethylamino)-1,4-pentadiene-3-ones (16a-c)

General Procedure: A mixture of α-oxoketene dithioacetals 10 (0.01 mol) and N,N-dimethylformamide diethylacetal 15 (1.80g, 0.012 mol) was heated (100°C) in a sealed tube for 5 h. The reaction mixture was cooled and passed through small silica gel column to give pure 16a-c.

1,1-Bis(methylthio)-5-(N,N-dimethylamino)-1,4-pentadiene-3-one (16a) was obtained as reddish brown crystalline solid (methanol); m.p. 109-110°C; yield 92%; spectral data given in text. (Found: C,49.54; H,6.71; N,6.72. Calc. for $C_9H_{15}NOS_2$(217.3): C,49.74; H,6.96; N,6.72%).

1,1-Bis(methylthio)-5-(N,N-dimethylamino)-2-methyl-1,4-pentadiene-3-one (16b) was obtained as dark red oil; yield 88%; i.r.(neat): ν_{max} = 1635, 1625, 1555 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.0(s,3H,CH_3); 2.15(s,3H,SCH_3); 2.28(s,3H,SCH_3); 2.90(s,6H,N-CH_3); 4.90(d,1H,J=12Hz, H-4); 7.22(d,1H,J=12Hz,H-5). (Found: C,52.07; H,7.41; N,6.05. Calc. for $C_{10}H_{17}NOS_2$(231,3): C,51.90; H,7.41; N,6.05%). m/z 231(M^+,12%).

1,1-Bis(methylthio)-2,4-dimethyl-5-(N,N-dimethylamino)-1,4-pentadiene-3-one (16c) was obtained as dark brown oil; yield 85%; i.r.(neat): ν_{max} = 1625, 1645 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.90(s,3H,CH_3); 2.80 (s,3H,CH_3);2.14(s,3H,SCH_3); 2.29(s,3H,SCH_3); 3.10(s,6H,NCH_3); 6.73 (s,1H,H-5). (Found: C,53.53; H,7.51; N,5.98. Calc. for $C_{11}H_{19}NOS_2$ (245.4): C,53.83; H,7.80; N,5.70%). m/z 245(M^+,59%).

5-Alkyl-1,1-bis(methylthio)-penta-1,4-diene-3-ones (17a-l); General Procedure: To a cooled (0°C) solution of the appropriate grignard reagent (0.015 mol) in dry ether (50 ml), 16 (0.01 mol) in anhydrous THF (20 ml) was added dropwise (5 min) under N_2 atmosphere. After stirring for 3 h, the reaction mixture was poured into a cold saturated solution of NH_4Cl(100 ml) and the solution was extracted with ether (3x25 ml). The ether phase was washed with water (2x50 ml), dried (Na_2SO_4) and evaporated and the residue was filtered through a small column of silica gel using ethylacetate:hexane (1:20) as eluent to give pure 17.

1,1-Bis(methylthio)-1,4-hexadiene-3-one (17a) was isolated as pale yellow oil; yield 91%; spectral data given in the text. (Found: C,50.78; H,6.74. Calc. for $C_8H_{12}OS_2$(186.3): C,51.02; H,6.43%).

1,1-Bis(methylthio)-1,4-heptadiene-3-one (17b) was isolated as pale yellow oil; yield 92%; i.r.(neat): ν_{max} = 1655, 1600, 1480 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.11(t,3H,J=7Hz,CH_3); 2.20(quintet d, 2H,J=7Hz, 1.5Hz,CH_3CH_2); 2.42(s,3H,SCH_3); 2.46(s,3H,SCH_3); 6.03(s,1H,H-2); 6.04(dt,1H,J=15Hz,1.5Hz,H-4); 6.71(dt,1H,J=15Hz,7Hz,H-5). (Found: C,53.69; H,7.26. Calc. for $C_9H_{14}OS_2$(202.3): C,53.43; H,6.97%). m/z 202(M^+,32%).

1,1-Bis(methylthio)-1,4-octadiene-3-one (17c) was isolated as pale yellow oil; yield 87%; i.r.(neat): ν_{max}= 1655, 1607, 1485, 1430 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.83(t,3H,J=7Hz,$CH_3CH_2CH_2$-); 1.50(sext,2H,J=7Hz, $CH_3CH_2CH_2$-); 2.16(qd,2H,J=7Hz,1Hz,$CH_3CH_2CH_2$): 2.39(s,3H,SCH_3); 2.46 (s,3H,SCH_3); 6.05(s,1H,H-2); 6.06(dt,1H,J=15Hz,1Hz,H-4); 6.71(dt, 1H,J=15Hz,7Hz,H-5). (Found: C,55.71; H,7.67. Calc. for $C_{10}H_{16}OS_2$ (216.4): C,55.50; H,7.45%). m/z 216(M^+,26%).

1,1-Bis(methylthio)-6-methyl-1,4-heptadiene-3-one (17d) was obtained as pale yellow oil; yield 89%; i.r.(neat): ν_{max}= 1652,1608,1480, 1430 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.04(d,6H,J=7Hz,CH_3); 2.35[m,1H, merged with SCH_3 signals $(CH_3)_2CH$]; 2.37(s,3H,SCH_3); 2.46(s,3H, SCH_3); 6.03(dd,1H,J=15Hz,1Hz,H-4); 6.12(s,1H,H-2); 6.68(dd,1H,J=15Hz, 7Hz,H 5). (Found: C,55.23; H,7.71. Calc. for $C_{10}H_{16}OS_2$(216.4): C,55.50; H,7.45%). m/z 216(M^+,60%).

1,1-Bis(methylthio)-2-methyl-1,4-hexadiene-3-one (17e) was obtained as pale yellow oil; yield 87%; i.r.(neat): ν_{max}= 1645, 1620,1440 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.91(dd,3H,J=7Hz,1.5Hz,5-CH_3); 2.02(s,3H,2-CH_3);

2.18(s,3H,SC$\underline{H}_3$); 2.36(s,3H,SC$\underline{H}_3$); 6.09(dq,1H,J=15Hz,1.5Hz,$\underline{H}$-4); 6.53(dq,1H,J=15Hz,$\underline{H}$-5). (Found: C,53.60; H,7.13; $C_9H_{14}OS_2$(202.3). Calc. for C,53.43; H.6.97%). m/z 202 (M^+,19%).

1,1-Bis(methylthio)-2-methyl-1,4-heptadiene-3-one (17f) was obtained as yellow oil; yield 82%; i.r.(neat): ν_{max}= 1556, 1618, 1550, 1432 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.12(t,3H,J=7Hz,C$\underline{H}_3$CH$_2$); 2.08(s,3H,2-C$\underline{H}_3$); 2.24 (s,3H,SC$\underline{H}_3$); 2.25(m,merged with SC$\underline{H}_3$ signals, 2H,CH$_3$C$\underline{H}_2$); 2.37(s, 3H,SC$\underline{H}_3$); 6.13(dt,1H,J=15Hz,1.5Hz,$\underline{H}$ 4); 6.66(dt,1H,J=15Hz,7Hz,$\underline{H}$-5). (Found: C,55.77; H,7.73. Calc. for $C_{10}H_{16}OS_2$(216.4): C,55.50; H,7.45%). M/z 216(M^+,34%).

1,1-Bis(methylthio)-2-methyl-1,4-octadiene-3-one (17g) was obtained as yellow oil; yield 88%; i.r.(neat): ν_{max}= 1654, 1614, 1430 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.93(t,3H,J=7Hz,C$\underline{H}_3$CH$_2$CH$_2$); 1.51(sext,2H,J=7Hz, CH$_3$C$\underline{H}_2$CH$_2$); 2.02(s,3H,2-C$\underline{H}_3$); 2.16(s,3H,SC$\underline{H}_3$); 2.20(m,merged with SC$\underline{H}_3$,C$\underline{H}_3$ signals, 2H,CH$_3$CH$_2$C$\underline{H}_2$); 2.31(s,3H,SC$\underline{H}_3$); 6.09(dt,br,1H, J=15Hz,7Hz,$\underline{H}$-5). (Found: C,57.07; H,8.15. Calc. for $C_{11}H_{18}OS_2$(230.4): C,57.34; H,7.87%). m/z 230(M^+,27%).

1,1-Bis(methylthio)-2,6-dimethyl-1,4-heptadiene-3-one (17h) was obtained as yellow oil; yield 81%; i.r.(neat): ν_{max}= 1651, 1615, 1460, 1430 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.10[d,6H,J=7Hz,(C$\underline{H}_3$)$_2$CH]; 2.01 (s,2H,2-C$\underline{H}_3$); 2.19(s,3H,SC$\underline{H}_3$); 2.31(s,3H,SC$\underline{H}_3$); 2.43[m,1H,(CH$_3$)$_2$C$\underline{H}$]; 6.60(dd,1H,J=16Hz,1Hz,$\underline{H}$ 4); 6.54(dd,1H,J=16Hz,7Hz,$\underline{H}$-5). (Found: C,57.59; H,8.15. Calc. for $C_{11}H_{18}OS_2$(230.4): C,57.34; H,7.87%). m/z 230(M^+,20%).

1,1-Bis(methylthio)-2,4-dimethyl-1,4-hexadiene-3-ones (17i) was obtained as yellow oil; yield 85%; i.r.(neat): ν_{max}= 1652, 1640, 1540, 1430 cm^{-1};

^{1}H n.m.r)CCl_4): δ 1.79(d,3H,J=1.5Hz,4-C<u>H</u>$_3$); 1.85(d,3H,J=7Hz,5-C<u>H</u>$_3$); 2.02(s,3H,2-C<u>H</u>$_3$); 2.11(s,3H,SC<u>H</u>$_3$); 2.30(s,3H,SC<u>H</u>$_3$); 6.38(qq,1H, J=7Hz,1.5Hz,<u>H</u>-5). (Found: C,55.23; H,7.73. Calc. for $C_{10}H_{16}OS_2$ (216.4): C,55.50; H,7.45%). m/z 216(M^+,41%).

<u>1,1-Bis(methylthio)-2,4-dimethyl-1,4-heptadiene-3-one (17j)</u> was obtained as yellow oil; yield 86%; i.r.(neat): ν_{max}= 1654, 1578, 1545, 1430 cm^{-1}; ^{1}H n.m.r.(CCl_4): δ 1.06(t,3H,J-7Hz,C<u>H</u>$_3$CH$_2$); 1.77(q,3H,J=1.5Hz,4-C<u>H</u>$_3$); 2.02(s,3H,2-C<u>H</u>$_3$); 2.20(s,3H,SC<u>H</u>$_3$); 2.20(m,merged with methyl signals 2H,CH$_3$C<u>H</u>$_2$); 2.29(s,3H,SC<u>H</u>$_3$); 6.21 (q,1H,H=7Hz,1.5Hz,<u>H</u>-5). (Found: C,57.52; H,8.12. Calc. for $C_{11}H_{18}OS_2$(230.4): C,57.34; H.7.87%). m/z 230(M^+,5%).

<u>1,1-Bis(methylthio)-2,4-dimethyl-1,4-octadiene-3-one (17k)</u>, was obtained as yellow oil; yield 85%; i.r.(neat): ν_{max}= 1650, 1575, 1540, 1428 cm^{-1}; ^{1}H n.m.r.(CCl_4): δ 0.93(t,3H,J=7Hz,C<u>H</u>$_3$CH$_2$CH$_2$); 1.46(sext,2H,J=7Hz,CH$_3$C<u>H</u>$_2$CH$_2$); 1.77(d,3H,J=1Hz,4-C<u>H</u>$_3$); 2.00(s,3H, 2-C<u>H</u>$_3$); 2.09(s,3H,SC<u>H</u>$_3$); 2.13(q,merged with SC<u>H</u>$_3$ and C<u>H</u>$_3$ signals, 2H,CH$_3$CH$_2$C<u>H</u>$_2$); 2.27(s,3H,SC<u>H</u>$_3$); 6.24(tq,2H,J=7Hz,1Hz,<u>H</u>-5). (Found: C,58.74; H,8.45. Calc. for $C_{12}H_{20}OS_2$(244.4): C,58.97; H,8.25%). m/z 244(M^+,91%).

<u>1,1-Bis(methylthio)-2,4,6-trimethyl-1,4-heptadiene-3-one (17l)</u> was obtained as yellow oil; yield 78%; i.r.(neat): ν_{max}= 1650, 1575, 1542, 1460, 1430 cm^{-1}; ^{1}H n.m.r.(CCl_4): δ 1.03[d,6H,J=7Hz, (CH$_3$)$_2$C<u>H</u>]; 1.76(d,3H,J=1Hz,4-C<u>H</u>$_3$); 2.01(s,3H,2-C<u>H</u>$_3$); 2.11(s,3H, SC<u>H</u>$_3$); 2.30(s,3H,SC<u>H</u>$_3$); 2.69[m,1H,(CH$_3$)$_2$C<u>H</u>]; 6.06(dq,7Hz,J=7Hz,1Hz, <u>H</u>-5). (Found: C,59.20; H,8.49. Calc. for $C_{12}H_{20}OS_2$(244.4): C,58.97; H,8.25%). m/z 244(M^+,8.9%).

Methyl 5-aryl-3-oxo-4-pentenoates (18a-g), Methyl 5-aryl-2-methyl-3-oxo-4-pentenoates (19a-c) and Methyl 7-aryl-3-oxo-4,6-heptadienoate (20); General Procedure: A suspension of α-oxoketene dithioacetal 11, 12 or 14 (0.01 mol) and Hg_2Cl_2 (2.70g, 0.01 mol) in anhydrous methanol (30 ml) was stirred at room temperature (10 min) and 1.5 ml (0.01 mol) of distilled boron trifluoride etherate was added and the reaction mixture was refluxed for 2 hr. It was then filtered through a sintered funnel to remove traces of mercuric chloride and the filtrate diluted with chloroform (100 ml), washed with saturated sodium bicarbonate solution (2x500 ml) and water (2x50 ml), dried (Na_2SO_4) and evaporated to give crude products, which were purified by column chromatography over silica gel. Elution with hexane and ethyl acetate (95:5) gave pure esters 18a-g, 19a-c and 20.

Methyl 5-phenyl-3-oxo-4-pentenoate (18a) was obtained as pale yellow crystalline solid; yield 70%; ;m.p. 79-80°C (exists in enol form in solid phase); spectral data are described in the text. (Found: C,70.84; H,6.11. Calc. for $C_{12}H_{12}O_3$(204.2): C,70.57; H,5.92%).

Methyl 5-(4-methylphenyl)-3-oxo-4-pentenoate (18b) was obtained as light yellow crystalline solid; yield 72%; m.p. 78-79°C; keto-enol ratio 33:67 (in CCl_4 solution); i.r.(KBr): ν_{max} = 1630, 1590 cm^{-1} (exists in enol form in solid phase); ^1H n.m.r.(CCl_4): δ 2.31(s, 3H,CH_3); 3.52(s,0.66H,CH_2); 3.62(s,3H,CH_3O); 5.00(s,0.67H,=CH); 6.23(d,J=15Hz,0.66H,-CH); 6.60(d,0.33H,J=15Hz,-CH); 6.88-7.60 (m,$5H_{arom+olefin}$); 11.68(s,0.67H,-OH). (Found: C,71.85; H,6.29. Calc. for $C_{13}H_{14}O_3$(218.2): C,71.54; H,6.45%). m/z 218(M^+,40%).

Methyl 5-(4-chlorophenyl)-3-oxo-4-pentenoate (18c) was obtained as pale yellow crystalline solid; yield 69%; m.p.83-84°C; keto-enol ratio 22:78 (in CCl_4 solution); i.r.(KBr): ν_{max}= 1645, 1628, 1588 cm^{-1}; (exists in enol form in solid phase); ^1H n.m.r.(CCl_4): δ 3.48(s,0.44H, $C\underline{H}_2$); 3.68(s,3H,$C\underline{H}_3O$); 5.08(s,0.78H,-C$\underline{H}$); 6.28(d,J=15Hz,0.78H,=C$\underline{H}$); 6.68(d,0.22H,J=15Hz,=C$\underline{H}$); 7.00-7.50(m,$5H_{arom+olefin}$); 11.70(s,0.78H, O$\underline{H}$). (Found: C,60.18; H,4.90. Calc. for $C_{12}H_{11}ClO_3$(238.7): C,60.30; H,4.65%). m/z 240(18%); 238(M^+,53%).

Methyl 5-(4-methoxyphenyl)-3-oxo-4-pentenoate (18d) was obtained as light yellow crystalline solid; yield 65%; m.p. 91-92°C; keto-enol ratio 75:25(in CCl_4 solution); i.r.(KBr): ν_{max}= 1642, 1622, 1588 cm^{-1} (exists in enol form in solid phase); ^1H n.m.r.(CCl_4): 3.58(s,1.5H,$C\underline{H}_2$); 6.64(s,3H,$C\underline{H}_3O$); 3.71(s,3H,$C\underline{H}_3O$); 5.05(s,0.25H, =C$\underline{H}$); 6.19(d,0.25H,J=15Hz,=C$\underline{H}$); 6.58(d,0.75H,J=12Hz,=C$\underline{H}$); 6.71-7.66 (m,$5H_{arom+olefin}$); 11.62(s,0.25H,O$\underline{H}$). (Found: C,66.80; H,5.96. Calc. for $C_{13}H_{14}O_4$(234.4): C,66.65; H,6.02%). m/z 234(M^+,77%).

Methyl 5-(3,4-dimethoxyphenyl)-3-oxo-4-pentenoate (18e) was isolated as yellow crystalline solid; yield68%; m.p. 82-83°C; keto-enol ratio 40:60(in CCl_4 solution); i.r.(KBr): ν_{max}= 1744, 1644, 1622, 1593 cm^{-1} (exists predominantly in enol form and shows small amount of keto forms in solid phase); ^1H n.m.r.(CCl_4): δ 3.60(s,0.8H,$C\underline{H}_2$); 3.67 (s,3H,$C\underline{H}_3O$); 3.80(s,6H,$C\underline{H}_3O$); 5.06(s,0.6H,=C$\underline{H}$); 6.21(d,0.6H,J=15Hz, -C$\underline{H}$); 6.59(s,0.4H,J=15Hz,=C$\underline{H}$); 6.71-7.10(m,$3H_{arom}$); 7.27(d,0.6H, J=15Hz,-C$\underline{H}$); 7.52(d,0.4H,J=15Hz,=C$\underline{H}$); 11.66(s,0.6H,O$\underline{H}$). (Found: C,63.43; H,5.81. Calc. for $C_{14}H_{16}O_5$(264.3): C,63.62; H,6.10%). m/z 264(M^+,49%).

Methyl 5-(3,4,5-trimethoxyphenyl) 3-oxo-4-pentenoate (18f) was isolated as crystalline solid; yield 66% m.p. 94-95°C; keto-enol ratio 67:33(in CCl_4 solution); i.r.(KBr): ν_{max}= 1738, 1640, 1625, 1590 cm^{-1} (exists in keto form in solid phase); ^1H n.m.r.(CCl_4): δ 3.63(s,1.34H,$C\underline{H}_2$): 3.68(s,3H,$C\underline{H}_3O$); 3.83(s,9H,$C\underline{H}_3O$); 5.10(s,0.67H, =C$\underline{H}$); 6.23(d,0.33H,J=15H,=C$\underline{H}$); 6.61(d,0.67H,J=15Hz,C$\underline{H}$); 6.62-6.81 (m,$2H_{arom}$); 7.28(d,0.33H,J=15Hz,=C$\underline{H}$); 7.51(d,0.67H,J=15Hz,=C$\underline{H}$); 11.66 (s,0.67H,O$\underline{H}$). (Found: C,61.47; H,6.28. Calc. for $C_{15}H_{18}O_6$ (294.3): C,61.22; H,6.16%). m/z 294(M^+,86%).

Methyl 5-(3,4-methylenedioxyphenyl)-3-oxo-4-pentenoate (18g) was isolated as crystalline solid; yield 64%; m.p. 91-92°C; keto-enol ratio 40:60 (in CCl_4 solution); i.r.(KBr): ν_{max}= 1740, 1630, 1590 cm^{-1}; (exists predominantly in enol form with small amount of keto form in solid phase); ^1H n.m.r.(CCl_4): δ 3.57(s,0.8H,$C\underline{H}_2$); 3.68(s,3H, $C\underline{H}_3O$); 5.02(s,0.60H,=C$\underline{H}$); 5.88(s,2H,-O-$C\underline{H}_2$-O); 6.18(d,0.6H,J=15Hz, C$\underline{H}$); 6.51(d,0.4H,J=15Hz,=C$\underline{H}$); 6.65-7.10(m,$3H_{arom}$); 7.30(d,0.6H, J=15Hz,=C$\underline{H}$); 11.65(s,0.6H,O$\underline{H}$). (Found: C,62.79; H,5.06; Calc. for $C_{13}H_{12}O_5$(248.4): C,62.90; H,4.87%). m/248(M^+,77%).

Methyl 2-methyl-5-phenyl-3-oxo-4-pentenoate(19a) was obtained as pale yellow viscous liquid; yield 85%; keto-enol ratio 80:20 (in CCl_4 solution); i.r.(neat): ν_{max}= 1740, 1688, 1660, 1610 cm^{-1} (exists in keto form in neat liquid phase); ^1H n.m.r.(CCl_4): δ 1.37(d,2.4H, J=7Hz,$C\underline{H}_3$); 1.88(s,0.6H,$C\underline{H}_3$); 3.67(s,3H,$C\underline{H}_3O$); 3.69(q,0.8H,J=7Hz, $CH_3C\underline{H}$); 6.81(d,0.8H,J=7Hz,$CH_3C\underline{H}$); 7.16-7.81(m,$6.2H_{arom+olefin}$); 12.50(s,0.19H,-O$\underline{H}$). (Found: C,71.75; H,6.67. Calc. for $C_{12}H_{14}O_3$(218.2): C,71.54; H,6.46%). m/z 218(M^+,39%).

Methyl 2-methyl-5-(4-chlorophenyl)-3-oxo-4-pentenoate (19b) was isolated as pale yellow oil; yield 84%; keto-enol ratio 20:80 (in CCl_4 solution); i.r.(neat): ν_{max}= 1640, 1620, 1590 cm^{-1} (exists in enol forms in neat liquid phase); ^1H n.m.r.(CCl_4): δ 1.44(d,0.6H,J=7Hz,CH_3); 1.93 (s,2.4H,CH_3); 3.73(q,0.2H,J=7Hz,CH_3CH); 3.82(s,3H,CH_3O); 6.80(d,0.2H, J=15Hz,=CH); 6.82(d,0.8H,J=15Hz,=CH); 7.21-7.71(m. $5H_{arom+olefin}$); 12.60(s,0.8H,-OH). (Found: C,61.95; H,4.96. Calc. for $C_{13}H_{13}ClO_3$ (252.7): C,61.79; H,5.18%). m/z 257(7%); 252(M^+,21%).

Methyl 2-methyl-5-(4-methoxyphenyl)-3-oxo-4-pentenoate (19c) was obtained as viscous liquid; yield 83%; keto-enol ratio 100:0 (in CCl_4 solution); i.r.(neat): ν_{max}= 1730, 1682, 1595 cm^{-1} (exists in keto form in neat liquid phase); ^1H n.m.r(CCl_4): δ 1.32(d,3H, J-7Hz,CH_3); 3.68(s,3H,-CH_3O); 3.80(s,3H,CH_3O); 3.81(q,1H,J=7Hz, $CHCH_3$); 6.55(d,1H,J=15Hz,=CH); 6.81(d,J=12Hz,$2H_{arom}$); 6.82-7.76 (m,3H+olefin). (Found: C,67.86; H,6.27; Calc. for $C_{14}H_{16}O_4$(248.3): C,67.72; H,6.50%). m/z 248(M^+,29%).

Methyl 7-phenyl-3-oxo-4,6-heptadienoate (20) was obtained as crystalline solid; m.p. 84°C; yield 30%; keto-enol ratio 30:70; i.r. (KBr): ν_{max}=1638, 1620, 1588, 1560 cm^{-1}; ^1H n.m.r(CCl_4): 3.63(s,0.6H, CH_2); 3.80(s,3H,CH_3O); 5.10(s,0.7H,=CH); 6.00(d,0.7H,J=15Hz,=CH); 6.71-7.83(m,$8.3H_{arom+olefin}$); 11.88(s,0.7H,-OH). (Found: C,72.92; H,5.88. Calc. for $C_{14}H_{14}O_3$(230.2): C,73.02; H,6.13%). m/z 230(M^+,63%).

2,5-dimethyl-3-methylthio-5-methoxy-4-aryl-2-cyclopentene-1-ones (21a-h); General Procedure: A suspension of α-oxoketene dithioacetal 13 (0.01 mol) and $HgCl_2$ (2.70g, 0.01 mol) in anhydrous methanol (30 ml) was stirred at room temperature (10 min) and 1.5 ml (0.01 mol)

of distilled boron trifluoride etherate was added and the reaction mixture was refluxed for 3-6 h. The reaction mixture was filtered through a sintered funnel to remove traces of mercuric chloride and the filtrate diluted with chloroform (100 ml) washed with saturated sodium bicarbonate solution and evaporated to give the crude products which were purified by column chromatography over silica gel. Elution with hexane and ethyl acetate (95:5) gave pure cyclopentenones (21a-h).

2,5-dimethyl-3-methylthio-5-methoxy-4-phenyl-2-cyclopentene-1-one (21a) was obtained as colourless crystals; m.p. 52°C ; yield 73%; spectral data described in the text. (Found: C,69.78; H,7.46. Calc. for $C_{15}H_{18}O_2S$(262.4): C,69.53; H,7.30%).

2,5-dimethyl-3-methylthio-5-methoxy 4-(4-methylphenyl) 2-cyclopentene-1-one-(21b) was obtained as viscous oil; yield 65%; refluxing time 3 hrs; i.r.(neat): ν_{max}= 1690, 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.70 (s,3H,CH_3); 1.80(d,3H,J=2.5Hz,CH_3); 2.03(s,3H,SCH_3); 2.32(s,3H, Ar-CH_3); 3.16(s,3H,CH_3O); 4.02(q,1H,J=2.5Hz,Ar-CH); 6.81-7.22(m, $4H_{arom}$). (Found: C,65.45; H,6.73. Calc. for $C_{16}H_{20}O_2S$(276.4): C,65.72; H,6.90%). m/z 276(M^+,3%); 246(M^+-20,100%).

2,5-dimethyl-3-methylthio-5-methoxy-4-(4-chlorophenyl)-2-cyclopentene-1-one (21c) was obtained as viscous liquid; refluxing time 3 hrs; yield 68%; ;i.r.(neat): ν_{max}= 1682, 1583 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.70(s,3H,CH_3); 1.83(d,3H,J=2.5Hz,CH_3); 2.06(s,3H,SCH_3); 3.21 (s,3H,CH_3O); 4.01(q,1H,J=2.5Hz,Ar-CH); 6.90-7.51(m,$4H_{arom}$). (Found: C,60.80; H,5.49. Calc. $C_{15}H_{17}ClO_2S$ (296.8): C,60.70; H,5.77%). m/z 296(M^+,1%); 266(M^+-30,100%).

2,5-dimethyl-3-methylthio-5-methoxy-4-(4-methoxyphenyl)-2-cyclopentene 1-one (21d) was obtained as viscous liquid; refluxing time 3 hrs; yield 60%; i.r.(neat): ν_{max}= 1680, 1580 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.71(s,3H,CH_3); 1.71(d,3H,J=1.5Hz,CH_3); 1.95(s,3H,-SCH_3); 3.10 (s,3H,CH_3O); 3.70(s,3H,CH_3O); 3.90(q,1H,J=2.5Hz,Ar-CH); 6.70-7.01 (m,4H_{arom}). (Found: C,65.45; H,6.73. Calc. for $C_{16}H_{20}O_3S$(292.4): C,65.72; H,6.90%). m/z 292(M^+,37%); 262(M^+-20,100%).

2,5-Dimethyl-3-methylthio-5-methoxy-4-(3-methoxyphenyl)-2-cyclopentene-1-one (21e) was obtained as viscous liquid; refluxing time 4 hrs, yield 60%; i.r.(neat): ν_{max}=1680, 1580 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.65(s,3H,CH_3); 1.82(d,3H,J=2.5Hz,CH_3); 2.06(s,3H,SCH_3); 3.22(s, 3H,CH_3O); 4.01(q,1H,J=2.5Hz,ArCH); 6.5-7.21(m,4H_{arom}). (Found: C,65.88; C,6.69. Calc. for $C_{16}H_{20}O_3S$(292.4): C,65.72; H,6.90%). m/z 292(M^+1%); 262(M^+-30,100%).

2,5-Dimethyl-3-methylthio-5-methoxy-4-(3,4-dimethoxyphenyl)-2-cyclopentene-1-one (21f) was obtained as viscous liquid; refluxing time 4 hrs; yield 52%; i.r.(neat): ν_{max}= 1681, 1580 cm^{-1}; ^1H n.m.r. (CCl_4): δ 0.73(s,3H,CH_3); 1.81(d,3H,J=2.5Hz,CH_3); 2.10(s,3H,SCH_3); 3.20(s,3H,CH_3O); 3.80(s,6H,OCH_3); 3.95(q,1H,J=2.5Hz,Ar-CH); 6.35-6.80(m,3H_{arom}). (Found: C,64.10; H,7.01. Calc. for $C_{17}H_{22}O_4S$(322.4): C,64.32; H,6.87%).

2,5-Dimethyl-3-methylthio-5-methoxy-4-(3,4,5-trimethoxyphenyl) 2-cyclopentene 1-one (21g) was obtained as viscous liquid; refluxing time 6 hrs; yield 61%; i.r.(neat): ν_{max} = 1680, 1580 cm^{-1}; ^1H n.m.r. (CCl_4): δ 7.90(s,3H,CH_3); 1.81(d,3H,J=2.5Hz,CH_3); 2.15(s,3H,SCH_3); 3.16(s,3H,OCH_3); 3.91(q,1H,J=2.5Hz,Ar-CH); 3.71(s,3H,OCH_3); 3.73

(s,6H,OC$\underline{H}_3$); 6.20-6.50(m,2H_{arom}). (Found: C,61.41; H,6.71; Calc. for $C_{18}H_{24}O_5S$(352.3): C,61.36; H,6.85%).

2,5-Dimethyl-3-methylthio-5-methoxy-4-(3,4-methylenedioxy)-2-cyclopentene-1-one (21h) was obtained as viscous liquid; refluxing time 6 hrs; yield 55%; i.r.(neat): ν_{max} = 1681, 1580 cm^{-1}; ^1H n.m.r. (CCl_4): δ 0.75(s,3H,-C$\underline{H}_3$); 1.81(d,3H,J=2.5Hz,C$\underline{H}_3$); 2.10(s,3H,SC$\underline{H}_3$); 3.15(s,3H,C$\underline{H}_3$O); 3.91(q,1H,J=2.5Hz,Ar-C$\underline{H}$); 5.90(s,2H,-O-C$\underline{H}_2$-O-); 6.41-6.90(m,3H_{arom}). (Found: C,62.55; H,6.22. Calc. for $C_{16}H_{18}O_4S$ (306.4): C,62.72; H,5.92%). m/z 306(M^+,59%); 276(M^+-30,100%).

Reaction of 1,1-Bis(methylthio)-2,4-dimethyl-5-(4-methoxyphenyl) 1,4-pentadien-3-one (13d) with $SnCl_4$: To a solution of the α-oxo-ketene dithioacetals 13d (3.08g, 0.01 mol) in dichloromethane, $SnCl_4$(1.20 ml; 0.01 mol) was added with cooling and stirring. The reaction mixturte was further stirred at room temperature for 5 h, poured over water (100 ml) extracted with dichloromethane (3x30 ml) dried (Na_2SO_4) evaporated to give a crude mixture of 31 and 32, which were isolated by column chromatography using 5% ethyl acetate hexane as eluent.

2,5-Dimethyl-3,4-dimethylthio-4-(4-methoxyphenyl)-2-cyclopentene 1-one (31) was obtained as viscous liquid; yield 30%; spectral data described in the text. (Found: C,62.41; H,6.64. Calc. $C_{16}H_{20}O_2S_2$ (308.4): C,62.30; H,6.54%).

2,5-Dimethyl-3-methylthio-5-hydroxy 4-(4-methoxyphenyl)-2-cyclopentene 1-one (32) was obtained as viscous liquid; yield 50%; i.r.(neat): ν_{max} = 3420, 1690, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.10(s,3H,C$\underline{H}_3$); 1.81(d,3H,J=2.5Hz,C$\underline{H}_3$); 2.12(s,3H,SC$\underline{H}_3$); 3.80(s,3H,OC$\underline{H}_3$); 4.40(q, 1H,J=2.5Hz,Ar-C$\underline{H}$); 6.60-7.35(m,4H_{arom}). (Found: C,64.86; H,6.61. Calc. for $C_{15}H_{18}O_3S$(278.4): C,64.70; H,6.52%).

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CHAPTER III

STUDIES ON THE SODIUM BOROHYDRIDE REDUCTION OF α-CINNAMOYL AND α-(5-ARYL-2,4-PENTADIENOYL) KETENE DITHIOACETALS

A. A NEW GENERAL METHOD FOR THE SYNTHESIS OF METHYL 7-ARYL-2,4,6-HEPTATRIENOATES*

B. A NOVEL SOLVOLYTIC REARRANGEMENT OF 1,1-BIS(METHYLTHIO)5-ARYL(OR STYRYL)-1,4-PENTADIENE-3-OLS TO CYCLOPENTENONE DERIVATIVES**

III.1 INTRODUCTION

The α-oxoketene dithioacetals 1 have been known to undergo regio-selective 1,2 reduction with sodium borohydride to give the corresponding carbinol acetals 2, which have been shown to undergo boron trifluoride etherate catalyzed methanolysis, stereoselectively, to afford the

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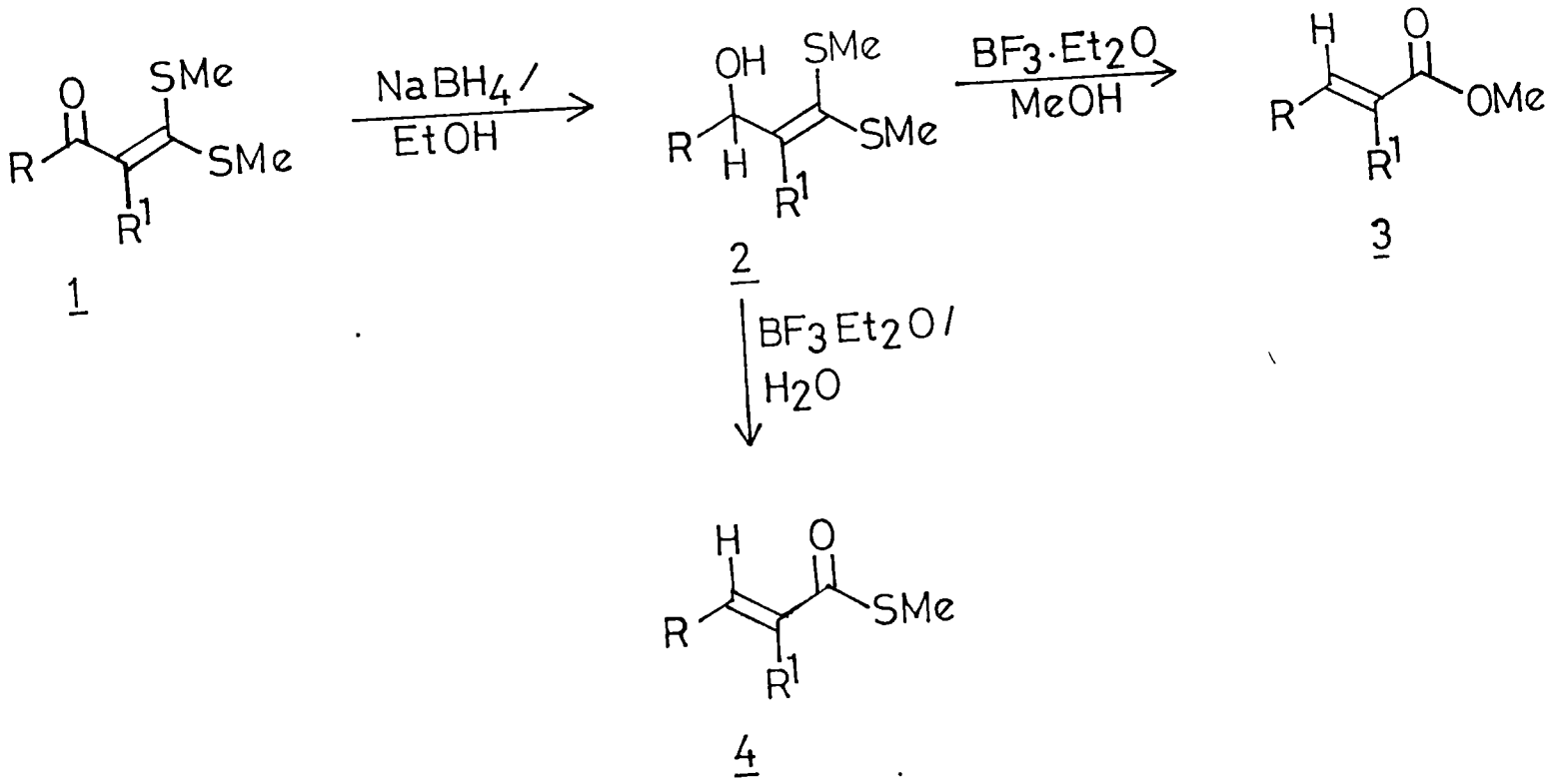
* C.V. Asokan, H. Ila and H. Junjappa, Synthesis, 163 (1985).

** C.V. Asokan, H.Ila and H. Junjappa, Tetrahedron Lett., 26, 1087 (1985).

corresponding α,β-unsaturated esters 3[1]. Also, the carbinol acetals 2 were partially hydrolysed in the presence of boron trifluoride etherate to afford the corresponding S-methyl esters 4. This reaction was considered of further importance if it can be extended to the conjugated polyene systems employing the α-oxoketene dithioacetals with appropriate structural modifications. The α-cinnamoyl ketene dithioacetals[2] (24a, 24b, Scheme 4) and the α-(5-Aryl 2,4-pentadienoyl) ketene dithioacetals (28a, 28b, Scheme 5), prepared by condensation of α-oxoketene dithioacetals derived from acetone or ethyl methyl ketone with benzaldehydes and cinnamaldehydes respectively would be ideal substrates for polyene synthesis. Apart from this, the α-cinnamoyl ketene dithioacetals or α-(5-Aryl-2,4-pentadienyl) ketene dithioacetals carrying substituents at the 2 & 4 positions would be of special interest, since the carbinol acetals, derived by their sodium borohydride reduction, under acid catalyzed solvolytic conditions may assume conformations, due to steric factors, in such a way, to enable them to undergo cationic ring closure to the corresponding cyclopentanoids. The importance of cyclopentanoids has grown considerably in the recent past due to discovery of several biologically important natural products containing this structural moiety[3]. The prostoglandins, hirsutic acids, Isocomine, Cedrene /a and a host of others are among the important compounds of natural origin belonging to cyclopentane family. Development of synthetic strategy to such cyclopentanoids was overshadowed by the preoccupation with their six membered counterparts. While excellent methods are available for six membered carbocyclics, synthetic solutions to

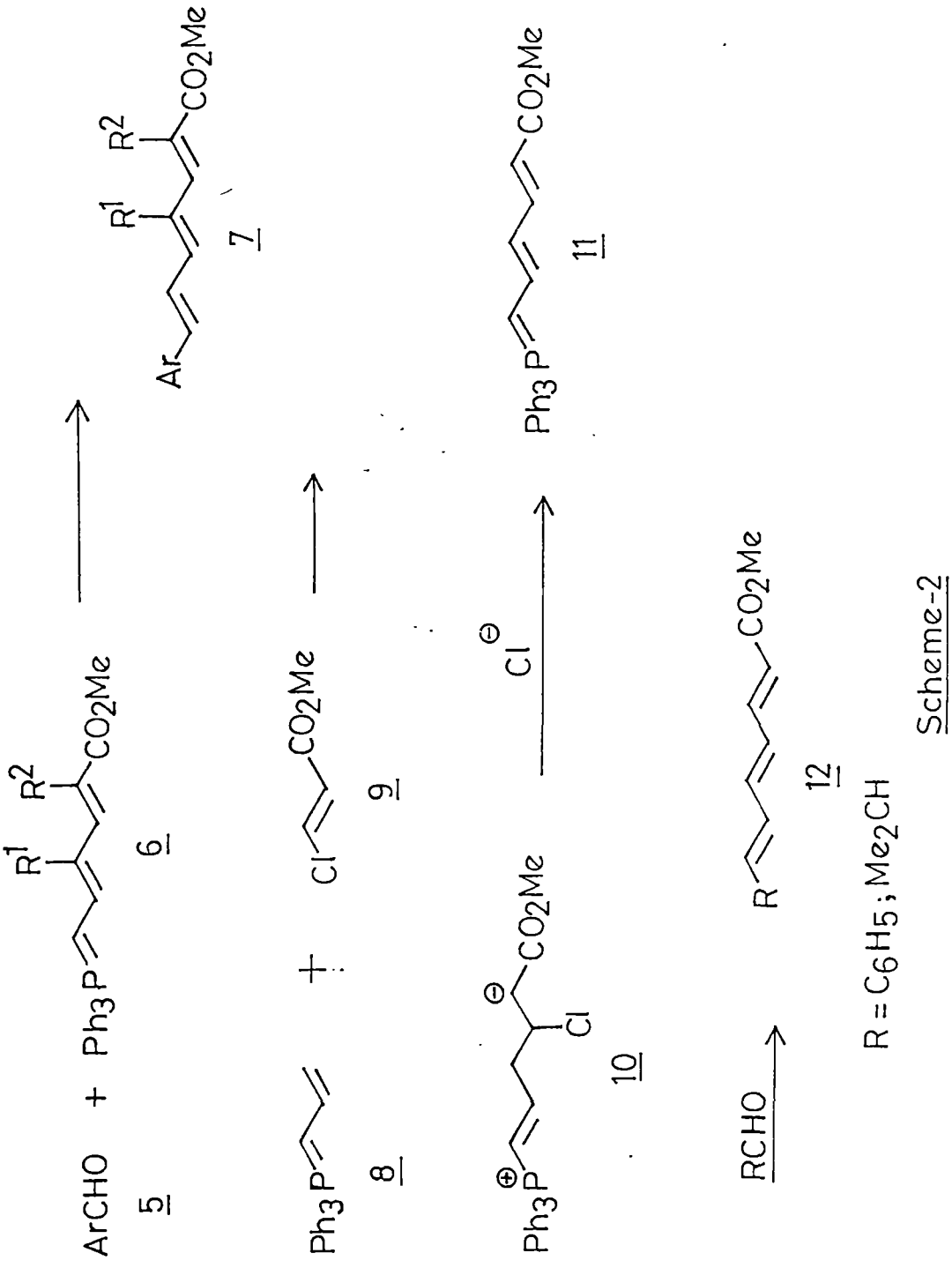


1 2 3 4

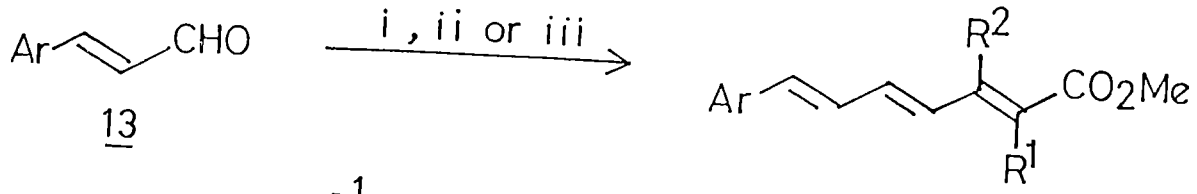
Scheme-1

corresponding cyclopentanoids were not many till recently. Besides it is now well documented that the efficient methods for the construction of six membered carbocyclics cannot be extended with the same efficiency to construct the corresponding cyclopentanoids. The classical methods such as Dieckmann cyclization or Friedel Craft's acylation have been used not always resulting in high yields. Novel synthetic methods for the construction of cyclopentanoids are therefore, of considerable importance. In the present chapter an attempt has been made to develop methodologies for the synthesis of cyclopentanoids and-polyene esters starting from appropriate α -oxoketene dithioacetals.

Our literature survey at this stage revealed that the methods described for the synthesis of heptatrienoates are not always satisfactory due to one reason or the other. The Wittig reaction has been widely used for polyene synthesis. Castells and co-workers have utilized the Wittig reagent 6[4] and Vedejs and co-workers have employed the reagent 11[5] (Scheme 2) for the preparation of similar heptatrienoates. However the difficulty in the preparation of the corresponding phosphonium salts, which involves several steps, makes the method unattractive. The reaction of cinnamaldehydes with the Wittig reagents[6,7] or Reformatsky reagents[8,9] derived from γ-bromocrotonates also affords the triene esters (Scheme 3). Condensation of cinnamaldehydes with β-substituted crotonates in presence of sodamide or potassium amide is reported to give the corresponding 3-substituted heptatrienoates[10,11,12] (Scheme 3). Another preparation of such compounds employs a Knoevenegel[13,14] or Wittig reaction on the



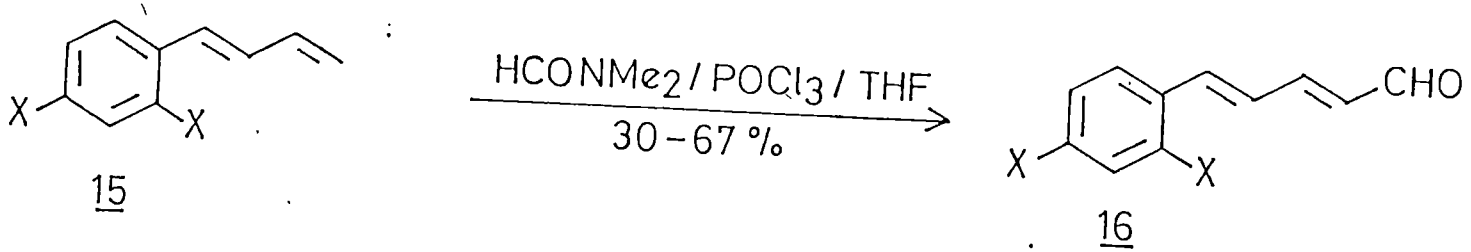
Scheme-2



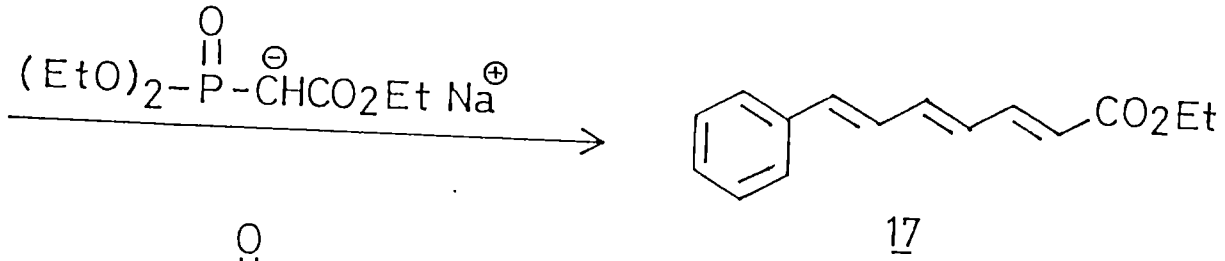
13 14

(i) $BrZn\,CH_2CH=\overset{R^1}{\underset{|}{C}}-CO_2Me$ (R^2=H); (ii) $Ph_3P=CH-CH=\overset{R^1}{\underset{|}{C}}-CO_2Me$ (R^2 = H)

(iii) $Me-\overset{R^2}{\underset{|}{C}}=CHCO_2Me$ (R^1=H) / $NaNH_2$



15 16



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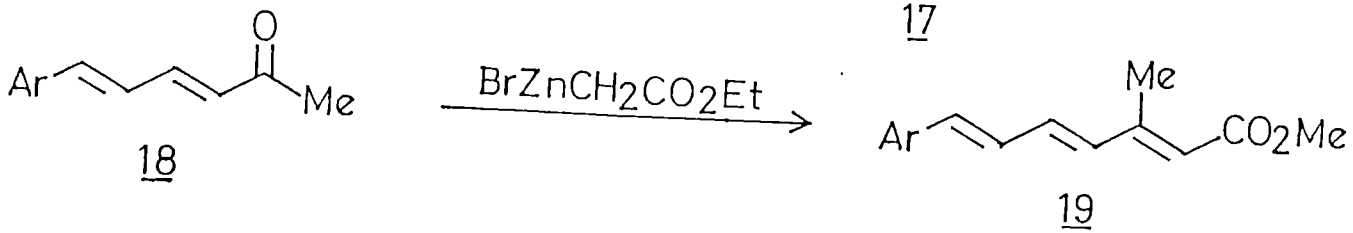
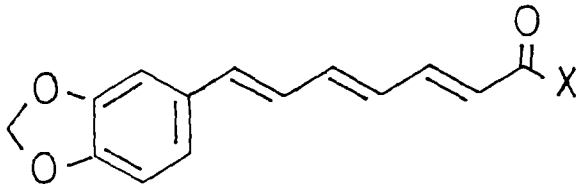


18 19

Scheme-3

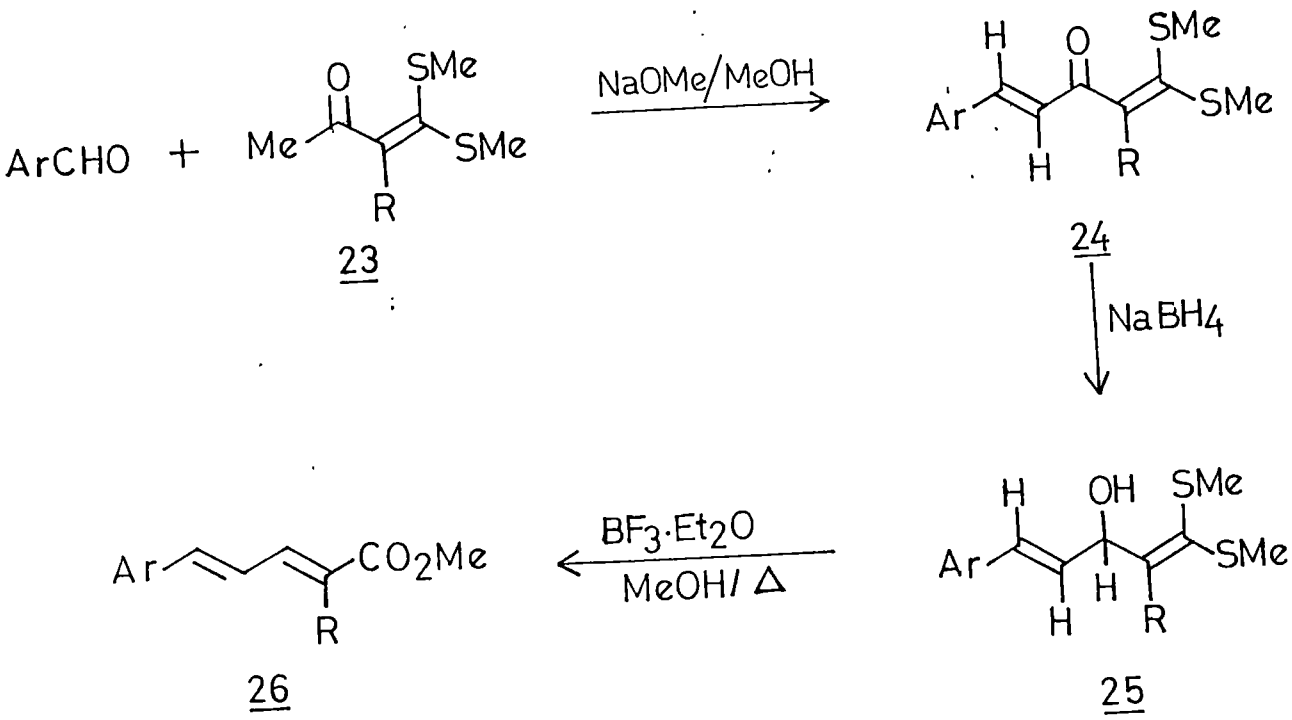
dienaldehydes 16, which may be obtained by a Vilsmeier formylation of the corresponding aryldienes 15. Dombrovski and co-workers[15] have reacted these dienaldehydes with the Wittig reagents derived from bromoacetate to give the trienesters 17. In yet another reaction, the aryldienone 18 has been used in a Reformatsky reaction to afford 3-methyltriene esters 19[16,17] (Scheme 3). Spring and Stark have isolated Piperettine (20) from the extracts of Piper nigrum and confirmed the structure by synthesis[18]. They have prepared methyl Piperettate (21) by reacting methyl γ-bromocrotonate in the presence of zinc with the corresponding cinnamaldehyde, hydrolysis of which yielded the piperittic acid (22). Condensation of the acid chloride from 22 with Piperidine gave the Piperttine 20. From this laboratory, a facile synthesis of methyl 5-aryl pentadienoates 26 has been reported by 1,2-reduction of the α-cinnamoyl ketene dithioacetals 24 to the corresponding carbinol acetals 25, followed by boron trifluoride etherate catalyzed methanolysis[19] (Scheme 4).



20 X = -N⟨ ⟩

21 X = -OMe

22 X = -OH



Ar = C_6H_5 ; p Me-C_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 3,4-Methelenedioxy C_6H_3

R = H, Me

Scheme-4

III.2 RESULTS AND DISCUSSION

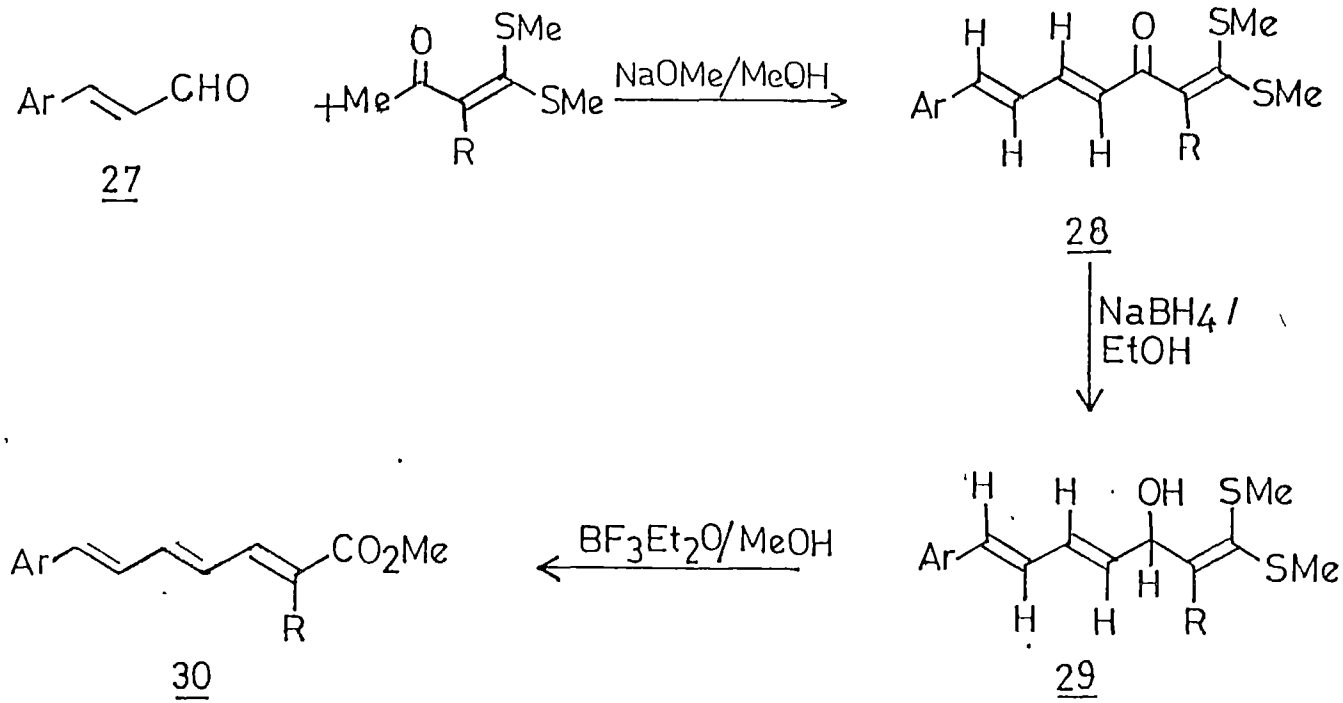
The 1,3-carbonyl transposition methodology, which has been used for the synthesis of α,β-unsaturated esters and pentadiene esters involving α'-oxoketene dithioacetals was considered of interest, if it can be extended to the corresponding triene esters, so that a new general methodology is available for their synthesis. The synthetic strategy is extremely simple and is described in Scheme 5. The α-(5-aryl-2,4-pentadionoyl) ketene dithioacetals 28a-h were obtained in high yields, by the known condensation[2] of cinnamaldehydes 27 with acyl ketene dithioacetals 23. The hitherto unreported pentadienoyl ketene dithioacetals 28a-h were fully characterized by their spectral and analytical data, and are described in the experimental section.

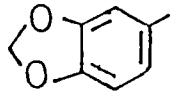
The 5-phenyl-2,4-pentadienoyl ketene dithioacetal 28a underwent exclusive 1,2-reduction with sodium borohydride to afford the corresponding hydroxy ketene dithioacetals 29a in nearly quantitative yield, which without further purification was subjected to boron trifluoride etherate assisted methanolysis to afford the methyl 7-phenyl-2,4,6-heptatrienoate 30a in 61% yield. The physical and analytical data of 30a were found in confirmity with those reported by earlier authors. The spectral data of the compound has been described in the experimental section. The compound was tentatively assigned trans-geometry, since stringent geometrical considerations were difficult as the olefinic protons appeared merged with the multiplet of the phenyl group in the ^{1}H n.m.r. spectrum. Similarly the trieneesters 30b-h were prepared from the dithioacetals 28b-h

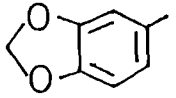
in 58-74% overall yields. Of the eight triene esters synthesized, four (30a,c,d and e) were reported earlier and their physical and spectral data were identical with those reported values. The hitherto unknown heptatrienoates 30b, 30f-h were fully characterized and the spectral and analytical data of all compounds are described in the experimental section.

Previous methods for the preparation of triene esters 30 employ one of the variants of aldol condensation using cinnamaldehyde and either crotonate ester (or its methyl analogs), bromocrotonates (Reformatsky) or the corresponding phosphonium salts (Wittig reaction). These methods and the other reported methods requires either reagents which are difficult to prepare or substrates which are not easily available, compared to the present method, which is simple and employs easily available starting materials with overall good yields. The acyl ketene dithioacetals 23 can be considered as synthetic equivalents of crotonic esters or their methyl derivatives which are transformed into 2-alkenoic ester moiety via reduction and transposition of the carbonyl group. The overall conversion (28-30) can be considered, as a 1,3-carbonyl transposition.

In the preceding paragraph, it has been demonstrated that the carbinol acetals 29 (Scheme 5) undergo facile methanolysis yielding the linear triene systems. Similarly the carbinol acetals 25 (Scheme 4) have also been shown to undergo methanolysis to afford diene esters. These carbinol acetals 25 and 29 are interesting 5-carbon units or 7-carbon units with a secondary hydroxyl group flanked by double bonds on either side. Such systems with substituents at 2,3 and

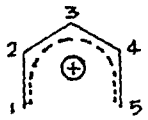


24,25	Ar	R
a	C_6H_5	H
b	4-MeC_6H_4	H
c	4-$MeOC_6H_4$	H
d		H

24,25	Ar	R
e	C_6H_5	CH_3
f	4-MeC_6H_4	CH_3
g	4-$MeOC_6H_4$	CH_3
h		CH_3

Scheme-5

4-position have been investigated by Sorenson and co-workers[22]. They have shown that such pentadienyl cations (31) undergo conrotatory



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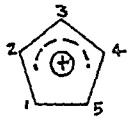
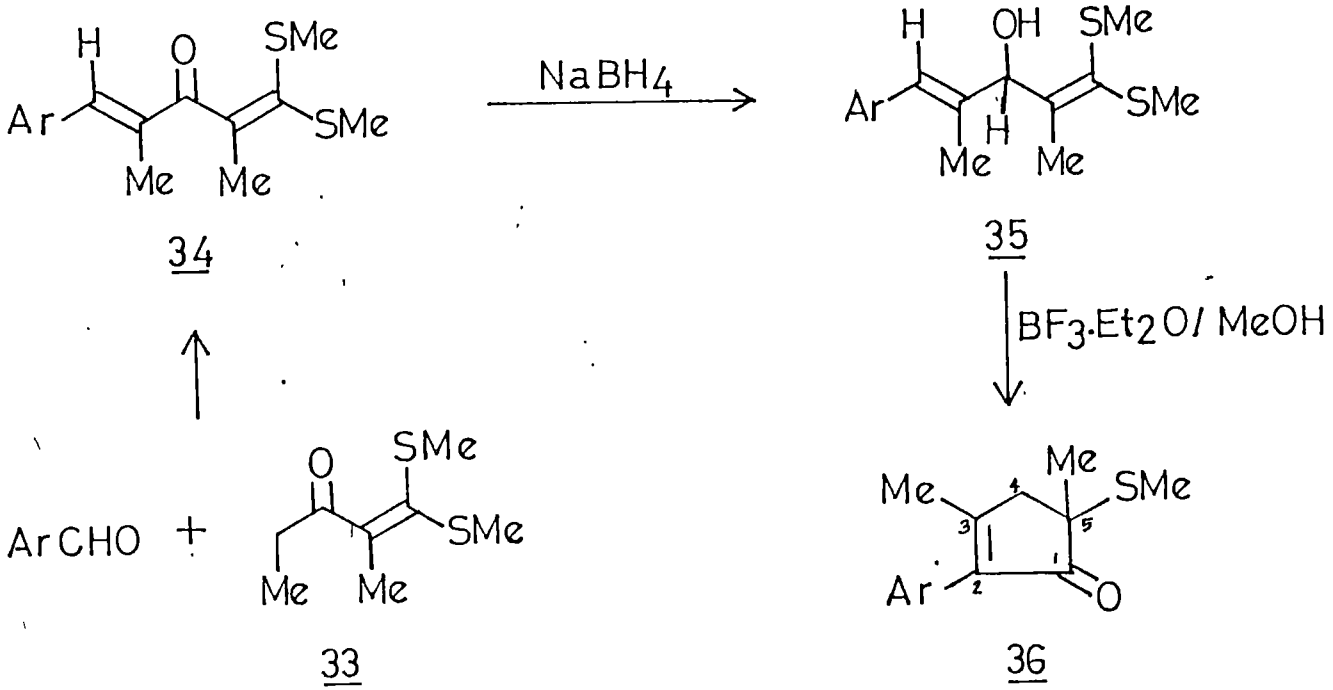


32

electrocyclic ring closure to give cyclopentenyl cations (32) and they have inferred that a molecule should have at least C-3-methyl group so that pentadienyl cation has a stabilizing effect on the non-polar 2Z, 3Z-confirmation, which favours the cyclization[21,22]. In this transformation the charge density is transferred from carbon atoms 1,3 and 5 to C-2 and C-4 manifesting that the methyl substitution at C-2 and C-4 should complement the stability of 2Z, 3Z conformation, thereby facilitating the electrocyclic ring closure. In view of this, the pentadienyl systems 35a-d described in Scheme 6 have the necessary substituents which could stabilize one of the favourable conformations, that might lead to the electrocyclic ring closure. The molecular systems with such structural features have been investigated by generating cations and subsequently to the irreversible cyclopentene cation and the products arising from it[21,22]. The required starting materials 34a-d (Scheme 6) were prepared by condensing appropriate aromatic aldehydes with the α-methyl- α-propionyl ketene dithioacetals 33 derived from diethyl ketone[2]. When 34a was subjected to borohydride reduction, the corresponding carbinol acetal 35a was obtained in nearly quantitative



34 35 36 33

34-36 a Ar = 4-MeC_6H_4

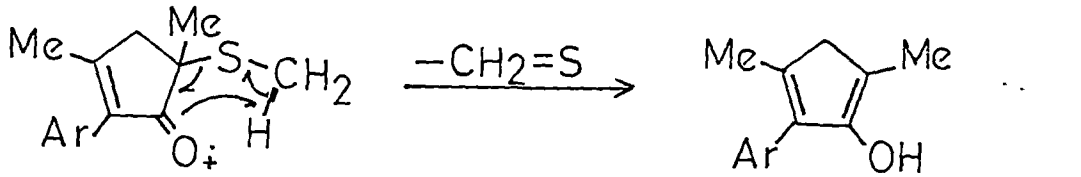
b Ar = C_6H_5

c Ar = 4-ClC_6H_4

d Ar = 4-$CH_3OC_6H_4$

Scheme-6

yield, which was directly subjected to boron trifluoride etherate assisted methanolysis. After work-up, the product was characterized as 2-aryl-3,5-dimethyl-5-methylthiocyclopentene-2-one (36a), formed in 70% yield. The structure of 36a was confirmed by both analytical and spectral data. Its elemental analysis was in agreement with the molecular formula $C_{15}H_{18}OS$ and its mass spectrum exhibited molecular ion peak at m/z 246(30%) and base peak at 200 ($M^+-CH_2=S$,100%). The base peak in mass spectrum at M^+-46 is probably due to the fragmentation of molecular ion 37 to 38. Its i.r.(KBr) spectrum exhibited a strong band at 1710, which is characteristic of the cyclopentenone carbonyl group, while in its n.m.r.(CCl_4) spectrum, the three singlets at δ 1.58(3H), 2.12(6H) and 2.30(3H) were assigned



37, m/z 246(M^+, 30%) 38, m/z 200 (M^+-CH_2S, 100%)

to the C-5 methyl group, the C-3-methyl group and the methylthio group, and the p-methyl groups respectively. The methylene protons appeared as a broad singlet at δ2.68, while the aromatic protons were present as a singlet at δ 7.15. The U.V. spectrum of 36a showed bands at λ_{max}(MeOH) 229 and 256 (ϵ,4000 and 9500). Its ^{13}C n.m.r. ($CDCl_3$) spectrum exhibited signals at δ 11.6, 17.8, 21.2, 22.0 which were assigned to four methyl groups. The absorption due to C-5 and

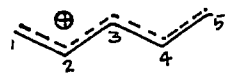
C-4 carbons appeared at δ 48.1(s) and 48.5(t) respectively. The signals at δ 129.0 and 129.1 were assigned to aromatic CH carbons whereas one of the quaternary carbon of aromatic ring appeared at δ 137.1 while the other was merged with aromatic signal. The other two ring quaternary carbons i.e. C-2 and C-3 appeared at δ 137.5 and δ 165.7 respectively. The signal at δ 204 was assigned to carbonyl carbon.

The generality of the reaction was confirmed by studying other systems 34b-d which under described reaction conditions yielded the corresponding 3-cyclopentenones 36b-d in 59-68% overall yields. The structures of all these compounds were confirmed with the help of analytical and spectral data and are described in the experimental section.

It was of particular interest to examine the behaviour of heptatrienyl cations derived from the α-pentadienoyl ketene dithioacetals 39, since Sorenson and co-workers have studied these cations and observed that they fail to undergo 1,7-cyclization and prefer 1,5 ring closure, because such ring closure is sterically more favoured[23]. The required 7-aryl-1,1-bis(methylthio)-2,4-dimethyl 3-oxo-1,4,6-heptatrienes were prepared by the condensation of α-methyl-α-propionyl ketene dithioacetals 33 with the corresponding cinnamaldehydes as reported earlier for the synthesis of similar compounds[2]. The spectral and analytical data of compounds 38a and 38b were in confirmity with the assigned structures and are described in the experimental section. In a typical experiment,

the α-oxoketene dithioacetal 39a after reduction with sodium borohydride afforded the corresponding carbinol acetal 40a, which was a suitable candidate for the study of cationic ring closure. When 40a was refluxed with boron trifluoride etherate in methanol, after work-up, the product was characterized as 2-styryl-3,5-dimethyl-5-methylthiocyclopenten-2-one 41a in 70% yield (Scheme 7). Similarly 39b afforded the corresponding 41b under the described conditions in 74% yield. The structures of 41a and 41b were confirmed with the help of analytical and spectral data which are described in the experimental section.

In the light of excellent work on the cyclopentenyl cation ring closure by Sorenson and co-workers the task of mechanism has become easy[24,25,26]. The most stable configuration of a pentadienyl cation is the 2E, 3E conformation 42 (or W configuration). The cyclization



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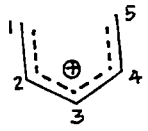
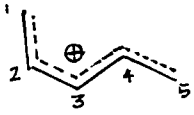


43



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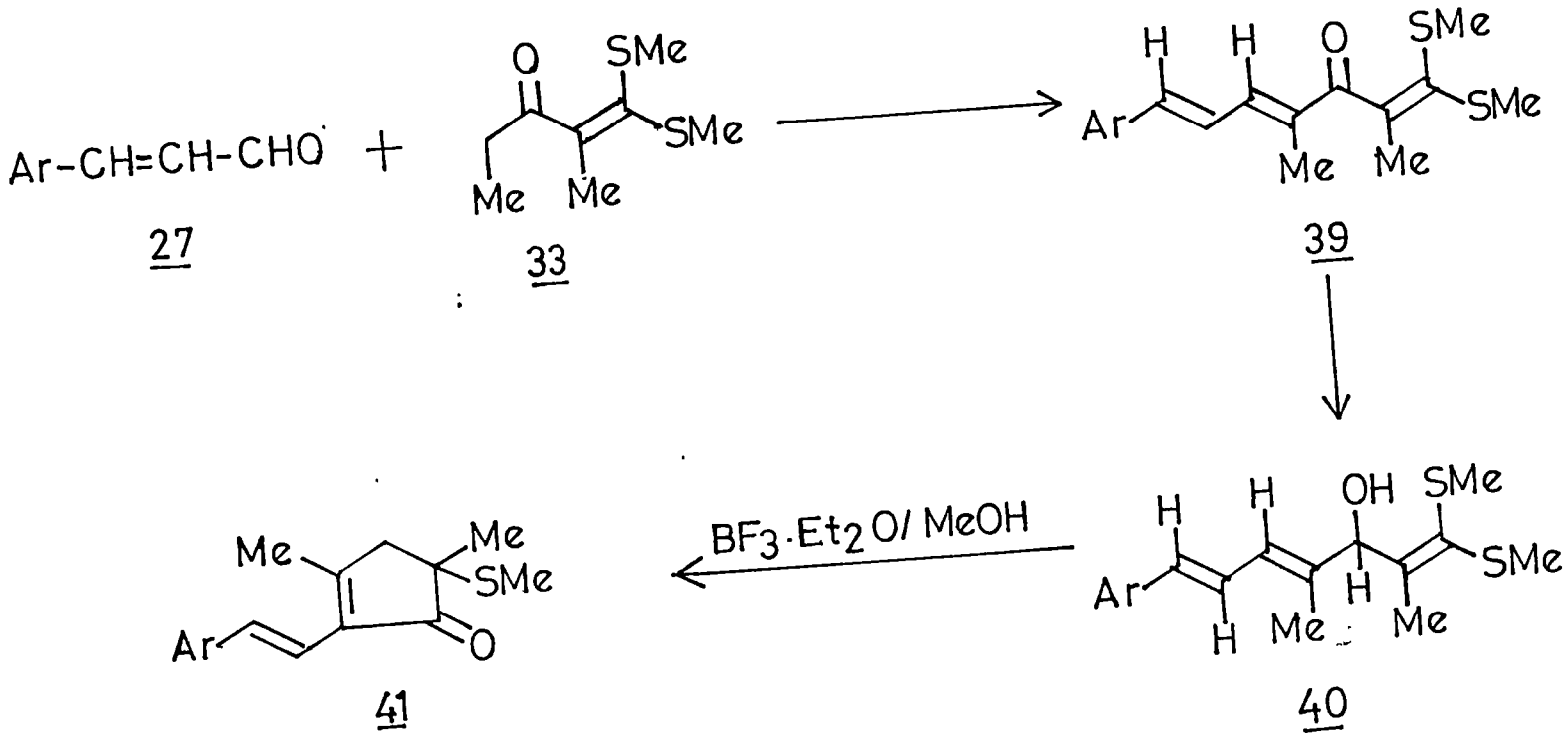
of 42 required a 2Z, 3Z,43 (U) conformation which is probably not planar due to steric repulsion between substituents of C-1 and C-5 carbon atoms. The third conformation possible is 2E, 3Z

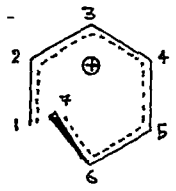


27, 39, 40, 41, a, Ar = C_6H_5

b, Ar = 4-MeC_6H_4

Scheme-7

(or sickle confirmation 44). The three conformations are interconvertable by rapid rotations about the C(2)-C(3) or C(3)-C(4) partial double bonds. Thus in the present investigation the pentadienyl cation 45 (2E, 3E) is comparitively less stable due to the non-bonded steric repulsion between the 2,4-methyl groups, and it equilibriates with less stable conformers 46 (2E, 3Z) and 47 (2Z, 3Z) (Scheme 8). The cation in the 2Z, 3Z conformation undergoes ring closure in a conrotatory fashion to the corresponding cyclopentenyl cation 48, which is further stabilized by the lone pair of the methylthio group through the episulphonium ion. Participation of methanol gives the cyclopentene 49, which on loss of a molecule of methanethiol gives 50. Hydrolysis of 50 affords the cyclopentenones 36. Similarly the cycloheptatrienyl cation 51 can have completely folded confirmation 54 or the 2Z, 3Z conformation 55, so that it may undergo an electrocyclic ring closure



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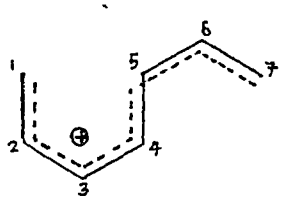
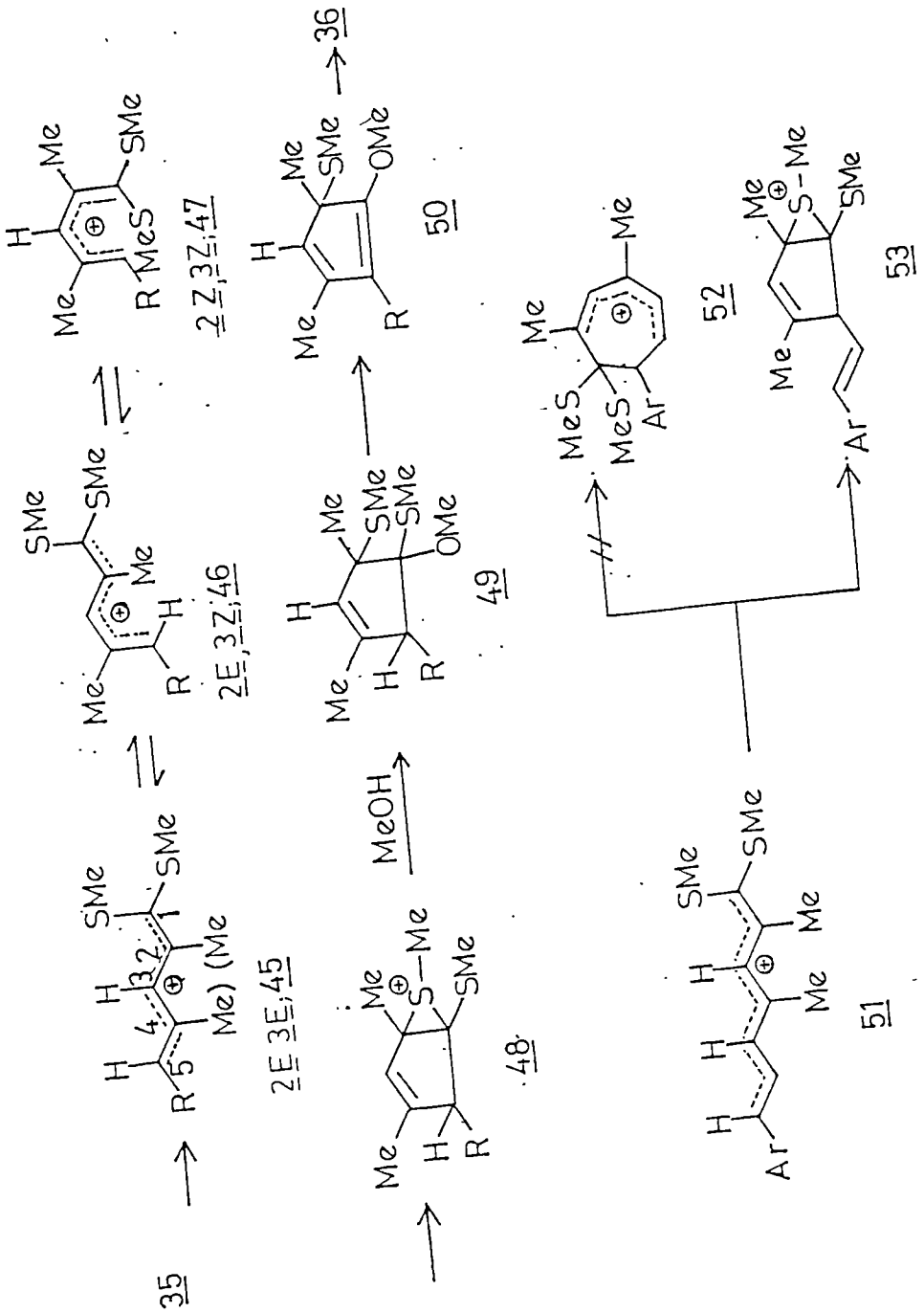


55

to afford a cycloheptadienyl cation or a cyclopentenyl cation respectively. However the 1,5-ring closure appears to be sterically the most favourable as the heptatrienyl cation 51 cyclizes to the styryl cyclopentenyl cation 53 rather than cycloheptadienyl cation 52.

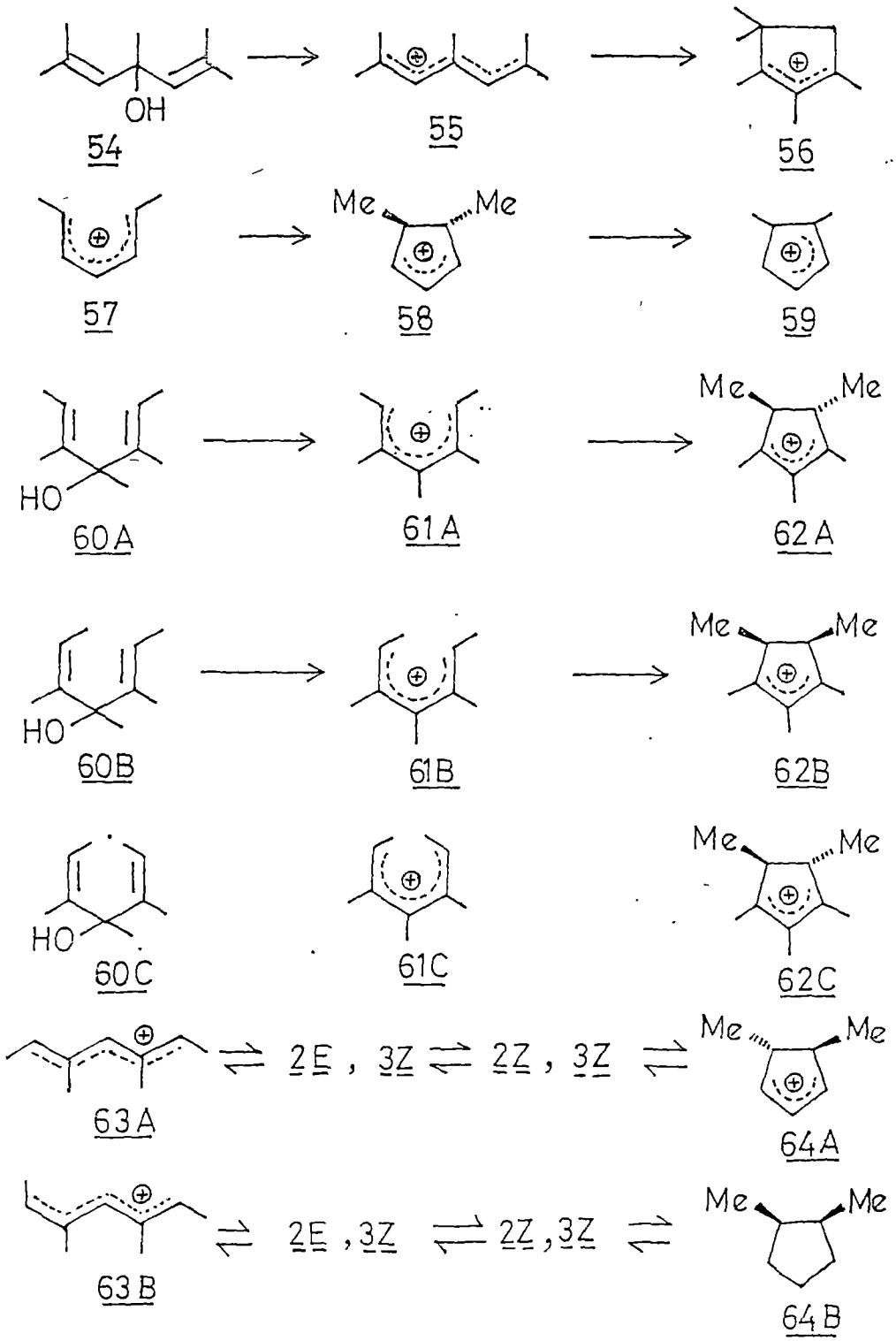


Scheme 8

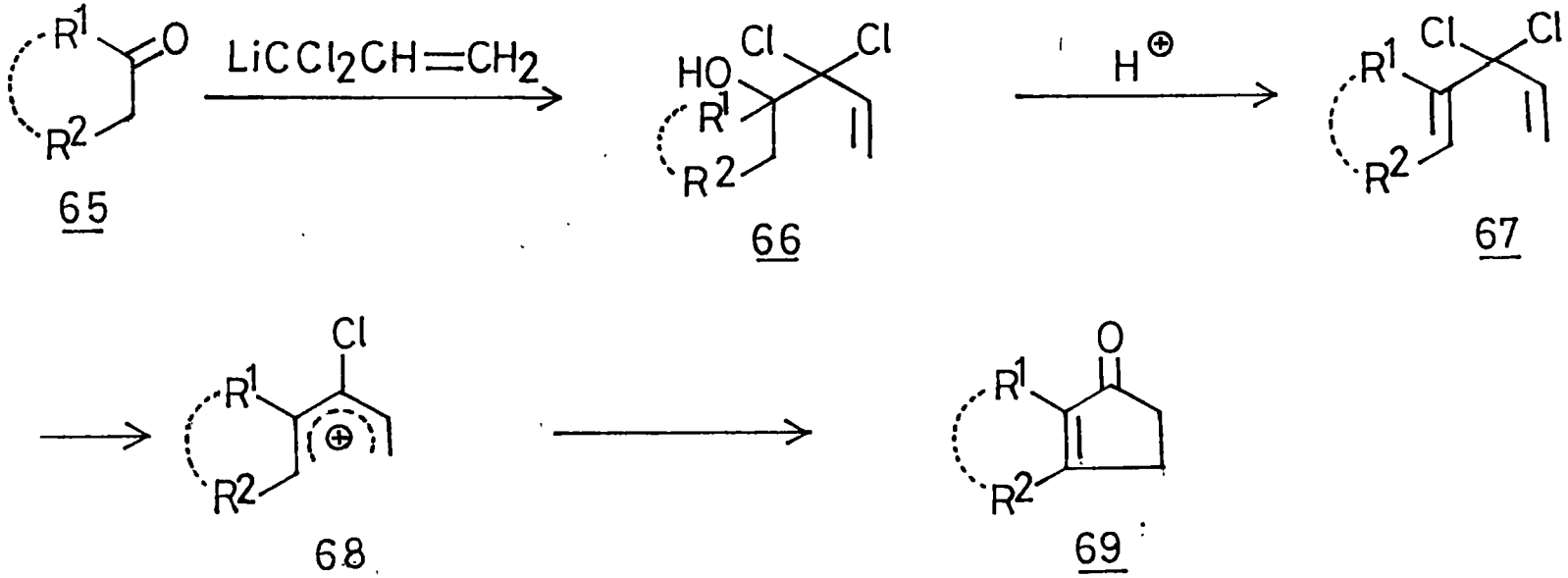
A similar participation of methanol and subsequent elimination of methanethiol followed by solvolysis affords the styrylcyclopentenones 41. These results fully confirm the observations made by Sorensøn and co-workers.

Construction of cyclopentanoids similar to the present work have been reported in the literature, though the examples are not many. Linear pentadienyl cations were first prepared by Deno and Pitman in 1964[27]. They observed that the carbocation 55, derived from the dienyl alcohol 54, undergoes ring closure in 96% H_2SO_4 to afford the cyclopentenyl cation 56, while the corresponding pentadienyl cation with no substitution at 3-position are stable and can be observed by standard spectroscopic techniques. Around the same time, Sorensøn has observed the cyclization of the cation 57 to 59[28]. Cambell and co-workers have studied stereochemistry of cyclization of pentadienyl cations 60A, B & C which showed formation of the predicted cyclopentenyl cations 62A, B & C (Scheme 9 Chiu and Sorensøn studied an analgous tetramethyl series where the pentadienyl cations 63A,B could be observed which were cyclized to to the cyclopentenyl cations 63A, 63B[21]. Sorensøn and Bladek have established through detailed kinetic studies that removal of the central methyl group in 60 slows down the rate of cyclization as it was predicted[22].

Another interesting study related to the present work was reported by Hiyama and co-workers[30] (Scheme 10). They have used the chloro-pentadienyl cation 68, derived from the dichlorohomoallyl alcohol 66,


OH
54
55
56
Me
Me
57
58
59
HO
60A
61A
62A
60B
61B
62B
60C
61C
62C
2E , 3Z ⇌ 2Z , 3Z
63A
64A
2E , 3Z ⇌ 2Z , 3Z
63B
64B

Scheme-9

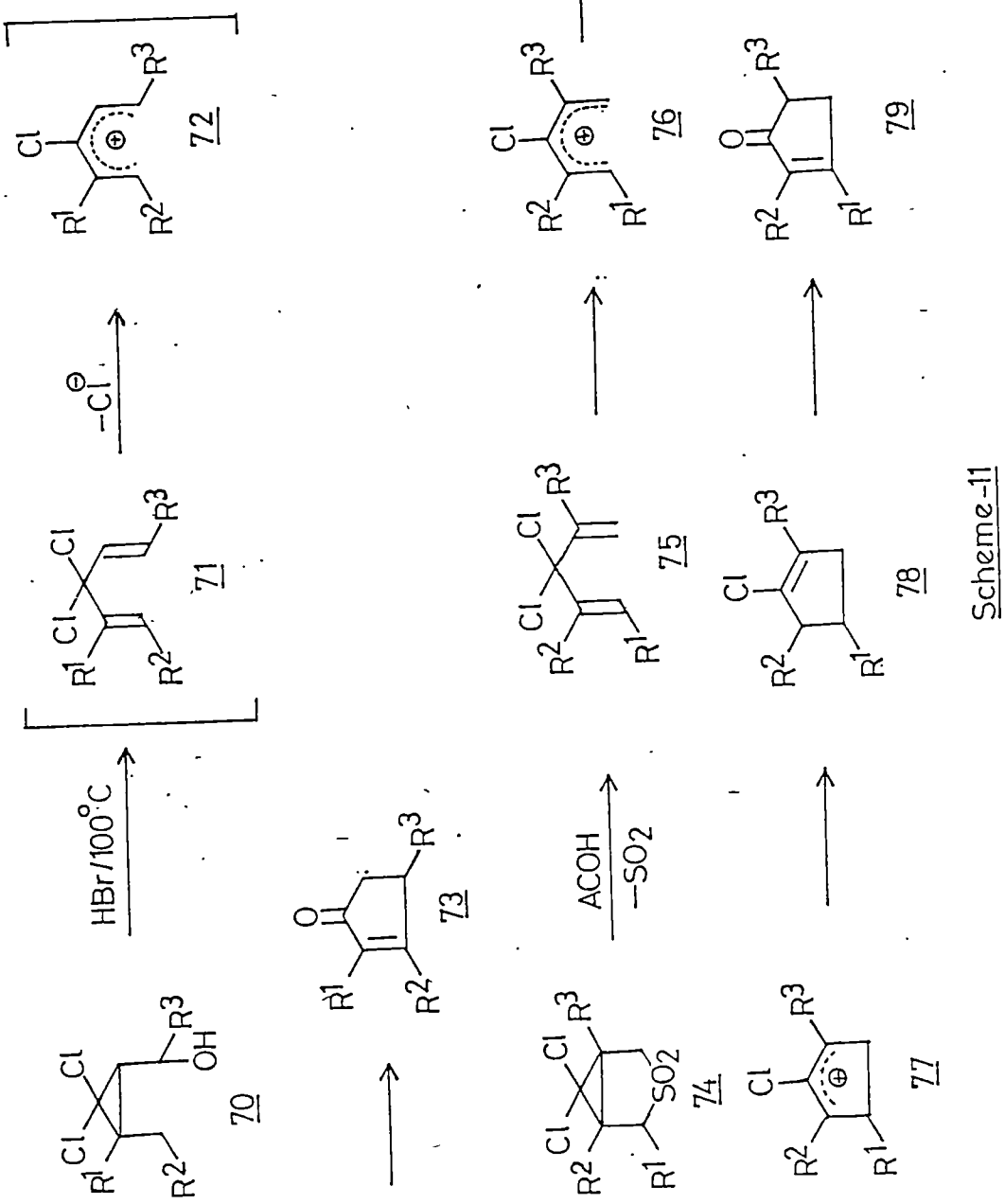


65 66 67 68 69

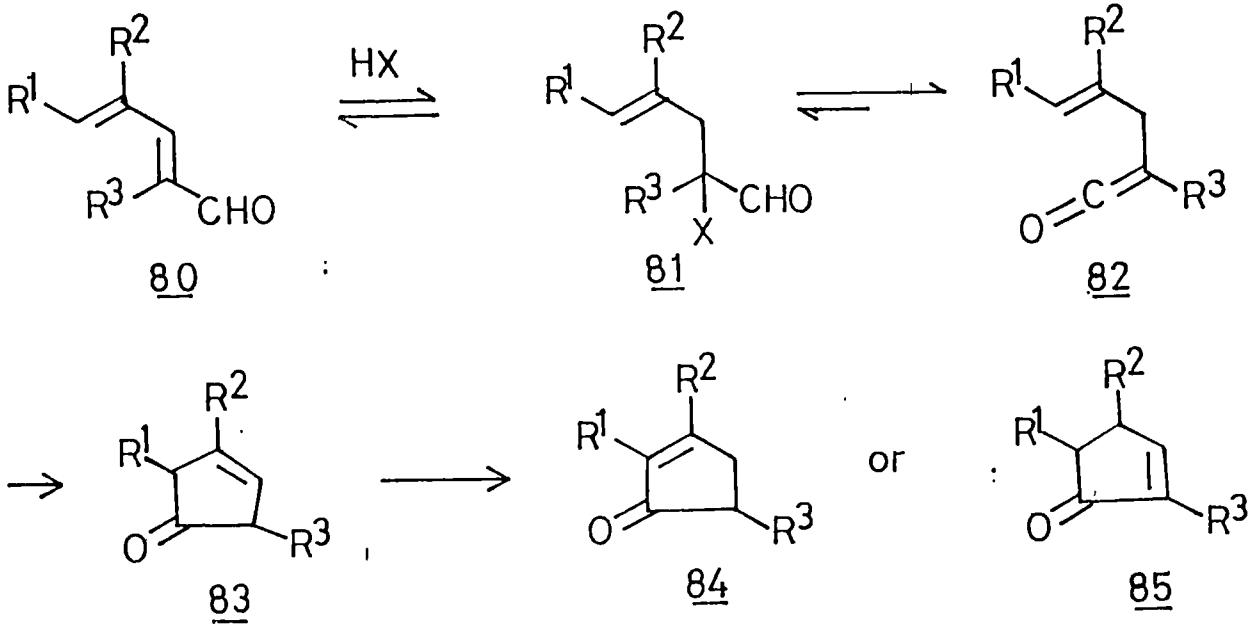
$R^1 = R^2 = -(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$, $-(CH_2)_{10}-$

$R^1 = Me$, $R^2 = n-C_5H_{11}$

Scheme-10



Scheme-11


R2
R1
R3
CHO
HX
X
O
C
80
81
82
83
84
85
or
R1 = 4-NO2C6H4
a, R2 = R3 = Me
b, R2 = Me, R3 = i-Pr
c, R2 = i Pr, R3 = Me
d, R2 = R3 = i-Pr

Scheme-12

which underwent acid catalyzed cyclization followed by hydrolysis to afford the cyclopentenones 69. The procedure is applicable to both cyclic and acyclic ketones 65. Hiyama and co-workers[31] have also employed the appropriately substituted dichlorocyclopropane 70 to generate the cyclopentenyl cations 72, which underwent ring closure and hydrolysis to give 2,3,4-trisubstituted cyclopentene-2-ones 73 (Scheme 11). Similarly Gaoni[32] has utilized almost identical cyclopentenyl cations 76 from yet another novel system 74 (Scheme 11) and obtained 2,3,5-trisubstitued cyclopentene-2-ones 79. As a model for determining dynamic equilibrium between possible geometrical isomers, Ogama and co-workers[33] have reported a novel rearrangement of 5-(p-nitrophenyl) 2,4-dialkylpentadienol 8 to cyclopentenones 84 and 85 (Scheme 12) in presence of hydrogen halides. They have further shown that the presence of bulkier allyl groups at 2 and 4-position in 80 forces them to twisted non-planar conforation and thus facilitating the formation of strain free HX adducts 81, which on subsequent elimination of HX followed by kinetically favoured electrocyclization of ketene intermediate 82 affords cyclopentenone 83 (Scheme 12).

III.2.3 EXPERIMENTAL

General experimental conditions were same as those described in the chapter II. ^{13}C n.m.r. spectra were measured at 67.89 MHz on a Brucker WH-270 spectrometer.

Starting Materials

The commercial samples of acetone, ethylmethyl ketone, diethyl ketone, benzaldehyde, 4-tolualdehyde, 4-chlorobenzaldehyde, anisaldehyde

and cinnamaldehyde were purified before use, while 4-methylcinnamaldehyde, 4-methoxycinnamaldehyde and 3,4-methylenedioxycinnamaldehyde were prepared according to the reported procedure[34]. The α-oxoketene dithioacetals 23a, 23b and 33 were prepared according to the procedure described in chapter II. The references for their physical data are also given in chapter II. The cinnamoyl ketene dithioacetals 24a-d, 5-aryl-2,4-pentadienoyl ketene dithioacetals 28a-h, 39a and 39b were prepared according to the reported procedure[2], as described in the second chapter. The spectral and analytical data of 34a-d are reported in the chapter II.

1,1-Bis(methylthio)-3-oxo-7-phenyl-1,4,6-heptatriene (28a) was isolated as yellow crystalline solid (MeOH); yield 76%; m.p.94°C; i.r. (KBr): ν_{max} = 1638, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.33(s,3H, SCH_3); 2.38(s,3H,SCH_3); 6.01(s,1H,H-2); 6.15(d,1H,J=15Hz,H-4); 6.61-7.48(m,$8H_{arom+olefin}$). (Found: C,65.93; H,5.45. Calc. for $C_{15}H_{14}OS_2$ (274.3): C,65.67; H,5.11). m/z 274(M^+).

1,1-Bis(methylthio)-3-oxo-7-(4-methylphenyl)-1,4,6-heptatriene (28b) was isolated as yellow solid; yield 81%; m.p.124-125°C; i.r.(KBr): ν_{max}= 1635, 1580 cm^{-1}; ^1H n.m.r.(CCl_4):δ2.11(s,3H,CH_3); 2.28(s,3H, SCH_3); 2.35(s,3H,SCH_3); 6.10(s,1H,H-2); 6.31(d,1H,J=15Hz,H-4); 6.84-7.4(m,$7H_{arom+olefin}$). (Found: C,66.42; H,5.32. Calc. for $C_{16}H_{16}OS_2$(288.3): C,66.65; H,5.55%). m/z 288(M^+).

1,1-Bis(methylthio)-3-oxo-7-(4-methoxyphenyl)-1,4,6-heptatriene (28c) was isolated as yellow crystalline solid (MeOH); yield 82%; m.p. 127-130°C; i.r.(KBr): ν_{max}= 1648, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.52 (s,6H,SCH_3); 3.78(s,3H,Ar-O-CH_3); 6.23-7.56(m,$9H_{arom+olefin}$). (Found:

C,63.45; H,5.45. Calc. for $C_{16}H_{16}O_2S_2$(304.3): C,63.15; H,5.30%). m/z 304(M^+).

1,1-Bis(methylthio)-3-oxo-7-(3,4-methylenedioxyphenyl)-1,4,6-heptatriene (28d) was isolated as yellow crystalline solid (MeOH); yield 80%; m.p. 134°C; i.r.(KBr): ν_{max} = 1650, 1592 cm^{-1}; ^1H n.m.r. (CCl_4): δ 2.21(s,3H,SCH_3); 2.32(s,3H,SCH_3); 5.88(s,2H,-O-CH_2-O-); 6.10(s,1H,H-2); 6.24(d,1H,J=15Hz,H-4); 6.58-7.26(m,$6H_{arom+olefin}$). (Found: C,60.46; H,4.61. Calc. for $C_{16}H_{14}O_3S_2$(318.3): C,60.37; H,4.43%). m/z 318(M^+).

1,1-Bis(methylthio)-2-methyl-3-oxo-7-phenyl-1,4,6-heptatriene (28e) was isolated as yellow crystalline solid (MeOH); yield 73%; m.p. 106-107°C; i.r.(KBr): ν_{max} = 1648, 1695 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.09(s,3H,CH_3); 2.21(s,3H,SCH_3); 2.32(s,3H,SCH_3); 6.31(d,1H, J=15Hz,H-4); 6.78-7.49(m,$8H_{arom+olefin}$). (Found: C,66.91; H,5.41. Calc. for $C_{16}H_{16}OS_2$(288.3): C,66.65; H,5.59%). m/z 288(M^+).

1,1-Bis(methylthio)-2-methyl-3-oxo-7-(4-methylphenyl)-1,4,6-heptatriene (28f) was isolated as yellow crystalline solid; yield 77%; m.p. 138-141°C; i.r.(KBr): ν_{max}= 1648, 1618 cm^{-1}; ^1H n.m.r. ($CDCl_3$): δ 2.09(s,3H,CH_3); 2.11(s,3H,Ar-CH_3); 2.22(s,3H,SCH_3); 2.31(s,3H,SCH_3); 6.26(d,1H,J=15Hz,H-4); 6.69-7.41(m,$7H_{arom+olefin}$). (Found: C,67.31; H,5.95. Calc. for $C_{17}H_{18}OS_2$ (302.3): C,67.54; H,6.01%). m/z 302(M^+).

1,1-Bis(methylthio)-2-methyl-3-oxo-7-(4-methoxyphenyl)-1,4,6-heptatriene (28g) was isolated as yellow crystalline solid (MeOH); yield 79%; m.p.92-93°C; i.r.(KBr): ν_{max}= 1648, 1590 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.12(s,3H,CH_3); 2.21(s,3H,SCH_3); 2.35(s,3H,SCH_3);

3.81(s,3H,OC$\underline{H}_3$); 6.31(d,1H,J=15Hz,$\underline{H}$-4); 6.61-7.59(m,7$H_{arom+olefin}$). (Found: C,64.31; H,5.79. Calc. for $C_{17}H_{18}O_2S_2$(318.3): C,64.14; H,5.69%). m/z 318(M^+).

1,1-Bis(methylthio)-2-methyl-3-oxo-7-(3,4-methylenedioxyphenyl)-1,4,6-heptatriene (28h) was isolated as yellow crystalline solid; yield 77%; m.p. 103-105°C; i.r.(KBr): ν_{max}= 1642, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): 2.13(s,3H,C$\underline{H}_3$); 2.21(s,3H,SC$\underline{H}_3$); 2.32(s,3H,SC$\underline{H}_3$); 5.89(s,2H,-O-C$\underline{H}_2$-O-); 6.25(d,2H,J=15Hz); 6.59-7.26(m,5$H_{arom+olefin}$). (Found: C,61.73; H,54.91. Calc. for $C_{17}H_{16}O_3S_2$: C,62.44; H,4.85%). m/z 332(M^+).

1,1-Bis(methylthio)-3-oxo-2,4-dimethyl-7-phenyl-1,4,6-heptatriene (39a) was isolated as pale yellow liquid; yield 78%; i.r.(neat): ν_{max}= 1635, 1610 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.99(d,3H,J=1.5Hz,C$\underline{H}_3$); 2.06(s,3H,C$\underline{H}_3$); 2.10(s,3H,SC$\underline{H}_3$); 2.30(s,3H,SC$\underline{H}_3$); 6.55-7.53(m,8$H_{arom+olefin}$). (Found: C,67.26; H,6.91. Calc. for $C_{17}H_{20}OS_2$(304.4): C,67.06; H,6.62%).

1,1-Bis(methylthio)-3-oxo-2,4-dimethyl-7-(4-methylphenyl)-1,4,6-heptatriene (39b)was isolated as pale yellow liquid; yield 78%; i.r. (neat): ν_{max}= 1641, 1615 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.00(d,3H,J=1.5Hz, C$\underline{H}_3$); 2.12(s,6H,C$\underline{H}_3$ and Ar-C$\underline{H}_3$); 2.32(s,6H,SC$\underline{H}_3$); 6.60-7.61(m,7$H_{arom+olefin}$) (Found: C,67.97; H,6.87. Calc. for $C_{18}H_{22}OS_2$(318.5): C,67.88; H,6.96%).

Methyl 7- Aryl-2,4,6-heptatrienoates (30a-h); General Procedure: To a well stirred suspension of the ketene S,S-acetal 28 (0.02 mol) in absolute ethanol (100 ml), excess of sodium borohydride (2.5g, 0.07 mol) is added and the mixture was refluxed for 2 hrs. The cooled mixture was then poured on to crushed ice (150g) and extracted with chloroform (2x150 ml). The chloroform extract was washed with saturated salt solution (2x100 ml), dried (Na_2SO_4) and evaporated under vacuum to give the crude carbinols 29 in nearly quantitative yields as an

undistillable thick viscous liquids. The crude carbinols were dissolved in absolute methanol (100 ml) and boron trifluoride etherate (10 ml) was added with stirring. The mixture was then refluxed for 20-24 hrs (30a-d) or 8-10 hrs (30e-h). The cooled mixture was poured into water (250 ml) and extracted with chloroform (2x100 ml). The chloroform extract was washed with saturated sodium hydrogen carbonate solution (2x100 ml) and with water (2x100 ml), dried (Na_2SO_4) and evaporated to give the crude esters 30 which were further purified by passing through a silica gel column, using hexane as eluent.

Methyl 7-phenyl-2,4,6-heptatrienoate (30a) was isolated as pale yellow crystalline solid; yield 61%; m.p. 111-113°C (reported m.p. 112°C)[9]; i.r.(KBr): ν_{max}= 1715, 1610 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 3.68(s,3H,OCH_3); 5.85(d,1H,J=15Hz,H-2); 6.45-6.85(m,$3H_{olefin}$); 7.11-7.62(m,$7H_{arom+olefin}$). (Found: C,78.3; H,6.61. Calc. for $C_{14}H_{14}O_2$(214.3): C,78.46; H,6.58%).

Methyl 7-(4-methylphenyl)-2,4,6-heptatrienoate (30b) was isolated as pale yellow crystalline solid; yield 62%; m.p. 131-132°C; i.r.(KBr): ν_{max}= 1716, 1600 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.32(s,3H,CH_3); 3.71(s, 3H,OCH_3); 5.85(d,1H,J=15Hz,H-2); 6.15-6.88(m,$3H_{olefin}$); 6.95-7.52(m, $6H_{arom+olefin}$). (Found: C,79.61; H,7.26. Calc. for $C_{15}H_{16}O_2$(228.3): C,79.91; H,7.06%). m/z 228(M^+98%).

Methyl 7-(4-methoxyphenyl)-2,4,6-heptatrienoate (30c) was isolated as pale yellow crystalline solid; yield 58%; m.p. 164-165°C (reported m.p. 167-168°C)[14]; i.r.(KBr): ν_{max} = 1716, 1600 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 3.70(s,3H,OCH_3); 3.78(s,3H,Ar-OCH_3); 5.80(d,1H,J=15Hz,H-2); 6.52-6.95(m,$5H_{arom+olefin}$); 7.10-7.55(m,$4H_{arom+olefin}$). (Found: C,73.81; H,6.81. Calc. for $C_{15}H_{16}O_3$(244.3): C,73.74; H,6.60%). m/z244 (M^+,89%).

Methyl 7-(3,4-methylenedioxyphenyl)-2,4,6-heptatrienoate (30d) was isolated as pale yellow crystalline solid; yield 68%; m.p. 172-173°C (reported m.p. 174°C)[18]; i.r.(KBr): ν_{max}= 1718, 1600 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 3.70(s,3H,OCH_3); 5.65-6.10(m,3H,O-CH_2-O + H-2); 6.15-7.00(m, $8H_{arom+olefin}$). (Found: C,69.34; H,5.69. Calc. for $C_{15}H_{14}O_4$(258.3): C,69.68; H,5.42%). m/z 258(M^+,89%).

Methyl 2-methyl-7-phenyl-2,4,6-heptatrienoate (30e) was isolated as pale yellow crystalline solid; yield 71%; m.p. 107-108°C (reported m.p. 108°C)[7]; i.r.(KBr): ν_{max}= 1698, 1600 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.95 (s,3H,-2-CH_3); 3.68(s,3H,OCH_3); 6.25-6.82(m,$4H_{olefin}$); 6.95-7.52(m, $6H_{arom+olefin}$). (Found: C,80.11; H,7.31. Calc. for $C_{15}H_{16}O_2$(228.3): C,78.91; H,7.06%). m/z 228(M^+,89%).

Methyl 2-methyl-7-(4-methylphenyl)-2,4,6-heptatrienoate (30f) was isolated as pale yellow crystalline solid; yield 68%; m.p. 101-102°C; i.r. (KBr): ν_{max} 1697, 1592 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.97(s,3H,2-CH_3); 2.32(s,3H,Ar-CH_3); 3.71(s,3H,OCH_3); 6.35-6.82(m,$4H_{olefin}$); 6.92-7.45 (m,$5H_{arom+olefin}$). (Found: C,79.51; H,7.54. Calc. for $C_{16}H_{18}O_2$(242.3): C,79.31; H,7.49%). m/z 242(M^+,98%).

Methyl 2-methyl-7-(4-methoxyphenyl)-2,4,6-heptatrienoate (30g) was isolated as pale yellow crystalline solid; yield 72%; m.p.95-96°C; i.r.(KBr): ν_{max} = 1698, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.98(s,3H,2-CH_3); 3.71(s,3H,OCH_3); 3.79(s,3H,Ar-OCH_3); 6.35-7.00(m,$6H_{arom+olefin}$); 7.10-7.55(m,$3H_{arom+olefin}$). (Found: C,74.45; H,7.16. Calc. for $C_{16}H_{18}O_3$(258.3): C,74.39p H,7.02%). m/z 258 (M^+,100%).

Methyl 2-methyl-7-(3,4-methylenedioxyphenyl)-2,4,6-heptatrienoate (30h) was isolated as pale yellow crystalline solid; yield 74%; m.p. 123°C; i.r.(KBr): ν_{max}= 1698, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.92(s,3H,2-CH_3); 3.71(s,3H,OCH_3); 5.90(s,2H,O-CH_2-O); 6.21-6.95(m,7$H_{arom+olefin}$); 7.05-7.35(m,1H_{olefin}). (Found: C,70.71; H,59.43. Calc. for $C_{16}H_{16}O_4$ (272.3): C,70.56; H,59.27%). m/z 272 (M^+89%).

2-Aryl-3,5-dimethyl-5-methylthio-2-cyclopenten-1-one (36a-d, 41a & 41b); General Procedure: To a well stirred suspension of the ketene S,S-acetals 34 or 39 (0.02 mol) in absolute ethanol (100 ml), excess of sodium borohydride (2.5g, 0.07 mol) was added and the mixture was refluxed for 2h. The cooled mixture was then poured into crushed ice (150g) and extracted with chloroform (2x150 ml). The chloroform extract was washed with saturated salt solution (2x100 ml), dried with sodium sulphate and evaporated under vacuum to give the crude carbinol 35 or 40 in nearly quantitative yields as an undistillable thick viscous liquid. The crude carbinol was dissolved in absolute methanol (100 ml) and boron trifluoride etherate (10 ml) was added with stirring. The mixture was then refluxed for 16-18 h. The cooled mixture was then poured into water (250 ml) and extracted with chloroform (2x100 ml). The chloroform extract was washed with saturated sodium hydrogen carbonate solution (2x100 ml) and with water (2x100 ml), dried with sodium sulphate and evaporated to give the crude cyclopentenones 36 and 41.

3,5-Dimethyl-5-methylthio-2-(4-methylphenyl)-2-cyclopentene-1-one (36a) was isolated as colourless crystals, yield 68%; m.p. 68-69°C; spectral data described in the text. (Found: C,73.26; H,7.47. Calc. for $C_{15}H_{18}OS$ (246.3): C,73.14; H,7.36%).

3,5-Dimethyl-5-methylthio-2-phenyl-2-cyclopentene-1-one (36b) was isolated as a pale yellow oil; yield 70%; i.r.(KBr): ν_{max}= 1718, 1650 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 1.55(s,3H,5-CH_3); 2.15(s,6H,SCH_3 and 3-CH_3); 2.64 (brs,2H,CH_2); 7.33(s,$5H_{arom}$). (Found: C,72.61; H,7.01. Calc. for $C_{14}H_{16}OS$ (232.3): C,72.36; H,6.94%). m/z 232(M^+,35%); 186(M^+-46,100%).

2-(4-Chlorophenyl)-3,5-dimethyl-5-methylthio-2-cyclopentene-1-one (36c) was isolated as pale yellow oil; yield 64%; i.r.(neat): ν_{max}= 1705, 1642 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.42(s,3H,5-CH_3); 2.06(s,6H,SCH_3 and 3-CH_3); 2.60(brs,2H,-CH_2-); 7.01-7.51(m,$4H_{arom}$). (Found: C,63.17; H,5.35. Calc. for $C_{14}H_{15}ClOS$ (266.7): C,63.04; H,5.67%). m/z 267 (M^+,29%); 221(M^+-46,100%).

3,5-Dimethyl-2-(4-methoxyphenyl)-5-methylthio-2-cyclopentene-1-one(36d) was isolated as pale yellow oil; yield 59%; i.r.(neat): ν_{max} = 1700, 1610 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.45(s,3H,5-CH_3); 2.03(s,3H,3-CH_3); 2.06(s,3H,SCH_3); 2.56(brs,2H,-CH_2-); 3.68(s,3H,Ar-OCH_3); 6.61-7.40 (m,$4H_{arom}$). (Found: C,68.83; H,69.26. Calc. for $C_{15}H_{18}O_2S$ (262.4): C,68.65; H,69.13%). m/z 262(M^+,49%); 216(M^+-46,100%).

3,5-Dimethyl-5-methylthio-2-styryl-2-cyclopentene-1-one (41a) was isolated as yellow oil; yield 72%; i.r.(neat): ν_{max}= 1700, 1600 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.40(s,3H,5-CH_3); 2.10(s,6H,SCH_3 and 3-CH_3); 2.51 (brs,2H,-CH_2-); 6.76(d,1H,J=16Hz,=CH); 7.00-7.61(m,$5H_{arom}$); 7.67(d, 1H,J=16Hz,=CH). (Found: C,74.64; H,7.30. Calc. for $C_{16}H_{18}OS$ (258.4): C,74.36; H,7.03%). m/z 258(M^+,38%); 212(M^+-46, 100%).

3,5-Dimethyl-2-(4-methylstyryl)-5-methylthio-2-cyclopentene-1-one(41b) was isolated a yellow oil; yield 74%; i.r.(neat): ν_{max}= 1690, 1600 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.31(s,3H,5-CH_3); 2.01(s,3H,3-CH_3); 2.06(s,3H,SCH_3);

2.23(s,3H,Ar-$\underline{CH}_3$); 2.50(brs,2H,-$\underline{CH}_2$-); 6.31-7.80(m,6H$_{arom+olefin}$).

(Found: C,74.76; H,7.35. Calc. for $C_{17}H_{20}OS$ (272.4): C,74.95; H,7.40%).

272(M^+,77%); 226(M^+-46,100%).

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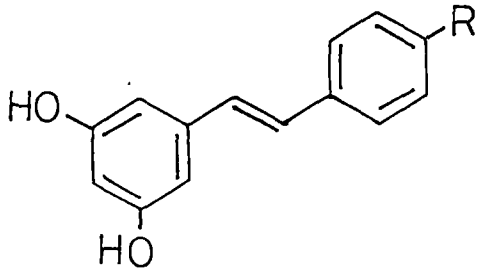
CHAPTER IV

1. REACTION OF ALLYL MAGNESIUM BROMIDE WITH CINNAMOYL KETENE DITHIOACETALS: A NEW EFFICIENT SYNTHESIS OF STILBENES*

2. ADDITION OF PHENYL AND METHYL GRIGNARD REAGENTS TO CINNAMOYL KETENE DITHIO-ACETALS: SYNTHESIS OF 5-SUBSTITUTED 3-OXOPENTANOATES

IV.1 INTRODUCTION

The naturally occuring Pinosilvin 1 and Resveratrol 2 have been isolated from wood and shown to have antifungul activity[1]. Diethyl Stilbestrol 3 is a stilbene derivative once employed as estrogenic hormone in human



1 R=H

2 R=OH

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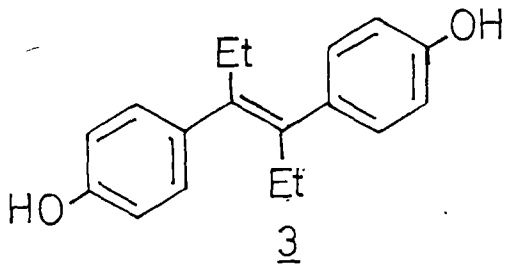
* C.V. Asokan, H. Ila and H. Junjappa, Synthesis, 284 (1987).

in human therapy[2]. Several commercial dyes are derivatives with stilbene structural moiety. The bis-stilbene 4 has been used as



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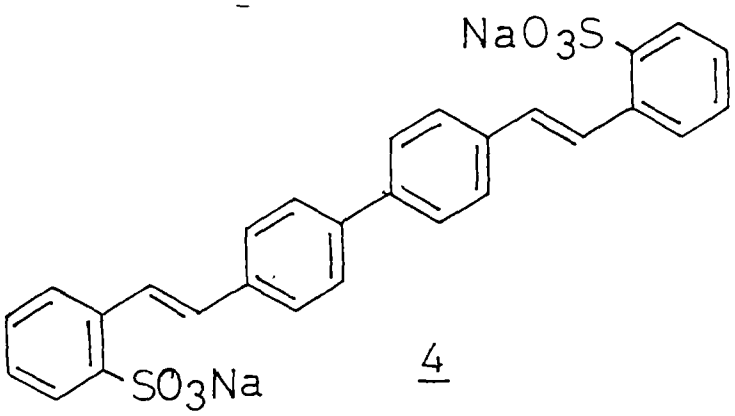
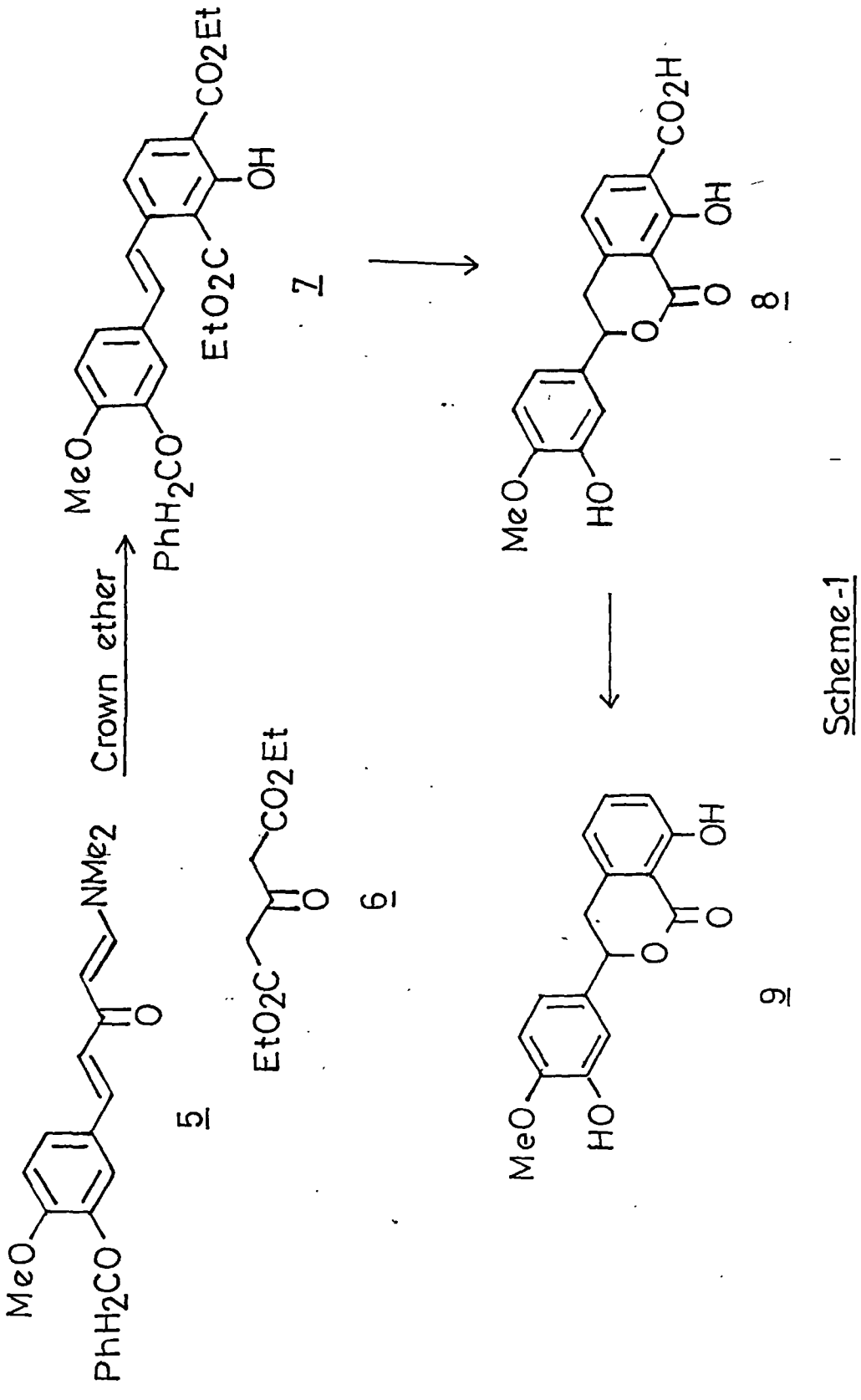
an optical brightner and also a detergent additive[3].



4

A number of approaches for the synthesis of both symmetric and asymmetric stilbenes have been described in the literature[4,5]. However many of these methods are not efficient for the synthesis of polyfunctional stilbenes, particularly substituents at ortho position to the projected stilbene double bond has a deleterious effect due to steric reasons or neighbouring group participation. Most of the methods described in the literature involve either transformation of aromatic precursors having built-in stilbene skeleton (Ar-C-C-Ar), or


MeO
PhH2CO
NMe2
O
5
Crown ether
EtO2C
CO2Et
O
6
MeO
PhH2CO
CO2Et
OH
EtO2C
7
MeO
HO
CO2H
OH
O
O
8
MeO
HO
OH
O
O
9

Scheme-1

coupling of aryl fragments with styrene or vinylarenes (Ar or Ar' + C=C-Ar). However there is only one report of the synthesis of stilbene involving direct construction of one of the aromatic ring from acyclic precursors. Thus the reaction of enaminoketone 5 (Scheme 1) with 3-oxoglutarate 6 leads to synthesis of (±)-Phyllodulcin 9[6].

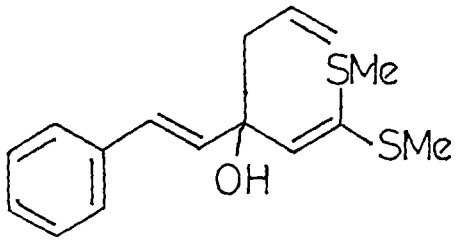
Aromatic annelation involving the reaction of allyl grignard reagents with α-oxoketene dithioacetals was first published from this laboratory and the method was subsequently shown to be of general applications with structural variation in both α-oxoketene dithioacetals and allyl grignard reagents as well[8]. It was therefore contemplated in the present work to study cycloaromatization of cinnamoyl ketene dithioacetals[9], which have been used in several investigation described in Chapter II and Chapter III of this thesis.

IV.2 RESULTS AND DISCUSSION

The starting cinnamoyl ketene dithioacetals 10a-g were prepared according to the reported procedure[8]. The structures of the dithioacetals 10a-d were confirmed by comparing their physical and spectral data with the reported values, while the hitherto unreported 10e-g were fully characterized with the help of spectral and analytical data (experimental).

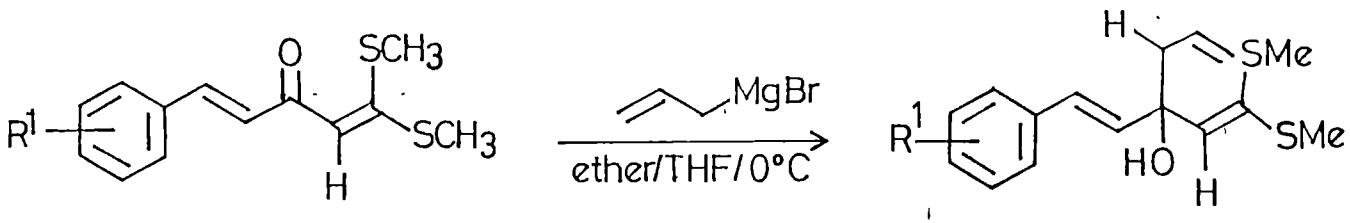
When 10a was reacted with allyl magnesium bromide in ether, the corresponding carbinol acetal 11a was obtained in nearly quantitative yield, which was subjected to boron trifluoride etherate catalyzed cycloaromatization in refluxing benzene to afford the corresponding 3-methylthiostilbene 12a in 68% yield. The spectral and analytical data of 12a were in confirmity with the assigned structure and are described in

the experimental section. The structure was further confirmed by its nickel boride (sodium borohydride/nickel chloride) desulphurization to the known[10a] trans-stilbene (18a) (Scheme 5). The method was found to be general when extended to the cinnamoyl ketene dithioacetals 10b-g which yielded the corresponding stilbene 12b-g under similar reaction conditions in 61-58% overall yields. The structures of all compounds were confirmed with the help of spectral and analytical data and are described in the experimental section. The stilbenes 12b and 12c were also desulphurized with Raney Nickel to give the known 4-methyl-(18b) and 4-chloro-(18c) stilbene in good yields (Scheme 5). Thus it is demonstrated that the synthesis of unsymmetrically substituted stilbenes can be achieved from preconstructed substituted cinnamoyl group carrying appropriate substituents, and converting the dithioacetal 3-carbon fragment into an aromatic ring through enol acetal intermediate 11. The present procedure was, however, not successful for the synthesis of 4-methoxy stilbene. The corresponding hydroxy dithioacetal 11h yielded intractable tar when reacted with ether boron trifluoride complex under varying conditions.

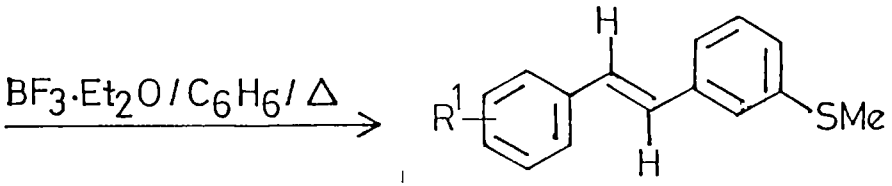


11a

When the carbinol acetal 11a was subjected to the boron trifluoride etherate catalyzed methanolysis at room temperature, the product obtained



10 11



12

10 - 12 a , R^1 = H e , R^1 = 2-Cl

b , R^1 = 4-CH_3 f , R^1 = 2,6-Cl_2

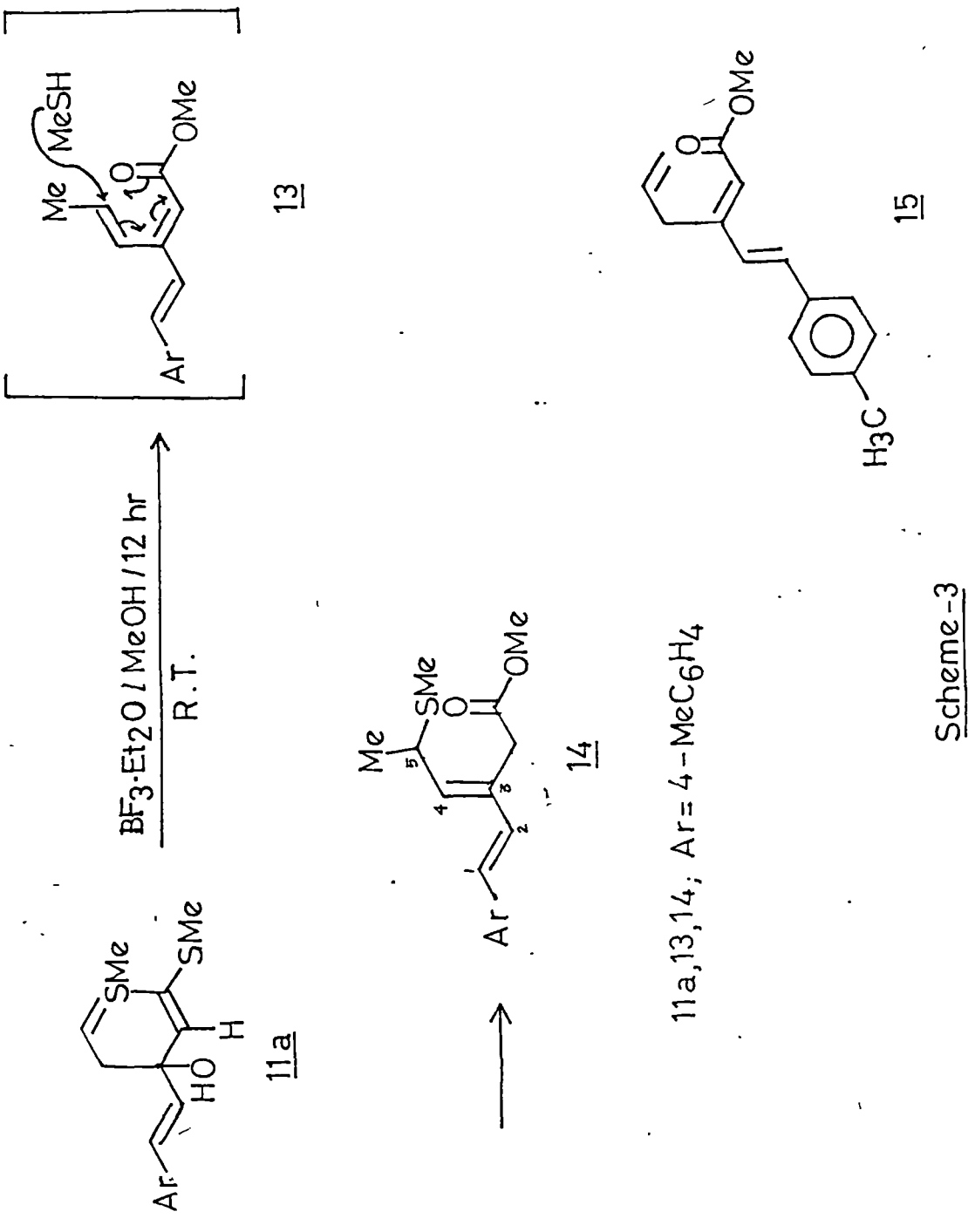
c , R^1 = 4-Cl g , R^1 = 3,4-Cl_2

d R^1 = 3-CH_3O

Scheme-2

in 65% yield after work-up and column chromatography was characterized as the saturated ester 14 while the expected methyl 3-allylpentadienoate 15 was not formed. The structure of 14 was confirmed by its spectral and analytical data. Thus it was analyzed for $C_{17}H_{22}O_2S$, its i.r.(neat) spectrum exhibited bands at 1735 and 1600 cm^{-1}. The ^1H n.m.r.(CCl_4) spectrum of 14 exhibited a doublet at δ 1.30(3H,J=7Hz) due to the methyl group and three singlets at δ 2.00, 2.32 and 3.68 due to methylthio, Ar-CH_3 and methoxy groups respectively. The methylene protons appeared at δ 3.25(d,J=5Hz,2H) while the H-4 and H-5 protons absorbed at δ 5.21-5.82(m,2H). The aromatic protons along with H-1 and H-2 appeared as multiplet between δ 6.25-7.35(m,6H). The mechanism of formation of 14 is depicted in Scheme 3. The initial product 13 is formed by methanolysis of the mercapto group. Subsequent 1,3-proton migration followed by Michel type addition of methylmercapto group gives the compound 14.

In another set of experiments, the crotyl magnesium bromide was reacted with the cinnamoyl ketene dithioacetals 10a-c, when the corresponding 1,2-adduct 16 was formed, while the isomeric adduct 16A was not detected. When the carbinol acetal 16a was subjected to boron trifluoride assisted cycloaromatization, the 2-methylstilbene 17a was formed in 51% yield. The compound was characterized with the help of its spectral and analytical data (experimental) and by dethiomethylation to the known trans-2-methylstilbene (18d) (Scheme 5) with nickel boride. The formation of this silbene carrying a methyl substituent to the ortho position of the projecting double bond is of particular interest since the existing methods either give poor yields, or fail when they have

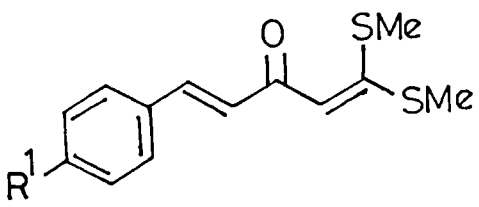

SMe
SMe
H
HO
Ar
11a
BF3·Et2O / MeOH / 12 hr
R.T.
Me
MeSH
O
OMe
Ar
13
Me
SMe
O
OMe
Ar
14
11a,13,14; Ar = 4-MeC6H4
OMe
O
H3C
15

Scheme-3

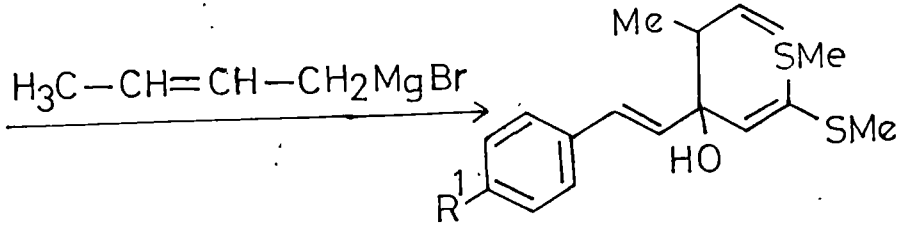
a substituent at the ortho position. Similarly 10b and 10c reacted with crotylmagnesium bromide to give the corresponding carbinol acetals 16b and 16c which underwent cycloaromatization to give the stilbenes 17b and 17c in 51 and 54% yields respectively. The spectral and analytical data of 17b and 17c were fully in confirmity with the assigned structures and are described in the experimental section.

It was then considered of interest to study 5-phenyl 2,4-pentadienoyl ketene dithioacetal 19 under similar reaction conditions to examine whether the corresponding cycloaromatized diene 21 could be formed. When 19 was reacted with allyl-magnesium bromide, the corresponding carbinol acetal 20 was obtained in quantitative yield, but subsequently failed to afford the expected 1,4-diaryldiene under various conditions. Similarly, the carbinol acetal 23 obtained by treatment of allyl magnesium bromide with 2-methyl cinnamoyl ketene dithioacetal (22) failed to undergo cycloaromatization to the corresponding 2-methyl stilbene (24) under described conditions.

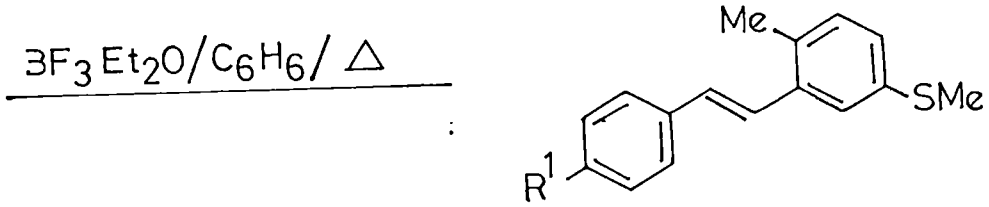
It has already been demonstrated that the 2,4-dimethyl- α -cinnamoyl oxoketene dithioacetals 25 behave differently from the unsubstituted dithioacetals 10 (Chapter II and Chapter III). It was therefore of interest to examine these systems under the described reaction conditions. When 25 was reacted with allyl magnesium bromide, the corresponding carbinol acetal 26 was formed in nearly quantitative yield. When 26 was subjected to $BF_3.Et_2O$ assisted ring annelation, after work-up, only one well defined compound was isolated in low yield (15%) which was characterized as 3-(p-chlorophenyl)-1-methyl-1-methylthioindene (32) (Scheme 7). The analytical and spectral data



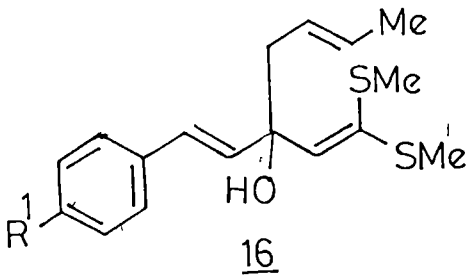
10 a-c



16



17 a-c



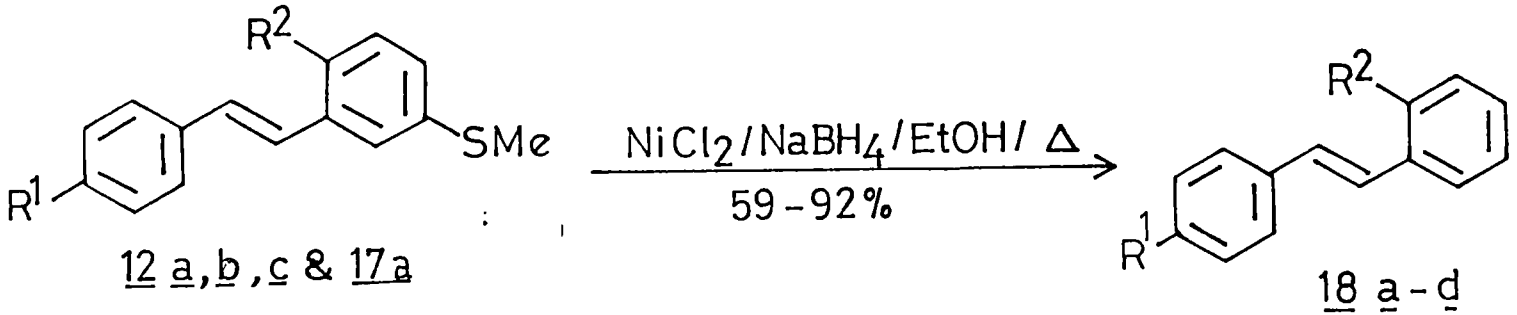
16

10 - 17 a, $R^1 = H$

b, $R^1 = CH_3$

c, $R^1 = Cl$

Scheme-4



12 a, b, c & 17a

18 a - d

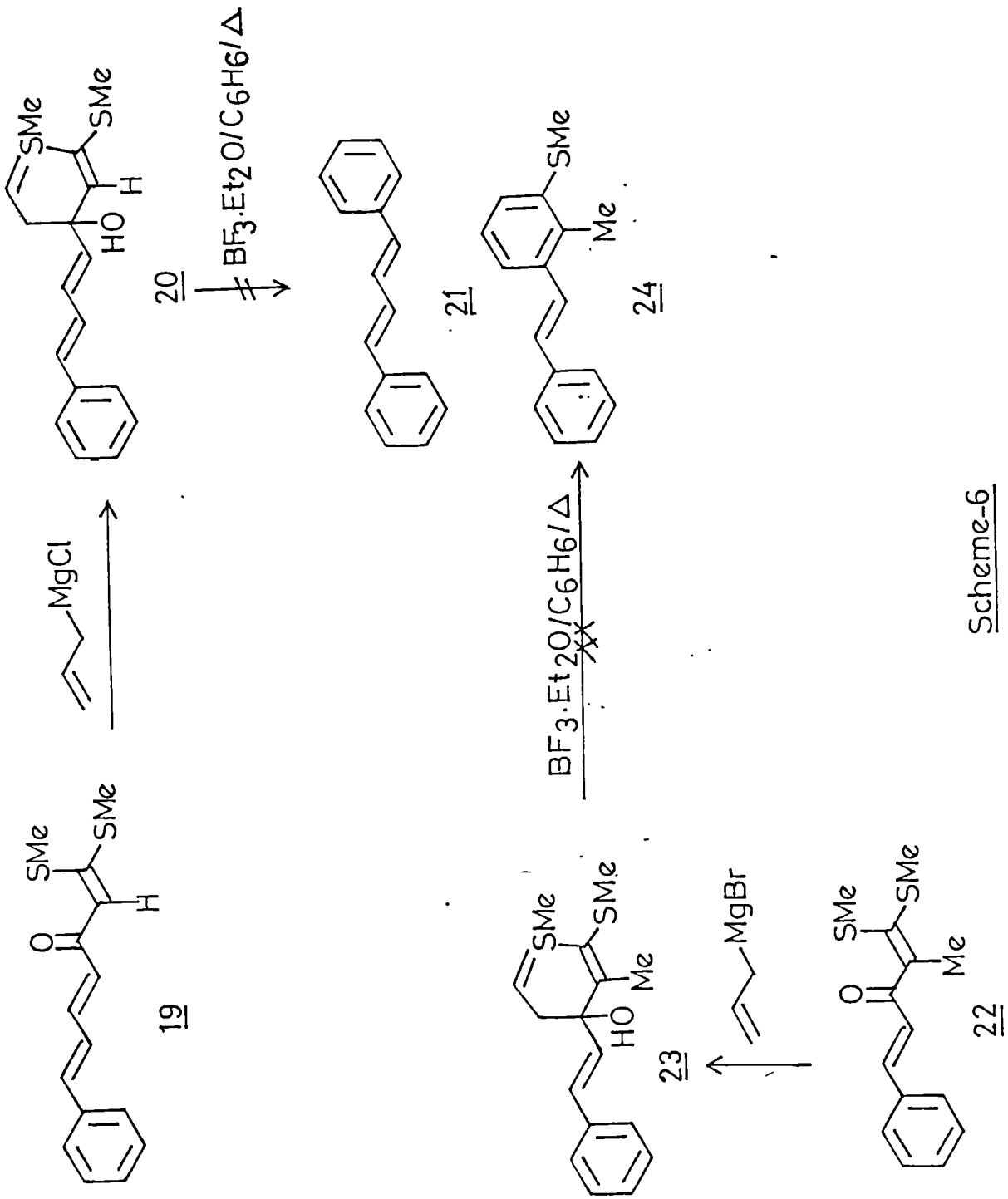
18 a , $R^1 = R^2 = H$

b , $R^1 = CH_3$, $R^2 = H$

c , $R^1 = Cl$, $R^2 = H$

d , $R^1 = H$; $R^2 = CH_3$

Scheme -5

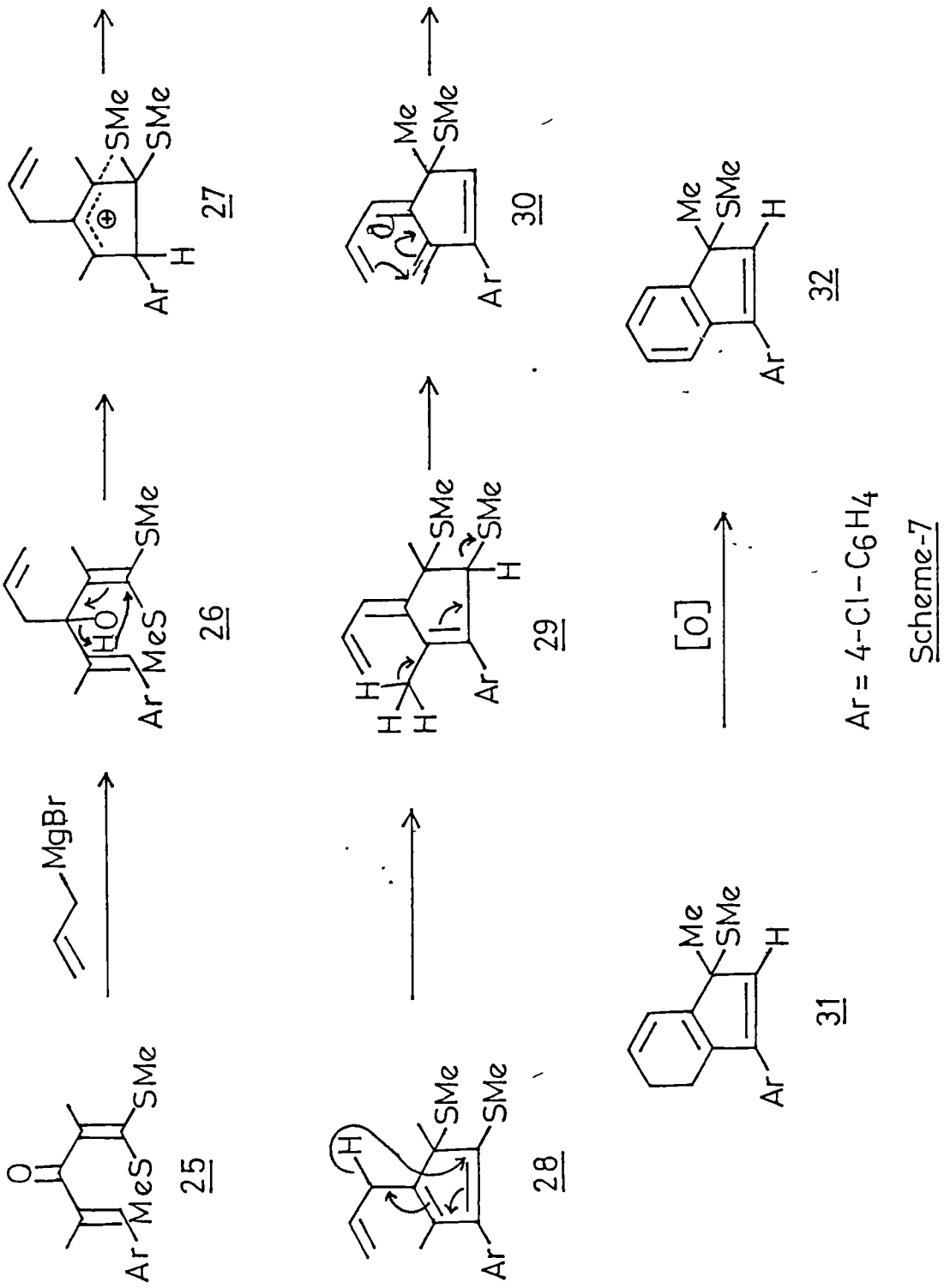

SMe
SMe
H
O
19
MgCl
SMe
SMe
H
HO
20
BF3.Et2O/C6H6/Δ
21
SMe
Me
24
BF3.Et2O/C6H6/Δ
SMe
SMe
Me
HO
23
MgBr
SMe
SMe
Me
O
22

Scheme-6

of 32 were in confirmity with its assigned structure. Thus it was analyzed for $C_{17}H_{15}ClS$, while its i.r. spectrum showed bands at 1580 and 1559 cm^{-1}. Further structural proof was obtained from ^1H n.m.r. spectrum ($CDCl_3$). The singlet at δ 2.32(3H) and δ 2.50(3H) were assigned to the methyl and methylthio groups respectively. The aromatic protons along with the H-2 proton were present as a multiplet between δ 6.98-7.55(9H). Its mass spectrum showed a base peak at m/z 240 (M^+-47,100%). The probably mechanism for the formation of 32 from 22 is shown in the Scheme 7. The conformational rigidity due to 2,3,4-trisubstitution in the carbinol 26 leads to a cyclopentenyl cation formation, which gives a 5-allyl cyclopentadiene intermediate 28 through a episulphonium ion 27. The intermediate 28 appears to undergo a very facile 1,5-sigmatropic shift to give 29 followed by homoallylic elimination of methyl mercaptan to give the cyclopentene 30 with conjugated triene framework. The triene 30 undergoes facile electrocyclic ring closure to give the dihydro compound 31, which on subsequent air oxidation affords the indene 32.

IV.3 ADDITION OF PHENYL AND METHYL GRIGNARD REAGENTS TO CINNAMOYL KETENE DITHIOACETALS: SYNTHESIS OF 5-SUBSTITUTED 3-OXOPENTANOATES

The α-cinnamoyl ketene dithioacetals 10a-c, 22a-c and 25 were selected for examining their reaction with phenyl magnesium bromide. When 10a was reacted with phenyl magnesium bromide, the product obtained in 78% yield, after work-up was characterized as the 1,1-bis(methylthio) 5,5-diphenyl-1-pentene-3-one (34a), which is obviously formed by the 1,4-addition of phenyl grignard reagent. The ketone 34a on subsequent methanolysis yielded the corresponding β-keto ester 35a in 70% yield. The structure of 34a and 35a were fully characterized with the help of



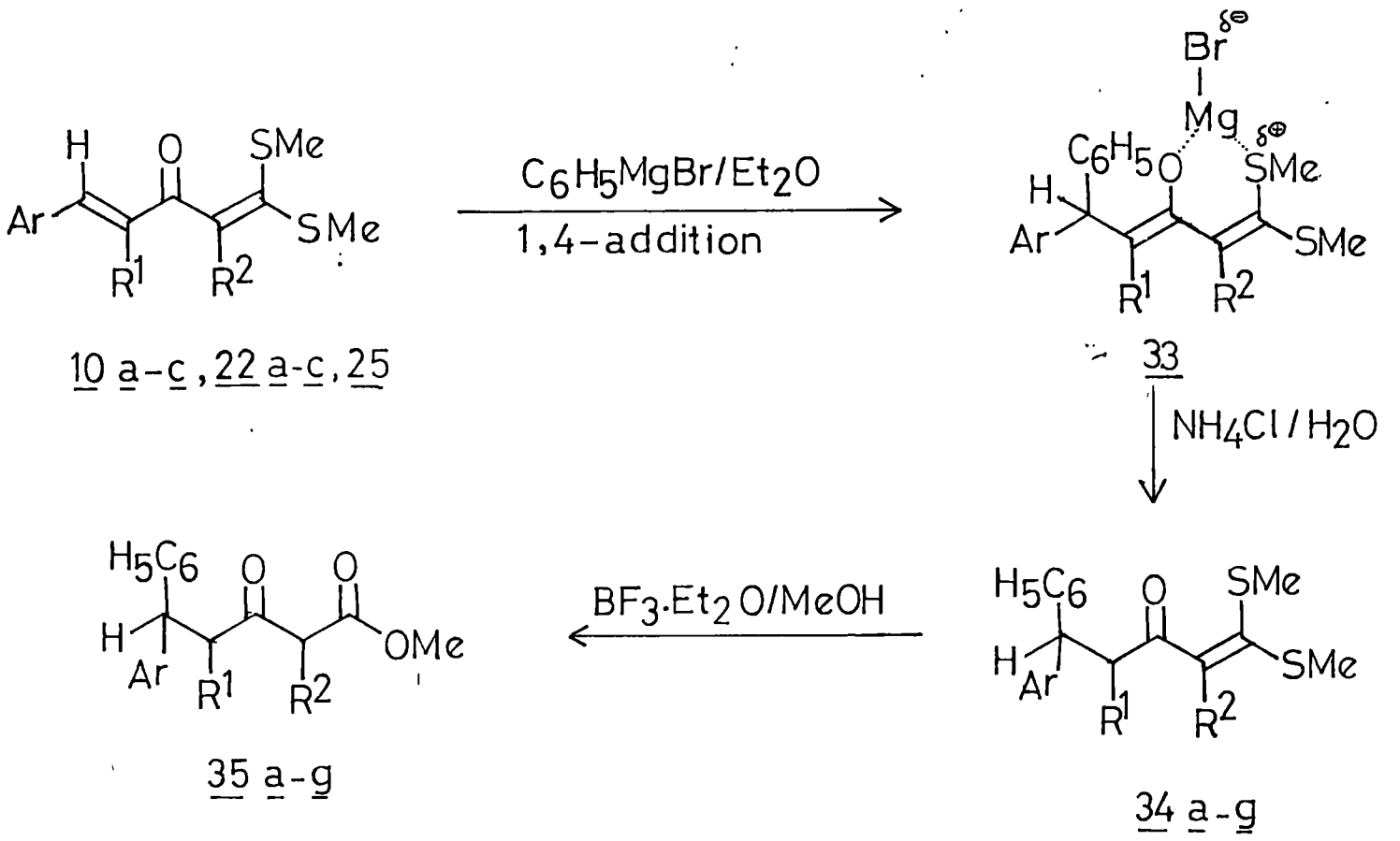
Scheme-7

Table-1

	Ar	R^1	R^2
10a, 35a	C_6H_5	H	H
10b, 35b	4-MeC_6H_5	H	H
10c, 35c	4-ClC_6H_4	H	H
22a, 35d	C_6H_5	H	Me
22b, 35c	4-MeC_6H_4	H	Me
22c, 35f	4-MeOC_6H_4	H	Me
25, 35g	C_6H_5	Me	Me

spectral and analytical data. Thus 34a was analyzed for $C_{19}H_{20}OS_2$. Its i.r.(KBr) spectrum exhibited bands at 1642, 1612 cm^{-1}. The ^1H n.m.r. spectrum of 34a showed two singlet at δ 2.18(3H) and δ 2.29(3H) due to two methylthio groups. The methylene protons appeared as a doublet (J=7Hz) at δ 3.01(2H), while the benzylic methine and H-2 protons were present at δ 4.52(t,1H,J=7Hz) and δ 5.67(s,1H) respectively. The aromatic protons appeared at δ 7.18(s,10H). The spectral and analytical data of β-oxoester 35a was also in confirmity with the assigned structure. Thus 35a analyzed for $C_{18}H_{18}O_3$ while its i.r. (KBr) spectrum exhibited two intense peaks at 1747 and 1716 cm^{-1} due to ester and keto carbonyl groups respectively. The ^1H n.m.r. spectrum of 35a showed a broad multiplet between δ 2.98-3.29(4H) due to methylene protons, while the absorption due to 5-methine proton was present as triplet (1H,J=7Hz) along with aromatic protons (s,5H) at δ 7.15. These data shows complete absence of enolic form for 35a in the solution which is further confirmed from its ^{13}C n.m.r. spectrum (CCl_4) which showed signals at δ 46.03($\underline{C}H_2$); 49.04($\underline{C}H_2$); 49.63($\underline{C}H$); 52.20(-O$\underline{C}H_3$); 126.64, 127.84, 128.71($\underline{C}H$-aromatic); 143.69(C-1' aryl); 167.32($\underline{C}$=O,ester) and 200.45($\underline{C}$=O). Similarly, the dithioacetals 10b-c, 22a-c, 25 also underwent 1,4-addition with phenyl magnesium bromide followed by methanolysis to give 3-oxopentanoates 35b-g in 58-76% overall yields under identical conditions. The structural assignments of 35b-g were fully confirmed with the help of spectral and analytical data and are described in the experimental section.

When phenyl magnesium bromide was added to 5-arylpentadienoyl ketene dithioacetal 19, the corresponding 1,4-adduct 36a was formed which on subsequent methanolysis gave methyl 5,7-diphenyl 3-oxo 6-heptenoate 36a



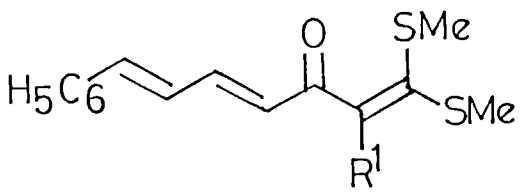
10 a-c, 22 a-c, 25

33

35 a-g

34 a-g

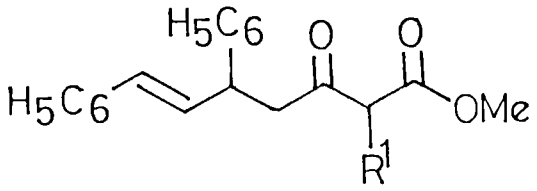
Scheme-8



19, R^1=H

19a, R^1 = Me

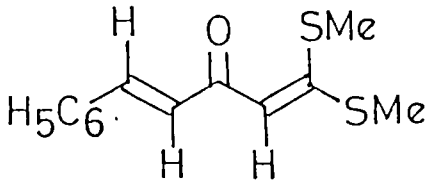
1. C_6H_5MgBr
2. $BF_3.Et_2O$/ MeOH



36 a - b

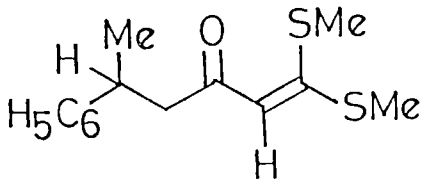
19, 36 a , R^1 = H

b , R^1 = Me



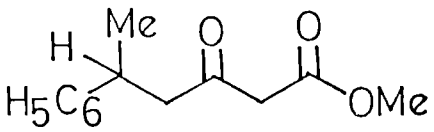
10a

1. MeMgBr
2. NH_4Cl



37

$BF_3.Et_2O$ / MeOH



38

Scheme-9

in 65% yield and its structure was confirmed with the help of spectral and analytical data (experimental). Similarly, the dithioacetal 19a afforded the corresponding 2-methyl-3-oxo-6-heptenoate (36b) under similar sequence of reactions.

The methylmagnesium bromide also underwent a 1,4-addition to the cinnamoyl ketene dithioacetal 10a to afford 1,1-bis(methylthio)-5-methyl-3-oxo-5-phenyl-1-pentene 37 in 70% yield. The ketone 37 also underwent boron trifluoride etherate assisted methanolysis to give the corresponding methyl 5-phenyl-3-oxohexanoate 38 in 60% yield. The assigned structure of 37 & 38 were confirmed with the help of spectral and analytical data (experimental).

Thus in conclusion, the cinnamoyl ketene dithioacetals undergo 1,2-addition with allyl and crotyl magnesium bromides followed by cyclo-aromatization to give trans-stilbenes, while with phenyl and methyl grignard reagents, 1,4-conjugate additions are observed.

IV.4 EXPERIMENTAL

General experimental conditions were same as those described in Chapter II.

Starting Materials

The commercial samples of acetone, ethylmethyl ketone, diethyl ketone, benzaldehyde, 4-tolualdehyde, 4-methoxybenzaldehyde, 3-methoxybenzaldehyde, 4-chlorobenzaldehyde, 2-chlorobenzaldehyde,2,6-dichlorobenzaldehyde, 3,4-dichlorobenzaldehyde, allyl bromide, crotyl bromide, methyl iodide and bromobenzene were purified before use. The α-oxoketene dithioacetals of acetone, ethylmethyl ketone and diethylketone were prepared according to the procedure described in Chapter II. The cinnamoyl ketene dithioacetals 10a-g, 25 and 33a-c were prepared

according to the reported procedure, as described in the second chapter. The spectral and analytical data of the new compounds prepared are given below.

1,1-Bis(methylthio)-3-oxo-5-(2-chlorophenyl)-1,4-pentadiene (10e) was isolated as yellow solid (MeOH); yield 75%; m.p.108°C; i.r.(KBr): ν_{max}= 1672, 1598 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.41(s,3H,$SC\underline{H}_3$); 2.48 (s,3H,$SC\underline{H}_3$); 6.23(s,1H,$\underline{H}$-2); 6.69(d,J=16Hz,1H,$\underline{H}$-4); 7.04-7.65(m, $4H_{arom}$); 7.89(d,J=16Hz,$\underline{H}$-5). (Found: C,54.62; H,4.30. Calc. for $C_{13}H_{13}ClOS_2$(283.3): C,54.83; H,4.57%).

1,1-Bis(methylthio)-3-oxo-5(2,6-dichlorophenyl)-1,4-pentadiene (10f) was isolated as yellow solid (MeOH); yield 72%; m.p.90°C; i.r.(KBr): ν_{max}= 1640, 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.51(s,6H,$SC\underline{H}_3$); 6.32(s, 1H,$\underline{H}$-2); 6.94(d,J=16Hz,1H,$\underline{H}$-4); 7.27-7.43(m,$3H_{arom}$); 7.76(d,J=16Hz, 1H,$\underline{H}$-5). (Found: C,48.67; H,3.52. Calc. for $C_{13}H_{12}Cl_2S_2$(319.3): C,48.90; H,3.79%).

1,1-Bis(methylthio)-3-oxo-5-(3,4-dichlorophenyl)-1,4-pentadiene (10g) was isolated as yellow solid (MeOH); yield 68%; m.p.149°C; i.r.(KBr): ν_{max}1640, 1590 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.51(s,6H,$SC\underline{H}_3$); 6.32(s,1H, $\underline{H}$-2); 6.94(d,J=16Hz,1H,$\underline{H}$-4); 7.27-7.43(m,$3H_{arom}$); 7.76(d,J=16Hz,1H, $\underline{H}$-5). (Found: C,48.67; H,3.52. Calc. for $C_{13}H_{12}Cl_2OS_2$(319.3): C,48.90; H,3.79%).

Reaction of 5-Aryl-1,1-bis(methylthio)-3-oxo-1,4-pentadienes 10a-g with allyl magnesium bromide; General Procedure: To a well stirred and cooled (0°C) suspension of allyl magnesium bromide (0.016 mol), [prepared from 1.92g(0.16 mol) of distilled allyl bromide,

and magnesium turnings, 1.2g (0.52 mol) in dry ether (40 ml), a solution of 10 (0.008 mol) in dry tetrahydrofuran (30 ml) was added and the reaction mixture was further stirred at 0°C for 1 hr. The reaction mixture was then poured into a saturated ammonium chloride solution (300 ml), extracted with ether (3x30 ml), dried with Na_2SO_4 and evaporated in vacuum to give crude 3-allyl-5-aryl-1,1-bis(methylthio)-penta-1,4-dien-3-ol (11) as yellow oils in nearly quantitative yields. Compounds 11a-g were unstable and therefore used as such for subsequent reactions without further purification.

Cycloaromatization of 11; Synthesis of Stilbenes 12a-g; General Procedure: To a solution of crude hydroxy dithioacetal 11 (0.008 mol) obtained as above, in dry benzene (60 ml), boron trifluoride etherate (10 ml) was added. The reaction mixture was refluxed for 45 minutes, poured into water, and the resultant mixture was neutralized with saturated $NaHCO_3$ solution (100 ml) and extracted with chloroform (4x30 ml). The organic extract was dried with Na_2SO_4 and evaporated to give crude 3-methylthiostilbenes 12a-g, which were purified by column chromatography over silica gel using hexane as eluent.

3-Methylthiostilbene (12a) was isolated as colourless crystalline solid; yield 68%; m.p. 61°C (hexane); i.r.(KBr): ν_{max} 1592 cm^{-1}; ^1H n.m.r. ($CDCl_3$): δ 2.40(s,3H,SCH_3); 6.90(s,$2H_{olefin}$); 7.01-7.65(m,$9H_{arom}$). (Found: C,79.91; H,6.41. Calc. for $C_{15}H_{14}S$(226.3); C,79.60; H,6.23%). m/z 226(M^+,100%).

4-Methyl-3'-methylthiostilbene (12b) was isolated as colourless crystalline solid; yield 62%; m.p.74-76°C (hexane); i.r.(KBr): ν_{max} 1590 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.31(s,3H,CH_3); 2.49(s,3H,SCH_3);

6.90(s,2H$_{olefin}$); 6.91-7.39(m,8H$_{arom}$). (Found: C,80.10; H,6.82. Calc. for $C_{16}H_{16}S$ (240.4): C,79.93; H,6.71%). m/z 240(M^+,100%).

4-Chloro-3'-methylthiostilbene (12c) was isolated as colourless crystalline solid; yield 68%; m.p.79°C (hexane); i.r.(KBr): ν_{max} 1595 cm^{-1}; ^1H n.m.r.($CDCl_3$): δ 2.48(s,3H,S$\underline{CH_3}$); 6.92(s,2H$_{olefin}$); 7.0-7.43(m,8H$_{arom}$). (Found: C,69.21; H,5.41. Calc. for $C_{15}H_{13}ClS$ (260.8): C,69.07; H,5.01%). m/z 260(M^+,100%); 262(37).

3-Methoxy-3'-methylthiostilbene (12d) was isolated as colourless oil; yield 57%; i.r.(neat): ν_{max} 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.41(s,3H, S$\underline{CH_3}$); 3.63(s,3H,O$\underline{CH_3}$); 6.90(s,2H$_{olefin}$); 6.92-7.38(m,8H$_{arom}$). (Found: C,75.01; H,6.37. Calc. for $C_{16}H_{16}OS$ (256.4): C,74.94; H,6.29%). m/z 256(M^+,100).

2-Chloro-3'-methylthiostilbene (12e) was isolated as colourless oil; yield 61%; i.r.(neat): ν_{max} 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.41(s, 3H,S$\underline{CH_3}$); 6.85(d,1H,J=16Hz,=$\underline{CH}$); 6.95-7.90(m,9H$_{arom+olefin}$). (Found: C,69.21; H,5.31. Calc. for $C_{15}H_{13}ClS$(260.8): C,69.07; H,5.01%). m/z 260 (M^+,30%); 262(12).

2,6-Dichloro-3'-methylthiostilbene (12f) was isolated as colourless oil; yield 52%; i.r.(neat): ν_{max} 1585 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.39 (s,3H,S$\underline{CH_3}$); 6.89(s,2H$_{olefin}$); 6.95-7.61(m,7H$_{arom}$). (Found: C,61.13; H,4.15. Calc. for $C_{15}H_{12}Cl_2S$ (295.2): C,61.02; H, 4.09%). m/z 294 (M^+,27%); 296(18).

3,4-Dichloro-3'-methylthiostilbene (12g) was isolated as colourless oil; yield 53%; i.r.(neat): ν_{max} 1582 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.49 (s,3H,S$\underline{CH_3}$); 6.89(s,2H$_{olefin}$); 6.95-7.51(m,7H$_{arom}$). (Found: C,61.31; H,4.22. Calc. for $C_{15}H_{12}Cl_2S$ (295.2): C,61.02; H, 4.09%).m/z 294(M^+,28%); 296(20).

Solvolysis of 1,1-Bis(methylthio)-3-allyl-5-(4-methylphenyl)-1,4-pentadiene-3-ol (11b): To a solution of crude hydroxydithioacetal 11b(2.45g, 0.008 mol) obtained by reaction of 10b with allyl magnesium bromide as described earlier, in dry methanol (50 ml) boron trifluoride etherate (2 ml) was added. The reaction mixture was stirred at room temperature for 14 hrs, poured into water (300 ml) and the resultant mixture is neutralized with saturated $NaHCO_3$ solution (100 ml) and extracted with chloroform (3x30 ml). The organic extract is dried with Na_2SO_4 and evaporated to give crude ester 14, which was purified by column chromatography over silica gel using hexane as eluent.

3-Carbomethoxymethyl-1-(4-methylphenyl)-5-methylthio-hexa -1,3-diene(14) was isolated as pale yellow oil; yield 65%; spectral data described in text. (Found: C,70.41; H,3.47. Calc. for $C_{17}H_{22}O_2S$(290.4): C,70.32; H,3.44%).

Reaction of 5-aryl-1,1-bis(methylthio)-3-oxo-1,4-pentadienes (10a-c) with crotylmagnesium bromide; General Procedure: To magnesium (1.2g, 0.52 mol) and a pinch of iodine in dry tetrahydrofuran (40 ml), two drops of crotyl bromide was added to initiate the reaction and a solution of crotyl bromide (2.20g, 0.016 mol) and dithioacetal (10, 0.008 mol) in dry tetrahydrofuran was added dropwise (30 min) at room temperature. After stirring the reaction mixture for 10-12 hrs at room temperature, it was poured over saturated ammonium chloride solution (300 ml), extracted with ether (3x30 ml), dried with sodium sulphate and evaporated in vacuo to give the crude 3-(1-buten-3-yl)-5-aryl-1,1-bis(methylthio)-penta-1,4-diene-3-ol (16a-c) which were used as such for further cycloaromatization.

Cycloaromatization of 16a-c; Synthesis of 2-methyl-5-methylthiostilbenes (17a-c): To a solution of crude hydroxydithioacetal 16 (0.008 mol), obtained as above, in dry benzene (60 ml), boron trifluoride etherate (10 ml) was added. The reaction mixture was refluxed for 45 min. poured into water (300 ml). The resultant mixture was neutralized with saturated $NaHCO_3$ solution (100 ml) and extracted with chloroform (4x30 ml). The organic layer was dried (Na_2SO_4) and evaporated to give crude 2-methyl-5-methylthiostilbenes (17a-c) which were purified by column chromatography over silica gel using hexane as eluent.

2-Methyl-5-methylthiostilbene (17a) was isolated as colourless oil; yield 52%; i.r.(neat): ν_{max} 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.30(s, 3H,CH_3); 2.4(s,3H,SCH_3); 6.9-7.51(m,$10H_{arom+olefin}$). (Found: C,79.83; H,6.81. Calc. for $C_{16}H_{16}S$(240.4): C,79.93; H,6.71%). m/z 240(M^+,100%).

4-Methyl-2'-methyl-5'-methylthiostilbene (17b) was isolated as colourless oil; yield 51%; i.r.(neat): ν_{max} 1595 cm^{-1}; ^1H n.m.r. (CCl_4): δ 2.30(s,6H,4-CH_3 and 2'-CH_3); 2.41(s,3H,CH_3); 6.7-7.35 (m,$9H_{arom+olefin}$). (Found: C,79.99; H,7.25. Calc. for $C_{17}H_{18}S$(254.4): C, 80.26; H,7.13%).

4-Chloro-2'-methyl-5'-methylthiostilbene (17c) was isolated as colourless oil; yield 51%; i.r.(neat): ν_{max} 1595 cm^{-1}; ^1H n.m.r. (CCl_4): δ 2.29(s,3H,CH_3); 2.40(s,3H,SCH_3); 6.86-7.45(m,$9H_{arom+olefin}$). (Found: C,65.67; H,5.67. Calc. for $C_{16}H_{15}ClS$(274.8): C,65.56; H,5.51%). m/z 274(M^+,100%); 276(28).

Dethiomethylation of stilbenes 12a-c and 17a; General Procedure: To a solution of methylthiostilbenes (12 or 17, 0.002 mol) in

methanol (200 ml), was added nickel (II) chloride hexahydrate (14.20g, 0.06 mol) followed by sodium borohydride (6.70g, 0.18 mol) in small portions with stirring and cooling (30 min). After refluxing for 6 hrs, the reaction mixture was filtered and the residue was washed with hot acetone (10x50 ml). The filtrate was evaporated and the viscous residue dissolved in chloroform (100 ml) and washed with water (100 ml) to remove trace nickel chloride. The chloroform layer was dried (Na_2SO_4) and evaporated to give crude desulphurized stilbenes 18a-d, which were further purified by passing through a silica gel column using hexane as eluent.

Stilbene (18a) was isolated as colourless crystals; yield 59%; m.p. 123-124°C (lit.[10a] m.p. 124°C);(superimposable i.r. and n.m.r. spectra).

4-Methylstilbene (18b) was isolated as colourless crystals; yield 61%; m.p. 119-120°C (lit.[10b] m.p. 120°C); (superimposable i.r. and n.m.r. spectra).

4-Chlorostilbene (18c) was isolated as colourless crystals; yield 62%; m.p. 127-128°C (lit.[10c] m.p. 129°C); (superimposable i.r. and n.m.r. spectra).

2-Methylstilbene (18d) was isolated as colourless crystals; yield 60%; m.p. 31-32°C (lit.[11] m.p. 31-32°C); (superimposable i.r. and n.m.r. spectra).

Reaction of 1,1-bis(methylthio)-5-(4-chlorophenyl)-2,4-dimethyl-3-oxo penta-1,4-diene (25) with allyl magnesium bromide: To a well stirred and cooled (0°C) suspension of allyl magnesium bromide (0.016 mol) in dry ether (40 ml) a solution of 25 (2.5g,0.008 mol) in tetrahydrofuran (20 ml) was added and the reaction mixture was further stirred

at 0°C for 1 hr. It was then poured over saturated NH_4Cl solution (300 ml) extracted with ether (2x50 ml), dried (Na_2SO_4) and evaporated to give crude 3-allyl-1,1-bis(methylthio)-5-(4-chlorophenyl)-2,4-dimethyl-penta-1,4-diene-3-ol 26 in 95% (2.69g) yield which was unstable and used as such for subsequent reaction.

Cyclization of 3-allyl-1,1-bis(methylthio)-5-(4-chlorophenyl)-2,4-dimethylpenta-1,4-diene-3-ol (26): To a solution of crude hydroxy dithioacetal 26 (2.69g, 0.0076 mol) obtained as above, in dry benzene (60 ml), boron trifluoride etherate (10 ml) was added. The reaction mixture was refluxed for 22 hrs, poured into water (300 ml) and the resultant mixture was neutralized ($NaHCO_3$) and extracted with chloroform (4x30 ml). The organic layer was dried (Na_2SO_4), evaporated and column chromatographed to give 3-(4-chlorophenyl)-1-methyl-1-methylthioindene 32 as colourless crystalline solid; yield 15%; m.p. 112°C; spectral data described in text. (Found: C,71.27; H,5.11. Calc. for $C_{17}H_{15}ClS$(286.8): C,71.19; H,5.27%). m/z 240(M^+-47,100%).

Reaction of phenyl magnesium bromide with 5-Aryl-1,1-bis(methylthio)-1,4-pentadiene-3-ones 10a-c, 25, 22a-c or 7-aryl 1,1-bis(methylthio)-1,4,6-heptatriene-3-ones 19 and 19a; General Procedure: To a well stirred and cooled (0°C)solution of phenyl magnesium bromide [0.015 mol, prepared from bromobenzene (2.34g, 0.015 mol) and magnesium turning (0.34g, 0.015 mol)] in dry ether (40 ml), a solution of 10, 25, 22 or 19 (0.01 mol) was added and the reaction mixture was poured in saturated NH_4Cl solution (300 ml), extracted with ether (3x30 ml), dried (Na_2SO_4) and evaporated to give 5-aryl-1,1-bis(methylthio)-5-phenylpent-1-ene-3-ones 34 or 1,1-bis(methylthio)-5,7-diphenyl hepta-1,7-diene-3-ones. The ketone 34a was further purified by

column chromatography over silica gel using EtOAc/hexane (1:20) as eluent.

1,1-Bis(methylthio)-5,5-diphenylpent-1-ene-3-one (34a) was isolated as pale yellow crystalline solid; yield 72%; m.p. 118°C; spectral data described in text. (Found: C,69.55; H,5.98. Calc. for $C_{19}H_{20}OS_2$(328.5): C,69.47; H,6.12%).

Solvolysis of 5-Aryl-1,1-Bis(methylthio)-5-phenylpent-1-ene-3-ones 34a-g and 7-aryl-1,1-bis(methylthio)-5-phenyl-hepta-1,6-diene-3-ones: Synthesis of methyl 5-Aryl-3-oxo-5-phenylpentanoates 35a-g and methyl 7-aryl-3-oxo-5-phenyl-6-heptenoate 36a and 36b; General Procedure:

To a solution of crude α-oxoketene dithioacetal 34 or the dithioacetal obtained from 19 (0.01 mol) in dry methanol (60 ml) boron trifluoride etherate (3 ml) was added and the reaction mixture was refluxed for 20-22 hr. It was then poured into water (200 ml), neutralized with $NaHCO_3$(12g), extracted with chloroform (3x50 ml), washed with water (2x50 ml) dried (Na_2SO_4) and evaporated to give crude β-ketoesters 35 or 36 which were further purified by column chromatography over silica gel using ethylacetate:hexane (1:20) as eluent.

Methyl 5,5-diphenyl-3-oxopentanoate (35a) was isolated as colourless crystalline solid; yield 73%; m.p. 128°C; spectral data described in the text. (Found: C,76.82; H,6.61. Calc. for $C_{18}H_{18}O_3$(282.3): C,76.57; H,6.42%).

Methyl 5-(4-methylphenyl)-5-phenyl-3-oxopentanoate (35b) was isolated as pale yellow semisolid; yield 75%; i.r.(neat): ν_{max} 1750, 1720 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.10(s,3H,Ar-CH_3); 3.00(m,4H,CH_2); 3.51(s,3H,-OCH_3); 4.33(t,1H,J=2.5Hz,H-5); 6.70-7.41(m,9H_{arom}). (Found: C,77.19; H,6.91. Calc. for $C_{19}H_{20}O_3$(296.3): C,77.01; H,6.80%).

Methyl 5-(4-chlorophenyl)-5-phenyl-3-oxopentanoate (35c) was isolated as pale yellow semisolid; yield 73%; i.r.(neat): ν_{max} 1748, 1721 cm^{-1}; ^1H n.m.r.(CCl_4): δ 3.50(m,4H,$C\underline{H}_2$); 3.78(s,3H,-$OC\underline{H}_3$); 4.46 (t,1H,$\underline{H}$ 5); 6.90-7.71(m,9H_{arom}). (Found: C,68.32; H,5.90. Cal. for $C_{18}H_{17}ClO_3$ (316.8): C,68.24; H,5.71%).

Methyl 5,5-diphenyl-2-methyl-3-oxopentanoate (35d) was isolated as colourless crystalline solid; yield 78%; m.p. 138°C; i.r.(KBr): ν_{max} 1735, 1710 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.21(d,3H,J=8Hz,-$C\underline{H}_3$); 3.20(q,1H,J=8Hz,CH_3-$\underline{C}$-$\underline{H}$); 3.26(d,2H,J=6Hz,$C\underline{H}_2$); 3.61(s,3H,$OC\underline{H}_3$); 4.58(t,1H,J=6Hz,$\underline{H}$ 5); 7.20(s,10H_{arom}); ^{13}C n.m.r.($CDCl_3$): δ 12.44 ($\underline{C}H_3$); 45.88($\underline{C}$-2); 47.65($\underline{C}$-4); 52.23($O\underline{C}H_3$); 53.32($\underline{C}$-5); 126.54, 127.86, 128.60($\underline{C}H_{arom}$); 143.80($\underline{C}$-1',aryl); 170.64($\underline{C}$=O,ester); 203.32($\underline{C}$=O). (Found: C,77.31; H,6.91. Calc. for $C_{19}H_{20}O_3$(296.3): C,77.01; H,6.80%). m/z 296(M^+,60%).

Methyl 2-methyl-5-(4-methylphenyl)-3-oxo-5-phenylpentanoate (35e) was isolated as pale yellow semisolid; yield 76%; i.r.(neat): ν_{max} 1750, 1720 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.10(d,3H,J=8Hz,$C\underline{H}_3$); 2.21 (s,3H,Ar-$C\underline{H}_3$); 3.01-3.34(m,3H,$\underline{H}$-2 and $C\underline{H}_2$); 3.50(s,3H,$OC\underline{H}_3$); 4.48 (t,1H,J=6Hz,$\underline{H}$-5); 6.70-7.60(m,9H_{arom}). (Found: C,77.61; H,7.32. Calc. for $C_{20}H_{22}O_3$(310.3): C,77.41; H,7.12%).

Methyl 2-methyl-5-(4-methoxyphenyl)-3-oxo-5-phenylpentanoate (35f) was isolated as pale yellow semisolid; yield 73%; i.r.(neat): ν_{max}1750, 1720 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.11(d,3H,J=8Hz,-$C\underline{H}_3$); 3.00-3.36(m,3H,$\underline{H}$-2 and -$C\underline{H}_2$); 3.50(s,3H,-$OC\underline{H}_3$); 3.61(s,3H,Ar-O-$C\underline{H}_3$); 4.45(t,1H,J=6Hz,$\underline{H}$-5); 6.42-7.42(m,9H_{arom}). (Found: C,73.69; H,6.91. Calc. for $C_{20}H_{22}O_4$ (326.3): C,73.61; H,6.80%).

Methyl 2,4-dimethyl-5,5-diphenyl-3-oxo-pentenoate (35g) was isolated as pale yellow oil; yield 75%; i.r.(neat): ν_{max} 1745,1715 cm^{-1}; ^1H n.m.r.(CCl_4): δ 0.84(d,3H,J=8Hz,$C\underline{H}_3$); 1.08(d,3H,J=8Hz,$C\underline{H}_3$); 2.81 (t,1H,J=8Hz,$\underline{H}$-2); 3.45-3.60(m,1H,$\underline{H}$-4); 3.61(s,3H,-$OC\underline{H}_3$); 3.95(d,1H, J=12Hz,$\underline{H}$-5); 7.01-7.60(m,$10H_{arom}$). (Found: C,77.63; H,7.26. Calc. for $C_{20}H_{22}O_3$(310.4): C,77.38; H,7.14%).

Methyl 5,7-diphenyl-3-oxo-6-heptenoate (36a) was isolated as pale yellow semisolid; yield 68%; i.r.(neat): ν_{max} 1750, 1720 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.85(d,2H,J=6Hz,$C\underline{H}_2$); 3.15(s,2H,$C\underline{H}_2$); 3.58(s,3H, -$OC\underline{H}_3$); 3.95-4.05(m,1H,$\underline{H}$-5); 6.19(brs,$2H_{styryl}$); 6.80-7.51(m,$10H_{arom}$). (Found: C,77.81; H,6.71. Calc. for $C_{20}H_{20}O_3$(308.4): C,77.88; H,6.54%).

Methyl 5,7-diphenyl-2-methyl-3-oxo-6-heptenoate (36b) was isolated as pale yellow semisolid; yield 65%; i.r.(neat): ν_{max} 1750, 1720 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.17(d,3H,J=7Hz,$C\underline{H}_3$); 2.90(d,2H,J=7Hz,$C\underline{H}_2$); 3.26 (q,1H,J=7Hz,$\underline{H}$-2); 3.50(s,3H,-$OC\underline{H}_3$); 4.05-4.15(m,1H,J=7Hz,$\underline{H}$-5); 6.25 (brs,$2H_{styryl}$); 7.00-7.51(m,$10H_{arom}$). (Found: C,78.02; H,6.77. Calc. for $C_{21}H_{22}O_3$(322.4): C,78.23; H,6.88%).

Reaction of Methyl magnesium iodide with 1,1-bis(methylthio)-5-phenyl 1,4-pentadiene-3-one (10a): To a well stirred and cooled suspension of methyl magnesiumbromide [0.015 mol prepared from methyl iodide (1 ml, 0.015 mol) and magnesium turnings(0.32g, 0.015 mol)] in dry ether (30 ml), the dithioacetal 10a(2.5g,0.01 mol) in ether (40 ml) was added and the reaction mixture was further stirred for 2 hrs. The mixture was poured over saturated ammonium chloride solution (100 ml), extracted with ether (3x50 ml), dried (Na_2SO_4) and evaporated to yield the crude

pentadienone (10a). Further purification by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluent gave 1,1-bis(methylthio)-5-phenyl-1-hexene-3-one (37) as pale yellow crystalline solid; yield 70%; m.p. 88°C; i.r. (KBr): ν_{max} 1650, 1501 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.26(d,3H,J=7Hz,CH_3); 2.38(s,3H,SCH_3); 2.47(s,3H,SCH_3); 2.80(d,2H,J=7Hz,CH_2); 3.25-3.35(m,1H,H-5); 5.82 (s,1H,H-2); 7.00-7.41(m,$5H_{arom}$). (Found: C,63.37; H,6.67. Calc. for $C_{14}H_{17}OS_2$(265.4): C,63.35; H,6.46%).

Solvolysis of 1,1-Bis(methylthio)-5-methyl-5-phenyl-1-pentene-3-one (37): To a solution of crude α-oxoketene dithioacetal 37 (1.3g, 0.005 mol) in methanol (50 ml), boron trifluoride etherate (3 ml) was added and the reaction mixture was refluxed for 15 hrs. The mixture was then poured over water, neutralized ($NaHCO_3$) and extracted with chloroform. The organic layer was washed with water dried (Na_2SO_4) and evaporated to give crude 38. Further purification by column chromatography using ethyl acetate:hexane (1:20) gave methyl 3-oxo-5-phenyl hexanoate 38 as pale yellow liquid; yield 71%; i.r.(KBr): ν_{max} 1748, 1718 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.27(d,3H,J=7Hz,CH_3); 2.81 (d,2H,J=7Hz,CH_2); 3.20(s,2H,CH_2); 3.25(m,1H,H-5); 7.00-7.30(m,$5H_{arom}$). (Found: C, 71.15; H,6.90. Calc. for $C_{13}H_{15}O_3$ (219.3): C,71.13; H,6.83%).

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CHAPTER V

STUDIES ON 1,5-, 1,7-, 1,9- AND 1,11-CARBONYL GROUP TRANSPOSITIONS VIA OXOKETENE DITHIOACETALS

V.1 INTRODUCTION

The term 'carbonyl group transposition' is defined as migration of carbonyl functionality within the same molecular framework[1,2]. The most intensively investigated carbonyl transpositions are the 1,2-carbonyl transpositions[3] and the examples of 1,3-carbonyl transpositions are relatively less in number. The methods for 1,4-carbonyl transpositions described in the literature are very few, whereas the studies involving 1,5-carbonyl transpositions are largely confined to isomerization of hydroxy ketones involving hydride migrations. Few 1,6-carbonyl transpositions involving hydride migrations are

known, and there appears to be no examples in the literature involving carbonyl transpositions beyond 1,6[4]. However, while the present investigation was in progress, Duhamel and co-workers[5,6] have reported the reactions of functionalized silyloxy or alkoxypolyenelithium reagents with aldehydes or ketones followed by hydrolysis in mild conditions which leads to polyenals. These reactions may be considered as special cases of alkylative 1,5 and 1,7 carbonyl group transpositions, where the carbonyl group migration is associated with homologation.

The carbonyl group is the most important functional group in organic chemistry. Although there is an abundance of carbonyl functionality in organic chemistry, serious studies involving carbonyl transpositions, which can be used as general methods for organic synthesis have not been attempted. Even the extensively studied 1,2-carbonyl transpositions have been developed as a part of specific design to introduce carbonyl group in an appropriate position in a given molecule. Since there exists no general methods in the literature, particularly for higher carbonyl transpositions, which may be used to design synthetic strategies for various biologically important molecules, it is desirable to investigate and evolve efficient methodologies for 1,5- and higher carbonyl transpositions. It was contemplated in the present investigation to undertake systematic investigation to develop new methodologies for higher carbonyl transpositions.

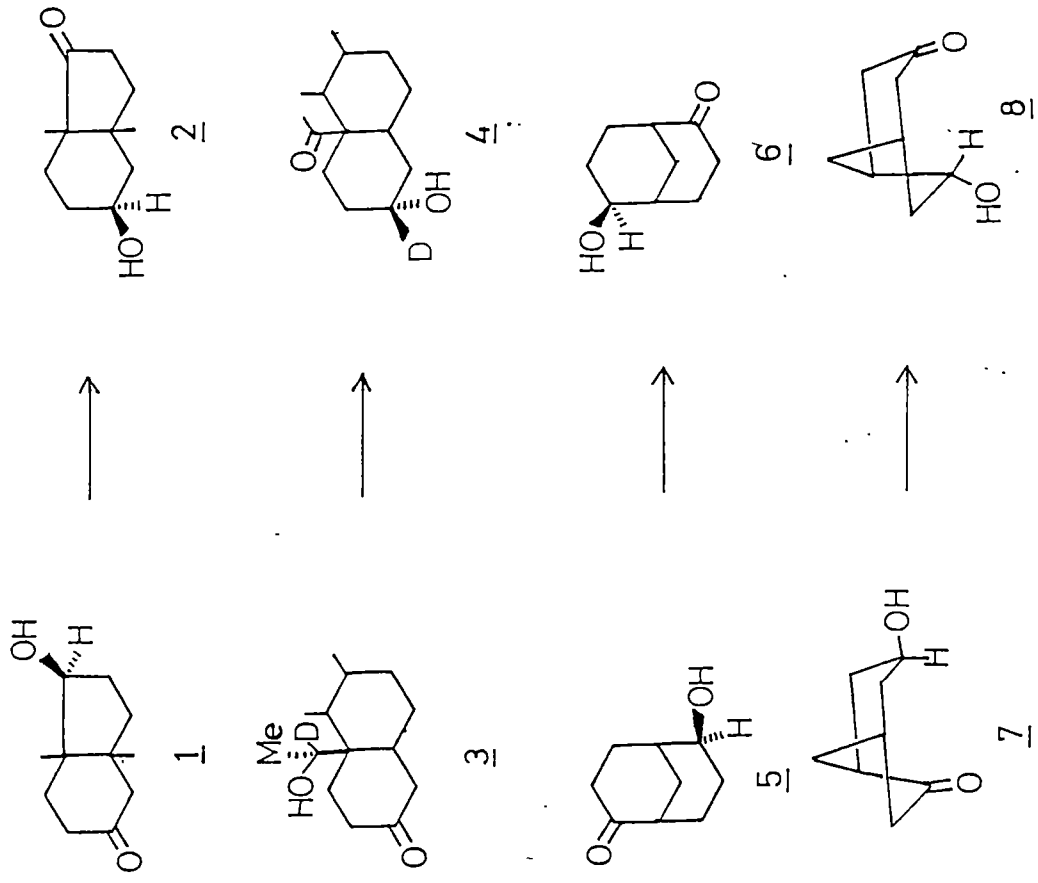
The oxoketene dithioacetals are a versatile group of synthons which have been extensively investigated to explore their synthetic potential and shown to be highly useful building blocks in organic

synthesis[7]. Their applications in 1,3 carbonyl transpositions involving borohydride reduction or reaction with Grignard or organo-lithium reagents to give the corresponding carbinol acetals followed by methanolysis to the corresponding ene-esters are well documented[8,9,10,11]. This 1,3 carbonyl transposition methodology has been further extended to the cinnámoyl and 5-aryl 2,4-pentadienolyl ketene dithioacetals to afford pentadienoates[12] and heptatrienoates[13] respectively. In the present work the acyl ketene dithioacetals have been successfully used to achieve 1,5-, 1,7-, 1,9- and 1,11- carbonyl group transpositions. Such methods will be of immense synthetic value particularly in the total absence of any carbonyl transpositions beyond 1,7.

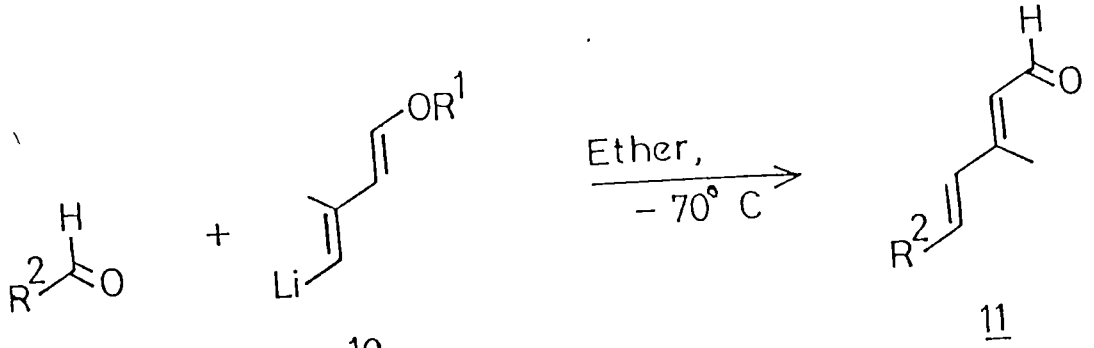
V.2. Current Status of Literature involving 1,5-, 1,6- and 1,7-Carbonyl Group Transpositions

V.2.1 1,5-Carbonyl Transposition

The first report on a 1,5 hydroxy-ketone transposition appears to have been that of Acklin and Prelog in 1959[14]. They have demonstrated that the hydroxy ketone 1 (Scheme 1) undergoes a 1,5-carbonyl transposition to give 2 in the presence of activated alumina. Similarly, Wicha and Caspi[15] have reported a migration of carbonyl group of cyclohexanone 3 to the exocyclic carbon to give 4 (Scheme 1) whereas the carbonyl group of 5 has been shown to be transposed to an adjascent fused ring by Parker and Stevenson[16]. The other example (7 → 8, Scheme 1) also involves a hydride transfer along with the 1,5 carbonyl transposition[17]. The variation and diversity in these examples of 1,5- carbonyl transposition is limited merely to intramolecular hydride transfer.



Scheme 1



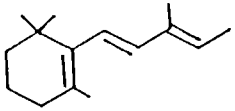
9 : 10 → 11

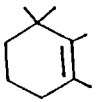
9, 11 a $R^2 = CH_3$

b $R^2 = Ph$

c $R^2 = Ph$–CH=CH–CH_3

d R^2 = 

e R^2 = 

f R^2 = 

10 a $R^1 = Et$

b $R^1 = Si(Me)_3$

Scheme 2

Recently Duhamel and co-workers[5] have developed a new reagent i.e. lithiosilyloxy or ethoxybutadiene 10 by reacting t-butyllithium with the corresponding bromo-, silyloxy- or ethoxybutadienes. The butadienyllithium reagents react with carbonyl compounds followed by hydrolysis to give polyenealdehydes 11 (Scheme 2). This reaction may be considered as an alkylative 1,5 carbonyl transposition where the migration of the carbonyl group is through the side chain introduced, involving simultaneous 4-carbon homologation as well.

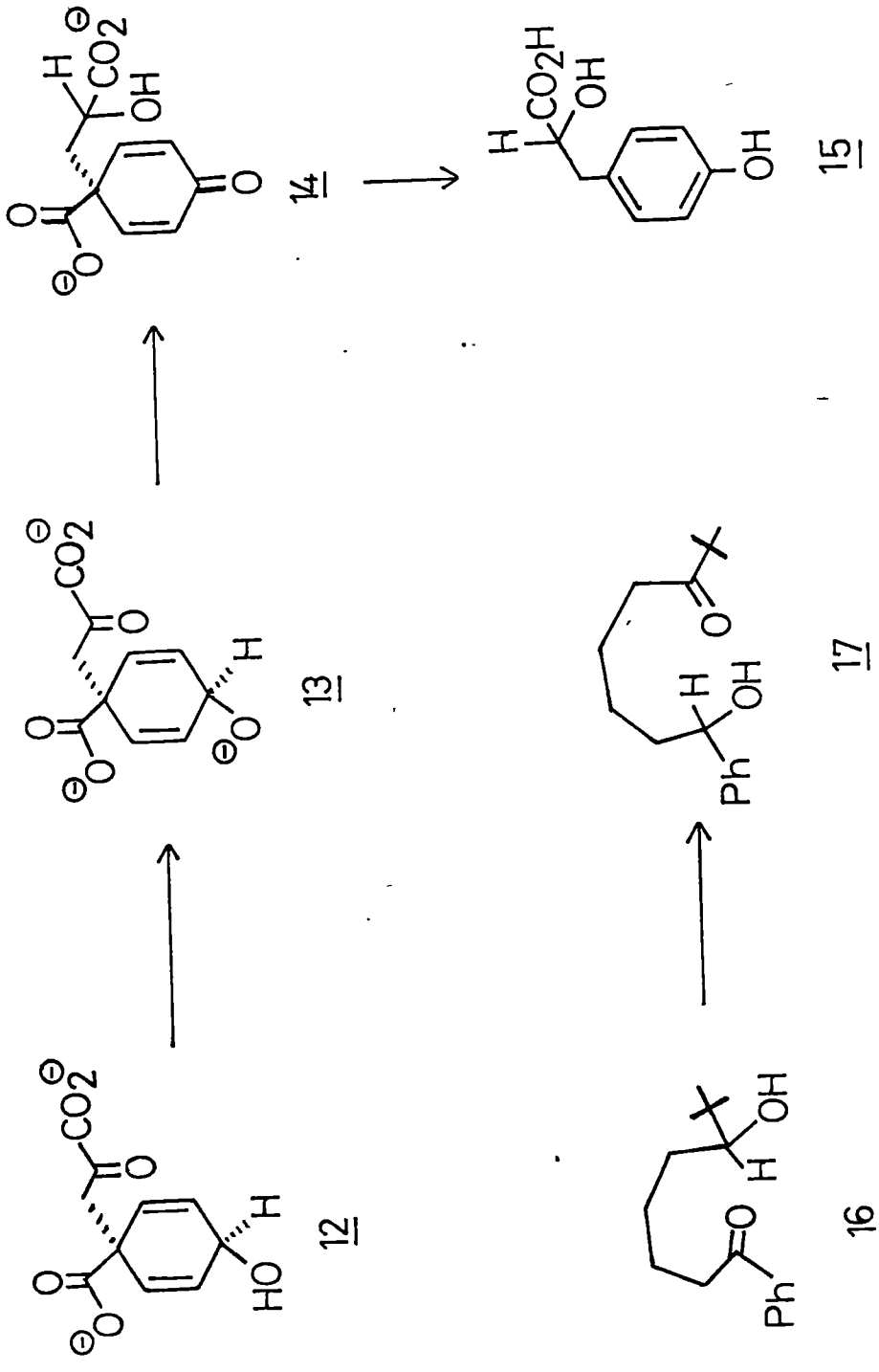
V.2.2 1,6-Carbonyl Transposition

Examples involving 1,6-carbonyl transpositions are limited to intramolecular hydride transfer. An interesting example is the preparation of p-hydroxyphenyl lactic acid 15 (Scheme 3) from 12 involving a 1,6-hydride migration[18]. Similarly, an example of 1,6-carbonyl transposition through hydride transfer in the conversion of acyclic hydroxy ketone 16 to 17 has also been reported (Scheme 3).

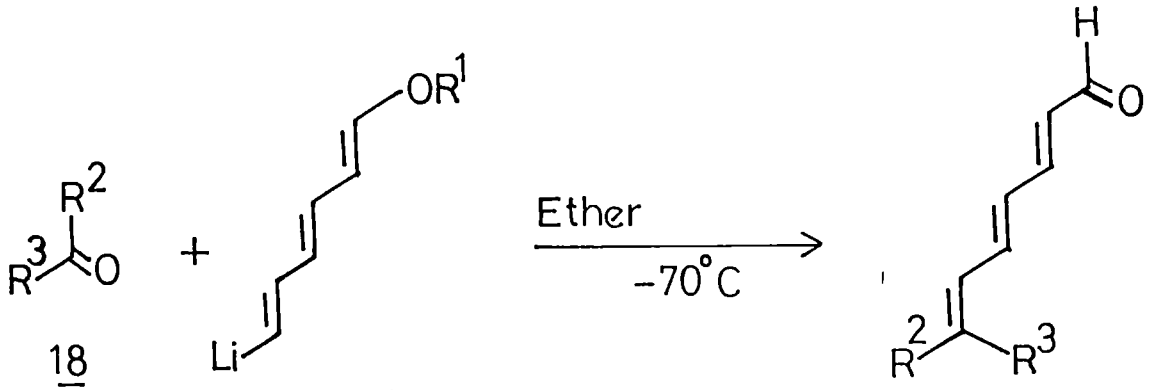
V.2.3 1,7-Carbonyl Transposition

The only report on a 1,7 carbonyl transposition is of Duhamel and co-workers[6], which appeared recently. They have prepared the vinylogous lithium reagents 19 by lithiation of the corresponding bromo compounds (Scheme 4). The reaction of these reagents with aldehydes or ketones leads to polyenaldehydes 20. The reaction involves an alkylative 1,7 carbonyl transposition, where the migration of the carbonyl group takes place through the side chain introduced. They have reported the synthesis of dehydrocitral, ψ-retinal and retinal through a one step reaction from acetone, α-ionone and β-ionone respectively.

The examples illustrated for 1,5-, 1,6-, and 1,7-carbonyl transpositions are very few in number and mostly confined to intramolecular hydride transfer.



Scheme 3

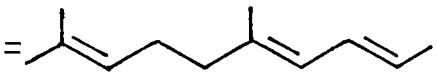


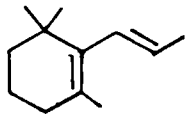
18 19 20

19 $R^1 = Et, SiMe_3$

18 20 a $R^2 = Ph$; $R^3 = H$

b $R^2 = CH_3$; $R^3 = CH_3$

c $R^2 =$  ; $R^3 = CH_3$

d $R^2 =$  ; $R^3 = CH_3$

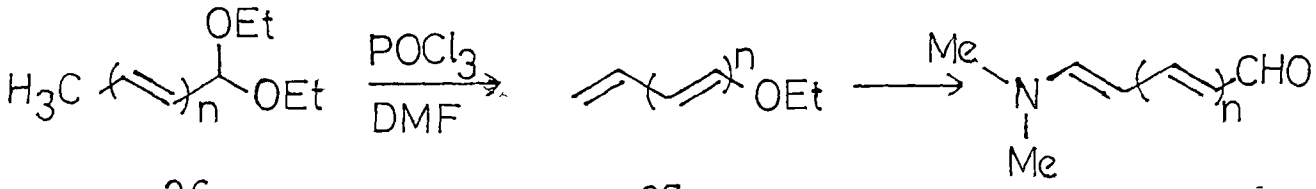
Scheme 4

V.3 RESULTS AND DISCUSSION

V.3.1 Synthesis of 5,5-Bis(methylthio)-pentadienals

During the course of this investigation it was considered that the pentadienals 23 (Scheme 5) would be suitable candidates for the 1,5 and 1,7 carbinol transpositions. These hitherto unreported dienaldehydes 25 were conveniently prepared by the Vilsmeir-Haack acylation of the carbinol acetals 22 obtained by a 1,2-reduction of the respective α-oxoketene dithioacetals 21. Thus the 5,5-bis(methylthio)-2,4-pentadienaldehyde 23a was obtained in 59% yield from the corresponding α-oxoketene dithioacetal 21a through the carbinol acetal 22a. It was analyzed for $C_7H_{10}OS_2$ and its i.r. spectrum displayed characteristic bands at 1670 and 1592 cm^{-1}. Further structural proof was obtained from its ^1H n.m.r. spectrum (CCl_4), which showed two singlets at δ 2.40(3H) and 2.41(3H) due to the two methylthio groups. The double doublet at δ 5.98(1H,J=16Hz,8Hz) which was assigned to H-2 proton thus showing trans along C_2C_3 double bond. The H-4 proton absorbed at δ 6.30(1H,J=12Hz), while the H-3 proton appeared as a double doublet at δ 7.47(1H,J=16Hz,12Hz). The doublet at δ9.52(1H, J=8Hz) was assigned to the aldehydic proton. The coupling constants of H-2 and H-3 confirm the 2-E geometry of the aldehyde formed and shows that the reaction is stereospecific unlike other formylations of polyenes under Vilsmeier-Haack reaction conditions. Similarly 23b and 23c were also prepared from the corresponding 21a and 21b respectively in 70 and 74% yields. They also show characteristic trans coupling at H-2 and H-3 confirming the 2-E geometry of the aldehydes.

The dienaldehydes 23 with a protected ester functionality at one terminal and a reactive aldehyde functionality at the other end, which can be used for new C-C bond forming reactions, such as aldol condensations, reactions with organolithium and magnesium reagents, Reformatsky and Wittig reactions, are of high synthetic importance, particularly when the other polyenaldehydes 28, which may be prepared by Vilsmeier reaction from the acetals are of limited use because of the dimethylamino substitution[20,21].

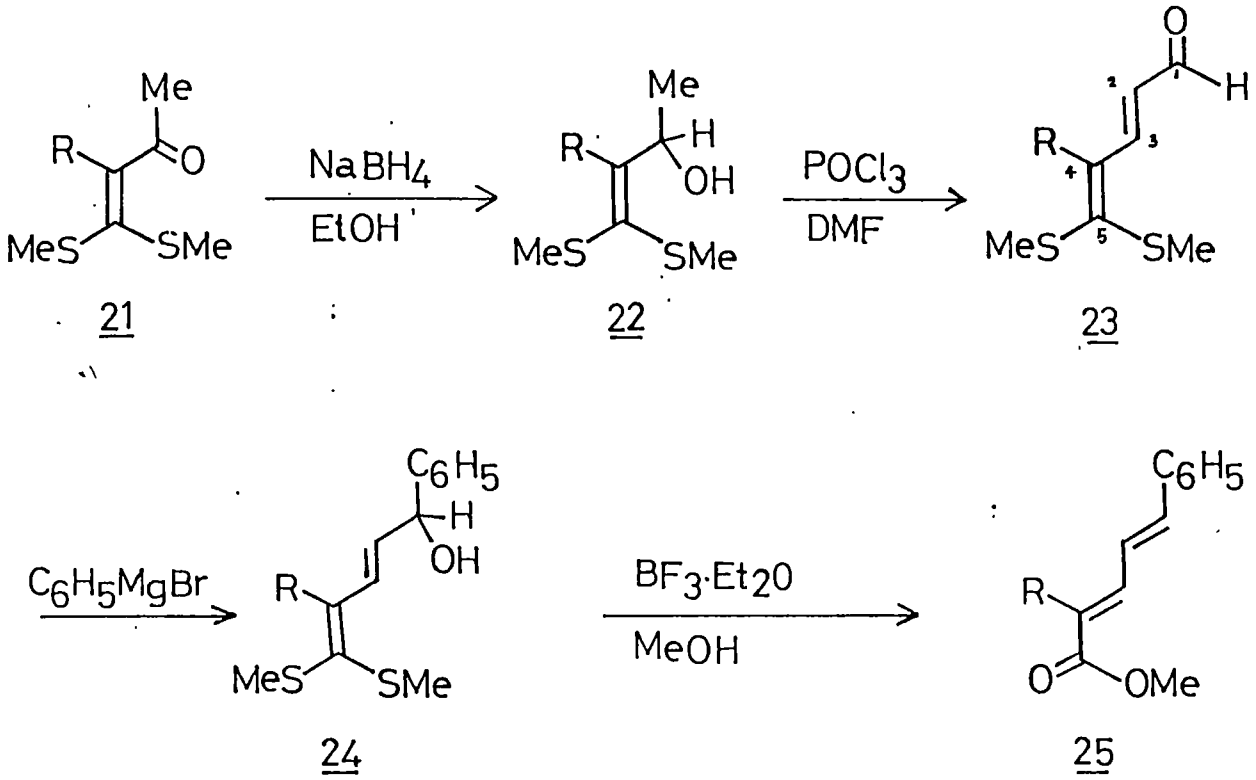


26 27 28

Scheme 6

V.3.2 Studies on 1,5-Carbonyl Transposition

The dienaldehydes 23a-c were considered as appropriate precursors for the study of 1,5 carbonyl transposition, as well as for the preparation of 7,7-bis(methylthio) heptatrienones and 7,7-bis(methylthio) heptatrienals which would be the precursors for 1,7 carbonyl transpositions. The 1,5 carbonyl transpositions were achieved from the bis(methylthio) dienaldehydes as described in the following section. When the dienaldehyde 23a was reacted with phenylmagnesium bromide the resultant pentadienol 24a was obtained in nearly quantitative yield (Scheme 5). The alcohol 24a was not characterized and used as such for the next step without further purification. After boron trifluoride etherate assisted methanolysis, work-up and column chromatography of the reaction mixture afforded the corresponding



21 22 23

24 25

21-25 a R=H

b R=CH_3

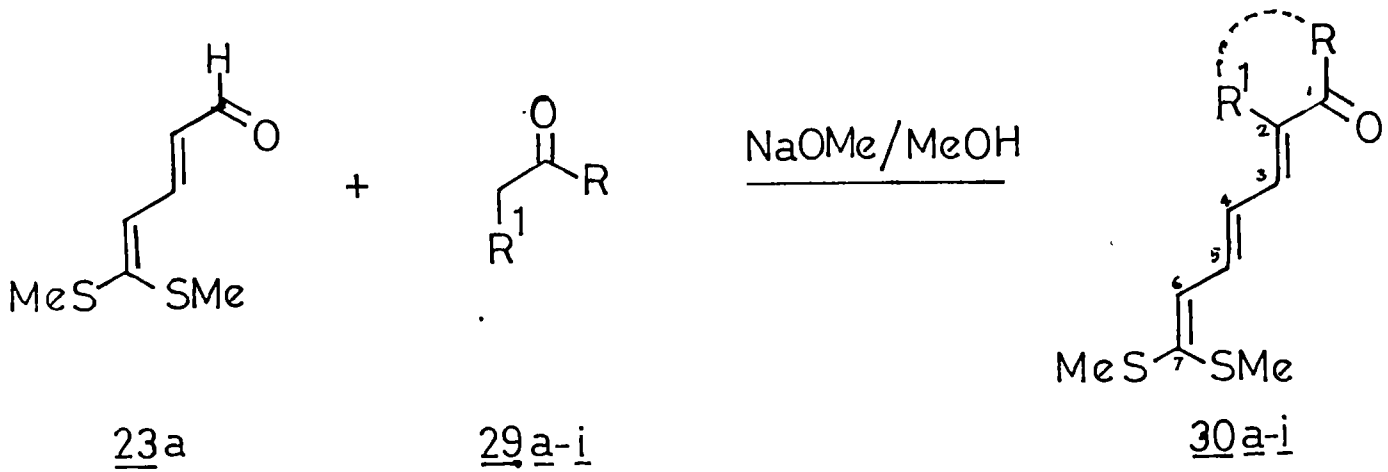
c R=C_2H_5

Scheme 5

methyl 2,4-pentadienoate 25a in 90% yield. The structure of 25a was confirmed by comparison with authentic sample prepared by methods reported earlier (m.m.p.; superimposable i.r. and n.m.r. spectra). The other diene esters 25b and 25c were also obtained in 85 and 87% yields from 23b and 23c respectively. The analytical and spectral data of all 25a-c were in conformity with the assigned structures and are described in the experimental. The diene esters were assigned 2-E, 4-E geometry based on the spectral data. The method is of particular synthetic importance, since it provides a facile route to dieneesters from the active methylene ketones via oxoketene dithioacetals through the sequence of reactions described (Scheme 5).

V.3.3 Synthesis of 7,7-Bis(methylthio)-1-aryl/alkyl (or cycloalkyl)-2,4,6-heptatriene-1-ones

According to the present scheme of investigation, the precursors for the study of 1,7 carbonyl transpositions can be of two kinds: (a) the heptatrienaldehyde 39 (Scheme 12); (b) the heptatrienone 30 (Scheme 7) or 31 (Scheme 8). The hitherto unreported 7,7-Bis (methylthio)heptatrienones 30a-i and 31a-i were prepared by condensation of the dienaldehyde 23a or 23b with various ketones. When the aldehyde 23a was reacted with acetophenone in the presence of sodium methoxide in methanol, the corresponding 7,7-bis(methylthio)-1-phenyl-2,4,6-heptatriene-1-one 30a was obtained in 95% yield. The structure and stereochemistry of the trienone 30a was established with the help of its spectral and analytical data. Thus the compound 30a exhibited the molecular ion peak in its mass spectrum at m/z 276 (M^+,10%) and was analyzed for $C_{15}H_{16}OS_2$. The i.r.(KBr) spectrum displayed



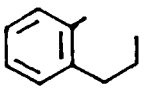
23a 29a-i 30a-i

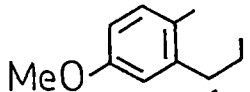
29-30 a R = C_6H_5 ; R^1 = H

b R = 4-MeC_6H_4 ; R^1 = H

c R = 4-MeOC_6H_4 ; R^1 = H

d R = 4-ClC_6H_4 ; R^1 = H

e R = R^1 = 

f R = R^1 = 

g R =  ; R^1 = H

h R =  ; R^1 = H

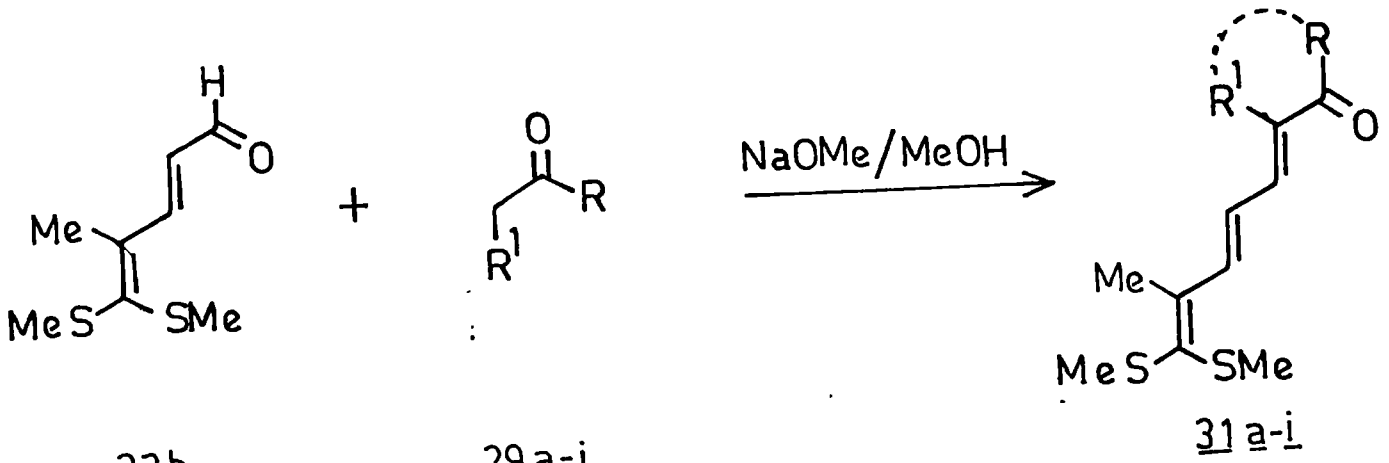
i R = CH_3 ; R^1 = H

Scheme-7

bands at 1643, 1590 and 1586 cm^{-1} due to the carbonyl and olefin groups respectively. The ^1H n.m.r. spectrum ($CDCl_3$, 300 MHz) showed two singlets at δ 2.39 and δ 2.40 due to the two methylthio groups. The doublet at δ 6.36(1H,J=11.4Hz) was assigned to the H-6 proton while the H-5 proton appeared as a double doublet at δ 6.45(1H,J=15Hz and 11.4Hz). The H-2 proton was present as a doublet at δ 6.96(1H, J=15Hz) while H-5 proton absorbed at δ 7.26(dd,1H,J=15Hz,11.1Hz). The multiplet at 7.40-7.60 (4H) was due to three aromatic protons along with H-3 and the other two aromatic protons absorbed between δ 7.92-7.94. The clear trans couplings of the H-3, H-4 and H-5 confirm the 2-E, 4-E geometry of the molecule. Similarly the heptatrienones 30b-i and 31a-i were prepared by the condensation of 23a or 23b with the active methylene compounds 29a-i in 80-95% overall yields (Scheme 7 and 8). The n.m.r. spectral data showed that the 2-E, 4-E geometry remained consistent in all these compounds. The structures and stereochemistry of all the heptatrienones were confirmed with the help of spectral and analytical data and are described in the experimental section.

V.3.4 Studies on 1,7-carbonyl transpositions of 7,7-bis(methylthio)-1-aryl 2,4,6-heptatrienones.

After the synthesis and structural assignment, the heptatrienones 30 and 31, were subjected to 1,7 carbonyl transposition studies and the results of the present investigation are depicted in the Scheme 9 and Scheme 10. Thus the heptatrienone 30a underwent smooth 1,2-reduction with sodium borohydride to give the corresponding heptatrienol 32a in nearly quantitative yield, which without further purification was subjected to boron trifluoride etherate assisted



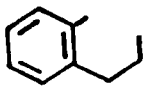
23b 29 a-i 31 a-i

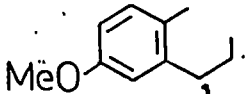
29, 31 a R = C_6H_5; R^1 = H

b R = 4-MeC_6H_4; R^1 = H

c R = 4-MeOC_6H_4; R^1 = H

d R = 4-ClC_6H_4; R^1 = H

e R = R^1 = 

f R = R^1 = 

R^1 = H

g R = 

R^1 = H

h R = 

R^1 = H

i R = CH_3 R^1 = H

Scheme-8

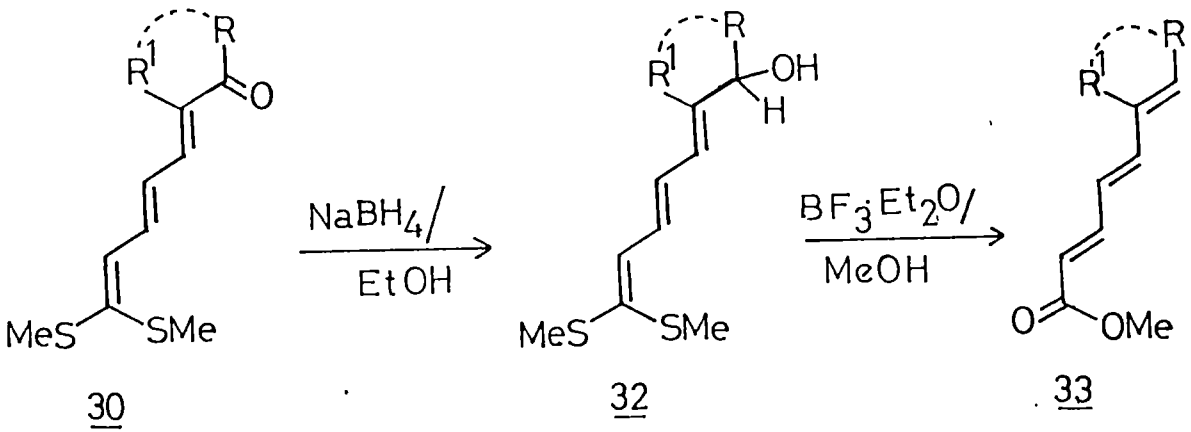
methanolysis and the corresponding transposed triene-ester 33a was obtained in 72% yield. The structure of the methyl 2,4,6-heptatrienoate 33a was confirmed by comparison with authentic sample prepared by reported methods as described in Chapter III of the thesis (m.m.p., superimposable i.r. and n.m.r. spectra). Other bis(methylthio) heptatrienones 30b-g and 31a-g also underwent 1,2-reduction with sodium borohydride, followed by boron trifluoride assisted methanolysis to give the heptatrienoates 33b-g (Scheme 9) and 35a-g (Scheme 10) respectively. However, the 7,7-bis(methylthio)-1-furyl -2,4,6-heptatrienones 30h and 31h though underwent the 1,2-reduction smoothly, failed to give the corresponding triene esters. It appears that the furan ring undergoes ring cleavage or polymerization in the presence of methanolic boron trifluoride etherate.

As a model reaction to examine the feasibility of alkylative 1,7 carbonyl transposition, the heptatrienone 31e was subjected to 1,2-addition with methyl magnesium iodide to give the carbinol acetal 36 in nearly quantitative yields. The triene alcohol 36, without further purification was subjected to boron trifluoride etherate catalyzed methanolysis to afford the methyl 2-methyl-5-(3,4-dihydro-1-methylnaphthyl)-2,4-pentadienoate 37 in 75% yield (Scheme 11). The structure of 37 was fully characterized with the help of spectral and analytical data. Thus its mass spectrum exhibited molecular ion peak at m/z 268(100%) and it was analyzed for $C_{18}H_{22}O_2$. Its i.r.(KBr) spectrum showed bands at 1700 and 1610 cm^{-1} due to ester carbonyl and olefinic groups respectively. The ^1H n.m.r. spectrum exhibited two singlets at δ 1.95(3H) and δ 2.22(3H) due to the methyl groups while the methylene protons appeared as a multiplet

between δ 2.36-2.88(4H). The absorption due to methoxy protons was present at δ 3.70(s,3H), while a double doublet at δ 6.57(1H,J=15Hz, 11Hz) was assigned to the H-4 proton. Other olefinic and aromatic protons were present as a multiplet between δ 6.98-7.41(6H). Thus it has been shown that the hexatrienones 30 and 31 can also be used as precursors for alkylative carbonyl transpositions, though a detailed investigation was not undertaken in the present study.

V.3.5 Synthesis of 7,7-Bis(methylthio)-2,4,6-heptatrienals

The reductive and alkylative 1,7 carbonyl transpositions have been achieved from the heptatrienones 30 or 31 as described in Scheme 9, 10 and 11. An alkylative carbonyl transposition can also be achieved from the heptatrienals 39 (Scheme 12) by reacting them with organo-lithium or grignard reagents followed by solvolysis. To study these transformations as well as the higher carbonyl transpositions, the heptatrienal 39 was prepared employing the sequence of reactions shown in Scheme 12. Thus the pentadienal 23a was reacted with methylmagnesium iodide to give the hexadienol 38 in nearly quantitative yield, which was subjected to formylation under Vilsmeier-Haack reaction conditions to give 7,7-bis(methylthio) 2,4,6-heptatrienal 39a in 56% yield. The structure of 39a was confirmed with the help of spectral and analytical data. Thus it was analyzed for $C_9H_{12}OS_2$. Its i.r.(neat) spectrum showed bands at 1670 and 1600 cm^{-1} due to the carbonyl and olefin functionalities. The structure was further confirmed from its ^1H n.m.r. spectrum (CCl_4). The two singlets at δ 2.31 and δ 2.32 integrating for 3H each were assigned to the two methylthio groups. The H-2 proton appeared at δ 6.01 (dd,J=16Hz,8Hz) thus showing trans configuration around 2,3 double



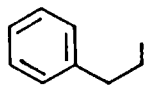
30 32 33

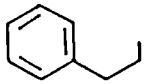
30,32,33 a R = C_6H_5 ; R^1 = H

b R = P-MeC_6H_4 ; R^1 = H

c R = P-$MeOC_6H_4$; R^1 = H

d R = P-ClC_6H_4 ; R^1 = H

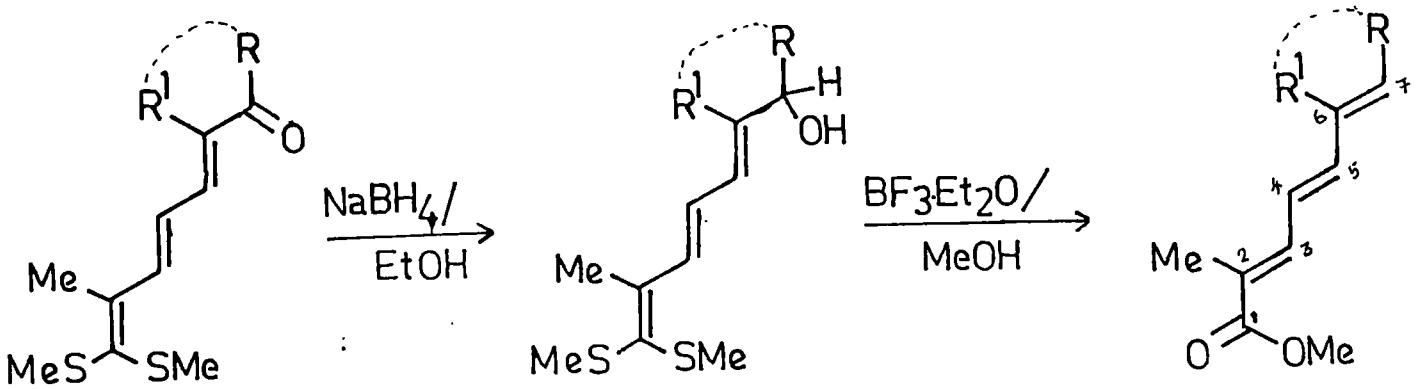
e R = R^1 = 

f R = R^1 = 

g R =  ; R^1 = H

30,32 h R =  ; R^1 = H

Scheme 9



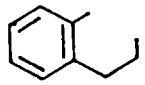
31 a-h 34 a-h 35 a-g

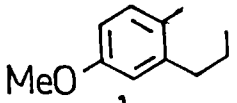
31,34,35 a R = C_6H_5; R^1 = H

b R = 4-MeC_6H_4; R^1 = H

c R = 4-$MeOC_6H_4$; R^1 = H

d R = 4-ClC_6H_4; R^1 = H

e R = R^1 = 

f R = R^1 = 

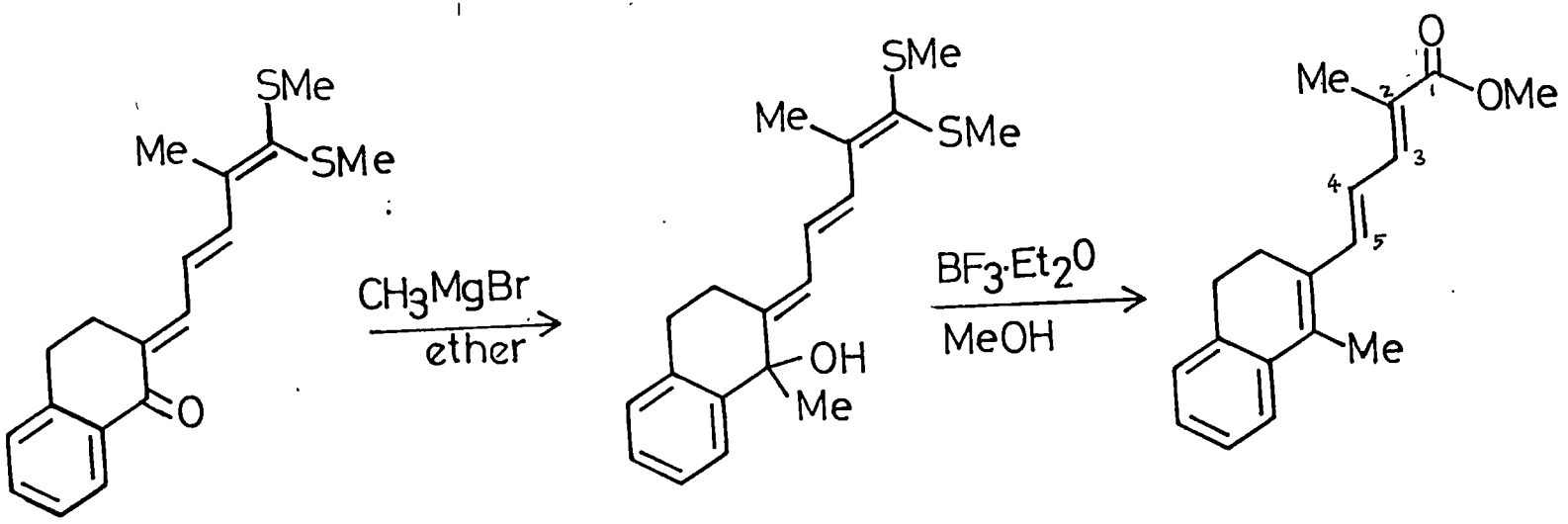
g R = 

; R^1 = H

31, 34 h R = 

; R^1 = H

Scheme 10



31e 36 37

Scheme 11

bond. The signal at δ 6.29(d,1H,J=12Hz) was assigned to H-6 proton while H-4 proton was present at δ 6.36(dd,1H,J=16Hz,12Hz). The signal due to H-5 proton appeared at δ 7.08(dd,1H,J=16Hz,12Hz) while another double doublet (J=15Hz,8Hz) at δ 7.29 was assigned to H-3 proton respectively. The low field signal at δ 9.52(d,1H, J=8Hz) was assigned to the aldehydic proton. The elegant spectral data in which all the protons of the molecule have appeared in highly distinguishable chemical shifts was helpful in the assignment of stereochemistry of the aldehyde. The coupling constants have been consistantly in favour of 2-E, 4-E, geometry of 39a. It is important to note that the polyenaldehydes obtained through Vilsmeier-Haack reactions have generally resulted in a mixture of geometrical isomers (Scheme 7), whereas in the present investigation, the geometries of 39a and other similar compounds described in this chapter have been obtained exclusively as a single isomer with all trans configuration. It appears that the $POCl_3$/DMF complex in association with sulphur lone pair leads to exclusive trans geometry. The validity of this reasoning requires further investigation and the present explanation is only a tentative one. The other heptatrienal 39b was obtained 80% yield from 23b, through the described sequence and its structure and stereochemistry were fully confirmed with the help of spectral and analytical data (experimental).

V.3.6 Reaction of Phenylmagnesium bromide with 7,7-bis(methylthio)-2,4,6-heptatrienals ; An alternative approach to 1,7-carbonyl transposition.

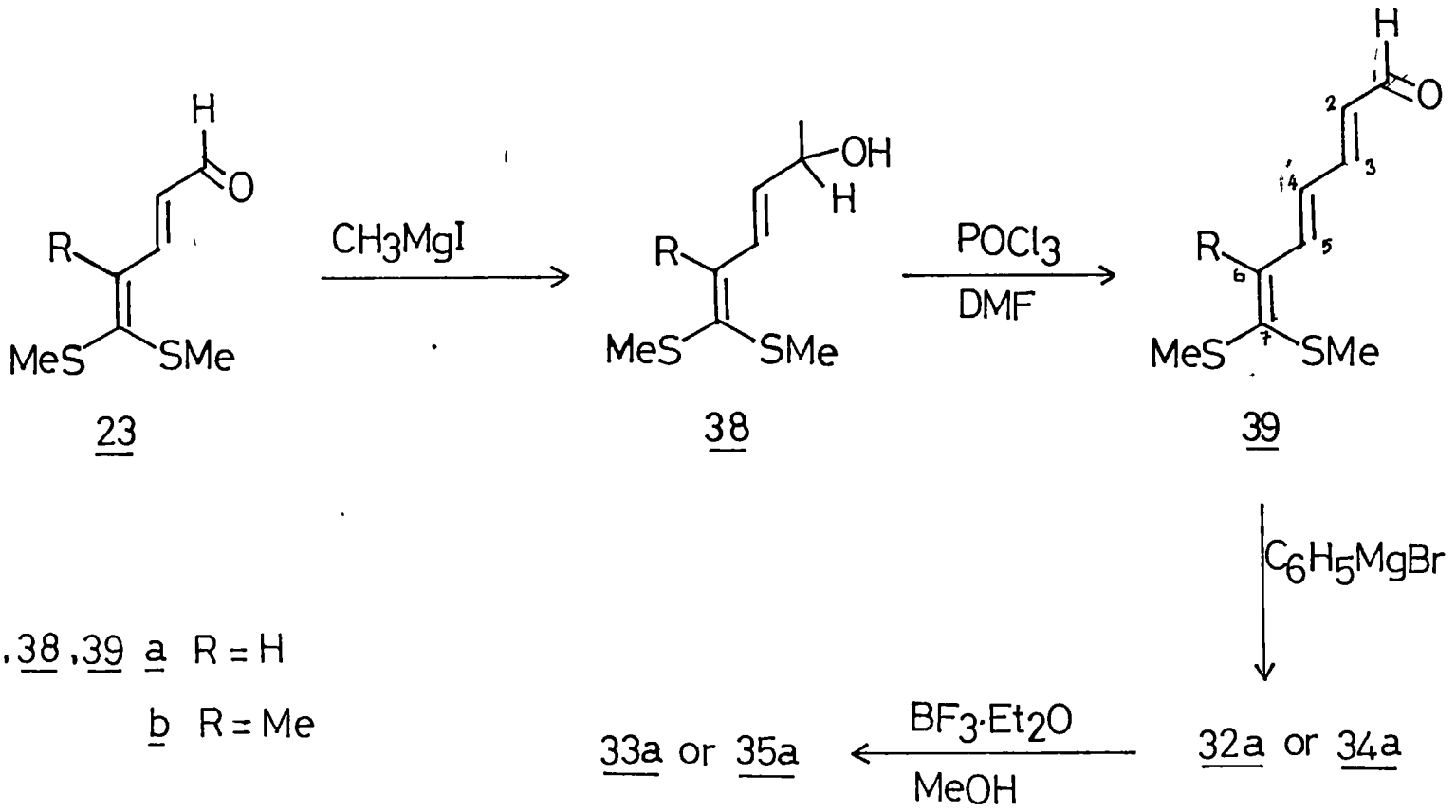
The objective of the synthesis of the heptatrienals 39a and 39b was to study their alkylative 1,7 carbonyl transpositions employing Grignard reagents as well as to use them as precursors in the

synthesis of polyenaldehydes and ketones required in the present studies. The 1,7 carbonyl transposition using Grignard reagents has been achieved as shown in Scheme 12.

The aldehyde 39a was reacted smoothly with phenylmagnesium bromide in a 1,2 fashion to yield the corresponding trienol 32a in nearly quantitative yields. The boron trifluoride etherate assisted methanolysis of the trienol 32a gave the corresponding heptatrienoate 33a in 80% yield (Scheme 12). The triene ester thus obtained was found to be exactly identical with the one prepared before as described in Scheme 9 (m.m.p., superimposable i.r., n.m.r. spectra). Similarly, 35a was prepared under identical conditions (Scheme 12) from 39b in 75% yield and found to be identical with the same triene ester which was prepared earlier (Scheme 10).

V.3.7 Synthesis of 1-Aryl(or cycloalkyl)-9,9-Bis(methylthio)-2,4,6,8-nonatetraenones

In the preceeding paragraph, synthesis of the heptatrienal 39 has been described which have been shown to undergo alkylative 1,7 carbonyl transposition. They have been now used for further condensation with active methylene ketones to give the corresponding tetraenones 40, which are suitable candidates for 1,9 carbonyl transposition studies (Scheme 13). Thus 39a was reacted with acetophenone in the presence of sodium methoxide in methanol to afford 9,9-Bis(methylthio)-1-aryl-2,4,6,8-nonatetraen-1-one 40a in 92% yield. The structure of 40a was elucidated from its analytical and spectral data. Thus it was analyzed for $C_{17}H_{18}OS_2$ (302.4) and in its i.r. (neat) spectrum, it exhibited bands at



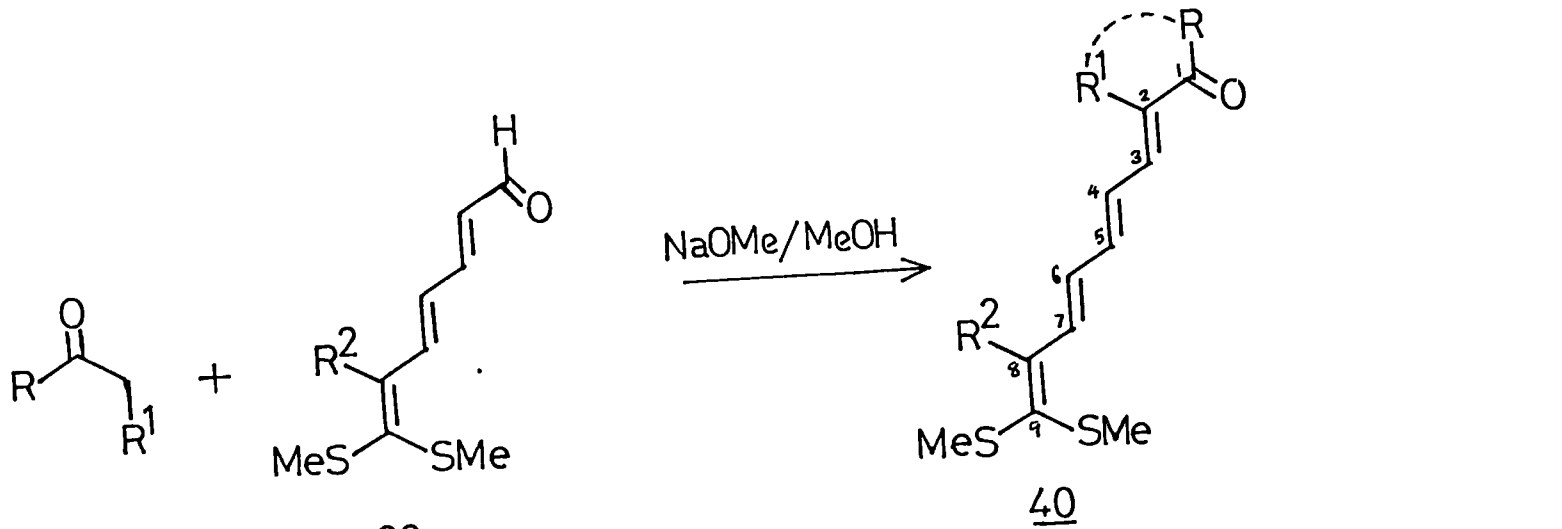
23 38 39

23, 38, 39 a R = H

b R = Me

33a or 35a ← 32a or 34a

Scheme 12



29 39 40

29a R = C_6H_5 R^1 = H

d R = 4-ClC_6H_4 R^1 = H

e R = R^1 = MeO

40a R = C_6H_5 ; R = R^2 = H

b R = C_6H_5 ; R^1 = H ; R^2 = Me

c R = 4-ClC_6H_4 ; R^1 = H ; R^2 = Me

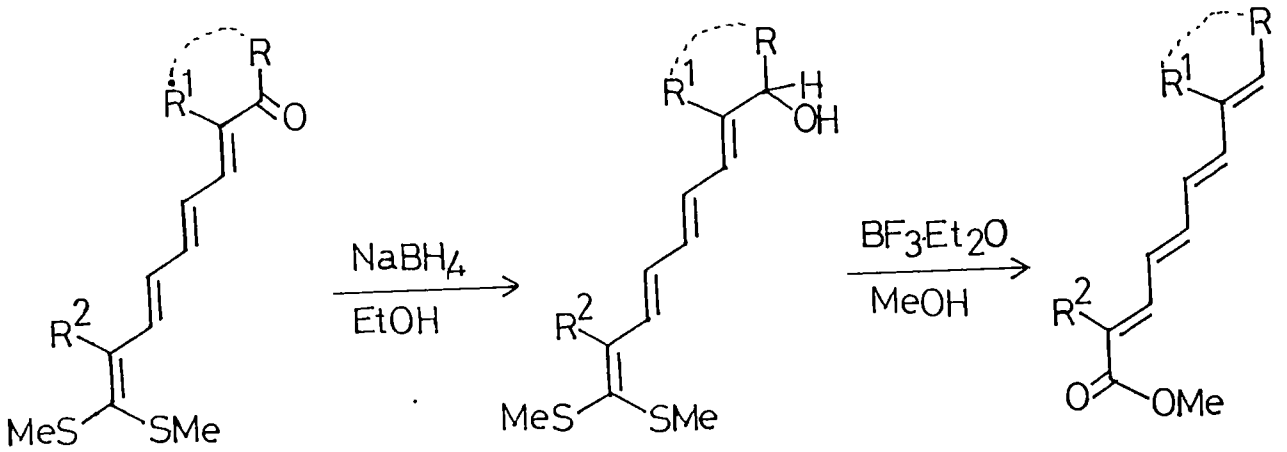
d R = R^1 = MeO ; R^2 = Me

Scheme 13

1652 and 1598 cm^{-1} which were atributed to the carbonyl group and the olefinic double bonds respectively. The structure was further confirmed by its ^1H n.m.r.(CCl_4) spectrum. The two singlets at δ 2.33(3H) and δ 2.34(3H) were assigned to the two methylthio groups, while the doublet (J=11Hz) at δ 6.29 was due to the H-8 proton. The H-2, H-4, H-5, H-6 and H-7 protons were present as a complex multiplet between δ 6.50-7.18. Aromatic protons along with H-3 also appeared as a multiplet from δ 7.23-8.01. The stereochemistry was assumed to be 2-E, 4-E,6-E on the basis of the assignments made earlier for analogous systems. Similarly, the nonatetraenones 40b-d were prepared from 39b and acetophenone, 4-chloroacetophenone and 6-methoxy tetralone respectively in 70-78% overall yields. The analytical and spectral data of 43b-d were in agreement with the assigned structures and are described in the experimental section.

V.3.8 1,9-Carbonyl Transposition Studies

After the synthesis and characterization of the bis(methylthio) nonatetraenyl ketones 40, their 1,9 carbonyl transposition studies were undertaken (Scheme 14). The tetraenone 40a was reduced with sodium borohydride in ethanol to give the corresponding tetraenol 41a in nearly quantitative yield, which on subsequent boron trifluoride etherate assisted methanolysis yielded the corresponding methyl 9-phenyl-2,4,6,8-nonatetraenoate 42a in 70% yield. The structure of 42a was confirmed from its analytical and spectral data. Thus it was analyzed for $C_{16}H_{16}O_2$ and its i.r.(KBr) spectrum exhibited bands at 1708 and 1618 cm^{-1} due to the ester carbonyl group and the olefinic double bonds respectively. The structure was further confirmed by its ^1H n.m.r. spectrum. The singlet at

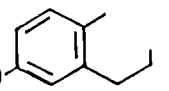


40 41 42

40, 41, 42 a $R = C_6H_5$; $R^1 = R^2 = H$

b $R = C_6H_5$; $R^1 = H$; $R^2 = Me$

c $R = 4\text{-}ClC_6H_4$; $R = H$; $R^2 = Me$

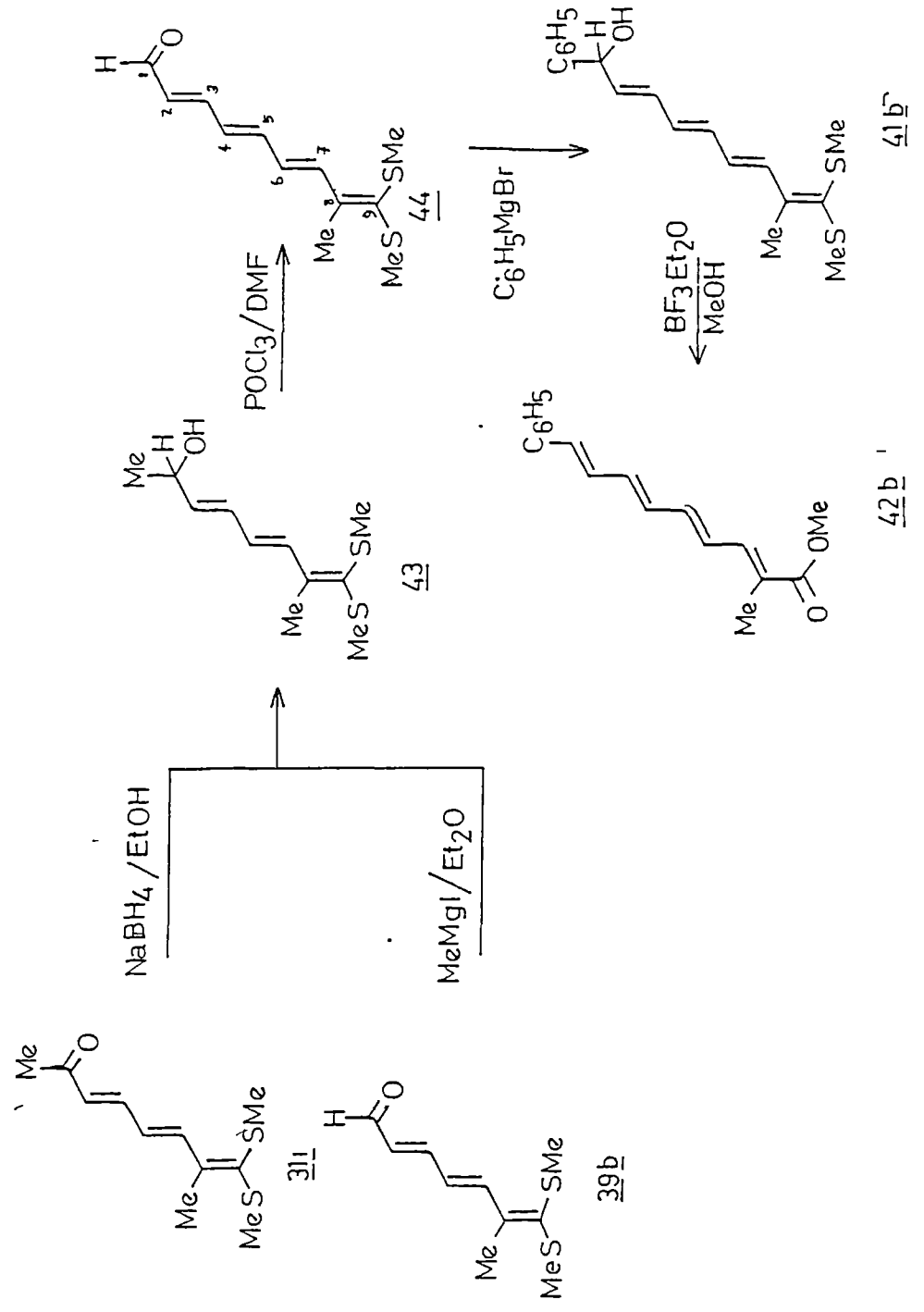
d $R = R^1 =$  ; $R^2 = Me$

Scheme 14

δ3.81(3H) was assigned to the methoxy protons. The H-2 proton appeared at δ 5.89(d,1H,J=15Hz) which was in confirmity with the trans geometry. The multiplet between δ 6.22-6.89(7H) were due to the various olefinic protons, whereas the other multiplet between δ7.02-7.25(5H) was assigned to the aromatic protons. The ester 42a was assumed to have all trans stereochemistry on the basis of earlier observations. The other tetraenoates 42b-d were similarly obtained in 70-80% overall yields. The spectral and analytical data of these compounds have been in agreement with the assigned structures and are described in the experimental section.

V.3.9 Synthesis of 9,9-Bis(methylthio)-8-methyl 2,4,6,8-nonatetraenal (44) and its 1,9 carbonyl transposition

The nonatetraenaldehyde 44 was prepared by employing the sequence of reactions described in Scheme 15. The intermediate alcohol 43 was obtained either by the reduction of the octatrieneone 31i, the preparation of which has been already described, or by reacting the heptatrienaldehyde 39b with methylmagnesium iodide. The alcohol 43 was subjected to formylation under Vilsmeier-Haack reaction conditions, and after work-up, 9,9-bis(methylthio)-8-methyl-2,4,6,8-nonatetraenal (44) was obtained in 70% yield. The structure of 44 was confirmed from its analytical and spectral data. Thus it was analyzed for $C_{12}H_{16}OS_2$(240.6) and it exhibited molecular ion peak in its mass spectrum at m/z 240(100%). The i.r. (neat) spectrum of 44 showed a strong band at 1675 cm^{-1} due to aldehyde functionality, whereas the bands at 1612 and 1585 cm^{-1} were due to the olefinic double bonds. The structure was further



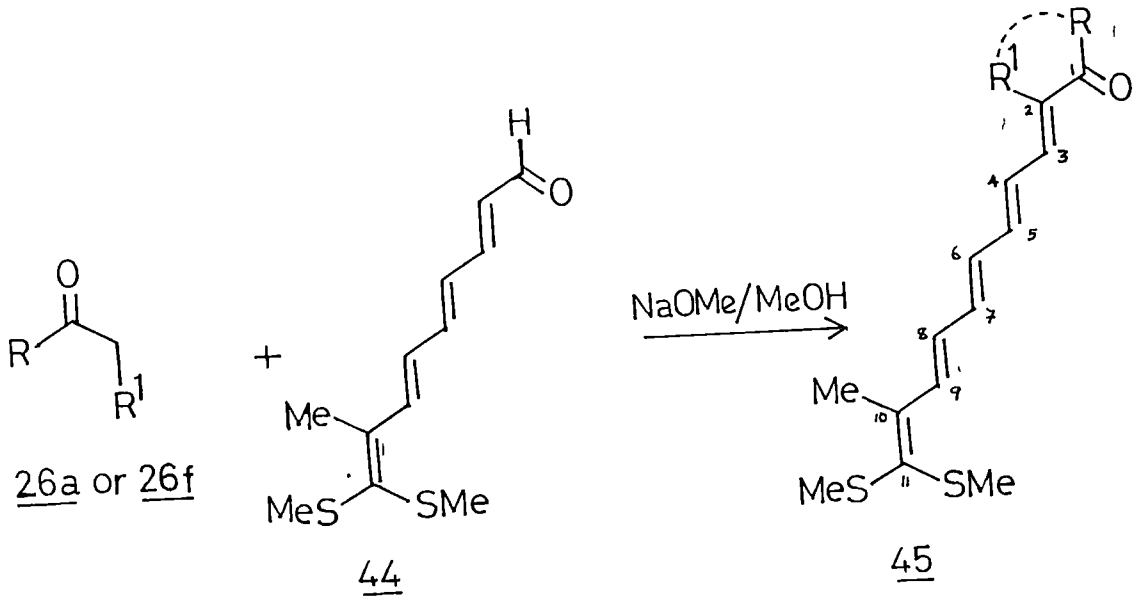
Scheme-15

confirmed by its ^1H n.m.r.(CCl_4) spectrum. The singlet (3H) at δ 2.11 was assigned to the methyl group, while the protons of the methylthio groups absorbed at δ 2.25(3H) and δ2.34(3H). The H-2 proton appeared as a double doublet (J=15Hz,8Hz) at δ 5.98 while the multiplet between δ 6.23-7.21 was assigned to four olefinic protons. The doublet (J=15Hz) at δ 7.42 was assigned to H-7 proton whereas the absorption due to aldehydic proton appeared at δ 9.49 (J=8Hz). The compound was assigned 2-E,4-E,6-E geometry, on the basis of n.m.r. data as well as in analogy with the dienaldehyde 23 and trienaldehyd 39 described earlier.

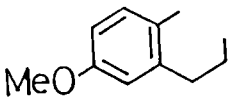
As an alternative approach towards 1,9 carbonyl transposition, the tetraenaldehyde 44 was reacted with phenylmagnesium bromide, when the corresponding alcohol 41b was obtained in quantitative yield, which was subsequently subjected to boron trifluoride etherate catalyzed methanolysis to afford the corresponding nonatetraenoate 42b in 70% yield. The nonatetraenoate 42b obtained by this reaction was found to identical with that obtained by reductive 1,9 carbonyl transposition of 40b (Scheme 14) (m.m.p., superimposable i.r. and n.m.r. spectra). Thus the synthesis of 42b from the tetraenal 44 further confirmed its structure. It is therefore possible to evolve at least two alternative methods for 1,9 carbonyl transposition, one through the tetraenyl ketone 40 and the other through the aldehyde 44.

V.3.10 Synthesis of 11,11-Bis(methylthio)-1-aryl(or cycloalkyl)-10-methyl 2,4,6,8,10-undecapentaene-1-ones

The pentaenones 45a and 45b were required as precursors for the study of 1,11 carbonyl transposition studies. They were conveniently



26,45 a $R = C_6H_5$; $R^1 = H$

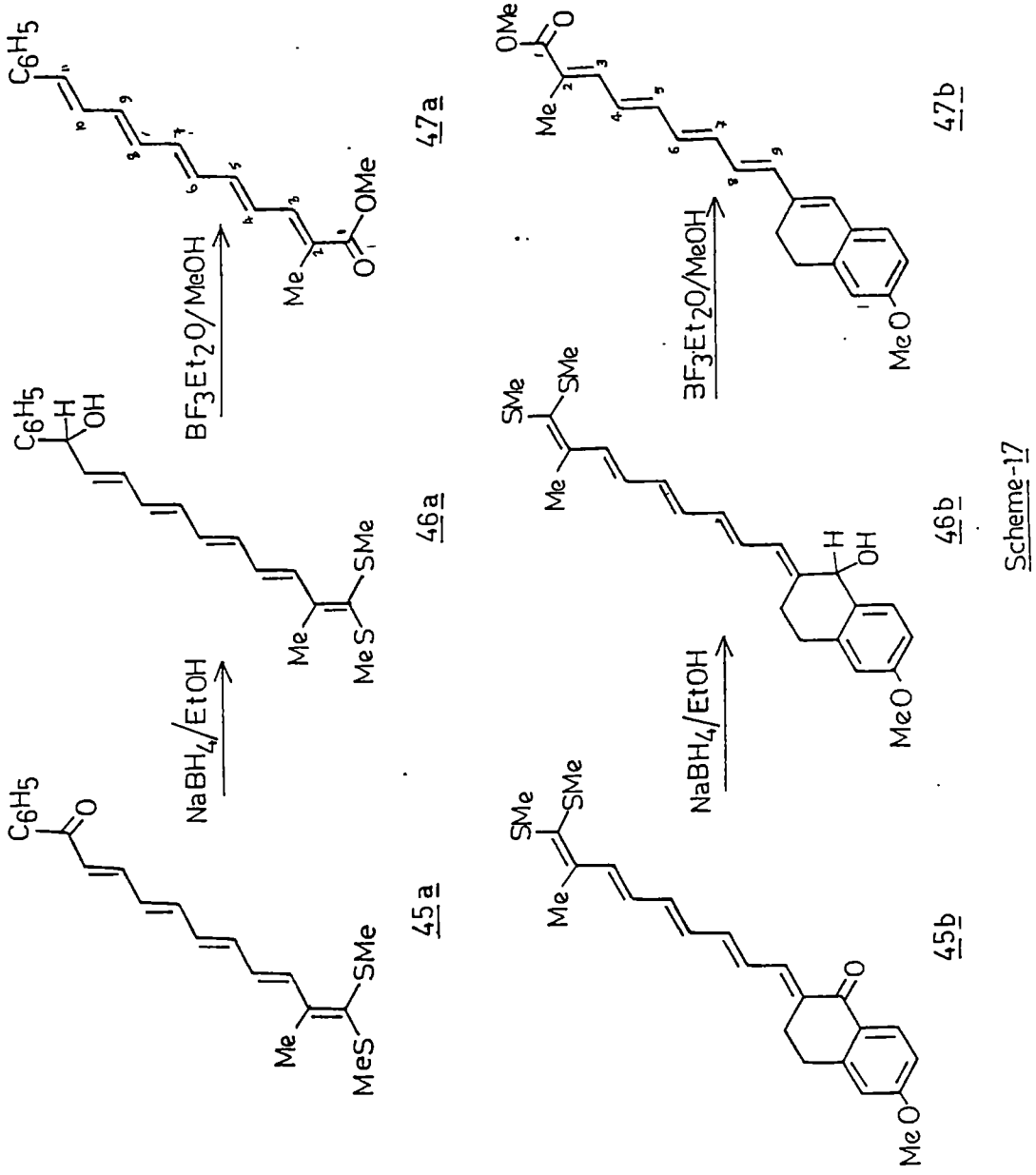
b $R = R^1 =$ 

Scheme 16

prepared by the condensation of the tetraenaldehyde 44 with acetophenone 26a and 6-methoxytetralone 26f respectively (Scheme 16). Thus when the tetraenaldehyde 44 was condensed with acetophenone in the presence of sodium methoxide and methanol the 11,11-bis (methylthio)-1-phenyl-9-methyl 2,4,6,8,10-undecapentaene-1-one 45a was obtained in 90% yield. The structure of 45a was confirmed with the help of spectral and analytical data. Thus 45a was analyzed for $C_{20}H_{22}OS_2$(342,6) and its i.r.(neat) spectrum showed bands at 1655 and 1595 cm^{-1} which were assigned to the carbonyl group and the olefinic double bond respectively. The structure was further confirmed from its ^1H n.m.r.(CCl_4) spectrum. The singlet at δ 2.00 was due to the CH_3 protons while the two methylthio groups were present at δ 2.13(s,3H) and δ 2.23(s,3H) respectively. The olefinic protons along with the aromatic protons appeared as a complex multiplet between 6.15-8.20(13H). The product was assigned 2-E, 4-E,6-E,8-E geometry in analogy with assignments made earlier for similar polyenones prepared by similar sequence of reactions. Similarly the condensation of the nonatetraenal 44 with 6-methoxytetralone gave the pentaenones 45b in 95% yield. The structure and stereochemistry was confirmed with the help of spectral and analytical data and are described in the experimental section.

V.3.11 1,11-Carbonyl Transposition Studies

After synthesis and characterization for the bis(methylthio) undecapentaenones 45, their 1,11 carbonyl transposition studies were undertaken. The pentaenone 45a underwent smooth 1,2-reduction with sodium borohydride in methanol to afford the bis(methylthio)pentaenols 46a in nearly quantitative yield. The polyene


C6H5
O
Me
MeS
SMe
45a
NaBH4/EtOH
C6H5
H
OH
46a
BF3Et2O/MeOH
47a
OMe
45b
46b
47b
MeO
3F3Et2O/MeOH

Scheme-17

alcohol, when subjected to boron trifluoride etherate assisted methanolysis yielded the corresponding methyl 11-phenyl-2-methyl 2,4,6,8,10 undecapentaenoate 47a in 85% yield (Scheme 17). The structure of the polyene ester 47a was confirmed with the help of its spectral and analytical data. Thus it was analyzed for $C_{19}H_{20}O_2$(280.4) and in its i.r.(KBr) spectrum exhibited bands at 1705 and 1617 cm^{-1} due to the ester carbonyl and olefinic double bonds respectively. Further proof for the structure was obtained from ^1H n.m.r.($CDCl_3$) spectrum, in which the methyl group appeared as a singletat δ 2.00(3H) and the methoxy protons were present at δ 3.36(s,3H). The multipletat 6.30-7.10(8H) was assigned to eight olefinic protons, while the aromatic protons along with an olefinic proton absorbed as a multiplet between δ7.10-7.85(6H). The polyene ester 47a was assigned all trans geometry in analogy with the other polyene esters prepared earlier. Similarly the bis(methylthio) pentaenone 45b also underwent 1,11 carbonyl transposition under the described reaction conditions to give the polyene ester 47b in 80% yield (Scheme 17). The structure and stereochemistry of 47b was confirmed with the help of its spectral and analytical data, and are described in the experimental section. Further proof for stereochemical assignment of polyenes 42, 44, 45 and 47 would be obtained from their high resolution ^1H n.m.r. and ^{13}C n.m.r. spectra, which is awaited.

V.4 EXPERIMENTAL

The general experimental conditions were same as in Chapter II. The ^1H n.m.r. spectra were recorded on a Varian EM 390(90 MHZ) or on a Varian XL 300(300 MHz) spectrometer.

Starting Materials

The commercial samples of acetone, ethylmethyl ketone, methylpropyl ketone, acetophenone, p-methylacetophenone, p-methoxyacetophenones, p-chloroacetophenone, tetralone, 6-methoxytetralone, 2-acetylthiophene and 2-acetylfuran were purified before use.

The previously reported ketene S,S-acetals 4,4-bis(methylthio)-3-butene-2-one (21a) m.p. 66-67°C[22], 4,4-bis(methylthio)-3-methyl-3-butene-2-one 21b, b.p. 68°C(0.1 mm)[23] and 4,4-bis(methylthio)-3-ethyl-3-buten-2-one 21c[23] were prepared by the general method described in Chapter II.

5,5-Bis(methylthio)-2,4-pentadienals (23a-c); General Procedure:

To a solution of α-oxoketene dithioacetal 21 (0.01 mol) in absolute ethanol, excess sodium borohydride (0.76g, 0.02 mol) was added slowly and the reaction mixture was then refluxed for 1.5 hrs. The mixture was cooled and poured over saturated ammonium chloride solution (200 ml), extracted with ether (4x50 ml) washed with water (2x50 ml) dried (Na_2SO_4) and evaporated to give the 4,4-bis(methylthio)-3-butene-2-ols 22 in nearly quantitative yields which were used as such for the next step without further purification. The hydroxy dithioacetal 22 (0.01 mol) in 5 ml DMF was added slowly to a well cooled (0°C) and stirred Vilsmeier reagent [prepared by adding phosphorous oxychloride (3.83g, 0.025 mol) to N,N-dimethyl formamide (20 ml, 0.25 mol) with stirring and cooling and further stirring for 30 min at room temperature]. The reaction mixture was stirred for 10-15 hrs for completion of reaction after which it was poured over crushed ice (300g) followed by slow addition of cold saturated potassium carbonate solution (100 ml) to liberate the aldehyde. The reaction mixture was then extracted with ether (4x100 ml) and the combined ether extracts were washed with water, dried (Na_2SO_4) and evaporated to give the crude pentadienals (23) which were further purified by column chromatography over silica gel using EtOAc:hexane (1:20) as eluent.

5,5-Bis(methylthio)-2,4-pentadienal (23a) was obtained as orange viscous liquid; yield 59%; spectral data described in text. (Found: C,48.39;

H,5.55. Calc. for $C_7H_{10}OS_2$(174.3): C,48.24; H,5.78%).

5,5-Bis(methylthio)-4-methyl-2,4-pentadienal (23b) was obtained as orange viscous liquid; yield 70%; i.r.(neat): ν_{max} 1660, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.11(s,3H,$C\underline{H}_3$); 2.33(s,3H,$SC\underline{H}_3$); 2.42(s,3H,$SC\underline{H}_3$); 6.11(dd,1H,J=16Hz,8Hz,$\underline{H}2$); 8.06(d,1H,J=16Hz,$\underline{H}$-3); 9.58(d,1H,J=8Hz, $C\underline{H}O$). (Found: C,51.30; H,6.34. Calc. for $C_8H_{12}OS_2$(188.3): C,51.02; H,6.43%). m/z 188(M^+,5%); 141(M^+-47,100%).

5,5-Bis(methylthio)-4-ethyl-2,4-pentadienal (23c) was obtained as orange liquid; yield 74%; i.r.(neat): ν_{max} 1710, 1660, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.18(t,3H,J=7Hz,$CH_2C\underline{H}_3$); 2.47(s,3H,$SC\underline{H}_3$); 2.58 (s,3H,$SC\underline{H}_3$); 2.78(q,2H,J=7Hz,$C\underline{H}_2CH_3$); 6.23(dd,1H,J=16Hz,7Hz,$\underline{H}$-2); 8.12(d,1H,J=16Hz,$\underline{H}$-3); 9.71(d,1H,7Hz,$C\underline{H}O$). (Found: C,53.56; H,6.86. Calc. for $C_9H_{14}OS_2$(202.3): C,53.42; H,6.97%). m/z 202(M^+,31%); 155(M^+-47,100%).

1,5-Carbonyl transpositions of 1,1-bis(methylthio)-2,4-pentadienals 23: Synthesis of Methyl 5-phenyl-2,4-pentadienoates (25a-c); General Procedure:

To a well stirred and cooled solution of phenyl magnesium bromide (0.015 mol) in ether (30 ml), the pentadienal 23 (0.01 mol) in ether (20 ml) was added slowly, the reaction mixture was stirred at room temperature for 1 hr, poured into a saturated ammonium chloride solution (100 ml), extracted with ether (2x50 ml), washed with water, dried (Na_2SO_4) and evaporated to give the crude dienol 24, which were used as such for further transformations, without purification.

The crude diene alcohol 24 (0.01 mol) was dissolved in absolute methanol (50 ml) and boron trifluoride etherate (2 ml) was added

with stirring, the mixture was then refluxed for 15-20 hrs. The cooled mixture was added to a saturated solution of sodium bicarbonate (100 ml), extracted with chloroform (2x50 ml), washed with water, dried (Na_2SO_4) and evaporated to give the crude pentadienoates 25 which were further purified by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluent.

Methyl 1-phenyl 2,4-pentadienoate (25a) was isolated as colourless crystalline solid; yield 90%; m.p. 70-71°C(reported m.p. 71°C)[24]. Spectral data reported earlier [25](superimposable i.r. and n.m.r. data). (Found: C,76.67; H,6.59. Calc. for $C_{12}H_{12}O_2$(188.2): C,76.56; H,6.43%).

Methyl 1-phenyl-2-methyl-2,4-pentadienoate (25b) was isolated as colourless crystalline solid; yield 85%; m.p. 86°C (reported m.p. 86-87°C)[26]. Spectral data reported earlier[25] (superimposable i.r. and n.m.r.spectra). (Found: C,77.25; H,6.81. Calc. for $C_{13}H_{14}O_2$ (202.2): C,77.21; H,6.98%).

Methyl 1-phenyl-2-ethyl-2,4-pentadienoate (25c) was obtained as a pale yellow liquid; yield 87%; i.r.(neat): ν_{max} 1720, 1620 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.09(t,3H,J=7Hz,$CH_2\underline{CH_3}$); 2.45(q,2H,J=7Hz,$\underline{CH_2}CH_3$); 3.68(s,3H,$O\underline{CH_3}$); 6.79-7.54(m,$8H_{arom+olefin}$). (Found: C,77.66; H,7.53. Calc. for $C_{14}H_{16}O_2$(216.2): C,77.77; 7.46%). m/z 216(93%).

7,7-Bis(methylthio-1-aryl/alkyl(or cycloalkyl)-2,4,6-heptatriene-1-ones 30a-i and 31a-i; General Procedure:

To a well stirred and cooled solution of sodium methoxide (0.54g, 0.01 mol) in methanol (20 ml),a mixture of dienaldehyde 23a or 23b (0.005 mol) and appropriate active methylene ketone 29 (0.005 mol)

in methanol (5 ml) was added dropwise and the mixture was stirred at room temperature for 6-8 hrs. The solid separated(30a,b,e,f, 31a, e, g,h)was filtered, washed with water and recrystallyzed from methanol to give pure 30 or 31. In cases where the products were viscous semisolid (30c,d,g-i, 31b-d,f), the reaction mixture was diluted with water (50 ml), extracted with chloroform (3x30 ml), washed with water (2x50 ml), dried (Na_2SO_4), evaporated and the crude products thus obtained were column chromatographed over silica gel using ethyl acetate:hexane (1:20) as eluent to give the pure 30 or 31.

7,7-Bis(methylthio)-1-phenyl-2,4,6-heptatriene-1-one (30a) was obtained as deep red crystals; yield 95%; m.p. 62°C; spectral data described in the text. (Found: C,65.30; H,5.97. Calc. for $C_{15}H_{16}OS_2$(276.4): C,65.17; H,5.83%). m/z 276(M^+,10%); 261(M^+-15,16%).

7,7-Bis(methylthio)-1-(4-methylphenyl)-2,4,6-heptatriene-1-one(30b) was obtained as reddish brown crystalline solid; yield 92%; m.p. 68-70°C; i.r.(KBr): ν_{max} 1640, 1600, 1575 cm^{-1}; ^1H n.m.r.(CCl_4): δ2.31(s,3H,CH_3); 2.32(s,3H,SCH_3); 2.33(s,3H,SCH_3); 6.31(d,1H,J=11Hz, H6); 6.33(dd,1H,J=15Hz,11Hz,H-4); 6.82(d,1H,J=15Hz,H-2); 7.00-7.91(m, $6H_{arom+olefin}$). (Found: C,66.30; H,6.40. Calc. for $C_{16}H_{18}OS_2$(290.4): C,66.16; H,6.25%).

7,7-Bis(methylthio)-1-(4-methoxyphenyl)-2,4,6-heptatriene-1-one(30c) was obtained as reddish brown semisolid; yield 90%; i.r.(neat): ν_{max} 1638, 1598 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.33(s,3H,SCH_3); 2.34(s,3H, SCH_3); 3.82(s,3H,OCH_3); 6.32(d,1H,J=11Hz,H 6); 6.34(dd,1H,J=15Hz,11Hz, H-4); 6.83(d,1H,J=15Hz,H-2); 7.00-8.01(m,$6H_{arom+olefin}$). (Found: C,62.80; H,5.81. Calc. for $C_{16}H_{18}O_2S_2$ (306.4): C,62.71; H,5.92%).

7,7-Bis(methylthio)-1-(4-chlorophenyl)-2,4,6-heptatriene-1-one (30d) was obtained as reddish brown semisolid; yield 94%; i.r.(Neat): γ_{max} 1640, 1600 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.32(s,6H,SCH_3); 6.23(d,1H, J=11Hz,H-6); 6.24(dd,1H,J=16Hz,11Hz,H-4); 6.81(d,1H,J=16Hz,1H,H-2); 7.22(dd,1H,J=16H,11Hz,H-5); 7.25-7.95(m,$5H_{arom+olefin}$). (Found: C,57.91; H,5.30. Calc. for $C_{15}H_{15}ClOS_2$(310.8): C,57.77; H,5.17%).

2-[1,1-Bis(methylthio)-1,3-pentadienylidene]-1-tetralone (30e) was obtained as orange crystalline solid; yield 92%; m.p. 102°C; i.r. (KBr): γ_{max} 1648, 1599 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.32(s,6H,SCH_3); 2.86(s,4H,CH_2); 6.36(d,1H,J=11Hz,H-2); 6.48(dd,1H,J=15Hz,11Hz,H-4); 7.00-8.21(m,$6H_{arom+olefin}$). (Found: C,67.61; H,6.09. Calc. for $C_{17}H_{18}OS_2$ (302.5): C,67.50; H,6.00%).

2-[1,1-Bis(methylthio)-1,3-pentadienylidene]-6-methoxy-1-tetralone (30d) was isolated as orange crystalline solid; yield 93%; m.p. 136°C; i.r. (KBr): γ_{max} 1647, 1603, 1571 cm^{-1}; ^1H n.m.r.(CCl_4)(300 MHz); δ 2.38 (s,3H,SCH_3); 2.39(s,3H,SCH_3); 2.85-2.95(m,4H,CH_2); 3.82(s,3H,OCH_3); 6.42(d,1H,J=11Hz,H-2); 6.56(dd,1H,J=16Hz,12Hz,H-4); 6.70-6.87(m, $2H_{arom}$); 7.27(dd,1H,J=15Hz,11Hz,H 3); 7.46(d,1H,J=12Hz,1H,H-5); 8.07 (d,J=8Hz,$1H_{arom}$). (Found: C,65.15; H,6.21. Calc. for $C_{18}H_{20}O_2S_2$(332.5): C,65.02; H,6.06%). m/z 332(M^+,13%); 317(M^+-15,24%).

7,7-Bis(methylthio)-1-(2-thienyl)-2,4,6-heptatriene-1-one (30g) was isolated as reddish brown semisolid; yield 90%; i.r.(neat): γ_{max} 1640, 1578 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.33(s,6H,SCH_3); 6.32(d,1H,J=15Hz,H-2); 6.33(dd,1H,J=15Hz,11Hz,H 4); 6.79(d,1H,J=11Hz,H 6); 7.05-7.85(m, $5H_{thienyl+olefinic}$). (Found: C,55.35; H,5.21. Calc. for $C_{13}H_{14}OS_3$(282.4): C,55.28; H,5.00%). m/z 282(M^+,9%); 267(M^+-15,15%).

7,7-Bis(methylthio)-1-(2-furyl)-2,4,6-heptatriene-1-one(30h) was isolated as reddish brown semisolid; yield 94%; i.r.(neat): ν_{max} 1645, 1580 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.33(s,6H,SCH_3); 6.31(d,1H,J=11Hz,H-2); 6.32(dd,1H,J=15Hz,11Hz,H-4); 6.79(d,1H,J=15Hz,H-6); 7.03-7.71(m, $5H_{furyl+olefinic}$). (Found: C,58.71; H,5.45. Calc. for $C_{13}H_{14}O_2S_2$ (266.4): C,58.62; H,5.30%). m/z 266(M^+,13%); 251(M^+-15,19%).

8,8-Bis(methylthio)-3,5,7-octatriene-2-one (30i) was obtained as reddish brown semisolid; yield 80%; i.r.(neat): ν_{max} 1670, 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.25(s,3H,CH_3); 2.32(s,6H,SCH_3); 5.98-6.49(m,3H,H-3, H-5 and H-7); 6.75-7.40(m,2H,H-4 and H 6). (Found: C,56.23; H,6.66. Calc. for $C_{10}H_{14}OS_2$(214.3): C,56.03; H,6.58%).

7,7-Bis(methylthio)-6-methyl-1-phenyl-2,4,6-heptatriene-1-one (31a) was isolated as reddish brown crystalline solid; yield 90%; m.p. 71°C; i.r.(KBr): ν_{max} 1640, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.16(s,3H, CH_3); 2.27(s,3H,SCH_3); 2.34(s,3H,SCH_3); 6.47(dd,1H,J=15Hz,11Hz,H-4); 6.96(d,1H,J=15Hz,H-2); 7.33-8.00(m,$7H_{arom+olefin}$). (Found: C,66.26; H,6.35. Calc. for $C_{16}H_{18}OS_2$(290.4): C,66.16; H,6.24%). m/z 290(M^+,5%); 275(M^+-15,17%).

7,7-Bis(methylthio)-6-methyl-1-(4-methylphenyl)-2,4,6-heptatriene-1-one (31b) was isolated as reddish brown semisolid; yield 88%; i.r. (neat): ν_{max} 1680, 1650, 1605 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.15(s,3H,CH_3); 2.31(s,3H,Ar-CH_3); 2.41(s,3H,SCH_3); 2.43(s,3H,SCH_3); 6.50(dd,1H,J=15Hz, 11Hz,H-4); 6.89-7.95(m,$7H_{arom+olefin}$). (Found: C,67.27; H,6.51. Calc. for $C_{17}H_{20}OS_2$(304.4): C,67.07; H,6.62%).

7,7-Bis(methylthio)-6-methyl-1-(4-methoxyphenyl)-2,4,6-heptatriene-1-one(31c) was isolated as reddish brown semisolid; yield 92%; i.r. (KBr): ν_{max} 1675, 1600 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.20(s,3H,CH_3); 2.31

(s,3H,SC$\underline{H}_3$); 2.38(s,3H,SC$\underline{H}_3$); 3.85(s,3H,OC$\underline{H}_3$); 6.56(d,1H,J=15Hz,11Hz, $\underline{H}$-4); 6.75-8.01(m,7H$_{arom+olefin}$). (Found: C,63.80; H,6.31. Calc. for $C_{17}H_{20}O_2S_2$(320.4): C,63.71; H,6.29%). m/z 320(M^+,2%); 305(M^+-15,4%).

7,7-Bis(methylthio)-6-methyl-1-(4-chlorophenyl)-2,4,6-heptatriene-1-one (31d) was isolated as reddish brown semisolid; yield 90%; i.r. (neat): ν_{max} 1658, 1591 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.20(s,3H,C$\underline{H}_3$); 2.31 (s,3H,SC$\underline{H}_3$); 2.33(s,3H,SC$\underline{H}_3$); 6.51(dd,1H,J=15Hz,11Hz,$\underline{H}$-4); 6.90(d,1H, 15Hz,$\underline{H}$-2): 7.26-8.09(m,6H$_{arom+olefin}$). (Found: C,59.26; H,5.21. Calc. for $C_{16}H_{17}ClOS_2$(324.8): C,59.15; H,5.09%).

2-[1,1-Bis(methylthio)-2-methyl-1,3-pentadienylidene]-1-tetralone(31e) was isolated as reddish brown crystallien solid; yield 94%; m.p.89-90°C; i.r.(KBr): ν_{max} 1647, 1599 cm^{-1}; ^1H n.m.r.(CCl_4,300MHz);δ2.22(s,3H, C$\underline{H}_3$); 2.30(s,3H,SC$\underline{H}_3$); 2.40(s,3H,SC$\underline{H}_3$); 2.92-2.93(m,4H,C$\underline{H}_2$); 6.65(dd, 1H,J=15Hz,12Hz,$\underline{H}$-4); 7.25(d,J=7.5Hz,1H$_{arom}$); 7.34(t,J=7.5Hz,1H$_{arom}$); 7.46(t,J=7.5Hz,1H$_{arom}$); 7.56(d,1H,J=12Hz,$\underline{H}$ 5); 7.77(d,1H,J=15Hz,$\underline{H}$ 3); 8.10(d,J=7.5Hz,1H$_{arom}$). (Found: C,68.40; H,6.21. Calc. for $C_{18}H_{20}OS_2$ (316.5): C,68.31; H,6.37%). m/z 316(M^+,5%); 301(M^+-15,43%).

2-[1,1-Bis(methylthio)-2-methyl-1,3-pentadienylidene]-6-methoxy-1-tetralone (31f) was isolated reddish brown semisolid; yield 94%; i.r.(KBr): ν_{max} 1640, 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.18(s,3H,C$\underline{H}_3$); 2.22(s,3H,SC$\underline{H}_3$); 2.31(s,3H,SC$\underline{H}_3$); 2.72-2.89(m,4H,C$\underline{H}_2$); 6.30-6.81(m, 3H$_{arom+olefin}$); 7.38(d,1H,J=12Hz,$\underline{H}$-5); 7.65(d,1H,J=15Hz,$\underline{H}$ 3); 7.92 (d,1H,J=7.5Hz,1H$_{arom}$). (Found: C,65.91; H,6.50. Calc. for $C_{19}H_{22}O_2S_2$ (346.5): C,65.86; H,6.40%).

7,7-Bis(Methylthio)-6-methyl-1-(2-thienyl)-2,4,6-heptatriene-1-one(31g) was isolated as reddish brown crystalline solid; yield 95%; m.p.105-106°C;

i.r.(KBr): ν_{max} 1659,1629, 1569 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.18 (s,3H,$C\underline{H}_3$); 2.29(s,3H,$SC\underline{H}_3$); 2.41(s,3H,$SC\underline{H}_3$); 6.51(dd,1H,J=15Hz, $\underline{H}$-4); 6.89(d,1H,J=15Hz,$\underline{H}$-2); 6.91-7.87(m,$5H_{thienyl+olefin}$). (Found: C,56.71; H,5.52. Calc. for $C_{14}H_{16}OS_2$(296.7): C,56.67; H,5.43%). m/z 296(M^+,4%); 281(M^+-15,48%).

7,7-Bis(methylthio)-6-methyl-1-(2-furyl)-2,4,6-heptatriene-1-one(31h) was isolted as reddish brown crystalline solid; yield 92%; m.p. 148-149°C; i.r.(KBr): ν_{max} 1640, 1590 cm^{-1}; ^1H n.m.r.(CCl_4,300MHz): δ 2.13 (s,3H,$C\underline{H}_3$); 2.30(s,3H,$SC\underline{H}_3$); 2.40(s,3H,$SC\underline{H}_3$); 6.54(dd,J=15Hz,11Hz, $\underline{H}$-4); 6.94(d,1H,J=15Hz,$\underline{H}$-2); 7.15(dd,J=4Hz,5Hz,$1H_{furyl}$); 7.59-7.77 (m,$4H_{furyl+olefin}$). (Found: C,59.81; H,5.61. Calc. for $C_{14}H_{16}O_2S_2$ (280.4): C,59.97; H,5.75%). m/z 280(M^+,32%); 265(M^+-15,98%).

8,8-Bis(methylthio)-7-methyl-3,5,7-octatriene-2-one (31i) was isolated as reddish brown semisolid; yield 85%; i.r.(KBR): ν_{max} 1658, 1600, 1580 cm^{-1}; ^1H n.m.r.(CCl_4): δ2.09(s,3H,$C\underline{H}_3$); 2.11(s,3H,$C\underline{H}_3$); 2.25 (s,3H,$SC\underline{H}_3$); 2.35(s,3H,$SC\underline{H}_3$); 6.09(d,1H,J=15Hz,$\underline{H}$-3); 6.31(dd,1H,J=11Hz, 15Hz,$\underline{H}$-5); 7.19(dd,1H,J=11Hz,15Hz,$\underline{H}$-4); 7.57(d,1H,J=15Hz,$\underline{H}$-6). (Found: C,57.90; H,7.21. Calc. for $C_{11}H_{16}OS_2$(228.4): C,57.83; H,7.06%). m/z 228(M^+,9%); 213(M^+-15,29%).

1,7-Carbonyl transposition of 7,7-Bis(methylthio)-1-aryl/cycloalkyl-2,4,6-heptatriene-1-ones 30a-g and 31a-g; General Procedure:

To a well stirred solution of heptatrienone 30 or 31 (0.01 mol) in absolute ethanol (50 ml), excess sodium borohydride (1.2g, 0.035 mol) was added and the reaction mixture was refluxed for 1 hr. The cooled reaction mixture was then poured onto crushed ice (100g) and extracted with chloroform (2x50 ml). The extract was washed with saturated

salt solution (2x50 ml) dried (Na_2SO_4) and evaporated under vacuum to give the crude heptatrienol 32 or 34 in nearly quantitative yields, which were used as such for the next step without further purification. The crude heptatrienol 32 or 34 (0.01 mol) was dissolved in absolute methanol (50 ml) and boron trifluoride etherate (2 ml) was added with stirring. The reaction mixture was then refluxed for 10-15 hrs. The cooled reaction mixture with chloroform (2x50 ml), washed with water, dried (Na_2SO_4) and evaporated to give the methyl heptatrienoates 33 or 35 which were further purified by column chromatography using hexane as eluent.

Methyl 1-phenyl-2,4,6-heptatrienoate (33a) was isolated as pale yellow crystalline solid; yield 80%; m.p. 111-112°C (reported m.p. 112°)[27]; (superimposable i.r. and n.m.r. spectra[28]).

Methyl 1-(4-methylphenyl)-2,4,6-heptatrienoate (33b) was isolated as isolated as pale yellow crystalline solid; yield78%; m.p. 131°C (reported m.p. 131-132°C[28]; superimposable i.r. and n.m.r. spectra[28]).

Methyl 1-(4-methoxyphenyl)-2,4,6-heptatrienoate (33c) was isolated as pale yellow crystalline solid; yield 76%; m.p. 166°C (reported m.p. 167-168°C[29] ; superimposable i.r. and n.m.r. spectra[28]).

Methyl 1-(4-chlorophenyl)-2,4,6-heptatrienoate (33d) was isolated as pale yellow crystalline solid; yield 75%; m.p. 152°C; i.r.(KBr): ν_{max} 1715, 1610 cm^{-1}; ^1H n.m.r.(CCl_4): δ 3.68(s,3H,OCH_3); 5.80(d, 1H,J=15Hz,H-2); 6.30-7.40(m,$9H_{arom+olefin}$). (Found: C,67.81; H,5.31. Calc. for $C_{14}H_{13}ClO_2$(248.7): C,67.60; H,5.26%).

Methyl 5-(3,4-dihydronaphth-2-yl)-2,4-pentadienoate(33e) was isolated as pale yellow crystalline solid; yield 78%; m.p. 86-87°C; i.r.(KBr):

ν_{max} 1716, 1605 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.33-3.13(m,4H,$C\underline{H}_2$); 3.80 (s,3H,$OC\underline{H}_3$); 5.86(d,J=16Hz,$\underline{H}$-2); 6.31-7.76(m,$8H_{arom+olefin}$). (Found: C,80.01; H,6.81. Calc. for $C_{16}H_{16}O_2$(240.3): C,79.97; H,6.71%).

Methyl 5-(3,4-dihydro-6-methoxynaphth-2-yl)-2,4-pentadienoate (33f) was isolated as pale yellow crystalline solid; yield 76%; m.p. 108-109°C; i.r.(KBr): ν_{max} 1710, 1608 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.31-3.12(m,4H, $C\underline{H}_2$); 3.81(s,3H,$OC\underline{H}_3$); 3.82(s,3H,Ar-$OC\underline{H}_3$); 5.86(d,1H,J=16Hz,$\underline{H}$-2); 6.20-7.60(m,$7H_{arom+olefin}$). (Found: C,75.75; H,6.61. Calc. for $C_{17}H_{18}O_3$(270.3): C,75.53; H,6.71%).

Methyl 7-(2-thienyl)-2,4,6-heptatrienoate (33g) was isolated as pale yellow semisolid; yield 70%; i.r.(neat): ν_{max} 1718, 1590 cm^{-1}; ^1H n.m.r. (CCl_4): δ 3.66(s,3H,$OC\underline{H}_3$); 5.79(d,1H,J=16Hz,$\underline{H}$-2); 6.31-7.50(m, $8H_{thienyl+olefin}$). (Found: C,65.50; H,5.58. Calc. for $C_{12}H_{12}O_2S$ (220.3): C,65.42; H,5.49%).

Methyl 2-Methyl-7-phenyl-2,4,6-heptatrienoate (35a) was isolated as pale yellow crystalline solid; yield 87%; m.p. 173°C (reported m.p. 174°C[30]; superimposable i.r. and n.m.r. spectra[28]).

Methyl 2-methyl 7-(4-methylphenyl)-2,4,6-heptatrienoate (35b) was isolated as yellow crystalline solid; yield 85%; m.p. 101-102°C (reported m.p. 101-102°C[28]; superimposable i.r. and n.m.r. spectra[28]).

Methyl 2-methyl-7-(4-methoxyphenyl)-2,4,6-heptatrienoate (35c) was isolated as yellow crystalline solid; yield 84%; m.p. 95-96°C (reported m.p. 95-96°C[28]; superimposable i.r. and n.m.r. spectra[28]).

Methyl 2-methyl-7-(4-chlorophenyl)-2,4,6-heptatrienoate (35d) was isolated as pale yellow crystalline solid; yield 82%; m.p. 115-117°C;

i.r.(KBr): ν_{max} 1705, 1600 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.95(s,3H,$C\underline{H}_3$); 3.71(s,3H,$OC\underline{H}_3$); 6.38-7.47(m,$9H_{arom+olefin}$). (Found: C,68.61; H,5.91. Calc. for $C_{15}H_{15}ClO_2$(262.7): C,68.58; H,5.76%).

Methyl 5-(3,4-dihydronaphth-2-yl)-2-methyl-2,4,-pentadienoate (35e) was isolated as yellow crystalline solid; yield 78%; m.p. 82-84°C; i.r.(KBr): ν_{max} 1700, 1608 cm^{-1}; ^1H n.m.r.(CCl_4,300 MHz): δ 2.00(s, 3H,$C\underline{H}_3$); 2.55(t,2H,J=8Hz,$C\underline{H}_2$); 2.89(t,2H,J=8Hz,$C\underline{H}_2$); 3.77(s,3H,$OC\underline{H}_3$); 6.57-7.35(m,$8H_{arom+olefin}$). (Found: C,80.30; H,7.21. Calc. for $C_{17}H_{18}O_2$(254.3): C,80.28; H,7.13%). m/z 254(M^+,99%).

Methyl 5-(3,4-dihydro-6-methoxynaphth-2-yl)-2-methyl-2,4-pentadienoate (35f) was isolated as yellow crystalline solid; yield 76%; m.p. 99-101°C; i.r.(KBr): ν_{max} 1700, 1605 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.95(s,3H,$C\underline{H}_3$): 2.23-2.84(m,4H,$C\underline{H}_2$); 3.60(s,3H,$OC\underline{H}_3$); 3.64(s,3H,Ar-$OC\underline{H}_3$); 6.31-7.31 ($m,7H_{arom+olefin}$). (Found: C,76.15; H,7.18. Calc. for $C_{18}H_{20}O_3$(284.3): C,76.04; H,7.09%).

Methyl 2-methyl-7-(2-thienyl)-2,4,6-heptatrienoate (35g) was isolated as pale yellow semisolid; yield 79%; i.r.(KBr): ν_{max} 1705, 1595 cm^{-1}; ^1H n.m.r.(CCl_4): δ1.98(s,3H,$C\underline{H}_3$); 3.68(s,3H,$OC\underline{H}_3$); 6.45-7.28(m, $8H_{thienyl+olefin}$). (Found: C,66.78; H,6.21. Calc. for $C_{13}H_{14}O_2S$ (234.3): C,66.64; H,67.03%).

Alkylative 1,7 carbonyl transposition of 2-[1,1-bis(methylthio)-2-methyl-1,3-pentadienylidene]-1-tetralone (31e):

To a well cooled and stirred solution of methyl magnesium iodide (0.015 mol) in dry ether (30 ml), the bis(methylthio) trienone 31e (3.1g, 0.01 mol) in dry ether (20 ml) was added dropwise (5 min) under nitrogen atmosphere, followed by stirring for 1.5 hrs. The reaction

mixture was poured into a cold saturtated solution of ammonium chloride (50 ml), was extracted with ether (3x50 ml), washed with water, dried (Na_2SO_4) and evaporated to give the crude heptatrienol 36 in nearly quantitative yield. The carbinol 36 (0.01 mol) was dissolved in absolute methanol (50 ml) and boron trifluoride etherate (2 ml) was added with stirring. The reaction mixture was then refluxed for 16 hrs, the cooled reaction mixture was poured into a saturated solution of sodium bicarbonate (100 ml) and extracted with chloroform (2x50 ml). The chloroform extract was.washed with water, dried (Na_2SO_4) and evaporated to give the crude triene ester 37 which was further purified by passing through a silica gel column using hexane as eluent.

Methyl 5-(3,4-dihydro-2-methylnaphth-2-yl)-2-methyl-2,4-pentadienoate (37) was isolated as pale yellow crystalline solid; yield 75%; m.p. 102°C; spectral data described in text. (Found: C,80.61; H,7.71. Calc. for $C_{18}H_{20}O_2$(268.3): C,80.56; H,7.51%). m/z 268(M^+,100%).

Synthesis of 7,7-Bis(methylthio)-2,4,6-heptatrienal (39a and 39b); General Procedure:

To a well cooled solution of methyl magnesium iodide (0.015 mol) in dry ether (30 ml), the pentadienal 23 (0.01 mol) in ether (20 ml) was added dropwise under nitrogen atmosphere. After stirring for 1.5 hrs the reaction mixture was poured into cold saturated solution of ammonium chloride (100 ml) and was extracted with ether (2x50 ml). The ether extract was washed with water (2x50 ml) dried (Na_2SO_4) and evaporated to give crude hexadienol 38 which was used as such for the subsequent Vilsmeier formylation.

The hexadienol 38 (0.01 mol) in 5 ml of DMF was added slowly to a well cooled (0°C) and stirred Vilsmeier reagent (0.025mol prepared as

described earlier). The reaction mixture was stirred for 10-15 hrs for completion of reaction, after which it was poured into crushed ice (300g) and a cold saturated potassium carbonate solution (100 ml) was added slowly to liberate the trienal. The reaction mixture was then extracted with ether (5x50 ml), the combined ether layer was washed with water dried (Na_2SO_4) and evaporated to give the crude heptatrienals 39 which were further purified by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluent.

7,7-Bis(methylthio)-2,4,6-heptatrienal (39a) was obtained as orange viscous liquid; yield 56%; spectral data described in text. (Found: C,54.01; H,6.15. Calc. for $C_9H_{12}OS_2$(200.3): C,53.96; H,6.04%).

7,7-Bis(methylthio)-6-methyl-2,4,6-heptatrienal (39b) was isolated as orange viscous liquid; yield 80%; i.r.(neat): ν_{max} 1670, 1600 cm^{-1}; ^1H n.m.r. (CCl_4): δ 2.14(s,3H,CH_3); 2.23(s,3H,SCH_3); 2.37(s,3H,SCH_3); 6.10(dd,1H,J=16Hz,8Hz,H-2); 6.41(dd,1H,J=16Hz,12Hz,H-4); 7.06(dd,1H, J=16Hz,12Hz,H-3); 7.62(d,1H,J=16Hz,H-5); 9.52(d,1H,J=8Hz,CHO). (Found: C,56.21; H,6.61. Calc. for $C_{10}H_{14}OS_2$(214,3): C,56.04; H,6.58%). m/z 214(M^+,12%); 192(M^+-15,39%).

Alkylative 1,7-carbonyl transposition of 7,7-bis(methylthio)-2,4,6-heptatrienals (39a and 39b); General Procedure:

To a well cooled solution of phenyl magnesium bromide (0.01 mol) in dry ether (30 ml), the heptatrienal 39 in ether (20 ml) was added dropwise (5 min) under a nitrogen atmosphere. After stirring for 2 hrs, the reaction mixture was poured into a cold saturated solution of ammonium chloride (50 ml), and extracted with ether (3x50 ml). The ether extract was washed with water (3x50 ml) dried and evaporated to give the crude heptatrienol 32a or 34a in nearly quantitative

yields. The heptatrienol 32a or 34a (0.01 mol) was dissolved in absolute methanol (100 ml) and boron trifluoride etherate (2 ml) was added with stirring and the reaction mixture was refluxed for 15-17 hrs. The cooled reaction mixture was poured into a saturated solution of sodium bicarbonate (50 ml) and extracted with chloroform, the extract was washed with water, and dried (Na_2SO_4) and evaporated to give crude heptatrienoates 33a or 35a which were further purified by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluent.

Methyl 7-phenyl-2,4,6-heptatrienoate (33a) was isolated as a pale yellow crystalline solid; yield 80%; m.p. 111-113°C (reported m.p. 112°C[25]; m.m.p. superimposable i.r. and n.m.r. spectra).

Methyl 2-methyl-7-phenyl-2,4,6-heptatrienoate (35a) was isolated as a pale yellow crystalline solid; yield 75%; m.p. 107-108°C (reported m.p. 107-108°C; m.m.p. superimposable i.r. and n.m.r. spectra).

Synthesis of 9,9-Bis(methylthio)-1-aryl/cycloalkyl-2,4,6,8-nonatetraene-1-ones (40a-d); General Procedure:

To a well stirred and cooled solution of sodium methoxide (0.54g, 0.01 mol) in methanol (20 ml), a mixture trienaldehyde 39 (0.005 mol) and active methylene ketone 29 (0.005 mol) in methanol (5 ml) was added dropwise and the reaction mixture was stirred at room temperature for 6-8 hrs. The solid separated (40c,d) was filtered washed with water and recrystallyzed from methanol to give pure 40. In the cases were the products were liquid (40a,b), the reaction mixture was diluted with water (50 ml), extracted with chloroform (3x30 ml) washed with water, dried (Na_2SO_4), evaporated and the crude products thus obtained were column chromatographed over silica gel using ethyl acetate:hexane (1:20) as eluent to give pure 40.

9,9-Bis(Methylthio)-1-phenyl-2,4,6,8-nonatetraene-1-one (40a) was obtained as reddish brown semisolid; yield 92%; spectral data described in text. (Found: C,67.60; H,6.21. Calc. for $C_{17}H_{18}OS_2$(302.4): C,67.51; H,6.00%).

9,9-Bis(methylthio)-8-methyl-1-phenyl-2,4,6,8-nonatetraene-1-one(40b) was isolated as reddish brown semisolid; yield 70%; i.r.(neat): ν_{max} 1658, 1590 cm^{-1}; ^1H n.m.r.(CCl_4): δ 2.10(s,3H,$C\underline{H}_3$); 2.21(s, 3H,$SC\underline{H}_3$); 2.35(s,3H,$SC\underline{H}_3$); 6.22-8.18(m,$11H_{arom+olefin}$). (Found: C,68.51; H,6.44. Calc. for $C_{18}H_{20}OS_2$(316.4): C,68.32; H,6.37%).

9,9-Bis(methylthio)-8-methyl-1-(4-chlorophenyl)-2,4,6,8-nonatetraene-1-one (40c) was isolated as reddish brown crystalline solid; yield 75%; m.p. 120-123°C; i.r.(KBr): ν_{max} 1642, 1597 cm^{-1}; ^1H n.m.r.(CCl_4,300 MHz): δ 2.17(s,3H,$C\underline{H}_3$); 2.29(s,3H,$SC\underline{H}_3$); 2.38(s,3H,$SC\underline{H}_3$); 6.45(dd,1H,J=15Hz, 11Hz,$\underline{H}$-6); 6.52(dd,1H,J=15Hz,11Hz,$\underline{H}$-4); 6.84(dd,1H,J=15Hz,11Hz,$\underline{H}$-5); 6.93(d,1H,J=15Hz,$\underline{H}$-2); 7.42-7.56(m,$4H_{arom+olefin}$); 7.87-7.90(m,$2H_{arom}$). (Found: C,61.82; H,5.66. Calc. for $C_{18}H_{19}ClOS_2$(350.8): C,61.62; H,5.46%). m/z 350(M^+,24%); 351(5%).

2-[1,1-Bis(methylthio)-1,3,5-heptatrienylidene]-6-methoxy-1-tetralone (40d) was isolated as reddish brown crystalline solid; yield 78%; m.p. 114-115°C; i.r.(KBr): ν_{max} 1647, 1602 cm^{-1}; ^1H n.m.r.($CDCl_3$,300 MHz): δ 2.17(s,3H,$C\underline{H}_3$); 2.29(s,3H,$SC\underline{H}_3$): 2.38(s,3H,$SC\underline{H}_3$); 2.93(s,4H,$C\underline{H}_2$); 3.86(s,3H,$OC\underline{H}_3$); 6.49(dd,1H,J=15Hz,11Hz,$\underline{H}$-4); 6.61-6.87(m,$4H_{arom+olefin}$); 7.43(d,1H,J=15Hz,$\underline{H}$-7); 7.47(d,1H,J=12Hz,$\underline{H}$-3); 8.07(d,1H,J=8Hz,aromatic). (Found: C,67.75; H,6.51. Calc. for $C_{21}H_{24}OS_2$(372.5): C,67.70; H,6.49%). m/z 372(M^+,49%).

1,9 Carbonyl transposition of 9,9-bis(methylthio)-1-aryl/cycloalkyl-2,4,6,8-nonatetraene-1-ones (40a-d); General Procedure:

To a well stirred solution of the tetraenone 40 (0.01 mol) in absolute ethanol (50 ml), excess sodium borohydride [1.2g (0.035 mol)] was added slowly and the reaction mixture was refluxed for 1.5 hrs. It was then cooled, poured into crushed ice (100g) and extracted with chloroform (3x50 ml). The chloroform extract was washed with saturated sodium chloride solution (2x50 ml) dried (Na_2SO_4) and evaporated to give the crude tetraene carbinol 41 in nearly quantitative yields, which were used as such without further purification for the next step. The tetraenol 41 (0.01 mol) was dissolved in absolute methanol (50 ml) and boron trifluoride etherate (2 ml) was added with stirring, the reation mixture was refluxed for 18-20 hrs and cooled reaction mixture was poured into saturated sodium bicarbonate solution (100 ml), washed with water dried and evaporated to give the crude tetraene esters 42 which were further purified by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluent.

Methyl 9-phenyl-2,4,6,8-nonatetraenoate (42a) was isolated as yellow crystalline solid; yield 70%; m.p. 151-153°C; spectral data described in text. (Found: C,80.11; H,6.91. Calc. for $C_{16}H_{16}O_2$(240.3): C,79.97; H,6.71%).

Methyl 2-methyl-9-phenyl-2,4,6,8-nonatetraenoate (42b) was isolated as isolated as yellow crystalline solid; yield 75%; m.p. 103-104°C; i.r.(KBr): ν_{max} 1695, 1598 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.95(s,3H,$C\underline{H}_3$); 3.69(s,3H,$OC\underline{H}_3$); 6.25-7.48(m,12$H_{arom+olefin}$). (Found: C,80.40; H,7.25. Calc. for $C_{17}H_{18}O_2$(254.3): C,80.28; H,7.13%).

Methyl 2-methyl-9-(4-chlorophenyl)-2,4,6,8-nonatetraenoate (42c) was isolated as yellow crystalline solid; yield 70%; m.p. 150°C; i.r.(KBr): ν_{max} 1705, 1608 cm^{-1}; ^1H n.m.r.($CDCl_3$,300 MHz): δ 1.98(s,3H,CH_3); 3.76 (s,3H,OCH_3); 6.41-6.86(m,$6H_{olefin}$); 7.24-7.34(m,$5H_{arom+olefin}$). (Found: C,70.75; H,6.01. Calc. for $C_{17}H_{17}ClO_2$(288.8): C,70.69; H,5.93%). m/z 288(M^+,100%).

Methyl 2-methyl-7-[3,4-dihydro-6-methoxynaphth-2-yl)-2,4,6-heptatrienoate (42d) was isolated as yellow crystalline solid; yield 80%; m.p.139-140°C; i.r. (KBr): ν_{max} 1700, 1608 cm^{-1}; ^1H n.m.r.($CDCl_3$,300 MHz): δ 1.97 (s,3H,CH_3); 2.48(t,2H,J=8.5Hz,CH_2): 2.85(t,2H,8.5Hz,CH_2); 3.76(s,3H, OCH_3); 3.79(s,3H,OCH_3); 6.41-6.70(m,$7H_{arom+olefin}$); 7.01(d,J=9Hz, $1H_{arom}$); 7.27(d,10Hz,$1H_{arom}$). (Found: C,77.591 H,7.29. Calc. for $C_{20}H_{22}O_3$(310.4): C,77.38; H,7.14%). m/z 310(M^+,100%).

9,9-Bis(methylthio)-8-methyl-2,4,6,8-nonatetraenal (44) (a) from Bis(methylthio)-7-methyl-3,5,7-octatriene-2-one (31i):

To a well stirred solution of trienone 31i (2.28g, 0.01 mol), excess sodium borohydride (1.25g, 0.035 mol) was added and the reaction mixture was refluxed for 1 hr. The cooled mixture was then poured into crushed ice (100g) and extracted with chloroform (2x150 ml). The chloroform extract is washed with saturated salt solution (2x100 ml) dried with sodium sulphate and evaporated under vacuum to give the crude octatrienol 43 in nearly quantitative yield.

To a well cooled (0°C) and stirred Vismeier reagent (0.025 mol, prepared as described earlier), the triene alcohol 43 was added slowly (10 min) and the reaction mixture was stirred at 0-10°C for 16 hrs, after which it was poured into crushed ice (300g) and the tetraenaldehyde

44 was liberated by a slow addition cold saturated potassium carbonate solution (100 ml). It was then extracted with ether (4x100 ml) and the combined ether layer was washed with water (4x50 ml), dried (Na_2SO_4), evaporated and column chromatographed over silica gel using ethylacetate:hexane (1:20) as eluent to give pure tetraenealdehyde 44.

9,9-Bis(methylthio)-8-methyl-2,4,6,8-nonatetraenal 44 was obtained as reddish brown liquid; yield 70%; spectral data described in text. (Found: C,60.01; H,6.80. Calc. for $C_{12}H_{16}OS_2$(240.4): C,59.96; H,6.71%), m/z 240(M^+,100%).

(b) Synthesis of 44 from 7,7-bis(methylthio)-6-methyl-2,4,6,-heptatrenal (39b): To a well stirred and cooled solution of methyl magnesium iodide (0.015 mol) in dry ether, a solution of the heptatrienal 39b in 20 ml dry ether was added dropwise and the reaction mixture was stirred for 1.5 hrs. It was then poured over saturated ammonium chloride solution (100 ml) and extracted with ether (3x50 ml). The combined organic layer was washed with water, dried (Na_2SO_4) and evaporated to give the octatrienol 43 in nearly quantitative yield. The crude triene alcohol 43 was subjected to Vilsmeier formylation as described above to give after work-up and column chromatography, the 9,9-bis(methylthio)-8-methyl-2,4,6,8-nonatetraenal 44 in 80% yield (superimposable i.r. and n.m.r. spectra).

Alkylative 1,9 carbonyl transposition of 9,9-bis(methylthio)-8-methyl-2,4,6,8-nonatetraenal 44:

To a well stirred and cooled solution of phenylmagnesium bromide in dry ether (40 ml), the tetraenaldehyde 44 (2.4g, 0.01 mol) in dry ether (20 ml) was added slowly and the reaction mixture was stirred

for 2 hrs. It was then poured over saturated ammonium chloride solution (100 ml) and extracted with ether (5x50 ml). The combined organic layer was washed with water and evaporated to give the crude tetraenol 41b in nearly quantitative yield. The tetraenol 41b was dissolved in methanol and boron trifluoride etherate (2 ml) was added with cooling and stirring. The reaction mixture was then refluxed for 16 hrs, cooled and poured into saturated sodium bicarbonate solution. It was then extracted with chloroform (3x50 ml) and the combined organic layer was washed with water, dried (Na_2SO_4), evaporated and purified by column chromatography over silica gel using ethyl acetate:hexane (1:20) as eluents to give methy 2-methyl-9-phenyl-2,4,6,8-nonatetraenoate 42b in 70% yield; (m.m.p. superimposable i.r. and n.m.r. spectra).

Synthesis of 11,11-Bis(methylthio)-1-aryl/cycloalkyl-1-methyl-2,4,6,8,10-undecapentaene-1-ones (45a-b); General Procedure:

To a well cooled and stirred solution of sodium methoxide (0.54g, 0.01 mol) in methanol (30 ml) a mixture of the tetraenaldehyde 44 (0.005 mol) and the active methylene ketone 26 (0.005 mol) as added dropwise. The reaction mixture was further stirred for 8 hrs, diluted with water (50 ml), extracted with chloroform (2x50 ml) and the combined organic layer was washed with water, dried (Na_2SO_4) and evaporated to give the crude nonapentaenone 45 which were further purified by column chromatography over silica gel using ethylacetate: hexane (1:20) as eluent to give the pure 45.

11,11-Bis(methylthio)-1-methyl-1-phenyl-2,4,6,8,10-undecapentaene-1-one (45a) was isolated as deep red semisolid; yield 90%; spectral

data described in the text. (Found: C,70.25; H,5.91. Calc. for $C_{20}H_{22}OS_2$(342.5): C,70.13; H,5.89%).

2-[1,1-Bis(methylthio)-2-methyl-1,3,5,7-nonatetraenylidene]-6-methoxy 1-tetralone (45b) was isolated as deep red semisolid; yield 95%; i.r.(neat): ν_{max} 1650, 1610 cm^{-1}; ^1H n.m.r.(CCl_4): δ 1.96(s,3H, CH_3); 2.10(s,3H,SCH_3); 2.23(s,3H,SCH_3); 2.73(s,4H,CH_2); 3.66(s,3H, OCH_3); 6.10-7.50(m,$9H_{arom+olefin}$); 7.93(d,J=8Hz,$1H_{arom}$). (Found: C,72.31; H,6.90. Calc. for $C_{23}H_{26}OS_2$(382.6): C,72.20; H,6.85%).

1,11 Carbonyl transposition of 11,11-Bis(methylthio)-1-aryl/cyclo-alkyl-10-undecapentaene-1-ones (45a-b); General Procedure:

To a well stirred solution of the pentaenone 45 (0.01 mol) in absolute ethanol (50 ml) excess sodium borohydride (1.25g, 0.035 mol) was added and the reaction mixture was refluxed for 2 hrs. It was then cooled and poured into crushed ice (100g) and extracted with chloroform (3x50 ml). The combined organic layer was washed with water, dried (Na_2SO_4) and evaporated to give the crude pentaene alcohols 46 in nearly quantitative yields which were used as such, without further purification for the next step.

The crude pentaene alcohol 46 was dissolved in absolute methanol and boron trifluoride etherate (2 ml) was added with cooling and stirring. The reaction mixture was then refluxed for 16 hrs, cooled, and poured into saturated sodium bicarbonate solution (100 ml), extracted with chloroform (3x50 ml), washed with water (2x50 ml), dried (Na_2SO_4) and evaporated to give the pentaene ester 47 which were further purified by column chromatography over silica gel using ethylacetate: hexane (1:20) as eluent.

Methyl 2-methyl-11-phenyl-2,4,6,8,10-undecapentaenoate (47a) was isolated as yellow crystalline solid; yield 85%; m.p. 142-143°C; spectral data described in text. (Found: C,81.41; H,7.20. Calc. for $C_{19}H_{20}O_2$(280.4): C,81.39; H,7.19%).

Methyl-2-methyl-[3,4-dihydro-6-methoxynaphth-2-yl]-2,4,6,8-nonatetraenoate (47b) was isolated as yellow crystalline solid; yield 80%; m.p. 149-151°C; i.r.(KBr): ν_{max} 1705, 1600 cm^{-1}; ^1H n.m.r. (CCl_4): δ 1.83(s,3H,CH_3); 2.20-2.80(m,4H,CH_2); 3.61(s,3H,OCH_3); 6.34(s,3H,OCH_3); 6.15-7.35(m,11$H_{arom+olefin}$). (Found: C,78.66; H,7.33. Calc. for $C_{22}H_{24}O_3$(336.4): C,78.54; H,7.19%).

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