INVESTIGATIONS ON OXOKETENE S,S-ACETALS NEWER SYNTHETIC METHODS FOR NOVEL CARBOCYCLES AND HETEROCYCLES

ABSTRACT

By

BISWAJIT DEB

DEPARTMENT OF CHEMISTRY
SCHOOL OF PHYSICAL SCIENCES

A THESIS
SUBMITTED IN FULFILMENT OF THE REQUIREMENT
FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

To

NORTH-EASTERN HILL UNIVERSITY

SHILLONG-793001

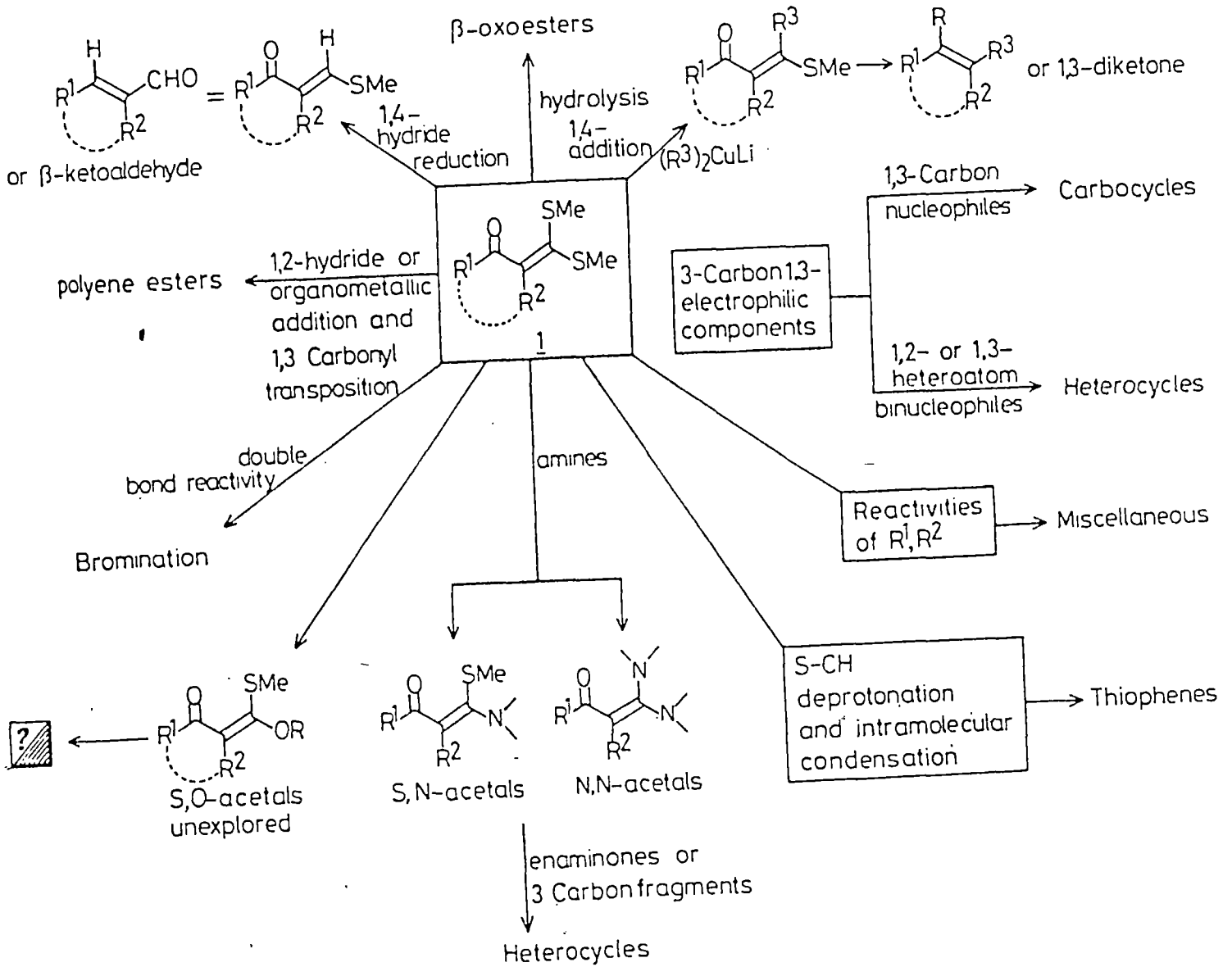
INDIA

1990

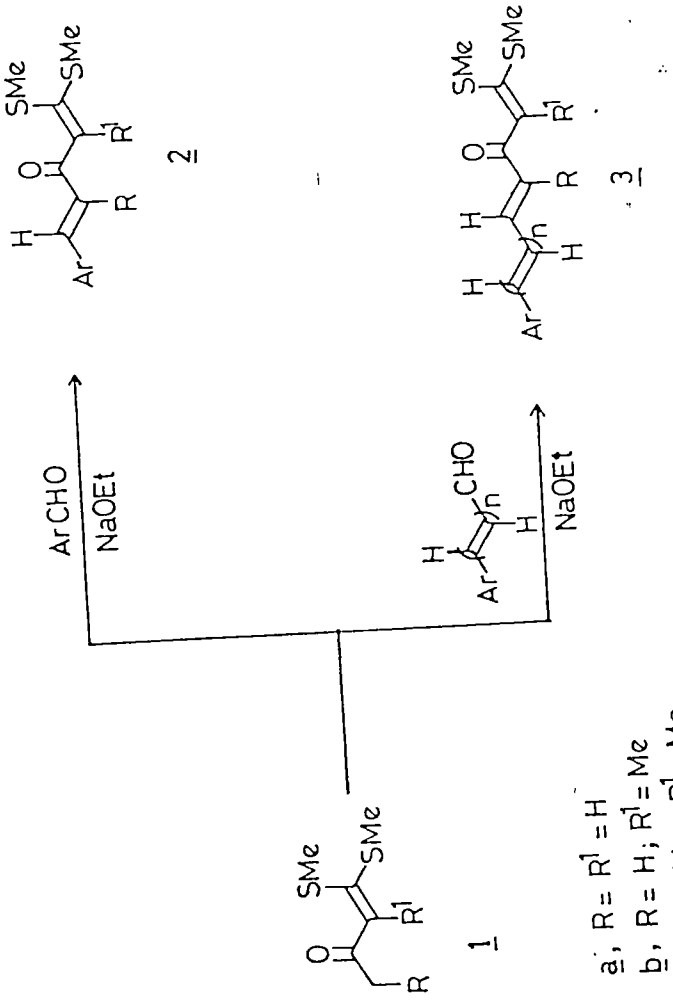
Chem
(Thesis)

The synthesis of α-oxoketene dithioacetals of general formula 1 was first reported in 1910, by Kelber and coworkers[1]. This class of compounds can be easily prepared from a wide variety of active methylene compounds and carbon disulfide in presence of a 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 be a one pot transformation. They are known to be versatile synthones and have been recognized as useful building block in various synthetic transformations[5]. The α-oxoketene dithioacetals posses 1,3-electrophilic centers with differing electrophilicity, this property has been extensively exploited for the construction of new bonds involving 1,2, 1,4 or both nucleophilic additions leading to a number of new synthetic methodologies for a wide range of organic molecules. (Scheme 1)

Among other uses of these compounds, the oxoketene dithioacetals 1 derived from aliphatic ketones (Scheme 2) are of particular interest, as they can be condensed with various aromatic aldehydes to afford the corresponding cinnamoyl ketene dithioacetals 2 and 3 in excellent yields[6]. In the present study, it was proposed to undertake some of the important transformations based on α-cinnamoyl ketene dithioacetals 3. The second chapter deals with the synthesis of substituted cyclopentanones 5, 6 and 7 obtained by acid catalyzed ring opening of the cyclopropyl ketene[7] 4 (Scheme 3). The cyclopropyl ketone 4


β-oxoesters
hydrolysis
1,4-addition
$(R^3)_2CuLi$
or 1,3-diketone
1,4-hydride reduction
or β-ketoaldehyde
1,2-hydride or organometallic addition and 1,3 Carbonyl transposition
polyene esters
1
3-Carbon 1,3-electrophilic components
1,3-Carbon nucleophiles
Carbocycles
1,2- or 1,3-heteroatom binucleophiles
Heterocycles
double bond reactivity
Bromination
amines
Reactivities of R^1, R^2
Miscellaneous
S-CH deprotonation and intramolecular condensation
Thiophenes
S,O-acetals unexplored
S,N-acetals
N,N-acetals
enaminones or 3 Carbon fragments
Heterocycles

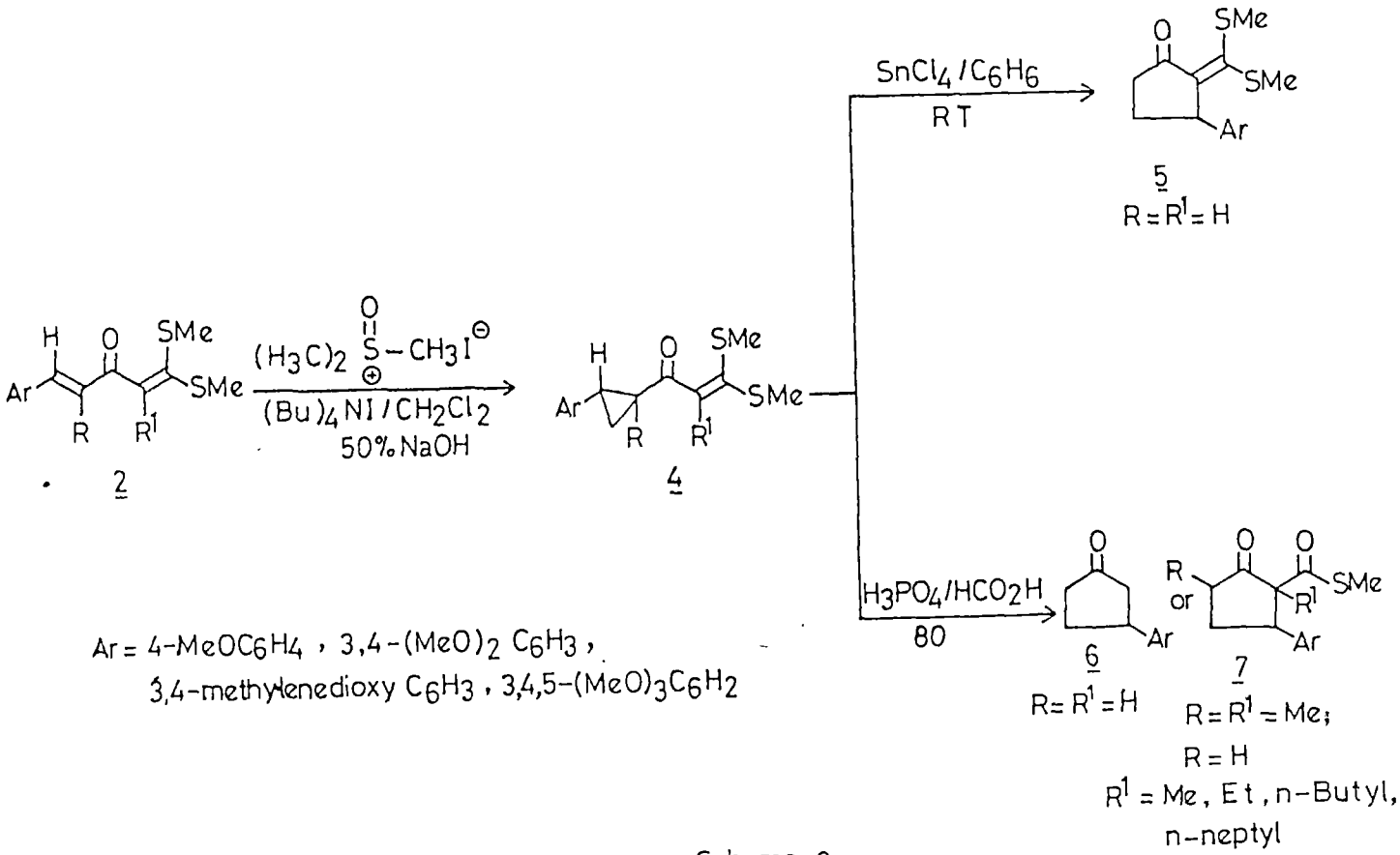
Scheme-1



a, R = R^1 = H
b, R = H; R^1 = Me
c, R = Me; R^1 = Me

n = 1, 2

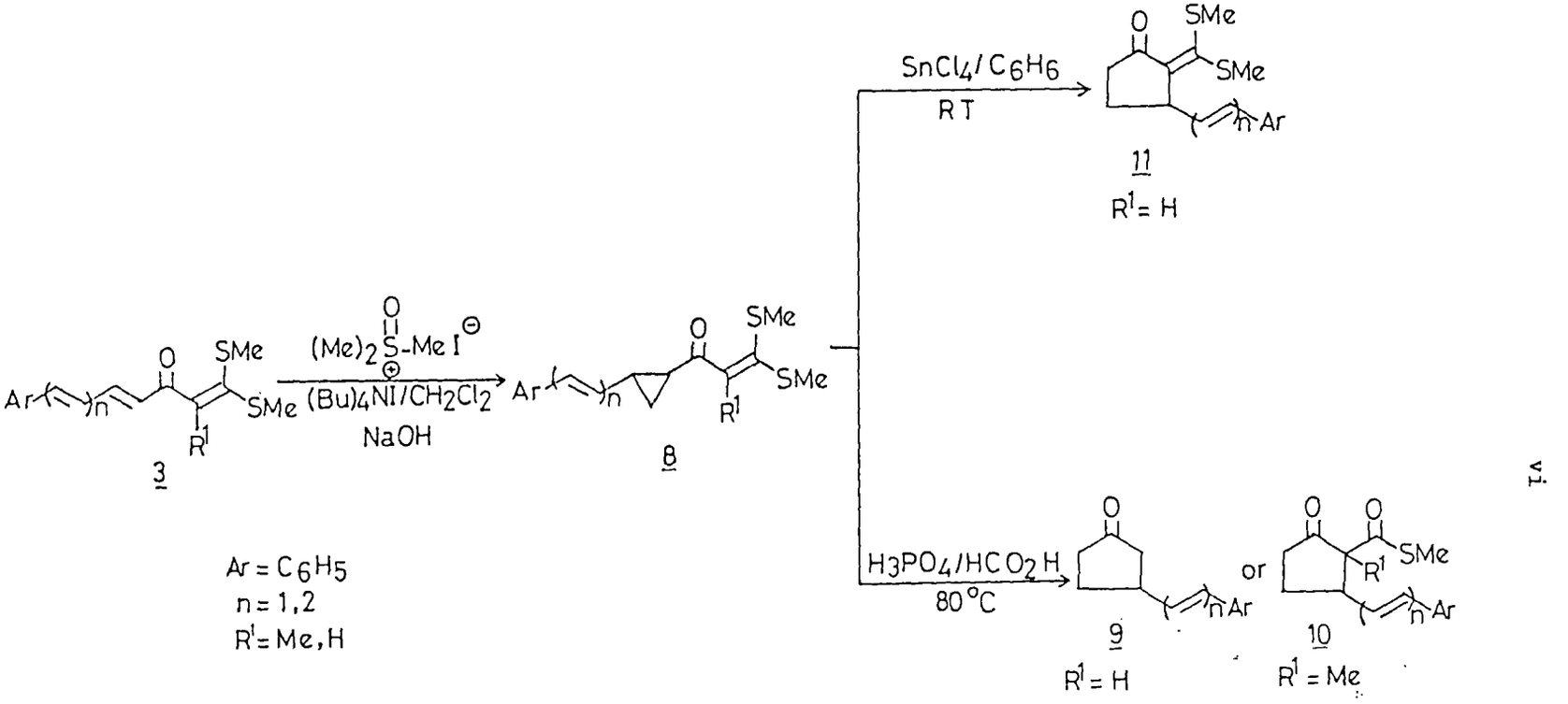
Scheme-2


SnCl4 / C6H6
RT
SMe
SMe
Ar
5
R = R1 = H
(H3C)2 S – CH3I
(Bu)4NI / CH2Cl2
50% NaOH
2
4
H3PO4/HCO2H
80
6
R = R1 = H
R
or
R1
SMe
7
R = R1 = Me;
R = H
R1 = Me, Et, n-Butyl,
n-neptyl
Ar = 4-MeOC6H4 , 3,4-(MeO)2 C6H3 ,
3,4-methylenedioxy C6H3 , 3,4,5-(MeO)3C6H2

Scheme- 3

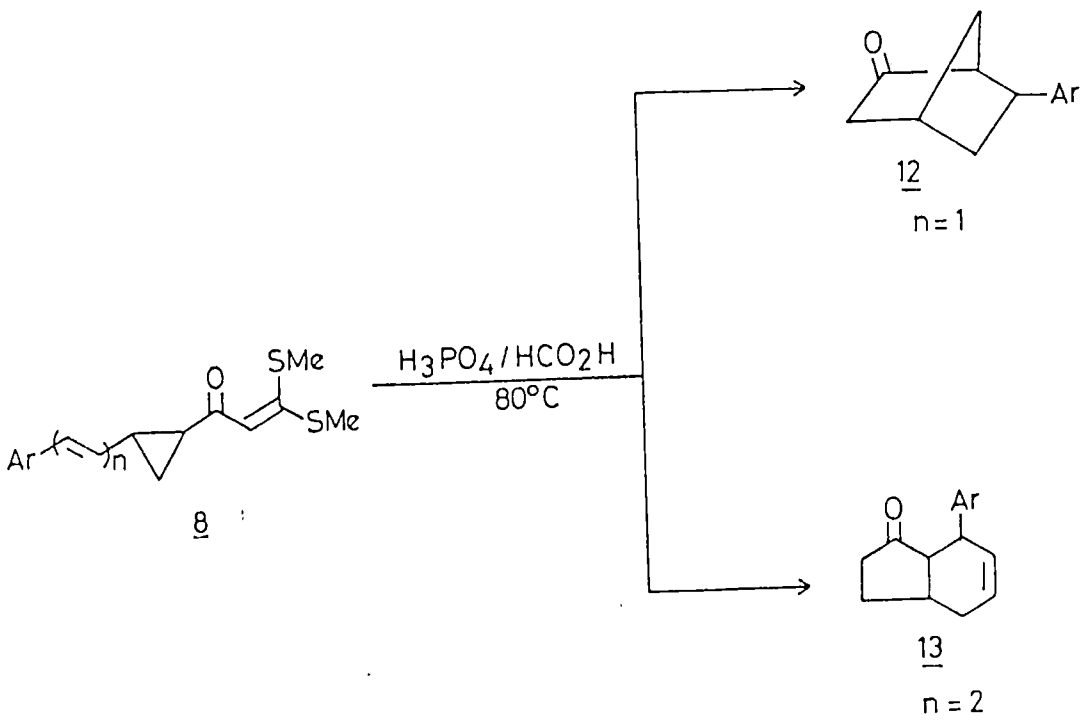
was obtained by conjugate addition of dimethylsulphoxonium methylide to 2 under phase transfer conditions. These cyclopropyl ketones 4 under different acidic conditions underwent ring opening with concomitant intramolecular π-participation of bis(methylthio)methylene double bond to give substituted cyclopentanones 5, 6, and 7. Similarly styrylcyclopropyl ketones and its higher enyl homologs 8 under similar conditions afforded the corresponding substituted cyclopentanones 9, 10 and 11 (Scheme 4). However, in the case of 4-methoxy styryl (n=1) and dienyl (n=2) cyclopropyl ketones under acidic condition, the product obtained were substituted bicyclo [2.2.1] heptane 12 and indanone derivative 13 respectively.(Scheme 5) Similarly a shorter route to cyclopentanoids 17 and 18, intermediates in the steroid synthesis[8], has been developed by employing this approach. Thus, these methods illustrates the successful utilization of α-oxoketene dithioacetal functionality as a latent β-ketoester equivalent and represents a novel intramolecular alkylative approach to cyclopentanones (Scheme 6).

In continuation with our studies on the cyclopropylketones 8, which undergoes a ring cleavage even at mild acidic medium, it was decided to utilize them in more synthetic purposes. Thus, the carbinol acetal 19 obtained by 1,2-reduction of 8 with sodium borohydride, on treatment with pyridinium tosylate underwent dehydration followed by ring opening to give 1,1 bis(methylthio)polyene acetals 20. On


SnCl4/C6H6
RT
11
R1 = H
(Me)2S-Me I
(Bu)4NI/CH2Cl2
NaOH
3
8
Ar = C6H5
n = 1,2
R1 = Me, H
H3PO4/HCO2H
80 °C
or
9
R1 = H
10
R1 = Me

Scheme-4

vi.



8

12

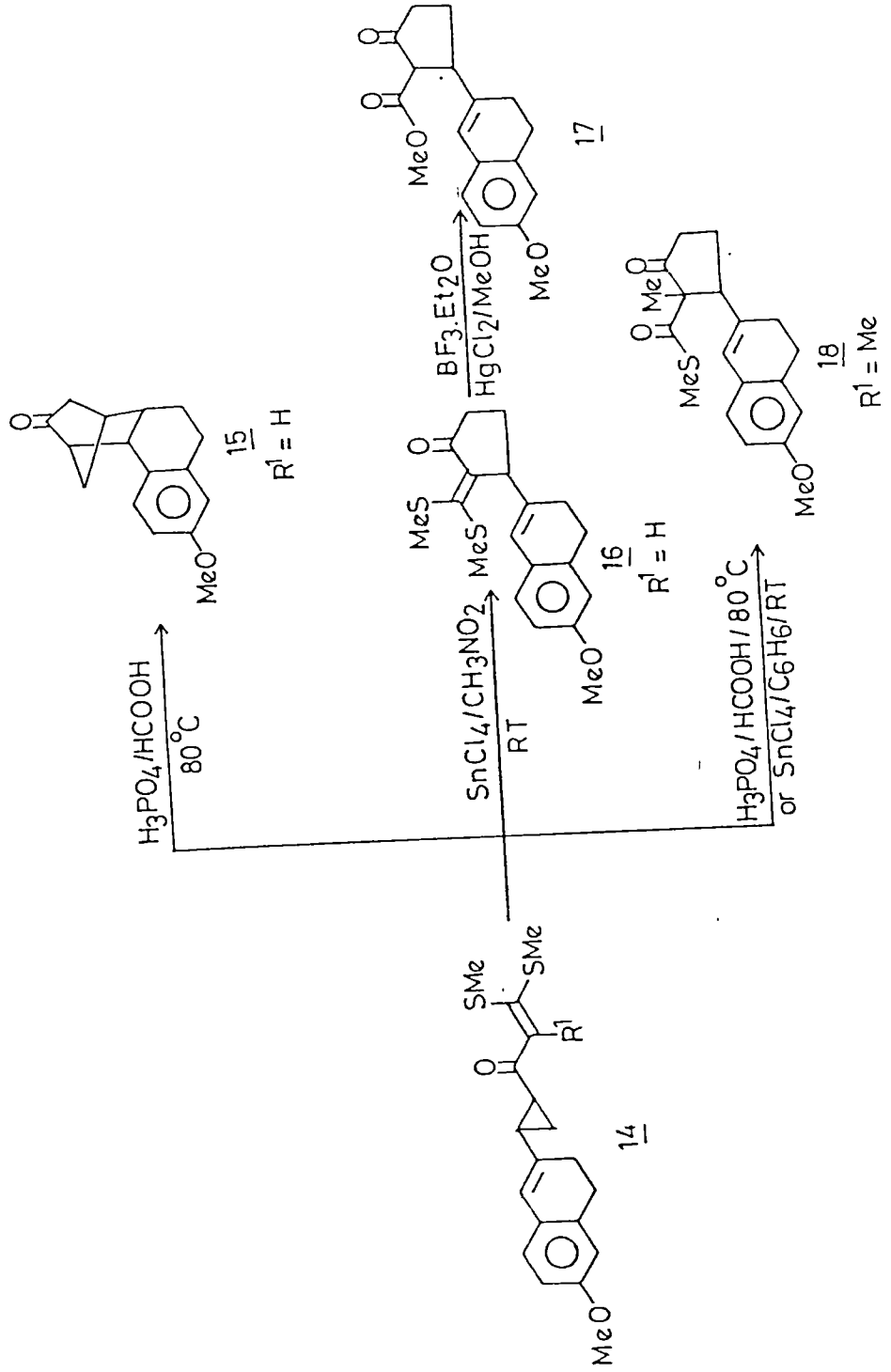
n = 1

13

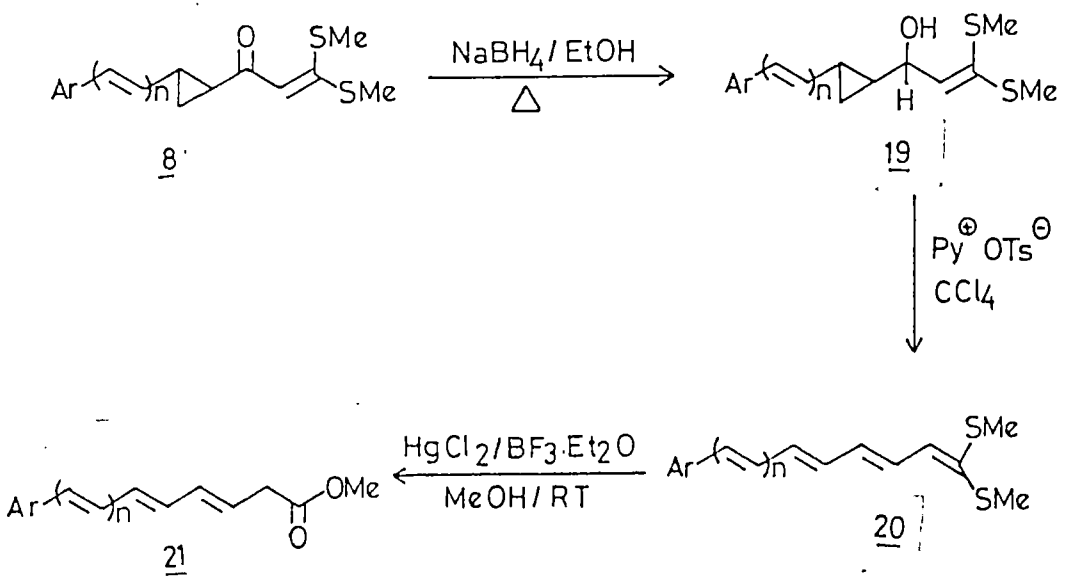
n = 2

Ar = 4-$MeOC_6H_4$

Scheme-5


SMe
SMe
R1
O
MeO
14
H3PO4/HCOOH
80°C
15
R1 = H
SnCl4/CH3NO2
RT
MeS
MeS
O
MeO
16
R1 = H
BF3.Et2O
HgCl2/MeOH
MeO
O
MeO
17
H3PO4/HCOOH/80°C
or SnCl4/C6H6/RT
MeS
O
MeO
18
R1 = Me

Scheme-6

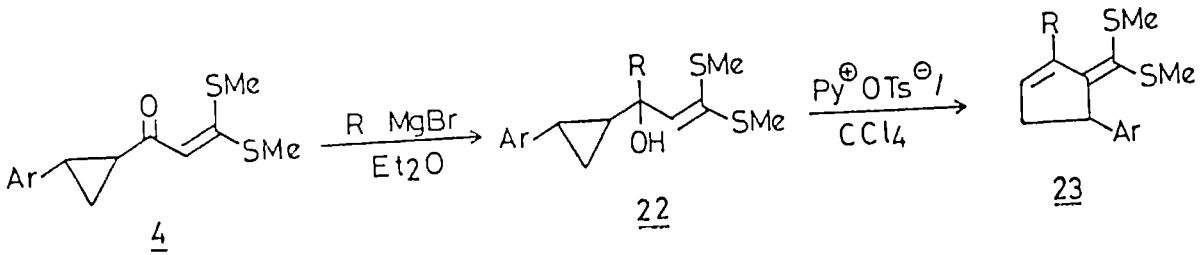


8 19 20 21

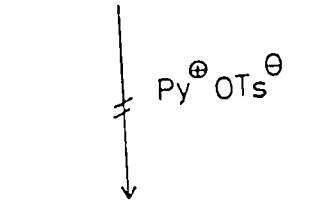
Ar = C_6H_5 , 4-$MeOC_6H_4$, 3,4-methylenedioxy C_6H_3 ,
3,4-$(MeO)_2$ C_6H_3 , 4-ClC_6H_4

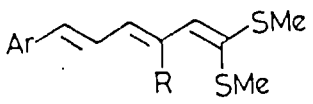
n = 0,1,2

Scheme-7



4 22 23



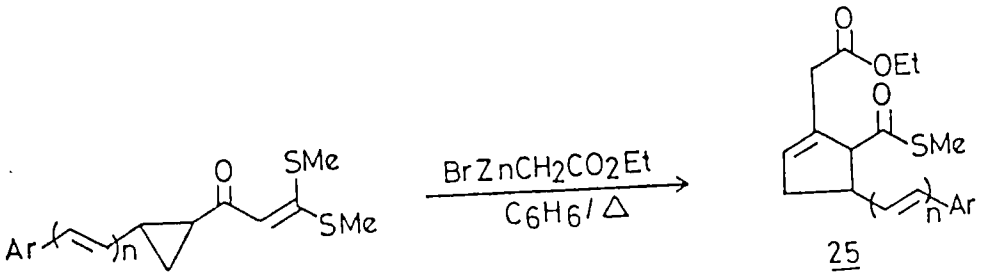


24

R = Me, n - Pr, C_6H_5, $-CH_2C_6H_5$

Ar = C_6H_5, 4-$MeOC_6H_4$

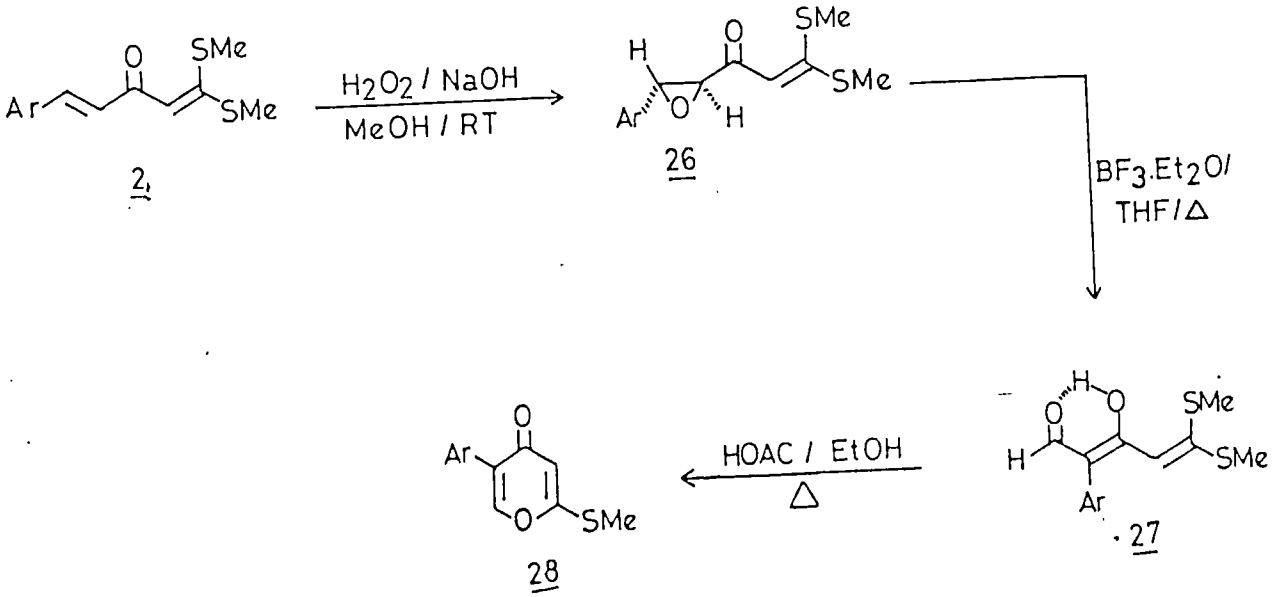
Scheme-8



8 25

Ar = C_6H_5 , 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$,
3,4- methylene dioxy C_6H_3
n = 0 , 1 , 2

Scheme- 9



2 26 27 28

Ar= C_6H_5 ; 4-MeC_6H_4 ; 4-ClC_6H_4 ; 4-$MeOC_6H_4$, 3-$MeOC_6H_4$;
3,4-$(MeO)_2C_6H_3$; 3,4,5-$(MeO)_3C_6H_2$; 3,4- methylenedioxy C_6H_3

Scheme- 10

subsequent Hg(II) assisted methanolysis 20 gave the corresponding β, γ-unsaturated esters 21 in good yields (Scheme 7). However, the 1,2-addition of Grignard and Reformatsky reagent to these cyclopropyl ketones and their future transformations gave the corresponding cyclopentenes 23 and 25 respectively, cyclized in *5-exo-trig* manner (Scheme 8 and 9). The details of these reactions have been described in the third chapter.

In the last chapter, a novel synthesis of substituted γ-pyrones 28 has been presented[9]. This synthesis was achieved in three successive steps. In the first step the styryl double bond of cinnamoyl ketene dithioacetals 2 were oxidized with alkaline hydrogenperoxide to give the corresponding epoxy ketones 26 in good yields. In the second step epoxy ketones 26 were subjected to rearrangement in the presence of borontrifluoride etherate to give the corresponding (α-formyl-α-phenylacetyl) ketene dithioacetals 27 in nearly quantitative yield, which were then cyclized in the third step by refluxing in acetic acid/ethanol to afford the desired pyran-4-one 28 in good yields. The generality of the method have been studied in greater details which is described in the present chapter.

REFERENCES

1. Kelber, C., *Chem.Ber.* 1910, *43*, 1252.

2. Thuillier, A.; Vialle, J., *Bull.Soc.Chim.Fr.*, 1962, 2187.

3. Chauhan, S.M.S.; Junjappa, H., *Tetrahedron*, 1976 *32*, 1779.

4. Dieter, R.K.; Jenkitkasemwong, L.; Dieter, J.W. *J.Org.Chem.*, 1984, *49*, 3183.

5. Dieter, R.K., *Tetrahedron*, 1986, *42*, 3029.

6. Thuillier, A.; Vialle, J., *Bull.Soc.Chim.Fr.*, 1962, 2182.

7. Deb, B.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*, 1988, *29*, 2111.

8. Trost, B.M. *Chem.Soc.Rev.*, 1982, *11*, 141.

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

INVESTIGATIONS ON OXOKETENE S,S-ACETALS : NEWER SYNTHETIC METHODS FOR NOVEL CARBOCYCLES AND HETEROCYCLES

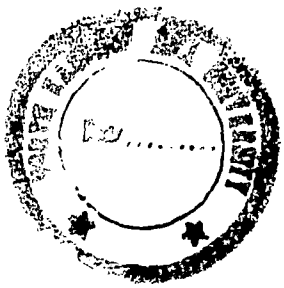
By

BISWAJIT DEB

DEPARTMENT OF CHEMISTRY
SCHOOL OF PHYSICAL SCIENCES

A THESIS
SUBMITTED IN FULFILMENT OF THE REQUIREMENT
FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY



To

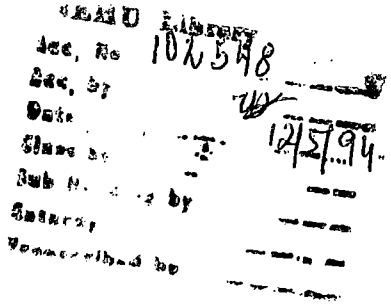
NORTH-EASTERN HILL UNIVERSITY

SHILLONG-793001

INDIA

1990

Chem (theirs).



Phone :
Grams : NEHU

North - Eastern Hill University

Bijni Complex
Bhagyakul, Shillong - 793003 (Meghalaya)

Department of.....

Professor H.Ila
Department of Chemistry

This is to certify that the work described in this thesis has been carried out by Mr. B. Deb 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.

H. ILA
Supervisor
Department of Chemistry
North-Eastern Hill University
Bhagyakul, Bijni Complex
Shillong — 793 003.

Phone :
Grams : NEHU

North - Eastern Hill University

Bijni Complex
Bhagyakul, Shillong - 793003 (Meghalaya)

Department of.....

Head
Department of Chemistry

This is to certify that Mr. B. Deb a Ph.D. student of the Department of Chemistry has satisfactorily completed the following courses as a part of his Ph.D programme.

Title	Course No.
1. Organic Photochemistry	Chem - 624
2. Chemical Kinetics	Chem - 640
3. Medicinal Chemistry	Chem - 631
4. German Language	SPS-602

H. Ila
Professor & Head

Head
Department of Chemistry
North-Eastern Hill University
Shillong — 793 003.

ACKNOWLEDGMENT

The research work described in this thesis was carried out in the Department of Chemistry, North-Eastern Hill University, Shillong under the supervision of Prof.(Mrs.) H. Ila, Head, Department of Chemistry. I take this opportunity to express my deep sense of gratitude for her excellent guidance and encouragement throughout the course of this investigation. I am also thankful to Prof. H. Junjappa, Department of Chemistry for his invaluable suggestions and encouragement.

I also wish to express my gratitude to my colleagues and friends with whom I have been associated throughout these years. I have taken the generosity of too many of them and to list them individually is impossible. I humbly say *"THANK YOU"*.

I further extend my thanks to Directors and Technical Staffs of RSIC, North-Eastern Hill University and Central Drug Research Institute, Lucknow for providing excellent analytical and spectral facilities. Also, quite a few spectral data were obtained from Dr. Gurdeep Singh, Institut Fur Organische Chemie, Universitat Hamburg, West Germany for which I remain grateful. Financial assistance from the Council of Scientific and Industrial Research, New Delhi, is also acknowledged.

Special recognition and gratitude are due to Mr. Sadhu for the help extended by him in processing this thesis.

Finally, I would like to thank my parents and all my family members, they not only endured, also encouraged, assisted and inspired.

Deb 18/5/90

B. Deb

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 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 interesting transformations of cinnamoyl ketene dithioacetals.

A brief account of some of the recent transformations of oxoketene dithioacetals as well as α-cinnamoyl ketene dithioacetals reported from this laboratory is presented in the first chapter. The second chapter deals with the results of a detailed investigation on the acid catalyzed ring opening of cyclopropyl ketones, obtained by the addition of dimethyl sulphoxonium methylide to the corresponding cinnamoyl ketene dithioacetals. In the third chapter of the thesis, 1,2-reduction and reaction of aryl and alkyl magnesium halide with the cyclopropyl ketones and further transformations of the resulting carbinol acetals have been described. The stereochemical consequences and the synthetic importance of these transformations have also been discussed in this chapter. The last chapter of the thesis deals with the synthetic investigation based on the epoxides of cinnamoyl ketene dithioacetals leading to highly substituted δ-pyrones.

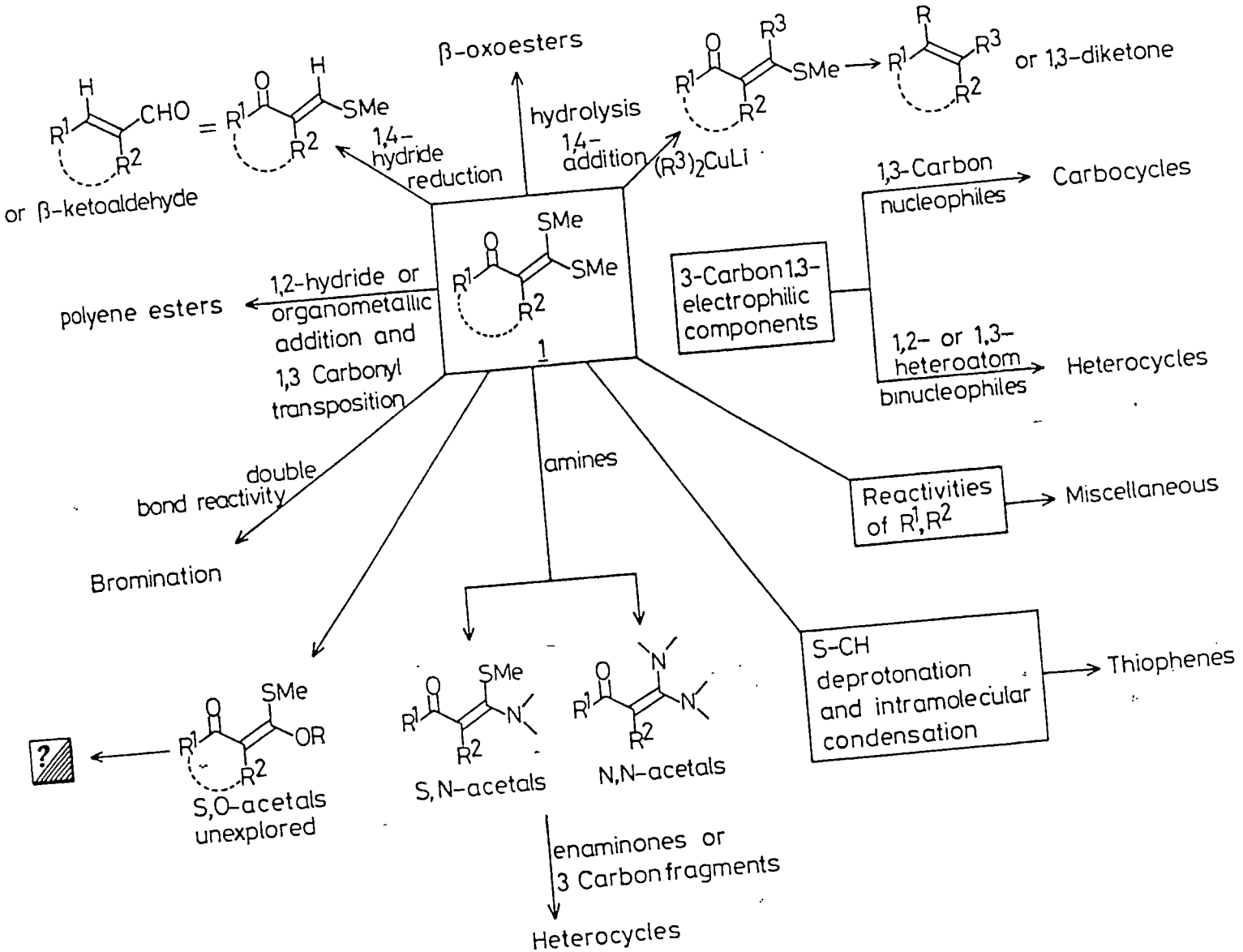
CHAPTER I

POLARIZED KETENE DITHIOACETALS : GENERAL INTRODUCTION

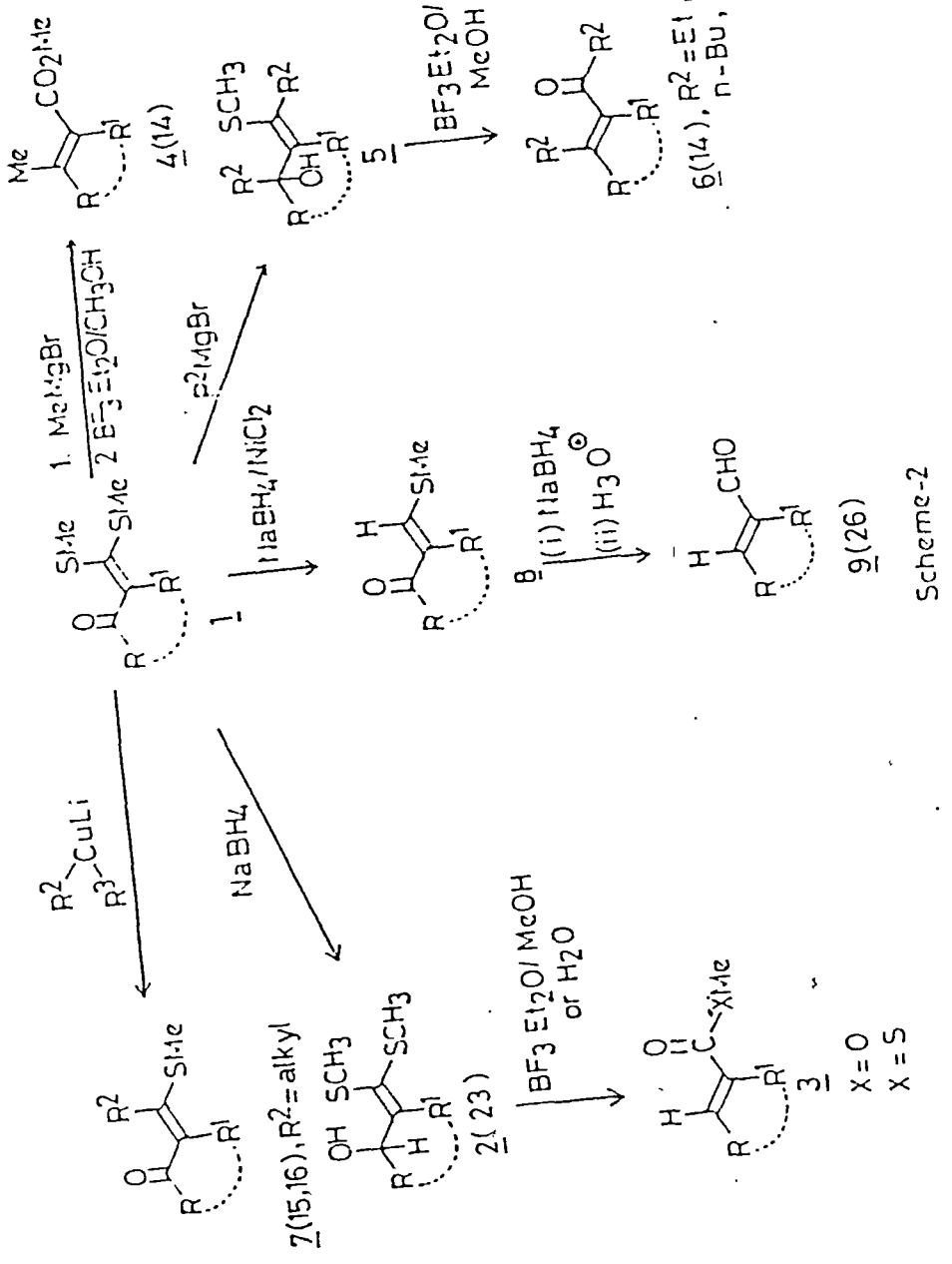
Polarized ketene dithioacetals are one of the simplest synthetic intermediates, and can be conveniently prepared[1-10] from a wide variety of active methylene compounds. They have been extensively explored in this laboratory for the development of new synthetic methods for a number of carbocycles and heterocyclic compounds. This class of compounds exhibit well defined physical properties either as crystalline solids or as distillable liquids and can be purified by conventional methods. They are stable at room temperature and can withstand mild

acidic and alkaline conditions. On the other hand the corresponding O,O-acetals are moisture sensitive and undergo hydrolysis under mild conditions.

Kelber and coworkers[11-13] reported the first synthesis of α-oxoketene dithioacetals in 1910. After the initial synthesis, for more than half a century the synthetic potential of this class of compounds remain unexplored until Thuillier and coworkers[1-4] prepared these compounds in high yields in one pot operation by reacting active methylene compound with CS_2 in the presence of base followed by alkylation. Subsequently, several modifications have been made in the choice of suitable base[5-10]. The general reactivity pattern of α-oxoketene dithioacetals 1 is outlined in Scheme 1. Hydrides and organometallic reagents add to the carbonyl carbon in a 1,2-manner, but this sequence can be altered to the 1,4-path by suitably changing reaction conditions and reagents[14-16]. The differential electrophilicity at 1,3-carbon of the oxoketene dithioacetals have been judiciously utilized for the synthesis of both 5- and 6-membered heterocycles by reacting with 1,2- and 1,3-heteroatom binucleophiles respectively. The 1,3-carbon binucleophiles have been similarly used in the synthesis of carbocycles. The enolate anion formed by the deprotonation (when R^1=alkyl) can undergo condensation with aldehydes to give α-enoyl ketene dithioacetals[17]. When R^2 is a methyl group an allylic anion is generated in


β-oxoesters
hydrolysis
1,4-addition
$(R^3)_2CuLi$
or 1,3-diketone
1,4-hydride reduction
or β-ketoaldehyde
1,2-hydride or organometallic addition and 1,3 Carbonyl transposition
polyene esters
1
1,3-Carbon nucleophiles
Carbocycles
3-Carbon 1,3-electrophilic components
1,2- or 1,3-heteroatom binucleophiles
Heterocycles
double bond reactivity
Bromination
amines
Reactivities of R^1, R^2
Miscellaneous
S-CH deprotonation and intramolecular condensation
Thiophenes
S,O-acetals unexplored
S,N-acetals
N,N-acetals
enaminones or 3 Carbon fragments
Heterocycles

Scheme-1

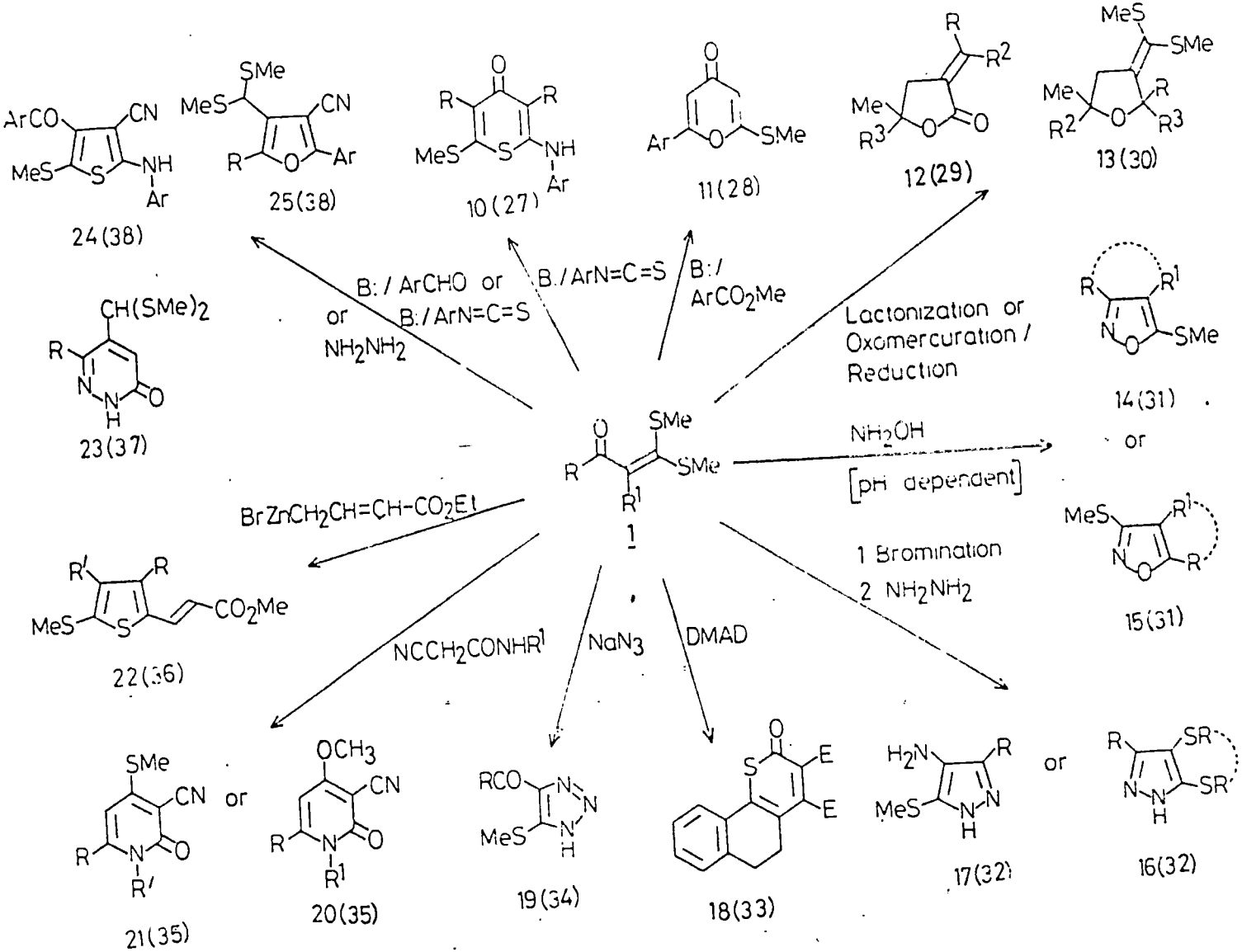


Scheme-2

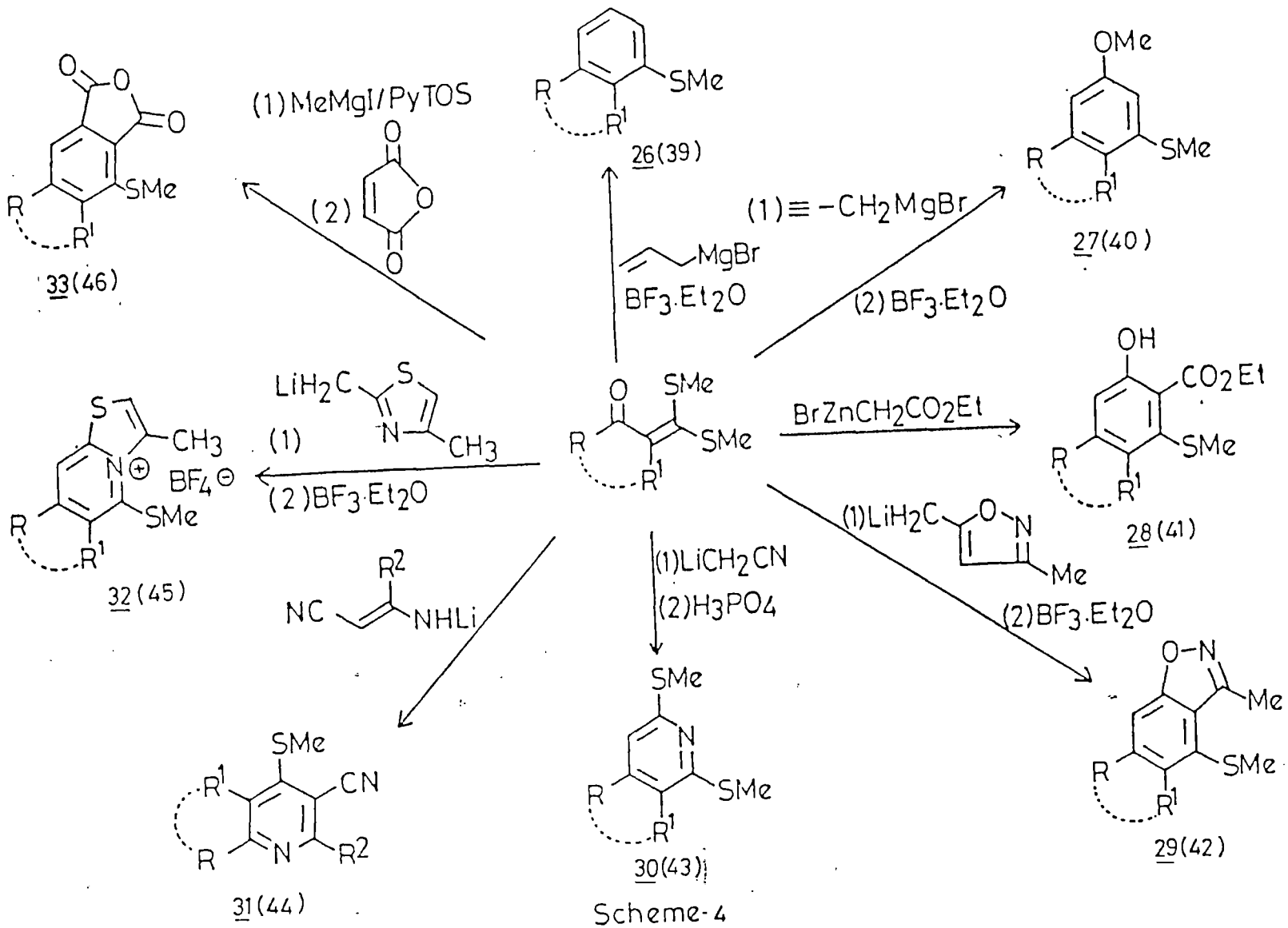
the presence of strong bases leading to rearranged products[18]. Deprotonation of the thiomethyl group followed by intramolecular aldol type condensation to afford thiophenes is also reported[19,20]. Nucleophilic substitution of one or both alkylthio groups in these intermediates by alkoxides or amines affords the corresponding O,S-, -N,S-, and N,N- acetals, which have also been shown to be versatile synthones for various transformations. The reactivity of double bond has also been studied with electrophiles. Thus, the bromination at α-position with N-bromosuccinimide has been carried out successfully[21,22].

The oxoketene dithioacetals have also been shown to undergo regio-, chemo-, and stereoselective C-C and C-H bond forming reactions[4,23]. The reactivity pattern of polarized ketene dithioacetals have been reviewed[24,25] and a few of the transformations have been depicted in Scheme 2. Numerous substituted and fused five and six membered heterocycles have been synthesized using oxoketene dithioacetals[27-38]. Some of the selected ones are shown in Scheme 3. However, these intermediates also serve as useful three carbon 1,3-electrophilic systems resulting in the formation of aromatic ring systems from acyclic precursors (Scheme 4).

As mentioned earlier the aldol condensation of acylketene dithioacetals with aromatic aldehydes and the corresponding higher enyl analogs afford α-cinnamoyl 34 or


24(38)
25(38)
10(27)
11(28)
12(29)
13(30)
23(37)
B:/ ArCHO or
or B:/ ArN=C=S
NH2NH2
B:/ ArN=C=S
B:/
ArCO2Me
Lactonization or
Oxomercuration /
Reduction
14(31)
or
15(31)
NH2OH
[pH dependent]
1 Bromination
2 NH2NH2
BrZnCH2CH=CH-CO2Et
22(36)
NCCH2CONHR1
NaN3
DMAD
1
21(35)
20(35)
19(34)
18(33)
17(32)
or
16(32)

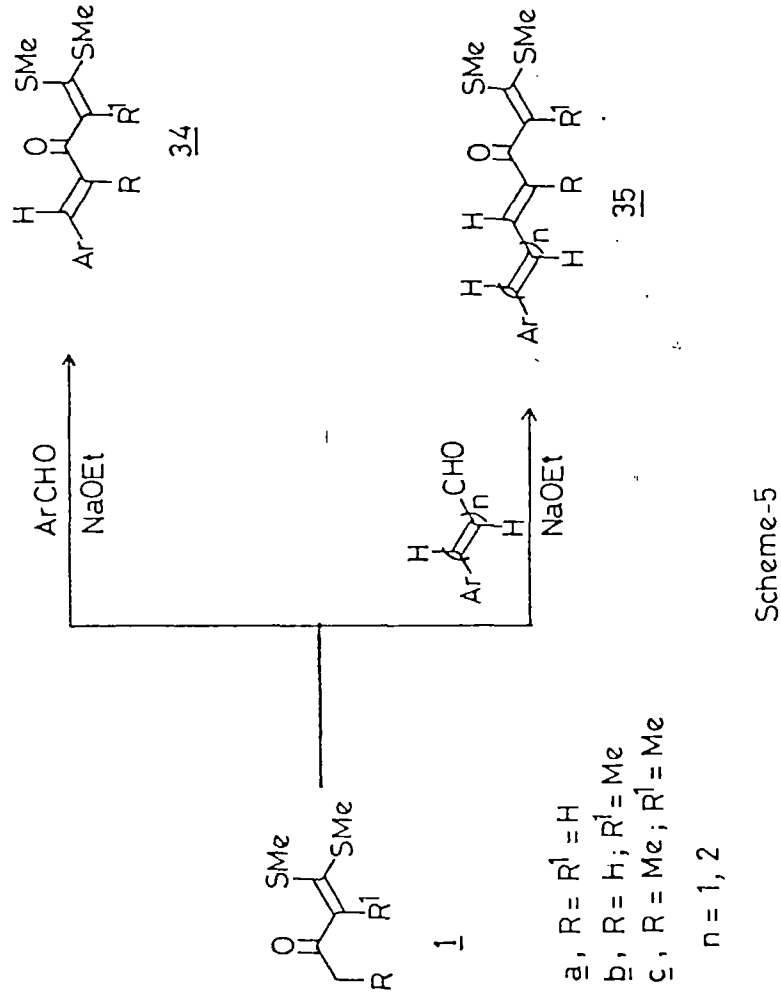
Scheme-3


(1) MeMgI/PyTOS
(2)
BF3·Et2O
MgBr
(1) ≡–CH2MgBr
(2) BF3·Et2O
BrZnCH2CO2Et
(1)
(2) BF3·Et2O
(1) LiCH2CN
(2) H3PO4
(1) LiH2C
(2) BF3·Et2O
33(46)
26(39)
27(40)
28(41)
32(45)
30(43)
29(42)
31(44)

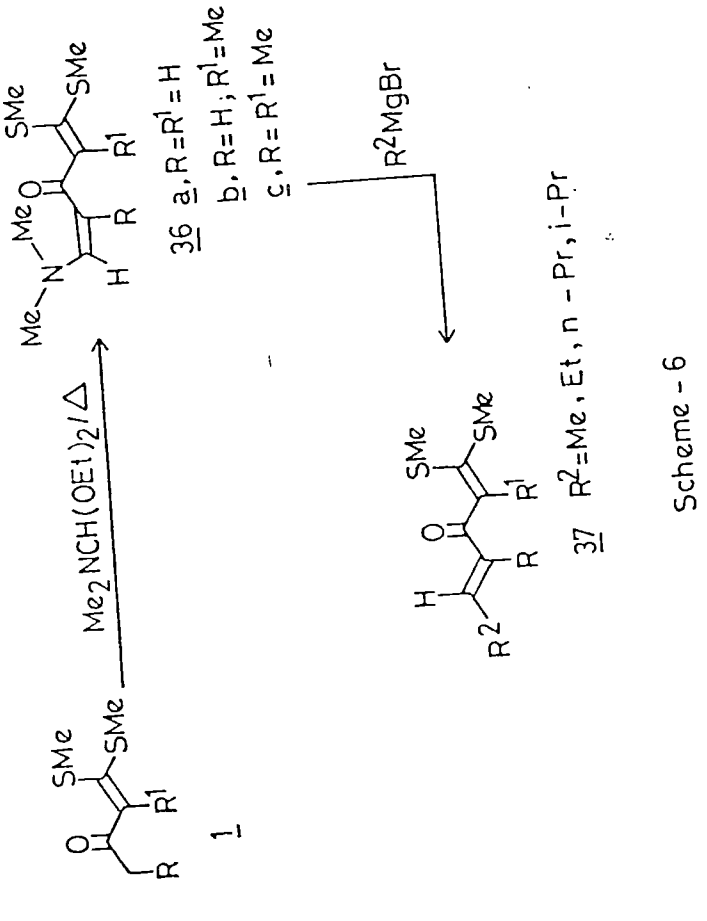
Scheme-4

5-aryl-2,4-pentadienoyl 35 ketene dithioacetals[17,47] as outlined in the Scheme 5. This methodology was not successful for the corresponding α-alkenoyl ketene dithioacetals as the aliphatic aldehydes underwent polymerization under these conditions. Therefore, an alternative route for these intermediates has been ~~achieved from~~ developed in our laboratory[48]. Condensation of acylketene dithioacetals with formamide acetals afforded the corresponding enamines 36, which underwent regioselective 1,4-addition with alkyl Grignard reagents to afford 37 (Scheme 6).

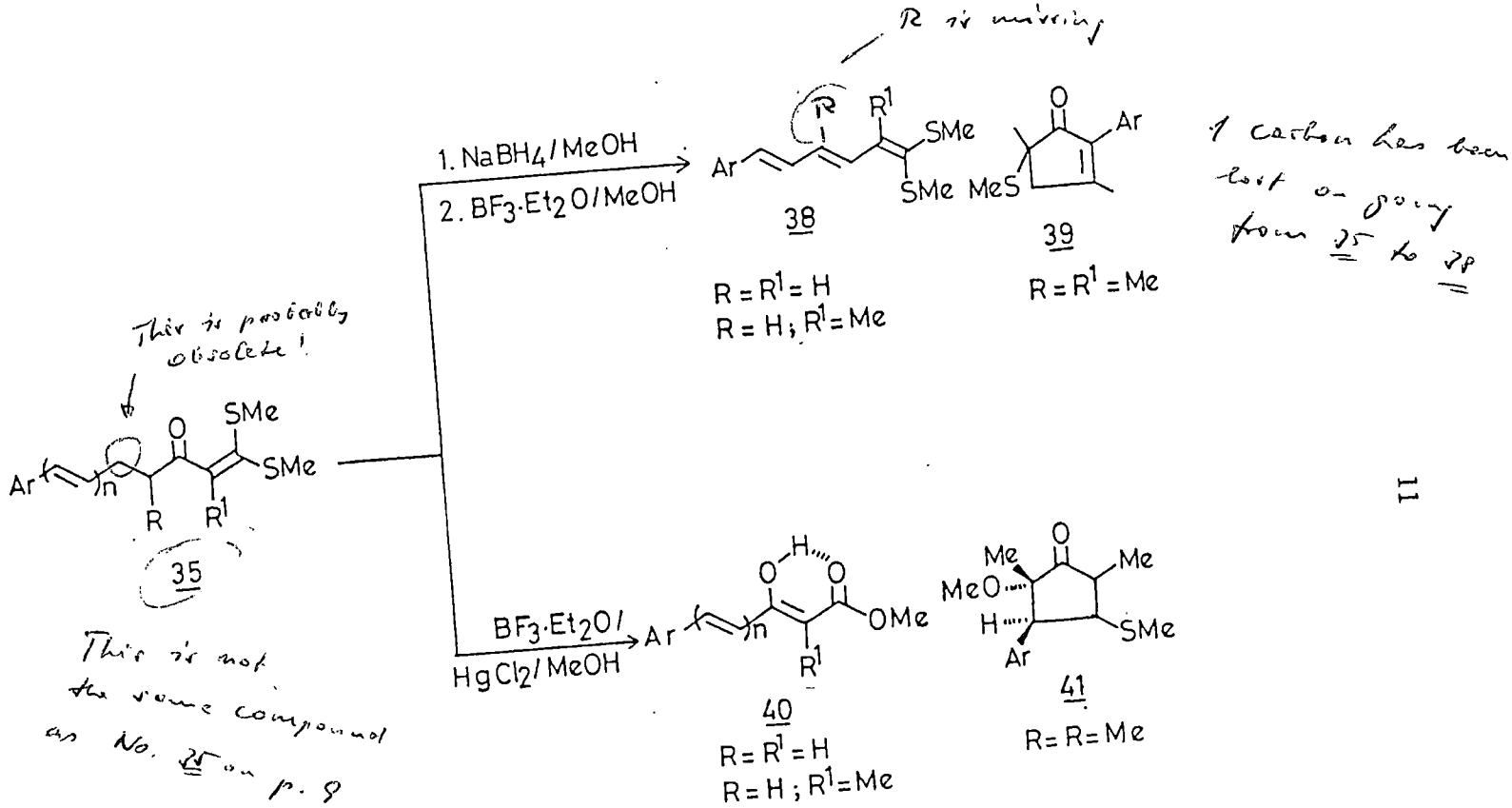
Several important transformations based on the intermediates 34,35 are shown in Scheme 7. Thus, a general method for the synthesis of polyene esters 38 has been reported by 1,2-reduction of 35 followed by methanolysis in the presence of borontrifluoride etherate. On the other hand, the carbinols derived from the corresponding 2,4-dimethyl cinnamoyl ketene dithioacetals underwent borontrifluoride etherate assisted electrocyclization through pentadienyl carbonium ion to give the rearranged cyclopentenes[50] 39 in good yields. Similarly, Hg(II) assisted methanolysis[51] of 35 gave γ,δ-unsaturated esters 40, while the corresponding 2,4-dimethyl cinnamoyl ketene dithioacetals underwent Nazarov cyclization to afford the corresponding cyclopentene 41 (Scheme 7). The cinnamoyl ketene dithioacetals 34 have also been utilized for the synthesis of substituted stilbenes 42 and salicylates 43 through benzoannelation. Thus, 34 undergoes 1,2-addition


SMe
SMe
O
R
R1
1
ArCHO
NaOEt
34
CHO
n
H
Ar
NaOEt
35
a, R= R1 =H
b, R= H; R1 = Me
c, R = Me; R1 = Me
n = 1, 2

Scheme-5


Me2NCH(OEt)2/Δ
R2MgBr
1
36 a, R=R1=H
b, R=H; R1=Me
c, R=R1=Me
37 R2=Me, Et, n-Pr, i-Pr

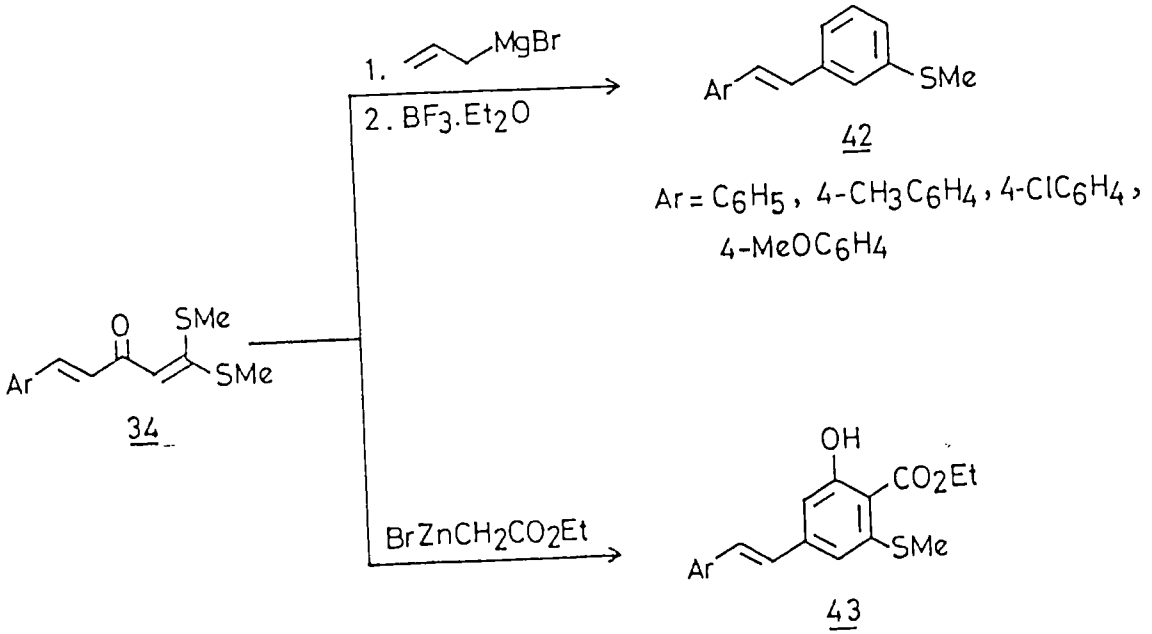
Scheme - 6


R is missing
1. NaBH4/MeOH
2. BF3·Et2O/MeOH
38
R = R1 = H
R = H; R1 = Me
39
R = R1 = Me
1 carbon has been lost on going from 35 to 38
This is probably obsolete!
35
This is not the same compound as No. 35 on p. 9
BF3·Et2O/
HgCl2/MeOH
40
R = R1 = H
R = H; R1 = Me
41
R = R = Me

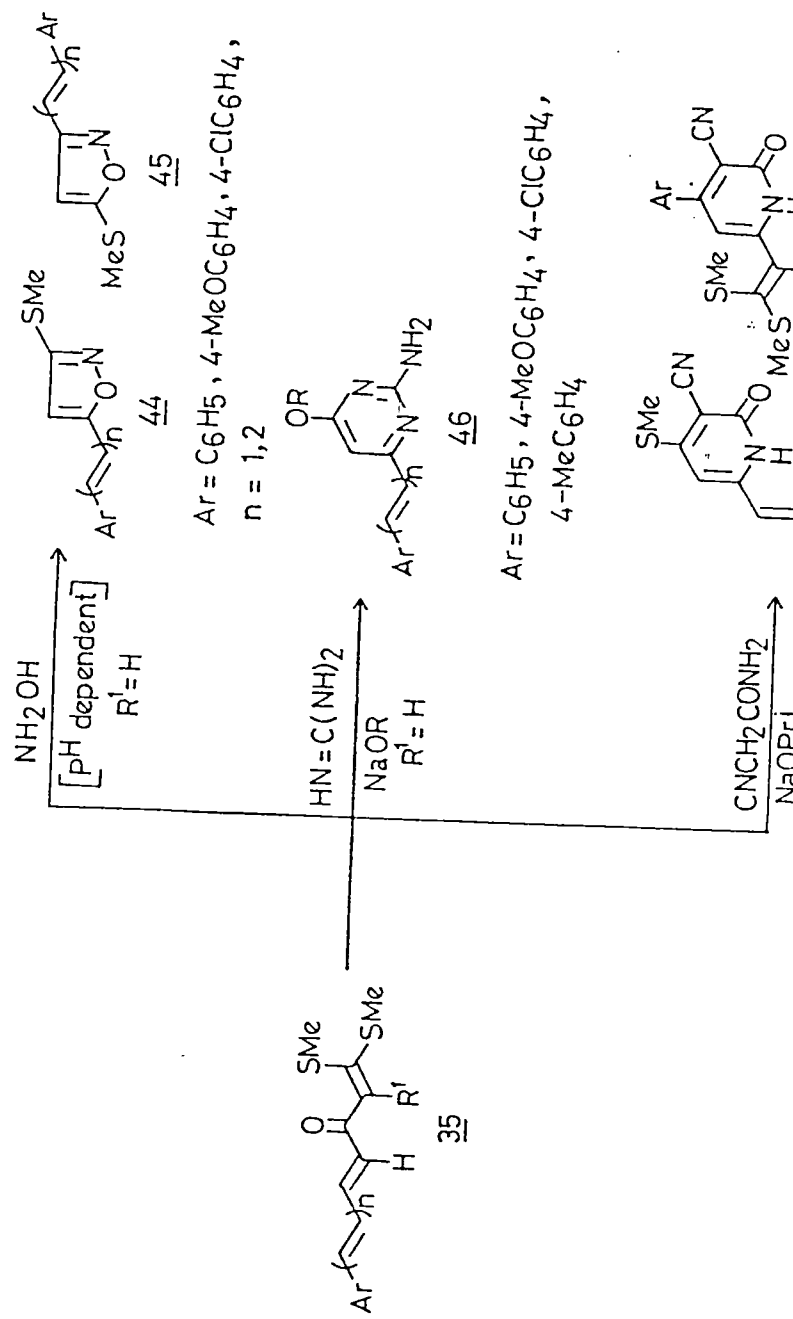
Scheme-7

with allylmagnesium bromide followed by cycloaromatization in the presence of $BF_3.Et_2O$ to afford the substituted stilbenes[52] 42. Similarly on addition of excess Reformatsky reagent to 34 under drastic condition yields 4-styrylsalicylates[53] 43 (Scheme 8). The α-cinnamoyl ketene dithioacetals 34 and their higher homologes 35 were found to be useful precursors for the synthesis of styryl and higher enyl substituted various heterocycles[31,54-55] (Scheme 9). The reaction of hydroxylamine is of greater interest since by manipulating the reaction conditions it was possible to synthesize both 3- and 5-styryl 44, 45 (and their higher homologs) in good yields, in regioselective manner[31].

The versatile synthetic applications of the cinnamoyl ketene dithioacetals 35 for a number of important heterocycles, carbocycles and ene esters prompted further study on their synthetic applications, which has been carried out as a part of the present programme. In the second chapter a new route for substituted 3-arylcyclopentanone 50-52 has been developed through the cationic ring opening of α-bis(methylthio)methylene alkyl cyclopropyl ketones[56] 49. The cyclopropyl ketones 49 were obtained in excellent yields by conjugate addition of dimethyloxosulphonium methylide to α-cinnamoyl ketene dithioacetals 34 under phase transfer conditions. These ketones 49 underwent facile ring opening and intramolecular cyclization in H_3PO_4/HCOOH through π-

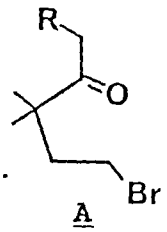

1. MgBr
2. $BF_3.Et_2O$
Ar
SMe
42
Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-$MeOC_6H_4$
O
SMe
SMe
Ar
34
$BrZnCH_2CO_2Et$
OH
CO_2Et
SMe
Ar
43
Ar = C_6H_5, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-$NO_2C_6H_4$

Scheme-8


NH2OH
[pH dependent]
R1=H
44
45
Ar = C6H5, 4-MeOC6H4, 4-ClC6H4,
n = 1,2
HN=C(NH)2
NaOR
R1=H
46
Ar=C6H5, 4-MeOC6H4, 4-ClC6H4,
4-MeC6H4
CNCH2CONH2
NaOPr-i
47
48
Ar= C6H5, 4-MeOC6H4, 4-ClC6H4,
2-MeOC6H4, 2-ClC6H4
35

Scheme-9

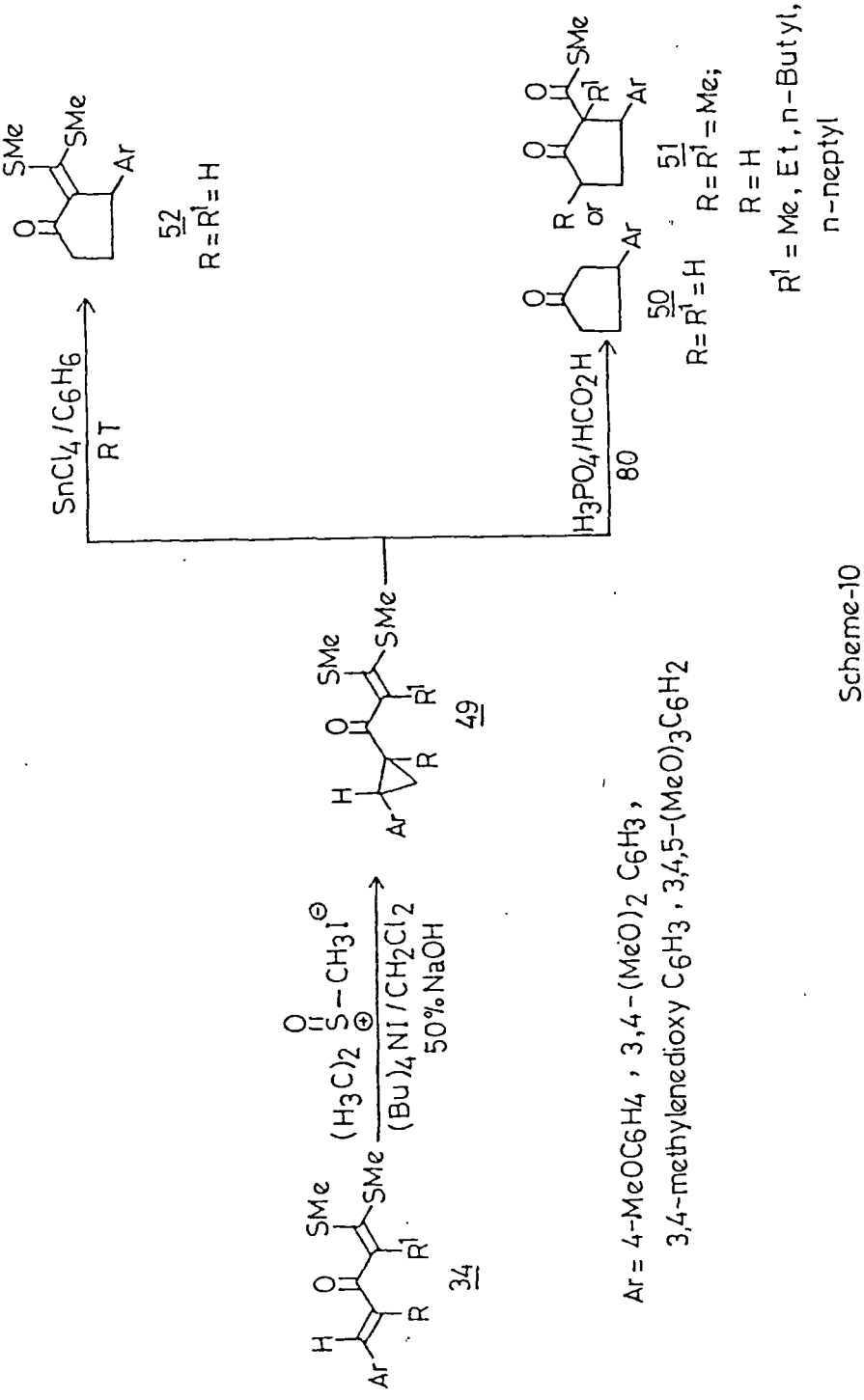
participation of bis(methylthio)methylene double bond to afford cyclopentanone 50 or 51 depending on substituents. Similarly, the corresponding 2-bis(methylthio)methylene cyclopentanones 52 were obtained from 49 on treatment with stannic chloride in benzene at room temperature. The rearrangement represents a novel intramolecular alkylation approach for substituted cyclopentanoids in which bis(methylthio)methylene group acts as a latent ester functionality. These results are important since earlier attempts to synthesize cyclopentanones through intramolecular alkylation of either γ-haloketone (A) or the corresponding β-ketoesters (B) in either basic or acidic



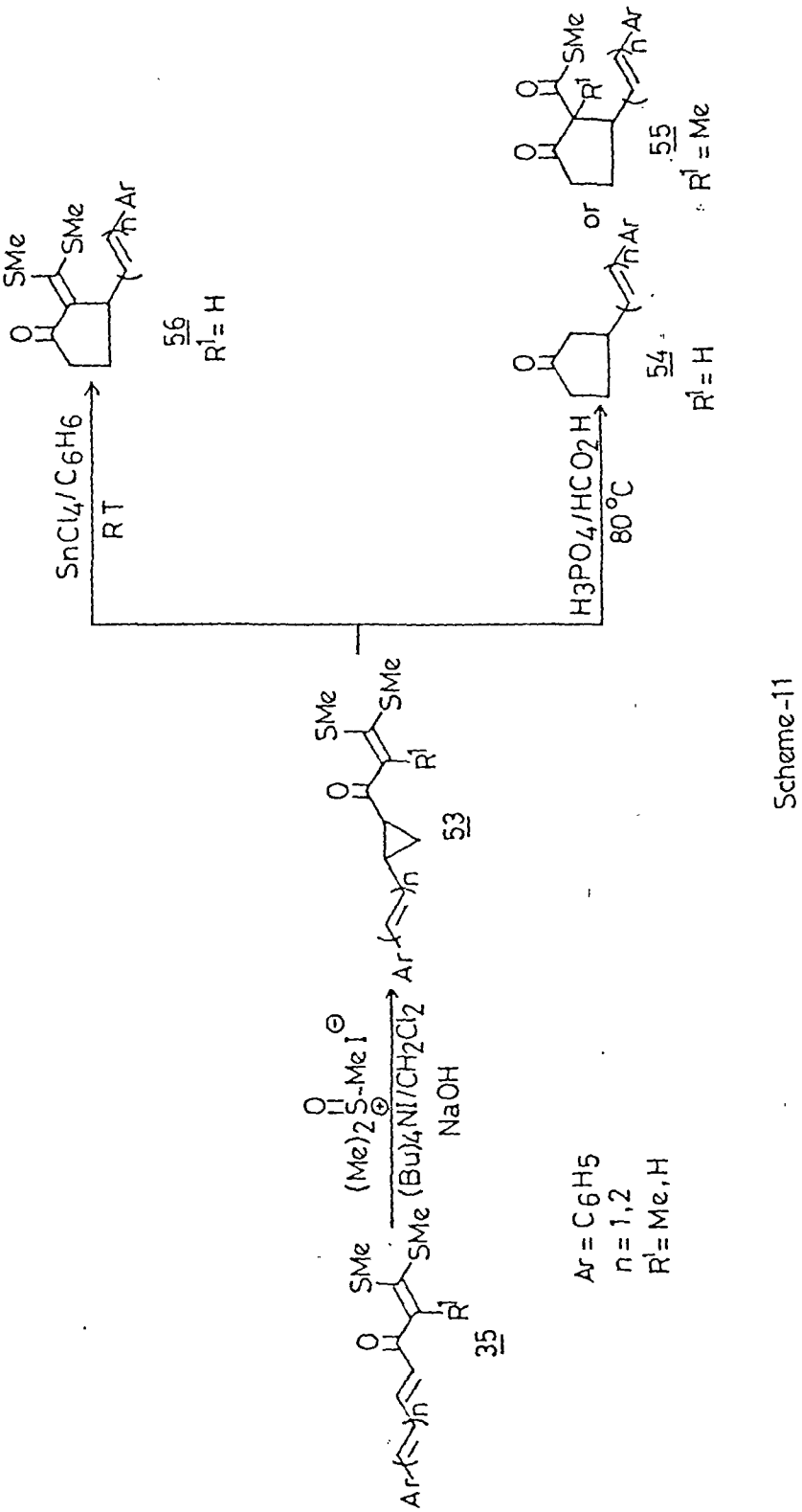
A

B

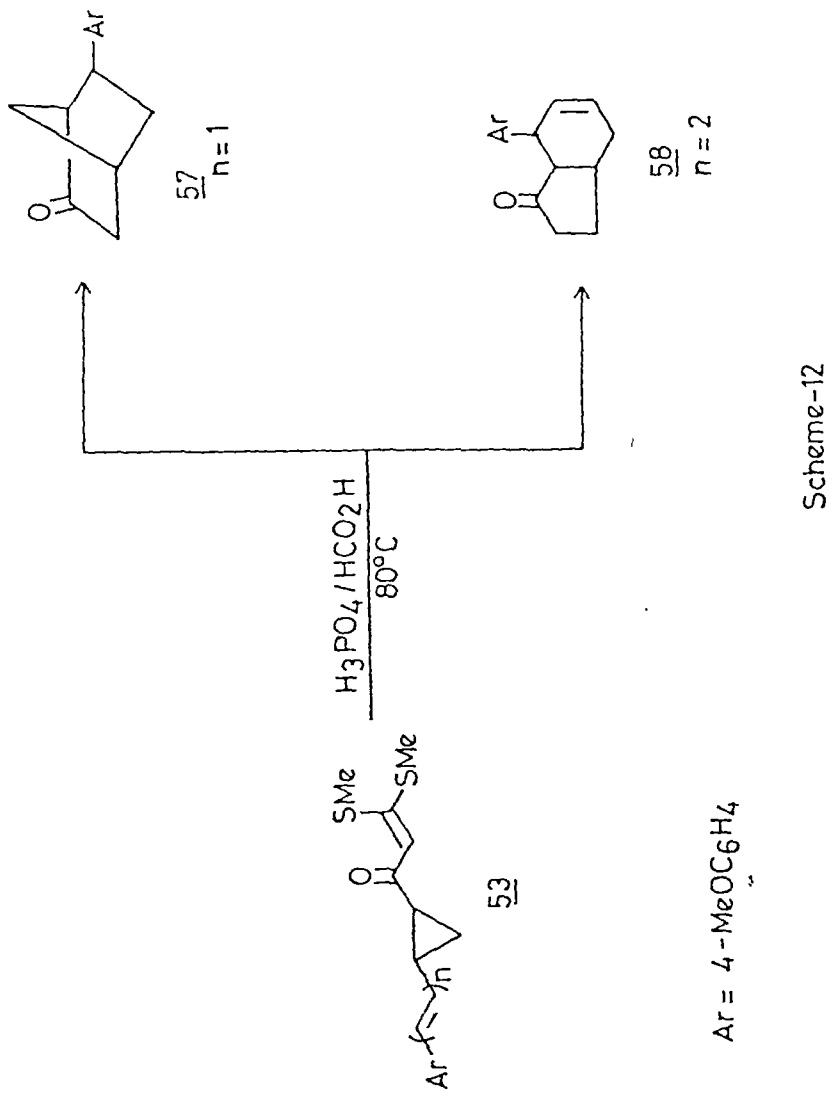
conditions gave the products of O-alkylation rather the C-alkylation due to stereoelectronic factors[57]. However, the present cyclopentanone synthesis (Scheme 10) was successful only with those cyclopropyl ketones with aryl substituents capable of stabilizing the benzylcarbonium ion on ring opening, while the phenyl substituted cyclopropanes yielded only open chain carbinol. A probable mechanism based on various experimental studies has been suggested for these transformations. The second part of this chapter deals with the studies based on cationic ring opening of styryl and 4-aryl-1,3-butadienyl cyclopropyl


SMe
SMe
Ar
O
52
R=R¹=H
SnCl4/C6H6
RT
H3PO4/HCO2H
80
O
R¹
SMe
R
or
Ar
O
50
R=R¹=H
51
R=R¹=Me;
R=H
R¹ = Me, Et, n-Butyl,
n-neptyl
SMe
SMe
R¹
O
R
H
Ar
49
(H3C)2 S⊕ CH3I⊖
(Bu)4NI/CH2Cl2
50% NaOH
34
Ar = 4-MeOC6H4, 3,4-(MeO)2 C6H3,
3,4-methylenedioxy C6H3, 3,4,5-(MeO)3C6H2

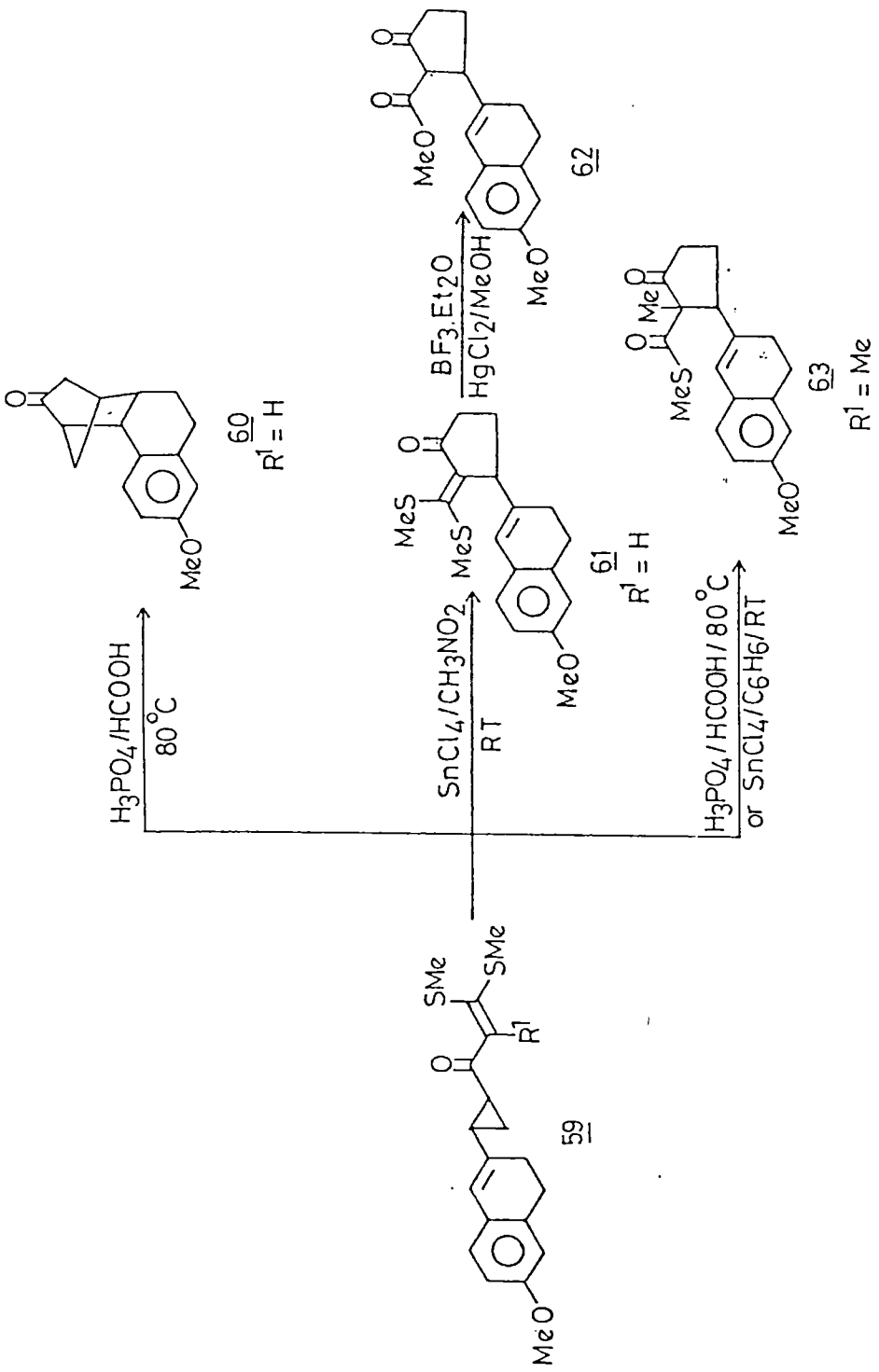
Scheme-10


SnCl4/C6H6
RT
56
R1= H
H3PO4/HCO2H
80°C
or
54
R1= H
55
R1 = Me
53
35
(Me)2S-MeI
(Bu)4NI/CH2Cl2
NaOH
Ar = C6H5
n = 1,2
R1= Me, H

Scheme-11



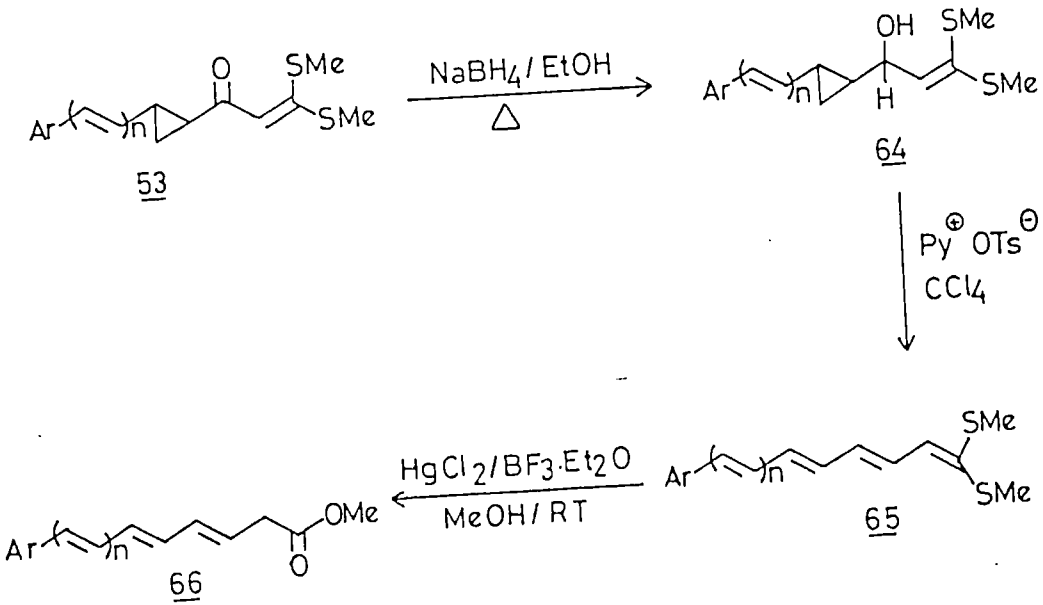
Scheme-12


H3PO4/HCOOH
80°C
60
R1 = H
SnCl4/CH3NO2
RT
61
R1 = H
BF3.Et2O
HgCl2/MeOH
62
H3PO4/HCOOH/80°C
or SnCl4/C6H6/RT
63
R1 = Me
59
MeO
MeS
SMe
Me

Scheme-13

ketones 53. These cyclopropyl ketones 53 were synthesized by similar manner as described above. Thus, on treatment of 53 with H_3PO_4/HCO_2H gave either 3-styrylcyclopentanone 54 or the corresponding β-oxothioester 55. While in the presence of stannic chloride the corresponding α-bis(methylthio)methylene cyclopentanone 56 (Scheme 11). However, the 4-methoxy derivative of the cyclopropane 53 behave differently under similar conditions. Thus, 53 on treatment with H_3PO_4/HCOOH gave 6-(4-methoxyphenyl)bicyclo [2.2.1] hept-2-one 57, while the corresponding dienyl analogue afforded the indanone derivative 58 in good yield. The probable mechanism for the formation of these compounds have been suggested. This methodology has been utilized for the synthesis of some target molecules like 11-oxosteroid precursors. Thus, the cyclopropyl ketone 59 on treatment with H_3PO_4/HCOOH gave the bicyclic compound 60, while in stannic chloride the corresponding 2-bis(methylthio)methylene cyclopentanone 61 was obtained in good yield. The subsequent methanolysis of 61 in the presence of $BF_3.Et_2O/HgCl_2$ gave the steroid precursor 62. Similarly the α-methyl-β-ketothioester analogue 63 was synthesized in good yield from the corresponding α-methyl derivative (Scheme 13).

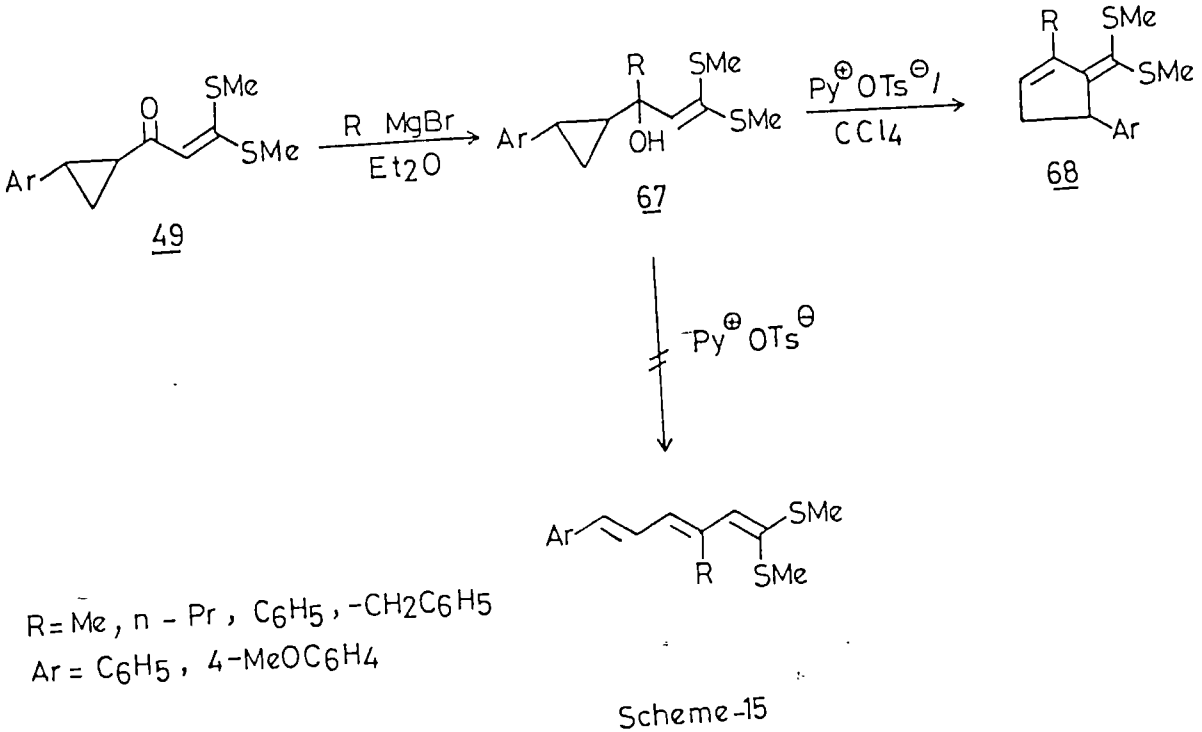
The third chapter of the thesis deals with the addition of hydride and carbon nucleophiles on cyclopropyl ketones 53. Thus, a new methodology for β, γ-unsaturated polyene esters 66 has been developed as shown in Scheme 14. The cyclopropyl ketones 53 and their higher enyl anologues



Ar = C_6H_5 , 4-$MeOC_6H_4$, 3,4-methylenedioxy C_6H_3 ,
3,4-$(MeO)_2C_6H_3$, 4-ClC_6H_4

n = 0,1,2

Scheme-14

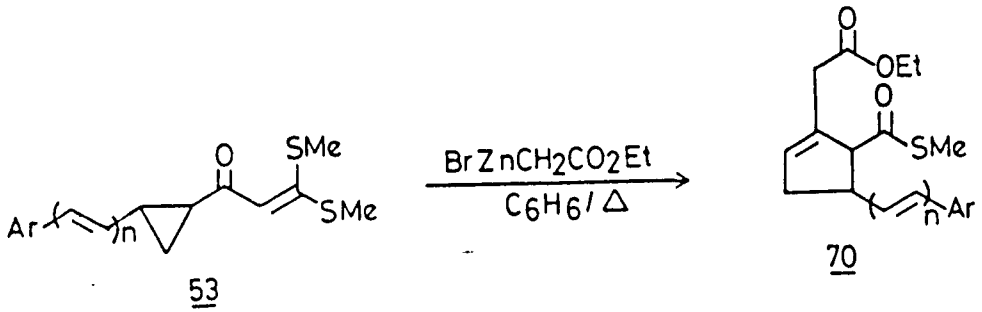


49 67 68

R = Me, n - Pr, C_6H_5, $-CH_2C_6H_5$

Ar = C_6H_5, 4-$MeOC_6H_4$

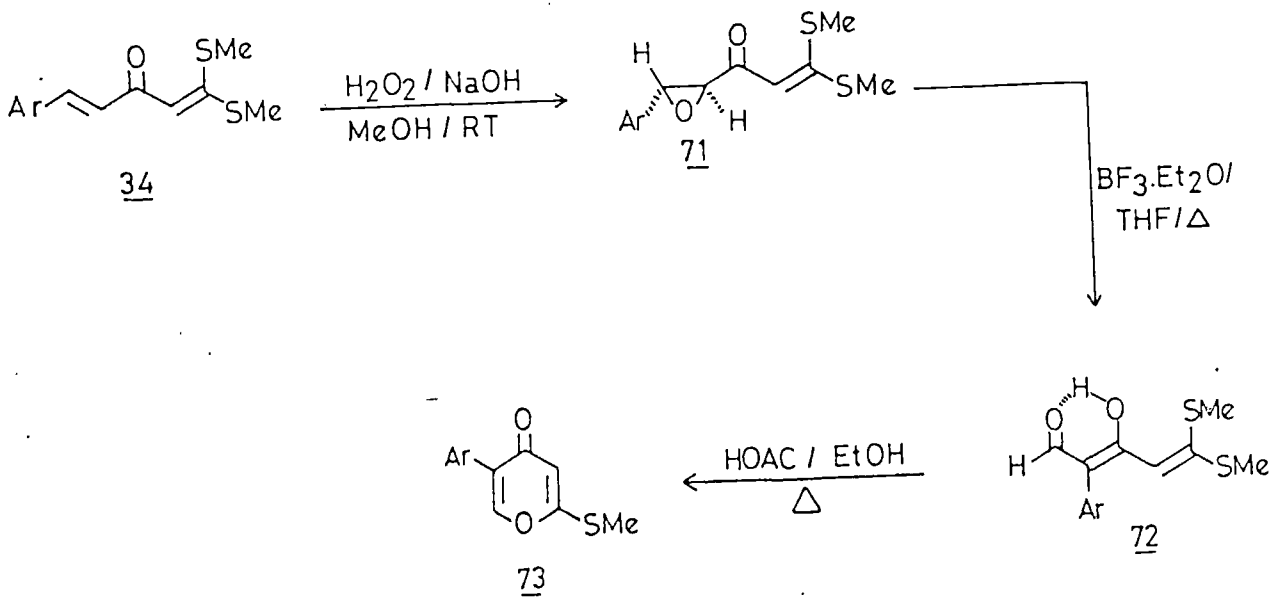
Scheme-15



53 70

Ar = C_6H_5 , 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$,
3,4- methylene dioxy C_6H_3
n = 0 , 1 , 2

Scheme-16



Ar= C_6H_5 ; 4-MeC_6H_4 ; 4-ClC_6H_4 ; 4-MeOC_6H_4 , 3-MeOC_6H_4 ;
3,4-$(MeO)_2C_6H_3$; 3,4,5-$(MeO)_3C_6H_2$; 3,4- methylenedioxy C_6H_3

Scheme-17

undergo regioselective 1,2-addition with sodium borohydride followed by ring opening and deprotonation in the presence of pyridinium tosylate to afford the respective *n*-aryl bis(methylthio)polyenes 65 in good yields. These polyenes on methanolysis under controlled conditions in the presence of $BF_3.Et_2O/HgCl_2$ afforded β,γ-unsaturated esters 66 (Scheme 14). Addition of alkyl and benzyl Grignard reagent to cyclopropyl ketones 49, gave the corresponding regioselectively carbinols 67. Interestingly, the ring opening of 67 in the presence of pyridinium tosylate afforded the cyclopentene derivative 68 instead of open chain polyene 69 (Scheme 15). A probable mechanism to rationalize these results has been suggested. Addition of Reformatsky reagent to cyclopropyl ketones 35 afforded δ-ketocyclopentene thioester 70 in one step in good yields (Scheme 16).

In the last chapter the synthetic transformations of epoxy ketones 71 by regioselective epoxidation of α-cinnamoyl ketene dithioacetals 34 ($H_2O_2/NaOH$) has been described[58]. Thus, the epoxy ketone 71 underwent borontrifluoride etherate catalyzed rearrangement to afford β-formyl oxoketene dithioacetals 72. These intermediates have been shown to be useful for the synthesis of 4-aryl-2-methylthio-pyran-4-ones 73 (Scheme 17).

Ref. 58 is not on p. 29

REFERENCES

1. Thuillier, A.; Vaille, J. *Bull.Soc.Chim.Fr.* 1959, 1398.
2. Thuiller, A.; Vaille, J. *Bull.Soc.Chim.Fr.*, 1962, 2187.
3. Thuilier, A.; Vialle, J. *Bull.Soc.Chim.Fr.*, 1962, 2194.
4. Saquet, M.; Thuillier, A. *Bull.Soc.Chim.Fr.*, 1966, 1582.
5. Gompper, R.; Schmidt, R.R.; Kutter, E. *Liebigs Ann.Chem.* 1965, *37*, 684.
6. Corey, E.J.; Chen, R.H.K. *Tetrahedron Lett.*, 1973, 3817.
7. Shahak, I.; Sasson, Y. *Tetrahedron Lett.*, 1973, 4207.
8. Chauhan, S.M.S.; Junjappa, H. *Tetrahedron* 1976, *32*, 1779.
9. Dieter, R.K. *J.Org.Chem.*, 1981, *46*, 5031.
10. Ali, S.M.; Tanimato, S. *J.Chem.Soc.Chem.Commun.* 1989, 684.
11. Kelber, C. *Chem.Ber.*, 1910, *43*, 1252.
12. Kelber, C.; Schwarz, A. *Chem.Ber.*, 1911, *44* 1693.
13. Kelber, C.; Schwarz, A. *Chem.Ber.*, 1912, *45*, 137.
14. Singh, G.; Purkayastha, M.L.; Ila, H.; Junjappa, H. *J.Chem.Soc.Perkin Trans I.* 1985, 1289.
15. Dieter, R.K.; Silks, L.A.; Fishpaugh, J.R.; Kastner, M.E. *J.Am.Chem.Soc.* 1985, *107*, 4879.

16. Dieter, R.K.; Fishpaugh, J.R.; Silks, L.A. *Tetrahedron Lett.*, 1982, *23*, 3751.

17. Myrboh, B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Synthesis*, 1984, 50.

18. Apparao, S.; Rahman, A.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1982, *23*, 971.

19. Marino, J.P.; Kostuysk, J.L. *Tetrahedron Lett.*, 1979, *20*, 2489.

20. Marino, J.P.; Kostuysk, J.L. *Tetrahedron Lett.*, 1979, *20*, 2493.

21. Singh, G.; Ila, H.; Junjappa, H. *Synthesis* 1985, 165.

22. Singh, G.; Deb, B.; Ila, H.; Junjappa, H. *Synthesis* 1987, 286.

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

24. Dieter, R.K. *Tetrahedron*, 1986, *42*, 3029.

25. Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron* (in press)., 1990.

26. Myrboh, B.; Singh, L.W.; Ila, H.; Junjappa, H. *Synthesis* 1982, 307.

27. Singh, L.W.; Ila, H.; Junjappa, H. *Synthesis*, 1985, 531.

28. Singh, L.W.; Ila, H.; Junjappa, H. *Synthesis*, 1987, 873.

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

30. Dutta, A.; Bhattacharjee, S.; Ila, H.; Junjappa, H. *Synthesis*, 1988, 729.

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

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

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

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

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

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

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

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

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

40. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1987, *28*, 1459.

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

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

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

44. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron* (in press), 1990.

45. Thomas, A.; Ila, H.; Junjappa, H. *Tetrahedron* (in press), 1990.

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

47. Thuillier, A.; Vialle, J. *Bull.Soc.Chim.Fr.* 1962, 2182.

48. Asokan, C.V.; Balu, M.P.; Ila, H.; Junjappa, H. *Synthesis*, 1988, 727.

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

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

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

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

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

54. Singh, L.W.; Gupta, A.K.; Ila, H.; Junjappa, H. *Sythesis*, 1984, 516.

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

CHAPTER II

ACID CATALYZED RING OPENING OF α-BIS(METHYLTHIO)-METHYLENEALKYL CYCLOPROPYL KETONES : A NOVEL APPROACH TO SUBSTITUTED CYCLOPENTANOIDS*

II.1 INTRODUCTION

As a part of ongoing research in this laboratory it was considered of interest to exploit the α-cinnamoyl ketene dithioacetals of general formula 99 (Scheme 16) as synthetic intermediates, to further explore the synthetic potential of this class of compounds. The activated styryl double bond in these intermediates could easily be converted into the corresponding cyclopropane ring and the resulting cyclopropyl ketones 100,which could be of

---

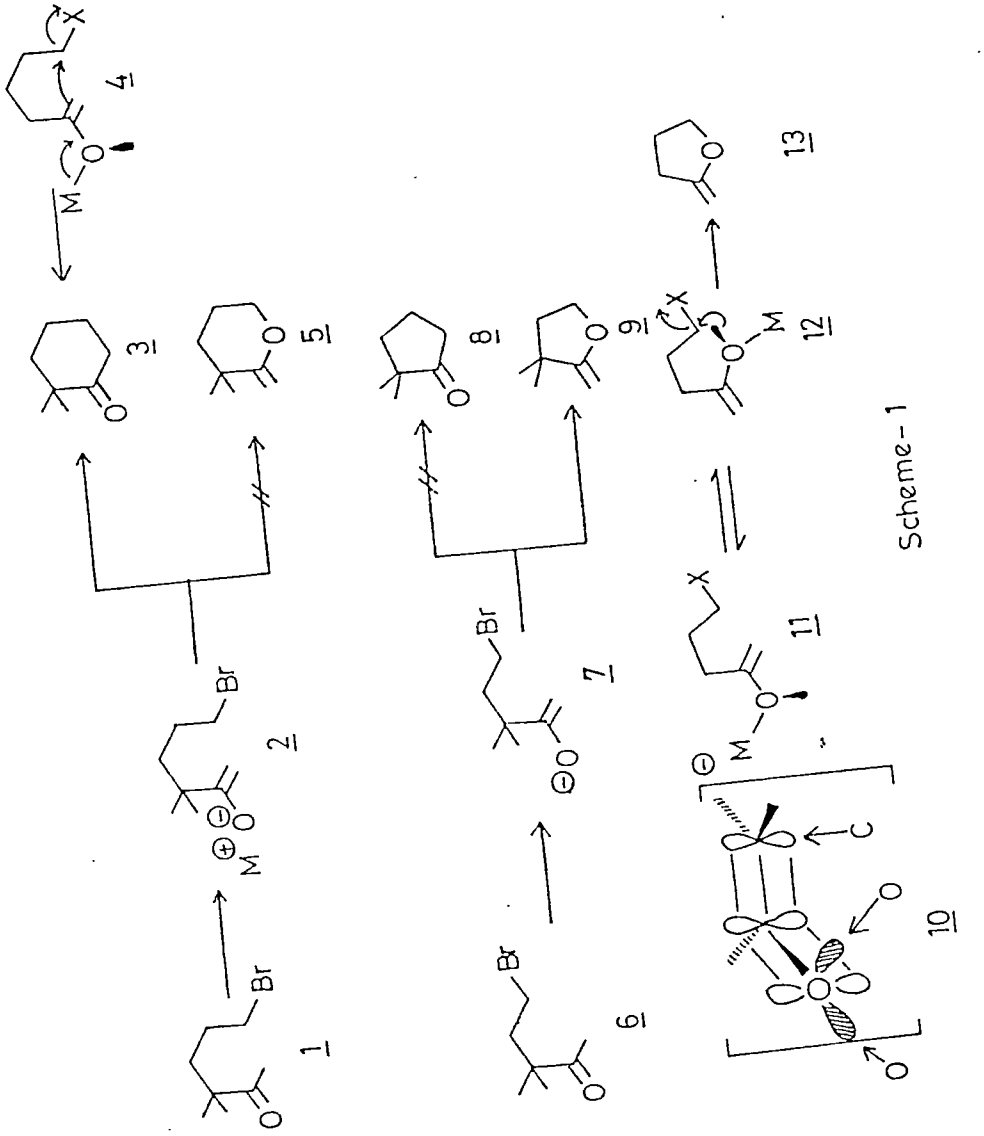
*Deb, B., Ila, H., Junjappa, H., *Tetrahedron Lett.* 1988, *29*, 2111.

considerable synthetic interest. The open chain cation 95, which is formed by an acid catalyzed ring opening, is intercepted intramolecularly by the suitably positioned olefinic double bond of the mercapto functionality to yield the corresponding cyclopentanones 103 (Scheme 17) or their derivatives. Therefore, the cyclopropyl ketones 100, constitute an important class of synthetic intermediates that could provide a new general methodology for the construction of cyclopentanoids. The cyclopropyl ketones 100 indeed underwent acid assisted cyclization and the detailed investigation of these transformations are described in the present chapter.

The cyclopropyl compounds have been the subject of intensive investigations[1] to construct carbocyclic ring systems *via* their acid catalyzed ring opening followed by intramolecular trapping by a suitable nucleophilic center. Thus, a number of approaches have been developed in the past several years to construct cyclopentanoids through the functionalized cyclopropyl ring systems. As an introduction to this chapter it was considered appropriate to briefly review some of the important transformations involving acid assisted cyclopropyl ring opening in the process of various carbocyclic synthesis. A few selected examples covering these aspects are reviewed as follows.

Though the construction of six membered rings using appropriate δ-halo ketones was known for long, the reaction conditions employed for the construction of five-

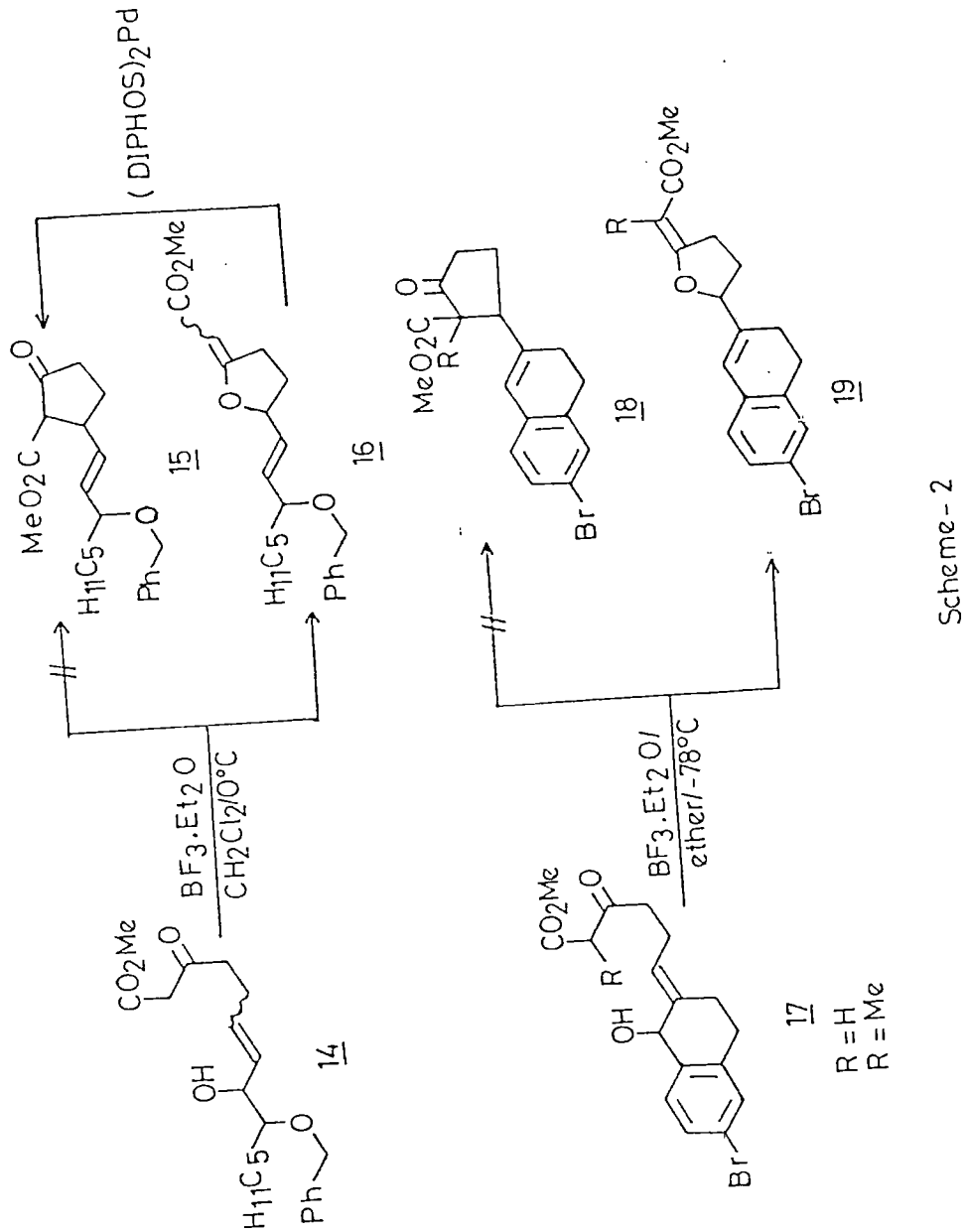
membered ring could not lead to identical ring closure to yield the corresponding cyclopentanoids[2-5]. It was often observed that the attempts for the construction of 5-membered rings from the corresponding δ-haloketones resulted in tetrahydrofuran derivative rather than the corresponding cyclopentanoids. A general set of rules governing various ring forming reactions were recently proposed by Baldwin[3]. These empirical rules help to appreciate and predict the feasibility of ring forming reactions, those concerning the formations of the 5-membered rings, are briefly discussed. So the substrate structure and its design becomes more rational in the planning of cyclopentanoid synthesis. Some of these examples depicted in the Scheme 1, where the metal enolates 2 derived from δ-bromoketone 1 should in principle yield either cyclohexanone 3, if it cyclized in the *endo* fashion, or pyran 5, *via* O-alkylation by *exo*-cyclization. However, only cyclohexanone 3 was formed confirming the preferred 6-*endo-trig* C-alkylative cyclization. However, the enolate anion 7 obtained by metalation of δ-haloketone 6 underwent intramolecular O-alkylation to give 9 instead of cyclopentanone 8 by C-alkylation. This ambiguity was explained by the empirical rule that 5-*endo-trig* is a disfavored process. And the preferred approach of the reacting sites leads to the formation of tetrahydrofuran derivatives. The remarkable difference between these two cyclizations results from stereoelectronic control of the alkylation of the ambident



Scheme-1

nucleophile i.e. the enolate ion. For such an ion 10, C-alkylation requires approach of the electrophile perpendicular to the plane of the enolate, whereas O-alkylation requires approach in the plane of the enolate. Consequently, during the formation of five-membered ring, the approach of the alkylating centre to the carbon site exists as *s-cis* and *s-trans*, as shown by 11 and 12 leading to the preferred enol ether product. On the other hand, in the six-membered precursor 2 the C-alkylation is sterically possible, for the same reasons as those by which 6-*endo-trig* process for ring closure are favoured. These rules which have been established to predict possible structural requirements in substrates in ring closure reactions have been used successfully in designing the substrates for the construction of cyclopentanoids in the present investigation.

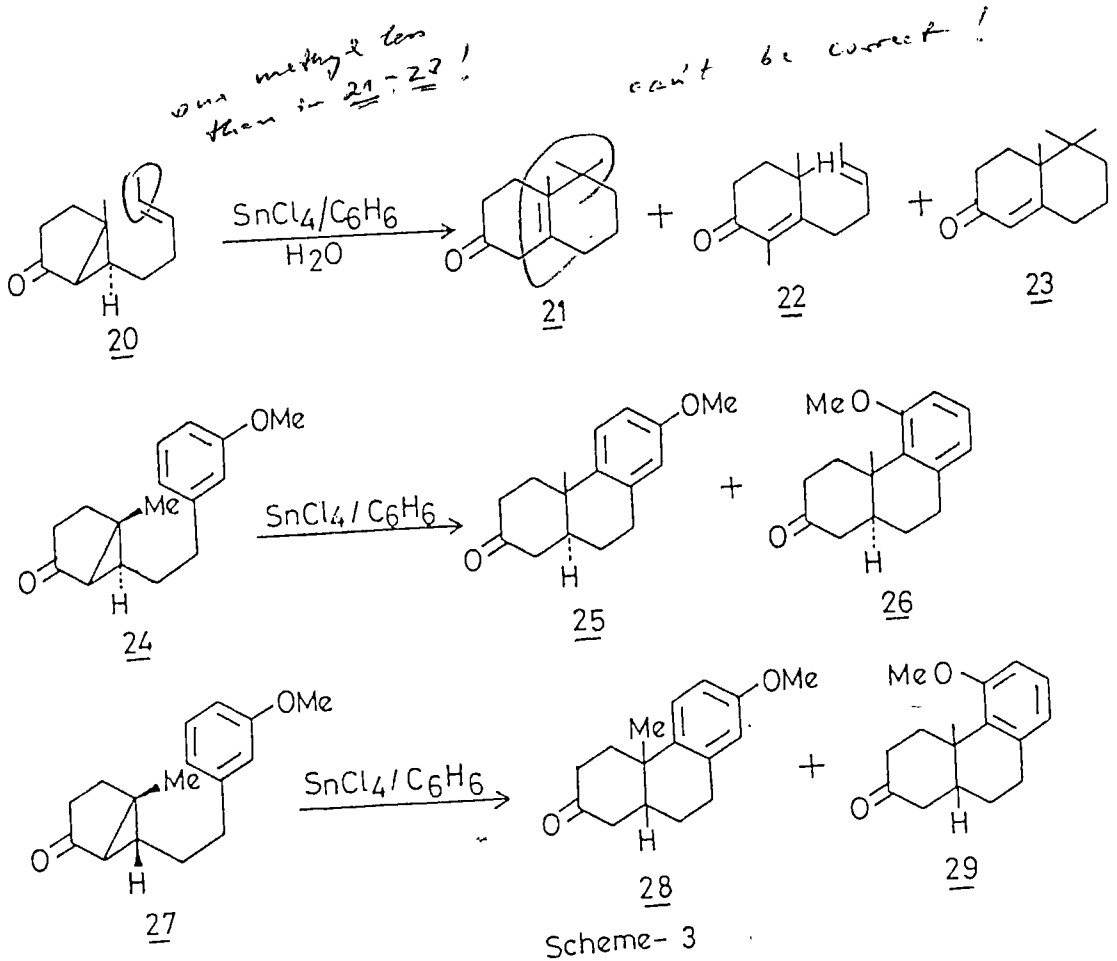
As seen in the preceding discussion the construction of cyclopentanoid ring system from δ-haloketones leads to preferred O-alkylated product rather than C-alkylation. These difficulties became serious constraints in the designing of appropriate precursors for the construction of cyclopentane rings. Trost and co-workers[6-9] have also faced the same thwarting situation when they attempted cyclization of β-ketoesters 14 and 17 resulting in O-alkylated product 16 and 19. However, Trost could circumvent these difficulties by treating furan derivatives 16 and 19 with palladium [0] catalyst so that


(DIPHOS)2Pd
MeO2C
H11C5
Ph
O
CO2Me
15
16
BF3.Et2O
CH2Cl2/0°C
14
OH
MeO2C
R
18
Br
CO2Me
19
BF3.Et2O/
ether/-78°C
17
R=H
R=Me

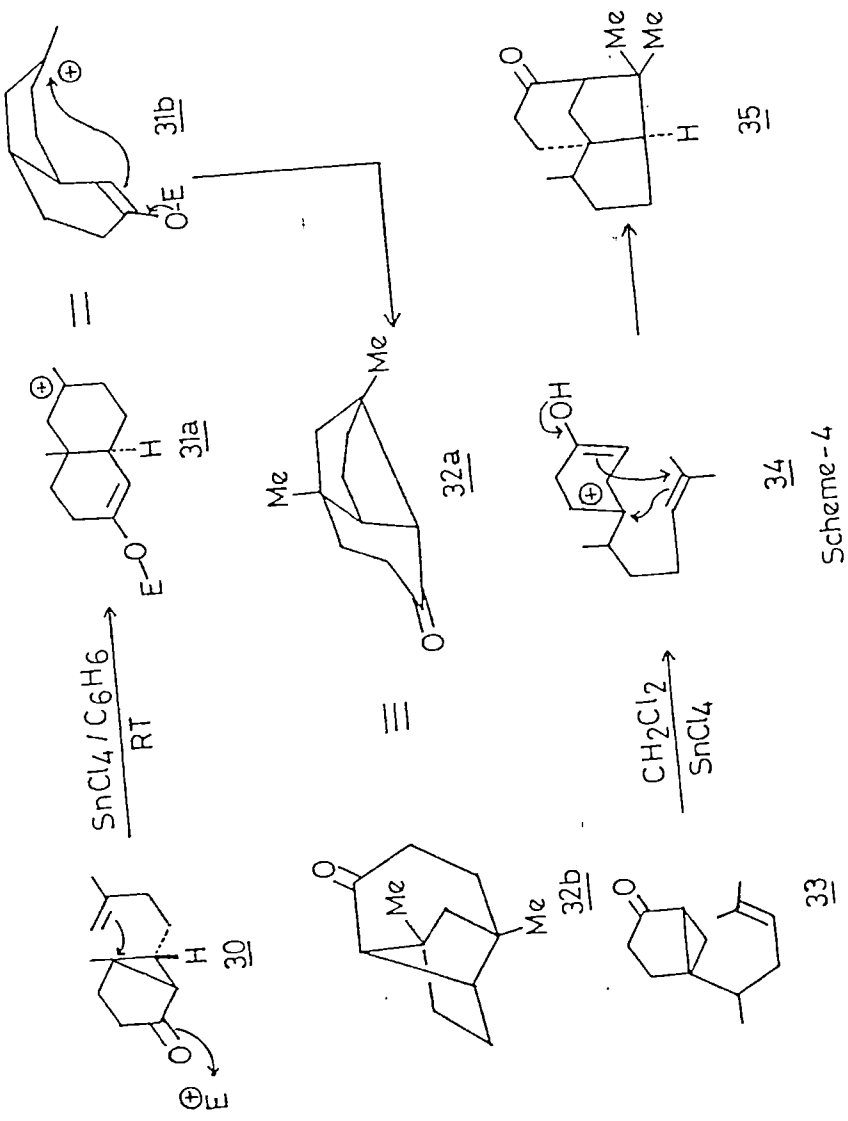
Scheme - 2

they follow a [1,3] rearrangement pathway to give the corresponding cyclopentanones 15 and 18 respectively (Scheme 2).

Stork and co-workers[10,11], have investigated the participation of olefinic functionality in the opening of cyclopropyl ring systems. They studied the reaction of model compound 20 in the presence of $SnCl_4$ and obtained three products, 21, 22 and 23. It was also shown that the compound 23 could be converted to its β,γ isomer 21[10] under similar reaction conditions. The mechanism governing the reaction involves the acid catalyzed cyclopropyl ring opening followed by intramolecular π-participation. They successfully extended these reactions to construct bicyclic ring systems 25, 26, 28 and 29 where the neighbouring participating group ~~being~~ an aromatic ring[11], (Scheme 3). The intramolecular olefin participation in acid catalyzed ring opening was further illustrated by the formation of bicyclo [2.2.1] heptane system[12] 32. Here again the *cis* cyclopropyl ketone 30 undergoes a ring closure *via* a *concerted* participation of the terminal olefin, so that the enol 31 is in a position to trap the resulting carbonium ion leading to 32. An elegant example for ~~the~~ Stork's cation-olefin cyclizations initiated by protonation of cyclopropyl ketones, was provided by Corey in the total synthesis of epi-cedrone[13] 35 (Scheme 4). The treatment of a mixture of two diastereomeric forms of 33 with acetyl methanesulfonate afforded 35 in 85% yield .



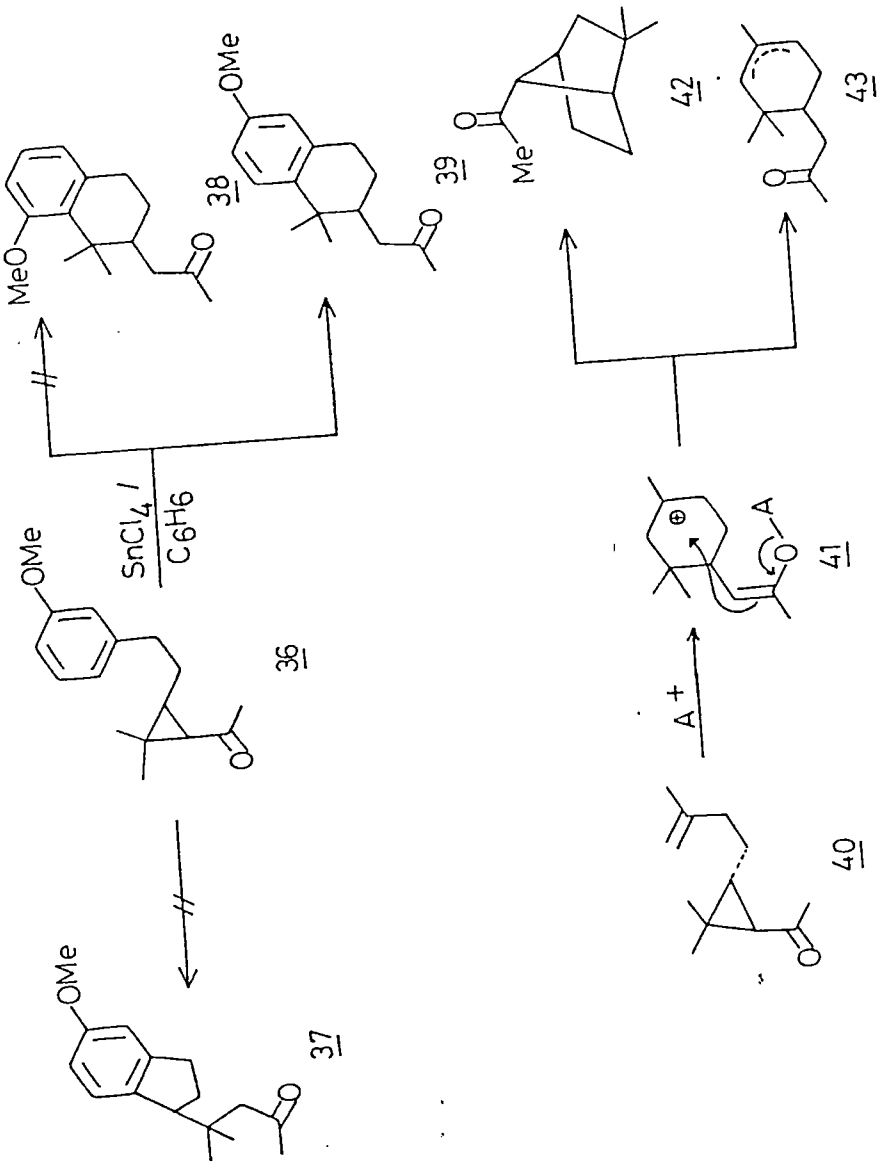
Scheme- 3



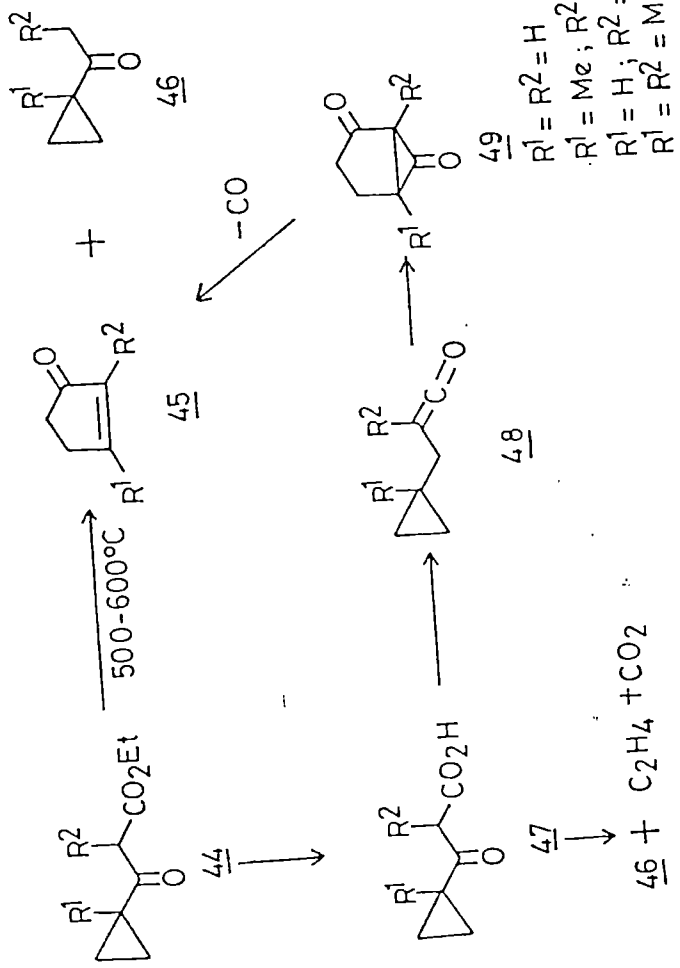
Scheme-4

The possibility of initiating acid catalyzed cationic biogenetic-like olefin cyclization in non-rigid cyclopropyl ketones 40 for the construction of bicyclic monoterpenes possessing the bicyclo[2.2.1]heptane 42 ring system was studied by Grieco and coworkers[14]. As a model they have taken the cyclopropyl ketone 36 which on treatment with stannic chloride in benzene gave 39 in 85% yield and no trace of 37 and 38 was isolated. This reaction was successfully extended to 40 to afford 42 and 43 in 80% and 20% yield respectively.

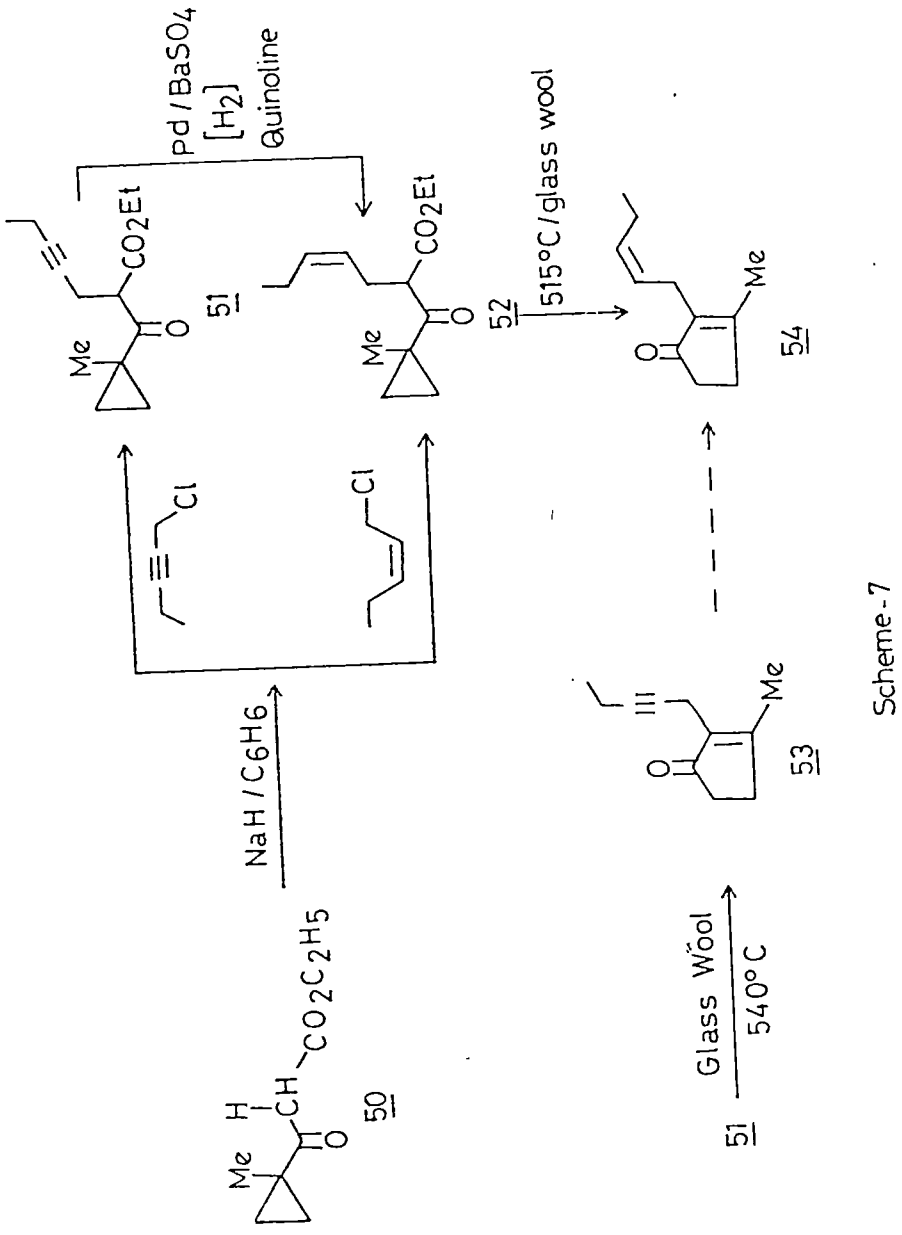
Berkowitz and coworkers[15] studied the behaviour of cyclopropyl ketone 44 under thermolytic condition. On pyrolysis at 500° - 600°C 44 gave a mixture of 45 and 46. The formation of 45 was explained through the 6-member intermediate 49, which on carbon monoxide extrusion yielded the product cyclopentanone. They extended this approach for the synthesis of *cis*-Jasmone[16] 54 as depicted in the Scheme 7. The cyclopropyl β-ketoester 50 on alkylation with *cis*-1-chloro-2-pentene or the corresponding chloro-acetylene compound yielded 51 and 52 respectively. The alkylated product 52 on thermolysis at 515°C in presence of glass wool under reduced pressure yielded *cis*-Jasmone 54 in good yields. Alternatively, 51 was cyclized under similar reaction conditions to yield 53, which was reduced in the presence of $Pd/BaSO_4$ catalyst to afford 54 (Scheme 7).



Scheme-5


500-600°C
-CO
44
45
46
47
48
49
$R^1 = R^2 = H$
$R^1 = Me ; R^2 = H$
$R^1 = H ; R^2 = Me$
$R^1 = R^2 = Me$
$C_2H_4 + CO_2$

Scheme-6

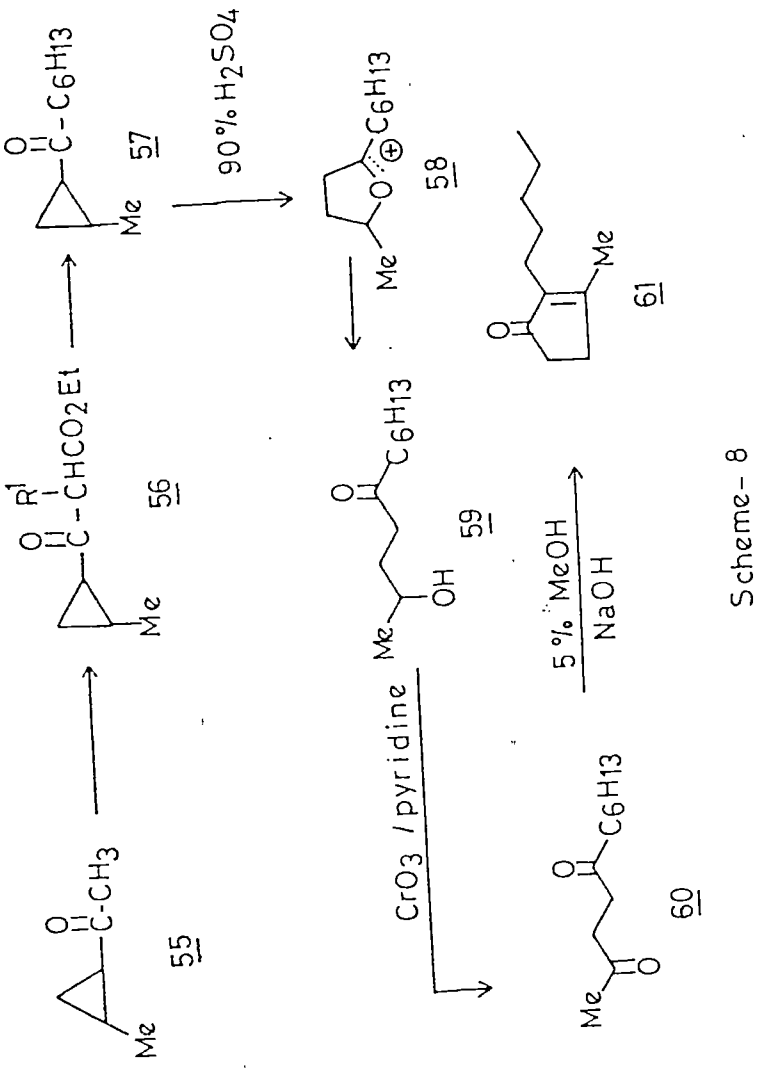

Pd/BaSO4
[H2]
Quinoline
CO2Et
Me
51
52
515°C/glass wool
54
Cl
NaH/C6H6
CO2C2H5
50
Glass Wool
540°C
53

Scheme-7

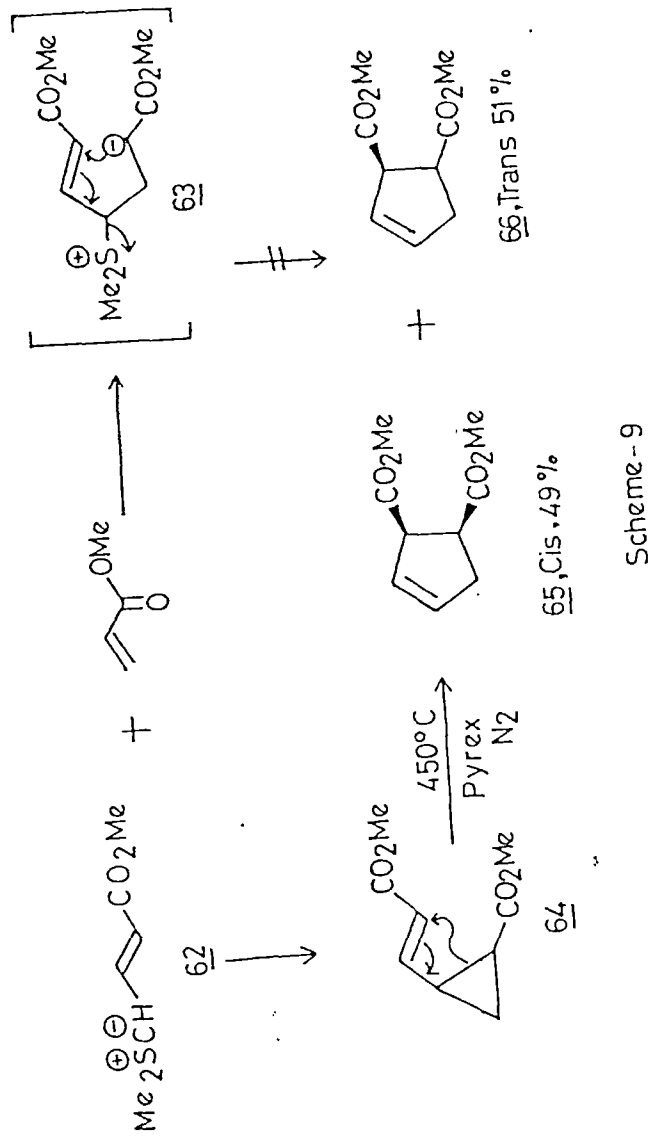
Nakai and coworkers[17] extended the Barkowitz's method for the synthesis of dihydrojasmone 61. The required δ-diketone 60 was obtained from the corresponding cyclopropyl ketone 55, through a sequence of acid catalyzed ring opening to 59 through 58 followed Cr_2O_3/pyridine oxidation. The δ-diketone 60 was then cyclized with 5% methanolic sodium hydroxide to dihydrojasmone 61 in 90% yield. They have thus demonstrated the utility of cyclopropyl ketones to afford 1,4-dicarbonyl compounds and cyclopentanones.

The thermal rearrangement of vinyl cyclopropane derivative 64 to yield the corresponding disubstituted cyclopentenes 65 and 66 has been described[18] (see Scheme 9). The desired vinyl cyclopropane 65 was obtained by treating the sulphur yield 62 with methyl acrylate. The intermediacy of cyclopropane 64 was proved by its isolation, thus ruling out the possibility of intramolecular cyclization of 63 after Michael addition of 62 to methyl acrylate.

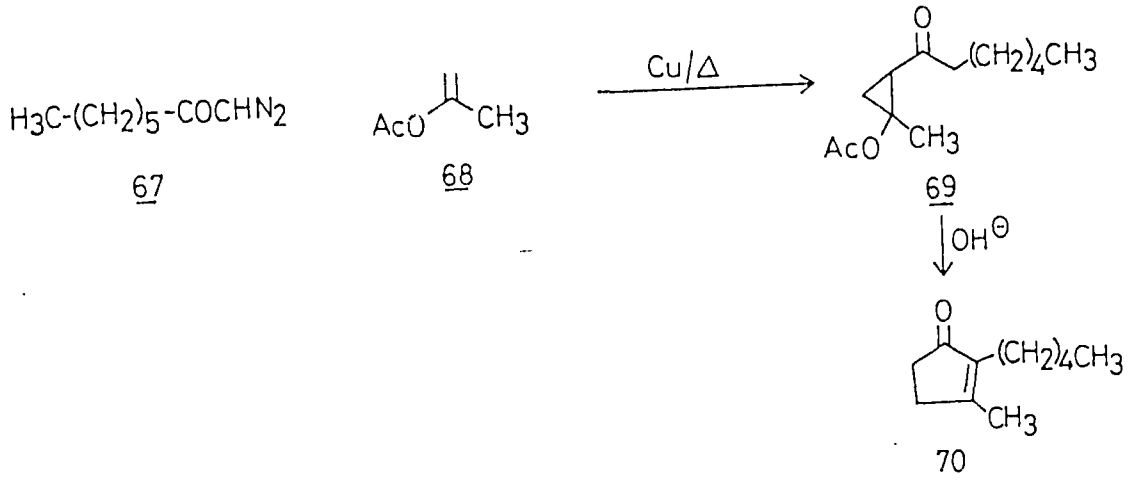
Wenkert and coworkers[19] have made extensive investigation on the ring opening reactions of a number of cyclopropanes. Among other systems studied by these authors the synthesis of dihydro jasmone 70 is noteworthy. The appropriate cyclopropyl ketone 69 was prepared by copper-assisted interaction of propenyl acetate 68 with β-diazocarbonyl compound 67. The cyclopropyl ketone 69 which has two vicinal functional groups, one is an electron donor and the other an electron acceptor, whose


55
56
57
58
59
60
61
90% H2SO4
CrO3 / pyridine
5% MeOH
NaOH
Me
C6H13
OH

Scheme- 8


CO2Me
CO2Me
Me2S
63
OMe
O
62
Me2SCH
CO2Me
450°C
Pyrex
N2
64
65, Cis, 49%
66, Trans 51%

Scheme-9

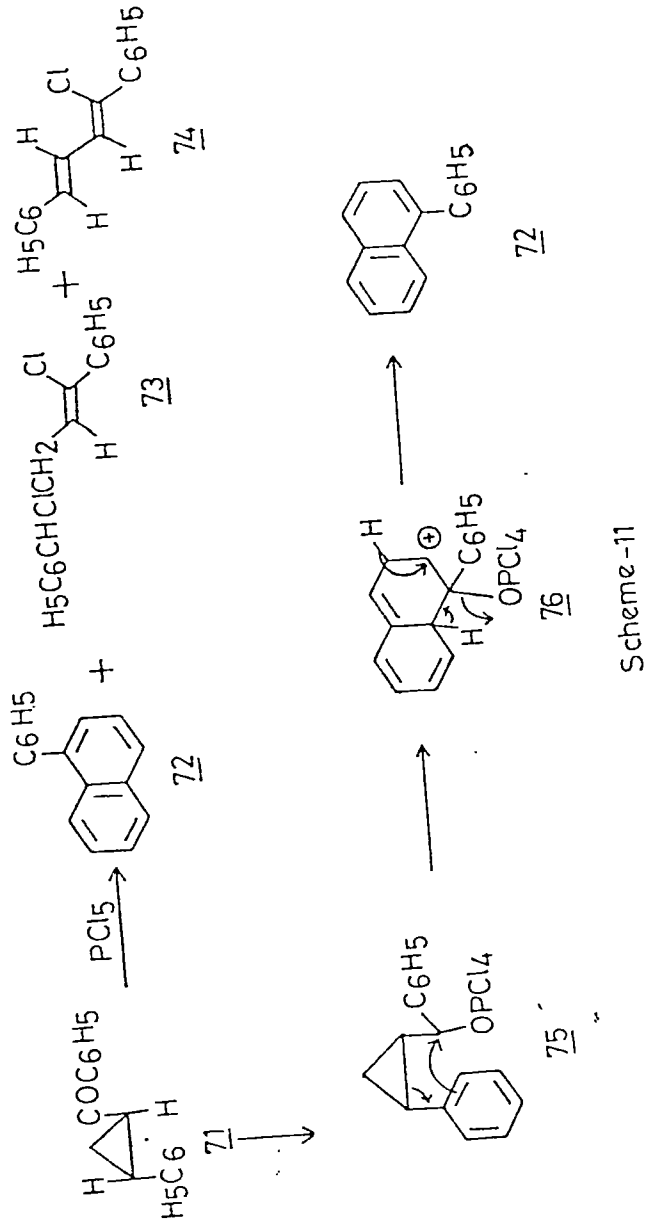

H3C-(CH2)5-COCHN2
67
AcO
CH3
68
Cu/Δ
O
(CH2)4CH3
AcO
CH3
69
OH⊖
O
(CH2)4CH3
CH3
70

Scheme-10

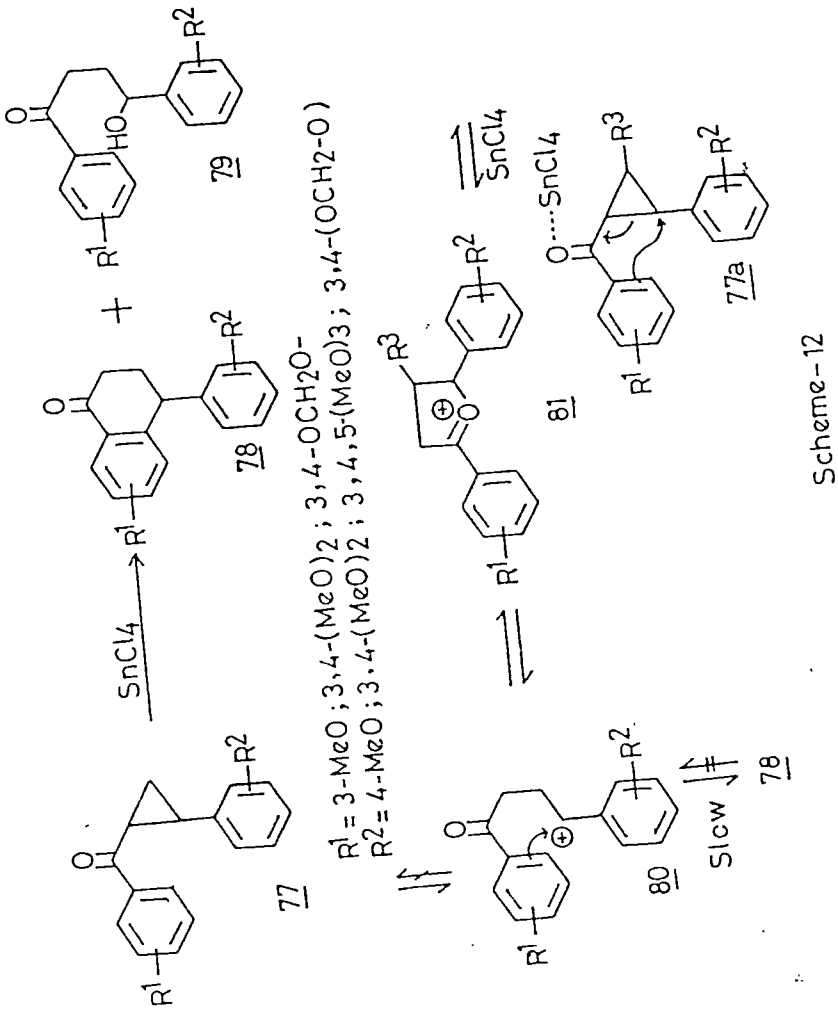
complementary reactivity enhances the cyclopropane ring fission in ionic reactions to yield 70.

The Scheme 11 depicts the intramolecular participation of aromatic ring to the cation formed by the ring opening of cyclopropyl ketone ring to give the substituted naphthelenes[20] 72. Thus, *trans*-2-phenylcyclopropyl phenyl ketone 71 on treatment with phosphorous pentachloride yielded 72 along with other chlorinated open chain olefins 73 and 74. The cyclization reaction is proposed to involved intramolecular alkylation.

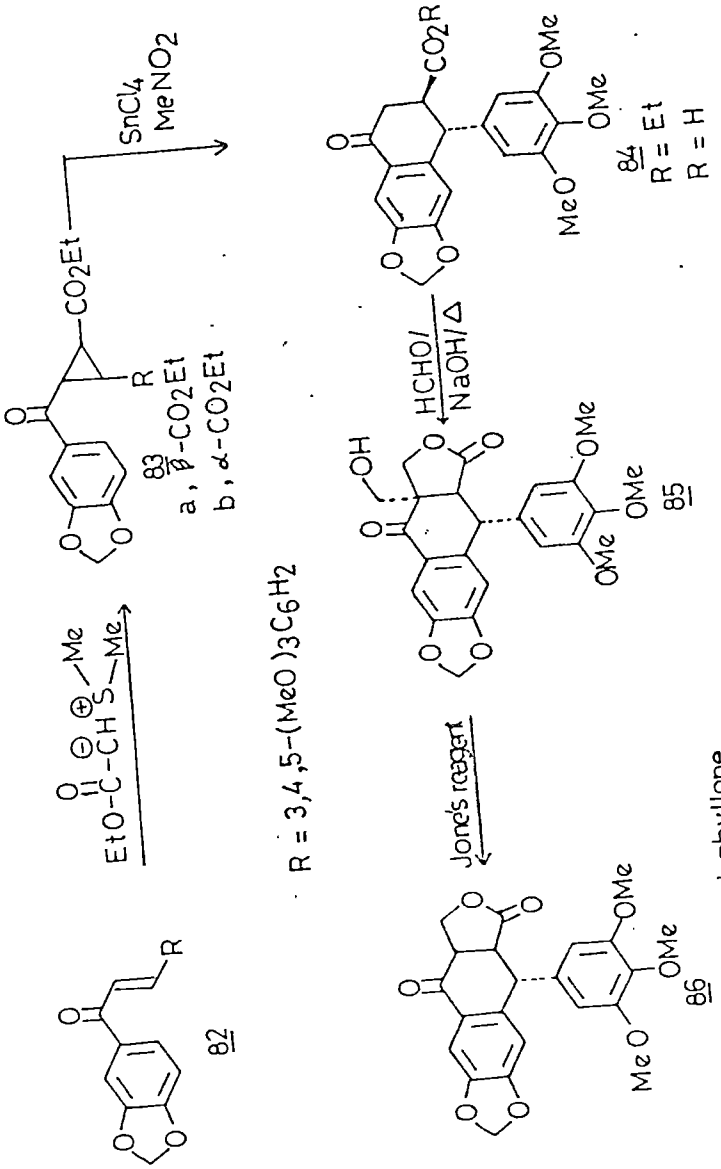
Murphy and coworkers[21-24] have published a series of papers on Lewis acid catalyzed cyclization of aryl cyclopropyl ketones 77 to aryl tetralones 78. These cyclizations have been explained through the benzylcarbocations 80, which is in equilibrium with cyclic oxonium intermediate 81. The corresponding open chain alcohol 79 was also occasionally obtained as a side product, which was presumed to formed due to step-wise process for the tetralone formation (Scheme 12). They successfully extended[25-26] this methodology for the synthesis of (±)Picropodophyllone 86, which is used as a cancer chemotherapeutic agent. The required cyclopropyl ketoester 83 was obtained by the reaction of appropriate chalcone 82 with carbethoxy suphomium ylide, which on treatment with stannic chloride gave the corresponding tetralone 84, followed by its cyclization by treatment with formaldehyde in the presence of aqueous base and Jone's oxidation gave



Scheme-11


SnCl4
R1 = 3-MeO ; 3,4-(MeO)2 ; 3,4-OCH2O-
R2 = 4-MeO ; 3,4-(MeO)2 ; 3,4,5-(MeO)3 ; 3,4-(OCH2-O)
Slow

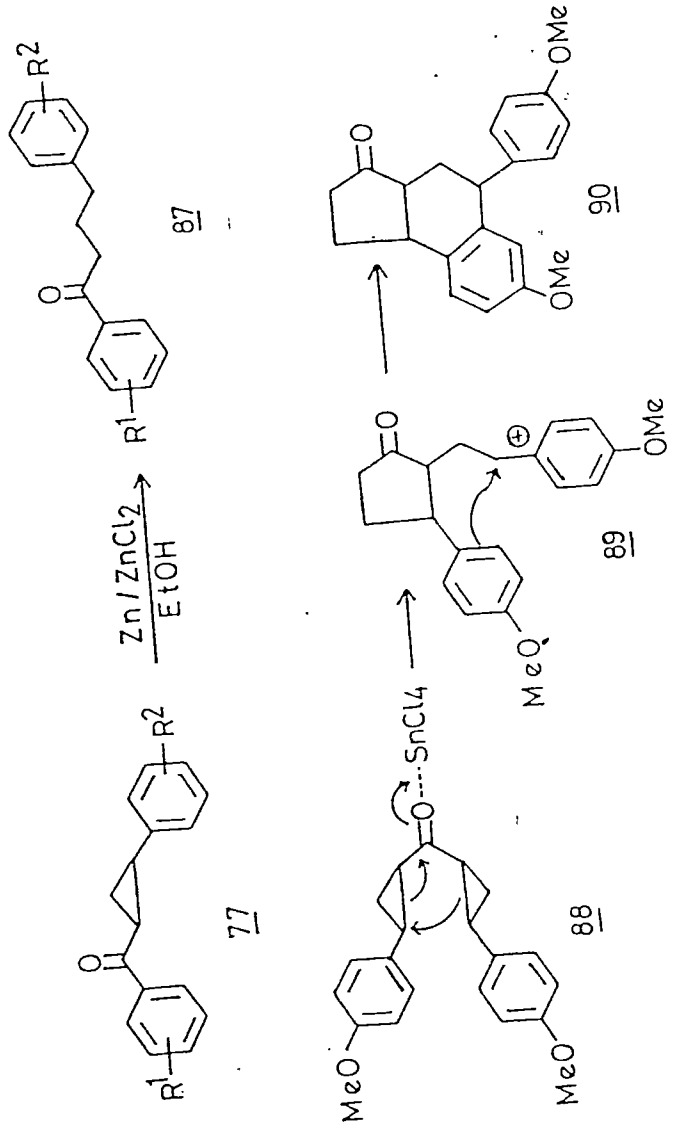
Scheme-12


SnCl4
MeNO2
CO2Et
R
83
a, β-CO2Et
b, α-CO2Et
EtO-C-CH-S-Me
Me
82
R = 3,4,5-(MeO)3C6H2
HCHO/
NaOH/Δ
CO2R
OMe
MeO
84
R = Et
R = H
OH
85
Jone's reagent
86
(±) picropodophyllone

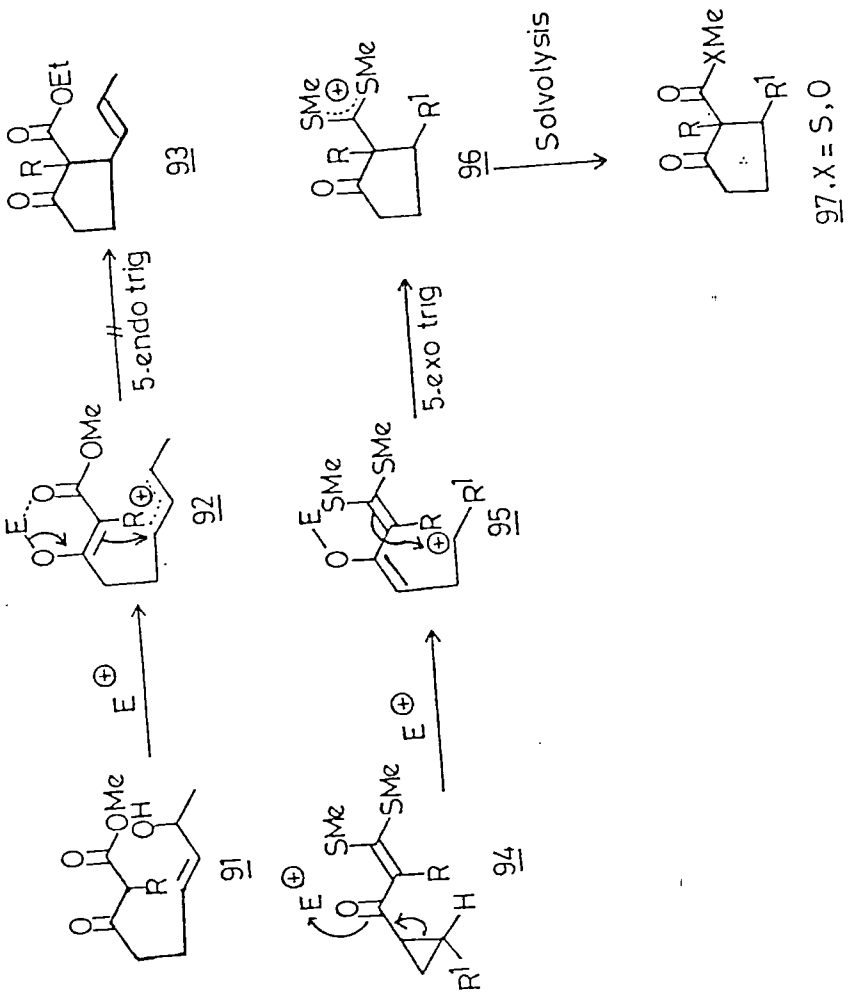
Scheme 13

86 in 72% yield (Scheme 13). They have also studied the reductive cleavage of arylcyclopropyl ketones 77 in the presence of zinc / zinc chloride in ethanol to give 4-aryl butyrophenones 87 in good yields[27,28]. The Lewis acid catalyzed ring closure was further exploited by the same group to synthesize indanone 90, by treating bis(arylcyclopropyl)ketone 88 with $SnCl_4$ in nitromethane[29] (Scheme 14).

In the preceding discussion some selected examples have been reviewed to illustrate the potential synthetic applications of ~~the~~ cyclopropyl ketones. It is apparent from the earlier studies that stereoelectronic factors are biased in γ-haloketones and β-ketoesters towards O-alkylation rather than intramolecular C-alkylation. Also, the carbocations of general formula 92 in their enol form, have to undergo ring closure via the disfavoured *5-endo-trig* process, apparently failing to yield the desired cyclopentanones 93. Therefore it became interesting and increasingly challenging problem, whether an intermediate with these structural features could be transformed into a ring ~~closure~~ through a favoured process. We therefore, became interested in the α-oxo cyclopropyl ketene dithioacetals 94, which are excellently suited to generate the intermediate carbocation 95,which possess the desired structural requirements for the favoured 5-*exo-trig* process to afford the corresponding cyclopentanones 97. In the present investigation it was therefore undertaken to examine on the development of this



Scheme-14



Scheme-15

general methodology, which is presented as follows. The chapter is divided into the following parts:

(a) Cationic ring opening of α-bis(methylthio)methylenealkyl cyclopropyl ketones : scope and mechanism

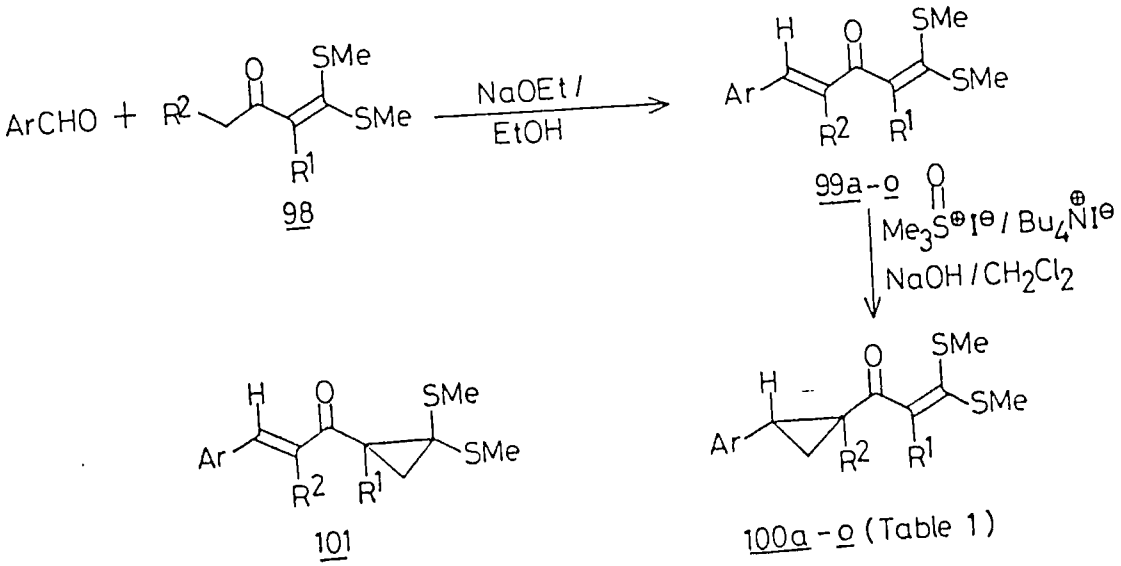
(b) Intramolecular alkylative cyclization involving α-bis (methylthio)methylene alkyl(α-alkenyl)cyclopropyl ketones : A shorter route to 11-oxo steroid precursors and substituted cyclopentanones.

II.2 RESULTS AND DISCUSSION

A series of hitherto unknown cyclopropyl ketene dithioacetals 100 required for the present studies was prepared in nearly quantitative yields. Also the precursors α-cinnamoyl ketene dithioacetals 99, were prepared according to the earlier reported procedure[30], by condensing various acylketene dithioacetals with various aromatic aldehydes. The structures of all the known dithioacetals (99a-g and 99k-o) were confirmed by comparison of their spectral and analytical data with those of authentic samples. The hitherto unknown oxoketene dithioacetals 99i-j were also prepared essentially by extending the described method and were characterized by their spectral and analytical data (experimental).

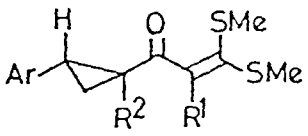
II.2a ACID CATALYZED REACTIONS OF α-BIS(METHYLTHIO)METHYLENE-ALKYL CYCLOPROPYL KETONES ; SCOPE AND MECHANISM

For the conversion of α-cinnamoyl ketene dithioacetals to their cyclopropyl analogs, dimethylsulphoxonium methylide was found to be highly efficient[31]. Thus, when 99a was treated with trimethylsulphoxonium iodide in the presence of tetrabutylammonium iodide in a phase transfer medium of aqueous sodium hydroxide and methylene chloride at 50°C after work up the product obtained was 1-[2-bis(methylthio)methyleneacetyl]-2-(4-methoxyphenyl)cyclopropane 100a in 98% yield (m.p. 97°-98°C). Apparently, the cyclopropyl ketone 100a was formed by the conjugate addition of dimethylsulphoxoniummethylide to the corresponding cinnamoyl ketene dithioacetals 99a. The structure of 100a was confirmed from its analytical and spectral data. Thus, it was analyzed for the molecular formula $C_{15}H_{18}O_2S_2$ and its molecular weight was confirmed by mass spectrum, m/z 294 (M^+, 24%). The prominent absorption bands in the IR spectrum (KBr) are observed at ν_{max} 1620 and 1480 cm^{-1}. The structure was further confirmed from its ^1H NMR spectrum (CCl_4). The signals at δ1.12-1.81 (2H), appeared as multiplets, were assigned to the cyclopropyl methylene protons. The two cyclopropyl methine protons appeared as two multiplets between δ1.89-2.15 (1H) and δ2.33-2.58 (1H). The singlets appeared at δ2.41 and 2.46 integrating for 3 protons each were attributed to the two methylthio groups. The three methoxy protons appeared as a singlet at δ3.76. A sharp singlet at


ArCHO +
SMe
SMe
O
R2
R1
98
NaOEt /
EtOH
H
O
SMe
Ar
SMe
R2
R1
99a-o
Me3S⊕I⊖ / Bu4N⊕I⊖
NaOH / CH2Cl2
H
O
SMe
Ar
SMe
R2
R1
101
H
O
SMe
Ar
SMe
R2
R1
100a-o (Table 1)

Scheme -16

Table 1

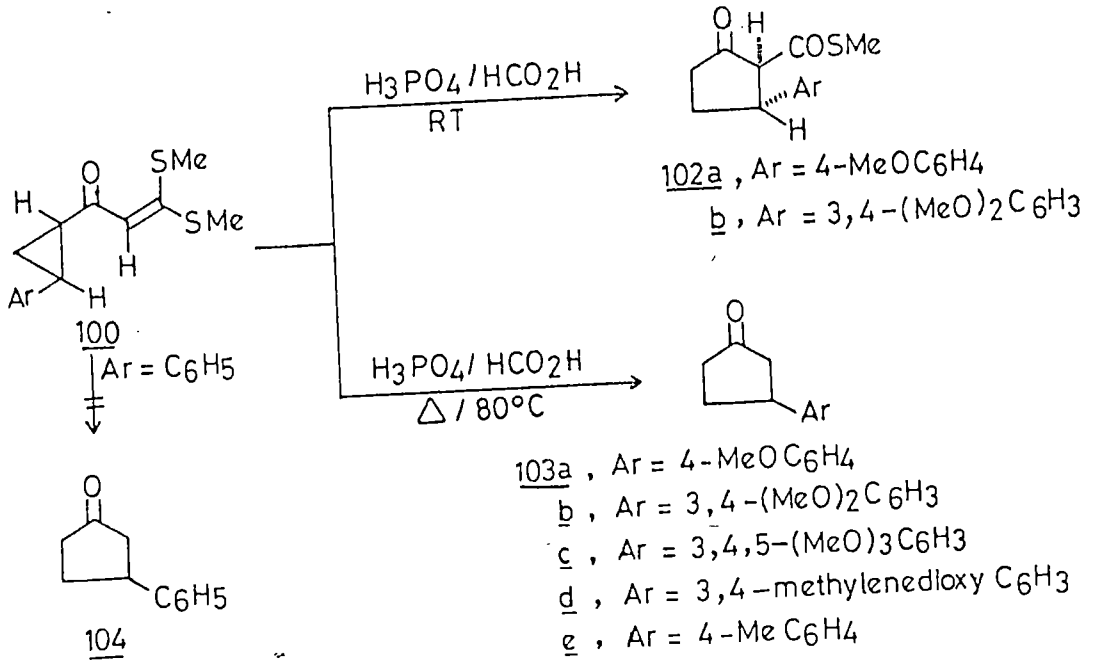


100

	Ar	R^1	R^2	% yield
a	4-MeOC$_6$H$_4$	H	H	98 %
b	3,4-(MeO)$_2$C$_6$H$_3$	H	H	98 %
c	3,4,5-(MeO)$_3$C$_6$H$_2$	H	H	96 %
d	3,4-methylenedioxy C$_6$H$_3$	H	H	94 %
e	4-MeC$_6$H$_4$	H	H	94 %
f	C$_6$H$_5$	H	H	97 %
g	4-MeOC$_6$H$_4$	Me	H	98 %
h	4-MeOC$_6$H$_4$	Et	H	84 %
i	4-MeOC$_6$H$_4$	n-Bu	H	87 %
j	4-MeOC$_6$H$_4$	n-heptyl	H	85 %
k	3,4-(MeO)$_2$C$_6$H$_3$	Me	H	95 %
l	3,4,5-(MeO)$_3$C$_6$H$_2$	Me	H	96 %
m	3,4-methylenedioxy C$_6$H$_3$	Me	H	96 %
n	4-MeOC$_6$H$_4$	Me	H	80 %
o	3,4-(MeO)$_2$C$_6$H$_3$	Me	H	79 %

δ6.16 (1H) was assigned to the olefinic proton and the aromatic protons appeared as two doublets (2H,J=9Hz) at δ6.75 and 7.01. The other cyclopropyl ketones 100b-o were similarly prepared in 79-89% overall yields. Their spectral data were fully established which are described in the experimental section. It is note-worthy that the cyclopropanation was found to be chemoselective, and the reagent attacks only at the styryl double bond, and the mercapto double bond remains being unaffected (Scheme 16).

The acid catalyzed ring opening of cyclopropyl ketones 100 was examined next. Thus, 100a when treated with a mixture of phosphoric acid and formic acid (1:3) at room temperature for 2 hr, after work-up and purification over silica gel column (EtOAc/Hexane 1:20) afforded a compound characterized as (*E*) S-methyl 5-(4-methoxyphenyl-2-oxo cyclopentane carbothioate 102a in 73% yield (m.p. 105-106°C). The structure of 102a was confirmed from its analytical and spectral data. Thus it was analyzed for molecular formula $C_{14}H_{16}O_3S$ (264) and the molecular weight was confirmed by its mass spectrum with a peak at m/z 264 (M^+,10%) along with another prominent peak at 189 [M^+ - 75(COSMe),100%]. The characteristic ring carbonyl and the thioester carbonyl stretching appeared at IR(KBr) 1750 and 1665 cm^{-1} respectively. The structure of 102a was further confirmed from its ^1H NMR($CDCl_3$) spectrum. The cyclopentane methylene protons appeared as multiplet at δ1.86-2.70 (4H). The singlets at δ2.30 and 3.80



100
Ar = C_6H_5

102a , Ar = 4-MeOC_6H_4
b , Ar = 3,4-$(MeO)_2C_6H_3$

103a , Ar = 4-MeOC_6H_4
b , Ar = 3,4-$(MeO)_2C_6H_3$
c , Ar = 3,4,5-$(MeO)_3C_6H_3$
d , Ar = 3,4-methylenedioxy C_6H_3
e , Ar = 4-MeC_6H_4

104

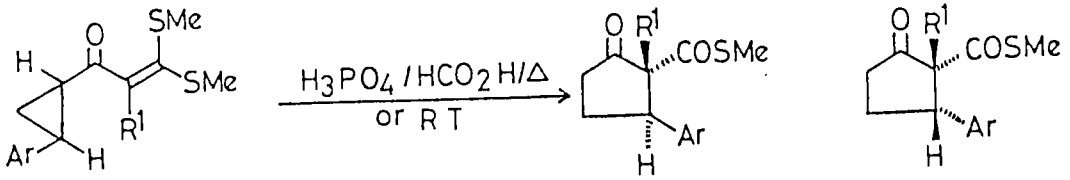
Scheme-17

integrating for 3-protons each were attributed to methylthio and methoxy protons respectively. The doublet appeared at δ3.42 (1H) with a coupling constant J=11Hz was due to the H-1.The methine proton H-5 appeared as a multiplet at δ3.66-4.01 (1H). The two doublets (J=9 Hz) at δ6.82 (2H) and 7.20 (2H) was attributed to the aromatic protons. On the basis of the coupling constant of H-1 proton, i.e. J=11 Hz and the down field shift of H-5 due to the deshielding by methylthio carbonyl group, it was decided that **102a** was having a single stereoisomer having (*E*)-geometry. Similarly, the cyclopentanone **102b** was obtained in 68% yield and found to be exclusively *E*-stereoisomer on the basis of its spectral and analytical data described in the experimental section.

In another experiment when **102a** was heated in the presence of a mixture of phosphoric and formic acid (1:3) at 80°C for 1 hr after work-up and purification as described above the product isolated was 3-(4-methoxyphenyl)cyclopentanone **103a** as low melting solid (m.p. 48-49°C) in 71% yield which was identical with that reported in the literature[32] (reported m.p. 47-48°C) The structure was further confirmed from its analytical and spectral data. It was analyzed for $C_{12}H_{14}O_2$ (190), which was confirmed by its mass spectrum m/z 190 (M^+,100%). The IR(KBr) spectrum showed absorption band at 1737 cm^{-1}. The structure of **103a** was further confirmed from its ^1H NMR spectrum (CCl_4). A multiplet appeared between δ1.61-2.50 (6H) due to ring methylene protons, while the benzylic proton, i.e. H-3

showed a multiplet at δ2.08-3.47 (1H). The singlet appeared at δ3.73 (3H) was attributed to the three methoxy protons while the aromatic protons appeared as two doublets with J=9 Hz at δ6.67 and 7.09 integrating for two protons each. Similarly, the cyclopropyl ketones 100b-e underwent cyclization with a loss of methylthiocarbonyl group to yield the corresponding 3-substituted cyclopentanones 103b-e in 37-72% overall yields. The cyclopentanones were confirmed by their spectral and analytical data. However, the phenyl substituted cyclopropyl ketone 100f failed to give the corresponding cyclopentanone 104 under similar reaction conditions and the reaction mixture resulted in an intractable tar, while the 4-methylphenyl substituted ketone 100e yielded the corresponding cyclopentanone 103e in only 37% yield. Apparently, these results testify the involvement of benzyl carbocation which is significantly stabilized by methoxy substituents under the observed experimental conditions.

When the reaction was extended to α-methylcyclopropyl ketone 100g under identical reaction conditions both at room and higher temperature, s-methyl-5-methoxyphenyl-1-methyl-2-oxocyclopentane carbothioate 105g (m.p. 75°-76°C) was obtained in 81% yield. The structure of the compound 105g was assigned on the basis of its spectral and analytical data. It was analyzed for $C_{15}H_{18}O_3S$ (278) and was confirmed with a molecular ion peak at m/z 278 (M^+,4%)

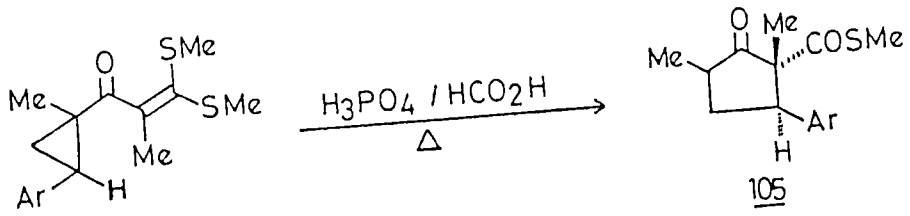


100g-m 105g-m (E) 105i, j (Z)

	Ar	R^1	% yield
g	4-$MeOC_6H_4$	Me	81
h	4-$MeOC_6H_4$	Et	71
i	4-$MeOC_6H_4$	n-Bu	60
j	4-$MeOC_6H_4$	n-heptyl	59
k	3,4-$(MeO)_2C_6H_3$	Me	76
l	3,4,5-$(MeO)_3C_6H_2$	Me	78
m	3,4-methylenedioxy C_6H_3	Me	77

Scheme-18

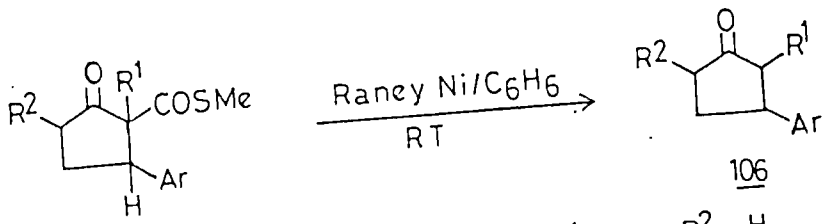
in its mass spectrum. The IR(KBr) spectrum showed prominent absorption bands at 1738 and 1665 cm^{-1}. The ^1H NMR($CDCl_3$) spectrum showed a singlet at δ0.98 (3H) for the methyl protons, while the multiplet appeared at δ1.90-2.61 (4H) was attributed to ring methylene protons. The singlets for methylthio protons and methoxy protons appeared at δ2.30 and 3.72 respectively integrating for 3-protons each. The benzyl methine proton appeared as a distorted triplet with J=7 Hz at δ4.05. It may be noted that chemical shift of benzylic proton at δ4.05 signifies its position with relation to methylthio carbonyl group in the *cis*-fashion, which is in conformity with the δ value reported by Trost and coworkers[8] on similar systems. Apparently, only one stereoisomer is formed with the methyl group *trans* to the benzylic proton, thus confirming an exclusive *E*-stereoisomer for 105g. The aromatic protons appeared as two doublets at δ6.76 and 7.0 with J=9 Hz. The compound 105g on prolonged heating (6 hr) at 80°C under similar reaction conditions did not undergo dithiocarbnylation and the reaction mixture remained unchanged. Thus methylthio carbonyl group appears to be more resistant in the tertiary-carbon atom. Similarly, the other α - alkylcyclopropyl ketones (100g-h and 100k-o) also underwent cyclization to yield only one (*E*) stereoisomer of 105, when the α-substituents were methyl or ethyl groups (105g-h and 100k-o). However, this stereoselectively was not maintained in the higher homologs 100i-j, when the α -substituents were *n*-butyl or



100 105

100, 105n , Ar = 4-MeOC$_6$H$_4$

– o , Ar = 3,4-(MeO)$_2$C$_6$H$_3$



105 106

105, 106a , Ar = 4-MeOC$_6$H$_4$; R^1 = Me ; R^2 = H

b , Ar = 4-MeOC$_6$H$_4$; R^1 = n-Bu ; R^2 = Me

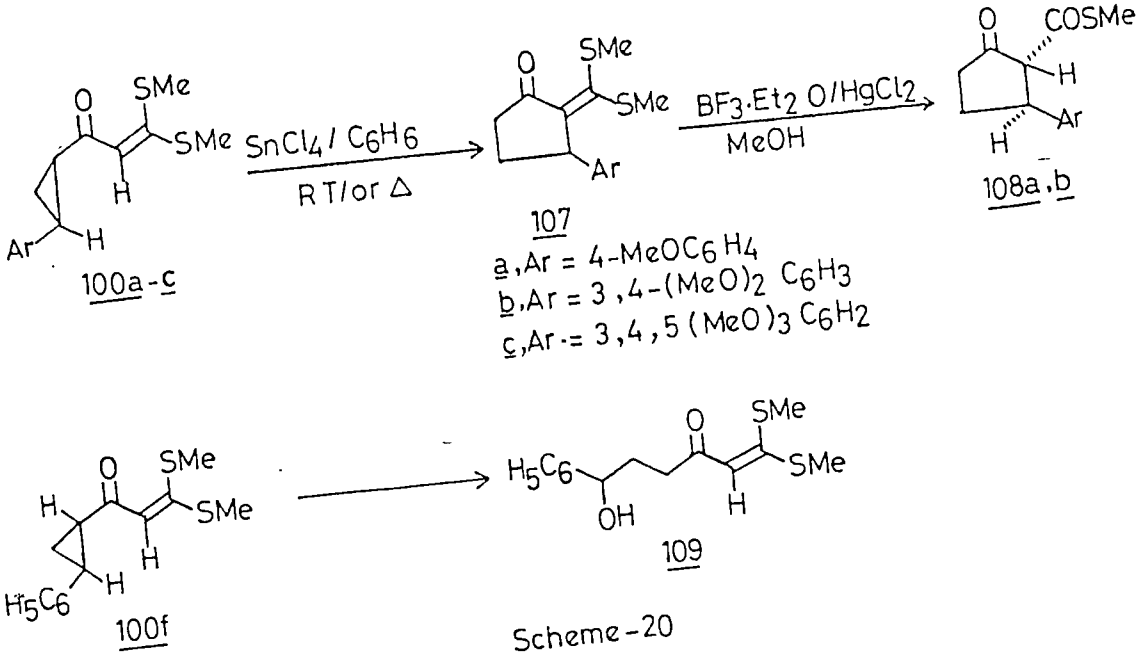
c , Ar = 4-MeOC$_6$H$_4$; $R^1 = R^2$ = Me

Scheme-19

n-heptyl groups. A mixture of *E* and *Z* isomers (105i-j) in varying proportions was obtained. The stereochemical assignments for 105i-j were also derived from their ^{1}H NMR spectral data. Thus, in the case of 105i the benzylic methine proton exhibited two signals at δ4.02 and δ3.49 due to *E* and *Z* isomers respectively. It appears that when the alkyl group at C-1 is bulkier, such as *n*-butyl and above, the product ratio results as a mixture of stereoisomers. Selected members of carbothioates 105g, 105i and 105n were subjected to demethylthiocarbonylation in the presence of Raney Nickel[33] at room temperature in benzene under nitrogen atmosphere to afford the corresponding cyclopentanones 106a-c in 78-89% yields respectively. The structure of these cyclopentanones 106a-e were in accord with their analytical and spectral data which are described in the experimental section (Scheme 18 and 19).

The aforesaid cyclopropanes 100a-c were next examined under Lewis acid condition. Thus, when 100a was stirred in the presence of stannic chloride in benzene, after work-up the product isolated was characterized as 2-bis(methylthio)methylene-3-(4-methoxyphenyl)cyclopentanone 107a in 83% yield. While the analytical and spectral data of 107a were in accord with the assigned structure (in the experimental section) the presence of two singlets at δ2.21 (3H) and δ2.42 (3H) was assigned to two methylthio groups in its ^{1}H NMR spectra, indicating that the mercapto functionality remained unaffected under these reaction

conditions. It is interesting to note that the bis(methylthio)methylene functionality can be utilized to transform into useful functional groups such as methyl carbothioate and carboalkyl etc. It can further be regioselectively reduced to the bis(methylthio) acetal, which could be subsequently hydrolysed to the corresponding aldehyde functionality. One of these transformations was attempted, when 107a was treated with $BF_3.Et_2O$ and $HgCl_2$ in refluxing methanol the product obtained was characterized as methyl 5-(4-methoxyphenyl)-2-oxo cyclopentane carboxylate 108a in 87% yield (m.p. 84°-85°C). The structure was established on the basis of its spectral and analytical data. The relative configuration ~~stereochemistry~~ of 108a was decided on the basis of the chemical shift of H-1 (δ3.25,d) and H-5 (δ3.52-3.96,m) and the coupling constant of H-1 (J=12 Hz) and was assigned *E* geometry. The analytical and spectral data of 108a-b were in full accord with the assigned structures and are described in the experimental section. Interestingly, when phenyl cyclopropyl ketone 100f was treated with a mixture of H_3PO_4/HCOOH only an intractable tar was formed. However, on treatment with stannic chloride in benzene it underwent a facile ring opening to yield the corresponding open-chain carbinol 1,1-bis(methylthio)-6-hydroxy-6-phenyl-1-hexene-3-one 109 in 73% yield. The product 109 exhibited a molecular ion peak at m/z 268 (M^+-18,6%) in its mass spectrum and was analyzed for $C_{14}H_{18}O_2S_2$. The IR(KBr) spectrum showed prominent absorption bands at 3440, 1620


O
SMe
SMe
H
Ar
H
100a-c
SnCl4 / C6H6
RT/or Δ
O
SMe
SMe
Ar
107
a, Ar = 4-MeOC6H4
b, Ar = 3,4-(MeO)2 C6H3
c, Ar = 3,4,5 (MeO)3 C6H2
BF3.Et2O/HgCl2
MeOH
O
COSMe
H
Ar
H
108a, b
O
SMe
H
SMe
H
H
H5C6
100f
H5C6
OH
O
SMe
SMe
H
109

Scheme-20

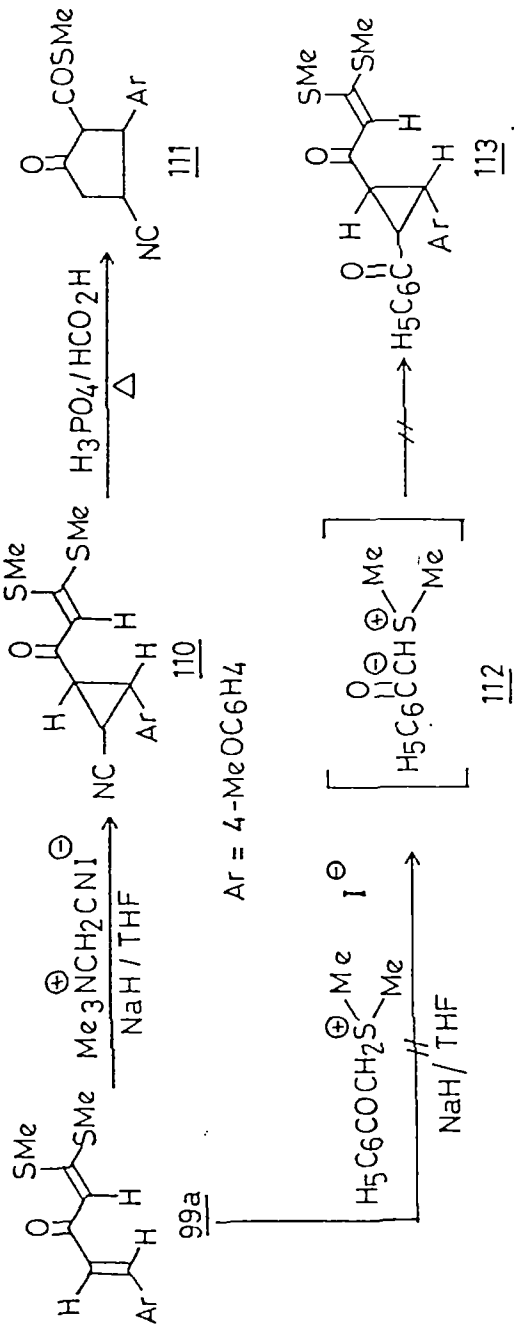
cm^{-1}. The structure was further confirmed by its ^1H NMR($CDCl_3$) spectrum. The triplet at δ2.05 (2H,J=7 Hz) was assigned to CH_2 methylene protons and two methylthio groups appeared as two singlets at δ2.40 and 2.49 each integrating for three protons. The other methylene protons adjacent to the carbonyl group appeared as triplet at δ2.58 (2H,J=7 Hz). A broad signal at δ2.71-3.28 (1H) was assigned to the hydroxyl group (exchangeable with D_2O). The benzylic protons appeared as triplet at δ4.71 (1H,J=7 Hz). The singlet appeared at δ5.98 (1H) was attributed the vinylic proton.The aromatic protons appeared as multiplet between δ7.12-7.42 (5H), thus confirming the open chain structure assigned as 109. Attempts to cyclize 109 on subsequent treatment with various Lewis acids as well as the treatment of 100f with these lewis acids for an extended time failed to yield the corresponding cyclopentanones and only the open-chain carbinol 109 was obtained in varying yields (Table 2).

The cyano-substituted cyclopropyl ketone 110 was obtained in 91% yield by addition of cyanotrimethylammonium ylide[34] to 99a in the presence of sodium hydride in dry tetrahydro furan. The cyclopropyl ketone 110 also underwent ring cleavage and cyclization in the presence of a mixture of H_3PO_4/HCOOH (1:3) at room temperature to afford the corresponding s-methyl 3-cyano-2-(4-methoxyphenyl)-5-oxo-cyclopentane carbothioate 111 in 81% yield. Other spectral data were in accord with the assigned structure, and the

Table 2

Reaction of Cyclopropyl ketone 100f with Lewis acids

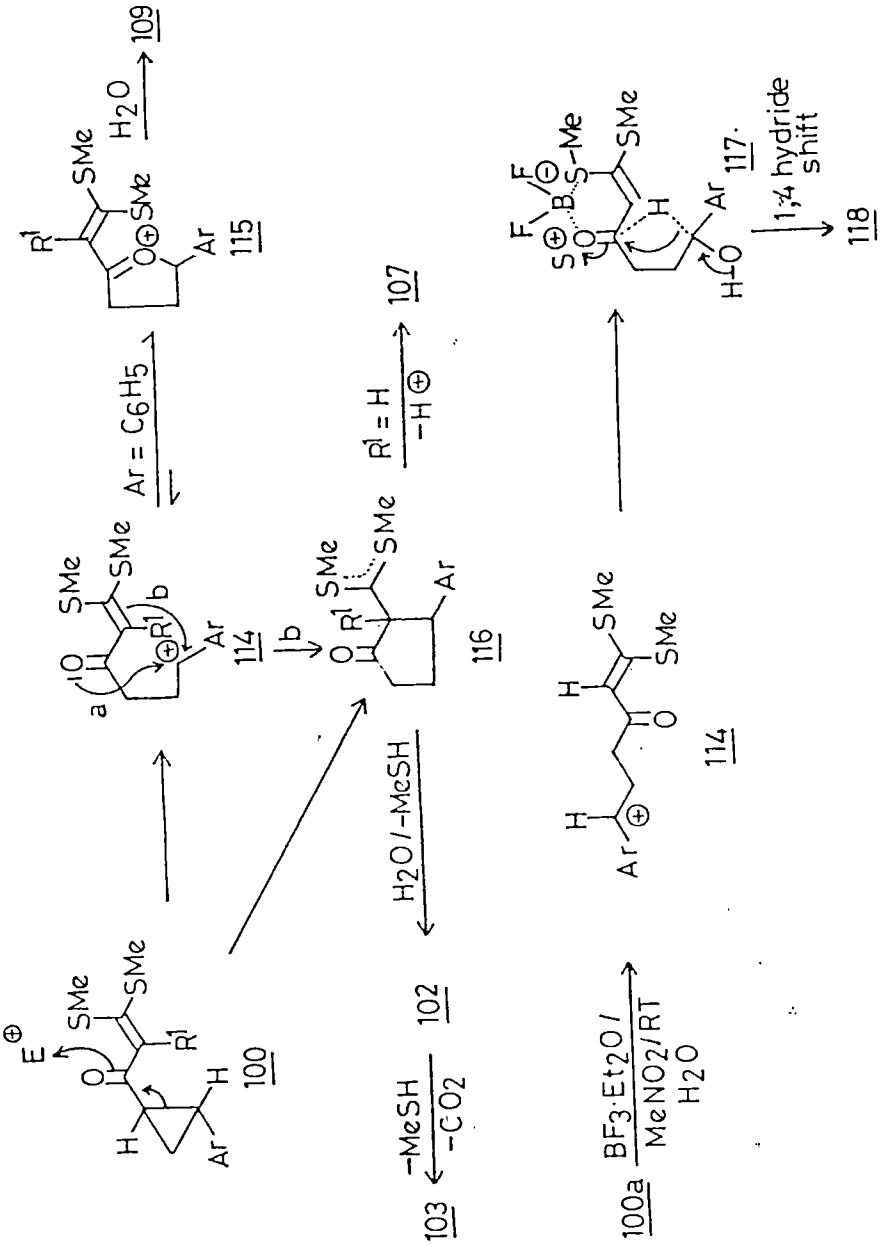
Entry	Lewis acid	Solvent	reaction conditions	Product % yield(10
1	$SnCl_4$	C_6H_6	RT, 12 h	73
2	$SnCl_4$	$MeNO_2$	0°C, 6h	81
3	$BF_3 \cdot Et_2O$	$MeNO_2$	RT, 5h	77
4	$BF_3 \cdot Et_2O$	C_6H_6	RT, 24h	83
5	$AlCl_3$	CH_2Cl_2	RT, 12h	87
6	$TiCl_4$	CH_2Cl_2	-78°C	83


99a
Me3NCH2CN I
NaH / THF
Ar = 4-MeOC6H4
110
H3PO4/HCO2H
Δ
111
H5C6COCH2S Me I
NaH/THF
112
Ar = 4-MeOC6H4
H5C6C
113

Scheme- 21

presence of nitrile group in IR(neat) was marked by the absorption at 2220 cm^{-1}. The rest of its spectral and analytical data are described in the experimental section. The conjugate addition of phenacylsulphonium ylide 112 to 99a under different conditions gave only a mixture of several products which could not be isolated in pure form.

The mechanism governing the cyclopropyl ring cleavage and the new C-C bond formation through mercapto double bond participation can either be stepwise or a concerted process. The structure of 100 is geometrically favourable for 5-*exo-trig* concerted ring closure. However, the failure of 100f to afford the corresponding cyclopentanone evidently supports the intermediacy of the benzylic carbocation and shows that the stability of the carbocation dictates the course of cyclopropyl ring opening. Attempted cyclization of 100f in the presence of Lewis acids in aprotic solvents yielded only the open-chain carbinol 109 in varying yields (Table 2). When 100a was treated with $SnCl_4$ in nitromethane at room temperature, the corresponding cyclopentanone 107a was formed within one hour in excellent yield (Table 3, entry 7), while the yield of 107a was lowered when the reaction temperature was reduced to -20°C (entry 8). The intermediate carbocation was trapped by quenching the above reaction mixture after 10 min. to afford the corresponding open-chain carbinol 109b in low yield (32%) along with cyclopentanone 107a in 43% yield (entry 9). Also the tri-~methoxyphenylcyclopropyl ketone 100c



Scheme-22

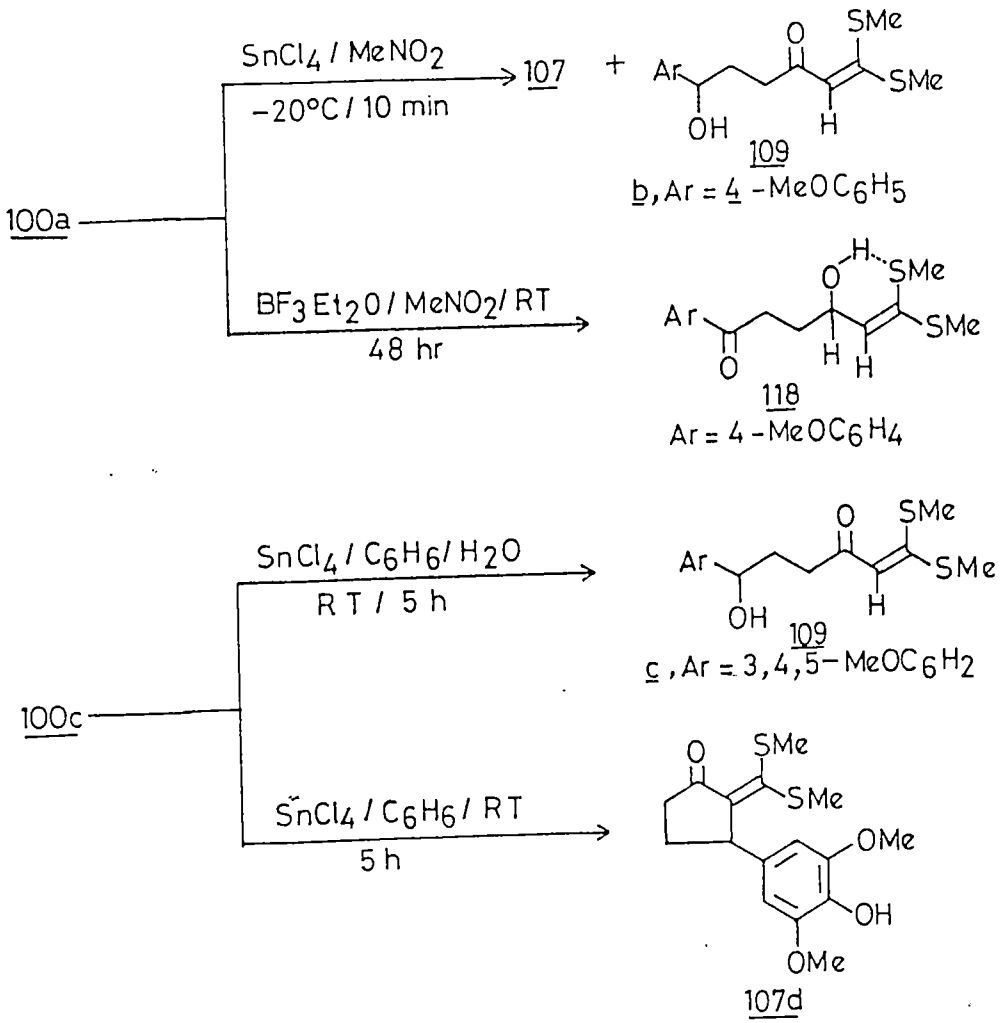
Table 3

Lewis acid catalyzed cyclizations of aryl cyclopropyl ketones 100

Entry	Reactant	Conditions	Products	%Yield
1	100a	$SnCl_4$, C_6H_6, RT, 2h	107a	83
2	b	$SnCl_4$, C_6H_6, RT, 2h	b	72
3	c	$SnCl_4$, C_6H_6, RT, 2h	c	52
4	a	TFA, CH_2Cl_2, RT, 2h	a	81
5	g	$SnCl_4$, C_6H_6, RT, 2h	105g	79
6	g	TFA, CH_2Cl_2, RT, 2h	g	79
7	a	$SnCl_4$, $MeNO_2$, RT, 1h	107a	83
8	a	$SnCl_4$, $MeNO_2$, -20°C, 1h	a	76
9	a	$SnCl_4$, $MeNO_2$, -20°C, 10min	107a, 109b	43, 32
10	c	$SnCl_4$, C_6H_6 / H_2O, RT, 5h	109c	73
11	c	$SnCl_4$, C_6H_6, RT, 5h	107d	41
12	a	BF_3·Et_2O, $MeNO_2$, RT, 48h	118	73
13	a	$SnCl_4$, C_6H_6, RT, 1h	107a	68
14	a	$SnCl_4$, CH_2Cl_2, RT, 1h	a	78
15	b	$SnCl_4$, $MeNO_2$, RT, 1h	b	61
16	c	$SnCl_4$, $MeNO_2$, 1h	c	52
17	d	$SnCl_4$, $MeNO_2$, RT, 1h	d	52

yielded the open-chain carbinol 109c exclusively (73%) on treatment with $SnCl_4$ in benzene with a few drops of water (entry 10). The same reaction mixture on continued stirring at room temperature (5hr) yielded the corresponding cyclopentanone 107d with demethylation of the 4-methoxy group (entry 11). Thus the isolation of the intermediate carbinols 109b and 109c further supports the formation of benzyl carbocation as intermediate which slowly cyclizes to cyclopentanone 107 on prolonged treatment with $SnCl_4$. Interestingly when 100a was stirred at room temperature in the presence of boron trifluoride etherate in nitromethane, the product isolated was characterized as carbinol acetal 118 on the basis of spectral and analytical data, [(described in the experimental section) (entry 12)(Scheme 22 and Scheme 23)].

A comparison of cyclization of 100a in the presence of $SnCl_4$ in various solvents (C_6H_6, CH_2Cl_2, CH_3NO_2) demonstrate[5] that the rate of cyclization is faster in polar solvents (Table 3, entries 7,13,14). Similarly variation of substituents in the aromatic ring influences the relative rates which become faster with the increasing ability of the substituents to stabilize benzyl carbocation (100b>100c> = 100d>100e) (Table 3, entries 7,15,16,17). The solvent and substituent effects evidently demonstrate that the benzyl carbocation is indeed an intermediate and the success of the reaction depends on


SnCl4 / MeNO2
-20°C / 10 min
107
+
Ar
OH
O
SMe
SMe
H
109
b, Ar = 4 -MeOC6H5
100a
BF3 Et2O / MeNO2 / RT
48 hr
H
O
SMe
Ar
SMe
O
H
H
118
Ar = 4 -MeOC6H4
SnCl4 / C6H6 / H2O
RT / 5 h
Ar
OH
O
SMe
SMe
H
109
c, Ar = 3,4,5-MeOC6H2
100c
SnCl4 / C6H6 / RT
5 h
O
SMe
SMe
OMe
OH
OMe
107d

Scheme -23

the substituents that extend increased stability to the developing cation. Based on these observations, a probable mechanism is depicted in the Scheme 22, which is similar to that suggested by Murphy[23,24] for tetralone formation. An open-chain benzyl cation 114 clearly accounts for the formation of products 107 and 109. Thus the intermediate cation appears to exist in equilibrium with oxonium ion 115 while in the presence of solvent with increasing polarity and a better stabilizing substituents on aryl group, the cation equilibrium is shifted to benzylic position 114 thus permitting the attack of bis(methylthio)methylene double bond. Subsequent loss of proton affords 107 or 103 when the reaction mixture is quenched with water. On the other hand, in the case of 100f, the equilibrium is essentially on the side of 115 due to instability of benzyl cation 114 a condition not favourable for π-participation. The oxonium ion yields the open-chain carbinol 109 on quenching the reaction mixture in aqueous basic media. However, none of these data preclude concerted ring opening and cyclization as major rule especially in the case of highly reactive cyclopropyl ketone such as 100a.

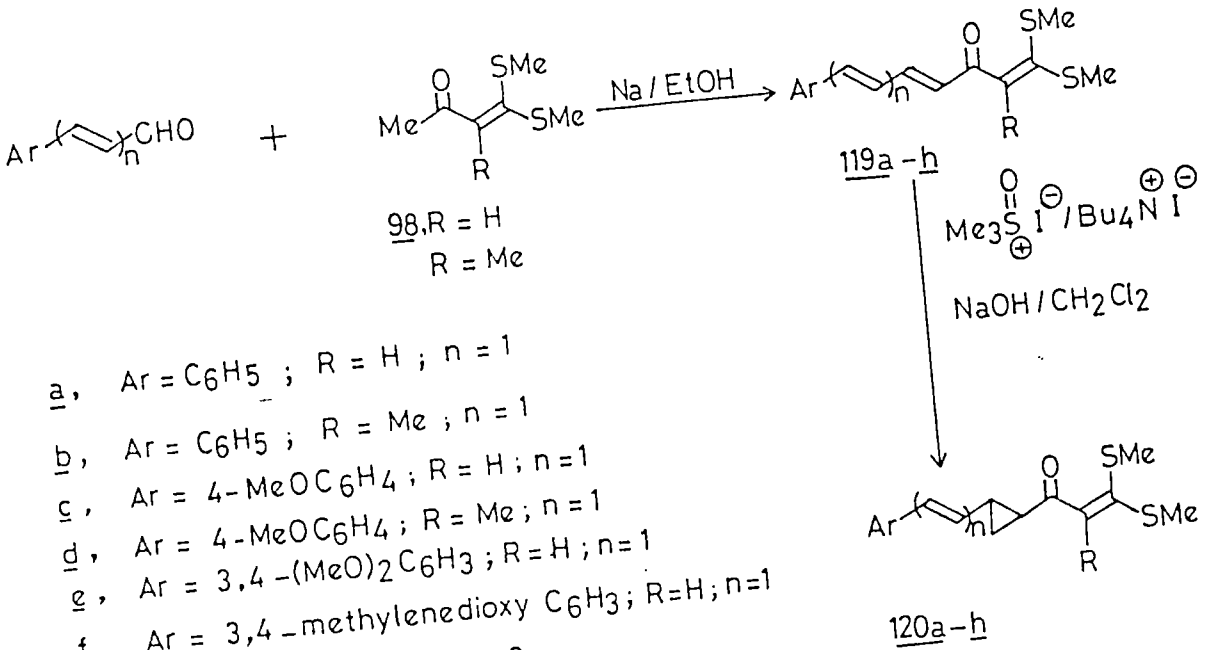
Formation of 118 from 100a in the presence of boron trifluoride etherate/nitromethane probably involves an inter or intramolecular 1,4-hydride transfer[35] in the initially formed carbinol 109b under the experimental conditions during workup.

II.2b INTRAMOLECULAR ALKYLATIVE CYCLIZATION INVOLVING α-BIS (METHYLTHIO)METHYLENE ALKYL (2-ALKENYL)CYCLOPROPYL KETONES : A SHORTER ROUTE TO 11-OXO STEROID PRECURSORS AND SUBSTITUTED CYCLOPENTANONES

In the preceding section of this chapter it was demonstrated that the cyclopropyl ketones 100 were found to be suitable precursors for the construction of functionalized cyclopentanones in good yields. The cyclopentanone ring closure was found to be a natural consequence of the favoured 5-*exo-trig* process. The mercapto double bond as a masked β-keto ester functionality serves the purpose of creating suitable structural parameters for the allowed *exo-trig* process. All the examples examined in the preceding section essentially carry the aryl substitution on the cyclopropyl ketones, but the phenyl substituted 100f failed to yield the envisaged cyclopentanone. However, in the presence of Lewis acids cyclopropyl ring cleaved to yield the corresponding open-chain carbinol 109 in high yield. Attempts to cyclize the cyclopropyl ketones 100f as well as the carbinol 109 failed. On the basis of these observations a step-wise mechanism was proposed involving benzyl carbocation intermidecy, which was trapped by the bis(methylthio)methylene double bond following the allowed *exo-trig* process. Thus, the presence of electron donating group on the aromatic ring capable of stabilizing the cation, was found to be essential for the ring closure. In continuation of these studies it was considered of

interest to circumvent the limitations observed in those cases. One possible alternative could be to prepare cyclopropyl ketones by introducing one or two π-bond bridges between the cyclopropane ring and the aromatic group. As a result the stability of arylallyl (or arylpentadienyl) cation may serve as better stabilizing parameters and enhance the scope of the present methodology of the cyclopentanone synthesis. Also, this approach has been successfully extended for the synthesis of 11-oxo steroid precursors as an application to a more important target molecule, in the present investigation. The results have been described as follows.

The cyclopropyl ketones 120a-h (Scheme 24) were selected to examine the potential synthetic application of the methodology described in the preceding part.They could conveniently be prepared following the sequence as depicted in Scheme 24. The α-enoyl ketene dithioacetals 119a-h were prepared by the condensation of various ene-aldehydes with acylketene dithioacetals 98 by earlier reported methods[30,36]. The structures of all these enoyl ketene dithioacetals 119a-h were in accord with their analytical and spectral data. In a typical experiment when 119a was reacted with dimethylsulphoxonium methylide under phase transfer conditions as described earlier to afford a colorless solid in 97% yield (m.p. 116°-117°C). It was characterized as 1-[2-bis(methylthio)methyleneacetyl]-2-styryl cyclopropane 120a on the basis of its spectral and



a, Ar = C_6H_5 ; R = H ; n = 1

b, Ar = C_6H_5 ; R = Me ; n = 1

c, Ar = 4-$MeOC_6H_4$; R = H ; n = 1

d, Ar = 4-$MeOC_6H_4$; R = Me ; n = 1

e, Ar = 3,4-$(MeO)_2C_6H_3$; R = H ; n = 1

f, Ar = 3,4-methylenedioxy C_6H_3 ; R = H ; n = 1

g, Ar = C_6H_5 ; R = H ; n = 2

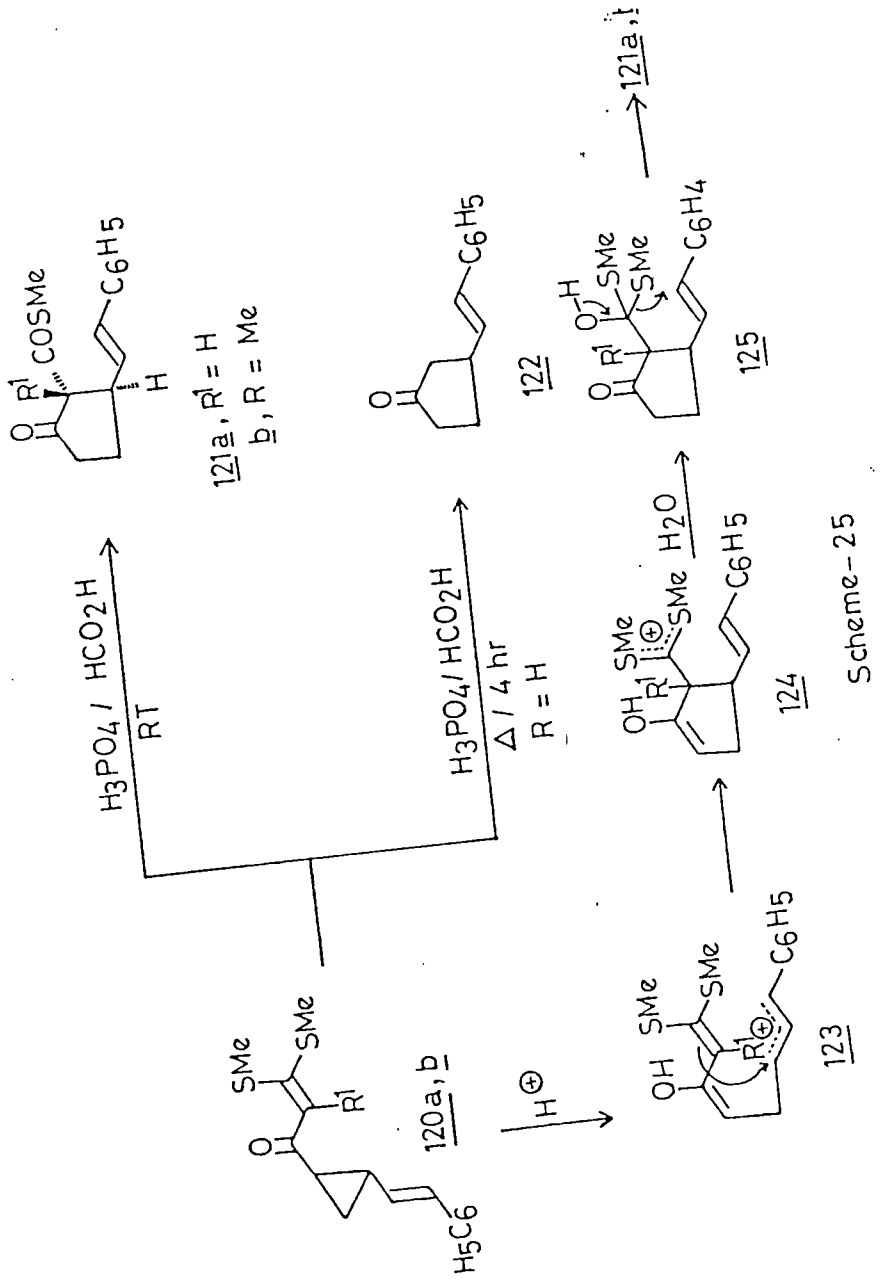
h, Ar = 4-$MeOC_6H_4$; R = H ; n = 2

Scheme-24

analytical data. It was analyzed for $C_{16}H_{18}OS_2$ (290) and the molecular weight was confirmed by its mass spectrum which gave a molecular ion peak at m/z 290 (M^+,8%). In IR(KBr) spectrum the absorption band at 1640 cm^{-1} was assigned to the carbonyl group. The structure was further confirmed from its ^1H NMR($CDCl_3$) spectrum. The cyclopropyl methine and methylene protons appeared at different chemical shifts δ0.85-1.20 (1H), δ1.46-1.71 (1H) and δ1.85-2.33 (2H) as multiplets respectively. The singlet appeared at δ2.42 integrating for 6-protons was attributed to the two methylthio groups. The styryl protons gave characteristic signals at δ5.75 (1H,dd,J=16,18 Hz) and δ6.49 (1H,d,J=16 Hz), showing stereochemistry of *trans* geometry. The mercapto vinylic proton appeared as a singlet at δ6.54 (1H). The multiplet appeared at δ7.0-7.41 integrating for 5-protons was attributed to the aromatic protons. Thus the data was in full confirmity with the assigned structure 120a. Similarly, the other cyclopropyl ketones 120b-h were prepared in 81-97% overall yields and their structures were established by their analytical and spectral data (Experimental).

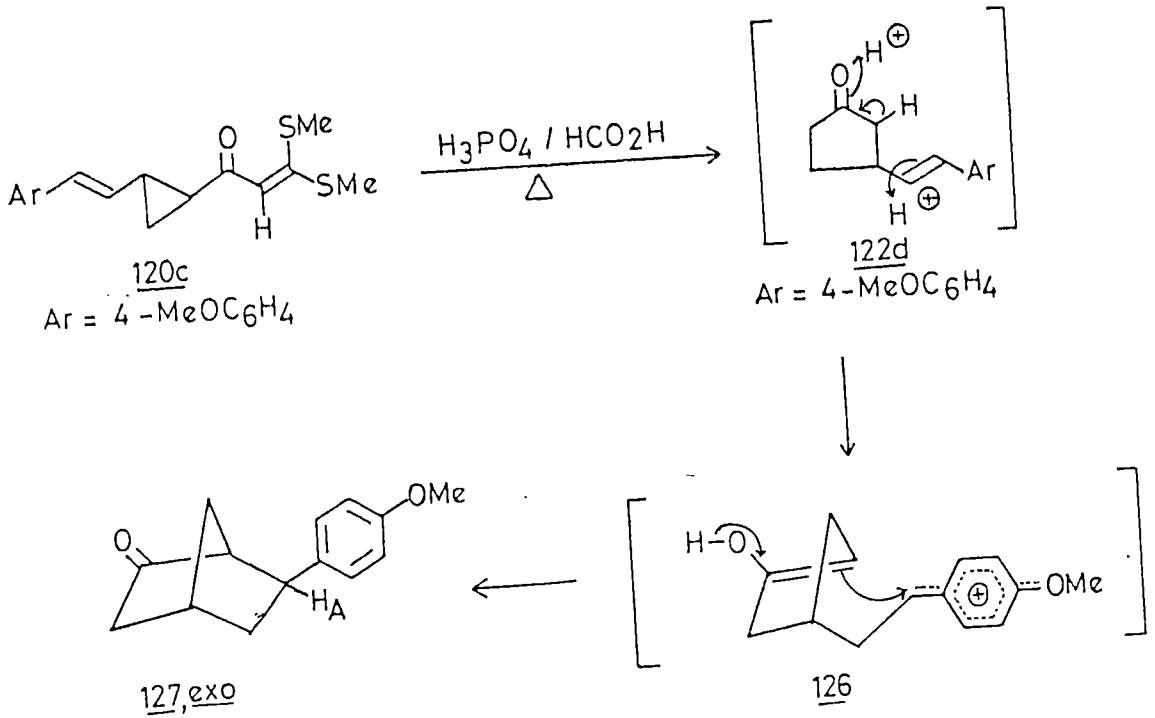
The acid catalyzed rearrangement of 120 to yield the corresponding cyclopentanones was next examined. When 120a was treated with a mixture of H_3PO_4/HCOOH (1:3) at room temperature the reaction mixture after work up and purification yielded s-methy-2-oxo-5-styryl cyclopentane carbothioate 121a in 77% yield (m.p. 111°C). The structure was confirmed from its analytical and spectral data. Thus

it was analyzed for $C_{15}H_{16}O_2S$ (260) and exhibited molecular ion peak at m/z 260 (M^+,7%). Its IR(KBr) spectrum showed absorption bands at ν_{max} 1753 and 1678 cm^{-1}. In its ^1H NMR($CDCl_3$) spectrum the multiplet between δ1.64-2.58 was assigned for the ring methylene protons. The thiomethyl protons appeared as singlet at δ2.33 (3H) and the signal due to H-1 proton appeared as a doublet (J=12 Hz) at δ3.25. The multiplet between δ3.38-3.67 (1H) was assigned to the H-5 methine proton. The olefinic protons of the styryl group appeared as double doublet (J=15,9 Hz) and doublet (J=15 Hz) at δ6.12 and δ6.52 respectively. The multiplet at δ7.18-7.49 (5H) was attributed to the aromatic protons. The product 121a was assigned *E* stereochemistry on the basis of chemical shift values for H-1 and H-5 methine protons and their coupling constants. Thus the H-1 methine proton appeared as a doublet at δ3.25 with J=12 Hz in accordance with the reported values in the similar systems for *trans* coupling constants. Similarly the downfield shift of H-5 methine proton is attributed to the deshielding of *cis* methylthiocarbonyl group which is also in accord with the similar systems reported earlier[8,9]. Also, the styryl double bond retained its *trans* geometry, which can be seen from the coupling constant value J=16 Hz. Similarly, the cyclopentanone 121b was also isolated in 71% yield and characterized to have an *E* configuration on the basis of the considerations mentioned above (Scheme 25).


H3PO4 / HCO2H
RT
H3PO4 / HCO2H
Δ / 4 hr
R = H
H2O
H⊕
120a, b
121a, R1 = H
b, R = Me
122
123
124
125
121a, b
Scheme-25

Interestingly, when the above reaction of 120a was carried out at 80°C (4 hr) the 5-styryl cyclopentanone 122 was isolated in 67% yield. Its structure was established by its analytical and spectral data. It was analyzed for $C_{13}H_{14}O$ (186) and its mass spectrum showed a molecular ion peak at m/z 186 (M^+,68%). In IR(KBr) the band due to ring carbonyl appeared at 1743 cm^{-1} and the ester carbonyl band around 1660 cm^{-1} was absent indicating the cleavage of carbothioate group. The structure of 122 was further confirmed by its ^1H NMR spectral data which are described in the experimental section.

However, the 4-methoxy styrylcyclopropyl ketone 120c did not yield the desired cyclopentanone under similar reaction conditions. The product isolated in 60% yield was characterized as 6-(4-methoxyphenyl)-2-oxo bicyclo[2.2.1]-heptane 127 on the basis of its spectral and analytical data. Thus, the *exo*-isomer was assigned on the basis of observed A_2B_2 pattern of aromatic protons and the triplet at δ2.98 for benzylic proton which is in accord with the earlier observations reported for *exo* substituted norbornane compounds[37]. The rest of the data which were all in agreement with the assigned structure are described in the experimental section. The formation of 127 appears to be not too unexpected under these acidic conditions. Thus, the initially formed cyclopentanone 122d has undergone intramolecular cyclization through trapping of highly stabilized 4-methoxybenzyl cation by enol 126 to afford 127[10-13] (Scheme 26).



120c
Ar = 4-$MeOC_6H_4$

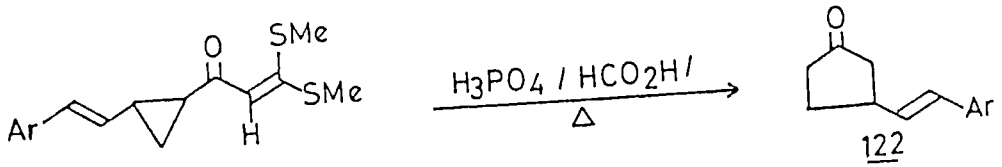
122d
Ar = 4-$MeOC_6H_4$

126

127, exo

Scheme-26

However, when the dimethoxystyrl 120e and methylenedioxystyryl 120f cyclopropyl ketones were treated with H_3PO_4/HCOOH (1:3) under similar conditions, the corresponding bicyclic ketones were not formed and the products were characterized as 3-(2-methylthio-2-aryl ethyl)cyclopentanones 129b (78%) and 129c (73%) respectively (Scheme 27). The structure assigned for 129b, c were confirmed by their analytical and spectral data (experimental). Further attempts to isolate the corresponding styryl cyclopentanones 122e-f under varying conditions did not succeed. On the other hand in the light of these examples, it was decided to re-examine the cyclization of 120a with H_3PO_4/HCOOH under controlled conditions (1 hr), when the corresponding was 129a indeed formed in 81% yield which underwent slow conversion to 122a on prolonged heating (4 hr). These results can be rationalized in terms of relative stabilities of the transient benzyl cation 128 formed by protonation of styryl double bond in the intermediate styryl cyclopentanone 122 (Scheme 27). In the case of 4-methoxyphenyl derivative, the benzyl cation 122d is stable enough to be trapped by the enol double bond intramolecularly to afford exclusively 127. On the other hand in an unsubstituted phenyl derivative, the equilibrium lies towards unprotonated 122a, apparently due to instability of unsubstituted benzyl cation 128a. Alternatively, benzyl cation 128b,c with intermediate



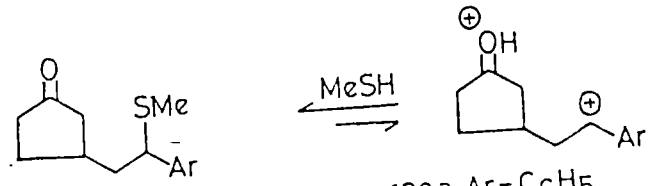
120

a Ar = C_6H_5

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

f Ar = 3,4 – methylenedioxy C_6H_3

122



129

a Ar = C_6H_5

b Ar = 3,4 – $(MeO)_2C_6H_3$

c Ar = 3,4 – methylenedioxy C_6H_3

128 a, Ar = C_6H_5

b, Ar = 3,4 – $(MeO)_2C_6H_3$

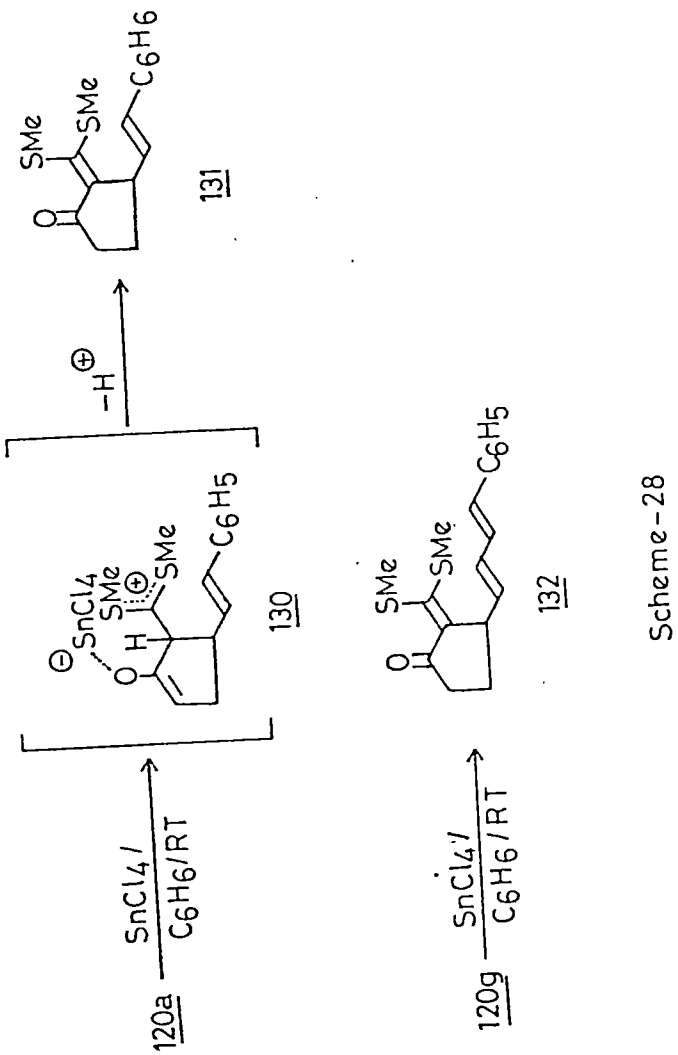
c, Ar = 3,4 – methylenedioxy C_6H_3

Scheme – 27

stability[24] was trapped by nucleophilic methylmercaptan to afford the cyclopentanones 129b,c.

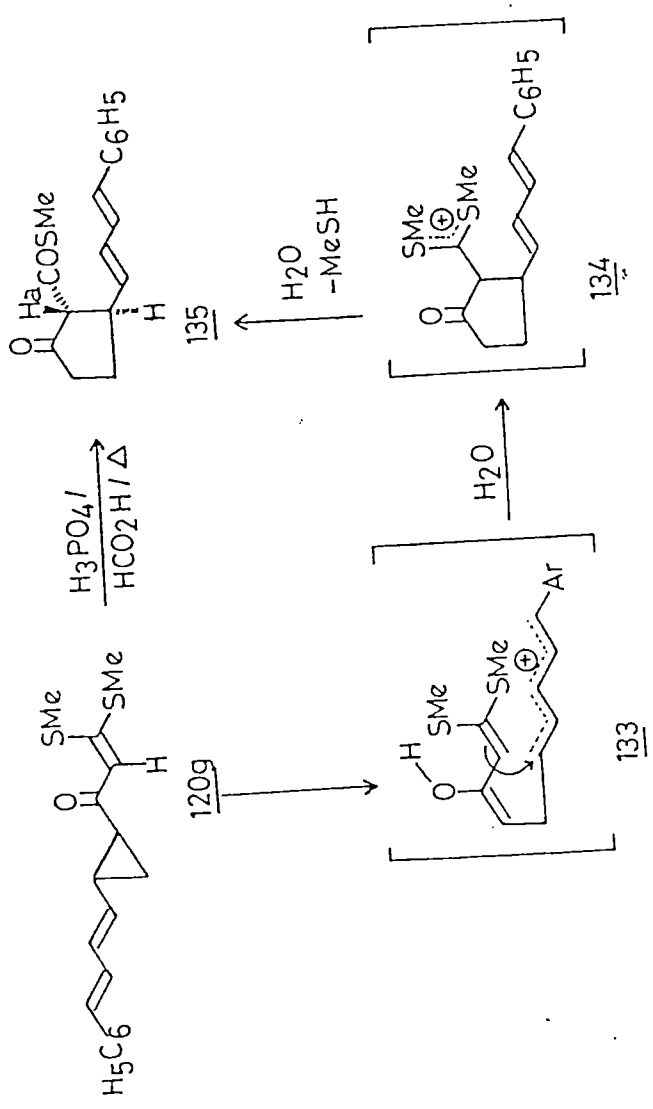
When 120a was treated with $SnCl_4$ in benzene at ambient temperature the product isolated after work up and purification over silica gel column was characterized as 2-bis(methylthio)methylene-3-styrylcyclopentanone 131 in 74% yield. It was analyzed for $C_{16}H_{18}OS_2$ (290) and showed a molecular ion peak at m/z 290 (M^+,21%) in its mass spectrum. The IR(neat) spectrum showed a carbonyl absorption band at 1693 cm^{-1}. The presence of two singlets at δ2.38 (3H) and 2.44 (3H) in its ^1H NMR(CCl_4) spectrum confirm the presence of two methylthio groups. The rest of the spectral data were in confirmity with the assigned structure and are described in the experimental section. Similarly, the dienyl cyclopropyl ketone 120g yielded the corresponding cyclopentanone 132 in 71% yield under similar reaction conditions. The spectral and analytical data of 132 were in full accord with the assigned structure (experimental). The formation of 131 appears to go through sulphur stabilized bis(methylthio)methyl carbocation 130 followed by loss of ring proton retaining the mercapto functionality (Scheme 28).

Cyclization of (4-aryl-1,3-butadienyl)cyclopropyl ketones 120g-h were next examined . When 120g was treated with a mixture of phosphoric acid and formic acid (1:3) at room temperature, the product isolated, after work-up and purification by column chromatography over silica gel, was

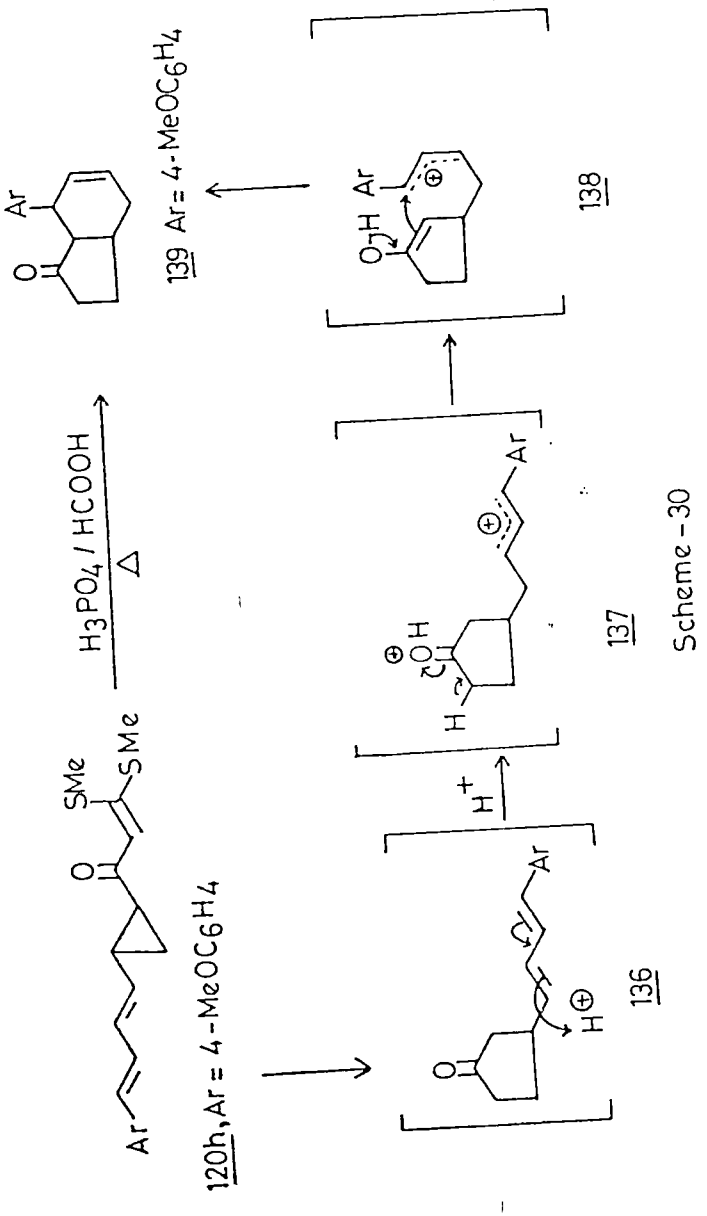

120a
SnCl4 /
C6H6/RT
SnCl4
SMe
SMe
C6H5
130
-H
SMe
SMe
C6H6
131
120g
SnCl4 /
C6H6/RT
SMe
SMe
C6H5
132

Scheme-28

5-(4-phenyl-1,3-butadienyl)-2-oxo cyclopentane carbothioate 135 in 76% yield (m.p. 108°-109°C). The compound gave satisfactory elemental analysis ($C_{17}H_{18}O_2S$). Its mass spectrum exhibited molecular ion peak at m/z 286 (M^+,40%). Its IR(KBr) spectrum showed characteristic bands at 1750 and 1675 cm^{-1} due to two carbonyl groups. It was found to be a mixture of *E* and *Z* (4:1) isomer on the basis of its ^1H NMR(CCl_4) spectrum. The signals at δ2.35 (2.4H,s) and δ2.26 (0.6H,s) were assigned to methylthio group in *E* and *Z* isomers respectively. The two H-1 (H_a) and H-5 (H_b) methine protons in *E* isomer appeared at δ3.12 (0.8H,d,J≈12 Hz,H-1) and 3.33 (0.8H,m,H-5) while signals due to these protons in *Z* isomer appeared as multiplet between δ2.55-2.80 (0.4H)[8,9]. The other analytical and spectral data were in agreement with the assigned structure which are described in the experimental section. Apparently, the product 134 was formed by 5-*exo-trig* ring closure followed by the hydrolysis of resulting sulphur stabilized carbocation 134 in the described reaction condition (Scheme 29). However, the corresponding 4-methoxy derivative 120h on treatment with H_3PO_4/HCOOH did not yield the expected dienyl cyclopentanone 136, instead the product formed (62%) was characterized as bridged bicyclic ketone 139 on the basis of its analytical and spectral data (Scheme 30). It was analyzed for $C_{16}H_{18}O_2$ and showed molecular ion peak at m/z 242 (M^+,100%) along with prominent peaks at 82(50%), 160(36%) and 198(30%). The characteristic cyclopentanone carbonyl frequency appeared



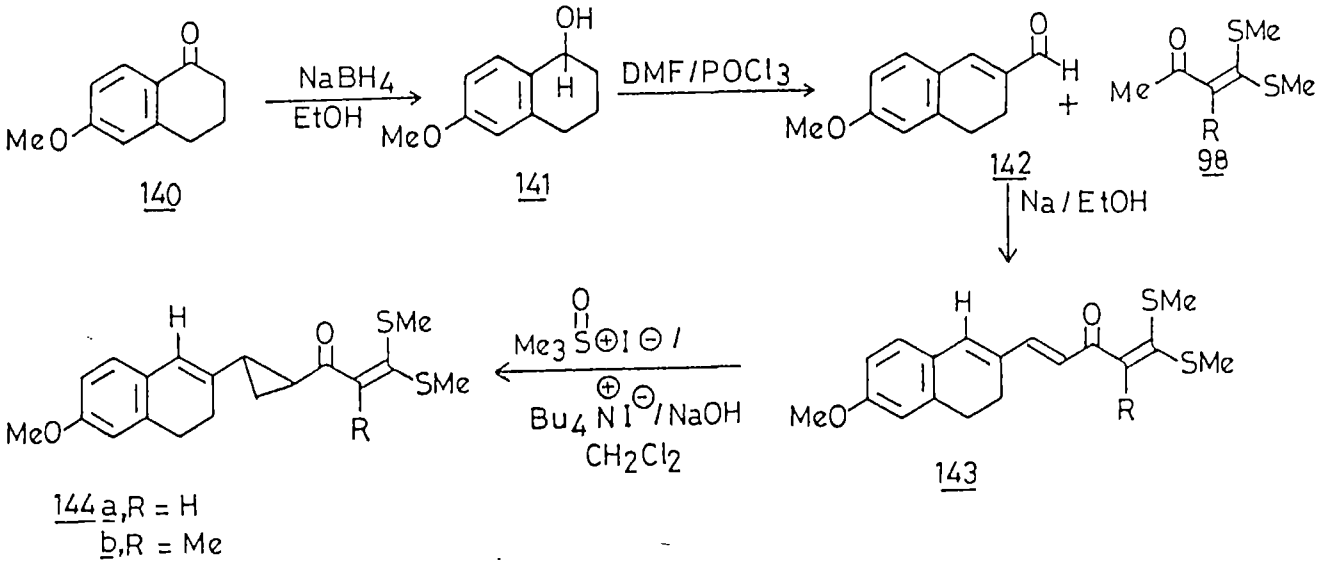
Scheme-29



Scheme-30

at 1743 cm^{-1}. Its ^1H NMR(CCl_4) showed a singlet at δ3.72 (3H) due to methoxy protons. The multiplet around δ1.10-2.80 (10H) was assigned to ring methylene and bridge head methine protons. The four aromatic protons appeared at δ6.8 (2H,d,J=8 Hz) and δ7.23 (2H,d,J=8 Hz). The olefinic protons appeared as multiplet between δ5.5-5.88 (2H) indicating that the double bond is not in conjugation with aryl group. The mechanism for the formation of **139** from **120h** is depicted in the Scheme 30. In the presence of acid the initially formed dienylcyclopentanone **136** could exist in its enol form with a highly stabilized 4-methoxyphenylallyl cation **138** which is trapped intramolecularly by enol double bond to yield **139** .

In continuation of these studies, an application of this methodology for the synthesis of 11-oxo steroidal precursors **149** and **150** was examined. The desired cyclopropyl ketones **144a,b** were synthesized as shown in Scheme 31. The enealdehyde **142** obtained through the *Vilsmeir-Haack* reaction on carbinol **141** was condensed with acylketene dithioacetals **98a,b** to afford the corresponding dienoyl ketene dithioacetals **143a,b** in the presence of sodium ethoxide in high yields. These dienes were then subjected to cyclopropanation as described earlier to afford the corresponding cyclopropyl ketones **144a** and **144b** in 93% and 81% yield respectively. The spectral and analytical data of **144a** and **144b** were in accord with the assigned structures and are described in the

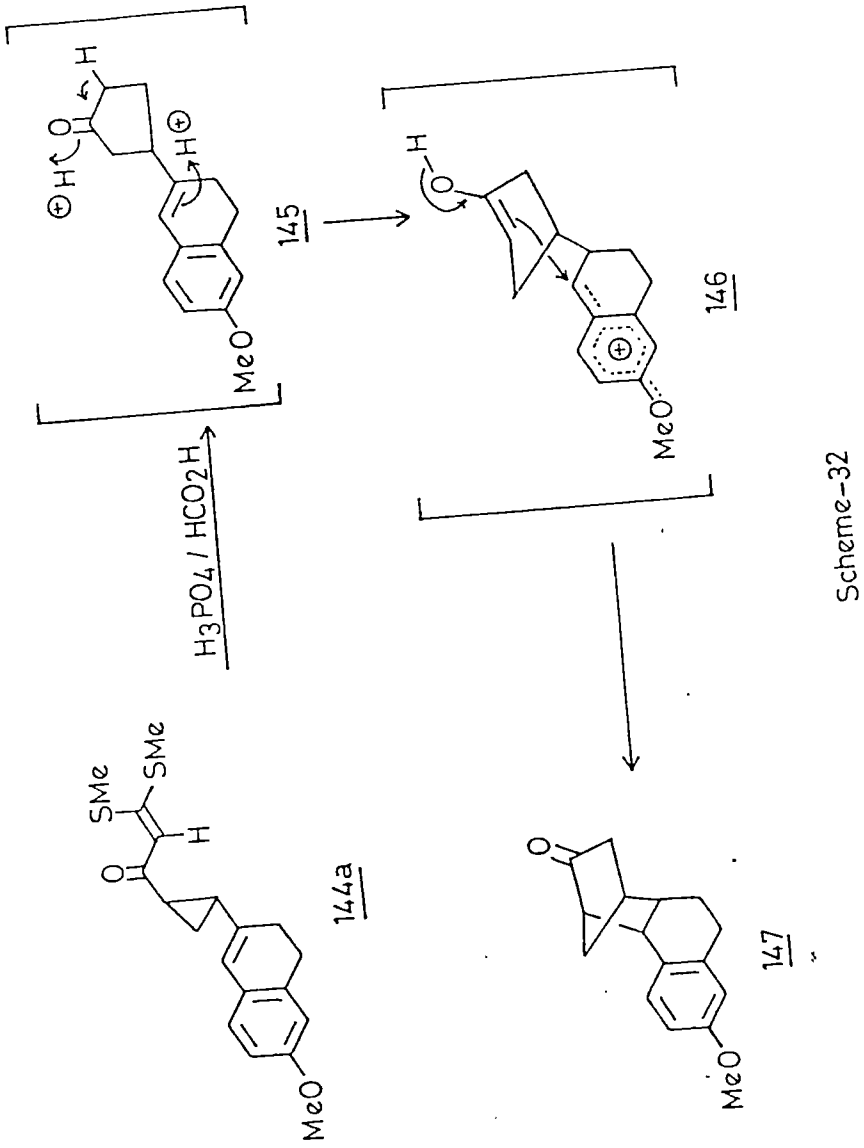


140 141 142 98 143

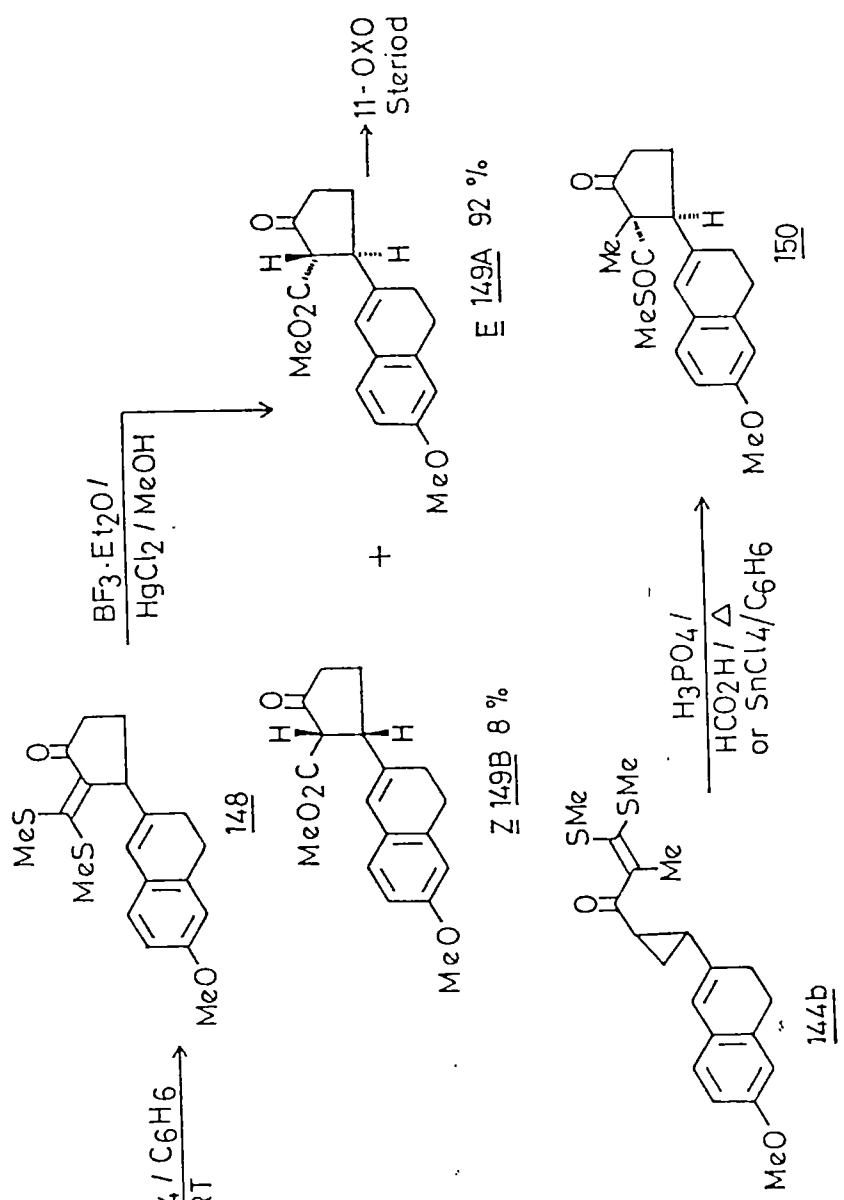
144 a, R = H
b, R = Me

Scheme -31

experimental section. The cyclopropyl ketone 144a when cyclized in presence of H_3PO_4/HCOOH yielded a product which was characterized as the bicyclic ketone 147 (Scheme 32) obtained in 62% yield and the desired cyclopentanone 145 was detected in the reaction mixture. The structural assignment was done on the basis of its spectral and analytical data. It was analyzed for $C_{16}H_{18}O_2$ (242) and showed a molecular ion peak at m/z 242 (M^+,100%). In its ^1H NMR(CCl_4) spectrum no vinylic protons were observed. The methylene and the methine protons appeared as multiplet between δ1.17-2.94 (12H). The signal at δ3.70 (3H,s) was due to methoxy protons. The aromatic protons appeared as multiplet between δ6.42-7.18 (3H). Here again, the intermediate cyclopentanone 145 has undergone an intramolecular ring closure in the acidic medium, which was proved by the disappearance of the B-ring olefinic proton. However, the desired β-ketoester 149 could be obtained in 78% overall yield by treating 144a with $SnCl_4$ in benzene at ambient temperature to afford initially 148 which on subsequent methanolysis ($BF_3.Et_2O/HgCl_2$/MeOH) gave the expected 149. The product 149 was found to be a single stereoisomer (*E*) and the assignment was based on their ^1H NMR spectrum which was in accordance with the corresponding 6-bromo isomer reported by Trost and coworkers[8,9]. Again, when 144b was heated at 80° in H_3PO_4/HCOOH (1:3) the expected product 150 was neatly formed in 83% yield (m.p. 118°-119°C). In its mass spectrum it exhibited molecular ion peak at m/z 330



Scheme-32


144a
SnCl4 / C6H6
RT
148
BF3·Et2O /
HgCl2 / MeOH
E 149A 92 %
Z 149B 8 %
11-OXO
Steriod
H3PO4 /
HCO2H / Δ
or SnCl4/C6H6
150
144b

Scheme-33

(M^+,28%) and was analyzed for $C_{19}H_{22}O_3S$. It was found to be a single stereoisomer as evident from its ^1H NMR spectrum. The sharp singlets for methyl (δ1.20, 3H), methylthio (δ2.32, 3H) and methoxy (δ3.77) and the olefinic proton at δ6.22 (1H) were observed. The methylene protons appeared as multiplet between δ1.41-2.88 (8H). The *E* stereochemistry of cyclopentanone ring was confirmed from the low field chemical shift for the methine proton H-5 which appeared at δ3.65 as a broad triplet merged with methoxy signal. Its low field shift was primarily due to deshielding effect of the *cis* methylthiocarbonyl group. The aromatic protons appeared as multiplet between δ6.51-6.77 (2H) and as doublet between δ6.95 (1H,J=9 Hz).

II.3 CONCLUSION

The cyclopropyl ketones have been shown to undergo a novel rearrangement through their cationic ring opening to give the corresponding 3-aryl cyclopentanones. The incipient carbocation developed in the presence of acid was successfully trapped by intramolecular π-participation of bis(methylthio) double bond to give the product cyclopentanones. The present method illustrates the successful utilization of α-oxoketene dithioacetal functionality as a latent β-ketoester equivalent and represents a novel intramolecular alkylative approach to substituted cyclopentanones. This new C-C bond formation is of particular interest since the attempted

intramolecular cyclization of δ-haloketones or the corresponding β-ketoesters yield the products of O-alkylation (furan) rather than intramolecular C-alkylation due to stereoelectronic factors. In the second part, the acid catalyzed ring opening of the cyclopropyl ketones with one or two double bonds flanked between aryl group and cyclopropane ring were successfully synthesized showing the phenylallyl (or phenylpentadienyl) carbocation can be trapped by the bis(methylthio)methylene double bond, whereas in the case of benzyl cation it was not successful, as shown in the preceding part. This methodology has been also extended for the synthesis of steroid precursors as an application to more important target molecules.

II.4 EXPERIMENTAL

General:- M.p.s were determined on a 'Thomas Hoover' capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian EM-390 (90 MHz) spectrometer in deuteriochloroform or carbon tetrachloride using TMS as internal standard. Mass spectra were obtained on a Jeol JMS D-300 spectrometer. Elemental analysis were carried out on a Heraeus CHN-O-RAPID instrument.

Starting Materials

Commercially available ketones were purchased (Aldrich) and were used as supplied. The other ketones were prepared by reported procedure. All liquid aldehydes were distilled and freed of acid before use. The substituted cinnamaldehydes, their higher homologues and 3,4-dihydro 6-methoxy-2-napthaldehyde 142 were prepared according to the reported procedure[38]. All acylketene dithioacetals were prepared according to the general procedure described below. The preparation for cinnamoyl ketene dithioacetals (99a-o), 5-aryl-2,4-pentadienoyl (119a-f,143a-b) and 7-aryl-2,4,6-heptatrienoyl (119g-h) ketene dithioacetals are also given below.

3,4-Dihydro-6-methoxy-2-napthaldehyde (142) colorless crystals (93%); m.p. 44°-45°C; ν_{max}(KBr) $\delta_H(CCl_4)$ 2.30-2.88 (4H,m,CH_2), 3.77 (3H,s,OCH_3), 6.53-6.76 (2H,m,=CH and ArH), 6.96-7.20 (2H,m,ArH), 9.53 (1H,s,CHO); (Found : C,76.81; H,6.62. $C_{12}H_{12}O_2$ requires C,76.57; H,6.43%).

General method for the preparation of α-oxoketene dithioacetals (98) : 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 (200 ml) and the reaction mixture was allowed to stir at room temperature for 5-6 hr. Acid free dimethyl sulphate (0.2 mol) was gradually added with stirring and cooling and the reaction mixture was allowed

to stir at room temperature for 6-10 hr. The reaction mixture was poured over ammonium chloride solution (250 ml) and the layers were separated. The aqueous layer was extracted with benzene (100 ml) and the combined benzene extracts were washed with water (4 x 250 ml), dried (Na_2SO_4) and evaporated to give crude dithioacetals 98, which were further purified by crystallisation or by distillation under reduced pressure. The physical and spectral data were compared with that of the reported values.

Condensation of α-acylketene dithioacetals with aldehydes : General procedure for the preparation of compounds (99a-o, 119a-h and 143a-b). To a cooled and stirred solution of sodium ethoxide in ethanol, prepared by dissolving sodium (0.06 mol) in ethanol (30 ml), a solution of the α-acylketene dithioacetal (0.03 mol) and aldehyde (0.03 mol) in minimum ethanol was added dropwise over a period of 5 minutes. The reaction mixture was brought to room temperature over a period of 20 minutes and further stirred at room temperature for 4-5 hr. The mixture was diluted with cold water (100 ml) and solid separates out was filtered, washed with water (4 x 50 ml) and dried. In the cases where the product is liquid (99h-j, 99n-o), the reaction mixture after dilution with water was extracted with chloroform (3 x 50 ml), washed with water (4 x 50 ml), dried (Na_2SO_4) and evaporated to give crude products which were further column chromatographed (ethylacetate :

hexane, 1:20 eluent). The data of unknown compounds are given below.

4,4-Bis(methylthio)methylene-1-(4-methoxyphenyl)-1-undecene-3-one (99j) yellow oil (59%); ν_{max} (neat) 1640, 1590 cm^{-1}; δ_H (CCl_4) 0.85 (3H,t,J 7Hz,CH_3), 1.10-1.61 (10H,m,CH_2), 2.18 (3H,s,SCH_3), 2.30 (3H,s,SCH_3), 2.57 (2H,t,J 7Hz,CH_2), 3.78 (3H,s,OCH_3), 6.5-7.6 (6H,m,=CH,ArH) ; (Found : C,66.85; H,7.61. $C_{21}H_{30}O_2S_2$ requires C,66.62; H,7.99%).

1,1-Bis(methylthio)-5-(3,4-dihydro-6-methoxy-2-napthyl)-1,4-pentadiene-3-one (143a) yellow crystals (87%); m.p. 104°-105°C; ν_{max} (KBr) 1643, 1495 cm^{-1}; δ_H ($CDCl_3$) 2.38-2.64 (2H,m,CH_2), 2.51 (6H,s,SCH_3), 2.73-3.02 (2H,m,CH_2), 3.78 (3H,s,OCH_3), 6.16 (1H,s,=CH), 6.32 (1H,d,J 16Hz,=CH), 6.61-6.81 (3H,m,=CH,ArH), 7.0-7.14 (1H,m,ArH), 7.47 (1H,d,J 16Hz,=CH). (Found : C,65.20; H,6.18. $C_{18}H_{20}O_2S_2$ requires C, 65.02; H, 6.05%).

1,1-Bis(methylthio)-5-(3,4-dihydro-6-methoxy-2-napthyl)-2-methyl-1,4-pentadiene-3-one (143b) yellow crystals (87%); m.p. 114°-115°C; ν_{max} (KBr) 1650, 1602 cm^{-1}; δ_H ($CDCl_3$) 2.11 (3H,s,CH_3), 2.24 (3H,s,SCH_3), 2.36 (3H,s,SCH_3), 2.43-2.61 (2H,m,CH_2), 2.70-3.02 (2H,m,CH_2), 3.81 (3H,s,OCH_3), 6.33 (1H,d,J 16Hz,=CH), 6.57-6.85 (3H,m,=CH,ArH), 7.08 (1H,d,J 9Hz,ArH), 7.26 (1H,d,J 16Hz,=CH); (Found : C,65.61; H, 6.23. $C_{19}H_{22}O_2S_2$ requires C, 65.86; H, 6.40%).

Synthesis of Cyclopropyl Ketones (100,120,144) from α-Cinnamoyl,dienoyl and trienoyl ketene Dithioacetal (99,119,143) and Dimethylsulphoxonium methylide: General Procedure: A suspension of the appropriate ketene dithioacetal (10 mmol), trimethylsulph- oxonium iodide (13 mmol), tetrabutyl ammonium iodide (15 mmol) in an aqueous solution of 50% NaOH (70 ml) and CH_2Cl_2 (70 ml) was stirred at 50°C for 7h except for(100m-o) (5days). The organic layer was separated and concentrated, the residue diluted with EtOAc to precipitate tetrabutylammonium iodide which was filtered off. The filtrate was evaporated to give crude cyclopropyl ketones which were purified by column chromatography over silica gel using EtOAc/hexane (1:20) as eluent. The analytically pure samples of cyclopropyl ketones were obtained by recrystallization from chloroform-hexane.

1-[2-Bis(methylthio)methyleneacetyl]-2-(4-methoxyphenyl) cyclopropane (100a) (98%), m.p. 97-98°C; ν_{max}(KBr) 1620(CO), 1480 cm^{-1}; $\delta_H(CDCl_3)$ 1.12-1.81 (2H, m, CH_2), 1.89-2.15 (1H, m, CH), 2.41 (3H, s, SMe), 2.46 (3H,s,SMe), 2.33-2.58 (1H, m, CH), 3.76 (3H,s,OMe), 6.16 (1H,s,=CH), 6.75 (2H,d,*J* 9Hz,ArH), 7.01 (2H,d,*J* 9Hz, ArH); (Found: C,61.35; H,6.2. $C_{15}H_{18}O_2S_2$ requires C,61.19; H,6.16%); m/z 294 (M^+,24%) and 279 (M^+-15,43).

1-[2-Bis(methylthio)methyleneacetyl]-2-(3,4-dimethoxy phenyl)cylopropane (100b) (95%), m.p. 104-105°C; ν_{max}(KBr) 1619 (CO),1495 cm^{-1}; $\delta_H(CDCl_3)$ 1.17-1.80 (2H, m, CH_2),

1.86-2.18 (1H, m, CH), 2.46 (3H,s,SMe), 2.49 (3H,s,SMe), 2.35-2.61 (1H,m,CH), 3.84 (3H,s,OMe), 3.87 (3H,s,OMe), 6.20 (1H,s,=CH), 6.54-6.88 (3H,m, ArH); (Found: C, 59.5; H, 6.3 $C_{16}H_{20}O_3S_2$ requires C, 59.23; H,6.21%); m/z 324 (M^+, 31%), 309 (M^+-15,31).

1-[2-Bis(methylthio)methyleneacetyl]-2-(3,4,5-trimethoxy phenyl)-cyclopropane (100c) (96%), m.p. 129-130°C; ν_{max}(KBr) 1620 (CO), 1478 cm^{-1}; $\delta_H(CDCl_3)$ 1.13-1.79 (2H,m,CH_2), 1.98-2.20 (1H,m, CH), 2.50 (3H,s,SMe),2.63 (3H,s,SMe) 2.30-2.56 (1H,m,CH), 3.76 (3H,s,OMe), 3.87 (6H, s, OMe), 6.28 (1H,s,=CH), 6.34 (2H,s,ArH); (Found: C,57.4; H, 6.4 $C_{17}H_{22}O_4S_2$ requires C,57.60; H, 6.26%); m/z 354 (M^+, 12%),339 (M^+-15,8).

1-[2-Bis(methylthio)methyleneacetyl)-2-(3,4-methylenedioxy phenyl)cyclopropane (100d) (94%), m.p. 130-131°C; ν_{max} (KBr) 1631(CO), 1490 cm^{-1};$\delta_H(CDCl_3)$ 1.13-1.80 (2H,m,CH_2), 1.93-2.21 (1H,m, CH), 2.46 (3H,s,SMe), 2.51 (3H,s, SMe), 2.38-2.66 (1H,m,CH), 5.94 (2H,s,CH_2), 6.21 (1H;s,=CH),6.56 -6.83 (3H,m,ArH); (Found: C, 58.6; H,5.4. $C_{15}H_{16}O_3S_2$ requires C, 58.41; H,5.23%); m/z 308 (M^+,20%), 297 (M^+-15,27).

1-[2-Bis(methylthio)methyleneacetyl]-2-(4-methylphenyl) cyclopropane (100e) (92%), m.p. 78-79°C; ν_{max}(KBr) 1623 (CO), 1480 cm^{-1};$\delta_H(CDCl_3)$ 0.95-1.75 (2H,m,CH_2), 1.81-2.15 (1H,m,CH), 2.13 (3H,s,Me), 2.28 (3H,s,SMe), 2.40 (3H,s, SMe), 2.09-2.45 (1H, m,CH), 6.11 (1H,s,=CH), 6.91-7.00

(4H,m,ArH); (Found: C, 64.9; H, 6.65. $C_{15}H_{18}OS_2$ requires C, 64.71, H, 6.52%); m/z 278 (M^+, 16%), 263 (M^+-15,100).

1-[2-Bis(methylthio)methyleneacetyl]-2-phenylcyclopropane (100f) (97%), m.p. 104-105°C; ν_{max}(KBr) 1620 (CO), 1490 cm^{-1}; δ_H($CDCl_3$) 1.15-1.80 (2H,m,CH_2), 1.92-2.21 (1H,m,CH), 2.44 (3H,s,SMe); 2.49 (3H,s,SMe), 2.41-2.67 (1H,m,CH), 6.17 (1H,s,=CH), 7.0-7.31 (5H,m, ArH); (Found: C, 63.7; H,6.2. $C_{14}H_{16}OS_2$ requires C, 63.60; H, 6.10%); m/z 264 (M^+,7%), 249 (M^+-15,100).

1-[2-Bis(methylthio)methylenepropanoyl]-2-(4-methoxy phenyl) cyclopropane (100g) (98%), oil; ν_{max}(neat) 1665 (CO), 1508 cm^{-1}; δ_H(CCl_4) 1.17-1.77 (2H,m,CH_2), 2.02 (3H, s,SMe), 2.08 (3H,s,SMe), 2.27 (3H,s,Me), 2.02-2.60 (2H,m, CH), 3.66 (3H,s,OMe), 6.69 (2H,d,*J* 9Hz, ArH), 6.96 (2H,d,*J* 9Hz, ArH); (Found: C,62.5; H,6.6. $C_{16}H_{20}O_2S_2$ requires C, 62.30; H,6.54%); m/z 308 (M^+,1%, 293 (M^+-15,47).

1-[2-Bis(methylthio)methylene-*n*-butanoyl]-2-(4-methoxy-phenyl) cyclopropane (100h) (84%), oil; ν_{max}(neat) 1667 (CO), 1510 cm^{-1}; δ_H(CCl_4) 1.00 (3H,t,*J* 7Hz,Me), 1.21-1.79 (2H,m,CH_2), 2.08 (3H,s,SMe),2.26 (3H,s,SMe), 2.50 (2H,q, *J* 7Hz,CH_2), 2.01-2.70 (2H,m,CH);3.69 (3H,s,OMe), 6.79 (2H,d,*J* 9Hz,ArH), 7.01 (2H,d, *J* 9Hz, ArH);(Found: C,63.5; H,6.75. $C_{17}H_{22}O_2S_2$ requires C,63.31;H, 6.88%); m/z 322 (M^+, 6%), 307 (M^+-15,100).

1-[2-Bis(methylthio)methylene-*n*-hexanoyl]-2-(4-methoxy-phenyl)cyclopropane (100i) (87%), oil; ν_{max}(neat) 1665

(CO), 1512 cm^{-1}; $\delta_H(CCl_4)$ 0.86 (3H,t,*J* 6Hz,Me), 1.17-1.81 (6H,m,CH_2), 2.10 (3H,s,SMe), 2.23 (3H,s,SMe), 2.03-2.31 (1H,m,ring CH), 2.37-2.67 (3H,m,CH_2,ring CH), 3.70 (3H,s,OMe), 6.69 (2H,d,*J* 9Hz, ArH), 7.04 (2H,d,*J* 9Hz, ArH); (Found: C,65.3; H, 7.6.$C_{19}H_{26}O_2S_2$ requires C, 65.10; H,7.48%); m/z 350 (M^+, 4%), 335 (M^+-15,100).

1-[2-Bis(methylthio)methylene-*n*-nonanoyl]-2-(4-methoxyphenyl) cyclopropane (100j) (85%), oil; γ_{max}(neat) 1669 (CO), 1515 cm^{-1}; $\delta_H(CCl_4)$ 0.88 (3H,t,*J* 7Hz,Me), 1.13-1.88 (12H,m,CH_2), 2.08 (3H,s,SMe), 2.32 (3H,s,SMe), 2.03-2.35 (1H,m,CH), 2.40-2.71 (3H,m,CH_2 and ring CH), 3.71 (3H,s,OMe), 6.71 (2H,d, *J* 9Hz, ArH), 7.01 (2H,d, *J* 9Hz, ArH); (Found: C, 67.45; H, 8.3. $C_{22}H_{32}O_2S_2$ requires C, 67.3; H, 8.22%); m/z 392 (M^+,6%), 377 (M^+-15,100)

1-[2-Bis(methylthio)methylenepropanoyl]-2-(3,4-dimethoxyphenyl) cyclopropane (100k) (95%), oil; γ_{max} 1662 (CO), 1508 cm^{-1}; $\delta_H(CCl_4)$ 1.17-1.73 (2H,m,CH_2), 2.03 (3H,s,SMe), 2.10 (3H,s,SMe), 2.27 (3H,s,Me), 2.01-2.64 (2H,m,CH), 3.71 (6H,s,OMe), 6.47-6.74 (3H,m,ArH); (Found: C, 60.2; H,6.7. $C_{17}H_{22}O_3S_2$ requires C, 60.32; H, 6.55%); m/z 338 (M^+;7%), 323 (M^+-15,39).

1-[2-Bis(methylthio)methylenepropanoyl]-2-(3,4,5-tri methoxyphenyl)cyclopropane (100l) (96%), oil; γ_{max}(neat) 1667 (CO),1505 cm^{-1}; $\delta_H(CCl_4)$ 1.19-1.75 (2H,m,CH_2), 2.05 (3H,s,SMe), 2.10 (3H,s,SMe), 2.26 (3H,s,Me),2.02-2.57 (2H, m,CH), 3.64 (3H,s,OMe), 3.76 (6H,s,OMe), 6.27 (2H,s,ArH);

(Found: C, 58.8; H, 6.7. $C_{12}H_{24}O_4S_2$ requires C, 58.67; H, 6.56%); m/z 368 (M^+,17%), 353 (M^+-15,97).

1-[2-Bis(methylthio)methylenepropanoyl]-2-(3,4-methylenedioxyphenyl)cyclopropane (100m) (96%), oil; ν_{max}(neat) 1668 (CO), 1490 cm^{-1}; $\delta_H(CCl_4)$ 1.18-1.80 (2H,m,CH_2), 2.06 (3H,s,SMe), 2.11 (3H,s,SMe), 2.29(3H,s,Me), 2.03-2.56 (2H, m,CH),5.82(2H,s,$CH_2{}^{O}{}_{O}$), 5.48-6.74 (3H,m,ArH); (Found: C, 59.8; H, 4.45. $C_{16}H_{18}O_3S_2$ requires C, 59.60, H, 6.63%); m/z 322 (M^+,9%), 307 (M^+-15,98).

1-[2-Bis(methylthio)methylenepropanoyl)-1-methyl-2-(4-methoxy-phenyl)cyclopropane (100n) (90%), oil; ν_{max}(neat) 1665 (CO), 1511 cm^{-1}; $\delta_H(CCl_4)$ 0.96 (3H,s,Me), 1.02-1.88 (2H,m,CH_2), 2.04 (3H,s,SMe), 2.22 (3H,s,SMe), 2.26 (3H,s, Me), 2.56-2.80 (1H,m,CH), 3.70 (3H,s,OMe), 2.56-2.80 (1H,m,CH), 6.74 (2H,d, *J* 9Hz, ArH), 7.07 (2H,d, *J* 9Hz, ArH); (Found: C, 63.5; H,6.75. $C_{17}H_{22}O_2S_2$ requires C,63.31; H, 6.88%); m/z 322 (M^+,1%), 245 (74), 217 (100).

1-[2-Bis(methylthio)methylenepropanoyl]-1-methyl-2-(3,4-dimethoxy phenyl)cyclopropane (100o) (88%), oil; ν_{max}(neat) 1667(CO), 1510 cm^{-1}; $\delta_H(CCl_4)$ 0.98 (3H,s,Me), 1.06-1.85 (2H,m,CH_2), 2.06 (3H, s, SMe), 2.19 (3H,s,SMe), 2.29 (3H,s,Me), 2.49-2.76 (1H,m,CH), 3.75 (6H,s,OMe), 6.63-6.78 (3H,m,ArH); (Found: C, 61.5; H, 6.93. $C_{18}H_{24}O_3S_2$ requires C, 61.33; H, 6.86%); m/z 352 (M^+, 1%), 322 (21) 275 (46).

1-[2-Bis(methylthio)methyleneacetyl]-2-styryl cyclopropane (120a) colorless crystals (97%), m.p. 116°-117°C; IR and

^{1}H NMR data described in the text.(Found: C,66.29; H,6.38. $C_{16}H_{18}OS_2$ requires C, 66.17; H, 6.25%); m/z 290 (M^+,8%), 275(36), 243(8).

1-[2-Bis(methylthio)methylenepropanoyl]-2-styrylcyclopropane (120b) yellow oil (93%); ν_{max} 1665, cm^{-1}; δ_H (CCl_4) 0.98-1.31 (1H,m,CH_2), 1.39-1.71 (1H,m,CH_2), 1.93-2.33 (2H,m,CH), 2.07 (3H,s,CH_3), 2.19 (3H,s,SCH_3), 2.25 (3H,s,SCH_3), 5.74 (1H,dd,J=16,18 Hz,=CH), 6.47 (1H,d,J=16 Hz,=CH), 6.98-7.34 (5H,m,ArH); (Found : C,67.19; H,6.79. $C_{17}H_{20}OS_2$ requires C,67.06; H,6.62%); m/z 304 (M^+,8%), 289(85).

1-[2-Bis(methylthio)methyleneacetyl]-2-[2-(4-methoxyphenyl)ethenyl]cyclopropane (120c) colorless crystals (87%), m.p. 108°-109°C; ν_{max} (KBr) 1625, 1495 cm^{-1}; δ_H ($CDCl_3$) 0.94-1.18 (1H,m,CH_2), 1.47-1.73 (1H,m,CH_2), 1.83-2.30 (2H,m,CH), 2.46(6H,s,SCH_3), 3.77 (3H,s,OCH_3) 5.64 (1H,dd,J=16,9 Hz,=CH), 6.18 (1H,s,=CH), 6.47 (2H,d,J=16 Hz,=CH), 6.80 (2H,d,J=9Hz,ArH), 7.22 (2H,d,J=9 Hz,ArH); (Found: C,63.86; H,6.42. $C_{17}H_{20}O_2S_2$ requires C,63.71; H, 6.29%); m/z 320 (M^+, 12%), 305(24), 273(16).

1-[2-Bis(methylthio)methylenepropanoyl)]-2-[2-(4-methoxyphenyl)ethenyl]cyclopropane (120d) yellow oil (86%); ν_{max} (neat) 1690 cm^{-1}; δ_H (CCl_4) 0.93-1.20 (1H,m,CH_2), 1.35-1.70 (1H,m,CH_2), 1.90-2.30 (2H,m,CH), 2.04 (3H,s,CH_3), 2.16 (3H,s,SCH_3), 2.25 (3H,s,SCH_3), 3.66 (3H,s,OCH_3), 5.66 (1H,dd,J=16,8 Hz,=CH), 6.48 (1H,d,J=16 Hz,=CH), 6.70 (2H,d

J=9 Hz, ArH), 7.10 (2H,d,J=9 Hz,ArH); (Found: C,64.81;H, 6.78. $C_{18}H_{22}O_2S_2$ requires C, 64.63; H,6.63%).

1-[2-Bis(methylthio)methyleneacetyl]-2-[2-(3,4-dimethoxyphenyl)ethenyl]cyclopropane (120e) colorless crystals (83%); m.p. 116°-117°C; ν_{max} (KBr) 1632, 1490 cm^{-1}; δ_H ($CDCl_3$) 0.79-1.38 (1H,m,CH_2), 1.48-1.80 (1H,m,CH_2), 1.87-2.36 (2H,m,CH), 2.46 (6H,s,SCH_3), 3.88 (6H,s,OCH_3), 5.68 (1H,dd,J=16,9 Hz,=CH), 6.21 (1H,s,=CH), 6.46 (1H,d,J=16 Hz,=CH), 6.67-6.94 (3H,m,ArH); (Found : C,61.82; H,6.21. $C_{18}H_{22}O_3S_2$ requires C,61.68; H,6.33%); m/z 350(M^+,11%), 335(38), 303(25).

1-[2-Bis(methylthio)methyleneacetyl]-2-[2-(3,4-methyledioxyphenyl)ethenyl]cyclopropane (120f) colorless crystals (81%), m.p. 114°-115°C; ν_{max} (KBr) 1645, 1495 cm^{-1}; δ_H (CCl_4) 0.76-1.06 (1H,m,CH_2), 1.35-1.66 (1H,m,CH_2), 1.77-2.20 (2H,m,CH), 2.40(3H,s,SCH_3), 2.44 (3H,s,SCH_3), 5.52 (1H,dd,J=16,9 Hz,=CH), 5.87 (2H,s,CH_2), 6.08 (1H,s,=CH), 6.35 (1H,d,J=16Hz,=C), 6.63 (2H,s,ArH), 6.72 (1H,s,ArH); (Found : C,61.21; H,5.59. $C_{17}H_{18}O_3S_2$ requires C,61.05; H, 5.42%).

1-[2-Bis(methylthio)methyleneacetyl]-2-(4-phenyl-1,3-butadienyl)cyclopropane (120g) colorless crystals (81%),m.p. 123°-124°C; ν_{max} (KBr) 1633, 1490 cm^{-1}; δ_H ($CDCl_3$) 0.85-1.10 (1H,m,CH_2), 1.45-1.70 (1H,m,CH_2), 1.78-2.23 (2H,m,CH) 2.44 (6H,s,SCH_3), 5.37 (1H,dd,J=16,9 Hz,=CH), 6.14 (1H,s, =CH), 6.27-6.84 (3H,m,=CH), 7.10-7.40 (5H,m,ArH); (Found :

C,68.46; H,6.53. $C_{18}H_{20}OS_2$ requires C,68.31; H,6.37%); m/z 316 (M^+, 10%), 301(26), 269(10).

1-[2-Bis(methylthio)methyleneacetyl]-2-[4-(4-methoxyphenyl)-1,3-butadienyl]cyclopropane (120h) colorless crystals (83%); m.p. 103°-104°C; ν_{max} (KBr) 1615, 1470 cm^{-1}, δ_H ($CDCl_3$) 0.74-1.16 (1H,m,CH_2), 1.38-1.72 (1H,m,CH_2), 1.81-2.20 (2H,m,CH), 2.42 (6H,s,SCH_3), 3.76 (3H,s,OCH_3), 5.38 (1H,dd,J=16,9 Hz,=CH), 6.18 (1H,s,=CH), 6.27-6.63 (3H,m,=CH), 6.83 (2H,d,J=9 Hz,ArH), 7.31 (2H,d,J=9 Hz,ArH) ; (Found : C, 65.98; H,6.56. $C_{19}H_{22}O_2S_2$ requires C, 65.86; H, 6.40%); m/z 346 (M^+,3%), 331(9).

1-[2-Bis(methylthio)methyleneacetyl]-2-(3,4-dihydro-6-methoxy-2-napthyl)cyclopropane (144a) colorless crystals (93%), m.p. 94°-95°C; ν_{max} (KBr) 1637 cm^{-1}; δ_H ($CDCl_3$) 0.77-1.24 (1H,m,CH_2), 1.29-1.53 (1H,m,CH_2), 1.74-2.50 (4H,m,CH_2 and CH),2.30(2H,t,J 6Hz,CH_2), 2.38 (3H,s,SCH_3), 2.43 (3H,s,SCH_3), 2.70 (2H,t,J=6 Hz,CH_2), 3.70 (3H,s,OCH_3), 6.06 (1H,s,=CH), 6.15 (1H,s,=CH), 6.36-6.63 (2H,m,ArH), 6.79 (1H,d,J=9 Hz,ArH); (Found : C, 65.98; H,6.55. $C_{19}H_{22}O_2S_2$ requires C, 65.86; H, 6.40%); m/z 346 ((M^+,21%), 331(30), 299(21).

1-[2-Bis(methylthio)methylenepropanoyl]-2-(3,4-dihydro-6-methoxy-2-napthyl)cyclopropane (144b) colorless crystals (81%), m.p. 67°-68°C; ν_{max} (KBr) 1665 cm^{-1}; δ_H (CCl_4) 1.09-1.36 (1H,m,CH_2), 1.38-1.67 (1H,m,CH_2), 1.96-2.37

(4H,m,CH_2 and CH), 2.08 (3H,s,CH_3), 2.20 (3H,s,SCH_3), 2.29 (3H,s,SCH_3), 2.71 (4H,m,CH_2), 3.70 (3H,s,OCH_3), 6.16 (1H,s,=CH), 6.40-6.67 (2H,m,ArH), 6.85 (1H,d,J=9 Hz, ArH); (Found : C,66.42; H,6.31. $C_{20}H_{24}O_2S_2$ requires C,66.28; H, 6.15%); m/z 360 (M^+, 11%), 345(41), 313(15).

Cyclopropanation of (99a) with Cyanotrimethylammonium methylide:[34] **1-[2-Bis(methylthio)methyleneacetyl]-2-cyano-3-(4-methoxyphenyl) cyclopropane (110):-** A suspension of cyanotrimethylammoniummethyl iodide (4g, 15 mmol), sodium hydride (1g, 20 mmol, 50% suspension) in dry THF (70 ml) was stirred at room temperature for 2 h. A solution of (1a) (2.8g, 10 mmol) in dry THF (100 ml) was added slowly (15 min.) and the reaction mixture was stirred at 40°C for 12h. It was quenched with water, exracted with $CHCl_3$ (3x60ml) the combined extract was dried (Na_2SO_4) and evaporated to give crude (110) which was purified by column chromatography over silica gel (EtOAc/hexane, 1:20); (92%), m.p. 141-142°C (Found: C, 60.35; H,5.4; N, 4.25. $C_{16}H_{17}O_2S_2N$ requires C, 60.16; H,5.37; N,4.38%); ν_{max} 2237(CN), 1630 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 2.27-2.42 (1H,m,CH), 2.50 (6H,s,SMe), 2.65-2.92 (2H,m,CH), 3.79 (3H,s,OMe), 6.23 (1H,s,=CH), 6.85 (2H,d, *J* 9Hz,ArH), 7.22 (2H, d, *J* 9Hz, ArH).

Cyclization of Cyclopropyl Ketones (100,120,144) in the Presence of Phosphoric acid/Formic acid: General Procedures:- A solution of appropriate cyclopropyl ketones (10 mmol) in HCO_2H (98%, 30 ml) and H_3PO_4 (85%,10

ml) was either stirred at room temperature (102a,b, 121a, 135) (2 h) or heated at 80°C (103a-e,105g-o, 122. 127, 129a-c.139, 147, 150) (2 h). The reaction mixture was poured over satd. $NaHCO_3$ solution (300 ml), extracted with $CHCl_3$, the organic layer was washed with water (2x100 mol), dried (Na_2SO_4) and evaporated to give crude products as viscous residues which were purified by column chromatography over silica gel using EtOAc/hexane (1:20) as eluent.

3-(4-Methoxyphenyl)cyclopentanone (103a) (71%), m.p. 48-49°C; lit.[14] 47-48°C; ν_{max}(KBr) 1737 (CO) cm^{-1}; δ_H(CCl_4) 1.61-2.50 (6H,m,CH_2), 2.08-3.47 (1H,m,ArCH), 3.75 (3H,s, OMe), 6.67 (2H,d,*J* 9Hz, ArH), 7.09 (2H,d,*J* 9Hz, ArH); (Found: C, 75.9; H, 7.55. $C_{12}H_{14}O_2$ requires C, 75.81; H, 7.42%); m/z 190 (M^+, 100%).

3-(3,4-Dimethoxyphenyl)cyclopentanone (103b) (68%), m.p. 73-74°C; ν_{max}(KBr) 1735 (CO) cm^{-1}; δ_H($CDCl_3$) 1.72-2.78 (6H,m,CH_2), 3.09-3.44 (1H,m,ArCH), 3.82 (3H,s,OMe), 3.87 (3H,s,OMe), 6.79 (3H,brs,ArH); (Found: C,70.95; H,7.45. $C_{13}H_{16}O_3$ requires C, 70.93; H, 7.33%); m/z 220(M^+, 100%), 189 (17).

3-(3,4,5-Trimethoxyphenyl)cyclopentanone (103c) (72%), oil ν_{max}(neat) 1737(CO) cm^{-1}; δ_H(CCl_4) 1.74-2.47 (6H, m, CH_2), 2.88-3.33 (1H,m,ArCH), 3.69 (3H,s,OMe), 3.79 (6H,s, OMe), 6.37 (2H,s,ArH); (Found: C, 67.3; H,7.35.$C_{14}H_{18}O_4$ requires C, 67.22; H, 7.25%); m/z 250 (M^+,100%), 235 (49).

3-(3,4-Methylenedioxyphenyl)cyclopentanone (103d) (71%), oil; ν_{max}(neat) 1738(CO) cm^{-1}; $\delta_H(CCl_4)$ 1.57-2.65 (6H,m, CH_2), 2.94-3.39 (1H,m,ArCH), 5.80 (2H,s,CH_2), 6.43-6.74 (3H,m,ArH); (Found:C,70.7; H, 5.8. $C_{12}H_{12}O_3$ requires C, 70.61; H, 5.93%); m/z 204 (M^+, 95%), 175(19).

3-(4-Methylphenyl)cyclopentanone (103e) (37%), oil; ν_{max} (neat)1740 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.76-2.72 (6H,m,CH_2), 2.31 (3H,s,Me), 3.01-3.51 (1H,m,ArCH), 6.92-7.16 (4H,m,ArH); (Found: C,82.85; H,8.20. $C_{12}H_{14}O$ requires C,82.72; H, 8.10%); m/z 174 (M^+, 73%).

(E)-S-Methyl-5-(4-Methoxyphenyl)-2-oxocyclopentane carbothioate (102a) (73%), m.p.105-106°C; ν_{max}(KBr) 1750(CO), 1665(CO) cm^{-1}; $\delta_H(CDCl_3)$ 1.86-2.70 (4H,m,CH_2), 2.30 (3H,s,SMe), 3.42 (1H,d,*J* 11Hz,COCH), 3.66-4.01 (1H,m, ArCH), 3.80 (3H,s,OMe), 6.82 (2H,d, *J* 9Hz,ArH), 7.20 (2H,d, J 9Hz, ArH); (Found: C, 63.75; H, 6.30. $C_{14}H_{16}O_3S$ requires C, 63.61; H, 6.10%); m/z 264 (M^+, 10%), 217 (27), 189 (100).

(E)-S-Methyl-5-(3,4-dimethoxyphenyl)-2-oxocyclopentane-carbothioate (102b) (68%), oil; ν_{max}(neat) 1747 (CO), 1663 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.57-2.71 (4H,m,CH_2), 2.16 (3H,s,SMe), 3.34 (1H,d,*J* 11Hz,COCH), 3.00-4.03 (1H,m,ArCH), 3.64 (3H, s,OMe), 3.69 (3H,s,OMe), 6.50-6.84 (3H,m,ArH); (Found: C, 61.35; H, 6.30. $C_{15}H_{18}O_4S$ requires C, 61.20; H, 6.16%); m/z 294 (M^+, 23%), 247(15), 219 (100).

(E)-S-Methyl-5-(4-methoxyphenyl)-1-methyl-2-oxocyclo-pentane carbothioate (105g) (81%), m.p. 75-76°C; ν_{max}(KBr) 1738 (CO), 1665 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 0.98 (3H,s,Me), 1.90-2.61 (4H,m,CH_2), 2.30 (3H,s,SMe), 3.72 (3H,s,OMe), 4.05 (1H,dt, *J* 7Hz,ArCH), 6.76 (2H,d, *J* 9Hz, ArH), 7.00 (2H,d, *J* 9Hz,ArH); (Found: C, 64.85; H, 6.65. $C_{15}H_{18}O_3S$ requires C, 64.75; H, 6.52%); m/z 278 (M^+, 4%), 232 (69), 203(100).

(E)-S-Methyl-1-ethyl-5-(4-methoxyphenyl)-2-oxocyclopentane carbothioate (105h) (74%), oil; ν_{max}(neat) 1740 (CO), 1667 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.66 (3H,t,*J* 7Hz,Me), 1.51 (2H,q,*J* 7Hz,CH_2), 1.90-2.71 (4H,m,CH_2), 2.30 (3H,s,SMe), 3.71 (3H,s,OMe), 4.03 (1H,t-like, *J* 7Hz,ArCH), 6.78 (2H,d, *J* 9Hz, ArH), 7.05 (2H,d, *J* 9Hz,ArH); (Found: C, 65.85; H, 6.8. $C_{16}H_{20}O_3S$ requires C, 65.76; H, 65.90%); m/z 292 (M^+, 2%), 245 (22), 217(100).

(E)-*(Z)*-S-Methyl-1-(*n*-butyl)-5-(4-methoxyphenyl)-2-oxo-cyclopentane carbothioate (105i) (*E/Z*, 4:1),(60%), oil; ν_{max}(neat) 1731 (CO), 1670 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.54-1.55 (9H,m,Me and CH_2); 1.77 (0.6H,s,*Z*-SMe), 2.30 (2.4H,s,*E*-SMe), 1.60-2.57 (4H,m,CH_2), 3.49 (0.2H,dd-like, *J* 7Hz, *Z*-ArCH), 3.69 (3H,s,OMe), 4.02 (0.8H, t-like,*J* 7Hz,*E*-ArCH), 6.51-7.20 (4H,m,ArH); (Found: C, 67.6; H,7.7. $C_{18}H_{24}O_3S$ requires C, 67.50; H, 7.56%); m/z 321(M^++1,33%), 273(61), 245(81).

(E), *(Z)*-S-Methyl-1-(*n*-heptyl)-5-(4-methoxyphenyl)-2-oxocyclo-pentane carbothioate (105j) (*E/Z*; 3:2), (59%),

oil; ν_{max}(neat) 1740 (CO), 1670 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.60-1.62 (13H,m,Me and CH_2), 1.62-2.61 (6H,m,CH_2), 1.78 (1.2H, s,*Z*-SMe), 2.29 (1.8H,s,*E*-SMe), 3.52 (0.4H,dd like, *J* 7Hz, *Z*-ArCH), 3.78 (3H, s, OMe), 4.03 (0.6H,t, *J* 7Hz,*E*-ArCH), 6.62-7.30 (4H,m,ArH); (Found: C, 69.7; H, 8.5. $C_{21}H_{30}O_3S$ requires C, 69.61; H, 8.35%); m/z 362 (M^+, 16%), 315(56), 287(100).

***(E)*-S-Methyl-5-(3,4-dimethoxyphenyl)-1-methyl-2-oxocyclopentane carbothioate (105k)** (76%), m.p. 88-89°C; ν_{max}(KBr) 1735 (CO), 1655 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 1.0 (3H,s,Me), 1.99-2.67 (4H,m,CH_2), 2.34 (3H,s,SMe), 3.74 (3H,s,OMe), 3.79 (3H,s,OMe), 4.15 (1H,dd,*J* 7,6Hz,ArCH), 6.58-6.87 (3H,m, ArH); (Found: C,62.4; H, 6.6. $C_{16}H_{20}O_4S$ requires C, 62.34; H, 6.54%); m/z 308 (M^+,14%), 261 (26), 233(100).

***(E)*-S-Methyl-1-methyl-5-(3,4,5-trimethoxyphenyl)-2-oxocyclopentane carbothioate (105l)** (78%), m.p. 104-105°C; ν_{max}(KBr) 1733(CO),1675(CO) cm^{-1}; $\delta_H(CDCl_3)$1.0 (3H,s,Me), 1.96-2.69 (4H,m,CH_2), 2.30 (3H,s,SMe), 3.70 (3H,s,OMe), 3.75 (6H,s,OMe), 4.07 (1H,dd like, merged with OMe,*J*7,6Hz, ArCH), 6.23 (2H,s,ArH); (Found: C, 60.45; H, 6.65. $C_{17}H_{22}O_5S$ requires C, 60.36; H, 6.56%); m/z 338 (M^+, 18%), 291(25), 263(100).

***(E)*-S-Methyl-5-(3,4-methylenedioxyphenyl)-1-methyl-2-oxocyclo-pentane carbothioate (105m)** (77%), oil; ν_{max}(neat) 1747(CO),1662 (CO)cm^{-1}; $\delta_H(CCl_4)$ 0.98 (3H,s,Me), 1.80-2.75 (4H,m,CH_2), 2.32 (3H,s,SMe), 4.11 (1H,dd,*J* 7,6Hz, ArCH), 5.88 (2H,s,CH_2), 6.48-6.74 (3H,m,ArH); (Found: C,61.75; H,

5.65. $C_{15}H_{16}O_4S$ requires C, 61.66; H, 5.52%); m/z 292 (M^+, 10%), 245(17), 217(100).

(E)-S-Methyl-1,3-dimethyl-5-(4-methoxyphenyl)-2-oxocyclopentane carbothioate (105n) (80%), oil; ν_{max}(neat)1740 (CO), 1660(CO) cm^{-1}; $\delta_H(CCl_4)$ 0.90 (3H,s,Me), 1.16 (3H,d, *J* 6Hz,Me), 1.16-2.20 (2H,m,CH_2), 2.13-2.69 (1H,m,3-CH), 2.27 (3H,s,SMe), 3.70 (3H,s,OMe) 4.05 (1H,dd like,*J* 12,5 Hz,ArCH), 6.73 (2H,d, *J* 9Hz, ArH), 7.01 (2H,d, *J* 9Hz, ArH); (Found: C,65.85; H, 7.0. $C_{16}H_{20}O_3S$ requires C, 65.76; H, 6.90%); m/z 292 (M^+, 14%), 245 (68), 217(100).

(E)-S-Methyl-5-(3,4-dimethoxyphenyl)-1,3-dimethyl-2-oxocyclopentane carbothioate (105o) (79%),m.p. 104-105°C; ν_{max} (KBr) 1736 (CO), 1657 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 0.95 (3H,s,1-Me), 1.25 (3H,d,*J* 7Hz,3-Me), 1.60-1.93 (1H,m,CH_2), 2.23-2.78 (2H,m,CH_2 and 3-CH), 2.33 (3H,s,SMe), 3.77 (3H,s,OMe) 3.81 (3H,s,OMe), 4.12 (1H,dd, *J* 12,5Hz,ArCH), 6.55-6.85 (3H,m,ArH); (Found: C, 63.45; H, 6.95. $C_{17}H_{22}O_4S$ requires C, 63.36; H, 6.88%); m/z 322 (M^+, 31%), 275(33), 247(100).

S-Methyl-4-cyano-5-(4-methoxyphenyl)-2-oxocyclopentane carbothioate (111) (81%), oil; ν_{max}(neat) 2220 (CN), 1740 (CO), 1695 (CO)cm^{-1}; $\delta_H(CCl_4)$ 2.20-2.42 (2H,m,CH_2), 2.30 (3H,s, SMe), 2.60-3.02 (2H,m,CH), 3.66-3.92 (1H,m, merged with OMe, ArCH), 3.73 (3H,s, OMe), 6.80 (2H,d,*J* 9Hz, ArH), 7.17 (2H,d,*J* 9Hz, ArH); (Found: C, 62.4; H, 5.35; N, 4.95. $C_{15}H_{15}O_3NS$ requires C, 62.27; H, 5.23; N, 4.85%); m/z 289(M^+,5%), 173(100).

(E)-S-Methyl-5-styryl-2-oxo-cyclopentane carbothioate (121a) colorless crystals (77%); m.p. 110°-111°C; ν_{max} (KBr) 1753, 1678, 1630 cm^{-1}; δ_H ($CDCl_3$) 1.64-2.58 (4H,m, CH), 2.33 (3H,s,SCH_3), 3.25 (1H,d, J=12 Hz,CH) 3.38-3.67 (1H,m,CH), 6.12 (1H,dd,J=16,7 Hz,=CH), 6.52 (1H,d,J= 16 Hz,=CH), 7.18-7.49 (5H,m,ArH); (Found : C, 69.34; H, 6.32. $C_{15}H_{16}O_2S$ requires C, 69.20; H, 6.20%); m/z 260 (M^+, 7%), 213(20), 185(67).

(E/Z)-S-Methyl-5-[4-phenyl-1,3-butadienyl]-2-oxocyclopentane carbothioate (135) (E/Z, 4:1) colorless crystals (76%); m.p. 108°-109°C, ν_{max}(KBr) 1750, 1675 cm^{-1}; δ_H ($CDCl_3$) 1.14-2.91 (4H,m,CH_2), 2.26 (0.6H,s,SCH_3), 2.35 (2.4H,s,SCH_3), 2.55-2.80 (0.4H,m,CH), 3.12 (0.8H,d,J=12 Hz,CH), 3.24-3.66 (0.8H,m,CH), 5.69 (1H,dd,J=16,7 Hz,=CH), 6.00-6.83 (3H,m,=CH), 7.03-7.44 (5H,m,ArH); (Found: C, 71.42; H, 6.47. $C_{17}H_{18}O_2S$ requires C, 71.30; H, 6.33%); m/z 286 (M^+,23%), 239(11), 211(100).

S-Methyl-1-methyl-5-styryl-2-oxocyclopentane carbothioate (121b) light yellow oil (71%); ν_{max}(neat) 1740, 1660 cm^{-1}; δ_H(CCl_4) 0.92-2.58 (4H,m,CH_2), 1.24 (3H,s,CH_3), 2.32 (3H,s,SCH_3), 3.39-3.85 (1H,m,CH), 6.03 (1H,dd,J= 16,8 Hz, =CH), 6.46 (1H,d,J=16 Hz,=CH), 7.03-7.52 (5H,m,ArH); (Found: C,70.18; H, 6.46. $C_{16}H_{18}O_2S$ requires C,70.04; H,6.61%); m/z 274(M^+,3%),227(16),200(74).

3-Styryl cyclopentanone (122) colorless oil (67%); ν_{max} (neat) 1743 cm^{-1}; δ_H (CCl_4) 1.17-3.07 (6H,m,CH_2), 2.68-3.15 (1H,m,=CH), 6.14 (1H,dd,J=16,7 Hz, =CH), 6.41 (1H,d,

J=16 Hz,=CH), 7.02-7.40 (5H,m,ArH); (Found: C, 83.96; H, 7.71. $C_{13}13H_{14}O$ requires C, 83.83; H, 6.61%); m/z 186 (M^+,68%).

3-[2-(methylthio)-2-phenylethyl]cyclopentanone (129a) yellow oil (81%); ν_{max} (neat) 1740 cm^{-1}; δ_H (CCl_4) 1.17-2.58 (9H,m,CH and CH_2), 1.76 (3H,s,SCH_3), 3.62 (1H, brt,J=7 Hz,ArCH), 7.03-7.49 (5H,m,ArH); (Found : C, 71.83; 7.86. $C_{14}H_{18}OS$ requires C,71.75; H,7.74%); m/z 234 (M^+,33%),187(85).

3-[2-(methylthio)-2-(3,4-dimethoxyphenyl)ethyl]cyclopentanone (129b) yellow oil (78%); ν_{max} (neat) 1743 cm^{-1}; δ_H (CCl_4) 1.19-2.37 (9H,m,CH and CH_2), 1.78 (3H,s,SCH_3), 3.6 (1H,brt,J=7 Hz,ArCH), 3.76 (3H,s,OCH_3), 3.80 (3H,s,OCH_3), 6.60-6.89 (3H,m,ArH); (Found : C,65.36; H,7.65. $C_{16}H_{22}O_3S$ requires C,65.27; H,7.53%); m/z 294 (M^+,17%), 247(74).

3-[2-(methylthio)-2-(3,4-methylenedioxyphenyl)ethyl]cyclopentanone (129c) yellow oil (73%); ν_{max} (neat) 1755 cm^{-1}; δ_H (CCl_4) 1.18-2.85 (9H,m,CH and CH_2), 1.80 (3H,s,SCH_3), 3.26 (0.33H,t,J=6 Hz,CH), 3.57 (0.67H, t, J=6 Hz,CH), 5.82 (0.66H,s,CH_2), 5.93 (1.34H,s,CH_2), 6.44-6.86 (3H,m,ArH); (Found : C,64.86; H,6.61. $C_{15}H_{18}O_3S$ requires C, 64.72; H,6.52%).

6-(4-Methoxyphenyl)bicyclo[2,2,1]-hept-2-one (127) colorless oil (60%); ν_{max}(KBr) 1748 cm^{-1}; δ_H (CCl_4) 1.48-2.27 (5H,m,CH_2 and CH), 2.02-2.56 (2H,m,CH_2), 2.72 (1H, brs,CH), 2.98 (1H,t,J=8 Hz,ArCH), 3.70 (3H,s,OCH_3),6.69

(2H,d,J=9 Hz,ArH), 7.05 (2H,d,J=9 Hz,ArH); (Found : C, 77.91; H,7.63. $C_{14}H_{16}O_2$ requires C,77.74; H,7.46%); m/z 216 (M^+, 96%).

7-(4-Methoxyphenyl)-4,7,3a,7a-tetrahydro-1-indanone (139): colorless viscous oil (62%); ν_{max} 1743 cm^{-1}; δ_H (250 MHz) $CCDCl_3$) 1.68-2.05 (3H,m,CH_2), 2.06-2.38 (4H,m,CH_2 and CH), 2.56 (1H,m,CH), 3.80 (3H,s,OCH_3), 3.82 (1H,m,ArCH), 5.67 (1H,brd,J 11Hz,=CH), 5.81 (1H,ddd,J 11,4,2Hz,=CH), 6.83 (2H,d,J 9Hz,ArH), 7.15 (2H,d,J 9Hz,ArH); δ_C ($CDCl_3$) 25.55, 26.12, 33.45 (CH_2), 29.67, 37.19 (CH) 55.14 (Ar), 56.43 (OCH_3), 113.81, 128.63 (ArCH), 125.54, 128.11 (=CH), 137.79 (C-1',Ar), 158.01 (C-4',Ar) 217.14 (C=O); (Found : C, 79.44; H, 7.56. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.49%).

***(E)*-S-Methyl-5-(3,4-dihydro-6-methoxy-2-napthyl)-1-methyl-2-oxocyclopantane carbothioate (150)** colorless crystals ($CHCl_3$/hexane) (83%); m.p. 118°-119°C; ν_{max} (KBr) 1738, 1660 cm^{-1}; δ_H ($CDCl_3$) 1.20 (3H,s,CH_3), 1.41-2.88 (8H,m, CH_2), 2.32 (3H,s,SCH_3), 3.65 (1H,brt,J=6 Hz,CH), 3.77 (3H,s,OCH_3), 6.22 (1H,s,=CH), 6.51-6.77 (2H,m,ArH), 6.95 (1H,d,J=9 Hz,ArH); (Found : C,69.21; H,6.86. $C_{19}H_{22}O_3S$ requires C,69.06; H, 6.71%); m/z 330 (M^+, 28%), 283(22), 255(100).

Bicyclo[2.2.1](1,2,3,4-tetrahydronapthyl)[2,1-e]hept-2-one (147) colorless oil (62%); ν_{max} (neat) 1750, 1610 cm^{-1}; δ_H (CCl_4) 1.18-2.95 (12H,m,CH_2 and CH), 3.70 (3H,s,OCH_3), 6.44-6.90 (2H,m,arom); 7.11 (1H,d,J=9 Hz,ArH); (Found :

C,79.48; H,7.65. $C_{16}H_{18}O_2$ requires C,79.31; H,7.49%); m/z 242 (M^+,100%).

Demethylthiocarbonylation of 2-oxocarbothioates (105): General Procedure:- A suspension of105(1 mmol), W-2 Raney Nickel (ca. 15-20 times by weight)in benzene (10 ml) was stirred under N_2 atmosphere for 6 h. The reaction mixture was filtered, washed with hot benzene and the combined filtrate were evaporated to give crude cyclopentanones (5a-c) which were purified by column chromatography over silica-gel using EtOAc/hexane (1:20) as eluent.

2-Methyl-3-(4-methoxyphenyl)cyclopentanone (106a) (87%), oil; ν_{max} 1737 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.63 (3H,d,*J* 7Hz,Me), 1.72-2.44 (5H,m,CH_2 and CH), 3.06-3.50 (1H, m,ArCH), 3.61 (3H,s,OMe), 6.60-7.08 (4H,m,ArH); (Found: C, 76.55; H, 7.8 $C_{13}H_{16}O_2$ requires C, 76.48; H, 7.90%); m/z 204 (M^+, 95%).

2-(*n*-Butyl)-3-(4-methoxyphenyl)cyclopentanone (106b) (78%), oil; ν_{max}(neat) 1743 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.60-1.62 (9H,m,CH_2 and Me), 1.73-2.88 (5H,m,CH_2 and CH), 3.14-3.53 (1H,m,ArCH),3.70 (3H,s,OMe), 6.60-7.18 (4H,m,ArH); (Found: C, 78.15; H, 9.1. $C_{16}H_{22}O_2$ requires C, 78.0; H, 9.0%); m/z 246 (M^+, 28%).

2,5-Dimethyl-3-(4-methoxyphenyl)cyclopentanone (106c) (89%), oil; ν_{max}(neat) 1740 (CO) cm^{-1}; $\delta_H(CCl_4)$ 0.31-1.30 (6H,m,Me), 1.45-2.63 (4H,m,CH_2 and CH), 2.80-3.23 (1H,m,ArCH), 3.63 (3H,s,OMe), 6.50-7.42 (4H,m,ArH);

(found: C, 71.9; H, 7.85. $C_{14}H_{18}O_2$ requires C, 71.77; H, 7.74%); m/z 216 (M^+, 52%).

Lewis Acid Catalyzed Cyclization of Cyclopropyl Ketones (100, 120 and 144): General Procedure:- A solution of cyclopropyl ketone (10 mmol) in the indicated solvent (80 ml) was treated with either of the Lewis acid catalysis i.e. $SnCl_4$ (1.5 eqv), TFA (1.5 eqv), $BF_3.Et_2O$ (1.5 eqv) $TiCl_4$ (1.5 eqv) and $AlCl_3$ (1.5 eqv) at the indicated temperature. The reaction mixtures were stirred at the given temperature for the time period given in Tables 1 and 2. It was then poured into cold aqueous sodium hydroxide (5%), extracted with $CHCl_3$ (3x60 ml), the organic layer was washed with water, dried (Na_2SO_4) and evaporated to afford products as viscous residues which were purified by column chromatography over silica gel using EtOAc/hexane (1:20) as eluent.

2-Bis(methylthio)methylene-3-(4-methoxyphenyl)cyclopentanone (107a) oil; ν_{max}(neat) 1695 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.70-2.58 (4H,m,CH_2), 2.21 (3H,s,SMe), 2.42 (3H,s,SMe), 3.73 (3H,s,OMe), 4.27 (1H,m,ArCH), 6.72 (2H,d,*J* 9Hz,ArH), 6.98 (2H,d, *J* 9Hz, ArH); (Found: C,61.3; H, 6.25. $C_{15}H_{18}O_2S_2$ requires C, 61.22; H, 6.17%); m/z 294 (M^+, 38%), 247(100).

2-Bis(methylthio)methylene-3-(3,4-dimethoxyphenyl)cyclopentanone (107b) oil; ν_{max}(neat) 1690 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.60-2.47 (4H,m,CH_2), 2.22 (3H,s,SMe), 2.40 (3H,s,SMe), 3.70 (3H,s,OMe), 3.75 (3H,s,OMe), 4.20 (1H,brt,*J* 7Hz, ArCH), 6.42-6.76 (3H,m,ArH); (Found:C,59.40; H,6.35.

$C_{16}H_{20}O_3S_2$ requires C, 59.26;, 6.22%); m/z 324 (M^+, 84%), 277(100).

2-Bis(methylthio)methylene-3-(3,4,5-trimethoxyphenyl)cyclopenta-none (107c) m.p. 77°C; ν_{max}(KBr) 1685 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 1.78-2.50 (4H,m,CH_2), 2.25 (3H,s,SMe), 2.40 (3H, s,SMe), 3.66 (3H,s,OMe), 3.71 (6H,s,OMe), 4.23 (1H,t,*J* 7Hz ArCH), 6.24 (2H,s,ArH); (Found: C,57.7; H,6.15. $C_{17}H_{22}O_4S_2$ requires C,57.63; H, 6.26%); m/z 354 (M^+, 25%), 307 (19).

1,1-Bis(methylthio)-6-hydroxy-6-phenyl-1-hexen-3-one (109) m.p. 115°C; ν_{max}(KBr) 3440 (OH), 1620(CO) cm^{-1}; $\delta_H(CDCl_3)$ 2.05 (2H,t, *J* 7Hz,CH_2),2.40 (3H,s,SMe), 2.49 (3H,s,SMe), 2.58 (2H, t, *J* 7Hz CH_2CO) 2.71-3.28 (1H,brs, exchangeable with D_2O,OH), 4.71 (1H, t, *J* 7Hz, ArCH), 5.98 (1H,s,=CH) 7.12-7.42 (5H,m,ArH); (Found: C, 59.7; H, 6.55. $C_{14}H_{18}O_2S_2$ requires C, 59.57; H, 6.43%); m/z 264 (M^+ -18,6%), 235 (M^+-47).

1,1-Bis(methylthio)-6-hydroxy-6-(4-methoxyphenyl)-1-hexen-3-one (109b) oil; ν_{max}(neat) 3420 (OH), 1610 (CO) cm^{-1}; $\delta_H(CDCl_3)$ 1.84-2.60 (4H,m,CH_2), 2.36 (3H,s,SMe), 2.40 (3H,s,SMe), 2.60-2.91 (1H,brs,OH, exchangeable with D_2O), 3.73 (3H,s,OMe), 4.58 (1H,t,*J* 6Hz,ArCH), 5.92 (1H,s,=CH), 6.75 (2H,d,*J* 9Hz, ArH), 7.20 (2H,d, *J* 6Hz,ArH); (Found: C, 57.75; H,6.6. $C_{15}H_{20}O_3S_2$ requires C, 57.66; H,6.45%); m/z 294 (M^+-18, 17%).

1,1-Bis(methylthio)-6-hydroxy-6-(3,4,5-trimethoxyphenyl)-1-hexen-3-one (109c) m.p. 140-141°C; ν_{max}(KBr) 3400 (OH),

1658(CO) cm^{-1}; $\delta_H(CDCl_3)$ 2.09 (2H,brq, *J* 6Hz, CH_2), 2.38 (3H,s,SMe), 2.46 (3H,s,SMe), 2.60 (2H,t,*J* 6Hz, CH_2CO), 2.92-3.42 (1H,brs, exchangeable with D_2O, OH), 3.78 (3H,s,OMe), 3.86 (6H,s,OMe), 4.70 (1H,t,*J* 6Hz, ArCH), 6.03 (1H,s,=CH), 6.60 (2H,s,ArH); (Found: C, 54.95; H, 6.65. $C_{17}H_{24}O_5S_2$ requires C, 54.81; H, 6.49); m/z 354 (M^+-18, 41%), 307 (26), 291(20), 259(37).

2-Bis(methylthio)methylene-3-(3,5-dimethyloxy-4-hydroxy-phenyl)-cyclopentanone (107d) oil; ν_{max}(neat) 3550 (OH), 1690 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.80-2.45 (4H,m,CH_2), 2.24 (3H,s,SMe), 2.42 (3H,s,SMe), 3.78 (6H,s,OMe), 4.28 (1H,t,*J* 6Hz, ArCH), 6.23 (2H,s,ArH);(Found: C, 56.6; H, 5.85. $C_{16}H_{20}O_4S_2$ requires C, 56.45;, 5.92%).

1,1-Bis(methylthio)-6-(4-methoxyphenyl)-6-oxo-1-hexen-3-ol (118) oil;ν_{max} (neat) 3420 (OH), 1703 (CO) cm^{-1}; $\delta_H(CCl_4)$ 1.78-2.41 (4H,m,CH_2), 2.16 (3H,s,SMe), 2.22 (3H,s,SMe), 3.73 (3H,s,OMe), 4.01 (1H,dd like, *J* 9,6Hz, CHOH), 5.91 (1H,d,*J* 8Hz,=CH), 6.77 (2H,d,*J* 9Hz,ArH), 7.10 (2H,d,*J* 9Hz, ArH), 10.81 (1H,brs,OH,exchangeable with D_2O); (Found: C, 57.75; H, 6.5. $C_{15}H_{20}O_3S_2$ requires C, 57.66; H, 6.45).

2-Bis(methylthio)methylene-3-styryl-cyclopentanone (131) yellow oil (74%); ν_{max} (neat) 1693 cm^{-1}; δ_H (CCl_4) 1.72 2.63 (4H,m,CH_2), 2.38 (3H,s,SCH_3), 2.44 (3H,s,SCH_3), 3.84 4.08 (1H,m,CH), 6.14-6.50 (2H,m,=CH), 7.08-7.45 (5H,m,ArH) ; (Found : C,66.31; H,6.37. $C_{16}H_{18}OS_2$ requires C,66.17; H,6.25%); m/z 290 (M^+,21%), 243(80).

2-Bis(methylthio)methylene-3-(4-phenyl-1,3-butadienyl) cyclopentanone (132) yellow oil (71%); ν_{max} (neat) 1680 cm^{-1}; δ_H (CCl_4) 2.45-2.51 (4H,m,CH_2), 2.39 (3H,m,SCH_3), 2.43 (3H,m,SCH_3), 3.89 (1H,brt,J=6Hz,ArCH), 5.76 (1H,dd, J=16,6Hz,=CH), 6.07 (1H,d,J=16Hz,=CH), 6.62 (2H,dd,J=16, 6Hz,=CH), 7.08-7.44 (5H,m,ArH); (Found: C,68.44; H,6.46. $C_{18}H_{20}OS_2$ requires C,68.31; H,6.37%); m/z 300 (M^+-16,26%)

2-Bis(methylthio)methylene-3-(3,4-dihydro-6-methoxy-2-napthyl)cyclopentanone (148) yellow oil (82%); ν_{max} (neat) 1690 cm^{-1}; δ_H ($CDCl_3$) 1.58-2.61 (6H,m,CH_2), 2.38 (3H,s, SCH_3), 2.47 (3H,s,SCH_3), 2.80 (2H,t,J=6Hz,CH_2), 3.65-3.98 (1H,m,ArCH), 3.75 (3H,s,SCH_3), 6.0 (1H,s,=CH), 6.55-6.78 (2H,m,ArH), 6.90 (1H,d,J=9Hz,ArH); (Found: C,65.93; H, 6.48. $C_{19}H_{22}O_2S_2$ requres C,65.86; H,6.40%); m/z 330. (M^+-16,26%).

Borontrifluoride Etherate Catalyzed Methanolysis of (107a-b, 148): Methyl 5-aryl-2-oxocyclopentane carboxylate (108a-b, 149): General procedure:- A suspension of the appropriate substrate (1 mmol), $HgCl_2$ (1.1 mmol) in anhydrous methanol (10 ml) was stirred at room temperature (10 min) followed by addition of $BF_3.Et_2O$ (1.5 ml). The reaction mixture was refluxed (3h), cooled, filtered and the filtrate was poured over satd. $NaHCO_3$ solution (50 ml) followed by extraction with $CHCl_3$ (3x30 ml). The combined extracts were washed with water (50 ml), dried (Na_2SO_4) and evaporated to give a viscous residues which on column

chromatography over silica gel (EtOAc/hexane, 1:20) afforded pure esters108.

(E)-Methyl-5-(4-methoxyphenyl)-2-oxocyclopentane carboxylate (108a) (87%), m.p. 84-85°C; ν_{max}(KBr) 1740 (CO) cm^{-1}; δ_H($CDCl_3$) 1.89-2.63 (4H,m,CH_2), 3.25 (1H,d, *J* 12Hz, CH), 3.52-3.96 (1H,m,ArCH), 3.71 (3H,s,OMe), 3.80 (3H,s,OMe), 6.87 (2H,*J* 9Hz, ArH), 7.20 (2H,d, *J* 9Hz, ArH); (Found: C, 67.85; H, 6.6. $C_{14}H_{16}O_4$ requires C, 67.76; H, 6.5%); m/z 248 (M^+, 19%), 216(11), 189 (100).

Methyl 5-(3,4-dimethoxyphenyl)-2-oxocyclopentane carboxylate (108b) (78%), oil; ν_{max}(neat) 1735 (CO) cm^{-1}; δ_H($CDCl_3$) 1.80-2.53 (4H,m,CH_2), 3.30 (1H,d,*J* 12Hz,CH), 3.49-3.82 (1H,m,ArCH), 3.61 (3H,s,OMe), 3.72 (3H,s,OMe), 3.78 (3H,s,OMe), 6.54-6.73 (3H,m,ArH); (Found: C, 64.85; H, 6.45. $C_{15}H_{18}O_5$ requires C, 64.77; H, 6.52%); m/z 278 (M^+, 39%), 246(18).

Methyl,5-(3,4-dihydro-6-methoxy-2-napthyl)-2-oxo-cyclopentane carboxilate (149) (*E:Z*=95:5), colorless oil (78%); ν_{max} (neat) 1730, 1760 cm^{-1}; δ_H ($CDCl_3$) 1.5-1.98 (1H,m,CH_2), 2.03-2.58 (5H,m,CH_2), 2.79 (2H,t, J=8Hz,CH_2), 3.10-3.43 (2H,m,CH), 3.71 (3H,s,OCH_3), 3.75 (3H,s,OCH_3), 6.27 (1H,s,=CH), 6.54-6.81 (2H,m,ArH), 6.91 (1H,d,J=9Hz, ArH); (Found : C,71.81; H,6.63. $C_{18}H_{20}O_4$ requires C,71.98; H,6.71%); m/z 300 (M^+,100%), 269(20), 241(72).

II.5 REFERENCES

1. Wong, H.N.C.; Hon, M.Y.; Tse, C.W.; Yip, Y.C.; Tanko, J.; Hudlicky, T. *Chem.Rev.* 1989, *89*, 165.
2. House, H.O.; Phillips, W.V.; Sayer, T.S.B.; Yau, C.C. *J.Org.Chem.* 1978 *43* 700.
3. Baldwin, J.E. *J.Chem.Soc.Chem.Comm.* 1976 734.
4. Baldwin, J.E.; Cutting, J.; Dupont, W.; Kruse, L.; Silberman, L.; Thomas, R.C. *J.Chem.Soc.Chem.Comm.* 1976, 736.
5. Baldwin, J.E.; Kruse, L.I. *J.Chem.Soc.Chem.Comm.*, 1977, 233.
6. Trost, B.M. *Chem.Soc.Rev.* 1982, *11*, 141.
7. Trost, B.M.; Jingheim, L.N. *J.Am.Chem.Soc.* 1980, *102*, 7910.
8. Trost, B.M.; Runge, T.A. *J.Am.Chem.Soc.*, 1981, *103* 7550.
9. Trost, B.M.; Runge, T.A. *J.Am.Chem.Soc.* 1981, *103*, 7559.
10. Stork, G.; Marx, M. *J.Am.Chem.Soc.*, 1969, *91*, 2371.
11. Stork, G.; Gregson, M. *J.Am.Chem.Soc.*, 1969, *91*, 2373.
12. Stork, G.; Grieco, P.A. *J.Am.Chem.Soc.*, 1969, *91* 2407.
13. Corey, E.J.; Balanson, R.D. *Tetrahedron Lett.* 1973, 3153.
14. Grieco, P.A.; Finkelhor, R.S. *Tetrahedron Lett.* 1974, 527.

15. Berkowitz, W.F.; Ozorio, A.A. *J.Org.Chem.*, 1971, *36*, 3787.
16. Berkowitz, W.F. *J.Org.Chem.*, 1972, *37*, 341.
17. Nakai, T.; Wada, E.; Okawara, M. *Tetrahedron Lett.*, 1975, 1531.
18. Neff, J.R.; Gruetzmacher, R.R.; Nordlander, J.E. *J.Org.Chem.*, 1974, *39*, 3814.
19. Wenkert, E. *Acc.Chem.Res.*, 1980, *13*, 27.
20. Newman, M.S.; Ream, B.C. *J.Org.Chem.*, 1966, *31*, 2175.
21. Murphy, W.S.; Wattanasin, S. *Tetrahedron Lett.* 1980, *21*, 1887.
22. Murphy, W.S.; Wattanasin, S. *Tetrahedron Lett.*, 1980, *21*, 3517.
23. Murphy, W.S.; Wattanasin, S. *J.Chem.Soc.Perkin Trans. I*, 1981, 2920.
24. Murphy, W.S.; Wattanasin, S. *J.Chem.Soc. Perkin Trans I*, 1982, 1029.
25. Murphy, W.S.; Wattanasin, S. *J.Chem.Soc. Perkin Trans I*, 1982, 271.
26. Murphy, W.S.; Wattanasin, S. *J.Chem.Soc.Chem.Comm.* 1980, 262.
27. Murphy, W.S.; Wattanasin, S. *Tetrahedron Lett.*, 1981, *22*, 695.
28. Murphy, W.S.; Wattanasin, S. *J.Chem.Soc.Perkin Trans I*, 1986, 1445.

29. Hantawong, K.; Murphy, W.S.; Russel, N.; Boyd, D.R. *Tetrahedron Lett.* 1984, *25*, 999.

30. Thuillier, A.; Vialle, J. *Bull.Soc.Chim.Fr.* 1962, 2182.

31. Marz, A.; Mark, G. *Angew Chem.Internat.Ed.*, 1973, *12*, 845.

32. Wilds, A.L.; Johnson, T.L. *J.Am.Chem.Soc.* 1945, *67*, 286.

33. Liu, H.J.; Lai, H.K.; Attah-Poku, S.K. *Tetrahedron Lett.*, 1979, *20*, 4121.

34. Bhattacharji, S.; Ila, H.; Junjappa, H. *Synthesis*, 1982, 301.

35. Morris, D.G. *Chem.Soc.Rev.* 1982, *11* 427-431.

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

37. Flautt, T.J.; Erman, W.F. *J.Am.Chem.Soc.*, 1963, *85*, 3212.

38. Reddy, M.P.; Krishnarao, G.S. *Synthesis*, 1980, 815.

CHAPTER III

NUCLEOPHILIC ADDITION TO α-BIS(METHYLTHIO) METHYLENEALKYL CYCLOPROPYL KETONES AND THEIR FURTHER TRANSFORMATIONS

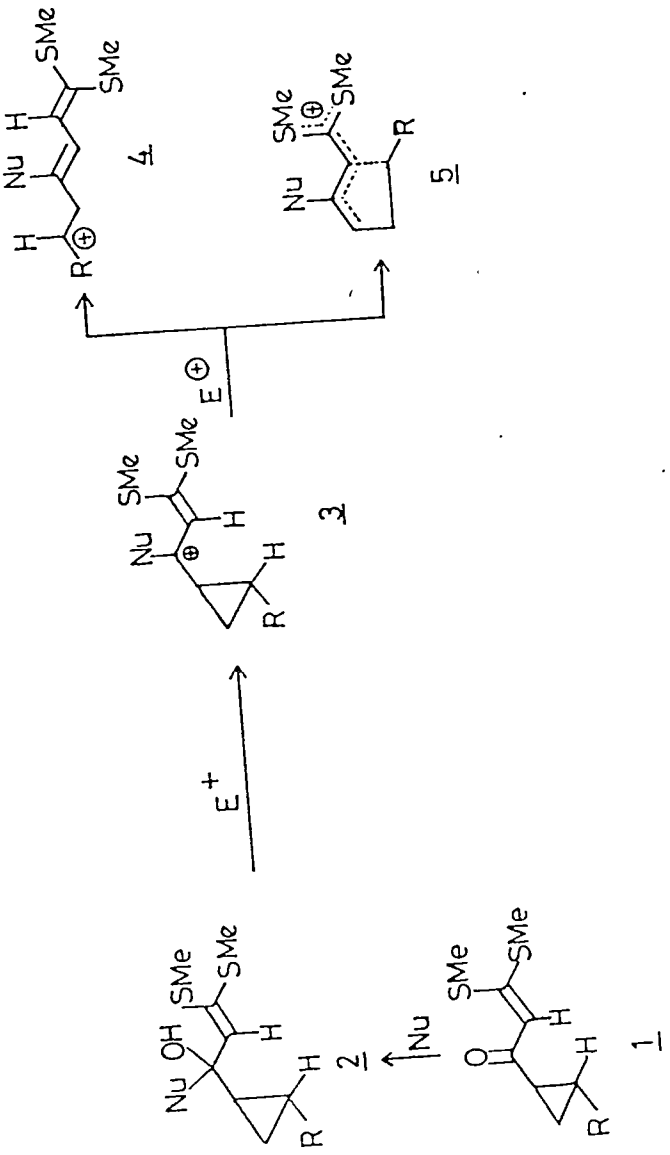
III.1 INTRODUCTION

In the preceding chapter we have described a new methodology based on cationic ring opening of cyclopropyl ketones 1, which afforded cyclopentanones with diverse structural features. It was further considered of interest to study the nucleophilic addition of hydride ions and organometallic reagents to these ketones since, the resulting carbinols 2, on subsequent Lewis acid treatment should afford cyclopropyl carbinyl cation 3 and the chemistry of cyclopropyl carbinyl cations and thier ring

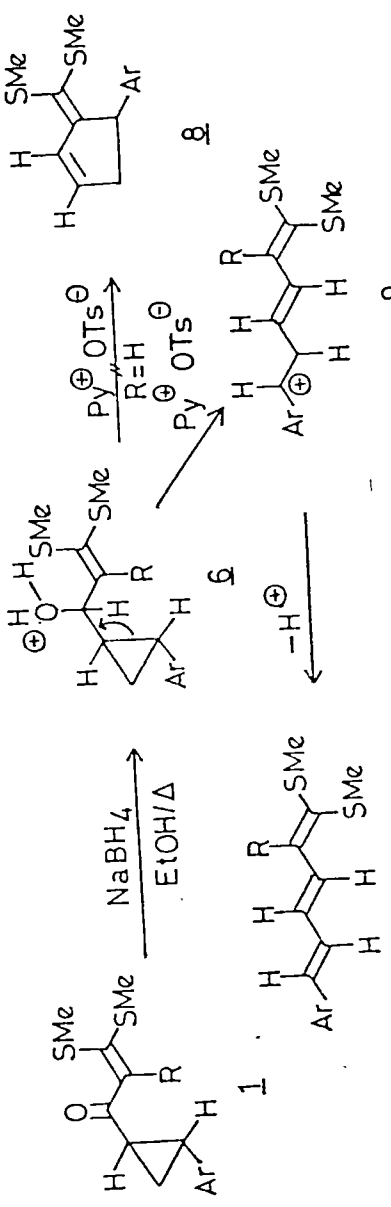
closure reactions are well documentated[1-5]. Thus, the cation 3 obtained from 2 may undergo ring opening to give an open chain hexadienyl cation 4 or it may as well rearrange through π-participation of bis(methylthio)-methylene double bond to cyclopentene derivatives (Scheme 1). In the present chapter we have described the results of our preliminary studies of nucleophilic addition of hydride as well as carbon nucleophiles to cyclopropanes 1 and their further transformations.

III.2 RESULTS AND DISCUSSION

When the ketene 1a was reacted with sodium borohydride in refluxing ethanol (2 hr), the carbinol 6a was obtained in nearly quantitative yield through 1,2-hydride addition. The attempted rearrangement of 6a in the presence of various protic and Lewis acids did not afford any clear cut product. However, 6a was refluxed with pyridinium tosylate in CCl_4, the product isolated was characterized as 1,1-bis(methylthio)-6-(4-methoxyphenyl)-1,3,5-hexatriene 7a (89%) and no trace of the corresponding cyclopentene derivative 8a was detected from the reaction mixture. The structure of triene 7a was confirmed on the basis of its analytical and spectral data. Thus, it was analyzed for $C_{15}H_{18}OS_2$ and its IR (neat) spectrum showed high intensity bands at 1500, 1600 and 1662 cm^{-1} due to $\nu_{C=C}$ vibrations. Its ^1H NMR (CCl_4) spectrum showed three sharp singlets at δ2.16 (3H), 2.21 (3H) and 3.61 (3H) due to two methylthio groups and a methoxy group respectively,


SMe
SMe
H
Nu
H
R⊕
4
SMe
SMe
Nu
R
5
E⊕
SMe
SMe
Nu
H
R
H
3
E+
Nu OH
SMe
SMe
H
R
H
2
Nu
O
SMe
SMe
H
R
H
1

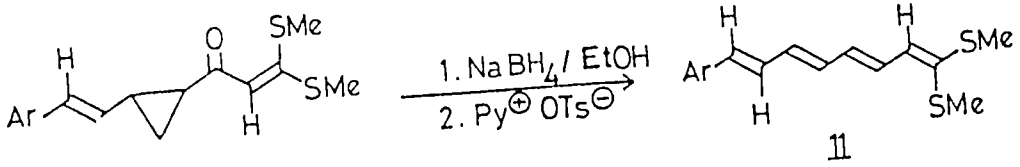
Scheme - 1



7 a, Ar = 4-MeOC$_6$H$_4$; R = H
b, Ar = C$_6$H$_5$; R = H
c, Ar = 3,4-(MeO)$_2$C$_6$H$_3$; R = H
d, Ar = 3,4-methylenedioxy C$_6$H$_3$, R = H
e, Ar = 2-ClC$_6$H$_4$; R = H
f, Ar = C$_6$H$_5$; R = Me

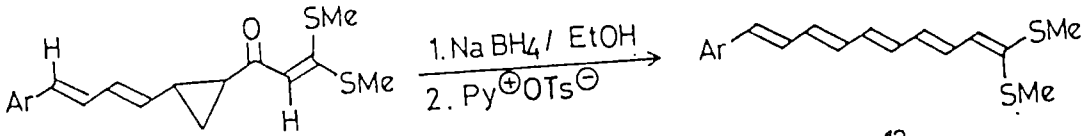
Scheme - 2

which shows the presence of only one stereoisomer. The aromatic protons appeared as A_2B_2 doublet at δ6.67 (2H,d,J=9 Hz) and 7.19 (2H,d,J=9 Hz), while the five olefinic protons were present as multiplet between δ5.94-6.53. The other substituted cyclopropyl ketones 1b-f similarly afforded the acyclic hexatriene 7b-f (78-87%) under identical conditions. Their stuctures were confirmed by analytical and spectral data (experimental). However, our attempts to isolate the corresponding cyclopentene derivatives 8 in any of the reactions were not successful. The trienes 7a-f are apparently formed through the loss of proton from the hexadienyl cation 9, formed by ring opening of carbinol 6 under the experimental conditions. When styrylcyclopropyl ketones 10a-d were subjected to similar treatment with sodium borohydride followed by pyridinium tosylate, the corresponding octatetraenes 11a-d were obtained in good yields.The structural assignment was confirmed by their analytical and spectral data which are descrived in the experimental section. Here again, formation of only one stereoisomer was observed as confirmed from their ^1H NMR spectra. The corresponding aryl butadienylcyclopropyl ketones 12a,b similarly afforded the decapentanenes 13a,b as yellow crystalline solids (87%-91%). The structures of 13a,b were confirmed with the help of spectral and analytical data which are described in the experimental section and the formation of only one stereoisomer (probably *trans*) was observed (Scheme 3).



10 11

a Ar = C_6H_5
b Ar = 4-$MeOC_6H_4$
c Ar = 4-MeC_6H_4
d Ar = 3,4-methylenedioxy C_6H_3

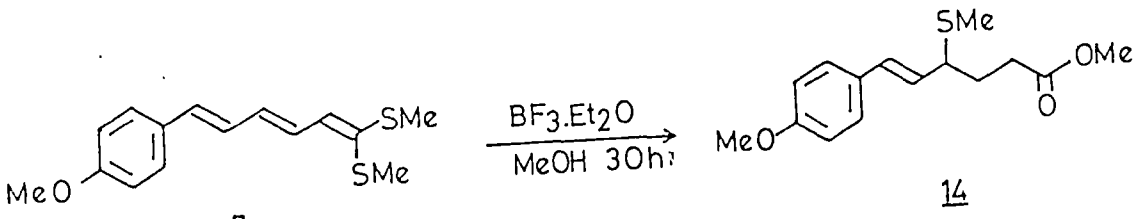


12 13

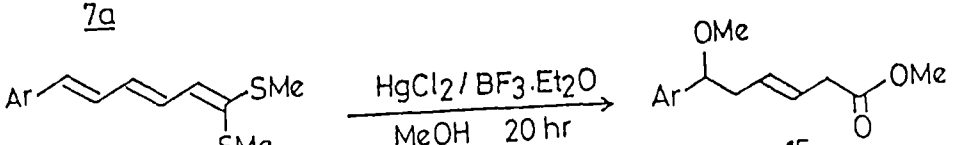
a , Ar = C_6H_5
b , Ar = 4-$MeOC_6H_4$

Scheme-3

The polyenes 7, 11 and 13 were subjected to solvolysis under a variety of conditions with a view to obtain β, γ-unsaturated esters. However, the solvolysis studies were complicated by the formation of several side products 14-16 as shown in the Scheme 4. The desired esters could be obtained by carrying out the solvolysis in the presence of $BF_3.Et_2O/HgCl_2$ in methanol at room temperature under controlled conditions. Thus, the hexatrienes 7a-d afforded 6-aryl-3,4-hexadienoates 18a-d in (67-84%) overall yields on methanolysis under described conditions (Scheme 5). The structures of 18a-d were confirmed with the help of their spectral and analytical data. Thus, 18a was analyzed for $C_{14}H_{16}O_3$ (232) and showed molecular ion peak at m/z 232 (M^+,100%) in its mass spectrum. Its IR (neat) spectrum exhibited absorption band at 1735 cm^{-1} due to unconjugated ester carbonyl group, while other significant bands appeared at 1515 and 1610 cm^{-1}. Similarly, its ^1H NMR (CCl_4) spectrum showed doublet at δ2.98 (J=7 Hz) due to two methylene protons besides two singlets at δ3.52 (3H) and 3.65 (3H) which were attributed to two methoxy groups. The four aromatic protons appeared as two doublets at δ6.68 (2H,J=9 Hz) and 7.14 (2H,J=9 Hz). However, the olefinic protons appeared as multiplet between δ5.37-6.54 (4H). The sharp singlets for various protons in the ^1H NMR spectrum of 18a further supported the formation of only one stereoisomer. The methanolysis of octatetraenes 11b-d and decapentaene 13a similarly afforded the corresponding



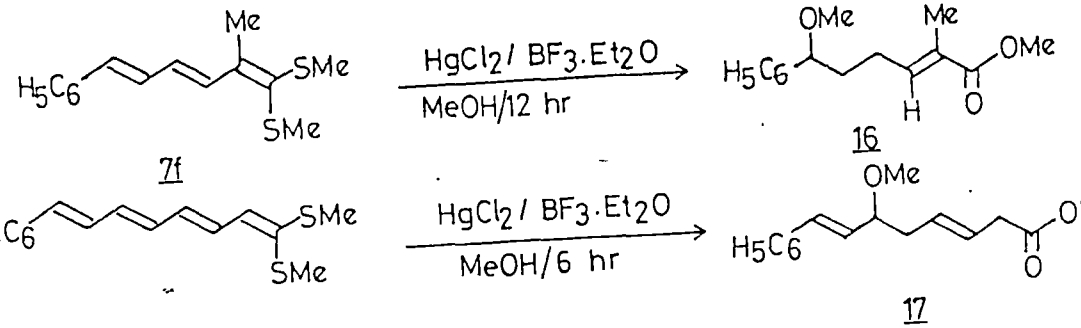
7a 14



7b 15

Ar = 3,4-methylene dioxy C_6H_3

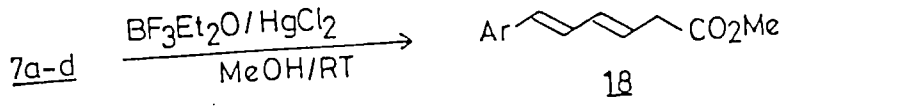
Ar = 2-ClC_6H_4



7f 16

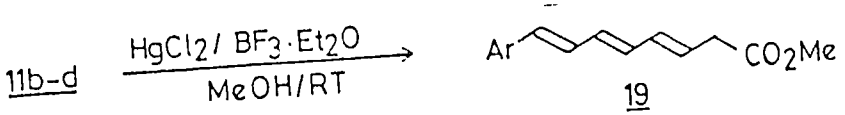
11a 17

Scheme-4



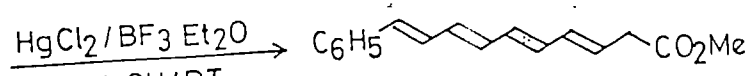
18

a Ar = 4-$MeOC_6H_4$
b Ar = C_6H_5
c Ar = 2,3-$(MeO)_2C_6H_3$
d Ar = 2,3-methylenedioxy C_6H_3



19

a Ar = 4-$MeOC_6H_4$
b Ar = 3,4-methylenedioxy C_6H_3
c Ar = 4-MeC_6H_4

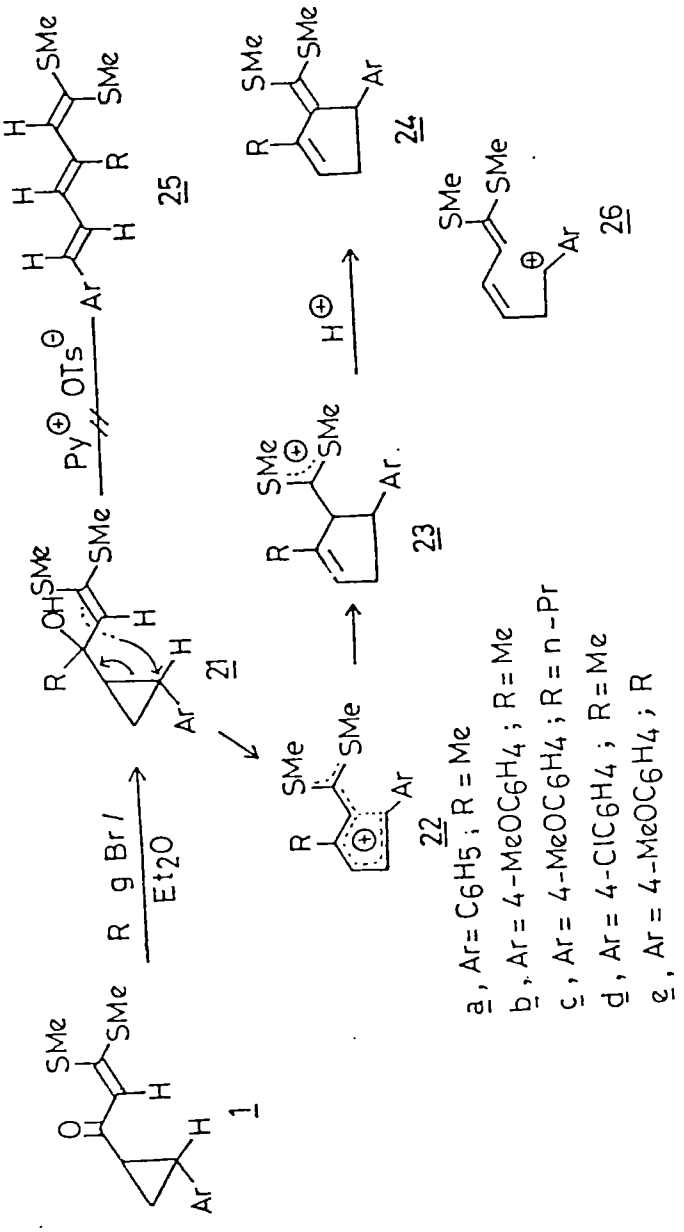


20

Scheme-5

8-aryl-3,5,7-octatrienoates 19a-c and 10-phenyl-3,5,7,9-decatetraenoate 20 in good yields. The spectral and analytical data of 19a-c and 20a were in confirmity with the assigned structure and showed the formation of only one stereoisomer (see experimental).

The addition of alkyl and aryl Grignard reagent to 1 was next investigated. Thus 1a underwent facile 1,2-nucleophilic addition to the carbonyl group with methylmagnesium iodide to afford carbinol 21a. However, when 21a was subjected to ring opening in the presence of pyridinium tosylate the expected 1,1-bis(methylthio)-3-methyl-6-(4-methoxyphenyl)-1,3,5-hexatriene 25a was not formed. The product isolated (87%) was characterized as 3-bis(methylthio)methylene-2-methyl-4-(4-methoxyphenyl) cyclopentene 24a on the basis of its spectral and analytical data. Thus, 24a was analyzed for $C_{16}H_{20}OS_2$ and exhibited molecular ion peak at m/z 292 (78%) in its mass spectrum. Its IR (neat) spectrum showed bands at 1240, 1504, 1604, 1661(m), 1686(m) cm^{-1}. The final confirmation of the structure of 24a was obtained from its ^1H NMR(CCl_4) spectrum, which exhibited three singlets at δ2.00 (3H), 2.23 (3H) and 3.73 (3H) due to two methylthio and methoxy groups respectively. The corresponding α-methyl group appeared as broad doublet at δ2.29 (3H,J=3 Hz) due to allylic coupling with the olefinic proton. The signals due to benzylic methine and olefinic protons appeared as double doublet (J = 7,9 Hz) and broad singlet at δ 4.30 (1H) and 6.0 (1H) respectively. The multiplets

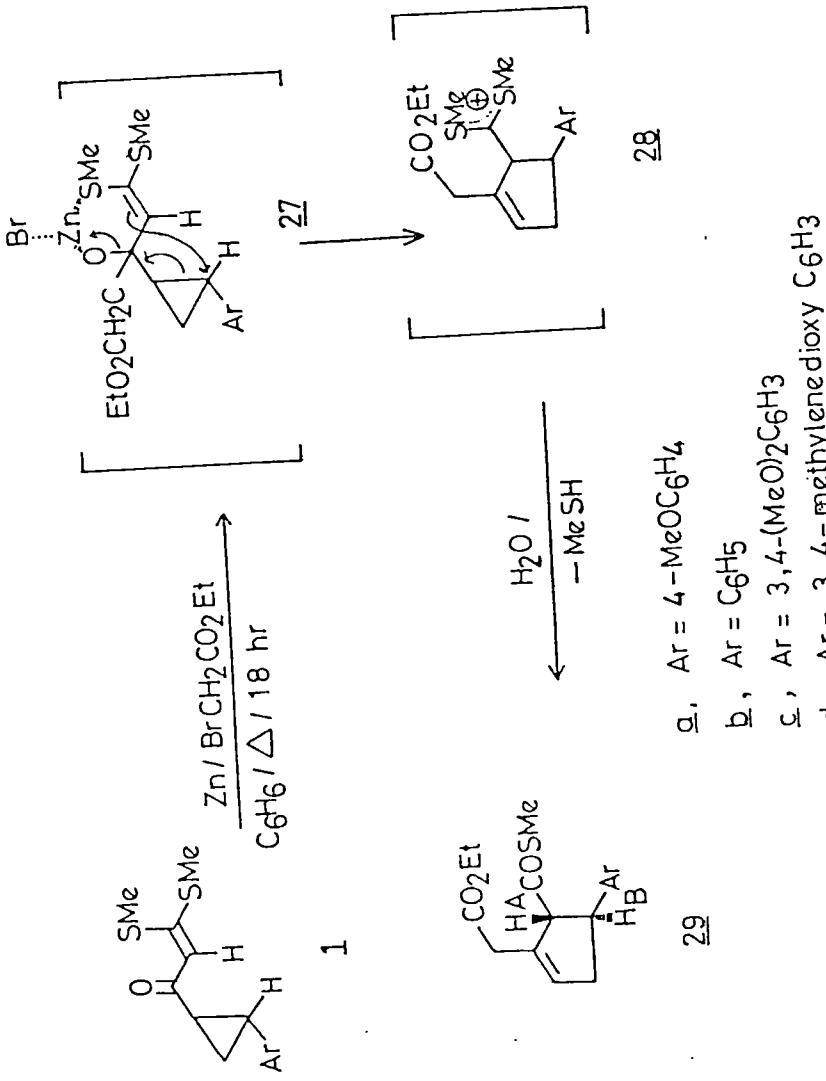


a, Ar= C_6H_5 ; R = Me
b, Ar = 4-$MeOC_6H_4$; R = Me
c, Ar = 4-$MeOC_6H_4$; R = n-Pr
d, Ar = 4-ClC_6H_4 ; R = Me
e, Ar = 4-$MeOC_6H_4$; R

Scheme-6

between δ 1.08-3.07 (2H) an A_2B_2 doublet at δ6.82 (2H) and 7.17 (2H) were assigned to two ring methylene and four aromatic protons respectively. The cyclopentene **24a** is evidently formed by *concerted* ring opening and π-participation of bis(methylthio)methylene double bond with the incipiant cyclopropyl carbinyl cation (intermediate **22**, Scheme 5). Our attempts to isolate trienes **25** under a variety of Lewis acid conditions were however not successful. Interestingly, the corresponding phenylcyclopropyl ketone **1b** also underwent a facile nucleophilic addition with methylmagnesium iodide and subsequent ring opening afforded the cyclopentene derivative **24b** in 78% yield. This observation is important in view of the failure of **1b** to undergo ring opening and π -participation with bis(methylthio)methylene double bond to afford 3-phenyl cyclopentanone on treatment with either H_3PO_4/HCOOH (1:3) or stannic chloride[6] (Chapter II). These results account for a mechanism involving *concerted* ring closure for the formation of **24** from **21**, rather than involving stepwise mechanism through a free benzyl cation **26**. Addition of propylmagnesium bromide to **1a** under similar conditions also afforded the corresponding 2-(*n*-propyl)cyclopentene derivative **24c** in 84% yield (Scheme 6).

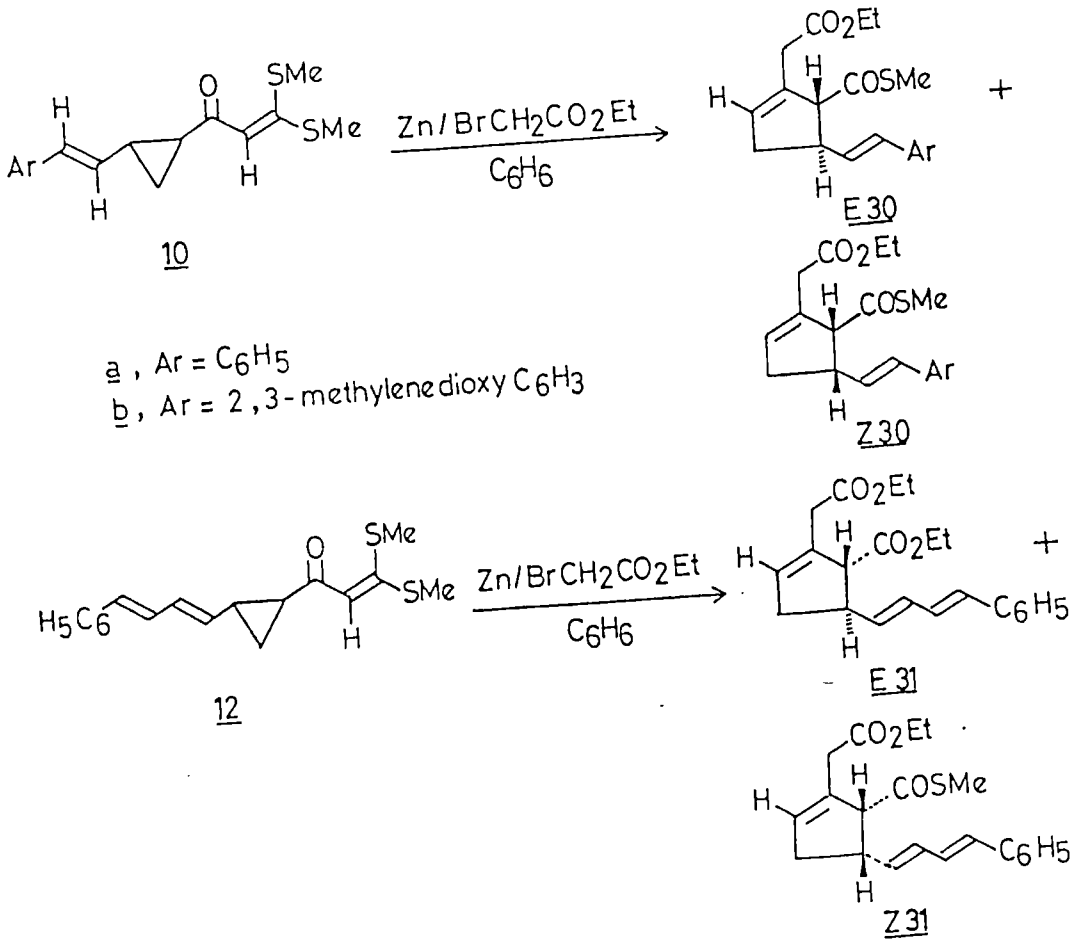
When **1a** was reacted with ethyl zincbromoacetate under Reformatsky reaction conditions, the reaction mixture on work up (10% H_2SO_4) yielded a product characterized as 2-


Zn / BrCH2CO2Et
C6H6 / Δ / 18 hr
1
27
28
H2O /
– MeSH
29
a, Ar = 4-MeOC6H4
b, Ar = C6H5
c, Ar = 3,4-(MeO)2C6H3
d, Ar = 3,4-methylenedioxy C6H3

Scheme-7

carboethoxymethyl cyclopentene-3-carbothioate 29a (81%). The spectral and analytical data of 29a was in full confirmity with the assigned structure. The signal of two methine protons at δ3.49-3.62 (1H,m,H_B) and 3.74-3.92 (1H,m,H_A) which accounts for *E*-stereochemistry at 3,4-carbon atoms. However, the final confirmation of the stereochemistry is being under investigations from its high resolution ^1H and ^{13}C NMR spectra. The other substituted cyclopentenes 30a,d and 31 were similarly obtained in 78 and 83% yields respectively. Apparently the zincnolate 27 undergoes *concerted* ring opening and hydrolysis through the intermediate carbonium ion 28 to afford the corresponding cyclopentene derivative 29. The mechanism was further supported by the isolation of the corresponding 4-phenyl derivative 29b from phenyl cyclopropyl ketone 1b (Scheme 7).

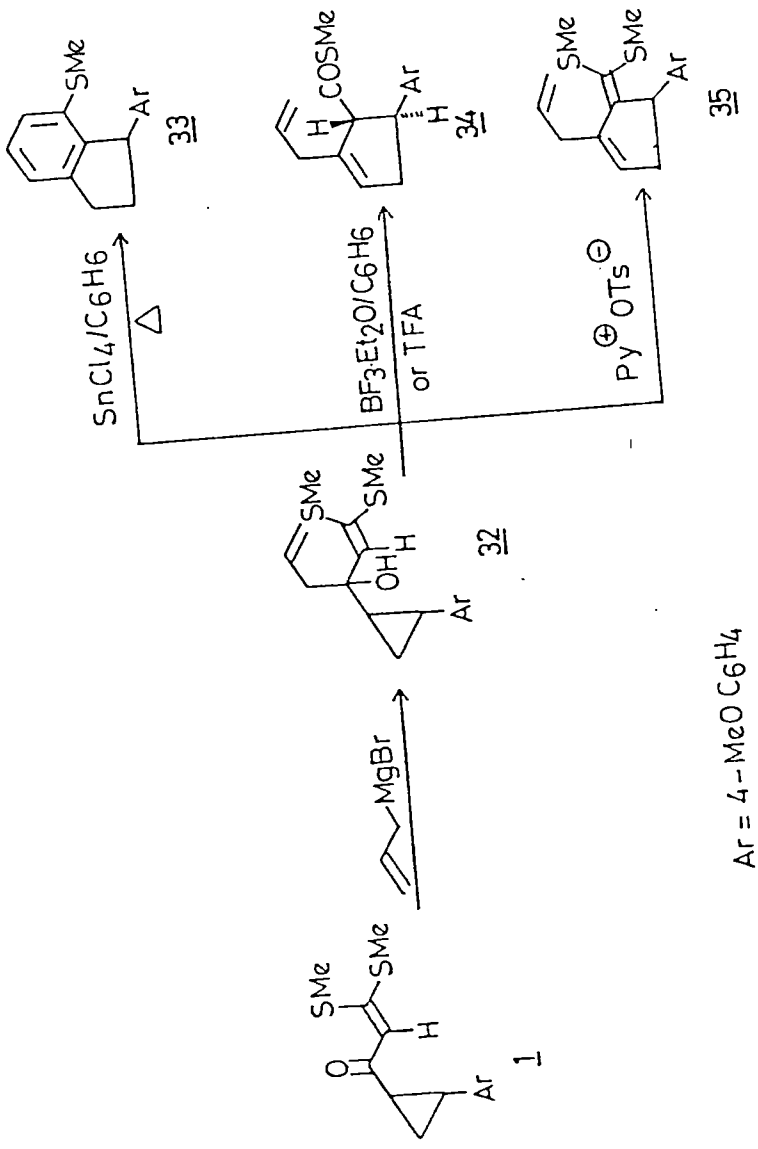
The styrylcyclopropyl ketone 10a also underwent a facile Reformatsky reaction and ring expansion with ethyl zincbromoacetate to afford 4-styrylcyclopentene-3-carbothioates 30a, which was found to be a mixture of *E* and *Z* isomers. Thus, the signals for methylthio group in *Z* - isomer (δ2.17) then in *E*-isomer (δ 2.27) appeared due to shielding by *cis* styryl double bond. The corresponding methylenedioxystyryl cyclopropane 10d gave styrylcarbothioate 30d in 73% yield as *E:Z* mixture (9:1). The reaction was equally sucessful with the higher 4-arylbutadienyl homolog 12 which afforded the respective 4-phenylbutadienyl cyclopropane-3-carbothioate 31


SMe
O
SMe
H
Ar
H
H
Zn/BrCH2CO2Et
C6H6
CO2Et
H
COSMe
H
Ar
H
+
E 30
CO2Et
H
COSMe
Ar
H
Z 30
10
a , Ar = C6H5
b , Ar = 2 ,3- methylenedioxy C6H3
SMe
O
SMe
H5C6
H
Zn/BrCH2CO2Et
C6H6
CO2Et
H
CO2Et
H
+
C6H5
H
E 31
CO2Et
H
COSMe
H
C6H5
H
Z 31
12

Scheme - 8

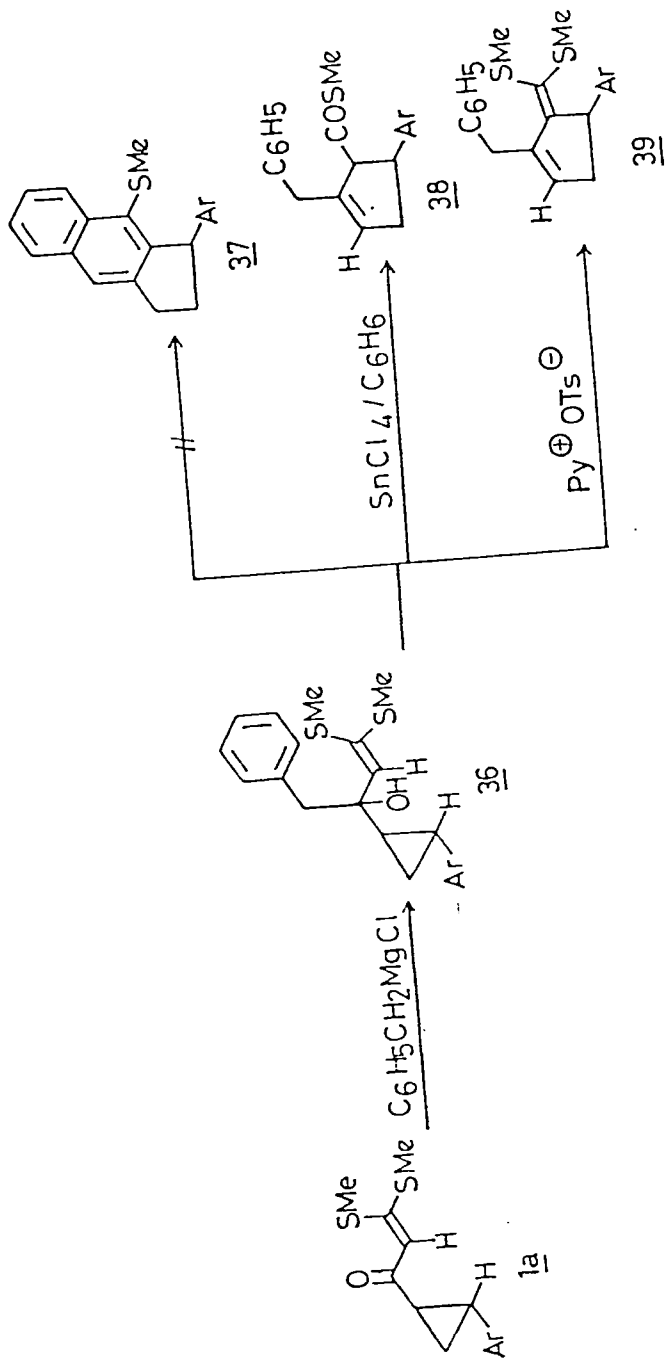
(*E:Z*,66:33) in 76% yield (Scheme 8). The structures of all the cyclopentenes 30 and 31 were confirmed with the help of spectral and analytical data (which are described in the experimental section).

The addition of allylmagnesium bromide to 1a was next investigated to explore the one pot synthesis of 1-aryl indane 33 through concurrent formation of benzene and cyclopentene ring through intramolecular cyclization and cycloaromatization of carbinol intermediate 32. The reaction proceeded in expected manner and the carbinol 32 was obtained in nearly quantitative yield on treatment with allylmagnesium bromide with 1a. When the carbinol 32 was subjected to simultaneous ring opening and cycloaromatization in the presence of stannic chloride in benzene, the desired 1-aryl-7-methylthio indane 33 was obtained in 61% yield. The structure of 33 was established with the help of spectral and analytical data.(see experimental) However, when the cyclization of 32 was attempted in the presence of other Lewis or protic acids like BF_3Et_2O or TFA, the product isolated was characterized as 2-allyl-4-(4-methoxyphenyl) cyclopentene carbothioate 34. The product 34 was found to be *E*-stereoisomer on the basis of the its ^1H NMR spectrum (experimental). Similarly when the carbinol 32 was subjected to cyclization in the presence of pyridinium tosylate, the corresponding 2-allyl-3-bis(methylthio) methylene cyclopentene 35 was obtained in 79% yield

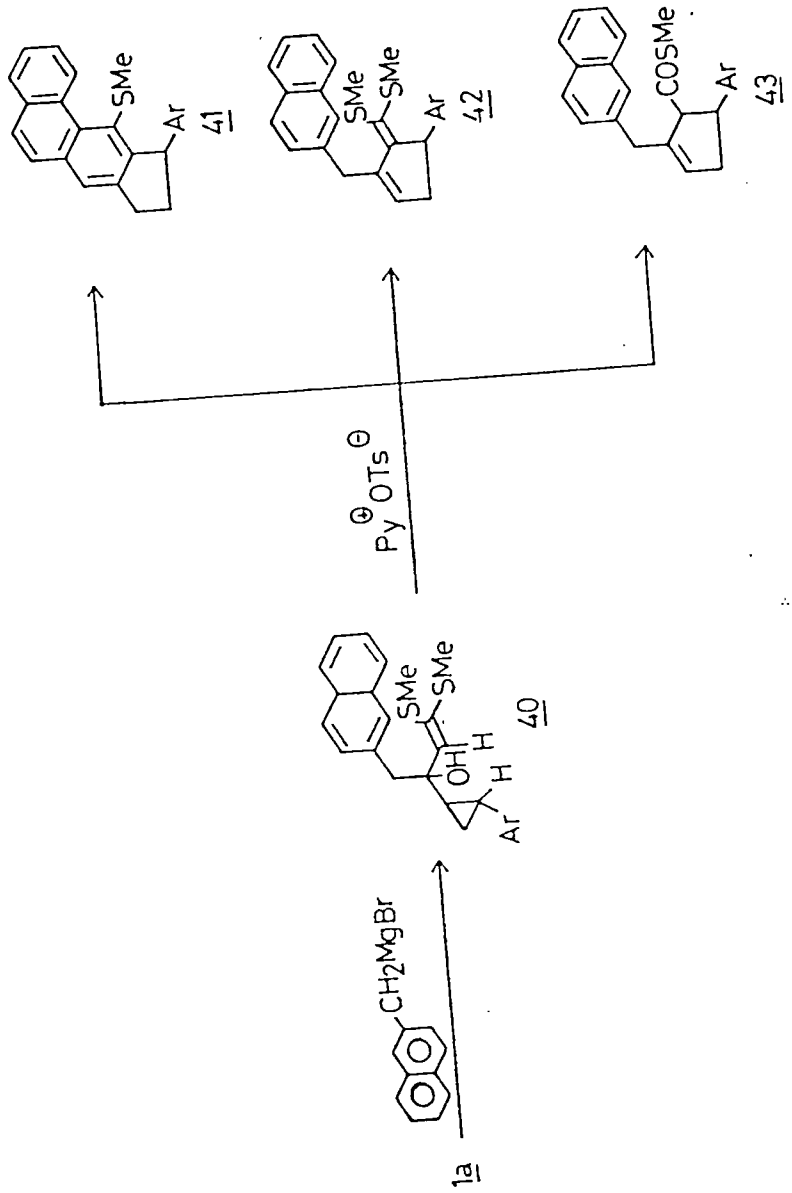


Ar = 4-MeO C_6H_4

Scheme-9


SMe
Ar
37
C6H5
COSMe
Ar
H
38
C6H5
SMe
SMe
Ar
H
39
SnCl4/C6H6
Py⊕ OTs⊖
SMe
SMe
OH
H
H
Ar
36
C6H5CH2MgCl
SMe
SMe
O
H
H
Ar
1a

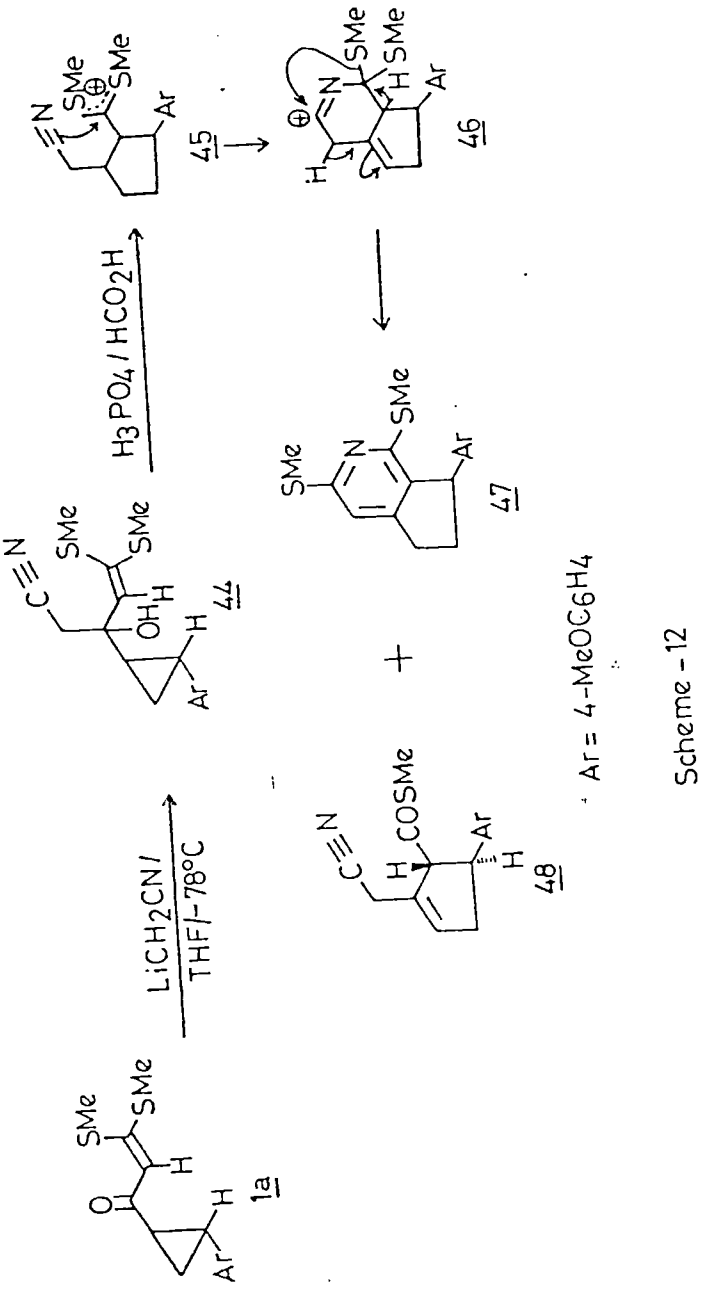
Scheme-10


1a
CH2MgBr
40
SMe
SMe
OH
H
H
Ar
Py⊖OTs⊖
41
SMe
Ar
42
SMe
SMe
Ar
43
COSMe
Ar

Scheme-11

(Scheme 9). Formation of all three products 33, 34, and 35 could be rationalized through a intermediate carbocation formed by cyclopropyl ring opening and π-participation of bis(methylthio)methylene double bond with incipiant carbonium ion. The subsequent π-participation of allyl double bond followed by elimination of methyl mercaptan and cycloaromatization gives indane 33, while hydrolysis or deprotonation affords the thioaster 34 or cyclopentene 35 respectively. Similar cycloaromatization of 1a with either benzyl or 2-napthyl magnesium chloride under identical conditions however did not afford the desired annilated napthelene 37 or phenanthrene 41 derivatives respectively. The products obtained by the treatment of carbinol 36 (from benzylmagnesium chloride) with various Lewis acids were found to be either 2-bis(methylthio)methylene cyclopentene 39 or the corresponding carbothioate 38 (Scheme10). Similarly the carbinol 40 obtained by addition of 2-napthylmagnesium chloride to 1a afforded 2-(2-napthylmethyl)cyclopentene-3-carbothioate 43 in 38% yield (Scheme 11). The structures of the products 39, 40 and 43 were confirmed with the help of their spectral and analytical data (experimental). The mechanism of formation of these products are similar to those described in Scheme 9.

The cyclopropyl ketone 1a was reacted with lithioacetonitrile with a view to study the behaviour of intermediate carbinol 44 with various protic and Lewis acids. Thus, the treatment of 44 with Lewis acids like

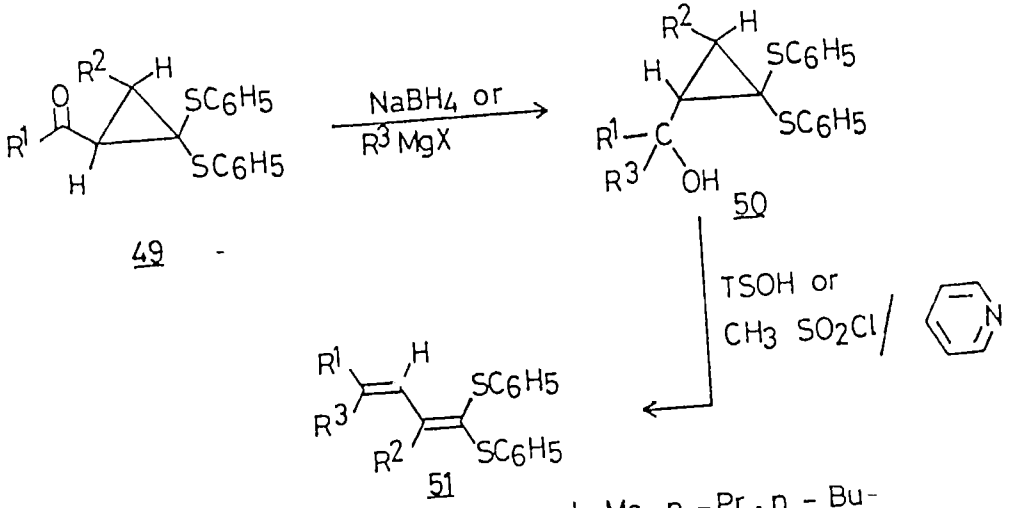

SMe
SMe
H
O
Ar
H
1a
LiCH2CN/
THF/-78°C
N
C
SMe
SMe
OH
H
Ar
H
44
H3PO4 / HCO2H
45
46
47
+
N
C
H
COSMe
Ar
H
48
Ar = 4-MeOC6H4

Scheme - 12

stannic chloride, $BF_3.Et_2O$ and TFA did not afford any clear cut product. However, when **44** was subjected to cyclization in the presence of H_3PO_4/HCOOH mixture (1:3) the workup of the reaction mixture afforded two products which were characterized as 2-(cyanomethyl)cyclopentene-3-carbothioate **48** (32%) and 3,4-cyclopentenopyridine **47** (63%). The mechanism of formation of **47** is similar to those described earlier from our laboratory[7] involving an intramolecular Ritter reaction and 1,3-methylthio shift in the intermediate carbocation **46**. The spectral and analytical data of **47** and **48** were in confirmity with the assigned structures (experimental).

III.3 CONCLUSION

From the above studies it was found that the carbinol formed by hydride addition undergoes ring cleavage and proton loss to give acyclic trienes or their higher enyl analogues. A similar kind of studies have also been described by Kulinkovich and coworkers[8] in the ring opening of cyclopropyl carbinols **50** to give the dienes **51** (Scheme 13). However, the carbinol obtained by addition of various carbon nucleophiles when subjected to electrophilic cyclopropyl ring opening affords the corresponding cyclopentene derivatives instead of acyclic polyenes. These results can be rationalized in terms of the conformation of intermediate carbocations **52** and **54** (Scheme 14). Thus when R=H, the carbocation **52** prefers to

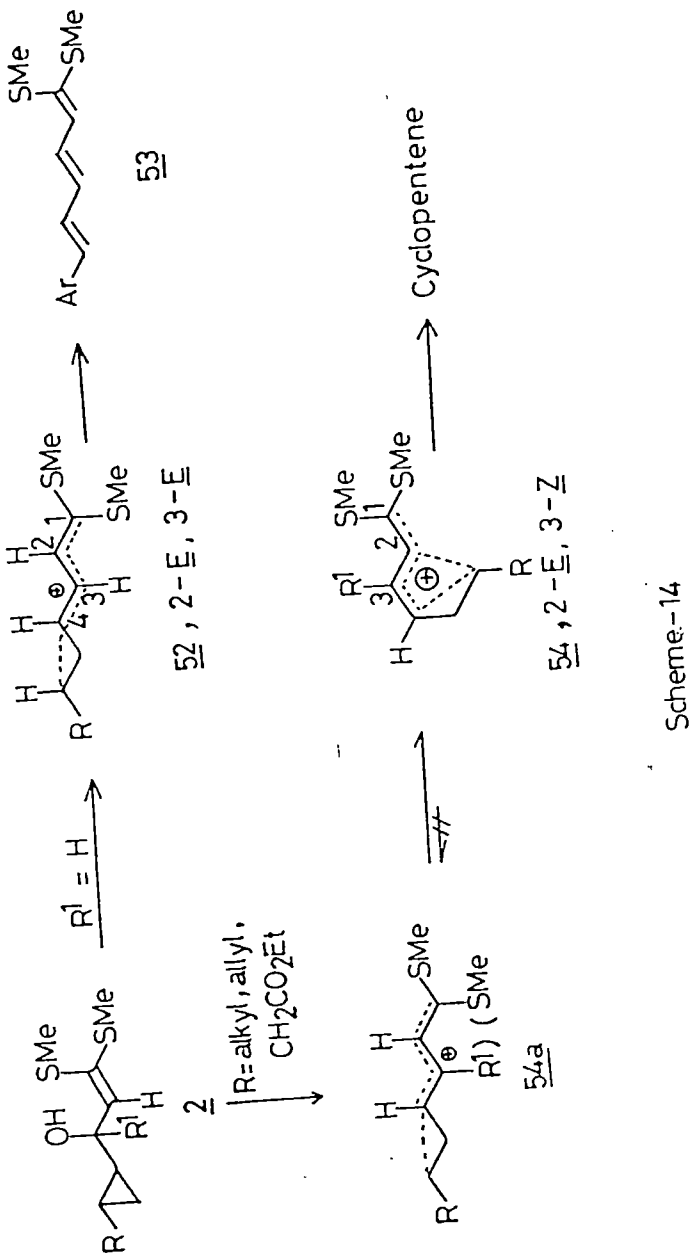


49 50 51

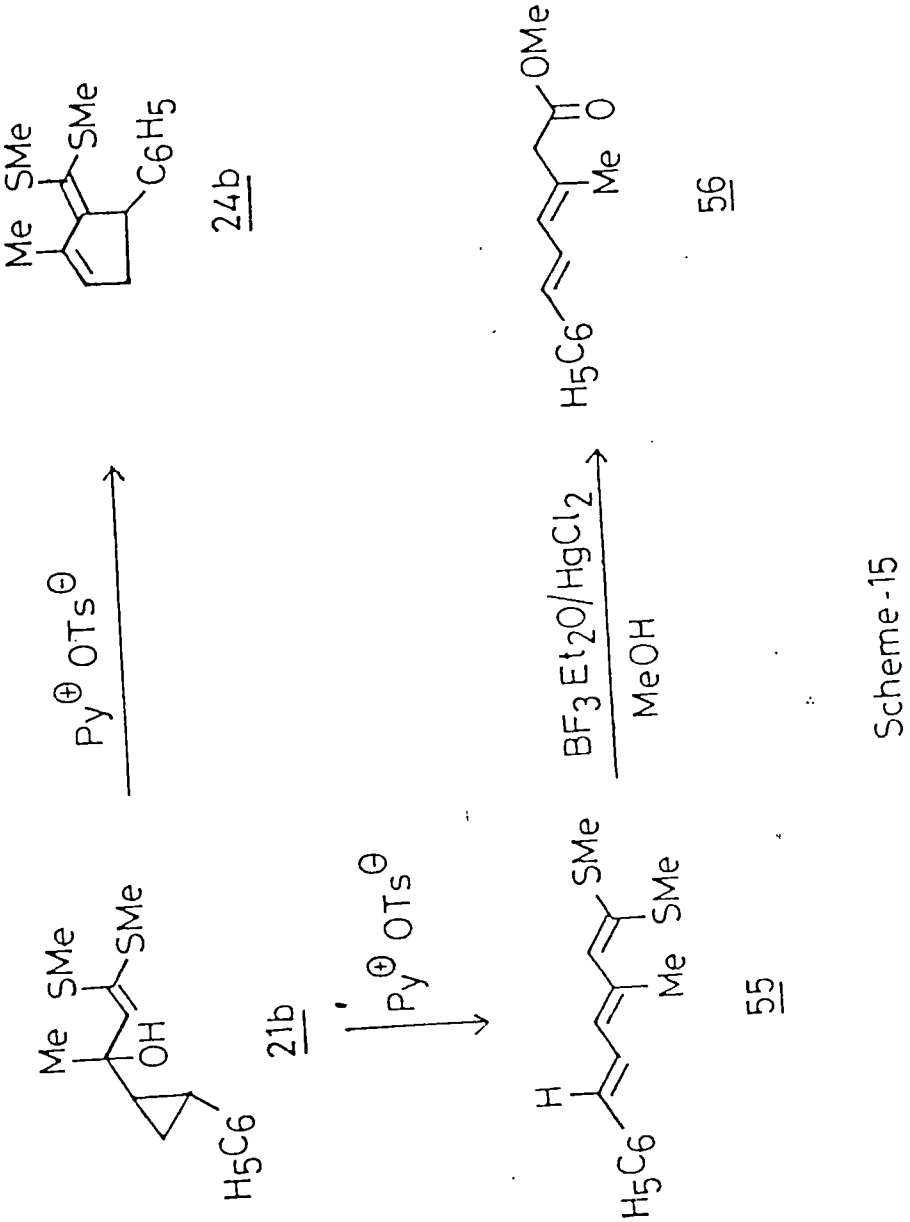
R^1 = substituted aryl, Me, n-Pr, n-Bu-

R^2 = H, Me, Ph, R^3 = H, Me, Ph

Scheme-13


SMe
SMe
Ar
53
R¹ = H
2
R=alkyl, allyl,
CH2CO2Et
52, 2-E, 3-E
54, 2-E, 3-Z
Cyclopentene
54a

Scheme-14


Me
SMe
SMe
C6H5
24b
Py⊕ OTs⊖
Me
SMe
SMe
OH
H5C6
21b
Py⊕ OTs⊖
H
SMe
Me
SMe
H5C6
55
BF3 Et2O/HgCl2
MeOH
OMe
O
Me
H5C6
56

Scheme-15

have *2E, 3E* conformation and undergoes proton loss to give triene. However, when R = alkyl or other carbon substituent the carbocation exists in *2E, 3Z* conformation resulting in favourable π-participation of bis(methylthio) methylene double bond with incipient benzyl carboniumion 54 to give various cyclopentene derivatives. Further studies are needed to fully rationalize these results. The formation of cyclopentene derivative 24b from the ring opening of unsubstituted phenylcyclopropyl carbinol 21b (Scheme 6) deserves further investigation to understand the mechanism of formation of cyclopentene ring in the light of our earlier results of ring opening of aryl cyclopropyl ketones[6] (Chapter II). The solvolysis of polyenes provides a novel route to hitherto unreported β, -unsaturated polyene esters. It is pertinent to note that 3-methyl-6-phenyl-3,5-hexadienoate 56 is the intermediate in the synthesis of antibiotic. However our attempts to synthesize triene 53 through treatment of carbinol 21b with various Lewis acids were not successful and in all the cases the corresponding cyclopentene 24b was obtained (Scheme 13). Our future studies are aimed at obtaining these trienes under different modified conditions.

III.4 Experimental

General

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were run either as KBr discs or neat film

on a Perkin-Elmer 297 spectrometer ^{1}H NMR, spectra were recorded on Varian EM-390 (90 MHz) spectrometer and chemical shift values are expressed as δ (ppm) down field from tetramethyl silane (TMS), as internal standard. The mass spectra were recorded on Jeol JMS D-300 instrument. Elemental analysis were carried out on a Heraeus CHN-O-RAPID instrument.

Starting Materials

The commercial samples of acetone, ethylmethyl, ketone, benzaldehyde, anisaldehyde, 3,4-dimethoxy benzaldehyde, 3,4 methylenedioxy benzaldehyde, and cinnamaldehyde were purified before use, while 4-methylcinnamaldehyde, 4-methoxycinnamaldehyde, 3,4-methylenedioxycinnamaldehyde and their higher homologues were prepared according to the reported procedure[9]. The α-oxoketene dithioacetals were prepared according to the procedure described in Chapter II. The cinnamoyl ketene dithioacetals, 5-aryl-2,4-pentadienoyl ketene dithioacetals, and 7-aryl-2,4,6-heptatrienoyl ketene dithioacetals were prepared according to the reported procedure[10] described in the chapter II. The cyclopropyl ketones were prepared according to the procedure[6], as described in the second chapter. The spectral and analytical data of are also reported in the chapter II.

Synthesis of n-aryl-1,1-bis(methylthio)polyenes (7,11,13): General Procedure : To a well stirred suspension of cyclopropyl ketones (10 mmol) in absolute ethanol (50 ml),

excess of sodium borohydride (1.25g, 35 mmol) is added and the mixture was refluxed for 2 hrs. The cooled mixture was then poured on to crushed ice (100 g) and extracted with chloroform (2 x 100 ml). The chloroform extract was washed with saturated salt (NaCl) solution (2 x 100 ml), dried (Na_2SO_4) and evaporated under vacuum to give the crude carbinols in nearly quantitative yields as an undistillable thick liquids. The crude carbinol was dissolved in carbontetrachloride (50 ml) and pyridiniumtosylate (5g, 20 mmol) was added with stirring. The solvent (CCl_4) from the reaction mixture was then distilled off slowly (15 min) over water-bath. The residue was taken as suspension in carbontetrachloride (75 ml) and filtered. The filtrate was evaporated to give the crude product which were further purified by passing through a silica gel column using hexane as eluent.

1,1-Bis(methylthio)-6-(4-methoxyphenyl)- 1,3,5-hexatriene (7a) (89%), oil; γ_{max} (neat) 1662, 1600 cm^{-1}; δ_H (CCl_4) 2.16 (3H,s,SCH_3), 2.21 (3H,s,SCH_3), 3.61 (3H,s,OCH_3); 5.94-6.53 (5H,m,=CH, 6.67 (d,2H,J 9Hz, ArH), 7.19 (d,2H, J 9Hz, ArH); (Found : C,64.89; H, 6.68. $C_{15}H_{18}OS_2$ requires C, 64.77; H, 6.52%).

1,1-Bis(methylthio)-6-phenyl-1,3,5-hexatriene (7b) (81%), oil; γ_{max} (neat) 1675 cm^{-1}; δ_H(CCl_4) 2.25 (3H,s,SCH_3), 2.31 (3H,s,SCH_3), 5.91-7.04 (5H,m,=CH), 7.10-7.52 (5H,m,ArH); (Found : C, 67.82; H, 6.58. $C_{14}H_{16}S_2$ requires C, 67.69; H, 6.49%); λ_{max} 359, 358 and C = 2.28057×10^4.

1,1-Bis(methylthio)-6-(3,4-dimethoxyphenyl)-1,3,5-hexatriene (7c) (78%), oil; ν_{max} (neat) 1680, 1585 cm^{-1}; δ_H (CCl_4) 2.20 (6H,s,SCH_3), 3.67 (3H,s,OCH_3), 3.73 (3H,s,OCH_3), 5.90-6.88 (8H,m,=CH and ArH); (Found : C, 62.47; H, 6.44. $C_{16}H_{20}O_2S_2$ requires C, 62.30; H, 6.54%).

1,1-Bis(methylthio)-6-(3,4-methylenedioxyphenyl)-1,3,5-hexatriene (7d) (86%), oil; ν_{max} (neat) 1686, 2672, 1595 cm^{-1}; δ_H (CCl_4) 2.34 (6H,s,SCH_3), 5.94 (2H,s,CH_2), 6.15-7.04 (8H,m,=CH and ArH); (Found : C, 61.76; H, 5.69. $C_{15}H_{16}O_2S_2$ requires C, 61.76; H, 5.69%).

1,1-Bis(methylthio)-6-(2-chlorophenyl)-1,3,5-hexatriene (7e) 82%; ν_{max} (neat) 1689, 1528 cm^{-1}; δ_H (CCl_4) 2.31 (6H,s,SCH_3), 6.05-7.71 (9H,m,=CH and ArH); (Found : C, 59.58; H, 5.51. $C_{14}H_{15}S_2Cl$ requires C, 59.45; H, 5.35%).

1,1-Bis(methylthio)-2-methyl-6-phenyl-1,3,5-hexatriene(7f) (87%), oil; ν_{max} (neat) 1675, 1595 cm^{-1}; δ_H (CCl_4) 2.11 (3H,s,CH_3), 2.25 (3H,s,SCH_3), 2.31 (3H,s,SCH_3), 6.24-6.98 (4H,m,=CH), 7.04-7.50 (5H,m,ArH); (Found : C,68.51; H, 6.83. $C_{15}H_{18}S_2$ requires C, 68.65; H, 6.91%). m/z 262 (M^+,74%), 247(52), 200(100).

1,1-Bis(methylthio)-8-phenyl-1,3,5,7-octatetraene (11a) (76%), oil; ν_{max} (neat) 1678, 1596 cm^{-1}; δ_H (CCl_4) 2.32 (6H,s,SCH_3), 6.28-7.04 (7H,m,=CH), 7.09-7.49 (5H,m,ArH); (Found : C, 70.21; H,6.73. $C_{16}H_{18}S_2$ requires C, 70.02; H, 6.61%).

1,1-Bis(methylthio)-8-(4-methoxyphenyl)-1,3,5,7-octatetra--ene (11b) (78%), m.p. 73°-74°C; ν_{max} (KBr) 1600, 1590, 1500 cm^{-1}; δ_H (CCl_4) 2.27 (3H,s,SCH_3), 2.30 (3H,s,SCH_3), 3.73 (3H,s,OCH_3), 6.09-6.60 (7H,m,=CH), 6.74 (2H,d,J 9Hz,ArH), 7.24 (2H,d, J 9Hz,ArH); (Found : C, 67.21; H, 6.78. $C_{17}H_{20}OS_2$ requires C, 67.05; H, 6.62%); m/z 304 (M^+, 100%), 257(12), 242(16).

1,1-Bis(methylthio)-8-(4-methylphenyl)-1,3,5,7-octatetra--ene (11c) (86%), m.p. 102°-103°C; ν_{max} (KBr) 1670, 1595 cm^{-1}; δ_H ($CDCl_3$) 2.40 (9H,s,CH_3 and SCH_3), 6.12-7.05 (7H,m,=CH), 7.13-7.54 (4H,m,ArH); (Found : C,70.86; H, 6.82. $C_{17}H_{20}S_2$ requires C, 70.78; H, 6.99%); m/z 289 (M^++1, 100%) 242(19), 227(18).

1,1-Bis(methylthio)-8-(3,4-methylenedioxyphenyl)-1,2,5,7-octatetraene (11d) (87%), oil; ν_{max} (neat) 1678, 1602 cm^{-1}; δ_H (CCl_4) 2.34 (6H,s,SCH_3), 5.67-7.44 (10H,m,=CH and ArH), 5.94 (2H,s,CH_2); (Found : C, 64.28; H, 5.83. $C_{17}H_{18}O_2S_2$ requires C, 64.12; H, 5.10%); m/z 318 (M^+, 32%), 271(14), 224(15).

1,1-Bis(methylthio)-10-phenyl-1,3,5,7,9-decapentaene (13a) (91%), m.p. 105°-106°C; ν_{max} 1670, 1597 cm^{-1}; δ ($CDCl_3$) 2.31 (3H,s,SCH_3), 2.34 (3H,s,SCH_3), 6.05-7.04 (9H,m,=CH, 7.13-7.51 (5H,m,ArH); (Found : C, 72.09; H, 6.84. $C_{18}H_{20}S_2$ requires C, 71.95; H, 6.71%); m/z 300 (M^+, 100%), 206(10).

1,1-Bis(methylthio)-10-(4-methoxyphenyl)-1,3,5,7,9,-decapentaene (13b) (87%),m.p. 109-110°C; ν_{max} (KBr) 1667,

1600 cm^{-1} ; δ($CDCl_3$) 2.34(6H,s,SCH_3), 3.87(3H,s,OCH_3), 6.20-6.81(9H,m,=CH), 6.92(2H,d,J 9Hz,ArH),7.40(2H,d,J 9Hz, ArH); (Found: C,69.15; H,6.87. $C_{19}H_{22}OS_2$ requires C,69.05; H,6.71%); m/z 330(M^+,100%) .

Synthesis of methyl 4-(methylthio)-6-(4-methoxyphenyl)-5-hexene carbothioate (14): To a solution of 7a (10 mmol) in methanol (40 ml), $BF_3.Et_2O$ (5 ml) was added. The reaction mixture was refluxed for 30hr, cooled and poured over saturated $NaHCO_3$ solution (100 ml). It was then extracted with chloroform (3x75 ml), the combined extracts were washed with water (2x100 ml), dried ($NaSO_4$) and evaporated to give a viscous residue, which on column chromatography over silicagel (hexene) afforded pure ester **14**.

yellow oil (83%), ν_{max} (neat) 1743, 1612 cm^{-1}; δ_H (CCl_4) 1.77-2.13 (2H,m,CH_2), 1.98 (3H,s,SCH_3), 2.44 (2H,t,J 7Hz, CH_2), 3.09-3.43 (1H,m,CH) 3.60 (3H,s,OCH_3), 3.79 (3H,s,OCH_3), 5.80 (1H,dd,J 12,16 Hz,=CH), 6.31 (1H,d,J 16 Hz), =CH), 6.81 (2H,d,J 9Hz,ArH), 7.30 (2H,d,J 9Hz, ArH); (Found : C, 64.38; H, 7.36. $C_{15}H_{20}O_3S$ requires C, 64.25; H, 7.19%).

Solvolytic studies on polyenes 7 and 11 in the presence of $BF_3.Et_2O/HgCl_2$ for prolonged time : General Procedure : To a solution of appropriate polyene (10 mmol) in methanol (40 ml), $HgCl_2$ (15 mmol) and $BF_3.Et_2O$ (5 ml) were added. The reaction mixture was stirred at room temperature for prolonged time (6-20 h). It was then filtered through a

sintered funnel to remove traces of mercuric chloride and the filtrate diluted with chloroform, washed with saturated sodium bicarbonate solution (2 x 100 ml) and water (2 x 50 ml) dried (Na_2SO_4 and evaporated to give crude products, which were purified by column chromatography over silica gel. Elution with hexane and ethylacetrite (20:1) gave pure ester.

Methyl 6-methoxy-6-(3,4-methylenedioxyphenyl)-3-hexene carboxylate (15d) : Colorless oil (63%); ν_{max} (neat) 1739 cm^{-1}; δ_H (CCl_4) 2.10-2.55 (2H,m,CH_2), 2.90 (2H,d,J 5Hz, CH_2), 3.09 (3H,s,OCH_3), 3.56 (3H,s,OCH_3), 3.93 (1H,t,J 7 Hz, CH), 5.39-5.56 (2H,m, =CH), 5.90 (2H,s, CH_2), 6.61-6.78 (3H,m,ArH); (Found : C, 64.89; H, 6.71. $C_{15}H_{18}O_5$ requires C, 64.74; H, 6.52%).

Methyl-6-methoxy-6-(2-chlorophenyl)-3-hexene carboxylate (15e) : Colorless oil (71%); ν_{max} (neat) 1743 cm^{-1}; δ_H (CCl_4) 2.23-2.50 (2H,m,CH_2) 2.94 (2H,d,J 5Hz,CH_2), 3.19 (3H,s,OCH_3), 3.60 (3H,s,OCH_3), 4.70 (1H,t, J 7Hz, CH), 5.44-5.64 (2H,m,=CH), 7.0-7.54 (4H,m,ArH); (Found : C, 62.73; H, 6.49. $C_{14}H_{17}ClO_3$ requires C,62.52; H, 6.38%).

Methyl 2-methyl-6-methoxy-6-phenyl-2-hexene carboxylate (16) : colorless oil (67%); ν_{max} (neat) 1703 cm^{-1}; δ_H (CCl_4) 1.60-2.35 (4H,m,CH_2), 1.80 (3H,s,CH_3), 3.20 (3H,s,OCH_3), 3.74 (3H,s,OCH_3), 4.04 (1H,t,J 7Hz,CH), 6.68-6.92 (1H,t,J 7Hz,=CH), 7.14-7.45 (5H,m,ArH); (Found : C, 72.73; H, 8.24. $C_{15}H_{20}O_2$ requires C, 72.55, H, 8.12%).

Methyl 6-methoxy-8-phenyl-3,7-octadiene carboxylate (17) : colorless oil (63%); $\bar{\nu}_{max}$ (neat) 1740 cm^{-1}; δ_H (CCl_4) 2.20-2.43 (2H,m,CH_2), 2.98 (2H,d,J 5Hz,CH_2), 3.24 (3H,s,OCH_3), 3.57 (3H,s,OCH_3), 3.70 (1H,t,J 7Hz,CH), 5.50-5.70 (2H,m,=CH), 6.01 (1H,dd,J 7,16Hz, =CH), 6.51 (1H,d,J 16Hz,=CH), 7.10-7.48 (5H,m,ArH); (Found : C,73.98; H,7.86. $C_{16}H_{20}O_3$ requires C, 73.82; H, 7.74%); m/z 260 (M^+, 2%).

Synthesis of Methyl n-aryl polyene carboxylate (18,19, 20) : General Procedure : To a solution of n-aryl polyene (10 mmol) in anhydrous methanol (50 ml), $HgCl_2$ (2.70g, 10 mmol) and $BF_3.Et_2O$ (5ml) were added and stirred at room temperature for 8-10 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 (3 x 100 ml) and water (2 x 50 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 (1:50) gave pure ester.

Methyl 6-(4-methoxyphenyl)-3,5-hexadienyl carboxylate(18a) (84%); m.p. 48°C; $\bar{\nu}_{max}$ (KBr) 1735, 1610 cm^{-1}; δ_H (CCl_4) 2.99 (1.5H,d,J 7Hz,CH_2), 3.15 (0.5H,d,J 9Hz,CH_2), 5.37-6.53 (4H,m,=CH), 6.68 (2H,d, J 9Hz,ArH), 7.14 (2H,d, J 9Hz,ArH); (Found : C,72.52; H,6.81. $C_{14}H_{16}O_3$ requires C, 72.39; H, 6.95%); m/z 232 (M^+, 100%), 200(3).

Methyl 6-phenyl-3,5-hexadienyl carboxylate (18b) (78%), oil; $\bar{\nu}_{max}$ (neat) 1720, 1645 cm^{-1}; δ_H (CCl_4) 3.11 (2H,d, J

7Hz, CH_2), 3.71 (3H,s,OCH_3), 5.56-6.96 (4H,m,=CH), 7.06-7.58 (5H,m,ArH); (Found : C,77.36; H,7.12. $C_{13}H_{14}O_2$ requires C, 77.20; H, 6.98%); m/z 202 (M^+, 2%), 171(3), 143(12).

Methyl 6-(3,4-dimethoxyphenyl)-3,5-hixadienyl carboxylate (18c)(67%), m.p. 61°-62°C; ν_{max} (KBr) 1730, 1598 cm^{-1}; δ_H ($CDCl_3$) 3.29 (2H,d,J 7Hz,CH_2), 3.70 (3H,s,OCH_3), 3.86 (s,3H,OCH_3), 3.91 (3H,s,OCH_3), 5.56-7.09 (7H,m,=CH and ArH); (Found : C, 68.81; H, 6.79. $C_{15}H_{18}O_4$ requires C, 68.68; H, 6.92%); m/z 262 (M^+, 17%), 203(11).

Methyl 6-(3,4-methylenedioxyphenyl)-3,5-hexadienyl carboxylate (18d) (83%); oil; ν_{max}(neat) 1735, 1600 cm^{-1}; δ_H (CCl_4) 3.03 (1.5H,d, J 7Hz, CH_2), 3.15 (0.5H,d, J 8Hz,CH_2), 3.60 (3H,s,OCH_3), 5.35-6.48 (4H,m,=CH), 5.83 (2H,s,CH_2), 6.54-6.88 (3H,m,ArH); (Found : C,68.13; H,5.59. $C_{14}H_{14}O_4$ requires C, 68.28; H, 5.73%) m/z 246 (M^+, 10%).

Methyl 8-(4-methoxyphenyl)-3,5,7-octatriene carboxylate (19a) (81%), oil; ν_{max} (neat) 1730, 1600, 1500 cm^{-1}; δ_H (CCl_4) 3.20 (0.5H,d,J 6Hz,CH_2), 3.33 (1.5H,d,J 7Hz,CH_2), 3.64 (3H,s,OCH_3), 3.71 (3H,s,OCH_3), 5.61-6.57 (6H,m,=CH), 6.82 (2H,d,J 9Hz,ArH), 7.30 (2H,d,J 9Hz, ArH); (Found : C,74.27; H,7.13. $C_{16}H_{18}O_3$ requires C, 74.39; H,7.02%); m/z 258 (M^+,99%), 199(30).

Methyl 8-(3,4-methylenedioxyphenyl)-3,5,7-octatriene carboxylate (19b) (84%), m.p. 61°-62°C; ν_{max} (KBr) 1740,

1600, 1500 cm^{-1}; δ_H (CCl_4) 3.05 (1.5H,d,J 9Hz,CH_2), 3.18 (0.5H,d,J 6Hz,CH_2), 5.27-6.54 (6H,m,=CH), 5.90 (2H,s,CH_2), 6.62-6.93 (3H,m,ArH); (Found : C,70.71; H,5.81. $C_{16}H_{16}O_4$ requires C, 70.57; H, 5.92%); m/z 272 (M^+, 94%), 213(20).

Methyl 8-(4-methylphenyl)-3,5,7-octatriene carboxylate (19c) (77%), oil; ν_{max} (neat) 1740, 1510 cm^{-1}; δ_H (CCl_4) 2.31 (3H,s,CH_3), 3.10 (1.5H,d,J 6Hz,CH_2), 3.24 (0.5H,d,J 6Hz,CH_2), 3.64 (3H,s,OCH_3), 5.38-6.82 (6H,m,=CH), 6.87-7.37 (4H,m,ArH); (Found : C, 79.19; H, 7.60. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.49%); m/z 242 (M^+, 71%).

Methyl 10-phenyl-3,5,7,9-decatetraene carboxylate (20), (87%), m.p. 84°-85°C; ν_{max}(KBr) 1733 cm^{-1}; δ_H (CCl_4) 3.11 (2H,d,J 6Hz, CH_2), 3.68 (3H,s,OCH_3), 5.46-6.97 (8H,m,=CH), 7.12-7.58 (5H,m,ArH); (Found : C,80.41; H, 7.22. $C_{17}H_{18}O_2$ requires C, 80.28; H, 7.13%); m/z 254 (M^+, 90%), 195(19).

Sythesis of 2-alkyl-4-aryl-3-bis(methylthio)methylene-1-cyclopentene (24) : General Procedure : To a cooled (0°C) solution of appropriate Grignard reagent (15 mmol) in dry ether (50 ml) appropriate cyclopropyl ketone 1 (10 mmol) in dry benzene (30 ml) was added drop wise (10 min) under nitrogen atmosphere. After stirring for 3 hr the reaction mixture was poured into cold saturated solution of NH_4Cl (100 ml) and was extracted with ether (3 x 30 ml). The ether phase was washed with water (2 x 50 ml), dried (Na_2SO_4) and evaporated. The corresponding carbinol 21 thus obtained was dissolved in CCl_4 (30 ml), treated with

pyridinium-tosylate (30 mmol) and the solvent was distilled off on a water bath. The crude residue was then washed with CCl_4 (3 x 30 ml) and filtered to remove the excess of pyridinium tosylate. The filtrate thus obtained was evaporated and the residue was purified over a column of silica gel using hexane as eluent.

3-Bis(methylthio)methylene-2-methyl-4-(4-methoxyphenyl)-1-cyclopentene (24a) : colorless oil (87%); γ_{max} (neat) 1610, 1507 cm^{-1}; δ_H (CCl_4) 1.08-3.07 (2H,m,CH_2), 2.0 (3H,s,SCH_3), 2.23 (3H,s,SCH_3), 2.29 (3H,d,J 3Hz,CH_3), 3.73 (3H,s,OCH_3), 4.30 (1H,t,dd,J 7,9 Hz,ArCH), 6.0 (1H,brs,=CH), 6.82 (2H,d,J 9Hz, ArH), 7.17 (2H,d,J 9Hz, ArH); (Found : C,65.89; H,6.96. $C_{16}H_{20}OS_2$ requires C, 65.71; H, 6.89%); m/z 292 (M^+, 78%).

3-Bis(mthylthio)methylene-2-methyl-4-phenyl-1-cyclopentene (24b): Colorless oil (78%); γ_{max} (neat) 1610, 1600 cm^{-1}; δ_H (CCl_4) 1.91 (3H, s, SCH_3), 2.17 (3H, s, SCH_3), 2.26 (3H, d, J 3Hz), CH_3), 2.61-3.04 (2H, m, CH_2), 4.34 (1H, t like, J 7Hz, ArCH), 5.90 (1H, brs, =CH), 6.95-7.32 (5H, m, ArH); (Found : C, 68.53; H, 6.73. $C_{15}H_{18}S_2$ requires C, 68.65; H, 6.91%); m/z 262 (M^+, 83%) 215(41).

3-Bis(methylthio)methylene-4-(4-methoxyphenyl)-2-propyl-1-cyclopentene (24c): Colorless oil (84%); γ_{max} 1611, 1512 cm^{-1}; δ_H (CCl_4) 0.89 (3H,t,J 6Hz, CH_3), 1.20-3.0 (6H, m, CH_2), 1.88 (3H, s, SCH_3), 2.14 (3H, s, SCH_3), 3.61 (3H, s, OCH_3), 4.20 (1H, dd, J 6,8Hz, ArCH), 5.88 (1H, brs, =CH),

6.61 (2H, d, J 9Hz, ArH), 6.93 (2H,d,J 9Hz, ArH); (Found : C, 67.22; H, 7.36. $C_{18}H_{24}OS_2$ requires C, 67.45; H, 7.55%); m/z 320 (M^+, 11%).

2-Allyl-3-bis(methylthio)methylene-4-(4-methoxyphenyl)-1-cyclopentene (35) : yellow oil (79%); ν_{max} (neat) 1608, 1503 cm^{-1}; δ_H (CCl_4); 1.69-3.08 (2H,m,CH_2), 1.98 (3H,s,SCH_3), 2.20 (3H,s,SCH_3), 3.54 (2H,brs,CH_2), 3.74 (3H,s,OCH_3), 4.27 (1H,t,J 7Hz,ArCH), 5.10 (2H,dd,J 5,9Hz,=CH_2), 6.0 (1H,brs, =CH), 6.67 (2H,d,J 9Hz,ArH), 6.99 (2H,d,J 9Hz, ArH); (Found : C, 67.63; H, 6.81. $C_{18}H_{22}OS_2$ requires C, 67.88; H, 6.96%); m/z 318 (M^+, 73%), 271 (83).

2-Benzyl-3-bis(methylthio)methylene-4-(4-methoxyphenyl)-1-cyclopentene (39) : colorless oil (77%); ν_{max} (neat) 1610, 1511 cm^{-1}; δ_H (CCl_4) 1.68-3.20 (2H,m,CH_2); 1.88 (3H,s,SCH_3) 1.95 (3H,s,SCH_3), 3.61 (3H,s,OCH_3), 4.08 (2H,s,$ArCh_2$), 4.34 (1H,+, J 6Hz, ArCH), 5.82 (1H,brs,=CH), 6.79 (2H,d, J 9Hz, ArH), 6.83-7.36 (7H,m,ArH); (Found : C, 71.93; H, 6.69. $C_{22}H_{24}OS_2$ requires C, 71.70; H, 6.56%); m/z 368 (M^+, 53%).

s-Methyl,2-(2-methylnapthyl)-5-(4-methoxyphenyl)-2-cyclopentene-1-carbothioate (43) : colorless oil (38%); ν_{max} (CCl_4) 1680, 1510 cm^{-1}; δ_H (CCl_4) 2.08-2.57 (2H,m,CH_2), 2.24 (3H,s,SCH_3), 3.34-3.85 (4H,m,$ArCH_2$,ArCH and CH), 3.65 (3H,s,OCH_3), 5.50 (1H,brs,=CH), 6.67 (2H,d,J 9Hz,ArH), 7.0 (2H,d,J 9Hz, ArH), 7.12-7.86 (7H,m,ArH); (Found : C,77.51;

H, 6.42. $C_{25}H_{24}O_2S$ requires C, 77.28; H, 6.23%); m/z 388.50 (M^+, 100%), 313(84).

Synthesis of 5-Methyl-5-aryl-2-(carbethoxymethyl)-2-cyclopentene-1-carbothioate (29,30,31) : General Procudure :
To a suspension of zinc (2.6g, 40 mmol preheated at 110°C for 1 hr) and a few crystals of iodine in dry ether (20 ml), ethyl bromoacetate (3.4g, 20 mmol) in dry ether (10 ml) was added dropwise (10 min) with stirring and the mixture refluxed for 1 hr. A solution of appropriate cyclopropyl ketone (10 mmol) in dry benzene (25 ml) is then added dropwise (30 min) and refluxing continued to another 20 hr. It was then passed over ice cooled 10% sulphuric acid (100 ml), organic layer separated, washed with water (50 ml), dried (Na_2SO_4) and solvent evaporated to give the crude product, which were then column chromotographed over silica gel using EtoAc/hexane (1:20) as eluent.

S-Methyl-2-(carbethoxymethyl)-5-(4-methoxyphenyl)-2-cyclopentene-1-carbothioate (29a) : Colorless oil (81%); ν_{max} (neat) 1740, 1695 cm^{-1}; δ_H (CCl_4) 1.20 (3H,t,J 7Hz, CH_3), 2.08-2.89 (2H,m,CH_2), 2.19 (3H,s,SCH_3), 3.02 (2H,brs,CH_2), 3.49-3.62 (1H,m,CH), 3.64 (3H,s,OCH_3), 3.74-3.92 (1H,m,CH), 3.99 (2H,q,J 7Hz,CH_2), 5.68 (1H,brs,=CH), 6.65 (2H,d,J 9Hz,ArH), 7.03 (2H,d,J 9Hz, ArH); (Found : C,64.51; H, 6.54. $C_{18}H_{22}O_4S$ requires C, 64.64; H,6,63%); m/z 334 (M^+, 4%), 287(4) 259(100).

S-Methyl-2-(carbethoxymethyl)-5-(3,4-dimethoxyphenyl)-2-cyclopentene-1-carbothioate (29c) : colorless oil (78%); ν_{max} (neat) 1742, 1692 cm^{-1}; δ_H (CCl_4) 1.21 (3H,t,J 7Hz, CH_3), 2.19-2.98 (2H,m,CH_2), 2.23 (3H,s,SCH_3), 3.11 (2H,brs,CH_2), 3.30-3.91 (2H,m,CH), 3.72 (3H,s,OCH_3), 3.79 (3H,s,OCH_3) 4.07 (2H,q,J 7Hz,CH_2), 5.77 (1H,brs,=CH), 6.64-6.78 (3H,m,ArH); (Found : C, 62.76; H, 6.71. $C_{19}H_{24}O_5S$ requires C, 62.61; H, 6.64%); m/z 364 (M^+, 63%), 289(100).

S-Methyl-2-(carbethoxymethyl)-5-(3,4-methylenedioxy)-2-cyclopentene-1-carbothioate (29d) : colorless oil (83%); ν_{max} (neat) 1735, 1686 cm^{-1}; δ_H (CCl_4) 1.25 (3H,t,J 7Hz, CH_3), 2.25-2.97 (2H,m,CH_2), 2.28 (3H,s,SCH_3), 3.12 (2H,brs,CH_2), 3.50-3.74 (1H,m,CH), 3.77-3.94 (1H,m,CH), 4.13 (2H,q,J 7Hz,CH_2) 5.81 (1H,brs,=CH), 5.90 (2H,s,CH_2), 6.65-6.85 (3H,m,ArH); (Found : C, 65.20; H, 6.17. $C_{18}H_{20}O_4S$ requires C, 65.04; H, 6.07%); m/z 332 (M^+, 9%), 257(12).

(*E/Z*)S-Methyl-2-(carbethoxymethyl)-5-styryl-2-cyclopentene-1-carbothioate (30a) : (*E/Z*, 2:1) colorless oil (73%); ν_{max} (neat) 1737, 1688 cm^{-1} δ_H (CCl_4) 1.23 (3H,t,J 7Hz, CH_3), 2.15-2.94 (2.6H,m,Ch_2 and *Z*-CH), 2.17 (1H,s,*Z*-SCH_3), 2.27 (2H,s,*E*-SCH_3), 3.06 (2H,brs,CH_2), 3.17-3.50 (0.6H,m,*E*-CH), 3.60-3.85 (0.6H,m,*E*-CH), 4.08 (2H,q,J 7Hz, CH_2), 5.70 (1H,brs,=CH), 6.13 (1H,dd,J 16,7Hz,=CH), 6.40 (1H,d,J 16Hz,=CH), 7.01-7.37 (5H,m,ArH); (Found : C,

69.22; H, 6.82. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71%); m/z 330 (M^+, 7%), 283(11), 255(53).

*(E/Z)*S-Methyl-2-(carbethoxymethyl)-5-[2-(3,4-methylene-dioxyphenyl)ethylene]-2-cyclopentene-1-carbothioate (30d), *(E/Z)* 9:1), colorless oil (73%); ν_{max} (neat) 1738, 1689 cm^{-1}; δ_H (CCl_4) 1.17 (3H,t,J 7Hz,CH_3), 2.03-2.87 (2.2H,m,CH_2 and *Z*-CH), 2.11 (0.3H,s,*Z*-SCH_3), 2.26 (2.7H,s,*E*-SCH_3), 2.99 (2b,brs,CH_2), 3.05-3.34 (0.9H,m,*E*-CH), 3.48-3.80 (0.9H,m,*E*-CH), 4.0 (2H,q,J 7Hz, CH_2), 5.64 (1H,brs,=CH, 5.80 (2H,s,CH_2), 5.39 (1H,dd,J 16,7Hz,=CH), 6.24 (1H,d,J 16Hz,=CH), 6.57-6.86 (3H,m,ArH); (Found : C, 64.03; H,5.84. $C_{20}H_{22}O_5S$ requires C, 64.15; H, 5.92%); m/z 374 (M^+, 22%), 298(100).

*(E/Z)*S-Methyl 2-(carbethoxymethyl)-5-[4-(phenyl)buta-dienyl]-2-cyclopentene-1-carbothioate (31) (*E/Z*, 2:1) colorless oil (76%); ν_{max} (neat) 1733, 1683 cm^{-1}; δ_H (CCl_4) 1.25 (3H,t,J 7Hz,CH_3), 2.09-2.92 (2.6H,m,CH_2 and *Z*-CH), 2.11 (1H,s,*Z*-SCH_3), 2.26 (2H,s,*E*-SCH_3), 3.06 (2H,brs,CH_2), 3.13-3.42 (0.6H,m,*E*-ArCH), 3.50-3.80 (0.6H,m,*E*-CH) 4.11 (2H,N,J 7Hz,CH_2), 5.70 (1H,brs,=CH), 5.79-6.90 (4H,m,=CH), 7.07-7.44 (5H,m,ArH); (Found : C, 70.87% H, 6.88. $C_{21}H_{24}O_3S$ requires C, 70.75; 6.79%); m/z 356 (M^+, 2%), 324(16), 294(26).

Reaction of 1-[2-bis(methylthio)methyleneacetyl]-2-(4-methoxyphenyl)cyclopropane (1a) with allylmagnesium bromide : General Procedure : To a well stirred and

cooled (0°C) suspension of allyl magnesium bromide (16 mmol) [prepared from 1.92g (160 mmol) of distilled allyl bromide and magnesium turnings, 1.2g (520 mmol) in dry ether (40 ml)], a solution of 1a (8 mmol) in dry benzene (30 ml) was added and the reaction mixture was further stirred at 0°C for 1hr. The reaction mixture was then poured into a saturated ammonium chloride solution (200 ml), extracted with ether (3 x 30 ml), dried (Na_2SO_4) and evaporated in vacuum to give crude carbinol (32) colorless oil in nearly quantitative yields. The carbinol 32 was unstable and therefore used as such for subsequent reaction without further purification.

Cycloaromatization of 32; synthesis of 1-(4-methoxyphenyl) -7-methylthio indane (33) : General Procedure : To a solution of the carbinol 32 (8 mmol) obtained as above, in dry benzene (60 ml), stannic chloride (6.25g, 24 mmol) was added. The reaction mixture was refluxed for 18hr. It was then poured into cold aqueous sodium hydroxide (5%) extracted with chloroform (3 x 60 ml), the combined organic layer was washed with water (100 ml), dried (Na_2SO_4) and evaporated to afford the product as viscous residue, which was purified by column chromatography over silica gel using hexane as eluent.

Colorless crystals (61%), m.p. 59°-60°C; ν_{max} (KBr) 1725, 1610 cm^{-1}; δ_H (CCl_4) 1.67-2.07 (1H,m,CH_2), 2.14 (3H,s,SCH_3), 2.28-3.26 (3H,m,CH_2), 3.60 (3H,s,OCH_3), 4.20 (1H,dd,J 7,4Hz, CH), 6.45-7.10 (7H,m,ArH); (Found : C,

75.73; H,6.91. $C_{17}H_{18}OS$ requires C, 75.51; H, 6.71%); m/z 270 (M^+,100%), 255(74), 223(44).

(E) S-Methyl, 2-allyl-5-(4-methoxyphenyl)-2-cyclopentene carbothioate (34); To a solution of carbinol 32 (10 mmol) in dry benzene BF_3Et_2O (5 ml) or trifluoroacetic acid (15 mmol) was added. It was then poured in saturated solution of $NaHCO_3$ (100 ml), extracted with chloroform (3x60 ml), the combined organic layer was washed with water (100 ml), dried (Na_2SO_4) and evaporated to afford the product as viscous residue, which was purified by column chromatography over silica gel using hexane as eluent.

(76%); γ_{max}(neat) 1680, 1610 cm^{-1}; δ_H (CCl_4) 2.24 (3H,s,SCH_3), 2.03-3.16 (4H, m,CH_2), 3.51-3.83 (2H, m, CH), 3.72 (3H,s,OCH_3), 5.02 (2H, brd, J 6Hz, =CH), 5.51-5.76 (2H, m, =CH), 6.73 (2H, d, J 9Hz, ArH), 7.10 (2H, d, J 9Hz, ArH); (Found: C, 63.88; H, 6.36. $C_{17}H_{20}O_2S$ requires C, 63.72; H 6.29%); m/z 321 (M^++1, 2%), 288(5) 241(6).

S-Methyl 2-benzyl-5-(4-methoxyphenyl)-2-cyclopentene-1-carbothioate (38) : the carbinol 36 obtained by addition of benzyl bromide was treated with stannic chloride in refluxing benzene as in the procedure described above. Colorless oil (63%); γ_{max} (neat) 1675, 1600(m) cm^{-1}; δ_H (CCl_4) 2.13 (3H,s,SCH_3), 2.27-3.21 (2H,m,CH_2), 3.27-3.36 (1H,m,CH), 3.41-3.62 (3H,m,CH_2 and CH), 3.60 (3H,s,OCH_3), 5.45 (1H,brs,=CH), 6.59 (2H,d,J 9Hz,ArH), 6.88 (2H,d,J 9Hz,ArH), 6.97-7.29 (5H,m,ArH); (Found : C, 74.71; H,

6.76. $C_{21}H_{22}O_2S$ requires C, 74.52; H, 6.55%) m/z 338 (M^+,61%), 291(16), 263(100).

The reaction of lithioacetonitrile with 1-[2-bis(methylthio)]-2-(4-methoxyphenyl)cyclopropane (1a) : General Procedure : To a stirred solution of freshly distilled acetonitrile (0.52g, 12.5 mmol) in dry tetrahydrofuran (25 ml), n-butylithium (12.5 mmol) was added under an efficient atmosphere of nitrogen maintaining the temperature at -78°C. After stirring for 0.5hr at -78°C, the cyclopropyl ketone 1a (2.9g, 10 mmol) in 50 ml of tetrahydrofuran was added. The reaction mixture was further stirred for 1hr, allowing the mixture to attain the room temperature slowly. It was then poured over a saturated solution of ammonium chloride and extracted with ether (3 x 50 ml), the combined extract was washed with water (100 ml), dried (Na_2SO_4) and evaporated to give crude carbinol **44** in nearly quantitative yield.

Cycloaromatization of 44 : General Procedure : The crude carbinol **44** (10 mmol) obtained as above was heated with a orthophosphoric acid and formic acid mixture (1:3) for 24hr at 80°C. The reaction mixture was then cooled and poured over cold water (0°C), extracted with chloroform (3 x 100 ml). The combined organic layer was then washed with water (150 ml), dried (Na_2SO_4) and evaporated to give a viscous residue, which was purified by column chromatography over silica gel using hexane as eluent to give two products **47** and **48**.

2,7-Bis(methylthio)-6-(4-methoxyphenyl)-4,5-dihydro-6H-cyclopenta [d] pyridine (47) Colorless crystals (63%), m.p. 117°-118°C; ν_{max} (KBr) 1610, 1570 cm^{-1}; δ_H (CCl_4) 1.64-2.17 (1H,m,CH_2), 2.40 (3H,s,SCH_3), 2.58 (3H,s,SCH_3), 2.67-3.26 (3H,m,CH_2), 3.72 (3H,s,OCH_3), 4.19 (1H,dd,J 10,4Hz,CH), 6.74-7.10 (5H,m,ArH); (Found : C, 64.53; H, 6.20; N, 4.62. $C_{17}H_{19}NOS_2$ requires C, 64.31; H, 6.03; N, 4.41%) ; m/z 317 (M^+, 100%), 302(36).

S-Methyl 2-(cyanomethyl)-5-(4-methoxyphenyl)-2-cyclopentene-1-carbothioate (48) Colorless oil (32%); ν_{max} (neat) 2240, 1676 cm^{-1}; δ_H (CCl_4) 2.30 (3H,s,SCH_3), 2.44-3.45 (3H,m,CH_2 and CH), 3.64 (2H,brs,CH_2), 3.74 (3H,s,OCH_3), 4.19 (1H,brd,J 10Hz,ArCH), 6.02 (1H,brs,=CH), 6.75 (2H,d,J 9Hz,ArH), 7.08 (2H,d,J 9Hz, ArH); (Found : C,66.65; H,5.81; N,4.73. $C_{16}H_{17}NO_2S$ requires C,66.87; H,5.96; N,4.87%); m/z 287 (M^+,27%), 240(14), 212(100).

III.5 REFERENCES

1. Wong, H.N.C.; Hon, M.Y.; Tse, C.W.; Yip, Y.C.; Tanko, J.; Hudlicky, T. *Chem.Rev.*, 1989, 165.
2. Marshall, J.A.; Ellison, R.H.; *J.Am.Chem.Soc.*, 1976, *98*, 4312.
3. Marshall, J.A.; Ellison, R.H. *J.Org.Chem.*, 1975, *40*, 2070.
4. Wender, P.A.; Howbert, J.J. *Tetrahedron Lett.*, 1982, *23*, 3983.
5. Ziegler, F.E.; Marino, A.F.; Petroff, O.A.C.; Studt, W.L. *Tetrahedron Lett.*, 1974, 2035.
6. Deb, B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron Lett.*, 1988, *29*, 2111.
7. Gupta, A.K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1988, *29*, 6633.
8. Kulinkovich, O.G.; Tishchenko, I.G.; Roslik, N.A.; Reznikov, *Synthesis*, 1983, 383.
9. Reddy, M.P.; Krishna Rao, G.S. *Synthesis*, 1980, 815.
10. Thuillier, A.; Vialle, *J.Bull.Soc.Chim.Fr.*, 1962, 2181.

CHAPTER IV

A NOVEL SYNTHESIS OF δ-PYRONES FROM CINNAMOYL KETENE DITHIOACETALS*

IV.1 INTRODUCTION

In the preceding chapter the cinnamoyl ketene dithioacetals of the general formula 1 have been shown to undergo chemoselective cyclopropanation in the presence of dimethyloxosulphonium methylide to yield the corresponding cyclopropyl ketones in high yields[1]. It was further

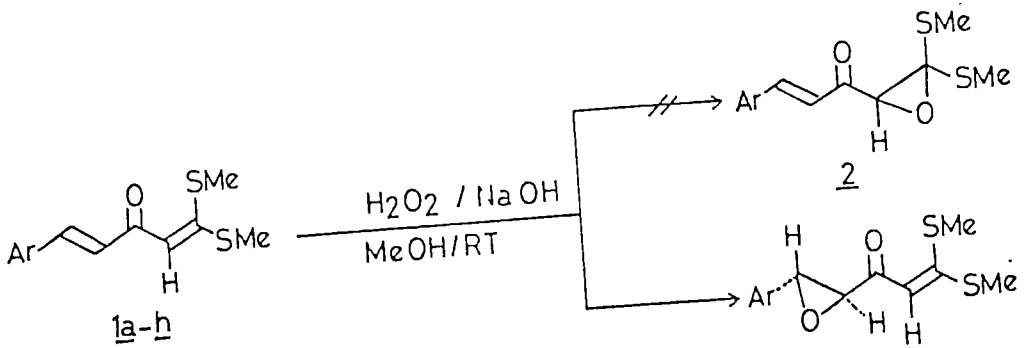
---

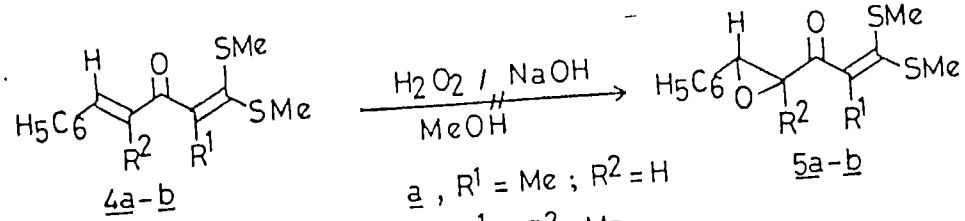
*Deb, B.; Asokan, C.V.; Ila, H.; Junjappa H. *Synthesis* 1987, 893.

considered of interest to subject these intermediates to a base catalyzed epoxidation to examine the behaviour of both the cross-conjugated double bonds. Thus cinnamoyl ketene dithioacetals 1 were preferentially oxidized at the cinnamoyl double bond to yield the corresponding epoxy compounds 3 in good yields (Scheme 1). These epoxides were found to be synthetically useful intermediates, since they underwent a facile boron trifluoride assisted rearrangement to yield the corresponding 3-hydroxy pentadienals 10, which on treatment with acetic acid underwent ring closure to give the corresponding 4*H*-pyran-4-ones 13 in excellent yields (Scheme 2) and the results are described in this chapter.

IV.2 RESULTS AND DISCUSSION

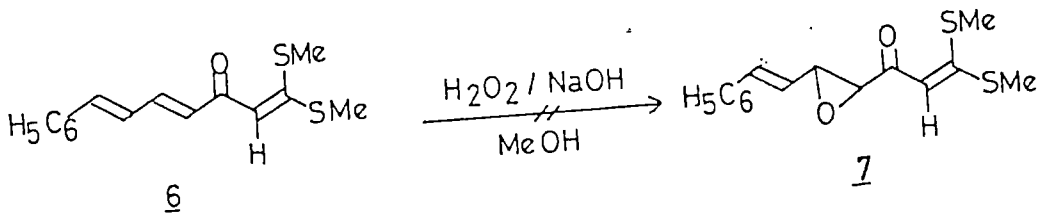
The synthesis of various cinnamoyl ketene dithioacetals employed in the present studies have been described in Chapter II, and their structural authenticity has therefore been fully established. When 1a was subjected to epoxidation in the presence of alkaline hydrogen peroxide at room temperature, after work up, the product isolated in 89% yield was characterized as 1,1-bis(methylthio)-4,5-epoxy-5-phenyl-1-pentene-3-one 3a. Apparently the entire epoxidation has taken place on the styryl double bond and the mercapto double bond has remained unaffected as confirmed by its analytical and spectral data. Thus, it was analyzed for a molecular formula $C_{13}H_{14}O_2S_2$ as confirmed by its mass spectrum which exhibited a molecular





a , R^1 = Me ; R^2 = H

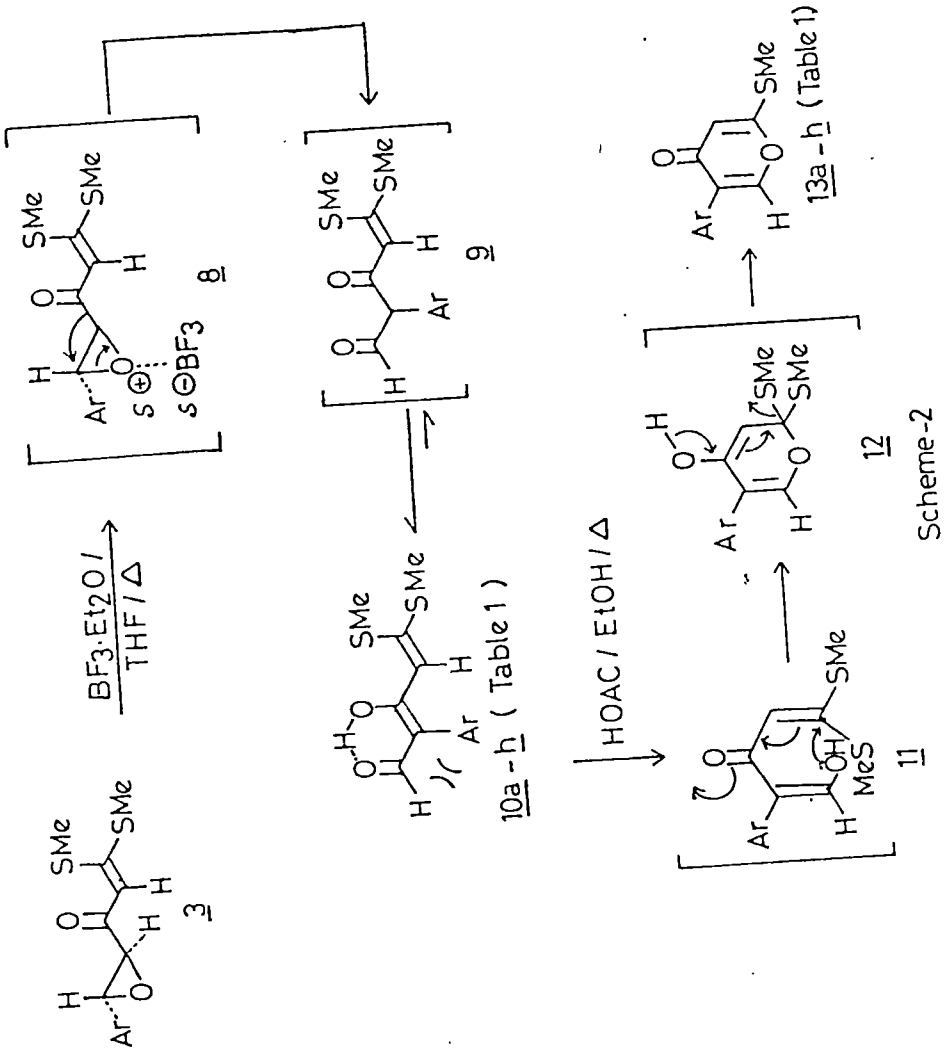
b , R^1 = R^2 = Me



Scheme - 1

ion peak at m/z 266 (M^+,5%). The prominent absorption bands in IR spectrum (KBr) are observed at ν_{max} 1630 and 1480 cm^{-1}. The structure was further confirmed from its ^1H NMR spectrum ($CDCl_3$). The signals at δ2.41 and δ2.42 as singlets integrating for 3H each, were assigned to the two methylthio groups. The characteristic *trans*-epoxy protons appeared as doublets at δ3.49 (J=2.5Hz,H-4) and δ3.90 (J=2.5Hz,H-5). The vinylic proton of the mercapto double bond appeared at δ6.20 (1H) as a singlet. Thus, the mercapto double bond was not involved in the oxidation as observed by its ^1H NMR spectrum. The other epoxy compounds **3b-h** were similarly obtained in 78-86% overall yields. All the epoxides (3b-h) thus prepared were confirmed by their spectral as well as analytical data which are described in the experimental section. However, dienoyl ketene dithioacetals **6** failed to undergo the described epoxidation, although it underwent smooth cyclopropanation with dimethyloxosulphonium methylide as observed in the preceding chapter. Similarly, the cinnamoyl ketene dithioacetals **4a-b** carrying alkyl substituents either at 2-position or both at 2 and 4 positions failed to undergo the oxidation under identical conditions or under modified conditions[2] to yield the corresponding epoxides **4a,b**.

The rearrangement of these epoxides were next examined. Thus, **3a** underwent a smooth 1,2 acyl shift in the presence of borontrifluoride etherate to afford, after purification, a bright yellow solid (92%)(m.p. 158-159°C). The product was characterized as 5,5-bis(methylthio)-3-

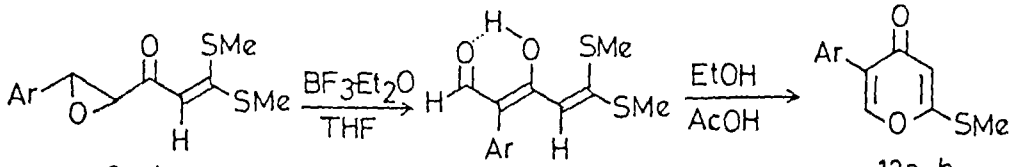

SMe
SMe
H
O
H
Ar
O
3
BF3·Et2O /
THF / Δ
SMe
SMe
H
O
H
Ar
S⊕
S⊖BF3
8
SMe
SMe
H
O
Ar
H
O
9
SMe
SMe
H
O
H
Ar
O
10a - h (Table 1)
HOAC / EtOH / Δ
SMe
SMe
H
O
Ar
H
O
12
SMe
O
Ar
OH
MeS
H
11
SMe
O
Ar
H
O
13a - h (Table 1)

Scheme-2

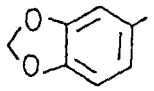
hydroxy-2-phenyl-2,4-pentadienal 10a on the basis its analytical and spectral data. Thus it exhibited molecular ion peak at m/z 266 (M^+) and was analyzed for $C_{13}H_{14}O_2S_2$. The IR spectrum (KBr) of 10a showed prominent absorption bands at ν_{max} 3200, 2830, 1580 and 1500 cm^{-1}. The structure of 10a was further confirmed from its ^1H NMR spectrum in $CDCl_3$ which exhibited two singlets at δ2.25 and δ2.60 integrating for 3H each due to the two methylthio groups. The vinylic proton appeared as singlet at δ5.85. The multiplet between δ7.50-7.55 (5H) was attributed to the aromatic protons. The aldehydic proton appeared as a singlet at δ7.80. The structure was further confirmed from its ^{13}C NMR spectrum ($CDCl_3$) which was in full agreement with the assigned structure (experimental). Thus, the rearrangement of 3a to 10a obtained in more than 92% yield was fully established. The rearranged other epoxy ketones 3b-h afforded the corresponding 2,4-pentadienals 10b-h 84-88% overall yields. The structures of all the dienals were in confirmity with their spectral and analytical data which are described in the experimental section.

The conversion of 2,4-pentadienals 10 to the corresponding 5-aryl-2-methylthio-4*H*-pyran-4-ones 13 was next examined. Thus, when 10a was refluxed in ethanolic acetic acid, after work up the product isolated in 75% yield was characterized as 2-methylthio-5-phenyl-4H-pyran-4-one 13a. The structure of 13a was established by its analytical and

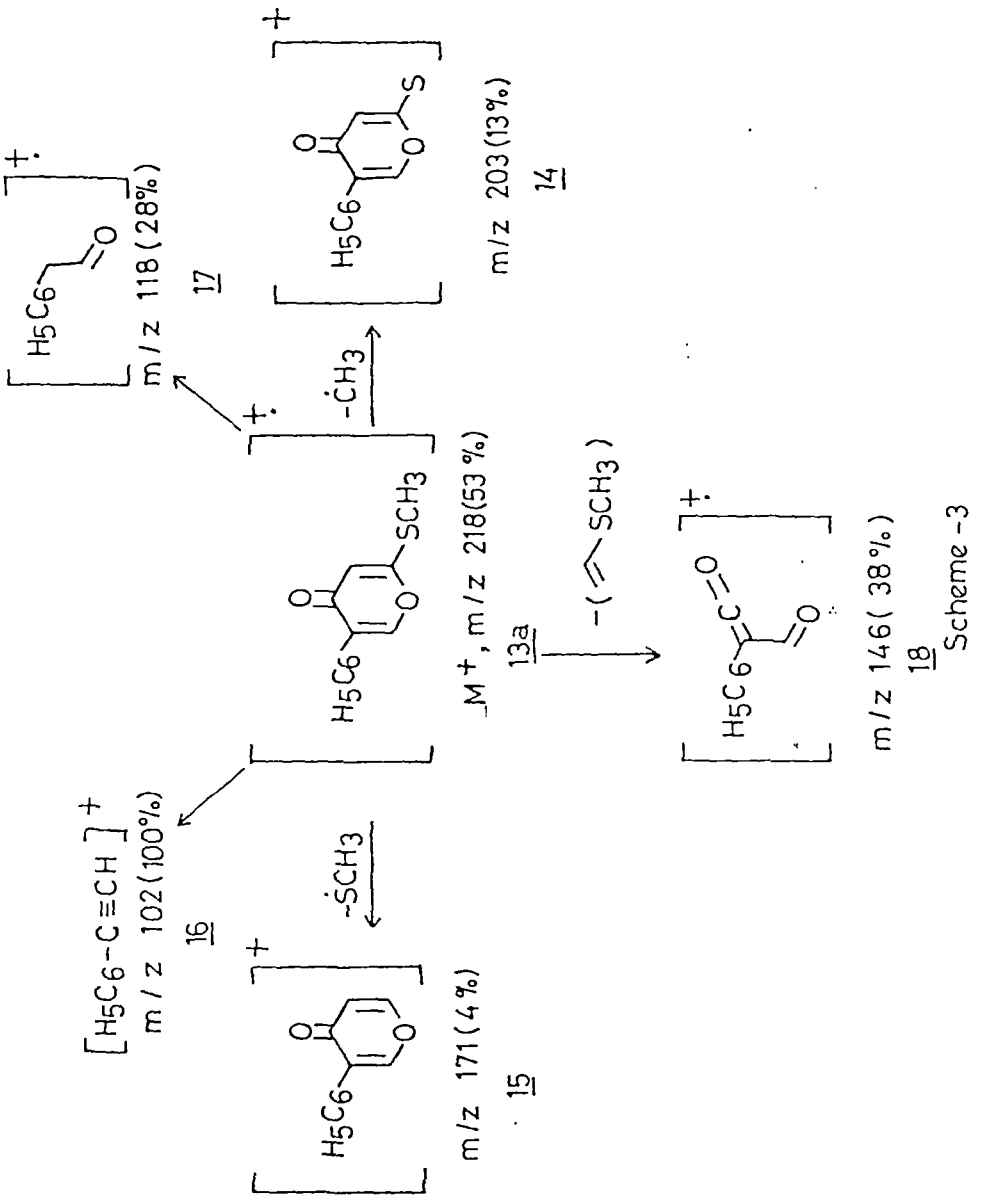
Table-1



3a-h 10a-h 13a-h

	Ar	% Yield 3	% Yield 10	% Yield 13
a	C_6H_5	89	92	75
b	4-MeC_6H_4	83	86	72
c	4-ClC_6H_4	80	87	76
d	4-$MeOC_6H_4$	86	88	73
e	3-$MeOC_6H_4$	78	85	72
f	3,4-$(MeO)_2$ C_6H_3	81	86	70
g	3,4,5-$(MeO)_3$ C_6H_2	80	88	69
h		83	84	71

spectral data. Thus, it was analyzed for $C_{12}H_{10}O_2S$ and confirmed by its mass spectrum with a molecular ion peak at m/z 218 (M^+,53%). The characteristic $\nu_{C=O}$ of γ-pyrone appeared at 1630 cm^{-1} in the IR spectrum. The structure was further confirmed from its ^1H NMR ($CDCl_3$) spectrum. The singlet at δ2.40 integrating for 3H was assigned to the methylthio protons, while signals for H-3 and H-6 appeared as singlets at δ6.10 and δ7.69 respectively. The aromatic protons appeared as multiplet between δ7.13-7.41 (5H). The other γ-pyrones 13b-h were similarly obtained from the corresponding 10b-h in 69-76% overall yields. The structures of all these pyrones were in confirmity with their spectral and analytical data as described in the experimental section. The table I describes the yields of epoxides 3, rearranged dienals 10 and pyran-4-ones 13. The Scheme 3 depicts the characteristic fragmentation pattern[3] of γ-pyrones to further establish the assigned structure. The first major fragment 14 appeared at m/z 203 (13%), was attributed to the loss of CH_3 radical and formation of the fragment m/z 171 was due to the loss of methylthio radical, 15. The fragment m/z 102 (100%) is due to the formation of phenylacetylene cation 16, which is characteristic of γ-pyrones. The most prominent feature of the spectrum was the formation of formylketene radical cation 18, m/z 146(38%), which arised by a retro-Diels-Alder cleavage of the molecular ion. The fragmentation pattern convincingly proves the structure of γ- pyrone. The pyran-4-ones are an important class of compounds, widely

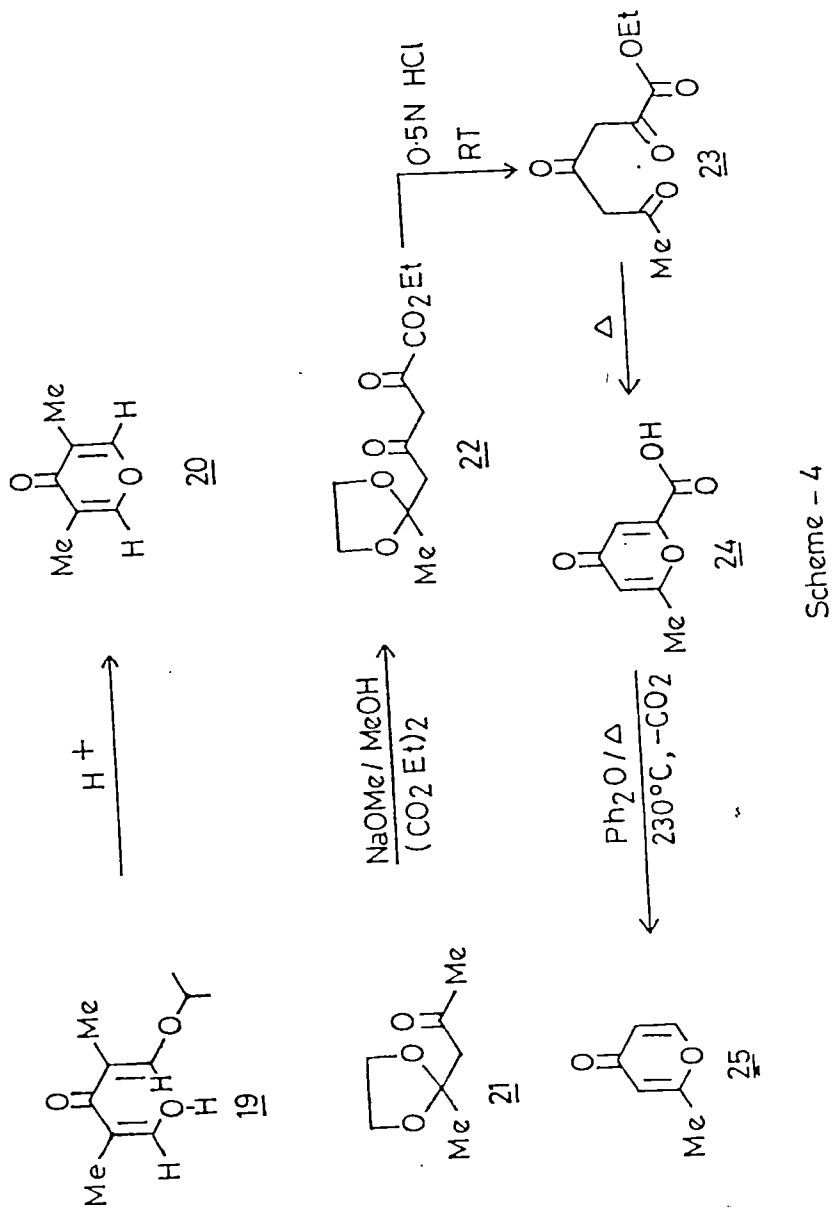

[H5C6-C≡CH]+
m/z 102(100%)
16
-ṠCH3
m/z 171(4%)
15
M+, m/z 218(53%)
13a
-(=SCH3)
m/z 146(38%)
18
-ĊH3
m/z 203(13%)
14
m/z 118(28%)
17

Scheme -3

distributed in nature, and a number of synthetic methods have been reported in the literature[4]. A few selected synthetic methods covering the literature on the construction of pyran-4-ones from open chain precursors have been reviewed as an appendix to the present chapter.

In connection with the studies on isotopic substitution, Beak and Carls[5] have reported the synthesis of 4-pyrones of general structure 20. The open chain precursor 19, was cyclized under acidic conditions to yield 3,5-dimethyl pyran 4-one in 25% yield. However, these authors have reported that their attempts to prepare 3,5-disubstituted γ-pyrones, utilizing the earlier reported methods[6], failed to because of the difficulty in condensing diethyl ketone with ethyl formate in desirable yields.

Subsequently, Dorman[7] has reported a novel approach for the synthesis of 2-methyl-4H-pyran-4-one 25 as described in the Scheme 4. The first step involved was to protect one of the carbonyl groups by ketalization of acetylacetone with ethylene glycol in the presence of p-toluene sulphonic acid. The ketal 21 was then subjected for acylation with diethyl oxalate in the presence of sodium methoxide to form the corresponding methyl 2,4-diketo-6-ethylenedioxyheptanoate 22. The ketal function was subsequently cleaved by 0.5 N hydrochloric acid to yield the triketo ester 23, which *in situ* underwent cyclization to afford the corresponding 6-methyl-4*H*-pyran-

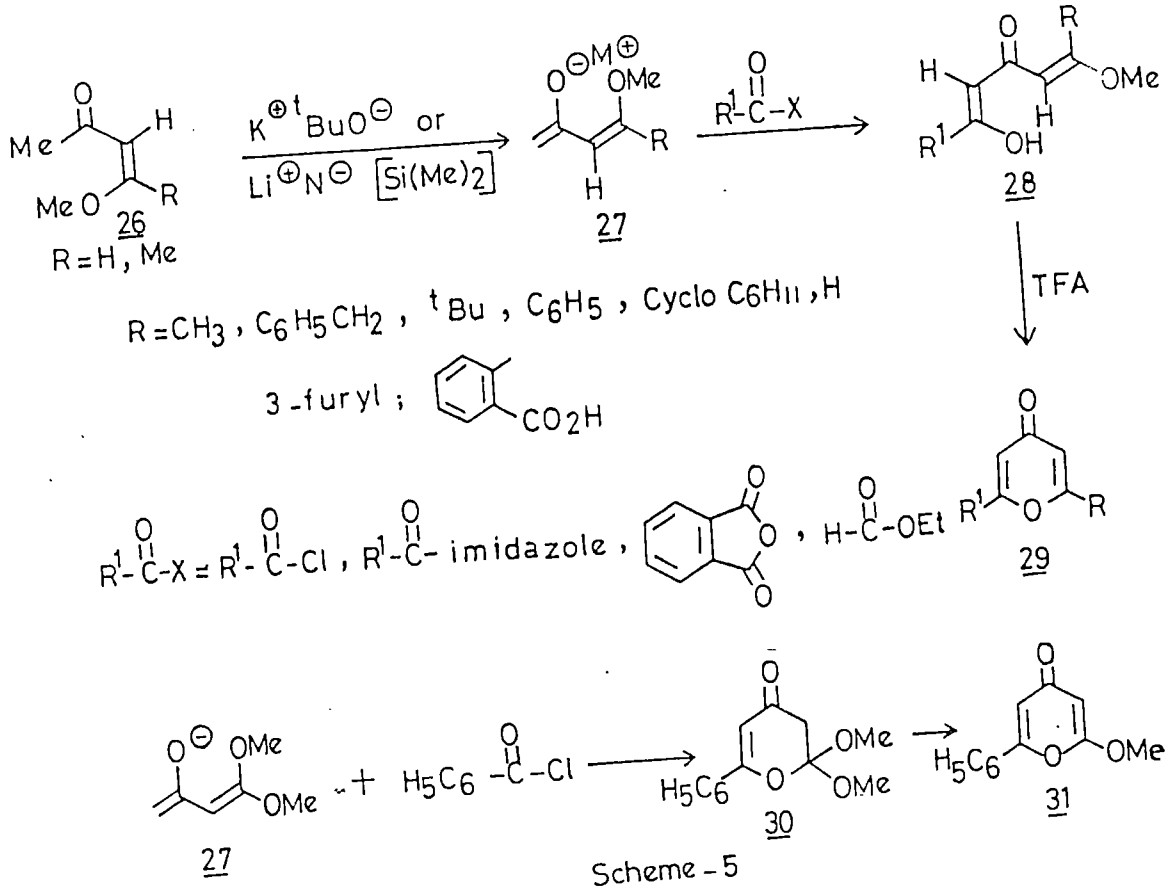

H+
NaOMe/ MeOH
(CO2 Et)2
0·5N HCl
RT
Δ
Ph2O/Δ
230°C, -CO2
19
20
21
22
23
24
25
Me
OH
OEt
CO2Et

Scheme - 4

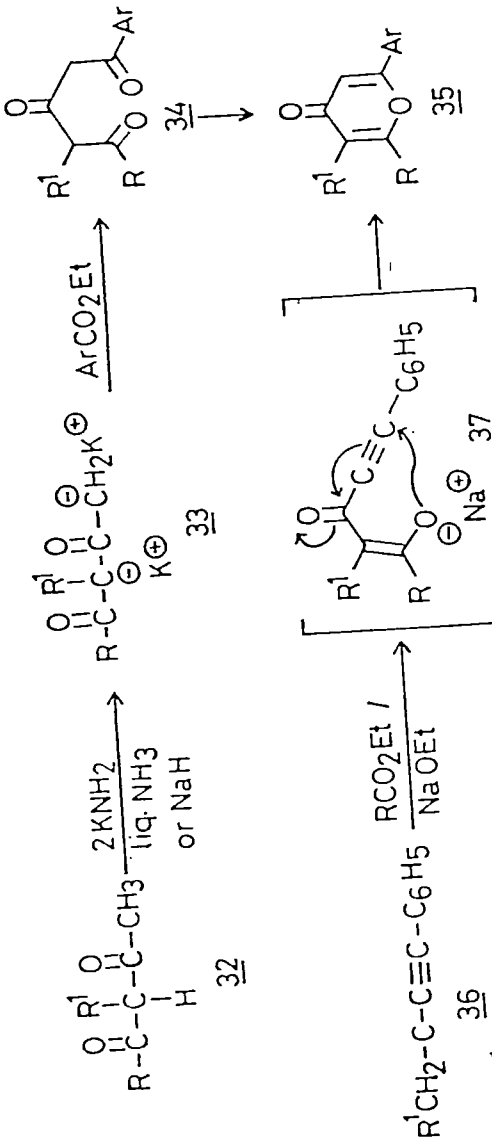
4-one-2-carboxylic acid 24. The acid 24 was converted to 2-methyl-4*H*-pyran-4-one 25 on heating in diphenyl ether.

A novel one step approach for γ-pyrone synthesis was reported by Morgan and Ganem[8], they generated the potassium enolate of 4-methoxy-3-butene-2-one 26 and reacted *in situ* with various acylating agents to afford the corresponding adduct 28. These acylated products 28 were cyclized under the same reaction conditions to yield the corresponding 2-substituted γ-pyrones 29. However, the same approach was extended by Koreeda and Akagi[9], who showed that the intermediate enols of general formula 28, obtained by condensation of 27 and acid chlorides, underwent smooth cyclization in the presence of a trace of trifluoroacetic acid as catalyst to afford the desired 2-methoxy-6-phenyl-4H-pyran-4-one 31 (Scheme 5).

The 2,5,6-trisubstituted γ-pyrones have also been prepared by Hauser and co-workers[10-12]. The required triketones 34 were obtained from the corresponding diketones 32 in moderate to good yields. Thus the dipotassium salts 33 or preferably dilithio butadiketones underwent smooth acylation with a number of aliphatic and aromatic esters to form the corresponding pyran-4-ones 35. The γ-pyrones 35, were also obtained by an alternative approach by Schiefer and Hensake[13] as shown in the Scheme 6. The phenylethynyl ketones 36 were conveniently acylated by acid esters in the presence of sodium ethoxide


Me
H
Me O
R
26
R = H, Me
K⊕ tBuO⊖ or
Li⊕ N⊖ [Si(Me)2]
O⊖ M⊕
OMe
H
R
27
R1-C-X
O
R
H
OMe
R1
OH
H
28
TFA
R = CH3 , C6H5CH2 , tBu , C6H5 , Cyclo C6H11 , H
3-furyl ;
CO2H
R1-C-X = R1-C-Cl , R1-C- imidazole ,
H-C-OEt
R1
R
29
O⊖ OMe
OMe
27
+ H5C6 -C-Cl
H5C6
OMe
OMe
30
H5C6
OMe
31

Scheme - 5



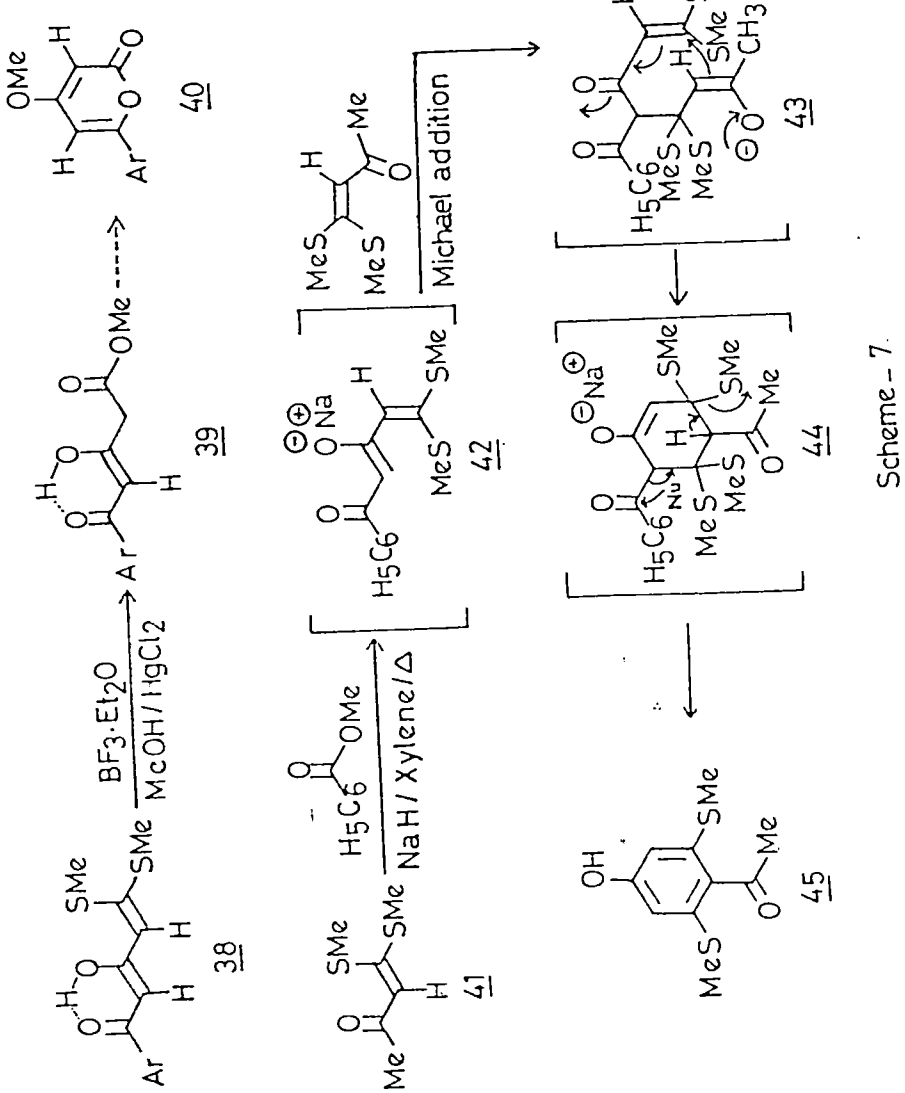
Scheme-6

to yield the corresponding sodio derivative of β-diketones 37, which instantly were cyclized to yield 35 on protonation .

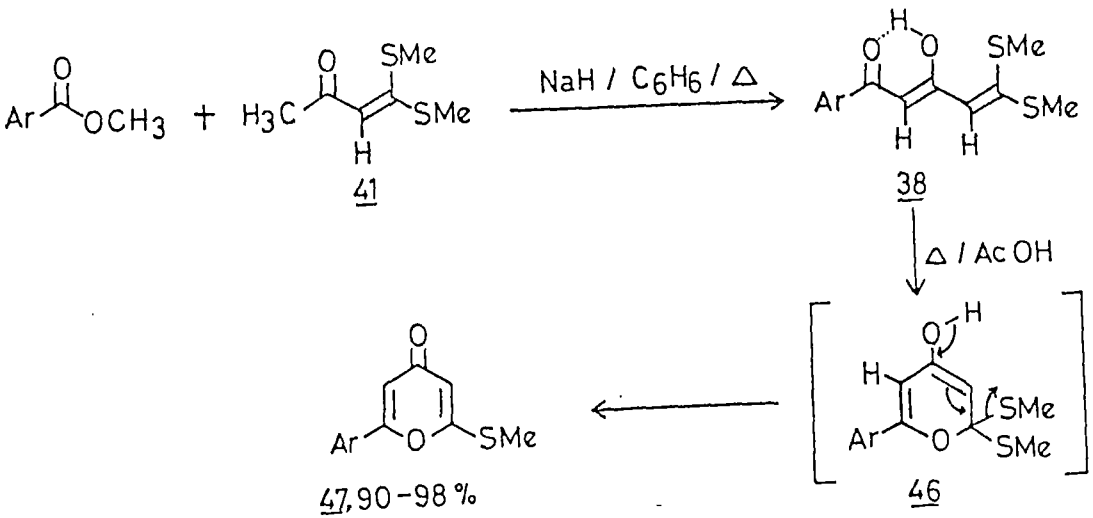
Singh, Ila and Junjappa[14,15] have studied the condensation of acylketene dithioacetals 41 with alkylbenzoates in the presence of a base to yield the corresponding diketones 38 in good yields. These diketones 38 underwent different course of cyclization reaction depending on the reaction conditions and reagents used. Thus, 38 on treatment with Hg(II) chloride and boron trifluoride in methanol afforded 6-aryl-4-methoxy-2H-pyran-2-ones 40 in high yields[13]. However, 4-hydroxy-2,6-dimethylthio acetophenone 45 was obtained[14] when 41 was refluxed with methyl benzoate in sodium hydride. Apparently the intermediate enolate anion 42 underwent Michael addition with 41 to afford the intermediate 43, which on intramolecular cyclization followed by elimination of two methylthio groups to yield 45 as shown in Scheme 7. The condensation product on treatment with acetic acid yielded the corresponding 2-methylthio-6-aryl-4H-pyran-4-ones 47 in high yields[14] (Scheme 8).

IV.3 CONCLUSION

The present method of 4*H* pyran-4-one synthesis from easily accessible α-oxoketene dithioacetals provides a new entry to hitherto unreported γ-pyrones. The 2-methylthio functionality can serve as a good leaving group which can be displaced by a suitable carbon and nitrogen



Scheme – 7



a-f, Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-$MeOC_6H_4$; 3-$MeOC_6H_4$; 2-ClC_6H_4

Scheme – 8

nucleophiles. The method however suffers from limitation since the epoxidation failed when the cinnamoyl ketene dithioacetals having substituents at 2 and 4-positions.

IV.4 EXPERIMENTAL SECTION

General

Melting points were determined on a Thomas Hoover melting point (capillary method) apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390, 90 MHz spectrometer and the chemical shift values are expressed as δ(ppm) down field from Me_4Si as internal standard. ^{13}C NMR spectra were recorded on 67.89 MHz Brucher WH-270 Spectrometer. IR and mass spectra were recorded on a Perkin-Elmer 297 Spectrophotometer and a Jeol D-300 mass spectrometer respectively. Elemental analysis were carried out on a Heraus CHN-O-RAPID instrument.

Starting materials

The commercial samples of acetone, ethylmethyl ketone, diethyl ketone, benzaldehyde, tolualdehyde, 4-chlorobenzaldehyde, 3-methoxy benzaldehyde, anisaldehyde, 3,4-dimethoxy benzaldehyde, 3,4,5-trimethoxy benzaldehyde, 3,4-methylenedioxy benzaldehyde and cinnamaldehyde were purified before use. The α-oxoketene dithioacetals were prepared according to the procedure described in Chapter II. The cinnamoyl ketene dithioacetals 1a-h, 4a-b and 5-

phenyl-2,4-pentadieneyl ketene dithioacetal were prepared according to the reported procedure[16], described in the Chapter II.

Synthesis of 5-aryl-1,1-bis(methylthio)-4,5-epoxy-1-pentene-3-ones (3) : General procedure : A solution of 30% H_2O_2 (5 ml) in 3 normal aqueous NaOH solution (5 ml) was added dropwise to a well stirred solution of α-cinnamoyl ketene dithioacetals 1 (10 mmol) in MeOH (150 ml) during 5 min. The mixture is stirred at room temperature for 6 h, diluted with water (100 ml) and left overnight in a refrigerator (0°C). The epoxy compounds 3 are filtered as white solids.

1,1-Bis(methylthio)-4,5-epoxy-5-phenyl-1-pentene-3-one (3a): white solid (89%); m.p. 82-83°C; IR and NMR data given in the text. (Found: C,58.62; H,5.3. $C_{13}H_{14}O_2S_2$ requires C,58.81; H,5.46%) m/z 266 (M^+, 5%), 250(17), 235(54), 219(37), 147(100).

1,1-Bis(methylthio)-4,5-epoxy-5-(4-methylphenyl)-1-pentene-3-one (3b) : white solid (83%); m.p. 96-97°C; ν_{max} (KBr) 1640, 1590, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.31 (3H,s,SCH_3), 2.78 (6H,s,SCH_3 and $ArCH_3$), 3.50 (1H,d,J=2.5 Hz,H-4), 3.88 (1H,d,J=2.5 Hz,H-5), 6.20 (1H,s,=CH), 7.08-7.28 (4H,m,ArH); (Found: C,59.77; H,5.61. $C_{14}H_{14}O_2S_2$ requires C, 59.97; H, 5.75%); m/z 280 (M^+,4%), 264(4), 249(13), 233(51), 147(100).

1,1-Bis(methylthio)-5-(4-chlorophenyl)-4,5-epoxy-1-pentene-3-one (3c) : white solid (80%); m.p. 105-106°C, ν_{max} (KBr) 1609, 1475 cm^{-1}; δ_H ($CDCl_3$) 2.50 (3H,s,SCH_3), 2.51(3H,s,SCH_3), 3.45(1H,d,J=2.5 Hz,H-4), 3.92 (1H,d,J=2.5 Hz,H-5), 6.25(1H,s,=CH), 7.13-7.55(4H,m,ArH); (Found: C, 51.71; H,4.67. $C_{13}H_{13}O_2S_2Cl$ requires C,51.90; H, 4.36%); m/z 300 (M^+, 10%), 302(5), 284(51), 286(20), 269(9), 271(4), 147(38).

1,1-Bis(methylthio)-4,5-epoxy-5-(4-methoxyphenyl)-1-pentene-3-one (3d) : white solid (86%); m.p.93-94°C; ν_{max} (KBr) 1636, 1609, 1488 cm^{-1}; δ_H ($CDCl_3$) 2.45 (3H,s,SCH_3), 2.46 (3H,s,SCH_3), 3.48 (1H,d,J=2.5 Hz,H-4), 3.85 (1H,d, J=2.5 Hz,H-5), 6.20 (1H,s,=CH), 6.75-7.30 (4H,m,ArH); (Found: C,56.86; H,5.61. $C_{14}H_{16}O_3S_2$ requires C,56.73; H, 5.44%); m/z 296 (M^+,18%), 280(6), 265(10), 249(100), 147(80).

1,1-Bis(methylthio)-4,5-epoxy-5-(3-methoxyphenyl)-1-pentene-3-one (3e) : white solid (78%); m.p. 84-85°C; ν_{max} (KBr) 1605, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.50 (6H,s,SCH_3), 3.42 (1H,d,J=2.5 Hz,H-4), 3.74 (3H,s,OCH_3), 3.88 (1H,d,J=2.5 Hz,H-5), 6.19 (1H,s,=CH), 6.72-7.38 (4H,m,ArH); (Found: C,56.81; H,5.56. $C_{14}H_{16}O_3S_2$ requires C,56.73; H,5.44%); m/z 296 (M^+,7%), 280(3), 265(4), 249(60), 147(100).

1,1-Bis(methylthio)-5-(3,4-dimethoxyphenyl)-4,5-epoxy-1-pentene-3-one (3f) : white solid (81%); m.p. 120-121°C; ν_{max} (KBr) 1620, 1590, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.50

(3H,s,SCH_3), 2.51 (3H,s,SCH_3), 3.55 (1H,d,J=2.5 Hz,H-4), 3.89 (7H,s,OCH_3 and H-5), 6.16 (1H,s,=CH), 6.60-6.79 (3H,m,ArH); (Found: C,55.36; H,5.71. $C_{15}H_{18}O_4S_2$ requires C,55.19; H, 5.56%); m/z M^+(absent), 310(17), 295(20), 279(15), 263(100), 147(82).

1,1-Bis(methylthio)4,5-epoxy-5-(3,4,5-trimethoxyphenyl)-1-pentene-3-one (3g) : white solid (80%); m.p. 184-185°C; ν_{max} (KBr) 1626, 1590, 1479 cm^{-1}; δ_H ($CDCl_3$) 2.49 (3H,s,SCH_3), 2.52(3H,s,SCH_3), 3.49 (1H,d,J=2.5Hz,H-4), 3.68 (3H,s,OCH_3), 3.80 (6H,s,OCH_3), 3.92 (1H,d,J=2.5 Hz,H-5), 6.28(1H,s,=CH), 6.58 (2H,s,ArH); (Found: C,53.78; H,5.49. $C_{16}H_{20}O_5S_2$ requires C,53.91; H,5.66%); m/z 356 (M^+,0.5%), 309(12), 147(92).

1,1-Bis(methylthio)-4,5-epoxy-5-(3,4-methylenedioxyphenyl)-1-pentene-3-one (3h) : white solid (83%); m.p. 124-125°C; ν_{max}(KBr) 1660, 1570 cm^{-1}; δ_H ($CDCl_3$) 2.49 (6H,s,SCH_3), 3.42 (1H,d,J=2.5 Hz,H-4), 3.82 (1H,d,J=2.5 Hz,H-5), 5.96 (2H,s,CH_2), 6.20 (1H,s,=CH), 6.62-6.90 (3H,m,ArH); (Found: C,54.32; H,4.86. $C_{14}H_{14}O_4S$ requires C,54.17; H,4.55%), m/z 310(M^+,5%), 294(3), 279(9), 263(73), 147(100).

Synthesis of 2-aryl-5,5-bis(methylthio)-3-hydroxy-2,4-pentadienals (10) : General Procedure : To a solution of 3 (10 mmol) in THF (50 ml), $Et_2O.BF_3$ (16 ml) is added and the mixture is refluxed for 5 h. The mixture is cooled and poured over ice cold saturated $NaHCO_3$ solution (200 ml). The product is extracted with EtOAc (4 x 50 ml), washed with water (3 x 100 ml), dried (Na_2SO_4) and concentrated

to give 10 as bright yellow to orange-red solids. These are used as such for subsequent reaction and crystallized from ether/$CDCl_3$ for spectral and analytical data.

5,5-Bis(methylthio)-3-hydroxy-2-phenyl-2,4-pentadienal (10a) : yellow crystals (92%); m.p. 158-159°C; IR and PMR data given in the text. $\delta_C(CDCl_3)$ 16.38(q,SCH_3), 17.67 (q,SCH_3), 106.32 (d,=CH), 115.7 (s,Ar-C=), 128.49, 129.07, 130.26 (d,Ar), 132.80 (s,C-1'of phenyl), 169.70 (d,CHO), 176.50 (s,=$C(SCH_3)_2$); 181.5 (s,HOC=); (Found: C,58.74; H,5.42. $C_{13}H_{14}O_2S_2$ requires C,58.62; H,5.3%); m/z 266 (M^+); 267 (M^++1).

5,5-Bis(methylthio)-3-hydroxy-2-(4-methylphenyl)-2,4-pentadienal (10b) : orange-red crystals (86%); m.p. 159-160°C; γ_{max}(KBr) 3200, 2830, 1595, 1480 cm^{-1}; $\delta_H(CDCl_3)$ 2.26 (3H,s,SCH_3), 2.40 (3H,s,SCH_3), 2.63 (3H,s,CH_3), 5.90 (1H,s,=CH), 7.05-7.50 (4H,m,ArH), 7.28 (1H,s,CHO); (Found: C,59.83; H,5.57. $C_{14}H_{16}O_2S_2$ requires C,59.97; H,5.75%); m/z 280 (M^+), 281 (M^++1).

5,5-Bis(methylthio)-2-(4-chlorophenyl)-3-hydroxy-2,4-pentadienal (10c) : yellow crystals (87%); m.p. 154-165°C; γ_{max}(KBr) 3200, 2840, 1595, 1500, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.26 (3H,s,SCH_3), 2.60(3H,s,SCH_3), 5.82 (1H,s,=CH), 7.05-7.50 (4H,m,A_2B_2,ArH), 7.65 (1H,s,CHO); (Found: C,51.76; H,4.23. $C_{13}H_{13}ClO_2S_2$ requires C, 51.90; H, 4.36%); m/z 300, 302 (M^+), 301,303 (M^++1).

5,5-Bis(methylthio)-3-hydroxy-2-(4-methoxyphenyl)-2,4-pentadienal (10d) : yellow crystals (88%); m.p. 140-141°C; γ_{max}(KBr) 3210, 2825, 1600, 1520, 1485 cm^{-1}; δ_H ($CDCl_3$) 2.20 (3H,s,SCH_3), 2.55 (3H,s,SCH_3), 3.80 (3H,s,OCH_3), 5.81 (1H,s,=CH), 6.75-7.26 (4H,m,A_2B_2,ArH), 7.66 (1H,s,CHO); (Found: C,56.88; H,5.57. $C_{14}H_{16}O_3S_2$ requires C, 56.73; H,5.44%); m/z 296 (M^+), 297 (M^++1).

5,5-Bis(methylthio)-3-hydroxy-2-(3-methoxyphenyl)-2,4-pentadienal (10e): yellow crystals (85%); m.p. 154-155°C; γ_{max}(KBr) 3250, 2825, 1590, 1490, 1475 cm^{-1}; δ_H ($CDCl_3$) 2.14 (3H,s,SCH_3), 2.50 (3H,s,SCH_3), 3.70 (3H,s,OCH_3) 5.83 (1H,s,=CH), 6.78-7.80 (4H,m,ArH), 7.70 (1H,s,CHO); (Found: C,56.88; H, 5.53. $C_{14}H_{16}O_3S_2$ requires C,56.73; N, 5.44%); m/z 296 (M^+), 297 (M^++1).

5,5-Bis(methylthio)-2-(3,4-dimethoxyphenyl)-3-hydroxy-2,4-pentadienal (10f): orange-yellow crystals (86%); m.p. 197-198°C; γ_{max}(KBr) 3215, 2831, 1590, 1495 cm^{-1}; δ_H ($CDCl_3$) 2.21 (3H,s,SCH_3), 2.60 (3H,s,SCH_3), 3.83 (6H,s,OCH_3), 5.84 (1H,s,=CH), 6.65-6.86 (3H,m,ArH), 7.66 (1H,s,CHO); (Found: C, 55.32; H, 5.71. $C_{15}H_{18}O_4S_2$ requires C,55.19; H,5.56%); m/z 327 (M^++1).

5,5-Bis(methylthio)-3-hydroxy-2-(3,4,5-trimethoxyphenyl)-2,4-pentadienal (10g): yellow crystals (88%); m.p. 178-179°C; γ_{max}(KBr) 3200, 2825, 1590, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.20 (3H,s,SCH_3), 2.57 (3H,s,SCH_3), 3.88 (9H,s,OCH_3), 5.90 (1H,s,=CH), 6.49 (2H,s,ArH), 7.44 (1H,s,CHO); (Found:

C,53.78; H,5.43. $C_{16}H_{20}O_5S_2$ requires C, 53.91; H,5.66%); m/z 357 (M^++1).

5,5-Bis(methylthio)-3-hydroxy-2-(3,4-methylenedioxy-phenyl)-2,4-pentadienyl (10h) : yellow crystals (84%); m.p. 174-175°C; ν_{max}(KBr) 3200, 2838, 1595, 1498, 1480 cm^{-1}; δ_H ($CDCl_3$) 2.30 (3H,s,SCH_3), 2.60 (3H,s,SCH_3), 5.81 (1H,s,=CH), 5.99 (2H,s,CH_2), 6.60-6.82 (3H,m,ArH), 7.67 (1H,s,CHO); (Found: C,54.28; H,4.69. $C_{14}H_{14}O_4S_2$ requires C,54.17; H,4.55%); m/z 310(M^+), 311 (M^++1).

Synthesis of 5-aryl-2-methylthio-4H-pyran-4-ones (13): **General Procedure:** A solution of 10 (7.5 mmol) in ethanol (15 ml) and glacial acetic acid (5 ml) is refluxed for 3-5h, cooled and poured over ice cooled saturated $NaHCO_3$ solution (70 ml). The product is extracted with CH_2Cl_2 (3 x 50 ml), dried (Na_2SO_4), evaporated and the residue is chromatographed on a neutral alumina column using EtOAc and hexane (1:20) as eluent to afford 13, as colorless solids which are crystallized from $CHCl_3$/hexane.

2-Methylthio-5-phenyl-4*H*-pyran-4-one (13a) : colorless IR and NMR data given in the text. (Found: C,66.18; H,4.83. $C_{12}H_{10}O_2S$ requires C,66.01; H,4.62%); m/z 218 (M^+,53%), 203(13), 146(38), 118(28), 102(100).

2-Methylthio-5-)4-methylphenyl)-4*H*-pyran-4-one (13b): colorless crystals (72%); m.p. 109-110°C; ν_{max}(KBr) 1630 cm^{-1}; δ_H ($CDCl_3$) 2.33 (3H,s,CH_3), 2.45 (3H,s,SCH_3), 6.28 (1H,s,H-3), 7.10-7.45 (4H,m,A_2B_2,ArH); (Found: C,67.46;

H,5.38. $C_{13}H_{12}O_2S$ requires C,67.21; H,5.21%); m/z 232 (M^+,48%), 217(11), 160(48), 132(14), 116(100).

5-(4-chlorophenyl)-2-methylthio-4*H*-pyran-4-one (13c): colorless crystals (76%); m.p. 114-115°C; ν_{max}(KBr) 1650 cm^{-1}; δ_H($CDCl_3$) 2.47 (3H,s,SCH_3), 6.28 (1H,s,H-3), 7.20-7.49 (4H,m,A_2B_2,ArH), 7.78 (1H,s,H-6); (Found: C,57.18; H,3.72. $C_{12}H_9ClO_2S$ requires C,57.03; H,3.59%); m/z 254(27%), 252(78), 239(7), 237(25), 182(20), 180(57), 154(9), 152(20), 138(47), 136(100).

2-Methylthio-5-(4-methoxyphenyl)-4*H*-pyran-4-one (13d) : colorless crystals (73%); m.p. 139-140°C; ν_{max}(KBr) 1632; δ_H($CDCl_3$) 2.45 (3H,s,SCH_3), 3.80 (3H,s,OCH_3), 6.29 (1H,s,H-3), 6.82-7.56 (4H,m,A_2B_2,ArH), 7.77 (1H,s,H-6); (Found : C,62.96; H,4.99. $C_{13}H_{12}O_3S$ requires C,62.88; H,4.87%); m/z 248 (M^+,100%), 2.33(15), 176(69), 148(10), 132(63).

2-Methylthio-5-(3-methoxyphenyl)-4*H*-pyran-4-one (13e): oil (72%); ν_{max}($CHCl_3$) 1635 cm^{-1}; δ_H ($CDCl_3$) 2.48 (3H,s,SCH_3), 3.80 (3H,s,OCH_3), 6.19 (1H,s,H-3), 6.73-7.37 (4H,m,ArH), 7.78 (1H,s,H-6); (Found: C,62.97; H,4.96. $C_{13}H_{12}O_3S$ requires C,62.88; H,4.87%); m/z 248(M^+, 100%), 233(17), 176(39), 148(80), 132(65).

5-(3,4-Dimethoxyphenyl)-2-methylthio-4*H*-pyran-4-one (13f): colorless crystals (70%); m.p. 144-145°C; ν_{max}(KBr) 1640 cm^{-1}; δ_H ($CDCl_3$) 2.45 (3H,s,SCH_3), 3.82 (6H,s,OCH_3), 6.19 (1H,s,H-3), 6.68-7.17 (3H,m,ArH), 7.72 (1H,s,H-6); (Found:

C,60.63; H,5.21. $C_{14}H_{14}O_4S$ requires C,60.42; H, 5.07%); m/z 278 (M^+,100%), 263(7), 206(4), 178(30), 162(25).

2-Methylthio-5-(3,4,5-trimethoxyphenyl)-4*H*-pyran-4-one (13g) : colorless crystals (69%); m.p. 63-69°C; ν_{max}(KBr) 1637 cm^{-1}; δ_H ($CDCl_3$) 2.45 (3H,s,SCH_3), 3.71 (3H,s,OCH_3), 3.81 (6H,s,OCH_3), 6.15 (1H,s,H-3), 6.60 (2H,s,ArH), 7.69(1H,s,H-6); (Found : C,58.63; H, 5.41. $C_{15}H_{16}O_5S$ requires C,58.41; H, 5.23%); m/z 308 (M^+,21%); 293(26), 208(7), 192(65).

2-Methylthio-5-(3,4-methylenedioxyphenyl)-4*H*-pyran-4-one (13h): colorless crystals (71%); m.p. 144-145°C; ν_{max}(KBr) 1625 cm^{-1}; δ_H($CDCl_3$) 2.46 (3H,s,SCH_3), 5.95 (2H,s,CH_2), 6.25 (1H,s,H-3), 6.77-7.05 (3H,m,ArH), 7.72 (1H,s,H-6); (Found: C,59.71; H,3.98. $C_{13}H_{10}O_{14}S$ requires C,59.52; H,3.84%); m/z 262 (M^+,100%), 247 (12), 190(71), 162(100), 146(64).

IV.5 REFERENCES

1. (a) Deb, B.; Asokan, C.V.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* 1988 *29*, 2111;
2. Bach, R.D.; Knight, J.W. *Org.Synth.*, 1981, *60*, 63.
3. Brogden, P.J.; Gobutt, C.D.; Hepworth, J.D. in : *Comprehensive Heterocyclic Chemistry*; Vol 3, Part 2B, Boulton, A.J.; McKillop, A.; Eds., Pergamon Press, Oxford, 1984, p. 611.
4. Hepworth, J.D. in : *Comprehensive Heterocyclic Chemistry*, Vol. 3, Part 2B, Boulton, A.J.; McKillop, A.; Pergamon Press, Oxford, 1984, p. 810-816 and references cited therein.
5. Beak, P.; Carls, G.A. *J.Org.Chem.*, 1964, *29*, 2678.
6. Benary, E.; Bitter, G.A. *Ber.* 1928, *61*, 1057.
7. Dorman, L.C. *J.Org.Chem.* 1967, *32*, 4105.
8. Morgan, T.A.; Ganem, B. *Tetrahedron Lett.* 1980, *21*, 2773.
9. Koreeda, M.; Akagi, H. *Tetrahedron Lett.*, 1980, *21*, 1197.
10. Hauser, C.R.; Harris, T.M. *J.Am.Chem.Soc.*, 1958, *80*, 6360.
11. Light, R.J.; Hauser, C.R. *J.Org.Chem.* 1960, *25*, 538.
12. Work, S.D.; Hauser, C.R. *J.Org.Chem.* 1963, *28*, 725.
13. Schiefer, H.; Henseke, G. *Angew.Chem.Int.Ed.Engl.* 1965, *4*, 527.
14. Singh, L.W.; Ila, H.; Junjappa, H. unpublished results.

15. Singh, L.W.; Ila, H.; Junjappa, H. *Synthesis* 1987, 873.

16. Thuiller, A.; Vialle, J. *Bull.Soc.Chim.Fr.*, 1962, 2181.