# SYNTHETIC STUDIES ON HETEROCYCLES OF BIOLOGICAL INTEREST
# AND
# REARRANGEMENT STUDIES ON CYCLOPROPYL KETONES

*By*

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DEDICATED IN THE MEMORY OF MY LATE UNCLE,

GRANDFATHER AND GRANDMOTHER

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

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# *PREFACE*

The α-oxoketene dithioacetals are a versatile group of 3-carbon fragments having ambident 1,3-electrophilic centres thus permitting to design various methodologies for both carbocyclic and heterocyclic syntheses. The differential electrophilicity of 1,3-carbon centres of these compounds has been exploited thoroughly by our group's continued efforts for the construction of new C-N and C-C bonds involving either 1,2- or 1,4- nucleophilic additions leading to a number of general synthetic routes for a wide range of organic molecules.

The work presented in this thesis is a part of our ongoing investigations on α-oxoketene S,S-, S,N- and O,S-acetals and cyclopropyl substituted oxoketene dithioacetal.

The first chapter brings a brief review on the reactivity of oxoketene dithioacetals. The use of oxoketene dithioacetals for a range of heterocycles, carbocycles, aromatics and heteroaromatics as well as construction of cyclopentanoids through acid catalyzed ring opening of cyclopropyl ketone is given.

A new efficient route to substituted carbazoles particularly having C-ring regiocontrolled substituents through the reaction of 1-alkylindole-3-acetonitrile with various α-oxoketene S,S-, N,S- and O,S-acetals is presented in second chapter.

Third chapter deals with aromatic annelation studies on S,S- acetal derived from 1,2,3,4-tetrahydro-N-benzenesulfonylquinol-4- one. The synthesis of a large variety of phenanthridines and benzo[j]phenanthridines is carried out following this route.

The acid catalyzed rearrangement studies on styryl cyclopropyl ketones via tandem carbocationic cyclization affording cyclopentanoids are described in the last chapter.

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## *CHAPT - 1*

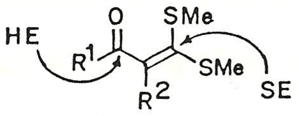
# POLARIZED KETENE DITHIOACETAL AS VERSATILE INTERMEDIATE IN ORGANIC SYNTHESIS: A BRIEF REVIEW

The versatile synthon family of polarized ketene dithioacetal has been proved to be among the simplest and potential synthetic intermediates in various synthetic transformations.[1] This family of compounds can be prepared conveniently from a wide variety of active methylene compounds by condensation of the corresponding enolate with carbon disulfide or trithiocarbonate followed by alkylation of the intermediate dithiolate species often in one pot operation in moderate to good yield.[2-9] They exhibit well defined physical properties either as crystalline solids or distillable liquids and can be purified by conventional chromatographic methods. They are stable at room temperature and can withstand mild acidic and alkaline conditions.

## 1.1 The polarized ketene dithioacetal

Kelber and co-workers reported the first synthesis of α-oxoketene dithioacetal in 1910.[10-11] However, the chemistry of these intermediates remained unexplored until Thuillier and co-workers prepared these compounds in higher yields using sodium amylate as base.[2-5] Subsequently, these reaction conditions have been greatly improved using different bases and careful manipulation of reaction conditions.[4,6-9] A large number of α-oxoketene dithioacetals have now been reported and they have emerged as very useful synthetic intermediates over the last two decades.[1]

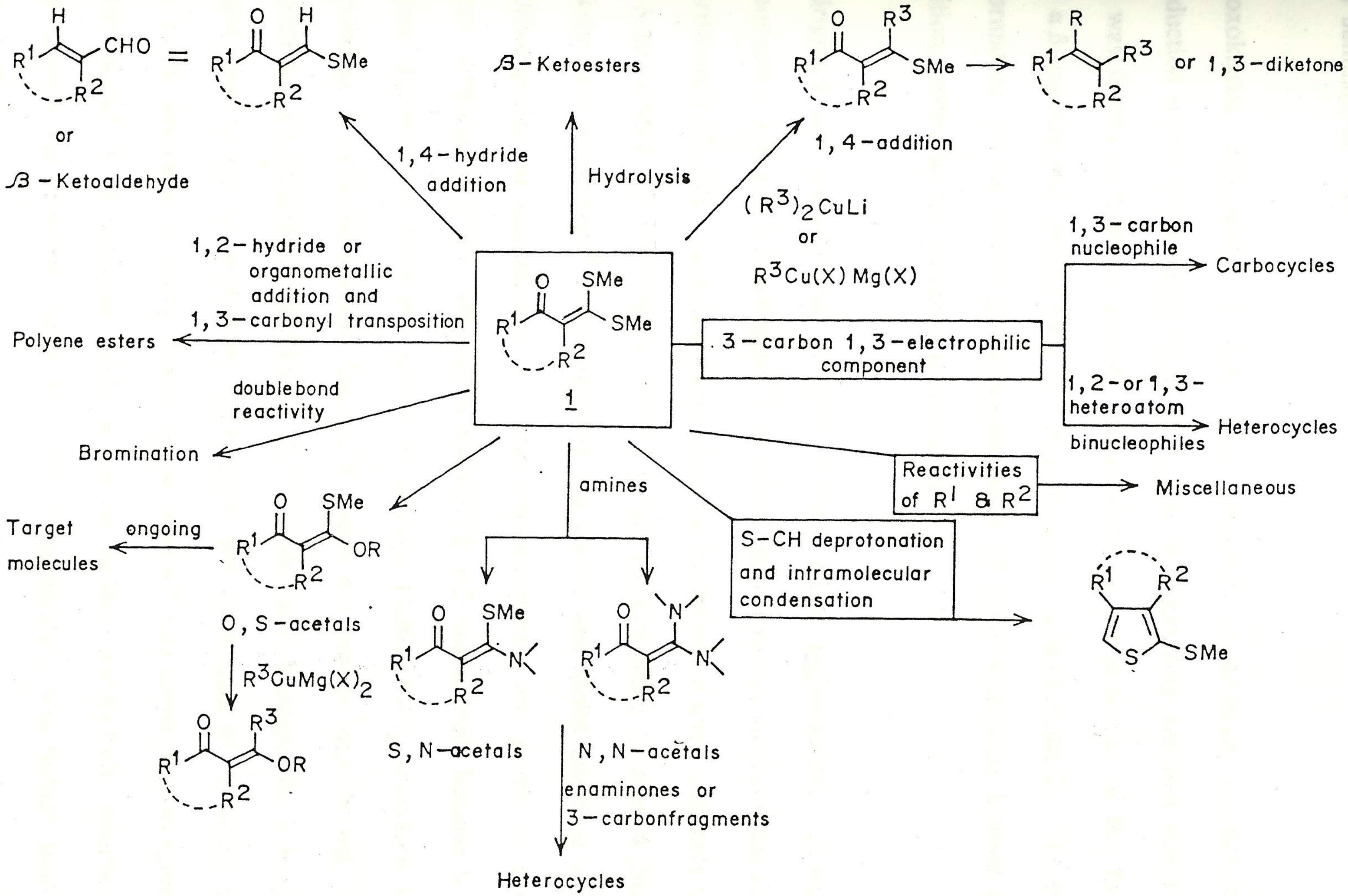
The oxoketene dithioacetals which can be prepared by easier methods in one pot and in high yields exhibit greater stability than the corresponding O,O-acetals,[12] which are moisture sensitive and undergo hydrolysis under mild conditions. They can be further converted to the corresponding ketene dihalogenides[13,14], N,S-[15], N,N-[16] and O,S-[17]acetals making them more important as precursors for a large variety of functionalized acetals. The oxoketene dithioacetals can also be visualized as masked ß-ketoester in which the ester functionality is manifested as a ketene dithioacetal moiety. Alternatively, they may be considered as α,ß-unsaturated ketones containing a highly functionalized carbon. The α-oxoketene dithioacetals have been shown to be excellent three carbon fragments possessing 1,3- electrophilic centres with differing electrophilic properties.[1]



HE = Hard electrophile
SE = Soft electrophile

Taking advantage of this difference, they have been exploited to construct stereo and regioselective bonds in various transformations. The oxoketene S,S-, N,S- N,N- and O,S-acetals have been extensively utilized in this laboratory for the synthesis of both heterocyclic and carbocyclic compounds.

Various reactivity profiles of α-oxoketene dithioacetals of general formula **1** are outlined in Scheme-1. Hydrides and organometallic reagents give 1,2-addition product characteristic of carbonyl function reactivity[18] but this sequence can be altered to the 1,4-path by suitably manipulating the reaction conditions and reagents.[18-20] Further transformations after the initial 1,2- or 1,4-addition have also been investigated extensively.[18] The α-oxoketene dithioacetal possess typical 1,3- electrophilic centres. These intermediates react with 1,2- and 1,3-heteroatom binucleophiles to give 5- and 6-membered heterocyclic compounds. The 1,3-carbon nucleophiles have been similarly used in the synthesis of carbocycles. The enolate anion formed by the deprotonation (when R=alkyl) can undergo condensation with aldehydes to give α-enoyl ketene dithioacetals.[3b,21] An allylic anion formation has been reported when $R^2$ is a methyl group leading to rearranged products.[22] Deprotonation of thiomethyl group followed by intramolecular aldol type condensation to afford thiophene is also reported.[23] As discussed, the α-oxoketene dithioacetal can be easily converted to O,S-, N,S- and N,N-acetals. They ($R^2$=H) also undergo bromination at α-position with N-bromosuccinimide.[24] Thus it is apparent that the α-oxoketene dithioacetal of general formula **1** constitute an important class of synthons with reactive electrophilic as well as nucleophilic centres distributed in various centres of its skeleton permitting

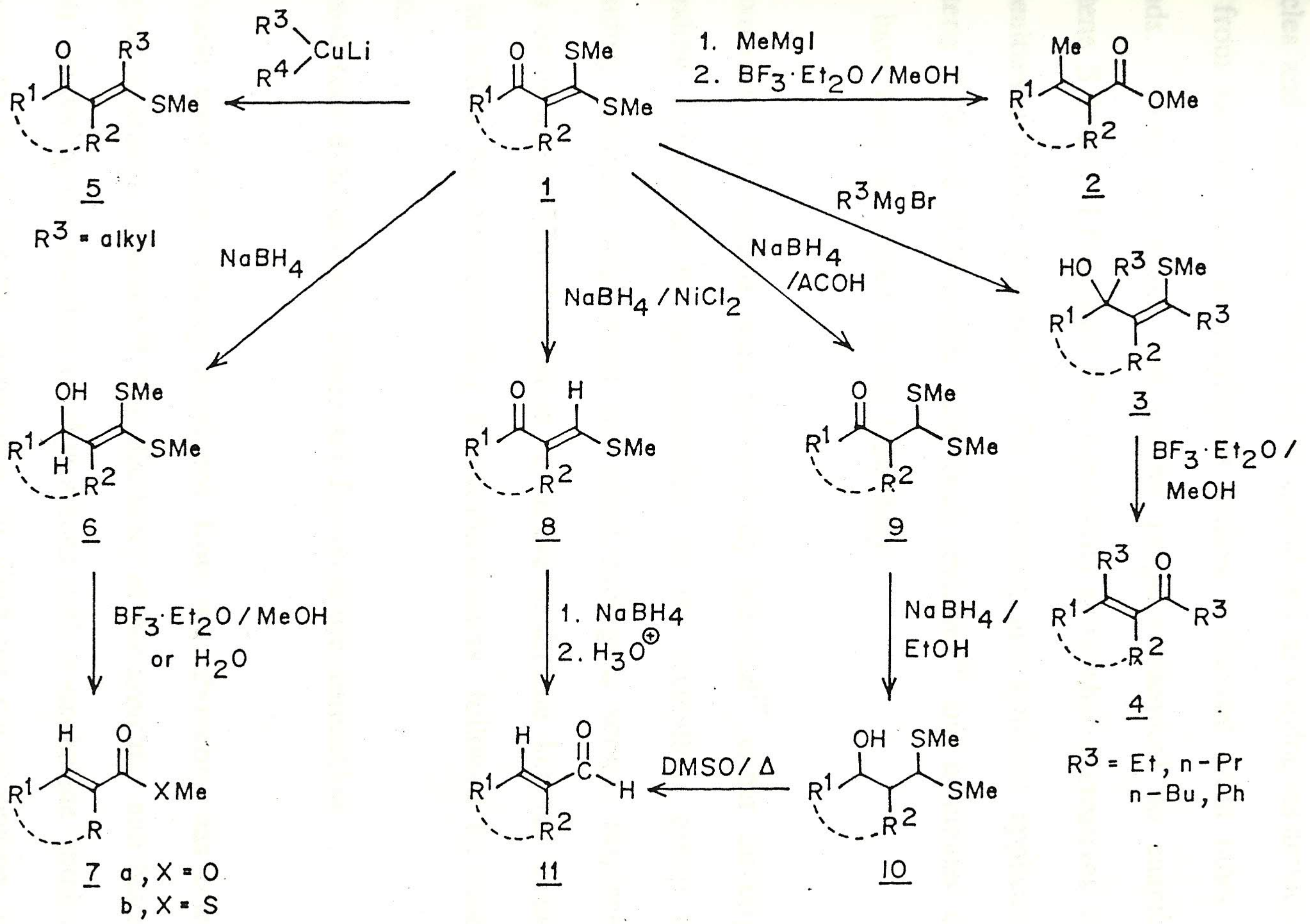

or
β-Ketoaldehyde
1,4-hydride addition
β-Ketoesters
Hydrolysis
1,4-addition
or 1,3-diketone
(R³)₂CuLi
or
R³Cu(X)Mg(X)
1,2-hydride or organometallic addition and 1,3-carbonyl transposition
Polyene esters
1
3-carbon 1,3-electrophilic component
1,3-carbon nucleophile
Carbocycles
1,2-or 1,3-heteroatom binucleophiles
Heterocycles
doublebond reactivity
Bromination
Reactivities of R¹ & R²
Miscellaneous
amines
Target molecules
ongoing
S-CH deprotonation and intramolecular condensation
O,S-acetals
R³CuMg(X)₂
S,N-acetals
N,N-acetals
enaminones or 3-carbonfragments
Heterocycles

Scheme – 1

reactions of great synthetic importance. Some of the important transformations are briefly summarized below.

The oxoketene dithioacetal **1** have been reported to undergo chemoselective 1,2-reduction with sodium borohydride to give the corresponding carbinol acetal **6**[25,26], which was shown to undergo smooth methanolysis in the presence of $BF_3.Et_2O$ to afford α,ß- unsaturated methyl ester **7a**[26] in quantitative yield (Scheme-2). The overall transformation can be viewed as the homologation of active methylene ketones at the α-position, involving 1,3- carbonyl transposition.

The Grignard and organolithium reagents undergo either regioselective 1,2-addition or a sequential 1,4- and 1,2- addition[18-20] to afford the α-hydroxy vinyl sulfides **3**. The borontrifluoride-etherate catalyzed solvolysis or the hydrolysis of these carbinols yield[18] either ß-substituted α,ß-unsaturated esters **2** or the corresponding ketenes **4** (Scheme 2). Dieter and co-workers[19,20] have reported the chemo and stereo selective addition of organocuprates to dithioacetals **1**. Thus organocuprates are shown to undergo conjugate addition to give ß- alkylthio-ß-substituted α,ß-unsaturated ketones **5**. The oxoketene dithioacetals were also shown to undergo $NaBH_4/NiCl_2$ reduction to the corresponding ß-methylthioalkenyl ketones **8** which are further transformed to the corresponding α,ß-unsaturated aldehydes **11**.[27] The exclusive regiospecific 1,4-addition of hydride ion to the α- oxoketene dithioacetal was accomplished by using excess $NaBH_4$ in the presence of strong proton donor solvent[28] like acetic acid to afford the ß-oxodithioacetal **9** in moderate yield which on further borohydride treatment in ethanol affords the carbinol acetal **10**. The carbinolacetal was further heated in DMSO to afford the corresponding α,ß-unsaturated aldehyde **11** in high yield.[29]



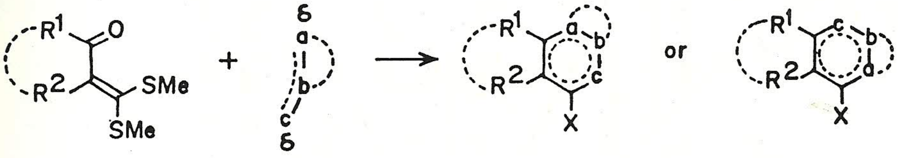
Scheme – 2

Like oxoketene S,S-acetals, the S,N- and N,N-acetals also possess 1,3-electrophilic centres and undergo a number of reactions with various binucleophiles to yield various heterocycles and carbocycles. They can be considered as vinylogous amides if they are derived from ketones and as vinylogous amines if derived from other methylene compounds. They are stable and exhibit property identical to enamines. The α-oxoketene S,N-and N,N-acetals were considered as suitable alternatives to enamines in the Nenitzescu indole synthesis.[30] The chemistry and synthetic applications of the α-oxoketene S,N- and N,N-acetals have been reviewed[1b] and a number of synthetic methods have been developed in this laboratory.

The α-oxoketene O,S-acetals were conveniently prepared[17] either directly from the corresponding S,S-acetals by quarternization of the methylthio group to give the corresponding activated sulphonium salt which undergoes smooth displacement with alkoxides or by alkoxythiocarbonylation of active methylene ketones in the presence of base to afford the corresponding ß- oxothionoesters followed by base catalyzed alkylation.

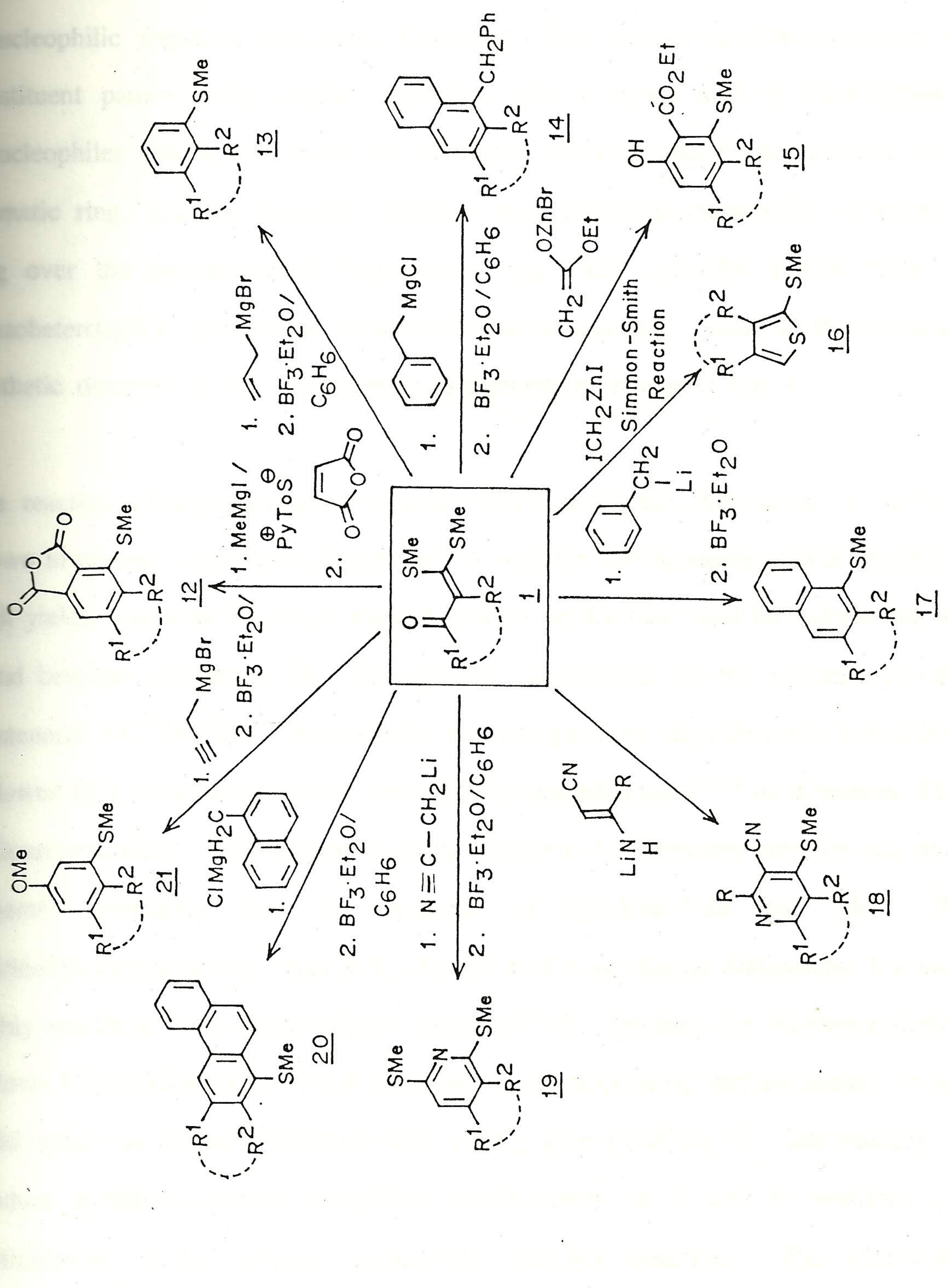
## I.2 α-Oxoketene dithioacetals: Precursor for aromatic annelation

The aromatic annelation strategy developed from our laboratory has emerged as an area of great synthetic potential.[61] The discovery of our aromatic and heteroaromatic annelation involving the reaction of allyl anions with α-oxoketene dithioacetals has been shown to be of general application to yield the corresponding benzenoids, naphthalenes, polycyclic aromatic and heteroaromatic compounds in good yields. The overall process was aimed at creating an aromatic (or heteroaromatic) system with diverse structural features from the easily available acyclic aliphatic precursors. The method offers for the first time a one pot reaction process for the construction of aromatic rings from the open chain precursors involving the combination of two 3-carbon fragments of which one possesses 1,3-dielectrophilic centres and the other 1,3-binucleophilic centres.



X = SMe or H

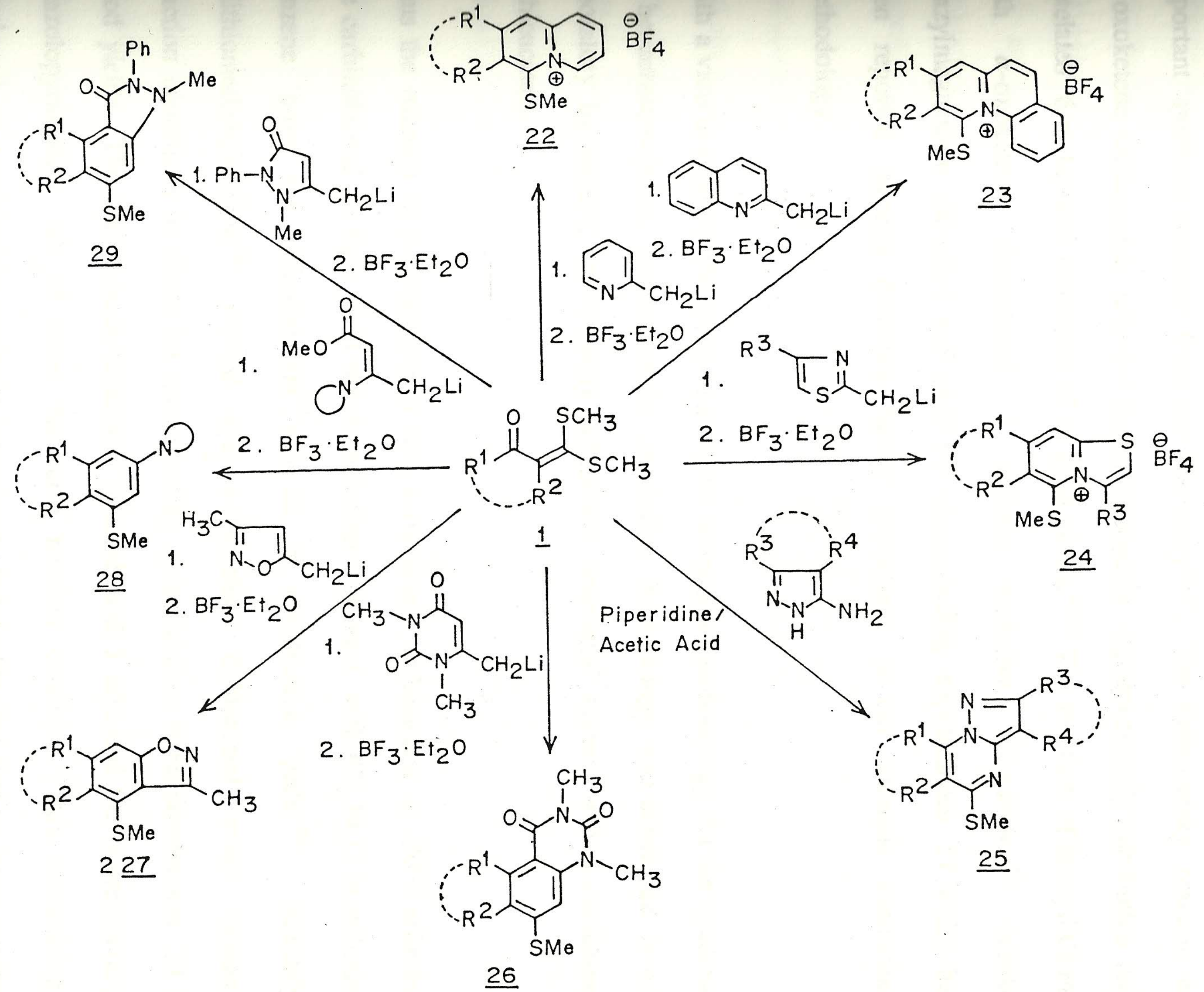
The α-oxoketene dithioacetals **1** derived from a variety of active methylene ketones and aldehydes constitute a large number of 1,3-electrophilic fragments that lend scope for liberal structural variation in the product aromatics. Similarly a variety of allyl anions have been shown to undergo facile 1,2-addition (Scheme-3 & 4) to the α-oxoketene dithioacetals to give the corresponding carbinolacetals in nearly quantitative yields. The carbinolacetals were then subjected insitu with Lewis acid catalyzed cyclization to afford the corresponding benzoannelated product. Thus a large variety of benzenoids, naphthalenes, phenanthrenes, anthracenes, benzanthracenes and many other condensed aromatics were synthesized by choosing appropriate allyl, benzyl, 1-(or 2-) naphthylmethyl anions and α-oxoketene dithioacetals. For the synthesis of substituted benzenes this approach is novel since the literature methods follow the substitution on the preconstructed aromatic ring. Such an approach suffers some limitations due to rigid aromatic orientation. In the present method the desired


1
12
13
14
15
16
17
18
19
20
21
SMe
1. MeMgI / $\overset{\oplus}{\text{Py}}\text{Tos}^{\ominus}$
2. maleic anhydride
1. allylMgBr
2. $BF_3\cdot Et_2O/C_6H_6$
1. PhCH2MgCl
2. $BF_3\cdot Et_2O/C_6H_6$
$CH_2=C(OZnBr)OEt$
$ICH_2ZnI$
Simmon-Smith Reaction
1. $PhCH_2Li$
2. $BF_3\cdot Et_2O$
LiNH–C(R)=CH–CN
1. $N\equiv C-CH_2Li$
2. $BF_3\cdot Et_2O/C_6H_6$
1. $ClMgH_2C$-naphthyl
2. $BF_3\cdot Et_2O/C_6H_6$
1. propargylMgBr
2. $BF_3\cdot Et_2O/$
$CH_2Ph$
$CO_2Et$
OH
OMe
CN
R
R1
R2

Scheme–3

substituents could be placed either in the open chain dielectrophilic fragment or in the binucleophilic fragment or in both, if required. Thus we can exercise control on the substituent pattern in the product aromatics. Also a variety of 1- or 1,3-heteroatom binucleophiles can be used so that an heteroatom or atoms can be incorporated in the aromatic ring. Another important variation is the successful construction of aromatic ring over the preconstructed heterocyclic ring which provides a new route for benzoheterocycles and related condensed heteroaromatics. Some of the important synthetic outcome of this methodology is depicted in Scheme-3 and 4.

The reaction of allylmagnesium bromide with α-oxoketene dithioacetal **1** has been shown to undergo exclusive 1,2-addition[31] to yield the corresponding carbinolacetals in high yields, which on $BF_3.Et_2O$ assisted cationic cyclization yield the substituted and fused benzene derivatives **13**. The approach is extended for the synthesis of other benzenoids **14**,[32]**20**,[33]**21**.[34] Interestingly, benzylmagnesium chloride reacts 1,4-addition followed by 1,2-addition sequence leading to benzyl substituted[32,33] naphthalenes **14** on cycloaromatization. This method is further shown to be extremely versatile and found general application for the synthesis of pyridines **18** and **19**. The β-lithioaminocrotonitriles react in 1,4-fashion with α-oxoketene dithioacetal **1** yielding highly substituted and functionalized pyridines[35] **18**. Similarly the lithioacetonitrile[36] follows 1,2-addition mode with **1** affording the corresponding carbinolacetals in high yield which on further cyclization with $H_3PO_4$ gave pyridines **19**. Interestingly the product pyridines contain methylthio unsubstituents at 2- and 6- positions, and participation of the external nucleophile was not observed. The Diels-Alder cycloadditions of vinylketene dithioacetals derived from the corresponding oxoketene dithioacetal **1** with maleic anhydride afforded the phthalic anhydride **12** in moderate


1
22
23
24
25
26
2 27
28
29
1. Ph–N–N(Me)–CH2Li
2. BF3·Et2O
1. CH2Li
2. BF3·Et2O
Piperidine/
Acetic Acid
SCH3
SMe
MeS
BF4

Scheme -4

yield[37]. The synthesis of thiophenes **16** by Simmon-Smith reaction on **1** is an very important synthetic outcome from our laboratory[38,39]. The Reformatsky reaction on α-oxoketene dithioacetals afforded the corresponding regiospecifically substituted and annelated 6-methylthio benzoates **15** in good yields.[40,41] The reaction of benzyllithium with α-oxoketene dithioacetal **1** follows exclusive 1,2-addition[42] (unlike benzylmagnesium chloride) and yield the corresponding naphthalenes **17** which has been reported recently describes further importance of our aromatic annelation methodology.

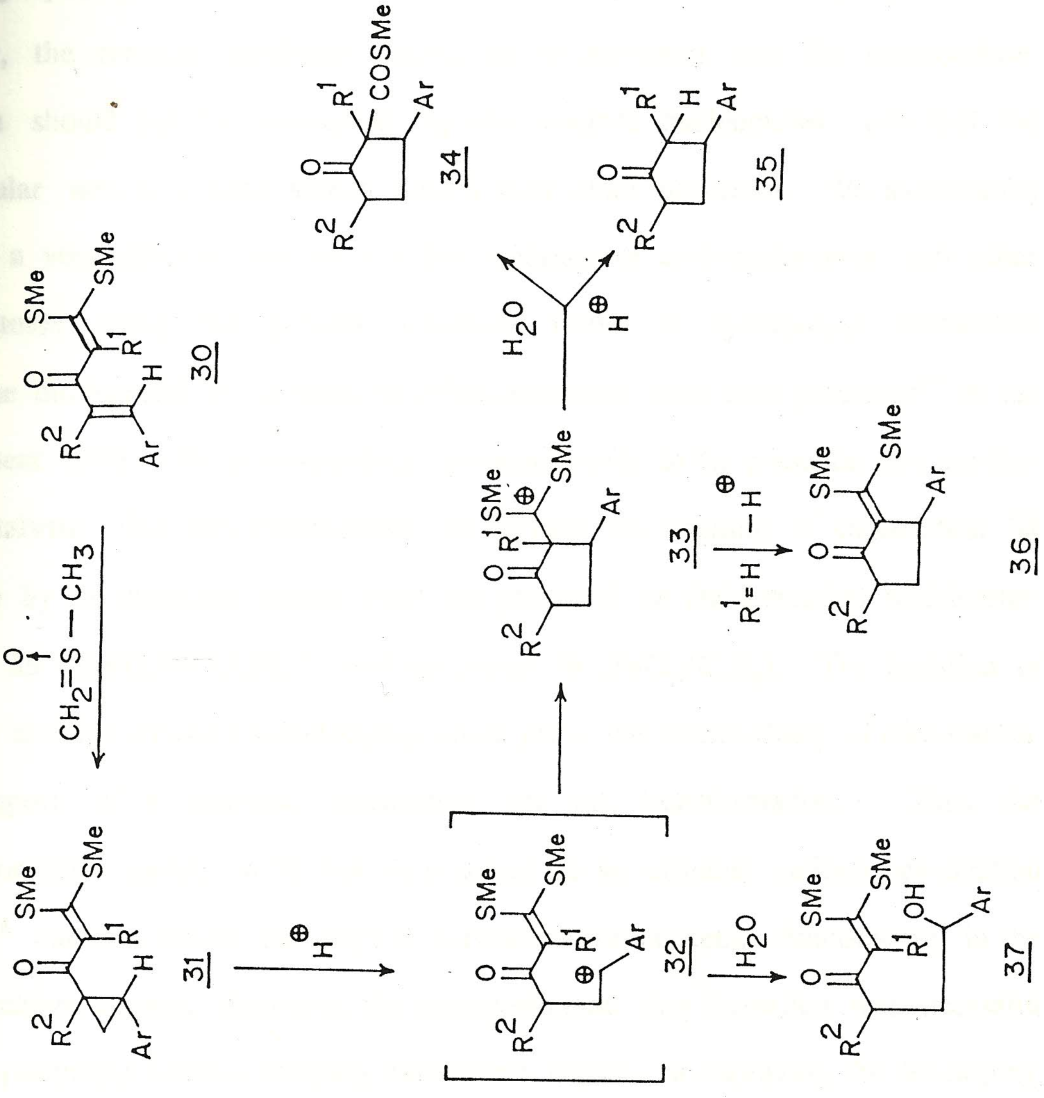
With a view to enhance the scope of aromatic annelation methodology for the synthesis of benzoheterocycles, heteroaromatic annelation methodology was developed in our laboratory by reacting appropriately substituted heteroallyl systems with α-oxoketene dithioacetals.

Thus the reaction of 2-picolyllithium with α-oxoketene dithioacetal at -30°C afforded the carbinolacetal in high yield which on further treatment with $BF_3.Et_2O$ in refluxing benzene gave the quinolizinium salt **22** in quantitative yield.[43a] Similarly, 2-lithiomethylquinoline[43b] reacted with α-oxoketene dithioacetal under identical reaction conditions to afford the corresponding quinolizinium tetrafluoroborates **23** in good yields. The 2-lithiomethylthiazole[44] reacted with **1** afforded the corresponding thiazolopyridinium salt **24** under the same reaction condition. This methodology developed as considerable synthetic importance due to the fact that, a large number of azallyl anions could be used to construct various synthetically important heterocyclic compound. The cycloaromatization of α-oxoketene dithioacetals **1** with 3-aminopyrazoles yielded the corresponding highly regioselectively substituted and condensed pyrazolo[a]- pyrimidines **25** in very good yields.[45] The reaction of 6-lithiomethyluracil and 1-phenyl-2-methyl-3-lithiomethyl pyrazolin -5-one reacted with α-oxoketene dithioacetal **1** in 1,4-fashion yielding the corresponding quinazolines[46] **26** and indazoles[62] **29** respectively. The regioselectivity was analysed by various spectral and analytical data. Similarly the lithiomethyl isoxazoles[47,48] and lithiomethyl aminocrotonates[46] reacted with **1** to afford the corresponding benziosoxazoles **27** and aminobenzenes **28** respectively in high yields.

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

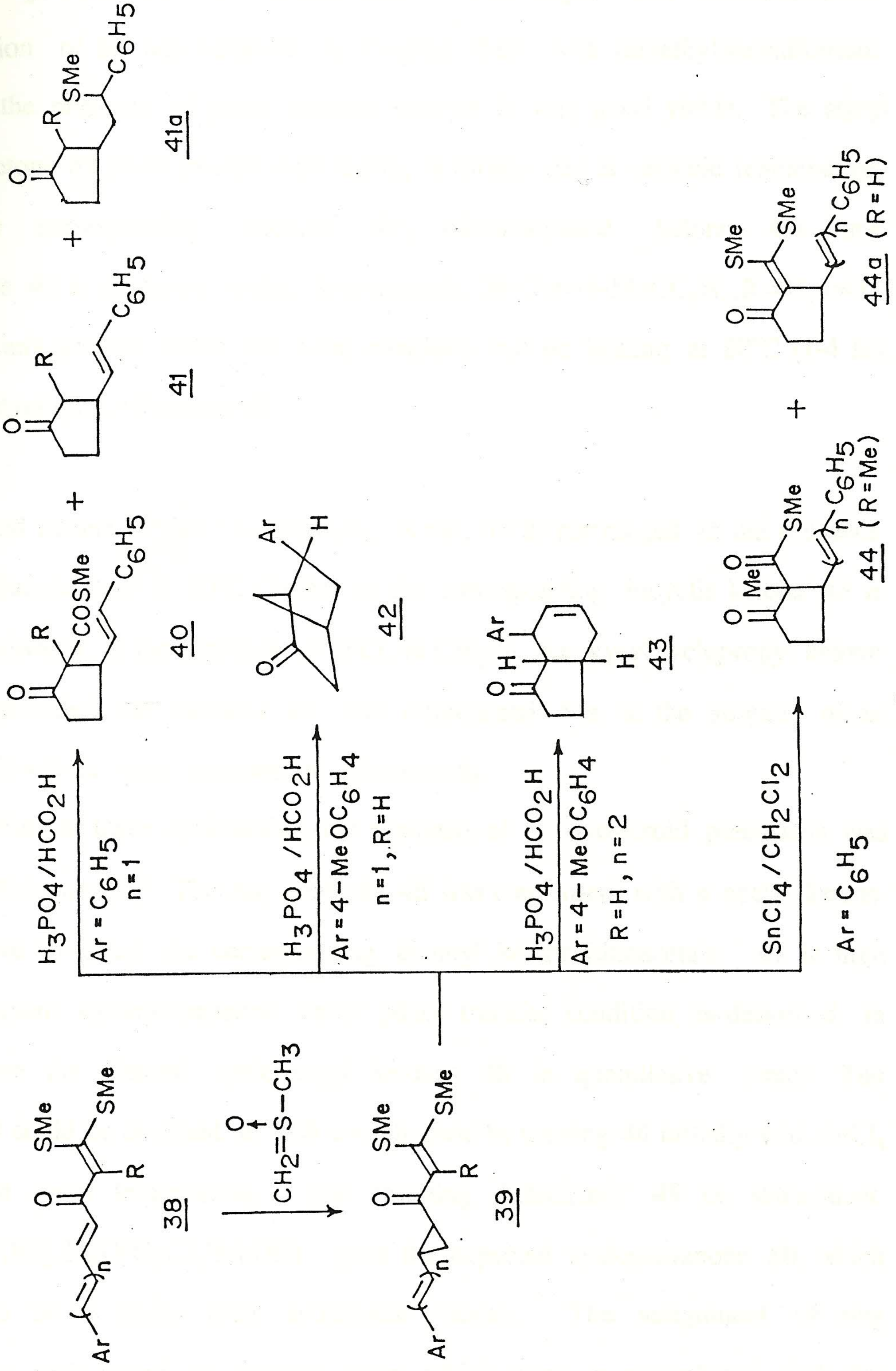
### I.3 α-Oxoketenedithioacetal: Precursor for cyclopentannelation

The development of newer synthetic strategies for the construction of five membered ring has been very active area of research in recent years.[49] Particularly impressive are a number of approaches involving cyclopropane ring expansion reactions.[50] A major contribution to these area has been Hudlicky's [4+2][51] annulation approach based on cyclopropanation of dienes and subsequent 1,3-sigmatropic rearrangement of the resulting vinylcyclopropanes to cyclopentene derivatives. The acid assisted rearrangement of cyclopropyl ketones has long been a subject of synthetic and mechanistic interest.[52] The carbocation generated in the presence of suitable acid catalyst is often intercepted either by an external nucleophile or by intramolecular participation of a neighbouring aryl or olefinic double bond.[53] This prompted us to



Scheme-5

synthesize cyclopropyl ketone of the general formula **31** and study their acid catalyzed ring opening. The bis(methylthio)methylene group in **31**, as masked ester functionality is expected to undergo intramolecular π-participation with the developing carbocation during ring opening and the new C-C bond thus formed lead to cyclopentanone. Apparently, the reaction condition should be so governed that the intermediate carbocation should not be intercepted by any external nucleophiles such that the intramolecular new C-C bond should prevail over other processes. We successfully developed a very efficient method for the synthesis of cyclopentanones and other cyclopentanoids using this general structural frame of cyclopropyl substituted α-oxoketene dithioacetal **31**. A series of communications have been published[54] on the rearrangement of **31** to the corresponding cyclopentanoids in the presence of a number of acid catalysts. The key intermediate **33** formed via trapping of carbocation **32** (Scheme-5) by the mercapto double bond was proposed for the formation of thioester **34**, ketone **35** ($H_3PO_4/HCO_2H$),[55] and thioacetal **36** ($SnCl_4/C_6H_6$). The isolation of open chain carbinol **37** (Ar=4-$MeOC_6H_4$) could prove the intermediacy of carbocation **32** in support of a stepwise mechanism for the transformation. Thus the ketenedithioacetal moiety in **31** not only serves as an efficient cationic cyclization terminator[56] but also retains the original α-oxoketenedithioacetal functionality in the product cyclopentanones. However, the cyclopentanone ring formation was successful only with cyclopropyl ketones carrying substituents capable of stabilizing the developing benzyl carbocation **32**. This limitation became a constraint on this methodology for side chain elaboration at the 3-position of the product cyclopentanones. It was therefore considered of interest to explore further structural changes so that the overall transformation results in the formation of cyclopentanones. The cyclopropyl ketones **39** (Scheme-6) were considered suitable precursors to meet these requirements. The

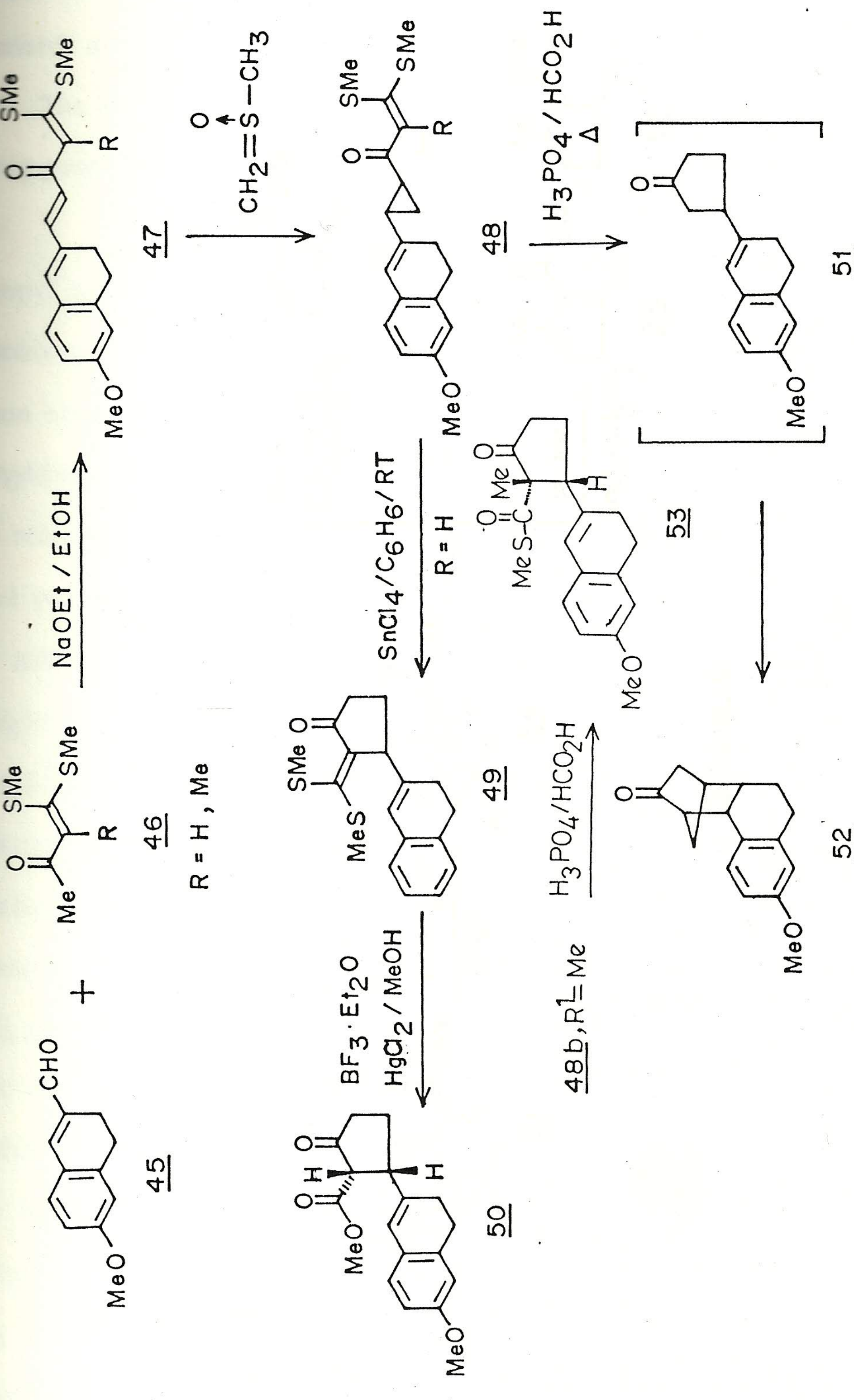

38
$CH_2=\overset{O}{\overset{\uparrow}{S}}-CH_3$
39
$H_3PO_4/HCO_2H$
Ar = $C_6H_5$
n=1
40
41
41a
$H_3PO_4/HCO_2H$
Ar = 4-MeO$C_6H_4$
n=1, R=H
42
$H_3PO_4/HCO_2H$
Ar = 4-MeO$C_6H_4$
R = H, n = 2
43
$SnCl_4/CH_2Cl_2$
Ar = $C_6H_5$
44 (R=Me)
44a (R=H)

Scheme-6

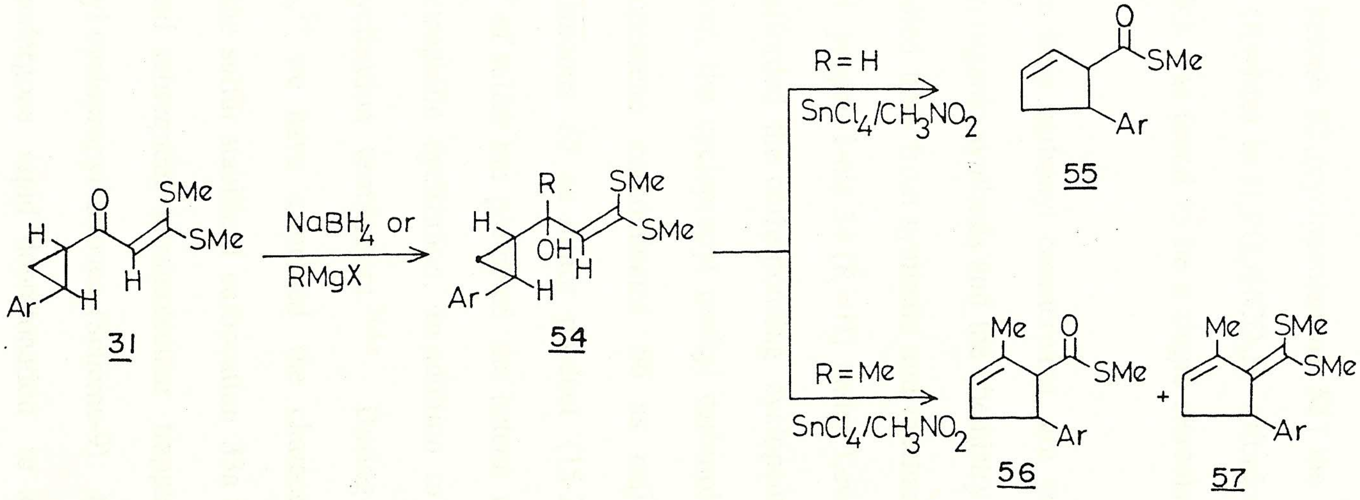
resulting 3-styryl cyclopentanones could be of further interest since they can be utilized as potential synthons for 11- oxostereoids. The regio- and chemoselective cyclopropanation of **38** was achieved by treating them with dimethyloxosulfonium methylide in the presence of phase transfer catalyst in very good yields. The styryl cyclopropyl ketone **39** when treated with $H_3PO_4$ in formic acid at variable temperature afforded the corresponding thioester **40**, thiomethylated ketone **40a** and cyclopentanone **41** in moderate yields. Interestingly, **39** (Ar=4-$MeOC_6H_4$,R=H,n=1) did not yield any product under the same condition but on heating at 80°C (1-4 hr) yielded oxobicyclo[2.2.1]heptane **42**.

The cyclopropyl ketone **39** (Ar=4-$MeOC_6H_4$, R=H, n=2) rearranged in the presence of $H_3PO_4$ in formic acid at 80°C (1-4hr) to the corresponding bicyclic ketone **43** in good yield. However, in the presence of $SnCl_4$ in $CH_2Cl_2$, the styryl cyclopropyl ketone **31** (R=Me) afforded the thioester **44** and dithioacetal **44a** in the absence of an α-proton i.e. R=H at room temperature (Scheme-6).

As an application of these cyclizations, the synthesis of 11- oxosteroid precursors was investigated (Scheme-7).[55] The ene aldehyde **45** was condensed with α-acetyl ketene dithioacetals **46** to afford the corresponding dienoyl ketenedithioacetals **47** in high yields. Subsequent cyclopropanation under phase transfer condition as described in Scheme-8 gave the desired cyclopropyl ketones **48** in quantitative yields. The β-ketoester **50** could be obtained in 78% overall yield by treating **48** initially with $SnCl_4$ in benzene at room temperature. The resulting dithioacetal **49** on subsequent methanolysis ($BF_3.Et_2O/HgCl_2/MeOH$) gave the expected cyclopentanone **50**, which was found to be a single trans substituted isomer. The assignment of ring stereochemistry was based on spectral datas which were in accordance with the


45
46
R = H, Me
NaOEt / EtOH
47
CH2=S(O)–CH3
48
SnCl4/C6H6/RT
R = H
49
BF3·Et2O
HgCl2 / MeOH
50
H3PO4 / HCO2H
Δ
51
53
H3PO4/HCO2H
48b, R1 = Me
52

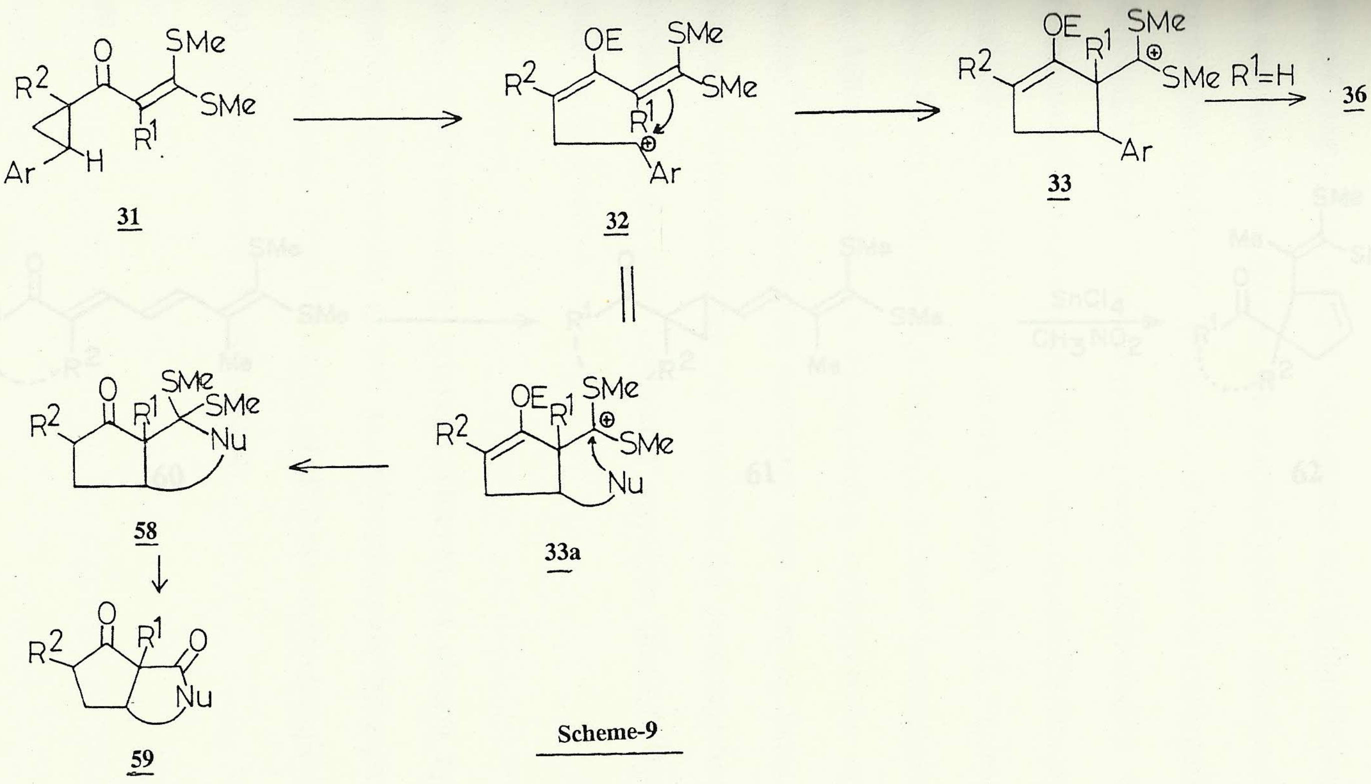
Scheme –7


H
O
SMe
SMe
H
Ar
H
31
NaBH$_4$ or
RMgX
R
SMe
H
OH
SMe
H
Ar
H
54
R = H
SnCl$_4$/CH$_3$NO$_2$
O
SMe
Ar
55
R = Me
SnCl$_4$/CH$_3$NO$_2$
Me
O
SMe
Ar
56
+
Me
SMe
SMe
Ar
57

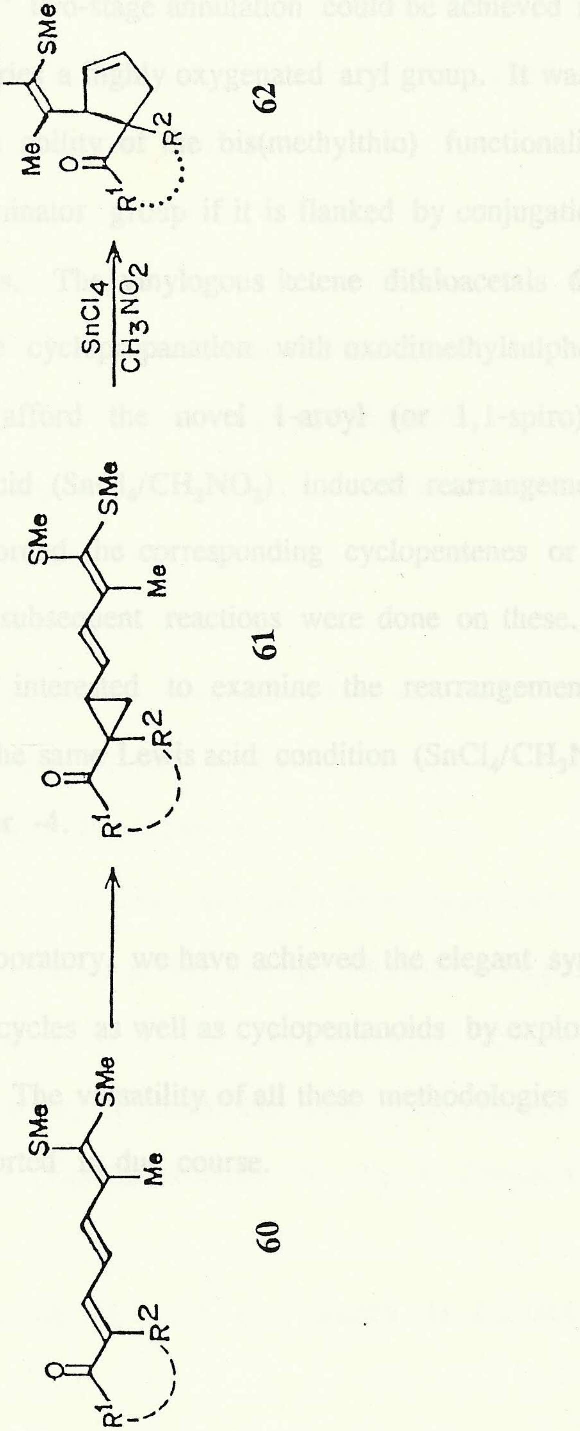
Scheme - 8

corresponding 6-bromo analogue reported by Trost and co- workers.[57] However, the cyclopropyl ketone **48** (R=H) when treated with $H_3PO_4/HCO_2H$ yielded a product characterized as bicyclic ketone **52**,(cyclopentanone **51**) the precursor of **52** was not detected. The ketone **48** (R=Me) in $H_3PO_4/HCO_2H$ afforded the expected thioester **53** in very good yield which was found to be a single stereoisomer.

Cyclopropyl carbinols like their carbonyl counterparts are well recognized as a class of important precursors in organic synthesis and the chemistry of their rearrangements have been extensively studied both from synthetic and mechanistic point of view. The bis(methylthio)cyclopropyl propen-1-ols **54** (R=H) under Lewis acid ($SnCl_4/CH_3NO_2$) assisted rearrangement afforded the corresponding cyclopentene carbothioates **55** as exclusive product. However, the cyclopropyl methyl carbinols (R=Me) afforded the methyl substituted cyclopentene carbothioates **56** as major product (55%) and bis(methylthio) cyclopentanones **57** as minor product (15-25%) (Scheme-8). The cation stabilizing ability[56] of sulfur has promoted the ketene dithioacetals as initiator in the intramolecular electrophilic cyclization. In addition to this they have proved to be excellent cationic cyclization terminators.[56d,e] During our earlier report on cyclopentanoid synthesis,[54] we have examined the characteristic $d^2$ step through 5-exotrig process to give the sulfur stabilized carbocation **33a** ($R^1$=Me, Ar=Nu) in the presence of Lewis acid and subsequent intramolecular trapping of these carbocations by suitably substituted aryl cyclopropyl ketones (Scheme-9). However, the cyclopropyl ketones having $R^1$=H undergone rapid deprotonation to afford the corresponding bis(methylthio) cyclopentanones as described in Scheme-5. The aryl ring having electron donating groups and the cyclopropyl ketone having α- substituent ($R^1$=Me) afforded the corresponding doubly annulated cyclopentanone rings of general formula



Scheme-9



Scheme-10

58 (Scheme-9). These thioketals were hydrolysed in $HgCl_2/aqCH_3CN$ to afford the corresponding diketones **59**. It was also extended to the corresponding carbinols. It was shown that Tandem[59] two-stage annulation could be achieved in the systems where the cyclopropyl ring carries a highly oxygenated aryl group. It was then considered of interest to examine the ability of the bis(methylthio) functionality to function as a cationic cyclization terminator group if it is flanked by conjugation of double bonds with cyclopropyl ketones. The vinylogous ketene dithioacetals **60** underwent highly regio and stereoselective cyclopropanation with oxodimethylsulphonium methylide in presence of PTC to afford the novel 1-aroyl (or 1,1-spiro) cyclopropanes **61** (Scheme-10). Lewis acid ($SnCl_4/CH_3NO_2$) induced rearrangement of these dienyl cyclopropyl ketones afforded the corresponding cyclopentenes or spiro derivatives **62** in good yields.[60] Then subsequent reactions were done on these. Encouraged by all these results, we were interested to examine the rearrangement studies on styryl cyclopropyl ketones in the same Lewis acid condition ($SnCl_4/CH_3NO_2$) and the results are described in Chapter -4.

In conclusion, in this laboratory, we have achieved the elegant synthesis of aromatics, heteroaromatics, heterocycles as well as cyclopentanoids by exploiting the open chain oxoketene dithioacetal. The versatility of all these methodologies are being examined further and will be reported in due course.

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