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SYNTHETIC STUDIES ON α-OXOKETENE DITHIOACETALS

By

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Dedicated To
My Late Father & Mother
(in their loving memory)

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TO WHOM IT MAY CONCERN

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Course No.	*Title*	*Grade*
1. SPS 601	French Language	O
2. SPS 629	Numerical Methods with application to Computer.	A
3. CHEM 620	Selected Topics in Physical Chemistry.	A
4. CHEM 622	Spectroscopic Methods in Chemistry	A

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This is to certify that the work described in this thesis has been carried out by Mr. Okram Mukherjee Singh, under my supervision. He has satisfactorily completed the Pre-Ph.D. courses prescribed and the minimum period of two years of investigation 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.

Shillong

H. Junjappa
Supervisor

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OMSingh

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OKRAM MUKHERJEE SINGH

CONTENTS

PREFACE

The α-oxoketene dithioacetals are a versatile group of 3-carbon synthons with ambident 1,3-electrophilic centres thus permitting to design various methodologies for both carbocyclic and heterocylic synthesis. They can be converted to the corresponding polarized ketone S,N- and N,N-acetals making them more important as precursors for a large variety of functionalized acetals. These polarized ketene S,S-, S,N- & N,N-acetals have been extensively explored in this laboratory for the development of new synthetic methods for a variety of heterocyclic and carbocyclic compounds. The work described in this thesis highlights further new interesting transformation of polarized ketene S,S-, S,N- & N,N-acetals.

The thesis consists of five chapters. The first chapter gives a general introduction to polarized ketene dithioacetals and some of the recent transformation reported from this laboratory.

The second chapter is divided into two parts. Part I contains a brief review on polarized ketene S,N- and N,N-acetals. In part II an improved and new method for the synthesis of polarized ketene S,N- and N,N-acetals in described.

The third chapter also, is divided into two parts. Part I contains a new versatile and efficient method for the synthesis of pyrido [1,2-a] pyrimidines via α-oxoketene S,N- and N,N-acetals.

In part II a new general method for novel imidazo [1,2-a] pyridines by copper (I) assisted intermolecular ring closure of S,N-acetals is described. Probable mechanism for the formation of various products is discussed.

In chapter IV, synthesis of cyclopropyl substituted heterocycles by reacting α-[bis (methylthio) methylene] cyclopropyl ketones with various 1,2- and 1,3- heteroatom bynucleophiles. The last chapter(CHAPTER V) of the thesis deals with studies on the reductive cleavage of C-O and C-S bonds of acetals and dithioacetals.

Each chapter is divided into introduction, results and discussion. experimental and conclusion. Relevant references have been included at the end of each chapter.

CHAPTER - I

GENERAL INTRODUCTION

The α-oxoketene dithioacetals and the corresponding S, N- and N, N- acetals are versatile synthetic intermediates in organic synthesis. This chapter is devoted to a brief review and discussion on the chemistry of these synthons in the context of their practical and potential application to organic synthesis. For convenience this chapter is divided into two sections. In the first section a brief survey of α-oxoketene dithioacetals is described and the present work has been described in the second section.

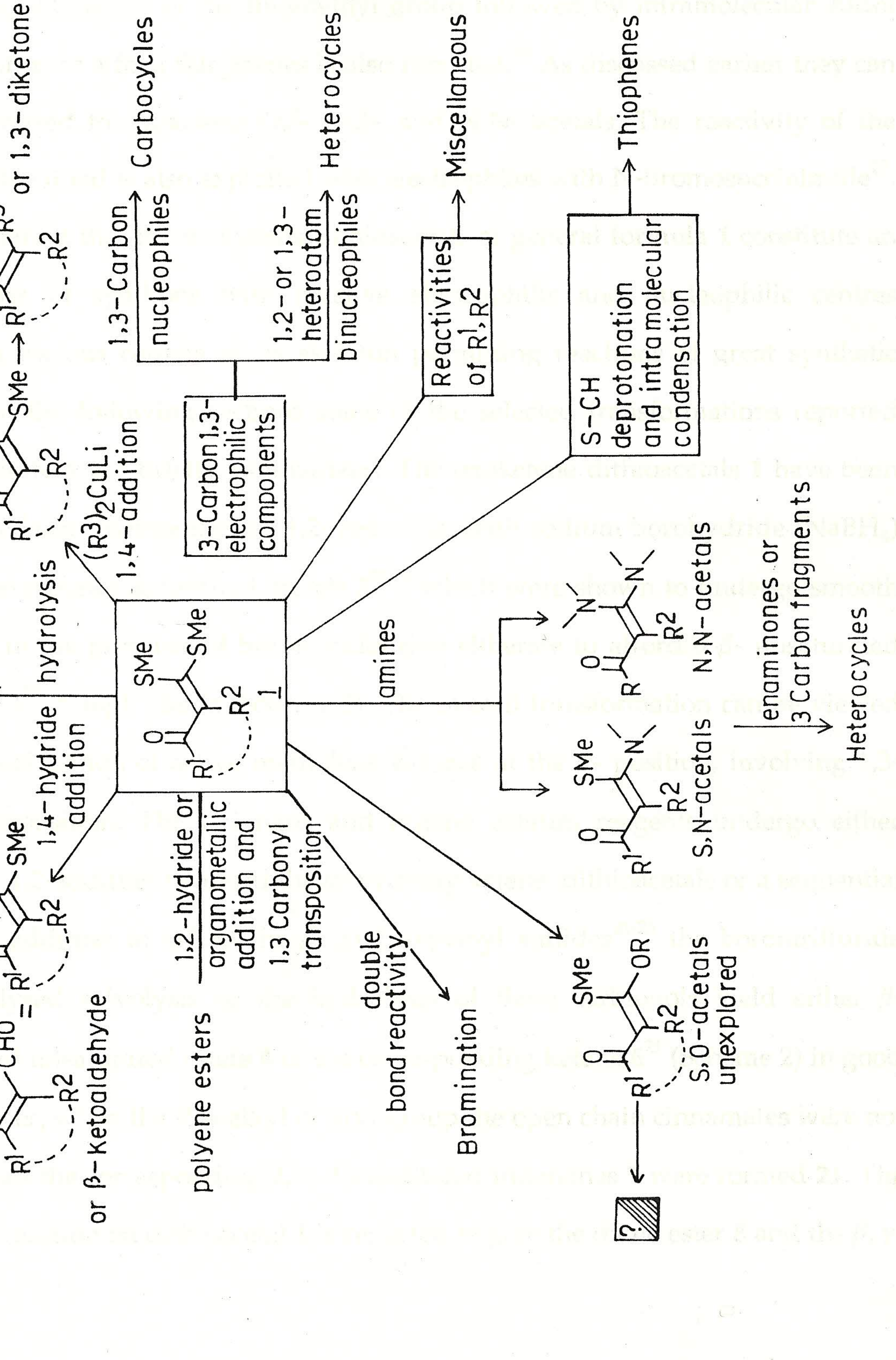
A. THE POLARIZED KETENE S, S - ACETALS

Polarized ketene S, S- acetals have been recognised as useful building blocks in many synthetic operations[1]. This class of compounds can be conveniently prepared by reacting any active methylene compound with two equivalents of base and carbon disulfide followed by alkylation[2,3,5]. Various bases and reaction conditions have been employed depending on the nature of the active methylene compound.

In 1910 Kelber and co-workers[10,11] reported the first synthesis of α-oxoketene dithioacetals. Much of the earlier works on oxoketene dithioacetals were confined to their preparation and properties, while little attention was paid for their synthetic utility. Hence, more than half a century the synthetic potential of these class of compounds remained unexplored. Later Thuillier and Vialle prepared these compounds in high yields in one pot reaction by reacting the active methylene ketone with carbondisulfide in the presence of sodium amylate followed by alkylation[2,3,5]. Subsequently, these reaction conditions have been greatly improved using different bases and reaction conditions[4,6-9]. A large number of α-oxoketene dithioacetals have now been reported and emerged as very useful synthetic intermediates over the last two decades and their chemistry has been reviewed by Dieter[1a] and Junjappa *et al.*[1b]

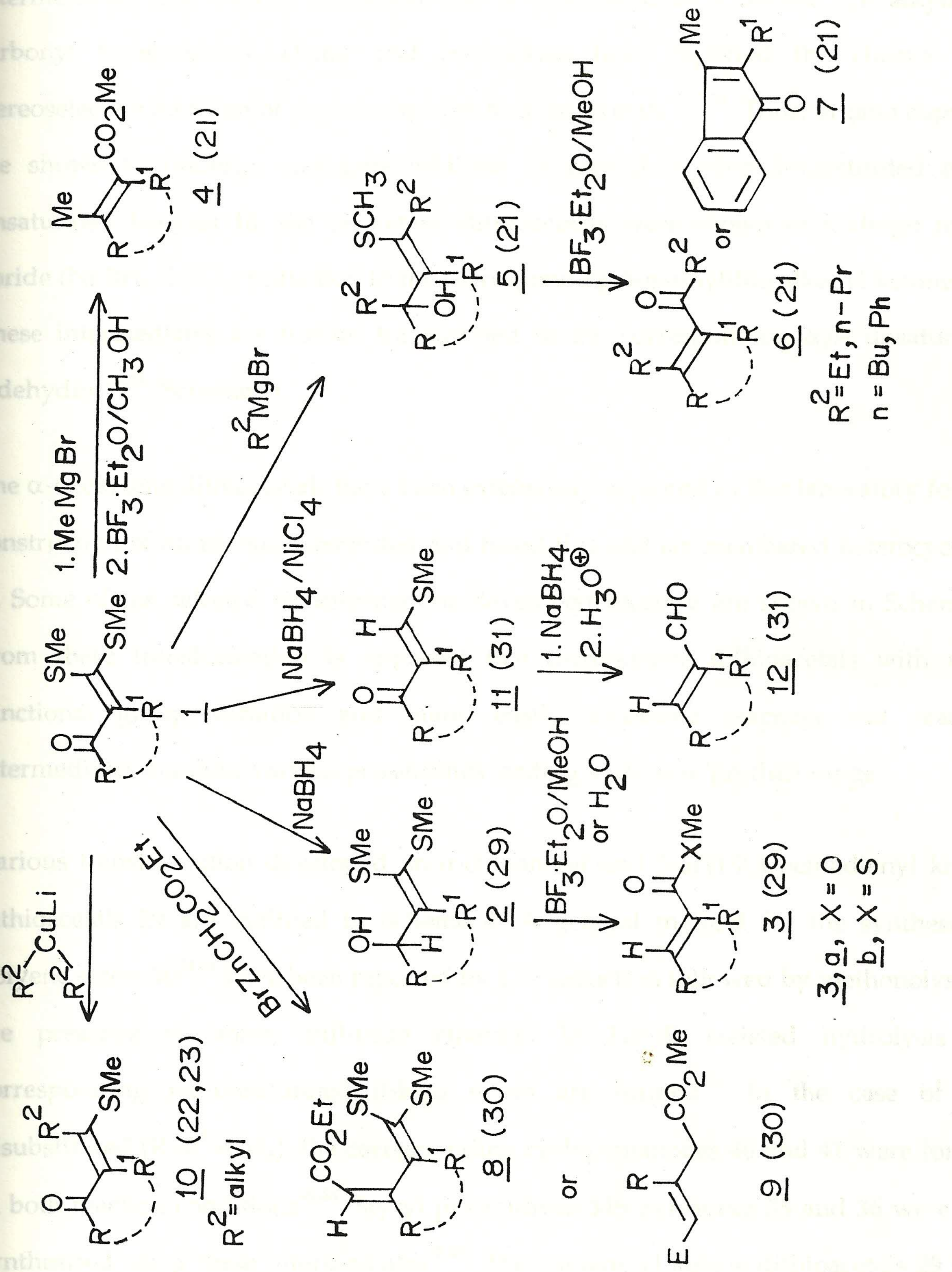
The α-oxoketene dithioacetals can be prepared by easier methods in one pot operation in high yields. They are stable compounds with well defined physical properties and can be easily purified by conventional methods. They are stable under mild acidic and alkaline conditions and can be stored indefinitely without decomposition. The corresponding α-oxoketene O,O- acetals[12] are moisture sensitive and undergo hydrolysis under mild conditions. The oxoketene dithioacetals are essentially a masked *β*-ketoester in which the ester functionality is protected as a ketene dithioacetal. Alternatively, it may be viewed as an α-β-unsaturated ketone containing a highly functionalised *β*-carbon. The oxoketene dithioacetals have been shown to be excellent three carbon fragments, with 1,3-carbon possessing differential electrophilic properties which is an important pre-requisite in designing various methodologies for both carbocyclic and heterocyclic compounds. They also possess considerable synthetic potential for the chemo-, stereo- and regioselective construction of new bonds via 1,2-nucleophilic additions to ketone carbonyl or by 1,4-conjugate addition to the β-carbon of the enone system. The intermediate allylic alcohols and enones can, in turn, be exploited in additional bond forming reactions. also, oxoketene dithioacetals can be further converted to the corresponding ketene dihalogenides[13,14], N,S[15] and N,N-acetals[16] making them more important as precursors for a large variety of functionalized acetals. The preparation of N,S-acetals is accomplished through the displacement of one of the thiomethyl groups by a suitable amine in refluxing ethanol[15,17]. Alternatively, they can be prepared directly from active methylene ketones by reacting their enolate anion with alkyl and arylisothiocyanates followed by alkylation[18]. The oxoketene N,N-acetals can be prepared in high yields by displacing both the thiomethyl groups by amines in refluxing acetic acid[17,19]. The preparation of O,S-acetals are accomplished through the displacement by an oxygen nucleophile of the sulfonium salt[2]. The oxoketene S,S- ,N,S- and N,N-acetals have been extensively used largely unexplored.

Scheme 1 outlines various reactivity profiles of α-oxoketene dithioacetals of the general formula **1**. Hydrides and organo metallic reagents give 1,2- addition products typical of carbonyl function reactivity[21]. These additions can be directed in a 1,4- manner by suitably manipulating the reaction condition and reagents[21-23]. Further transformations of these 1,2- or 1,4- addition products have also been investigated extensively[21]. 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 hetero atom binucleophiles respectively. The 1,3- carbon binucleophiles have been similarly used in the synthesis of carbocycles. The enolate


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

Scheme-1

anoin formed by the deprotonation (when R=alkyl) can undergo condensation with aldehydes to give α-enoyl ketene dithioacetals[3b,24]. When R^1 is a methyl group and allylic anion is generated in the presence of strong bases leading to rearranged products[25]. Deprotonation of the thiomethyl group followed by intramolecular Aldol type condensation to afford thiophenes is also reported.[26] As discussed earlier they can be easily converted to oxoketene O,S-, N,S- and N,N- acetals. The reactivity of the mercapto double bond is also exploited with electrophiles with N-bromosuccinimide[27]. Thus, it is apparent that the oxoketene dithioacetals of general formula **1** constitute an important class of synthons with reactive electrophilic and nucleophilic centres distributed in various centers of its skeleton permitting reactions of great synthetic importance. In the following sections some of the selected transformations reported from this laboratory are briefly summarized. The oxoketene dithioacetals **1** have been reported to undergo chemoselective 1,2- reduction with sodium borohydride ($NaBH_4$) to give the corresponding carbinol acetals **2**[28,29] which were shown to undergo smooth methanolysis in the presence of boron triflouride eltherate to afford α-β- unsaturated methyl esters 3[29] in high yields (Scheme 2). The overall transformation can be viewed 90 as the homologation of active methylene ketones at the α- position, involving 1,3-carbonyl transposition. The Grignard and organo lithium reagents undergo either regioselective 1,2-addition to afford the α- hydroxy ketene dithioacetals or a sequential 1,4- and 1,2- addition to afford the β- hydroxyvinyl sulfides[21-23] the borontrifluride etherate catalysed solvolysis or the hydrolysis of these carbionols yield either β-substituted α-β unsaturated esters **4** or the corresponding ketene **6**[21] (Scheme 2) in good yields. However, when the R is alkyl or aryl group the open chain cinnamates were not formed, instead the corresponding 2,3- disubstituted indenones **7** were formed **21**. The Reformatsky reaction on dithioacetal **1** is reported to give the diene ester **8** and the β, γ-

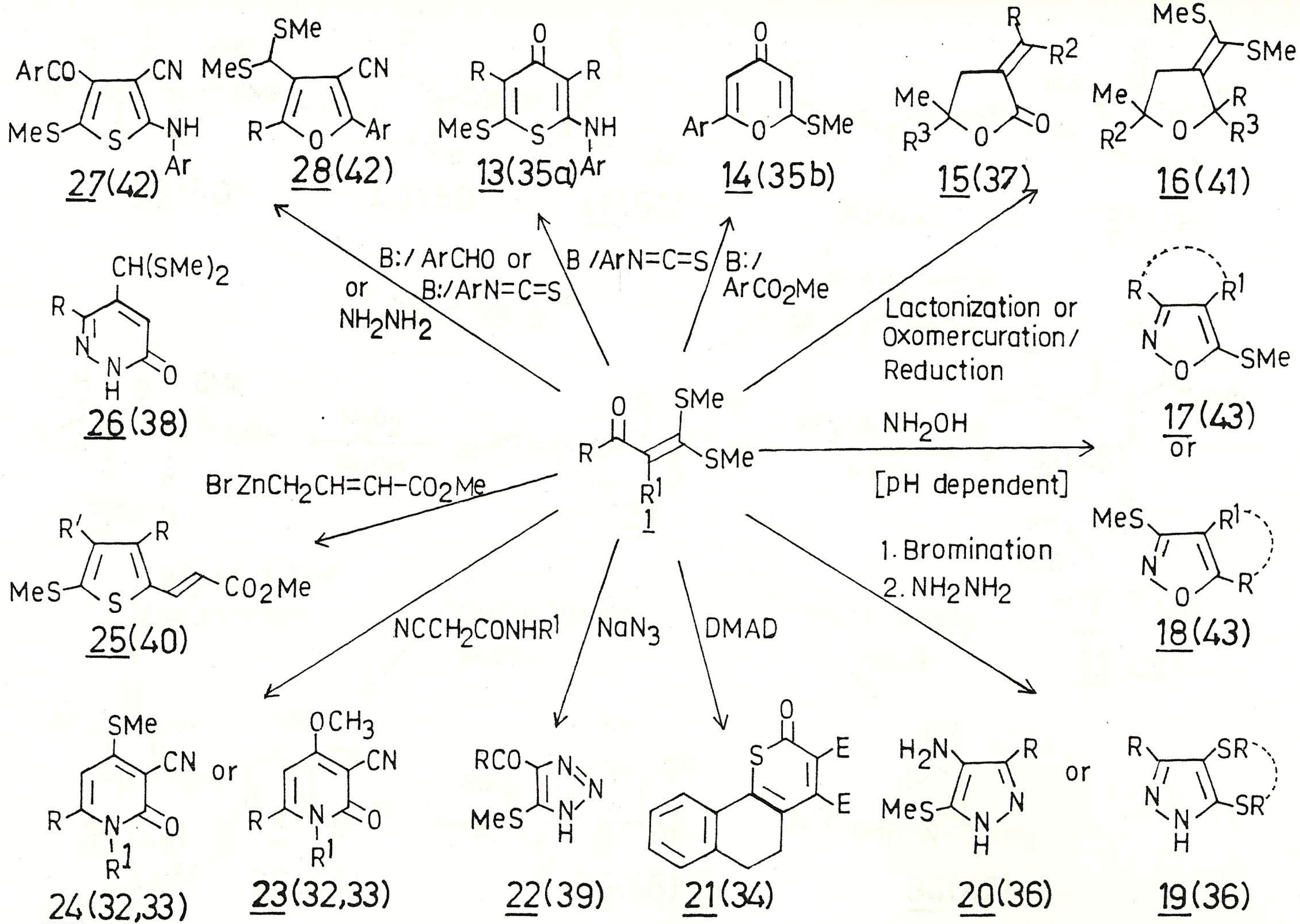

1
1. MeMgBr
2. BF$_3$·Et$_2$O/CH$_3$OH
4 (21)
R^{2}MgBr
5 (21)
BF$_3$·Et$_2$O/MeOH
6 (21)
7 (21)
R^2 = Et, n-Pr
n = Bu, Ph
NaBH$_4$/NiCl$_4$
11 (31)
1. NaBH$_4$
2. H$_3$O$^⊕$
12 (31)
NaBH$_4$
2 (29)
BF$_3$·Et$_2$O/MeOH or H$_2$O
3 (29)
3, a, X = O
b, X = S
BrZnCH$_2$CO$_2$Et
8 (30)
or
9 (30)
R$^2_2$CuLi
10 (22,23)
R^2 = alkyl

Scheme-2

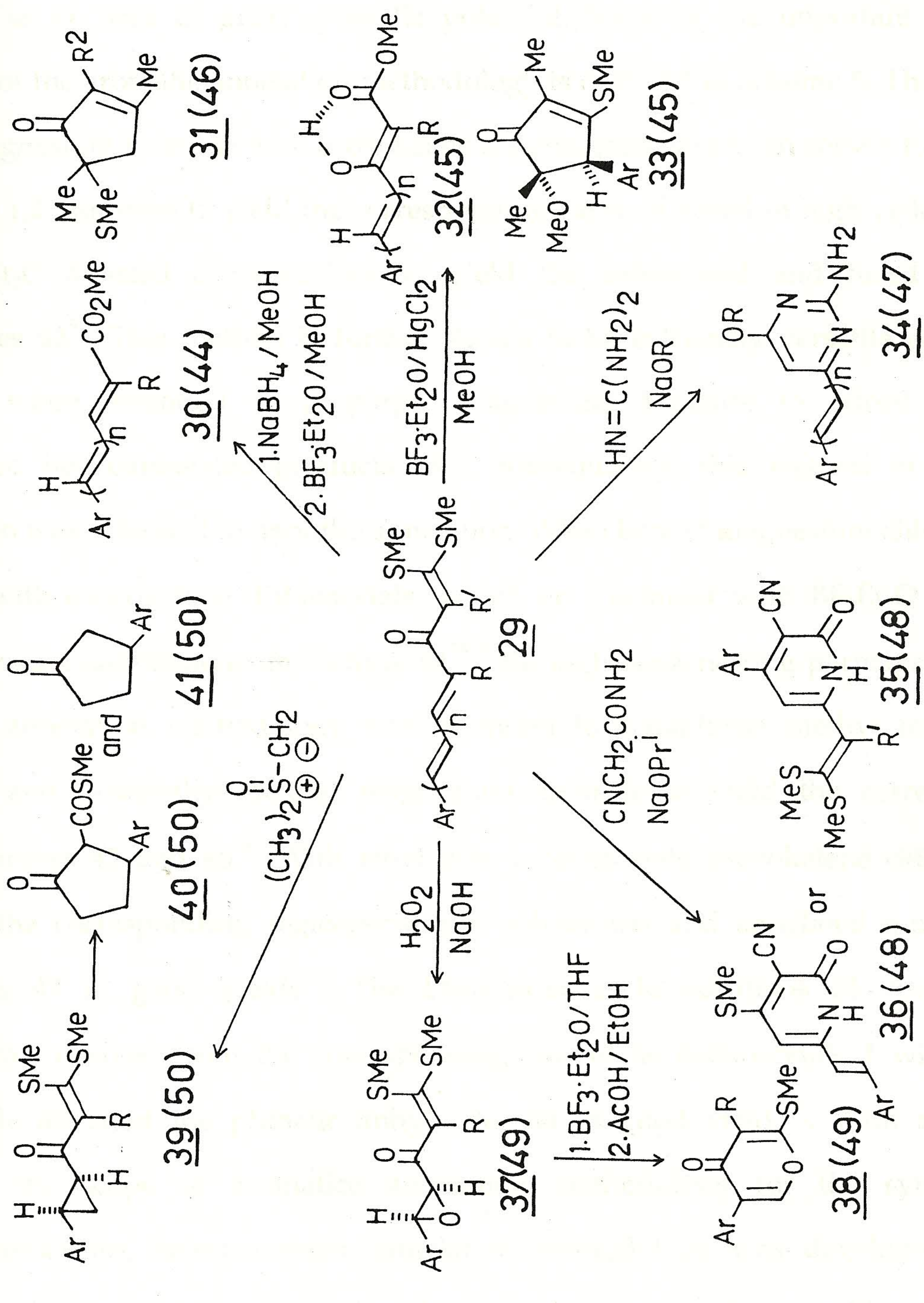
unsaturated ester **9**[30], these dienes hold considerable promise as useful synthetic intermediates. The overall transformation is considered as a double 1,3- alkylative carbonyl transposition. Dieter and co-workers have reported the chemo- and stereoselective addition of organo cuprates to dithioacetals **1**[22,23]. Thus, organo cuprates are shown to undergo conjugate addition to give β-alkythio β-substituted α, β-unsaturated ketones **10**. the oxoketene dithioacetals were shown to undergo nickel boride ($NaBH_4/NiCl_2$) reduction to the corresponding β-methylthio alkenyl ketones **11**. These intermediates are further transformed to the corresponding α,β- unsaturated aldehydes **12**[31] (Scheme 2).

The α-oxoketene dithioacetals have been extensively explored in this laboratory for the construction of numerous substituted and fused five and six membered heterocycles[32-43]. Some of the selected transformations developed recently are shown in Scheme 3. From these transformation is apparent that α-oxoketene dithioacetals with wide functional group variation and many easily accessible reagents and reaction intermediates manifest various possibilities leading to diverse product range.

Various transformation developed on α-cinnamoyl and 5-aryl-2,4-pentadienyl ketene dithioacetals **29** are outlined in Scheme 4. A general method for the synthesis of polyene esters **30**[24,44] have been reported by 1,2- reduction followed by methonolysis in the presence of boron trifluride etherate. In Hg(II) assisted hydrolysis the corresponding γ-δ-unsaturated β-keto esters are formed[45]. In the case of 2,4-disubstituted ($R=R^1=CH_3$), the corresponding cyclopentanones **40** and **41** were formed in both reaction conditions[45,46]. Styryl pyrimidines **345** pyridones **35** and **36** were also synthesised using these intermediates[47,48]. The cinnamoyl ketene dithioacetals **29** have been reported to undergo regioselective epoxidation and cyclopropanation at the styryl


27(42)
28(42)
13(35a)
14(35b)
15(37)
16(41)
26(38)
B:/ ArCHO or
or
NH2NH2
B:/ArN=C=S
B /ArN=C=S
B:/
ArCO2Me
Lactonization or
Oxomercuration/
Reduction
NH2OH
[pH dependent]
17(43)
or
18(43)
1
BrZnCH2CH=CH-CO2Me
25(40)
1. Bromination
2. NH2NH2
NCCH2CONHR1
NaN3
DMAD
or
or
24(32,33)
23(32,33)
22(39)
21(34)
20(36)
19(36)

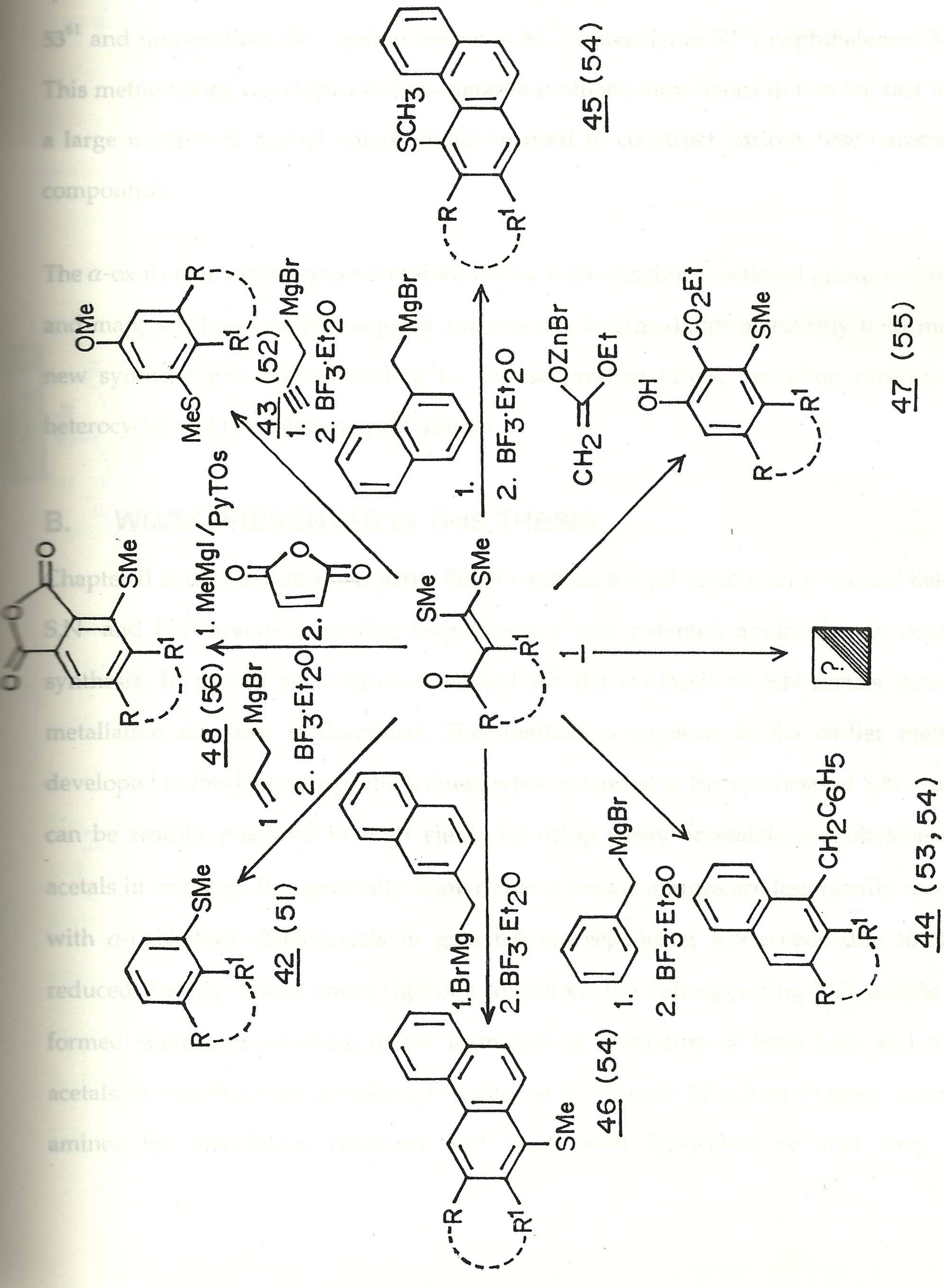
Scheme -3


39(50)
40(50)
and
41(50)
30(44)
31(46)
(CH3)2S-CH2
1.NaBH4/MeOH
2.BF3·Et2O/MeOH
H2O2
NaOH
29
BF3·Et2O/HgCl2
MeOH
32(45)
37(49)
33(45)
1.BF3·Et2O/THF
2.AcOH/EtOH
CNCH2CONH2
NaOPr^i
HN=C(NH2)2
NaOR
38(49)
36(48)
or
35(48)
34(47)
Ar
R
R'
SMe
MeS
CN
OR
NH2
CO2Me
COSMe
OMe
Me
MeO
R2

Scheme -4

double bond[49,50]. The intermediates **37** and **39** were further explored for the synthesis of pyrones **38** and cyclopentanones **40** and **41** respectively.[49,50]

Aromatic annelation via α-oxoketene dithioacetals, developed from this laboratory has emerged as an area of great synthetic potential. Some of the important synthetic outcome of the aromatic annelation methodology is outlined in Scheme 5. The reaction of allymagnesium bromide with α-oxokeene dithioacetals have been shown to undergo exclusive 1,2- addition to yield the corresponding carbinol acetal in high yields, which on $BF_3.Et_2O$ assisted cationiccylization yield the substituted and fused benzene derivatives **42**[51]. This method is further shown to be extremely versatile and found general, when extended to propargyl magnesium bromide to afford methoxy substituted benzoannelated products **43**[52]. Subsequently, this method of aromatic annelation was extended to naphtho annelation. When benzyl magnesium chloride was reacted with α-oxoketene dithioacetals, which on treatment with BF_3Et_2O gave the corresponding naphthalene derivatives **44**[53,54] through benzene ring participation. This naphtho annelation methodology was extended to α-naphthyl methyl magnesium chloride and β-naphthyl methyl magnesium chloride to yield the corresponding phenanthrenes **45** and **46**[54]. With ethyl zinc bromoacetate α-oxoketene dithioacetals yielded the corresponding regiospecifically substituted and annelated 6-methylthio benzoates **47** in good yields[55]. The Diels-alder cyclo additions of vinyl ketene dithoacetals derived from the corresponding oxoketene dithioacetals **1** with maleic anhydride afforded the phthalic anhydrides **48** in good yields[56]. With a view to enhance the scope of aromatice annelation methodology for the synthesis of benzoheterocycles, heteroaromatic annelation methodology was developed in this laboratory by reacting appropriately substituted heteroallyl systems with α-oxoketene dithioacetals. Thus, the reaction of lithiomethylisoxazole with α-oxoketene dithioacetals


SMe
SMe
O
R
R1
1. MeMgI / PyTOs
2. maleic anhydride
48 (56)
1. allylMgBr
2. BF3·Et2O
42 (51)
1.BrMg
2.BF3·Et2O
46 (54)
1. benzylMgBr
2. BF3·Et2O
44 (53, 54)
CH2C6H5
1
?
47 (55)
CH2=C(OZnBr)OEt
OH
CO2Et
1. naphthylmethylMgBr
2. BF3·Et2O
45 (54)
SCH3
1. propargylMgBr
2. BF3·Et2O
43 (52)
MeS
OMe

Scheme — 5

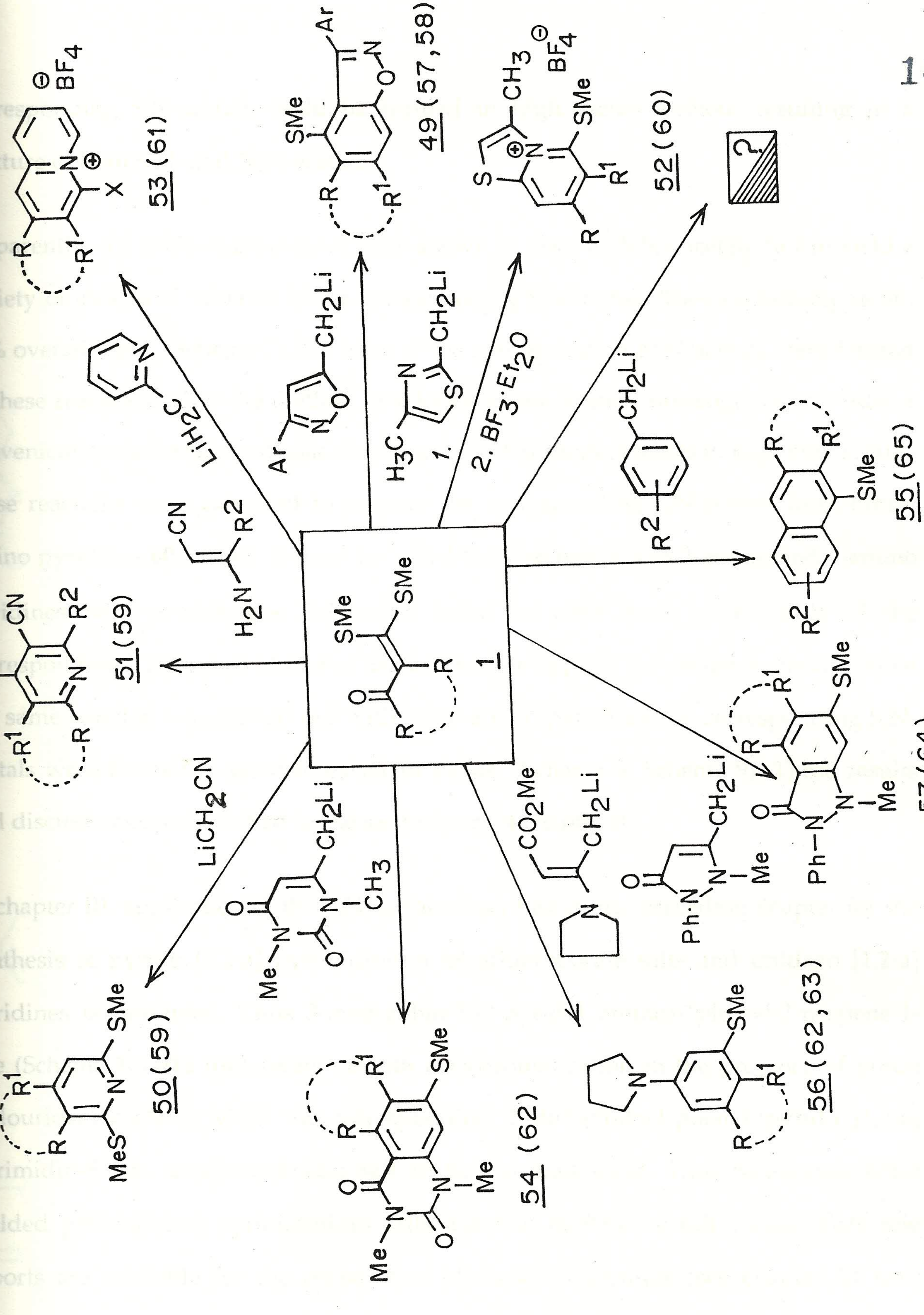
yielded the corresponding benzisoxazoles **49** in excellent yield[57,58] (Scheme 6). This method was further shown to be extremely versatile and general when extended for the synthesis of pyridines **50** and **51**[59], thiazolopyridinium salts **52**[60], quinolizinium salts **53**[61] and quinazolines **54**[62], amino benzenes **56**[63], indazolenes **57**[64], naphthalences **55**[65]. This methodology developed as considerable synthetic importance due to the fact that, a large number of azallyl anions could be used to construct various heteroaromatic compounds.

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

B. WORK PRESENTED IN THIS THESIS

Chapter II is divided into two parts. Part-I contains a brief review on polarised ketene S,N- and N,N-acetals regarding their practical and potential application in organic synthesis. In part II an improved method for the synthesis of S,N-acetals through metallation reactions is described. This method is superior to the earlier method developed in this laboratory which failed when extended to the synthesis of S,N-acetals can be readily prepared in high yields by using easily accessible α-oxoketene S,S-acetals in one step. It is generally known that aromatic amines are less readily reacted with α-oxoketene dithioacetals to give the corresponding S,N-acetals due to their reduced basicity. Under more rigorous conditions the corresponding N,N-acetals are formed sometimes resulting in the formation of a mixture of both S,N- and N,N-acetals. It was therefore, considered of interest to generate N-anions of these aromatic amines by metallation reactions and react with S,S-acetals so that only the

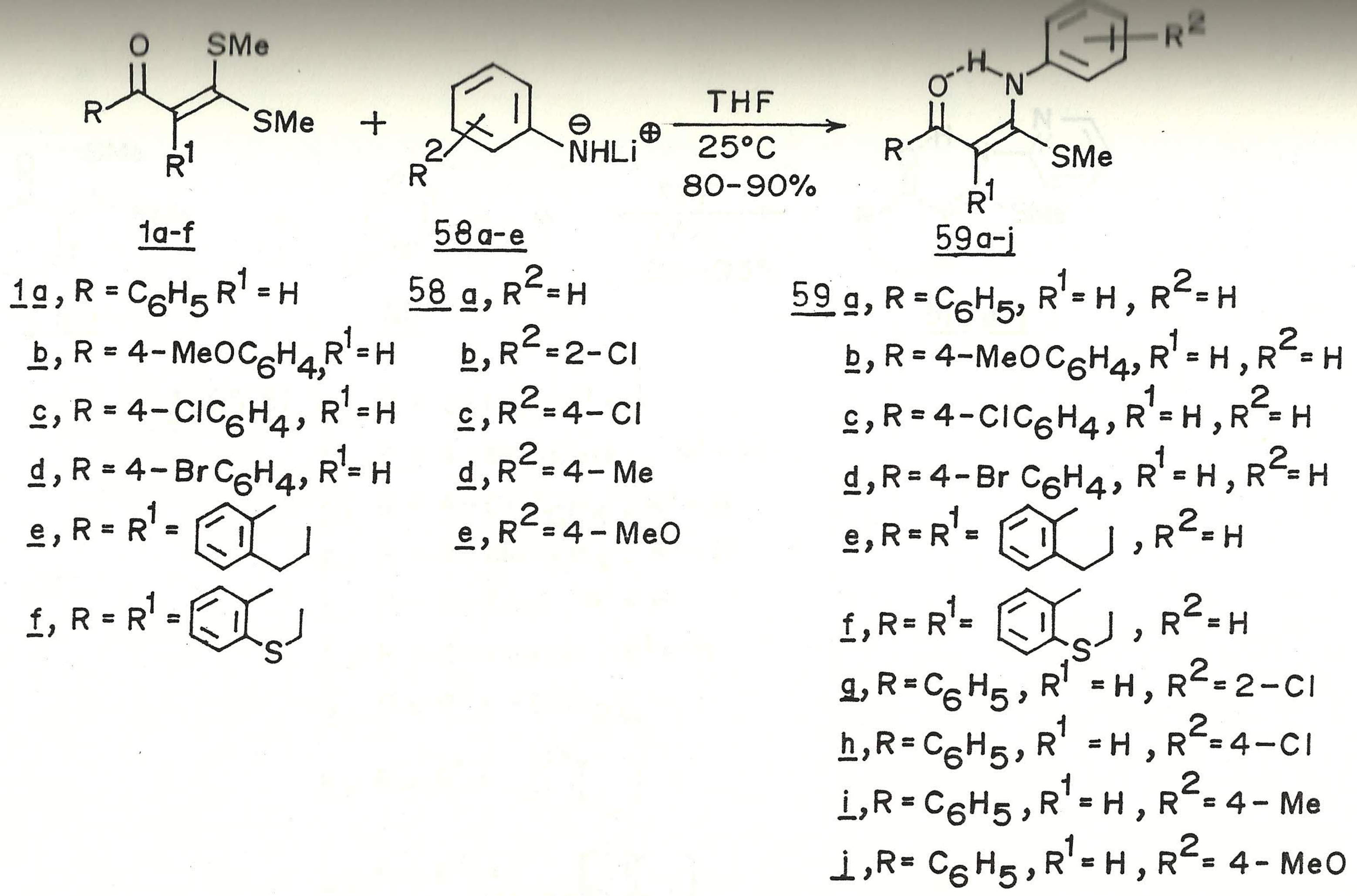
Scheme-6


1
LiCH$_2$CN
50 (59)
H$_2$N, CN, R^2
51 (59)
LiH$_2$C
53 (61)
CH$_2$Li
49 (57,58)
1. CH$_2$Li
2. BF$_3$·Et$_2$O
52 (60)
?
CH$_2$Li
55 (65)
57 (64)
CO$_2$Me, CH$_2$Li
56 (62,63)
CH$_2$Li
54 (62)

corresponding S,N-acetals could be formed in high yields without resulting in a mixture of both S,N- and N,N-acetals.

Apparently, the lithio-anilines have been shown to react with S,S-acetals 1a-f to yield a variety of structural variants of the corresponding S,N-acetals **59a-j** exclusively in 80-90% overall yield. (Scheme-7). No trace of the corresponding N,N-acetals were formed in these reactions. Thus the method developed in the present investigation provides a convenient route for the synthesis of S,N-acetals of aromatic amines in high yields. Also these reactions were extended to prepare the corresponding S,N-acetals from lithio-amino pyridines **60** and **62**. It must be noted that the reaction of 2-amino and 3-amino pyridines with α-oxoketene S,S-acetals failed to yield even poor yields of the corresponding S,N-acetals **61a-j** and **63a-e** when we applied the earlier methods. When the same reaction was carried out with lithio amino pyridines the corresponding S,N-acetals were formed in good to excellent yields. (Scheme 8, Scheme 9). These results and discussions are described in the second part of chapter II.

In chapter III, application of the S,N-acetals described in the preceding chapter for the synthesis of pyrido [1,2-a] pyrimidinium tetrafluoroborate salts and imidazo [1,2-a] pyridines is presented. Thus 3-methylthio-3-(2-pyridyl amino)-1phenyl-2-propene-1-one (Scheme 10) **61a** underwent smooth cycloaromatization in the presence of boron triflourideetherate to yield the corresponding 2-Methylthio-4-phenyl pyrido [1,2-a] pyrimidin-5-ium tetrafluoroborate salt in 82% overall yield. Thus S,N-acetals 61b-f yielded pyrido[1,2-a] pyrimidinium salts **64b-f** in 80-90% overall yields. Very few reports are available for the preparation of these compounds (see chapter III text) involving the reaction of 1,3 dicarbonyl compounds with 2-amino pyridines in the presence of perchloric acid under drastic conditions to get overall poor yields of the



1a-f + 58a-e $\xrightarrow[\text{25°C, 80-90\%}]{\text{THF}}$ 59a-j

1a, R = C_6H_5 R^1 = H

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

c, R = 4-ClC_6H_4, R^1 = H

d, R = 4-BrC_6H_4, R^1 = H

e, R = R^1 =

f, R = R^1 =

58 a, R^2 = H

b, R^2 = 2-Cl

c, R^2 = 4-Cl

d, R^2 = 4-Me

e, R^2 = 4-MeO

59 a, R = C_6H_5, R^1 = H, R^2 = H

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

c, R = 4-ClC_6H_4, R^1 = H, R^2 = H

d, R = 4-Br C_6H_4, R^1 = H, R^2 = H

e, R = R^1 = , R^2 = H

f, R = R^1 = , R^2 = H

g, R = C_6H_5, R^1 = H, R^2 = 2-Cl

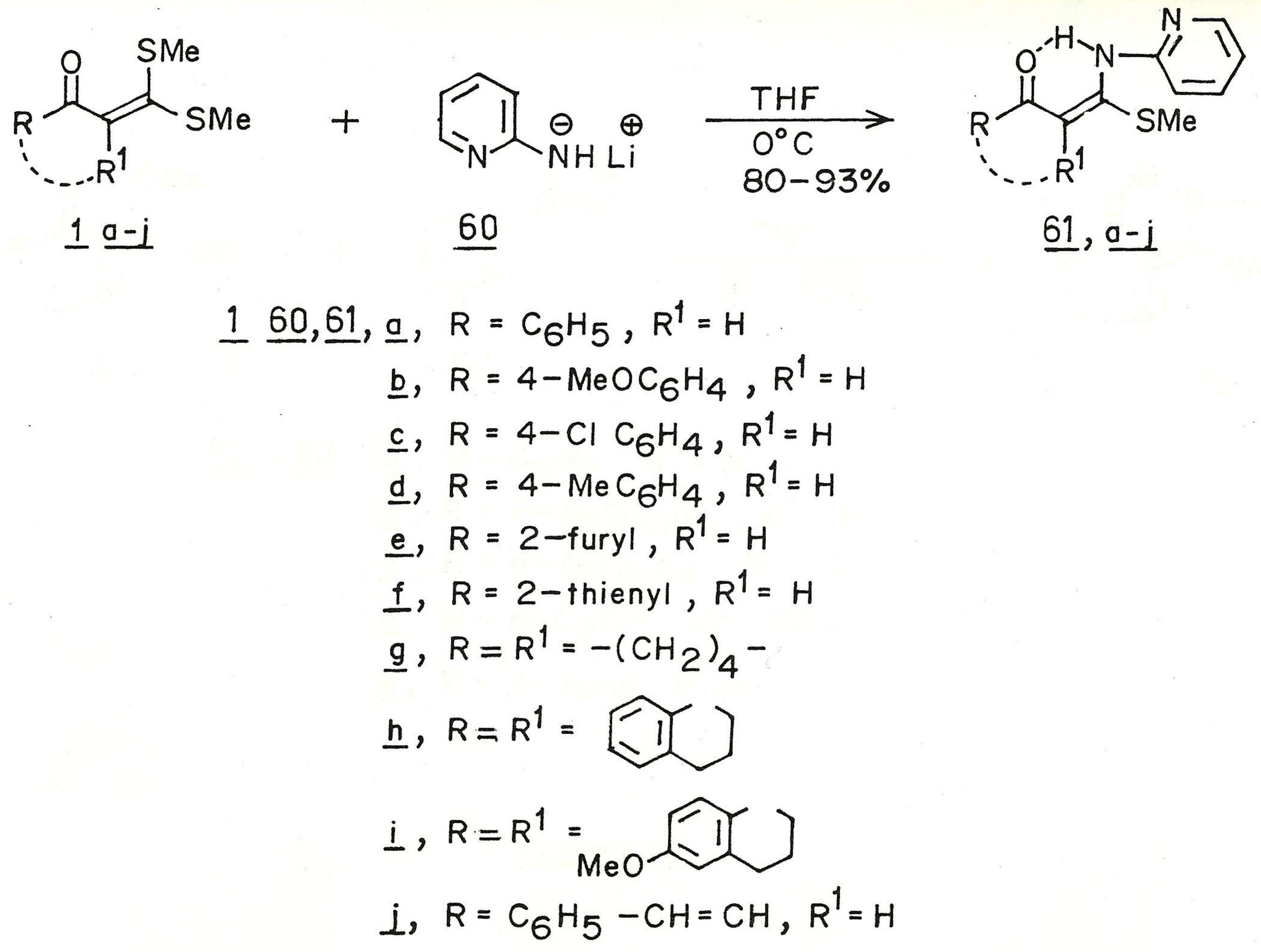
h, R = C_6H_5, R^1 = H, R^2 = 4-Cl

i, R = C_6H_5, R^1 = H, R^2 = 4-Me

j, R = C_6H_5, R^1 = H, R^2 = 4-MeO

Scheme-7

(See Table-1)



1 a-j

60

61, a-j

1 60,61, a, $R = C_6H_5$, $R^1 = H$

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

c, $R = 4\text{-}Cl\ C_6H_4$, $R^1 = H$

d, $R = 4\text{-}MeC_6H_4$, $R^1 = H$

e, R = 2–furyl, $R^1 = H$

f, R = 2–thienyl, $R^1 = H$

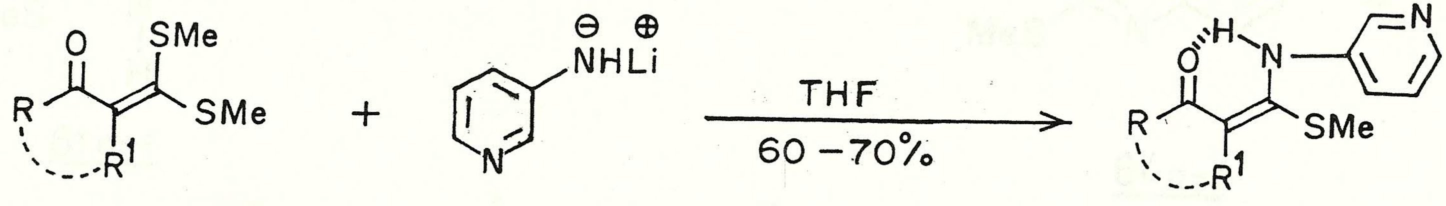
g, $R = R^1 = -(CH_2)_4-$

h, $R = R^1 =$

i, $R = R^1 =$

j, $R = C_6H_5-CH=CH$, $R^1 = H$

Scheme-8



1 62 63

62, 63, a, R = C_6H_5 , R^1 = H

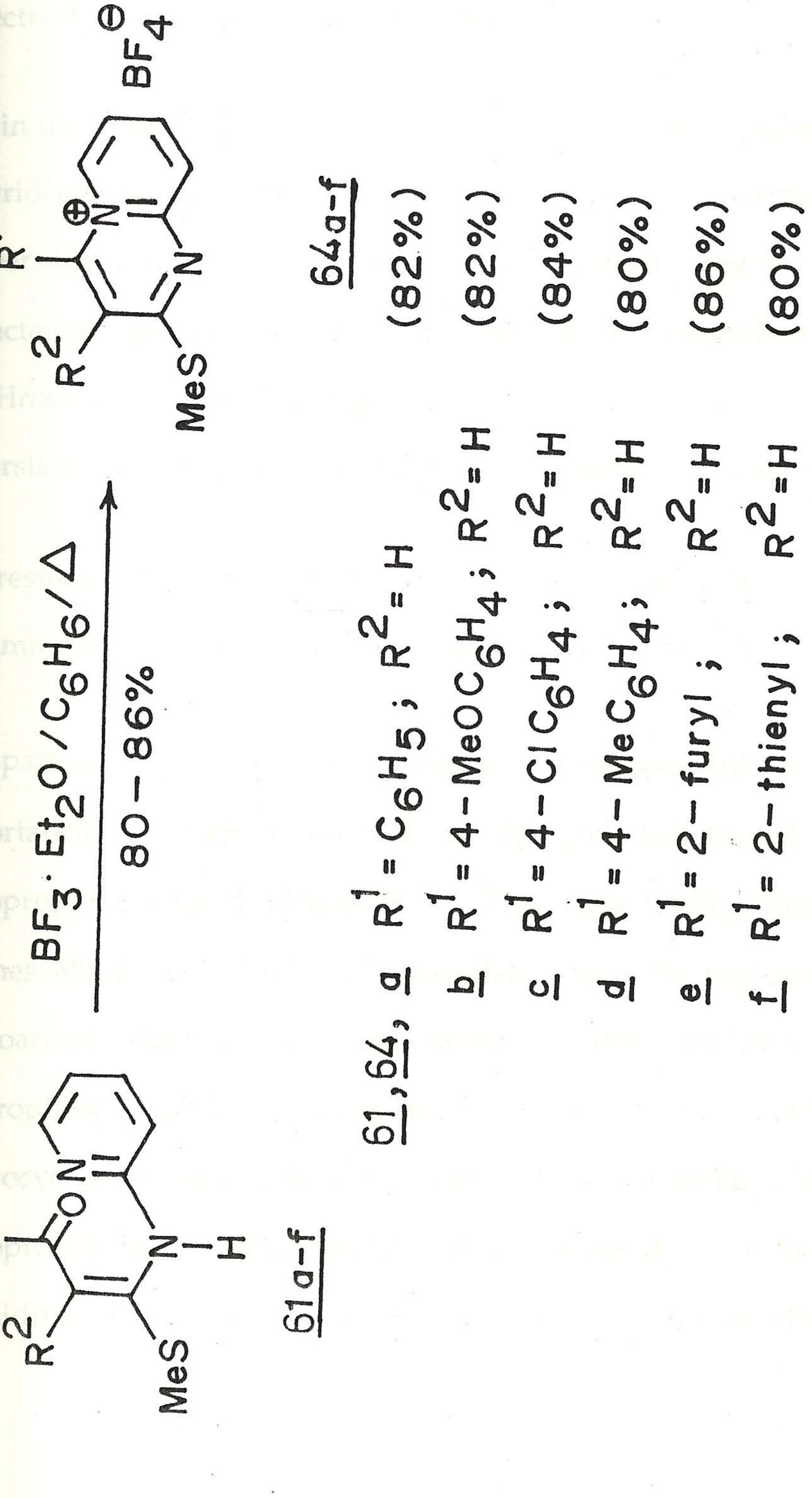
b, R = 4−MeOC_6H_4 , R^1 = H

c, R = 4−MeC_6H_4 , R^1 = H

d, R = H_5C_2O− , R^1 = CN

e, R = 2− furyl , R^1 = H

Scheme-9



61a-f

64a-f

61, 64, a $R^1 = C_6H_5$; $R^2 = H$ (82%)

b $R^1 = 4\text{-}MeOC_6H_4$; $R^2 = H$ (82%)

c $R^1 = 4\text{-}ClC_6H_4$; $R^2 = H$ (84%)

d $R^1 = 4\text{-}MeC_6H_4$; $R^2 = H$ (80%)

e $R^1 = 2\text{-}furyl$; $R^2 = H$ (86%)

f $R^1 = 2\text{-}thienyl$; $R^2 = H$ (80%)

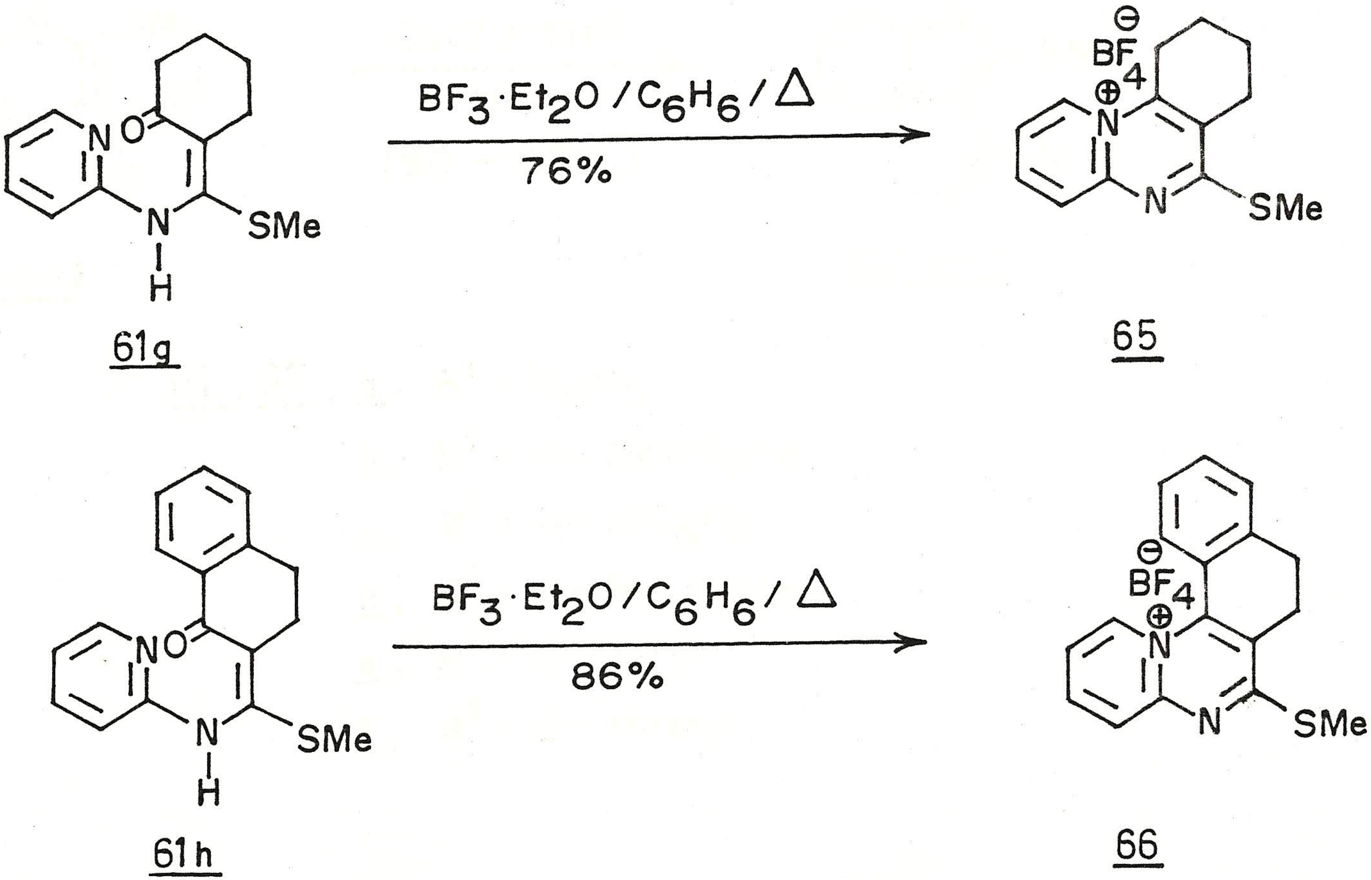
Scheme—10

corresponding pyrido [1,2-a] pyrimidinium perchlorates. Thus the method developed in the present investigation is shown to provide convenient route for the synthesis of these compounds under mild reaction conditions with more flexible structural variants. S,N-acetals **61g** and **61h** derived from mercaptals of cyclohexanone and tetralone also yielded the pyrido [1,2-a] quinazolinium tetraflouroborates 65(76%) and 66(86%) respectively under the same reaction conditions (Scheme 11).

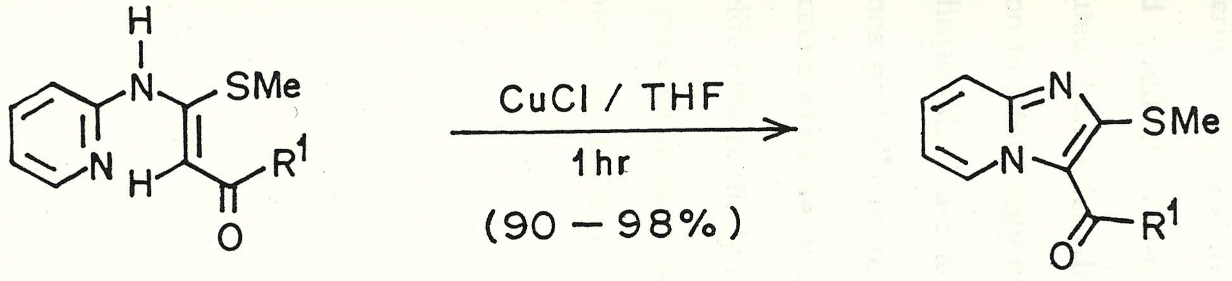
Also in the same chapter, a new general method for the synthesis of novel imidazo [1,2-a] pyridines is described. Thus S,N-acetals **61a-f** when treated with one equivalent of Copper (1) chloride in refluxing tetrahydrofuran the compounds obtained were characterised as imidazo [1,2-a] pyridines **67a-f** with excellent yields (85-93%) (Scheme-12). However the reaction mechanism governing these transformations is not clearly understood and the possible tentative mechanism is discussed.

The results describing synthesis of both pyrido [1,2-a] pyrimidinium tetra florobates and imidazo [1,2-a] pyridines are described in chapter - III.

As a part of our programmed studies on α-oxoketene dithioacetals it was considered of importance to prepare several cyclopropyl substituted heterocycles by using cyclopropyl ketene dithioacetals **69**. The *α*-bis (methylthio) methylene cyclopropyl ketones **69a-f** were obtained in excellent yields by regioselective cinnamoyl ketene dithioacetals 68a-f under phase transfer conditions (Scheme 13). The 3-carbon 1,3-electrophilic structural frame is utilized for the synthesis of both 5- and 6-membered keterocycles by reacting with 1,2- and 1,3-heteroatom binucleophiles respectively. The cyclopropyl ketene dithioacetals **69** are reacted with hydrazine, hydroxylamine, guanidine and cyanoacetamide to obtain cyclopropyl substituted pyrazoles **70a-f**,



Scheme-11



61 a – f

67 a – f

61, 67, a, $R^1 = C_6H_5$

b, R^1 = 4 – MeOC_6H_4

c, R^1 = 4 – cl C_6H_4

d, R^1 = 4 – Me C_6H_4

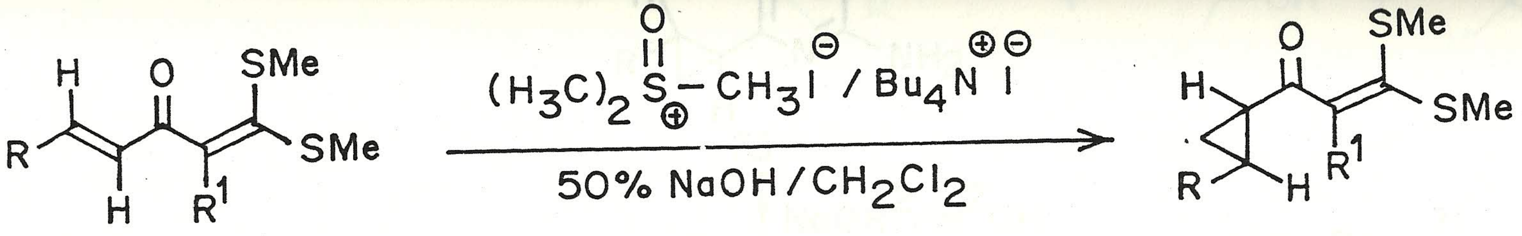
e, R^1 = 2 – furyl

f, R^1 = 2 – thienyl

Scheme – 12 12

isomeric isoxazoles **71a-e**, **72a-e**, pyrmidines **73a-f**, and the pyridones **74a-d** (Scheme 14) respectively. These results are described in chapter - IV.

In chapter V, some studies on the reductive cleavage of C-O and C-S bonds in the presence of zinc and acetic acid has been described. When acetals **75a-h** are treated with zinc in acetic acid and refluxed for 20-24 hours the products obtained were characterised as a mixture of acetals **76a-d** alcohols **77a-c,h** and sometimes completely reduced products **78d-g** (Scheme 15). The acetals **75d-g** derived from alkoxy substituted benzaldehydes underwent facile cleavage under the same reaction condition to afford only the completely reduced products exclusively. However when the dithioacetals **79a-e** are treated with zinc in acetic acid under similar reaction conditions partially reduced mercaptans **80a-e** (Scheme 16) were obtained. Similarly dithioacetals **81a-c** derived from aromatic bezaldehydes and ketones and thiophenol also yielded the partially reduced products **82a-c** along with traces of thiophenol in the overall product mixture are (Scheme 17). The results of this study and the plausible mechanism are also described in this chapter.



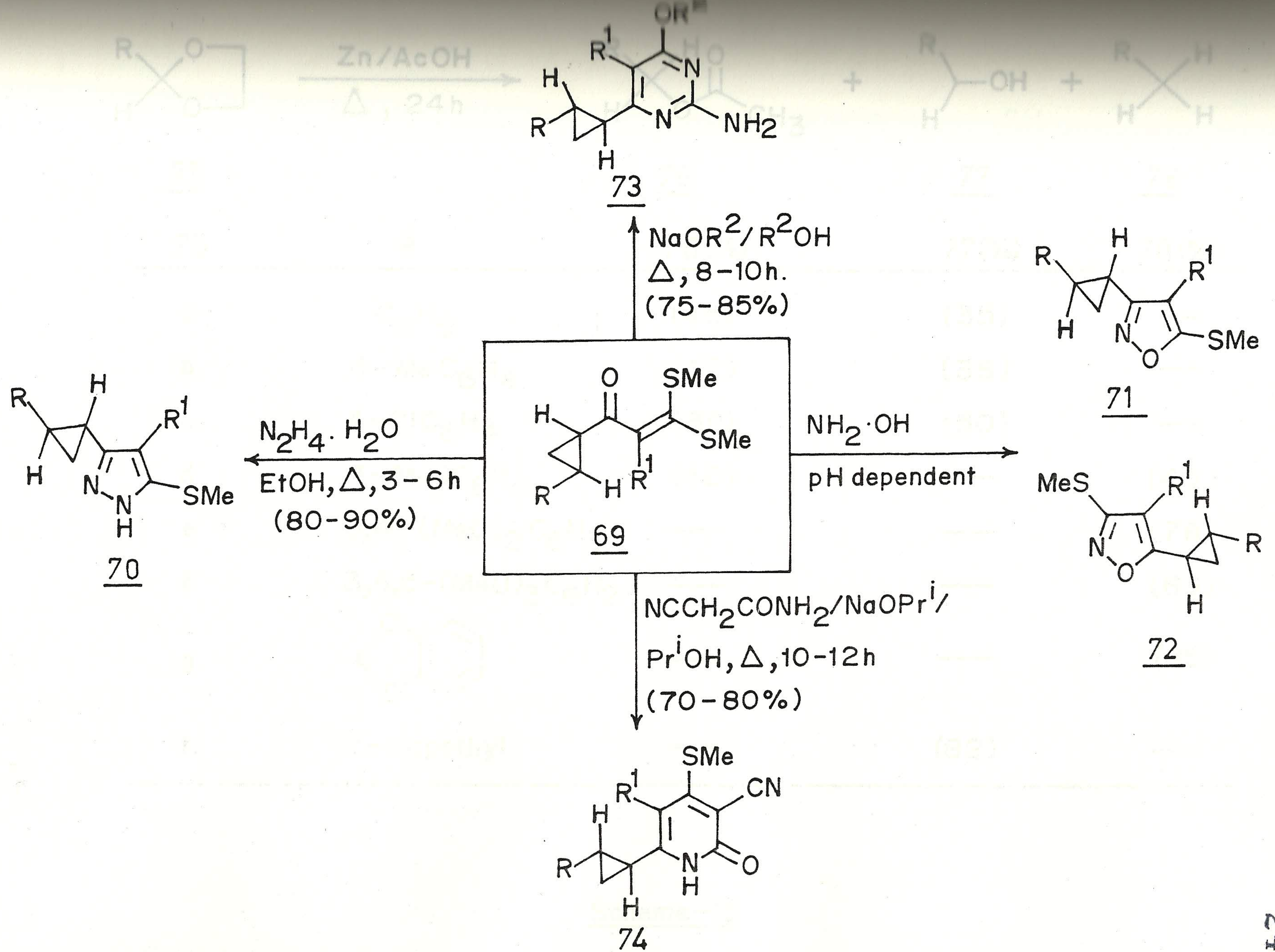
68 a–f

69 a–f

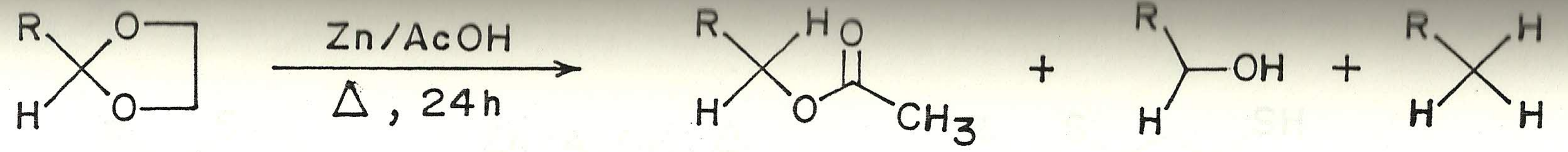
68, 69

a, R = C_6H_5 , R^1 = H
b, R = 4–MeOC_6H_4 , R^1 = H
c, R = 3,4–$(MeO)_2C_6H_3$, R^1 = H
d, R = 3,4,5–$(MeO)_3C_6H_2$, R^1 = H
e, R = 4–ClC_6H_4 , R^1 = H
f, R = 4–MeC_6H_4 , R^1 = H

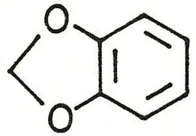
Scheme – 13


73
NaOR^2/R^{2}OH
Δ, 8–10h.
(75–85%)
70
N$_2$H$_4$·H$_2$O
EtOH, Δ, 3–6 h
(80–90%)
69
NH$_2$·OH
pH dependent
71
72
NCCH$_2$CONH$_2$/NaOPr^i/
Pr^{i}OH, Δ, 10–12h
(70–80%)
74

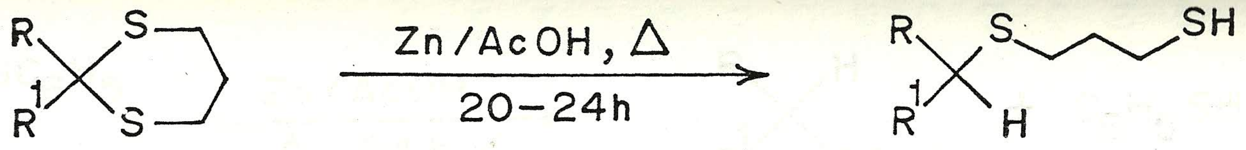
Scheme-14



75 76 77 78

75	R	76 (%)	77(%)	78 (%)
a	C_6H_5	(45)	(35)	—
b	4-Me C_6H_4	(42)	(36)	—
c	4-ClC_6H_4	(30)	(50)	—
d	4-MeOC_6H_4	(40)	—	(40)
e	3,4-$(MeO)_2$ C_6H_3	—	—	(78)
f	3,4,5-$(MeO)_3C_6H_2$	—	—	(63)
g		—	—	(65)
h	2-Naphthyl	—	(82)	—

Scheme-15

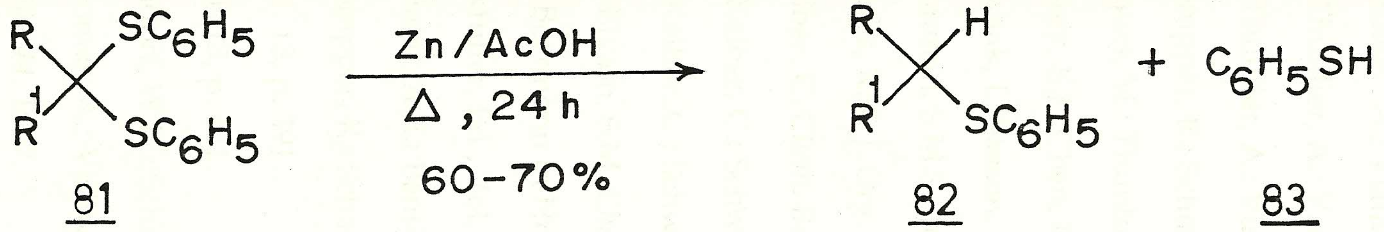


79

80
72 – 85%

79, 80, a, R = C_6H_5 , R^1 = H
b, R = 4–ClC_6H_5 , R^1 = H
c, R = 4MeOC_6H_4 , R^1 = H
d, R = 2– naphthyl, R^1 = H
e, R = R^1 = C_6H_5

Scheme–16



81, 82, a, $R = C_6H_5$, $R^1 = H$

b, $R = C_6H_5-CH=CH$, $R^1 = H$

c, $R = R^1 = C_6H_5$

Scheme-17

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