HETEROCYCLIC SYNTHESIS INVO
1,3-DIAZA-1,3-BUTADIENES A
RELATED SYSTEMS

By

PARAMITA D. DEY
DEPARTMENT OF CHEMISTRY
SCHOOL OF PHYSICAL SCIENCES

A THESIS
SUBMITTED
IN FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

To

NORTH-EASTERN HILL UNIVERSITY
SHILLONG - 793 022
MEGHALAYA (INDIA)
DECEMBER, 1998

Dedicated

to

my Parents

and

my Son

Bob

पूर्वोत्तर पर्वतीय विश्वविद्यालय
बिजनी परिसर, शिलांग-७९३००३ (मेघालय)
North-Eastern Hill University
Bijni Complex, Shillong-793 003 (Meghalaya)

Phone :
Grams: NEHU

Dr. Mahendra K. Mahanti
Professor and Head
Department of Chemistry

I certify that the Thesis entitled "Heterocyclic Synthesis Involving 1,3-Diaza-1,3-Butadienes And Related Systems" submitted by Mrs. Paramita D. Dey for the degree of Doctor of Philosophy of the North-Eastern Hill University, Shillong, embodies the record of original investigation carried out by her under my supervision. She has duly registered and the Thesis is worthy of being considered for the Ph.D. Degree. This work has not been submitted for any degree of any other University.

Place: Shillong

Date: 09 December 1998

Mahendra K. Mahanti
Signature of the Supervisor

पूर्वोत्तर पर्वतीय विश्वविद्यालय
बिजनी परिसर, शिलांग-७९३००३ (मेघालय)

North-Eastern Hill University
Bijni Complex, Shillong-793 003 (Meghalaya)

Phone :
Grams: NEHU

This is to certify that Mrs. Paramita D. Dey has satisfactorily completed the following Pre-Ph.D. courses prescribed by the University.

1. French Language
   (University level)
2. Numerical Methods in Computer Programming
   (School level)
3. Spectroscopic Methods in Chemistry
   (Departmental)
4. Advanced Topics in Physical Chemistry
   (Departmental).

Mahendra K. Mohanti
09/12/98
Professor and Head
Department of Chemistry

HEAD
DEPARTMENT OF CHEMISTRY
NORTH-EASTERN HILL UNIVERSITY
LAITUMKHRAH; SHILLONG-793003

ACKNOWLEDGEMENTS

It gives me immense pleasure to express my deep sense of gratitude to my research guide, Dr. M. P. Mahajan presently, Professor, Department of Pharmaceutical Sciences, Guru Nanak Dev University, Amritsar for his guidance, inspiration and constant encouragement throughout the course of my Ph.D. programme.

I want to express my sincere thanks to Prof. M.K. Mahanti, Head, Department of Chemistry, NEHU, for accepting to supervise me in the absence of Dr. M.P. Mahajan, to complete my research work and for rendering valuable suggestions and help.

I wish to express my heart felt thanks to all my laboratory colleagues, Dr. S.N. Majumdar, Dr. A.K. Sharma, Dr. S. Mukherjee and Mr. Senthil Kumar for their cooperation and help.

I take this opportunity to thank all the non-teaching staff members of this Department and library, who have helped me in various ways during my research period.

I am extremely thankful to RSIC, NEHU for providing me analytical and spectral facilities.

Thanks are also due to Mr. Avijit Roy for taking pain in neatly typing the thesis, Miss. Baphimon Rynjah for her help and Mr. Partha Pratim Dey who with his computer skill gave a proper shape to the thesis.

The list of acknowledgements would be incomplete if I do not mention the inspiration and encouragement rendered over the years by my parents and brother.

Lastly the encouragement, help and moral support provided by my husband, Dr. Debashis Dey, are unforgettable. The thesis also owes a great deal to my son, Bob.

The financial support extended by UGC, New Delhi, is gratefully acknowledged.

Paramita D. Dey

CONTENTS

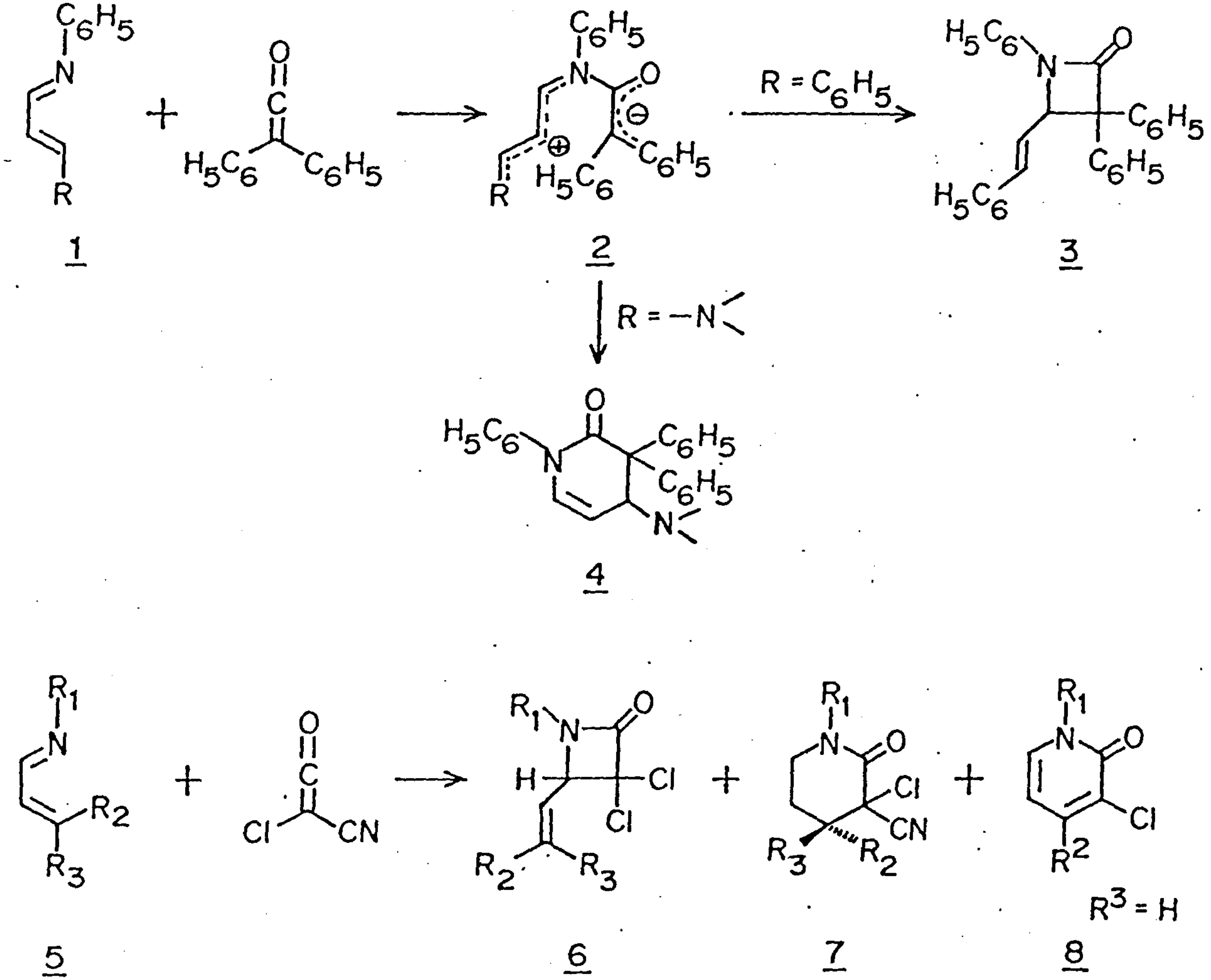
CHAPTER-I

REGIOSELECTIVE [4+2] CYCLOADDITION VERSUS NUCLEOPHILIC REACTIONS OF N-ARYLAMINO SUBSTITUTED 1,3-DIAZA-1,3-BUTADIENES WITH MONOHALO, PHENYL AND CONJUGATED KETENES.

1.1: *GENERAL INTRODUCTION*

Diels-Alder reactions have secured an immutable and well deserved stature in the minds and hands of chemists. It is the best known pericyclic reaction which turned out to be an important tool in synthetic organic chemistry[1]. It has been the subject of extensive preparative[2-9], theoretical[10,11] and mechanistic[12] studies, contributing towards the ease and predictability with which this reaction may be carried out. For the synthesis of polycyclic natural products, it provided an unique opportunity for regioselective and stereospecific introduction of multiple centres of configuration. Moreover, it has been known that reactive species can be generated in which one or more carbon atoms of diene and/or dienophile have been replaced by heteroatoms, and that cycloaddition reactions of these systems with dienophiles or conjugted dienes can yield a variety of heterocyclic compounds. Much less attention has been paid to the cycloaddition reactions of such systems, which may probably be due to: (i) uncertainty in the question of concerted versus polar stepwise nature of cycloaddition; (ii) ambiguities surrounding the observed or predicted regio/ steroselectivity; and (iii) the relative lack of methods concerning the preparation of starting materials.

It has been observed that the conjugated systems containing nitrogen, that is, azabutadienes[2,3,5,8,10,12-14], show diminished reactivity towards electron-deficient dienophiles, which lends credence to the electrophilic character of such systems.These observations, together with the recognised shortcomings in attempting cycloaddition reactions with 2π and 4π components of a similar electrophilic nature, led to



Scheme – 1

the development of several general approaches for useful azadiene Diels-Alder reactions.

Azadienes have proven to be an important key intermediate in organic synthesis for the construction of both heterocylic systems and open chain polyfunctionalized molecules[15,16]. Their studies have highlitghted many synthetic and mechanistic aspects associated with their chemistry. Cycloaddition reactions of heterodienes with ketenes have been shown to be very useful in the synthesis of natural products and molecules of biological importance[15b,17-21]. The imine-ketene cycloaddition is well established, but in recent years the discovery of several β-lactam derivatives[22] in nature have given a new impetus to the study of reactions involving conjugated carbon-nitrogen double bonded systems, as for example, azadienes and ketenes.

The literature survey clearly reveals that ketenes add to carbon-carbon double bonds and carbon-nitrogen double bonds resulting mostly in the preferential formation of [2+2] cycloadducts. The azadienes containing either carbon-carbon double bonds and carbon-nitrogen double bonds or both carbon-nitrogen double bonds in conjugation, have been reported to undergo [2+2] and/or [4+2] cycloaddition with ketenes. Thus, 1-aza-1,3-butadiene **1** and diphenyl ketene gave azetidinone **3** and dihyropyrimidinone **4**, and these reactions was explained through the intermediacy of zwitter ion **2**. Subsequently, the formation of [2+2] and [4+2] cycloadducts **6** and **7/8** respectively, in the reaction of chlorocyanoketene with a similar 1-aza-1,3-butadiene, re-established the intermediacy of zwitter ion of type **2** (Scheme-1)[24].

Suschitzky et al.[25] reported that the reactions of 3-(aryliminomethyl)-chromones **9** and 2-(aryliminomethyl)- chromones **10** with chloroketenes followed [4+2] and [2+2] cycloaddition pathways, yielding pyridone **11** and β-lactam derivative **12**, respectively (Scheme-2).

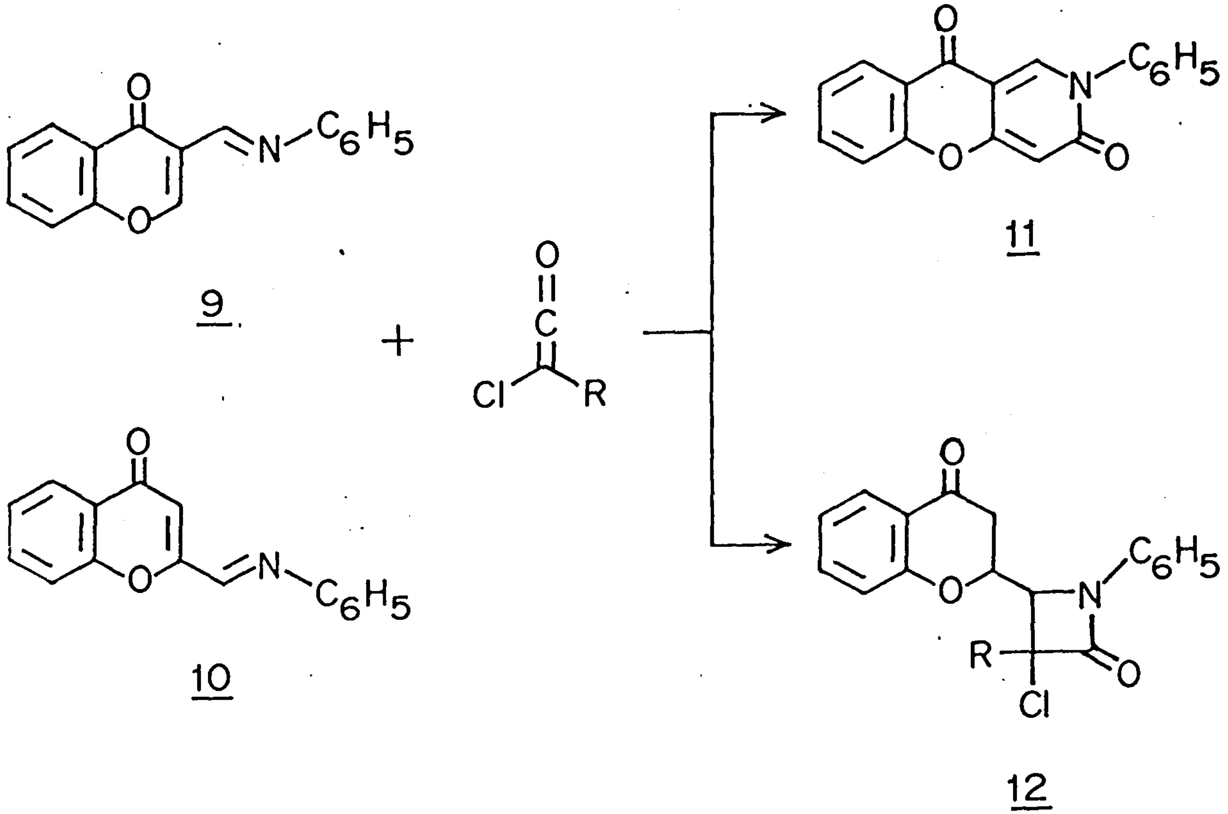
A few more similar reports[26-29] are also available in the literature.

The reports regarding the reactions of 2-aza-1,3-butadienes with ketenes are very rare[30,31]. For example, the Lewis acid catalyzed addition of anils **13** to ketene resulted in [4+2] cycloadduct **14**[32] (Scheme-3).

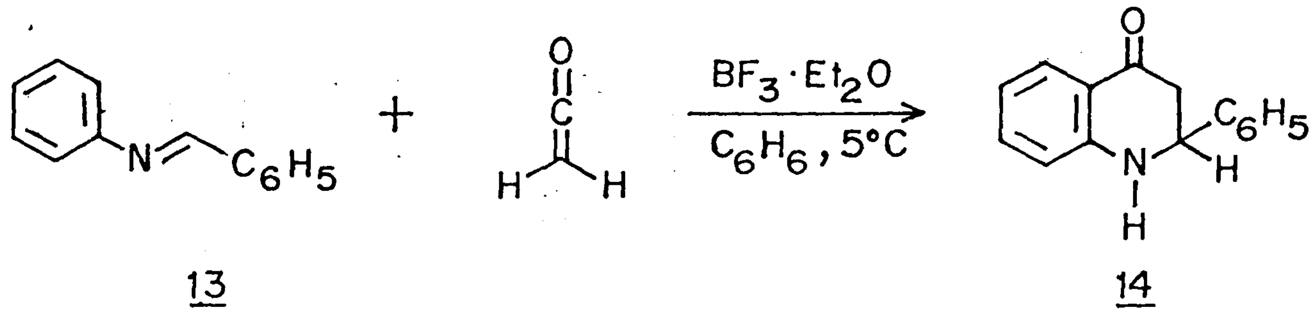
A few cycloaddition reactions of ketenes and 1,4-diaza-1,3-butadienes, have also been reported. For example, the reactions of diphenylketene with α-diimides **15** yielded [2+2] cycloadduct **16**, which were initially mistaken to be [4+2] cycloadducts **17**[34-36]. However, *o*-benzoquinonediimines **18** were shown to give [4+2] cycloadducts **19** with diphenylketene[37] (Scheme-4).

The heterocyclic 1,3-diaza-1,3-butadienes **20** are known to undergo facile [4+2] cycloaddition reactions with diphenylketene[38,39] and diketene. In contrast, the simple acyclic 1,3-diaza-1,3-butadienes **22** failed to give a formal cycloadduct with diketene, and instead resulted in oxazinone **24**. Also, the reaction of **22** with diphenyl ketene did not give any [4+2] cycloadduct, but underwent [2+2] cycloaddition leading to β-lactam **23**[40] (Scheme-5).

The successful incorporation of heteroatoms in dienes have extended the synthetic versatility of cycloaddition reactions by allowing rapid and easy access to a variety of heterocyles. In this context, 1,2- and 1,4-diaza-1,3-butadienes have been extensively studied, whereas reports concerning the comparable reactions of 1,3-diaza-1,3-butadienes were rare[41-43], probably due to: (i) the lack of methods available for the preparation of 1,3-diaza-1,3-butadienes; (ii) their reluctance to participate in [4+2] cycloaddition reactions because of their inverse electron demand tendency due to the unfavourable position of the second nitrogen at position 3- of 1,3-diaza-1,3-butadienes; and (iii) because of their preferred s-trans geometry. In view of the reported lack of synthetic approaches, together with reports of the failure of acylic 1,3-diaza-1,3-butadienes as an effective 4π component in Diels-Alder cycloaddition reactions, we devised simple methods for the preparation of stable acylic 1,3-diaza-1,3-butadienes[44]. Such 1,3-diazabutadienes with polarising functions at 4- and 2/4- position (Scheme-6 and 7) were successfully utilised in [4+2] cycloaddition reactions with various ketenes.



Scheme −2

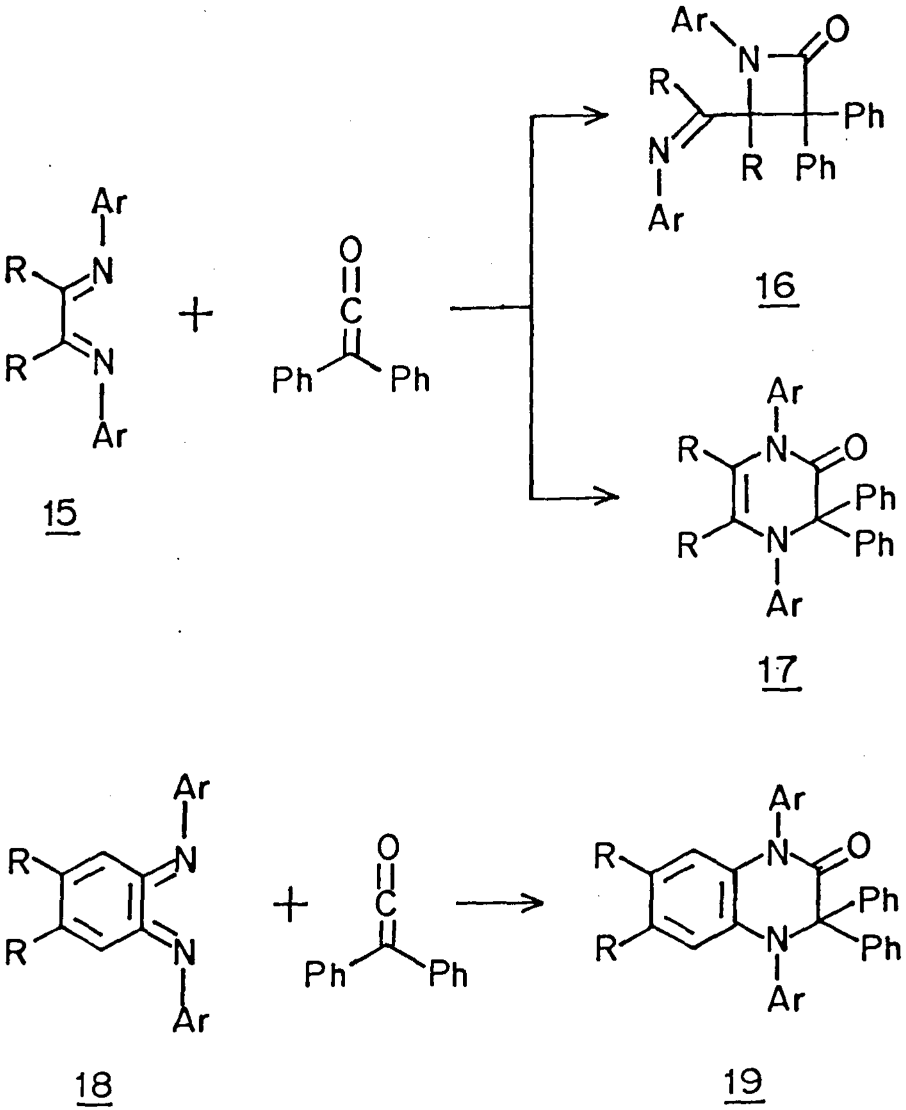


Scheme – 3

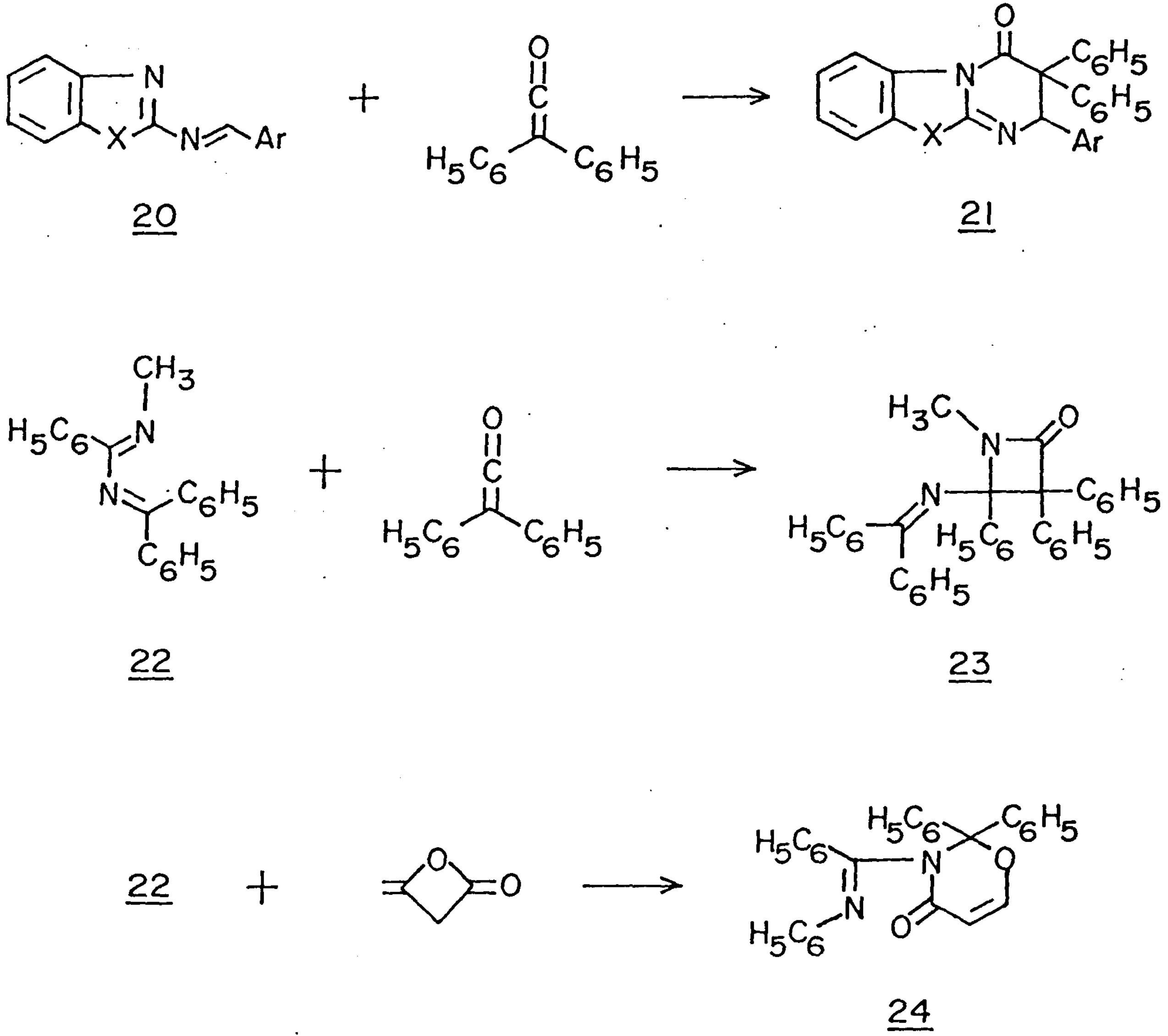
The cycloaddition reactions of monophenylketene, generation of which is simple and easy, could not evoke much interest among synthetic organic chemists, possibly because of its instability[45]. However, cycloaddition could be realised by its slow generation in the presence of reactive substrates. Accordingly, the reactions of 1,3- diaza-1,3-butadienes **(25-28)** with phenylketene **29** were found to follow the [4+2] cycloaddition pathway, resulting in excellent yields of previously unknown pyrimidinones **(30-32)**[46] (Scheme-8). It was also observed that the reactions of diphenylketene with 1,3-diaza-1,3-butadienes **27** followed the [2+2] cycloaddition pathway, yielding β-lactams **33**, whereas 1,3-diaza-1,3-butadiene **28** gave the pyrimidinone **34** as [4+2][47] cycloadduct (Scheme-9).

There are quite a few reports on the addition of halogenated ketenes in carbon-nitrogen double bonded systems. Dibromo-and dichloroketenes were found to add readily to dialkyl diimides **35** to yield the β-lactams. The cycloadditions of imines **36** and dihaloketenes were shown to result in almost quantitative yields of α,α- dihalo-β-lactams, whereas the α,β-unsaturated imines, (for example, 1-aza-1,3-buta-1,3-dienes **37**) yielded both 1,2- and 1,4-cycloadducts[51] (Scheme- 10). This was shown to be possible since cycloadditions across C=N as a two step process involving a dipolar intermediate[52,53], was well established.

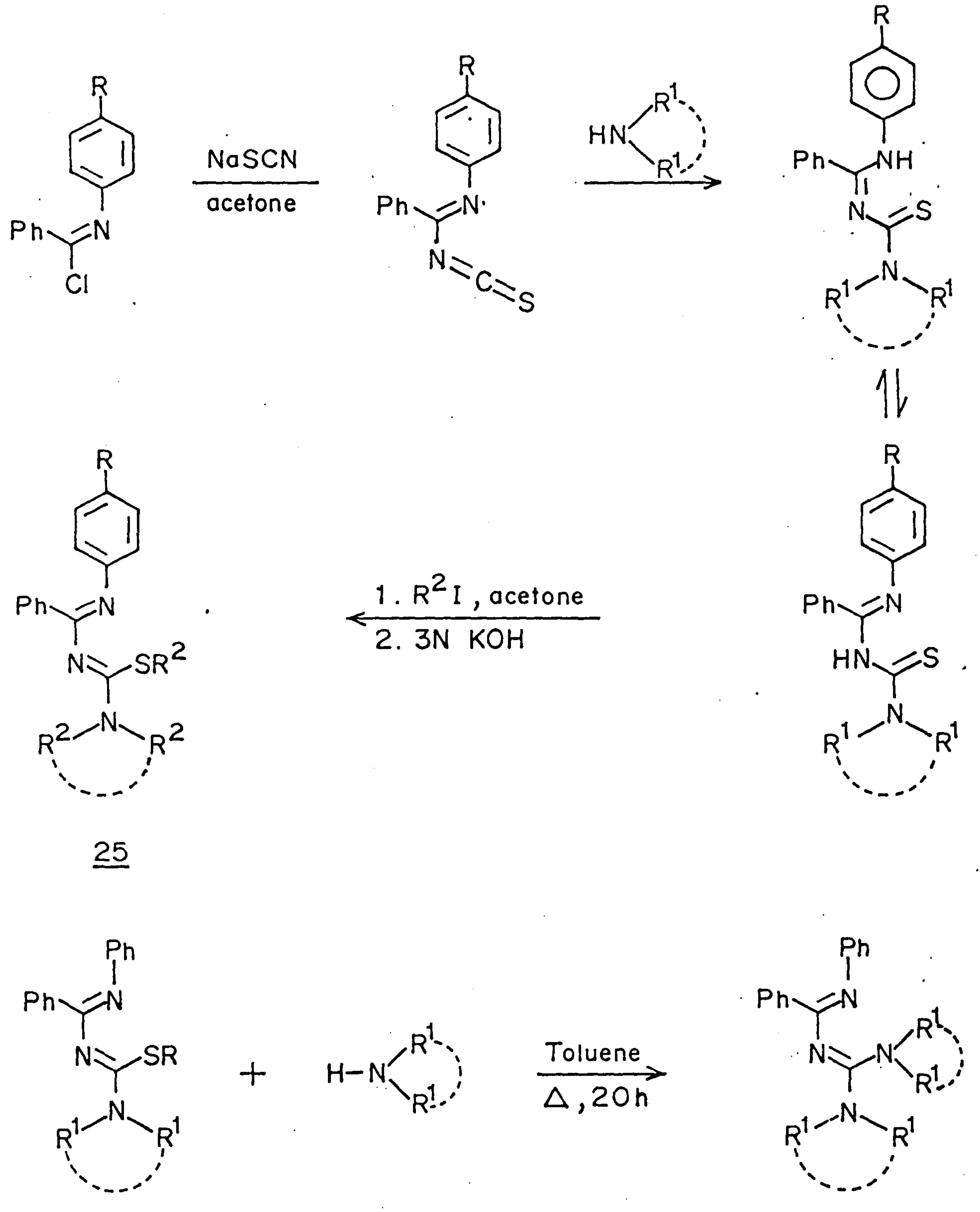
There are very few reports concerning the cycloaddition of azadienes with haloketenes, which may be due to lack of reactivity of azadienes or the fast polymerisation of haloketenes. Keeping these observations in view, we have recently reported the simple methods for the preparation of various reactive acylic 1,3-diaza-1,3-butadienes[44] which were successfully utilized in [4+2] cycloaddition with haloketenes[46,54]. These reactions were found to follow exclusively the 1,4-addition mode, resulting in high yields of previously unknown pyrimidinones. Thus, the reactions of 1,3-diaza-1,3-butadienes **27** and **28** with chloroketene gave pyrimidinones **38** and **39**, formed via the base-induced elimination of dialkylamine from the initially formed [4+2] cycloadduct as an intermediate. The higher polarisability of 1,3-diaza-1,3- butadienes could be considered as one of the reasons


Ar
R
N
R
N
Ar
15
+
O
C
Ph
Ph
Ar
N
O
R
N
Ph
R
Ph
Ar
16
Ar
R
N
O
Ph
R
N
Ph
Ar
17
Ar
R
N
R
N
Ar
18
+
O
C
Ph
Ph
Ar
R
N
O
Ph
R
N
Ph
Ar
19

Scheme - 4



Scheme -5

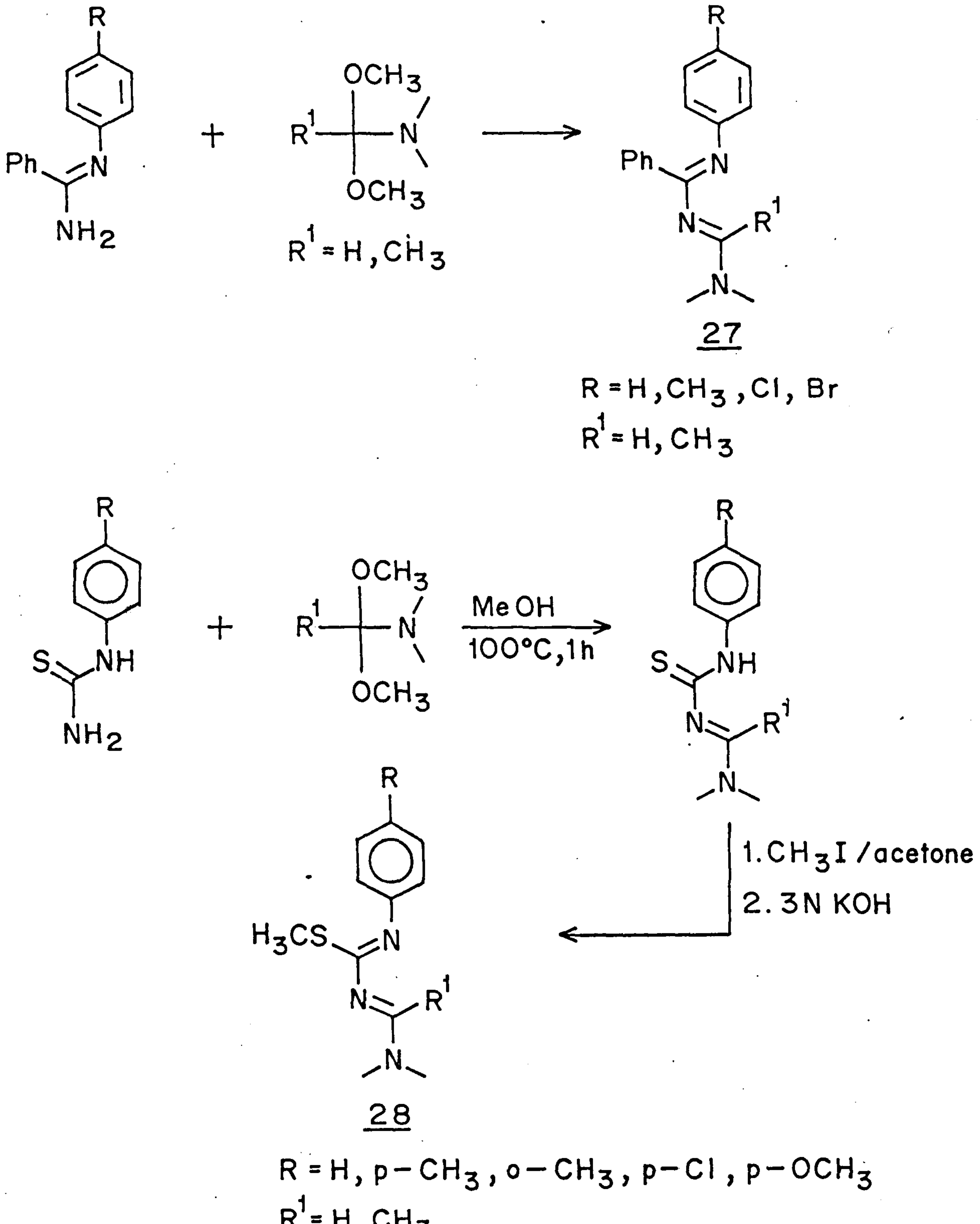


25

25

26

Scheme - 6



27

$R = H, CH_3, Cl, Br$

$R^1 = H, CH_3$

28

$R = H, p-CH_3, o-CH_3, p-Cl, p-OCH_3$

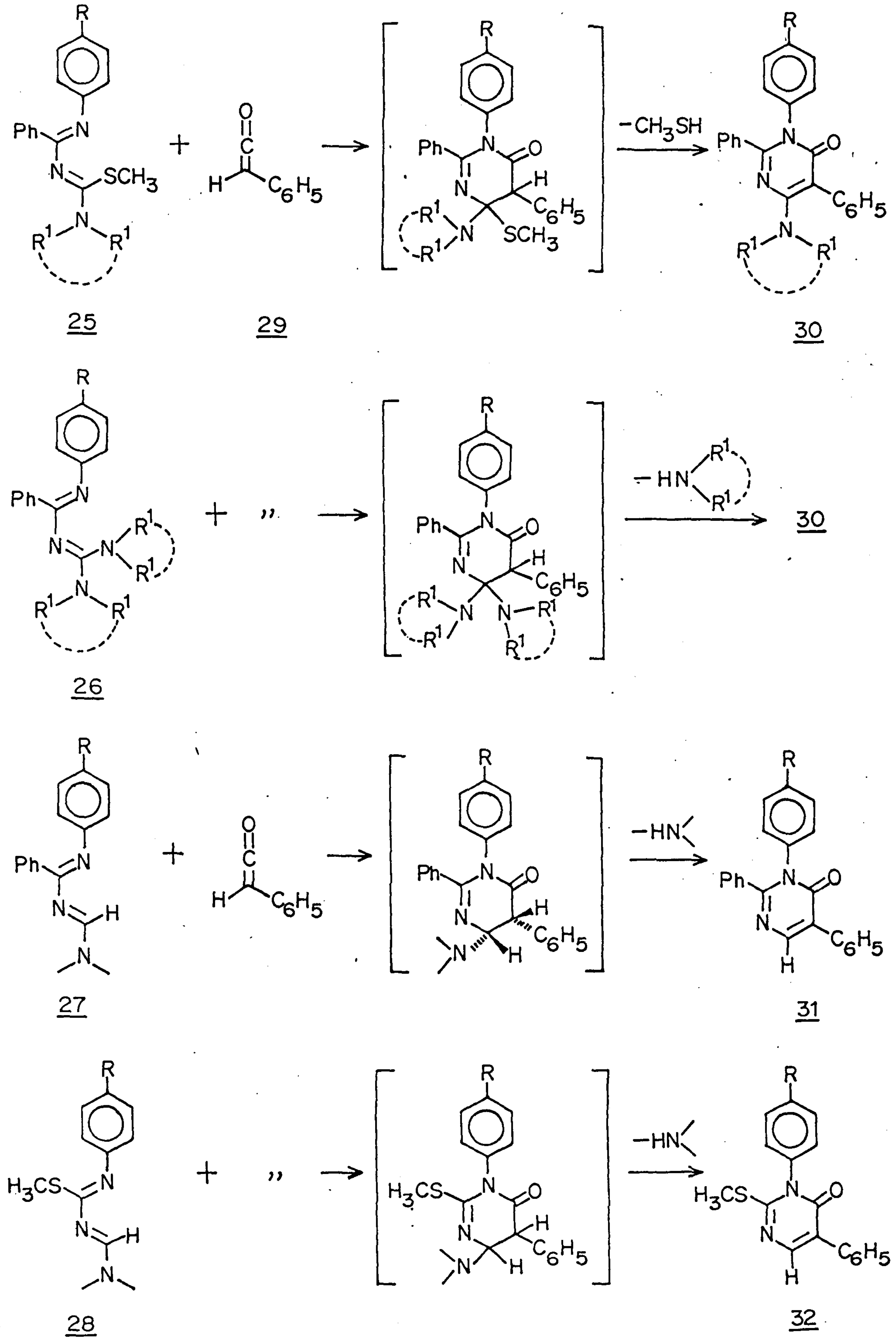
$R^1 = H, CH_3$

Scheme-7

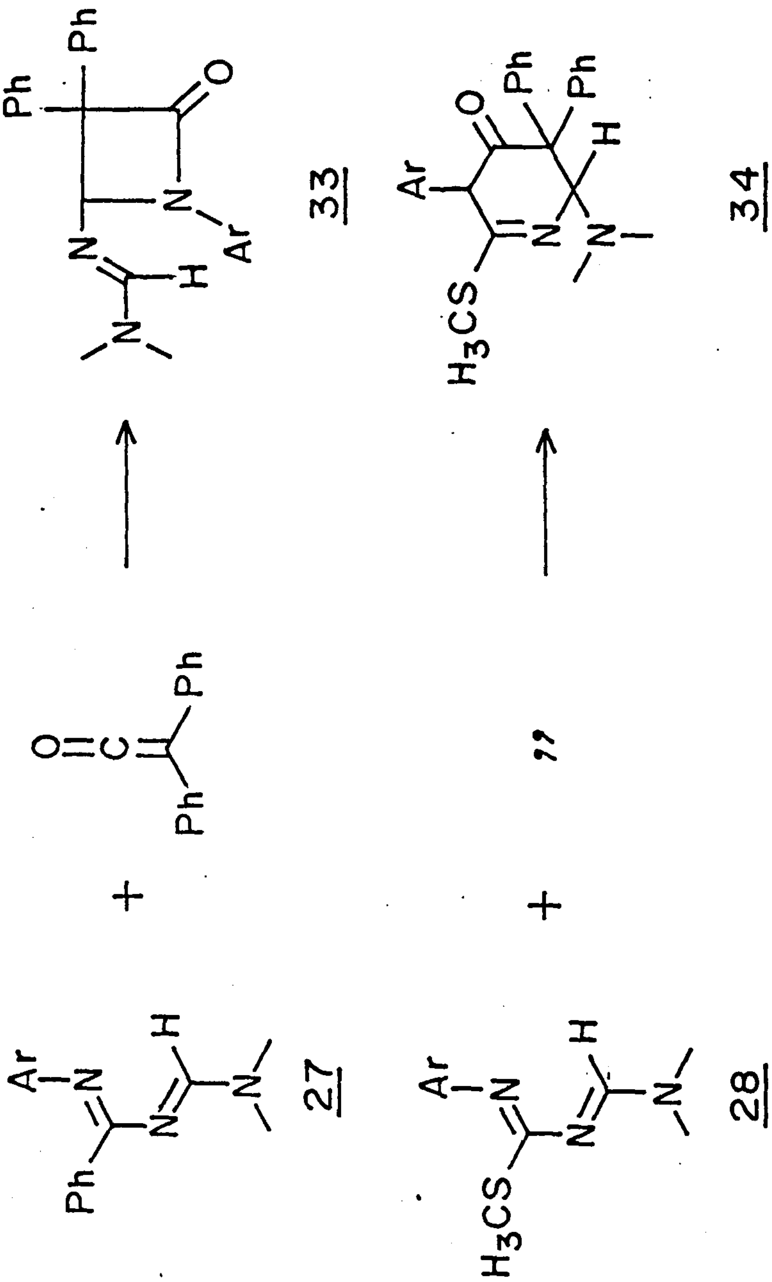
for the formation of δ-lactam, in preference to β-lactam, as in the case of 1-aza-1,3-butadienes[55] (Scheme-11).

Interestingly, the reactions of 1,3-diaza-1,3-butadienes **25** with monochloroketene resulted in products which indicated the presence of methylthio, as well as secondary amino functions and loss of hydrogen chloride. The products were characterized as pyrimidinones **42** and involved transposition of -SMe from position 6- to position 5- of initially formed [4+2] cycloadducts **40** as an intermediate[56]. The probable mechanistic pathway proposed for the formation of rearranged pyrimidinone **42** involves the transformation of intermediate **40** into an episulfonium intermediate **41**. This intermediate then rearranges by the loss of a proton and migration of an alkylthio function to give pyrimidinones **42** (Scheme-12). Further, the reactions of 1,3-diaza-1,3-butadienes **25** with bromo- and iodoketenes have been investigated, since it was thought that the mechanistic pathway followed in their cycloadditions may be influenced by their larger size and better leaving group ability. However, it was found that the reactions of 1,3-diaza-1,3-butadiene **25** with mono bromo/iodoketene resulted in the isolation of identical pyrimidinones **42**. The pyrimidinones obtained in the case of reactions of bromo and iodoketenes showed undepressed melting point and superimposable IR spectra with the corresponding samples obtained in case of chloroketene reactions. The formation of identical pyrimidinones **42** in good yields, in the cases of chloro-, bromo- and iodoketenes, clearly indicated the presence of a common intermediate in all these reactions (Scheme-12)[54] . In the case of reactions of 1,3-diaza-1,3-butadienes **26**, having two secondary amine functions at the 4- position, with haloketenes, no such rearrangement was observed and these reactions yielded pyrimidinones **44**, with the elimination of one of the secondary amine functions from intermediate **43** (Scheme-13).

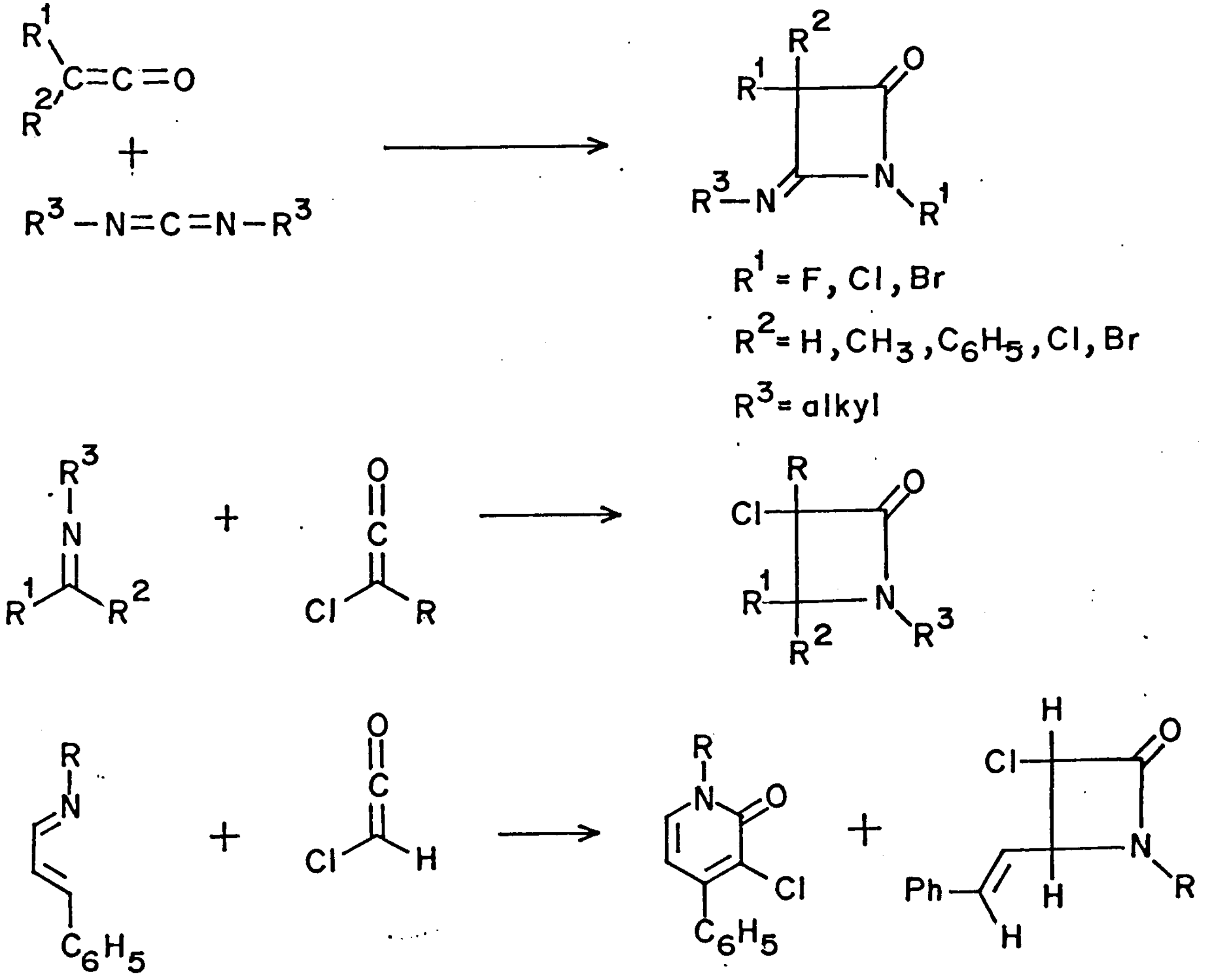
There are also reports of [4+2] cycloaddition reactions of 1,3- diaza-1,3-butadienes **25**, **27** and **28** with 2-oxazolin-5-ones **45**, leading to the formation of various pyrimidinones. Sandhu et al[57,58] reported that 1,3- diaza-1,3-butadienes **27** and **28** reacted with 2-oxazolinones **45** to yield pyrimidinones **46** and **47**, respectively, as single diastereoisomers with reverse stereochemistry. Also,



Scheme - 8

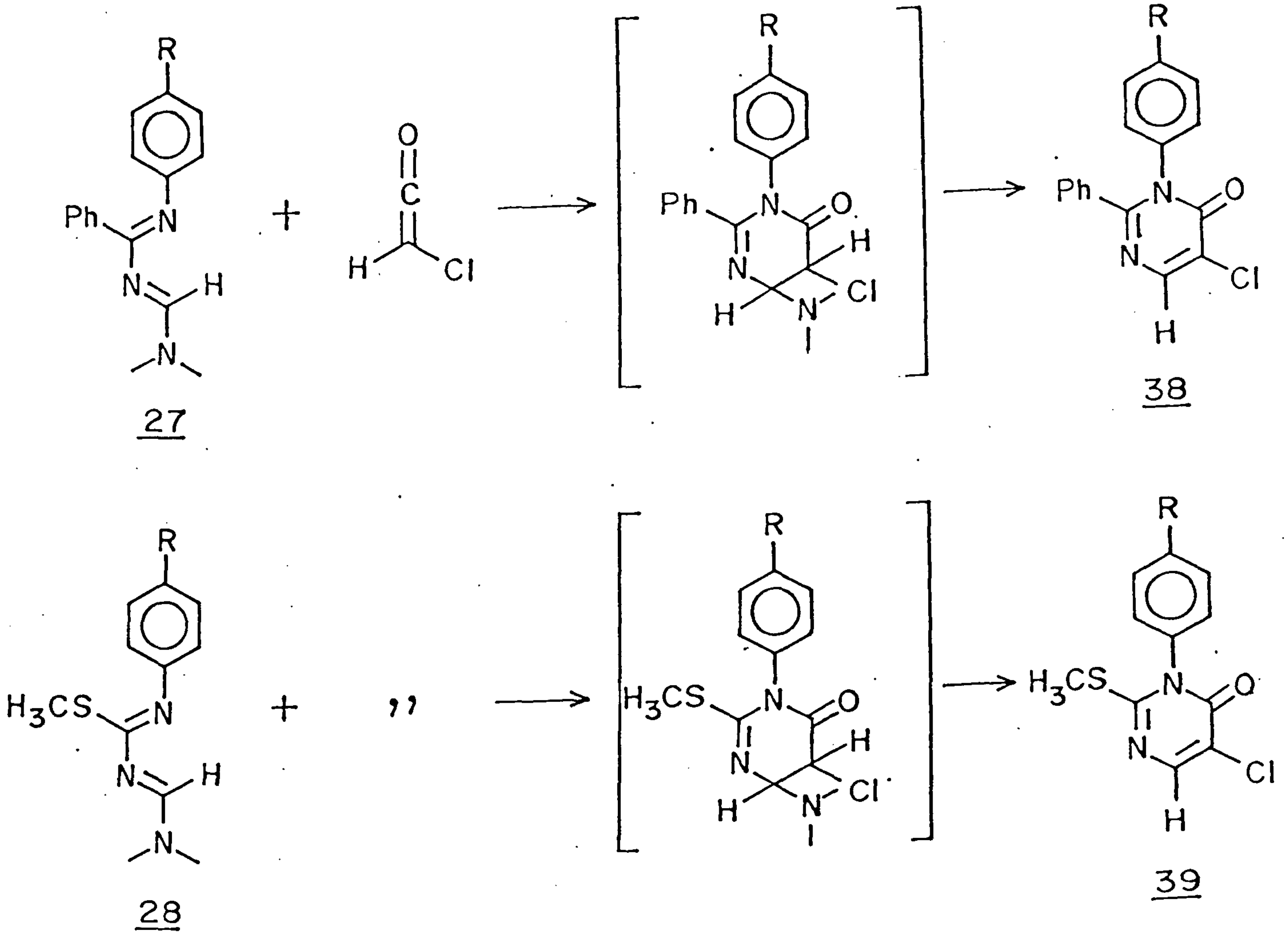


Scheme - 9



37

Scheme-10



Scheme -11

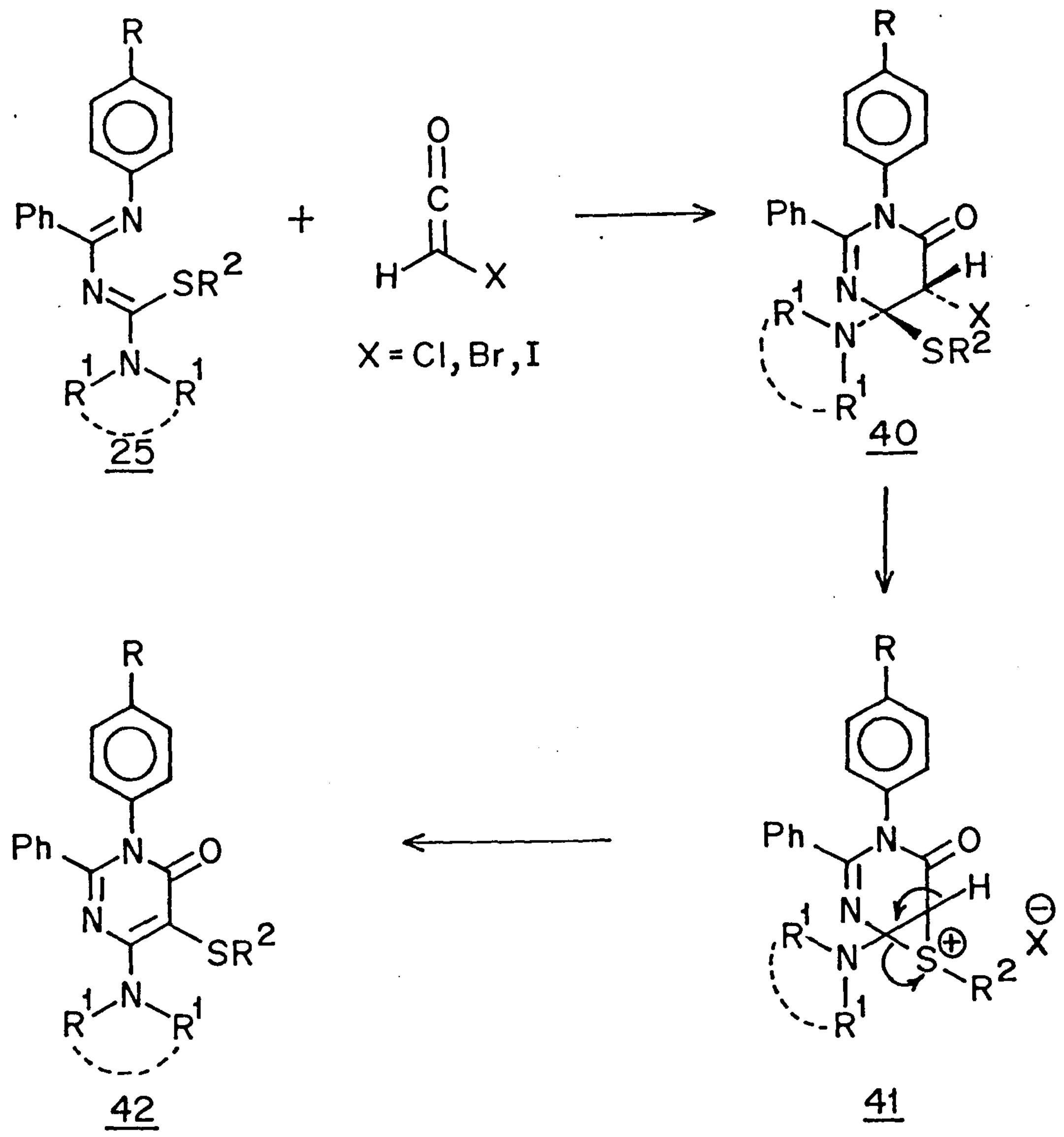
the reactions of 1,3-diaza-1,3-butadienes **25** with **45**, leading to pyrimidinones **48**, have been reported in the literature[58] (Scheme-14).

Very recently, Rossi et al[59] reported the synthesis of 1-(4-methylphenyl)-2,4-diphenyl-1,3-diaza-1,3-butadiene[60] **50**, starting from dibutylphosphoramidate **49** and benzaldehyde (Scheme-15), and their reactions with monophenyl, diphenyl, monochloro and ethoxycarbonylketenes in dry toluene giving rise to the dihydro-pyrimidin-6-ones **52 (a-d)** are also reported (Scheme-16). It is worthwhile to note that the formation of dihydropyrimidinone **52b** represents the first example of a [4+2] cycloaddition reaction between a fully aryl substituted diazabutadiene **50a** and diphenylketene, such a mode of cycloaddition being observed only with bulky alkyl substituted diazabutadienes[61]. Further, in the reaction of **50a** with chloroketene, both **52c** and **53** could be isolated. Poorer yields were observed with the ethoxycarbonyl ketene which underwent partial polymerization also in dilute solution. The reactions performed with 1,3-diaza-1,3-butadines **50b**, bearing a benzyl group on N-1 and ketenes **51(a-c)**, had resulted in the isolation of the [2+2] cycloaddition products, the azetidinones **54 (a-c)** (Scheme-17).

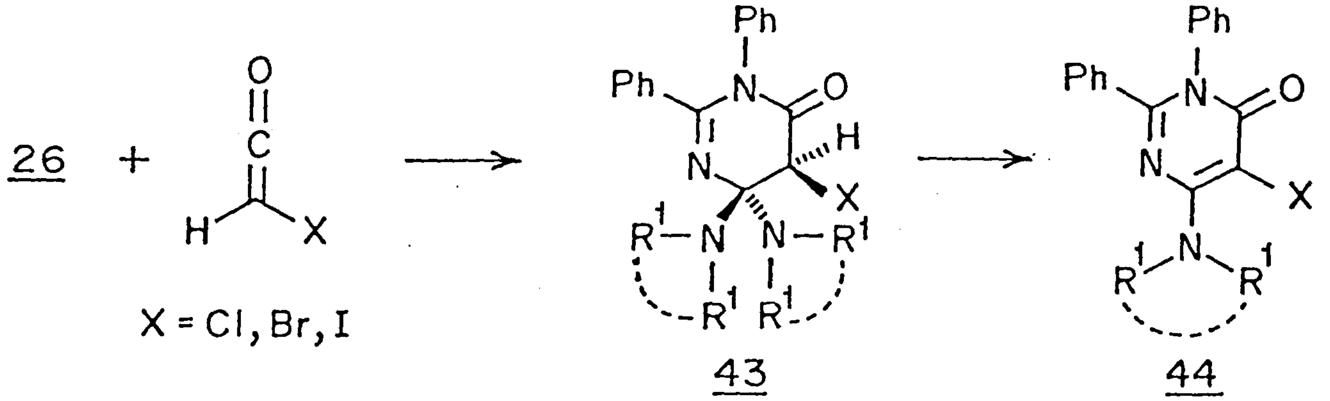
The novelty in this case is represented by the [2+2] cycloaddition observed with phenyl and chloroketene **51 (a,c)**, which react in a [4+2] mode with all diazabutadienes tested until now by Mahajan et al from our laboratories[46,54].

There are numerous reports concerning [2+2] cycloadditions of imines with various ketenes, extended recently to vinyl/ isopropenyl ketenes[62-65] acting as 2π components, leading to a variety of substituted β-lactams[66-69], which, in certain cases, have even been converted to important penicillin derivatives. There are also reports of vinylketenes participating as 4π component in [4+2] cycloaddition reactions[70,71]. Recent disclosures from our laboratories have shown the effective participation of vinylketenes as 2π component in [4+2] cycloaddition reactions with polarised acyclic 1,3-diaza-1,3-butadienes[72] (Scheme-18).

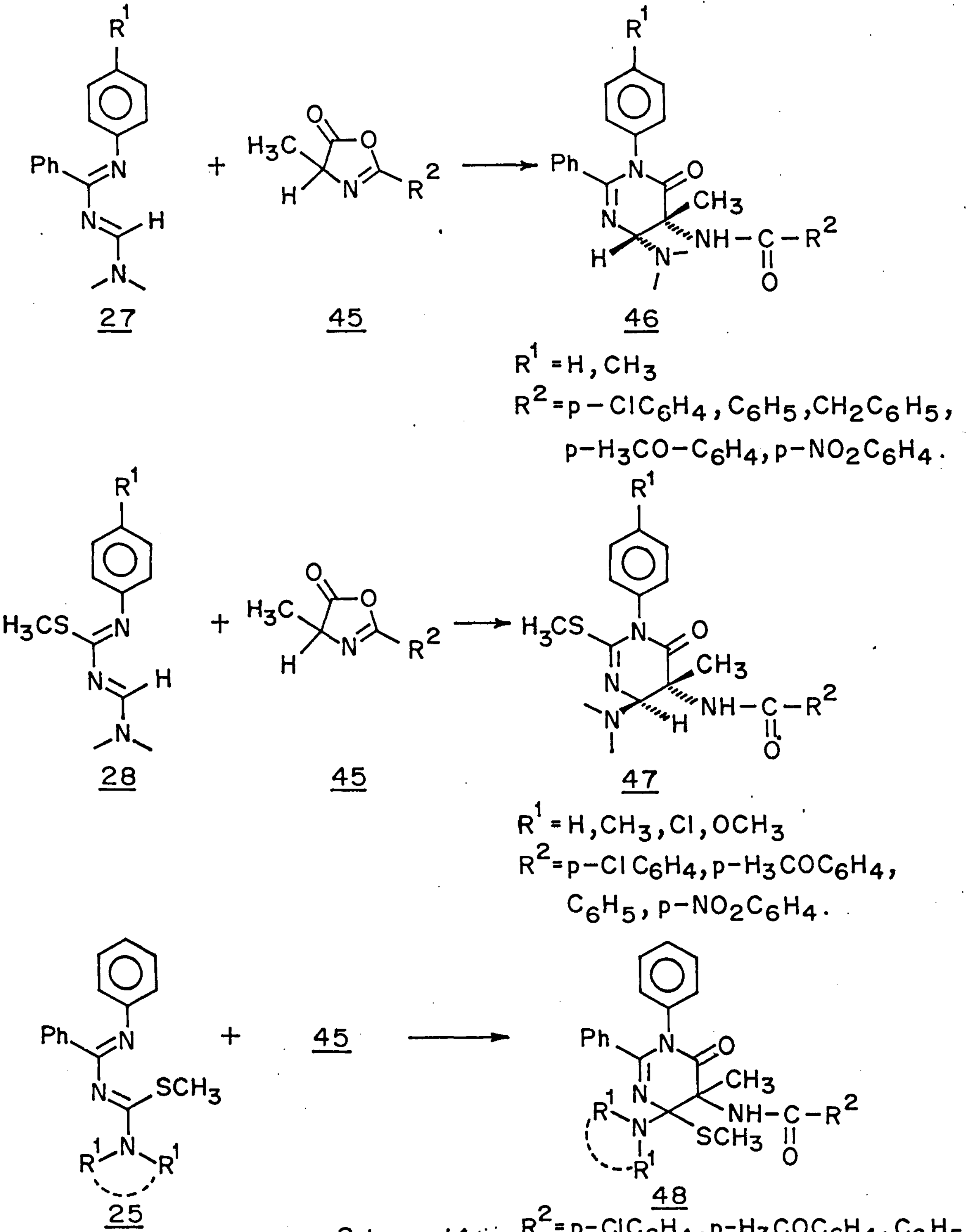
Recent investigations in our laboratories have led to a new method for the generation of butadienylketene, and the successful utilization of this ketene in [2+2]



Scheme-12



Scheme-13

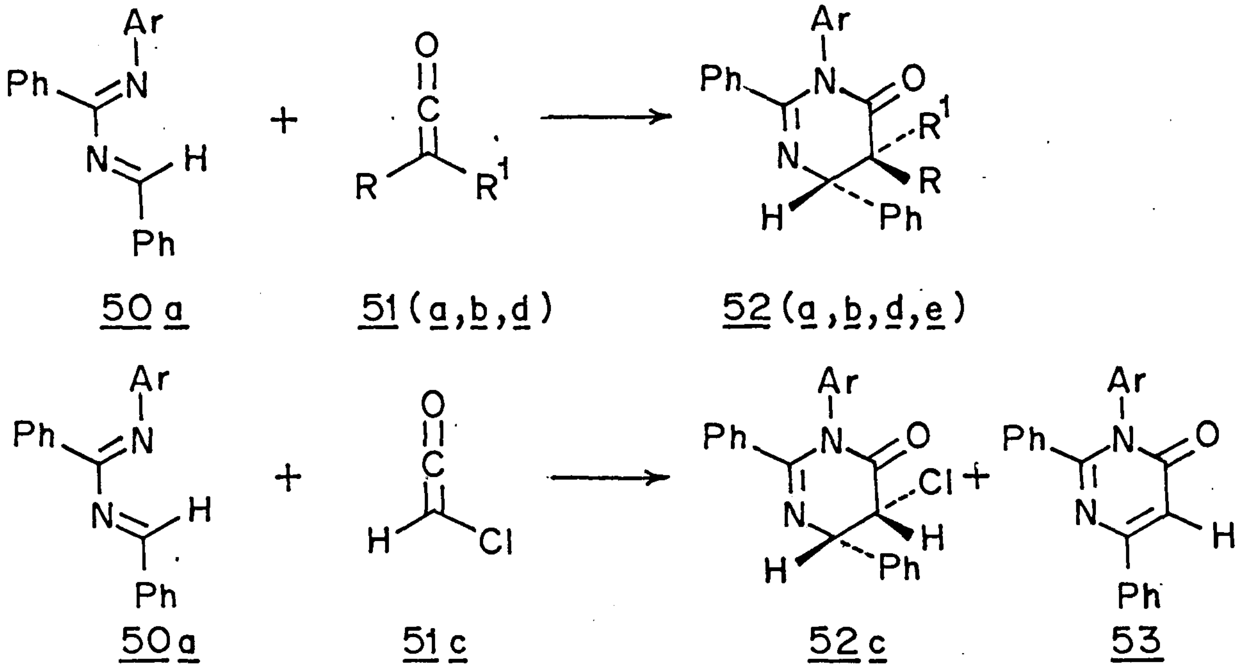


$R^1 = H, CH_3$
$R^2 = p\text{-}ClC_6H_4, C_6H_5, CH_2C_6H_5,$
$p\text{-}H_3CO\text{-}C_6H_4, p\text{-}NO_2C_6H_4.$

$R^1 = H, CH_3, Cl, OCH_3$
$R^2 = p\text{-}Cl\,C_6H_4, p\text{-}H_3COC_6H_4,$
$C_6H_5, p\text{-}NO_2C_6H_4.$

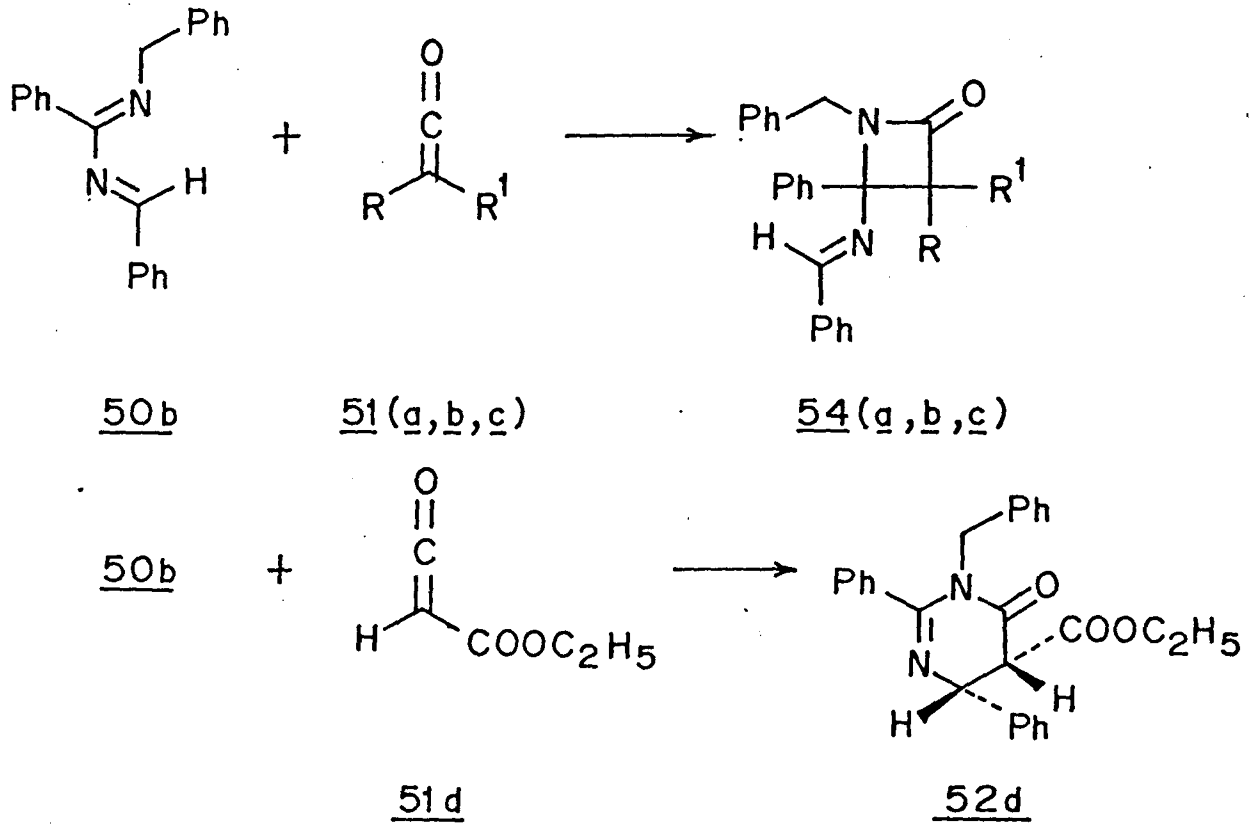
Scheme-14

$R^2 = p\text{-}ClC_6H_4, p\text{-}H_3COC_6H_4, C_6H_5$



52. a R = H, R^1 = Ph, Ar = $CH_3C_6H_4$
b R = Ph, R^1 = Ph, Ar = $CH_3C_6H_4$
c R = H, R^1 = Cl, Ar = $CH_3C_6H_4$
d R = H, R^1 = $COOC_2H_5$, Ar = $CH_3C_6H_4$
e R = Ph, R^1 = H, Ar = $CH_3C_6H_4$
53 R = H, Ar = $CH_3C_6H_4$

Scheme-16



50b 51(a,b,c) 54(a,b,c)

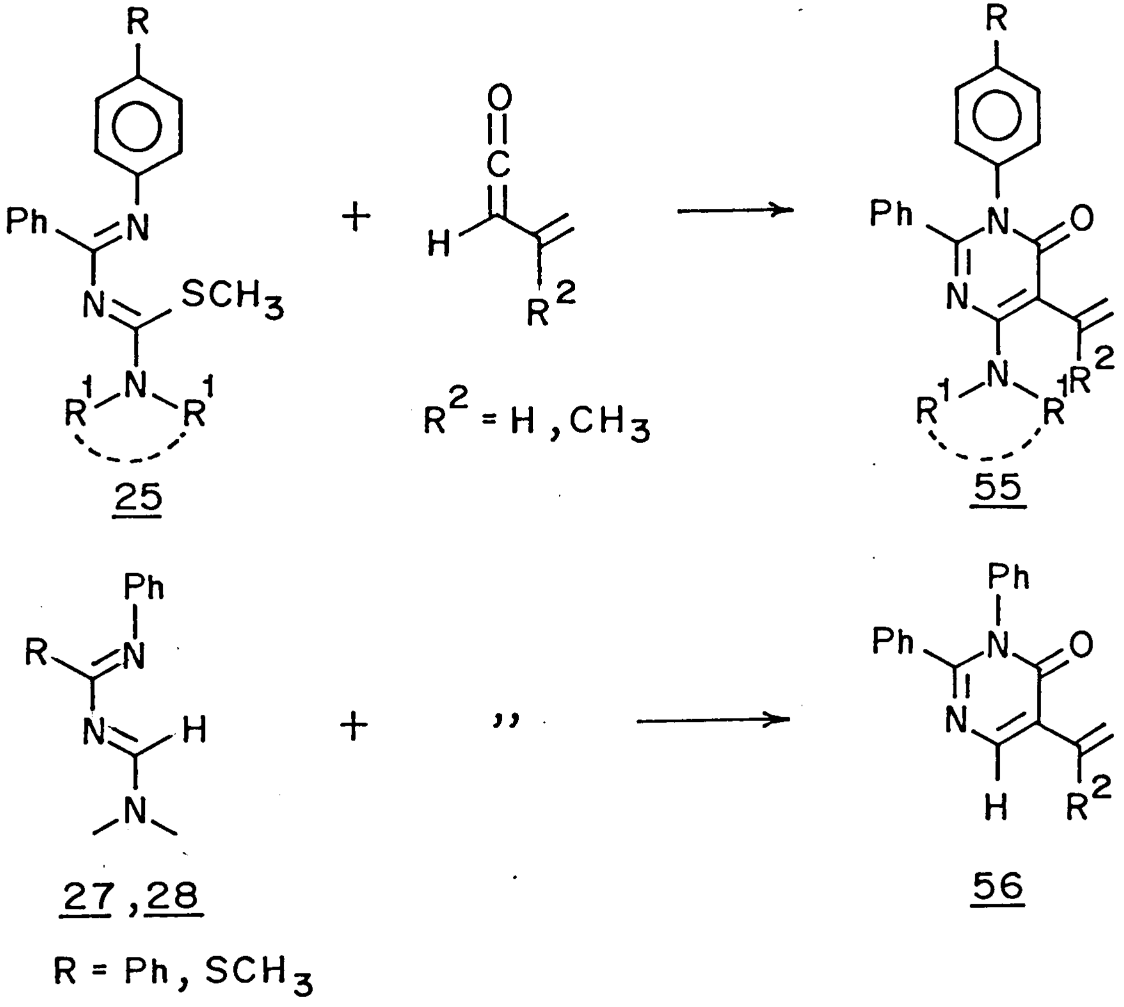
50b + 51d → 52d

54 a. R = Ph , R^1 = H

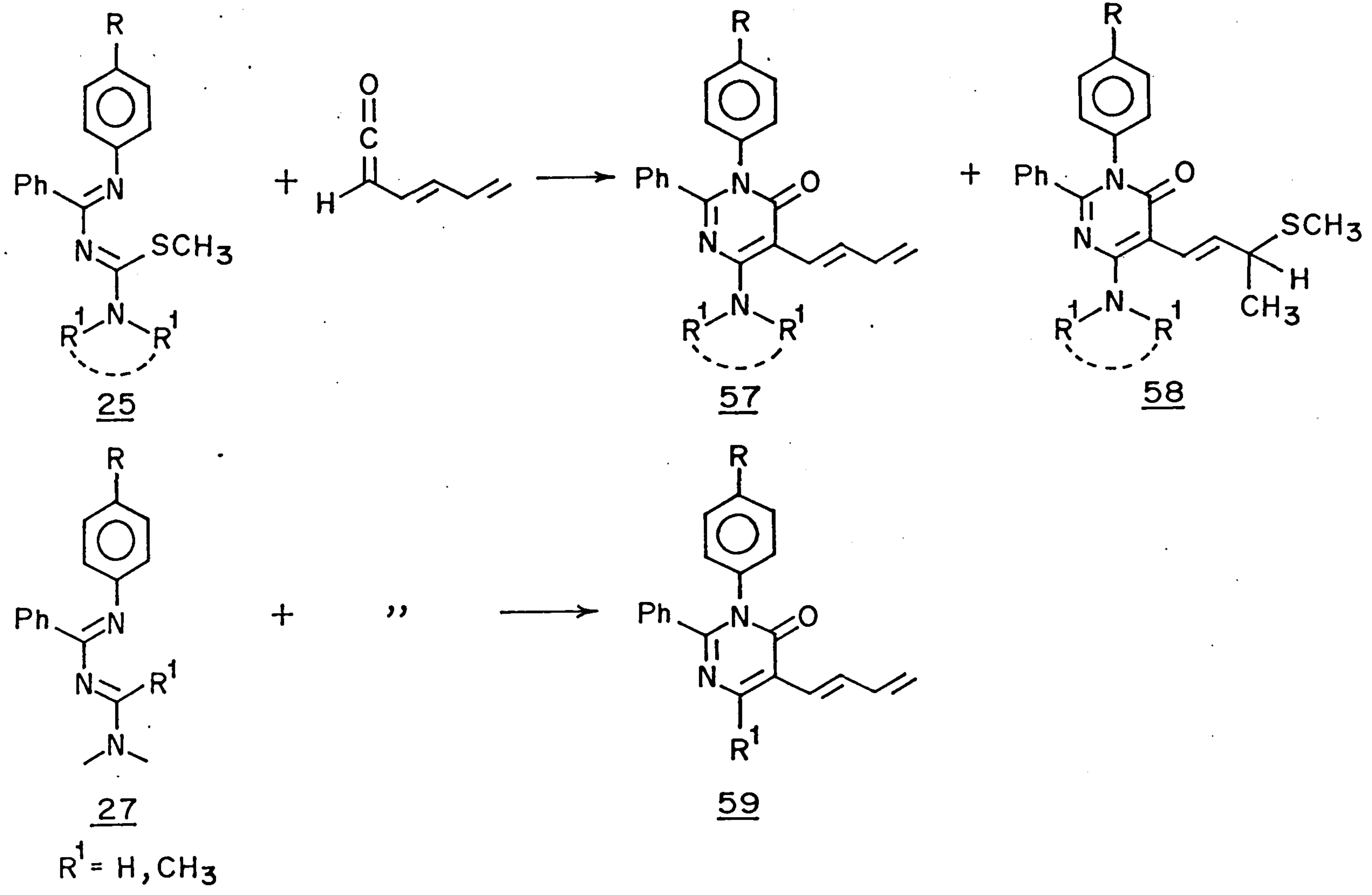
b. R = Ph , R^1 = Ph

c. R = H , R^1 = Cl

Scheme-17



Scheme-18



Scheme—19

cycloaddition reactions with imines, and [4+2] cycloaddition reactions with a variety of 1,3-diaza-1,3-butadienes[73]. To our knowledge, this involves the first use of butadienylketene in cycloaddition reactions. The reactions of 1,3-diaza-1,3-butadienes **25** with butadienyl ketene gave pyrimidinone **57** and pyrimidinone **58** involving suprafacial 1,5-alkythio shift. However, the reactions of **27** with butadienylketene gave pyrimidinone **59** as the only isolable product (Scheme-19).

In view of the interesting disclosures involving the reactions of various 1,3-diaza-1,3-butadiene with ketenes, and to further exploit such reaction pathways for the synthesis of various substituted/fused pyrimidinones, it was thought worthwhile to extend these studies to N-arylamino-1,3-diazabutadines[74,75]. Here, we have investigated the reactions of these diazabutadines with phenyl-, halo-,vinyl-, isopropenyl- and butadienylketenes with a view to examine the regiochemical aspects and to understand the nature of the reaction pathways followed in these reactions. The results of these investigations are described in sections **1.2**, **1.3** and **1.4** of this chapter.

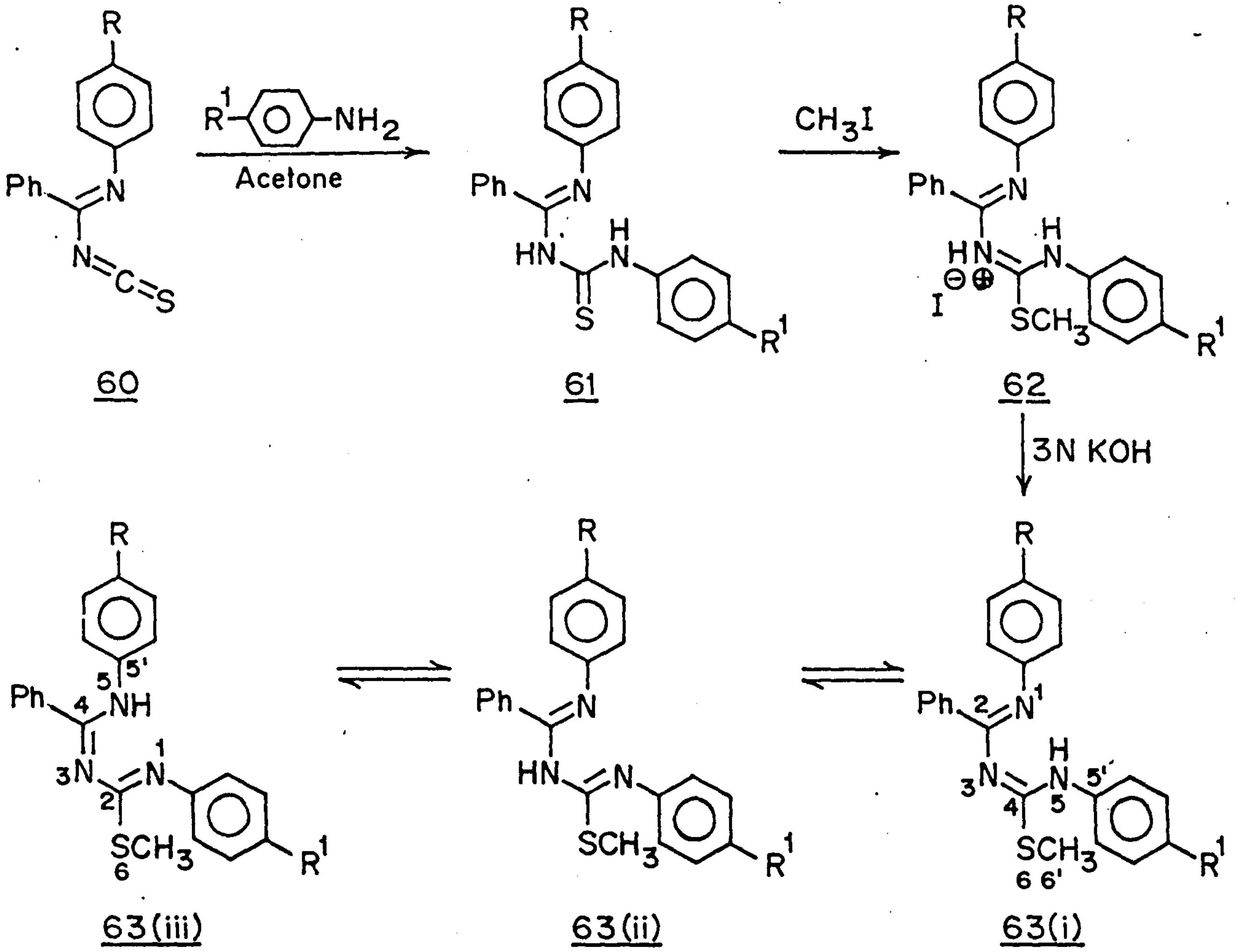
1.2: *REACTIONS OF N-ARYLAMINO-1,3-DIAZA-1,3-BUTADIENES WITH PHENYL- AND HALOKETENES*

The advent of various diazabutadienes as potential 4π components has extended their versatility by allowing an easy access to various functionalised six membered heterocyclic systems. Keeping in view the growing significance of the synthetic utility of heterodienes[76-79], the development of synthetic approaches to newer 1,3-diazabutadienes is thought to be of immense importance.

Results and Discussion

The desired N-arylamino -1,3-diazabuta-1,3-dienes **63** have been synthesised by the reactions of N-arylbenzimidoyl isothiocyanates[80] **60** with primary aromatic amines, followed by S-methylation of the resultant thioureas **61** (Scheme-20). It was felt that 1,3-diazabutadienes **63** could possibly exist in a number of tautomeric forms, namely, 1-aryl-4-(N-arylamino)-4-methylthio-2-phenyl 1,3-diaza-1,3-butadienes form **63i**, N-imidoylthioimidate **63ii** and 1-aryl-4-(N-arylamino)-2-methylthio-4-phenyl-1,3-diaza -1,3-butadiene form **63iii**. In order to investigate the regiochemical aspects and to understand the nature of the reaction pathway followed, we have examined the reactions of such systems with various ketenes. Further, it was felt that the comparison of the dienic properties of tautomeric forms **63i** and **63iii** could be an interesting scientific enquiry, which in the case of heterodienes in general, and azadienes in particular, have not been well attended to.

Thus, the reactions of **63** with monosubstituted ketenes **64**, namely, phenyl and chloroketenes, generated in situ from phenyl acetyl chloride/ chloroacetyl chloride and triethylamine in methylene chloride, resulted in very good yields (75-95%) of products which were characterised as pyrimidinones **66**, on the basis of analytical and spectral evidences. In the **IR** spectra (KBr) of these adducts, strong absorption peak around 1680 cm^{-1} indicated the presence of an α,β-unsaturated carbonyl group, and the absence of any peak around 1730 cm^{-1} clearly ruled



63. a. $R = H$, $R^1 = H$

b. $R = H$, $R^1 = Cl$

c. $R = H$, $R^1 = CH_3$

d. $R = H$, $R^1 = OCH_3$

e. $R = Cl$, $R^1 = H$

f. $R = CH_3$, $R^1 = H$

g. $R = CH_3$, $R^1 = Cl$

h. $R = CH_3$, $R^1 = OCH_3$

Scheme-20

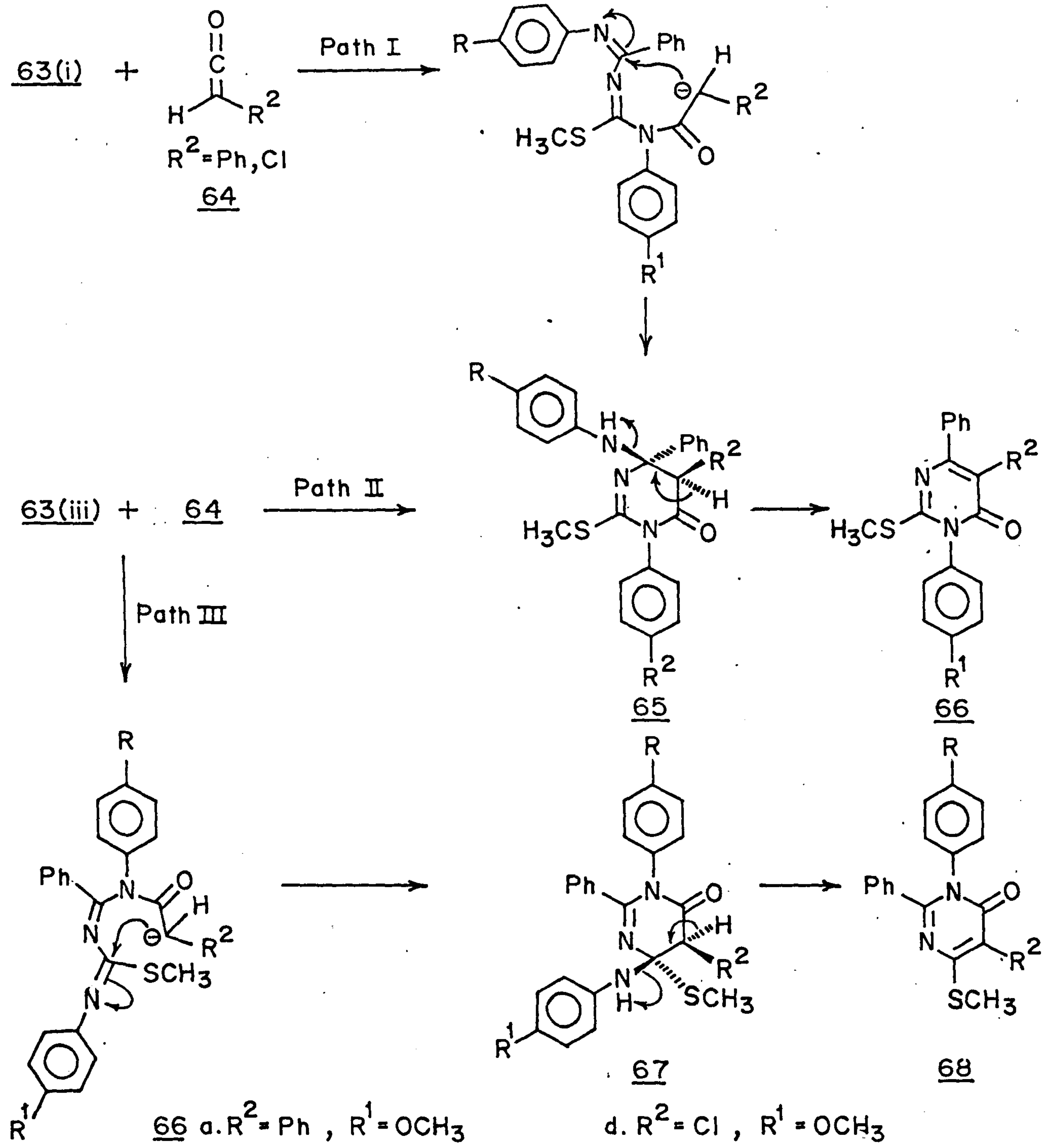
out the formation of any β-lactam. Their ^{1}**H NMR** spectra showed the presence of methylthio protons, and the loss of the proton signals from one N-arylamino function. On the basis of these data, the products could be characterised either as 3-aryl-2-methylthio- 6-phenyl-4(*3H*)-pyrimidinones **66** or 3-aryl-6-methylthio-2-phenyl-4(*3H*)-pyrimidinones **68**. However, the absence of protons due to N-arylamino functions next to the carbon bearing the phenyl group in the ^{1}**H NMR** spectra of all these products indicated a preference for pyrimidinones **66** over pyrimidinones **68**. The compound **66a** for example analysed for $C_{24}H_{20}N_2O_2S$ and its mass spectrum showed in addition to the molecular ion peak at 400 (58.7%) , peaks at 353 (30.1%, M-SCH_3), 192 (37.1%), 175 (60.1%), 163 (94.5%), 147 (30.2%), 121 (99.3%) and 77 (18.5%). The probable mechanism leading to the formation of pyrimidinones **66** is outlined in Scheme-21. In this scheme, it is assumed that the reaction of 1,3-diaza-1,3-butadienes **63** with ketenes **64** can follow three different pathways. The pathway I assumes initial nucleophilic attack by amino nitrogen of 1-aryl-4-(N-arylamino)-4-methylthio-2-phenyl-1,3-diazabutadienes **63i** at the ketene carbonyl, followed by cyclisation to give the intermediate **65**, which undergoes elimination of aromatic amines to give pyrimidinones **66**. The pathway II, involving regioselective [4+2] cycloadditions of 1-aryl-4-(N-arylamino)-2-methylthio-4-phenyl-1,3-diaza-1,3-butadiene **63iii** with ketenes **64** can yield the intermediate **65**, which in the presence of excess of triethylamine, undergoes elimination of aromatic amines resulting in pyrimidinones **66**. According to pathway III, the nucleophilic attack by the arylamino nitrogen of **63iii** at the ketene carbonyl, followed by cyclisation, may result in an intermediate **67** which, on elimination of aromatic amines, yield pyrimidinones **68**, isomeric with pyrimidinones **66**. The formation of pyrimidinones **68** may further be ruled out since it has been reported that the intermediate of the type **67** prefers elimination of methyl mercaptan over that of amines[46,72].

The pathways (I and III), assume initial nucleophilic attack by N-5 of structure **63i** and **63iii** respectively (Table-I). It was felt that the relative electron densities at these nitrogen atoms may help in discriminating one mechanism over the other. Keeping this in view, we have carried out the semi empirical AM1 calculations[81] for structures **63i** and **63iii**. The calculations were performed by using the MOPAC program package[82], without imposing any geometrical constraints. The results are presented for both structures in Table-I, where the charge on the skeleton atoms are given. Earlier theoretical (ab initio) studies on 1,3-diaza-1,3-butadienes showed that the S-*trans* arrangement corresponds to a stable molecule, and the S-*cis* arrangement does not correspond to a minimum on the potential energy surface. However, in substituted 1,3-diaza-1,3-butadienes like **63**, the substituents (NHR) provide the hydrogen atom for the formation of intramolecular hydrogen bond and stabilize the S-cis isomers. AM1 calculations showed that the S-*cis* isomers are at least 6-7 K cal/ mole more stable that the S-*trans* isomers. The N H...N hydrogen bond lengths are in the range of 2.1 Å to 2.2 Å. This distance corresponds to strong intramolecular hydrogen bonding interactions. For example, the H_2O....H-OH hydrogen bond distance is 2.14 Å according to AM1 calculations. The amino group is planar in **63**, as evidenced by the sum of angles around amino N (360°).

Tautomer **63i** is more stable than **63iii** by about 0.81 k cal/mole. Though the difference is very small, it may be concluded that in solution, **63i** exists predominantly. In **63i**, the amino nitrogen is more charged and in **63iii**, the imino nitrogen is more charged. Hence, it is evident that the N- atom (No.5) in structure **63i**, having greater charge density as compared with the N-atom (No.5) in structure **63iii**, is more nucleophilic.

Table I: **Semi Empirical AM1 Calculations**

Structure 63i			Structure 63iii		
Atom No.	Chemical Symbol	Charge	Atom No.	Chemical Symbol	Charge
1	N	-0.3353	1	N	-0.2763
2	C	0.3331	2	C	0.2977
3	N	-0.3295	3	N	-0.3225
4	C	0.1860	4	C	0.2467
5	N	-0.3532	4’	C	-0.0628
5’	C	0.0651	5	N	0.2466
6	S	-0.0549	5’	C	0.0479
6’	C	0.0537	6	S	-0.0888



66 a. R^2 = Ph , R^1 = OCH_3
b. R^2 = Ph , R^1 = H
c. R^2 = Cl , R^1 = OCH_3
d. R^2 = Cl , R^1 = OCH_3
e. R^2 = R^1 = Cl

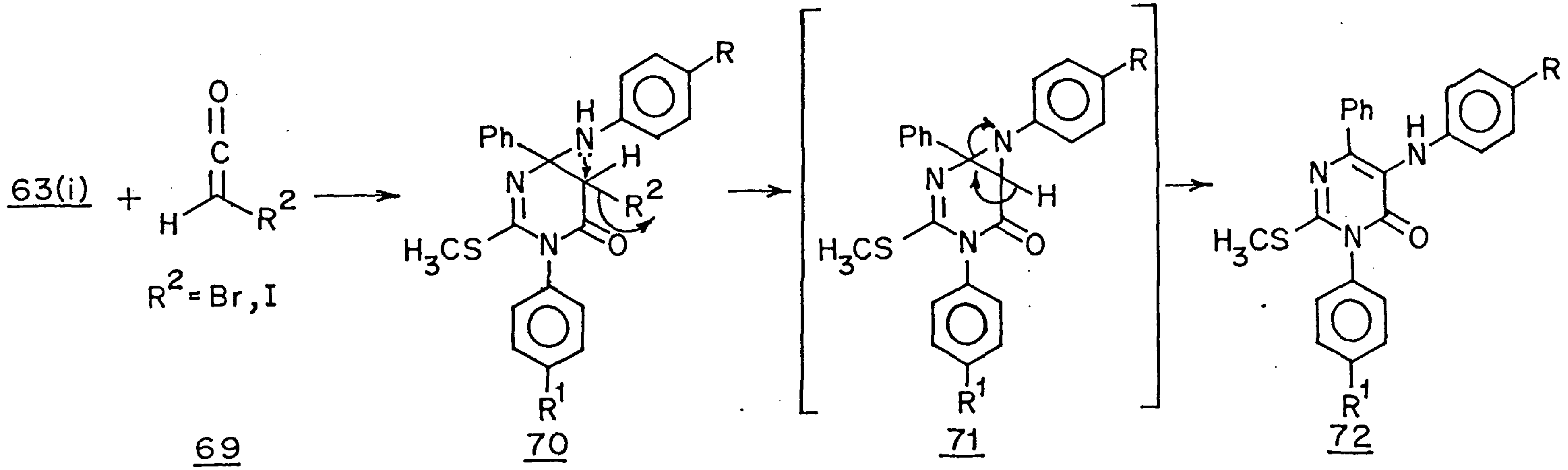
Scheme- 21

Based on these calculations, it may be concluded that for the formation of pyrimidinones **66** in these reactions, the pathway I, involving initial nucleophilic attack of amino nitrogen of **63i** at the ketene carbonyl[74] may indeed be preferred over pathways II and III. On the basis of the above conclusion, it may also be inferred that 1,3-diaza-1,3-butadienes **63** perhaps exist predominantly in the tautomeric form **63i.**

Further to our investigations, we have examined the reactions of 1,3-diaza-1,3-butadienes **63** with bromo- and iodoketenes, since it was felt that the intermediate **70**, because of better leaving group abilities of bromide and iodide, may undergo either elimination of aromatic amines or hydrobromic/hydroiodic acid. Interestingly, the reactions of 1,3-diaza-1,3-butadienes **63** with bromo- and iodoketenes, generated in situ from bromoacetylbromide/triethylamine and iodoacetic acid/*p*-toluene sulfonyl chloride/triethylamine, respectively, resulted in good yields of novel rearranged pyrimidinones **72**, which were characterised on the basis of analytical results and spectral data (Scheme-22).

The compound **72a**, analysed for $C_{23}H_{19}N_3OS$, and its mass spectrum, gave the molecular ion peak at 385 (100%), and showed peaks at 352 (22.9%), 294(4.5%), 276(5.4%), 207(10.2%), 193(10.7%), 150(18%), 136 (15.2%), 104(33.4%) and 77 (44.1%). Its **^{1}H NMR** spectrum exhibited signals both for N-aryl and methylthio protons. The probable mechanism leading to the formation of rearranged pyrimidinones **72** is outlined in Scheme-22. In this Scheme, it is assumed that the initial nucleophilic attack by the preferred tautomeric form **63i** at the ketene carbonyl, followed by cyclisation, leads to an intermediate **70**, which transforms into aziridinium intermidiate **71** by the nucliophilic attack of N-aryl nitrogen at the C-5 bearing the bromide/iodide leaving group, and finally rearranges to pyrimidinones **72**.

Although we have recently reported the 1,2- alkylthio shifts involving episulfonium intermediates in the case of cycloaddition reactions of 1,3- diaza-1,3-



$\underline{72}$. a. R = R^1 = H

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

c. R = H , $R^1 = OCH_3$

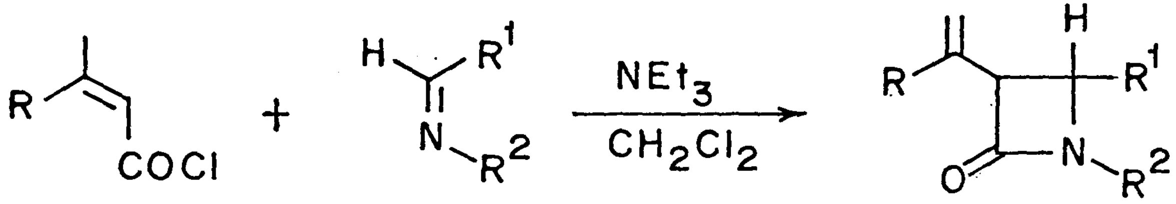
d. R = CH_3, R^1 = Cl

Scheme-22

butadienes **25** with haloketenes[54], the intermediacy of aziridinium ions could not be observed even in the reactions of 1,3- diaza-1,3-butadienes **26** and **27** with bromo- and iodoketenes. To our knowledge, this may represent one of the rare examples of 1,2- amino shifts involving aziridinium intermediates in the case of heterocyclic compounds.

1.3: *REACTIONS OF N-ARYLAMINO-1,3-DIAZA-1,3-BUTADIENES WITH VINYL/ ISOPROPENYL KETENES*

The cycloaddition reactions of ketenes continue to be an important area of scientific quest[83], which is dominated by [2+2] cycloaddition reactions and such cycloaddition reactions with carbon-nitrogen double bonds of imines, monoaza-and diazabutadienes have been successfully exploited for the synthesis of important β-lactam derivatives[15b,84]. However, very few reports describe the synthesis of α-alkyl, α-acyl or α-alkylidene β-lactams based on acid chloride imine cycloadditions[85]. Synthesis of α-alkyl or α-acetyl β-lactams became an important target after the discovery of various carbepenem antibiotics which demanded the use of ketenes such as vinyl/ isopropenyl ketenes to generate such β-lactams. The reactions of acid chloride **73** with various Schiff bases **74**, in the presence of triethylamine, resulted in the formation of various α-vinyl/ isopropenyl azetidinones[86-89], the stereochemistry of which was found to depend on the substituents **R^1** and **R^2** (Scheme-23). This reaction, developed in 1971 by Bose et al was later utilised by Zamboni and Just[87] for preparing various α-vinyl-β-lactams, the potential synthons for β-lactam antibiotics. Such α-vinyl azetidinones have been converted to pyrrolidine derivatives, intermediates for carbepenem antibiotics[89], and sulfur containing bicyclic β-lactam[90]. The [2+2} cycloaddition reactions of vinylketenes **77**, generated in situ, to electron rich alkynes **76** have also been reported[91-95]. The 4-vinyl cyclobutenones **78** thus obtained were transformed into various catechols[96] **80** through putative dienylketene intermediates **79** (Scheme-24). Following the same strategy, the judicious heteroatom permutations of dienylketene provided direct synthetic entry to a variety of valuable heterocyclic systems via intramolecular vinyl ketene cyclisations on to the C=X (X = N,O) double bonds [97-99]. Using this methodology, a novel approach to α-pyridone **81** has been developed[97,98]. A large variety of substituted ring fused α-pyridone derivatives **82** have been synthesised by the thermal rearrangements of substituted cyclobutenones via vinylketene intermediates[99] (Scheme-25). Ab initio calculations



73 74 75

75. $R = H, CH_3$

$R^1 = Ph, \text{furfuryl}, Ph-CH=CH, CO_2Me, COPh$

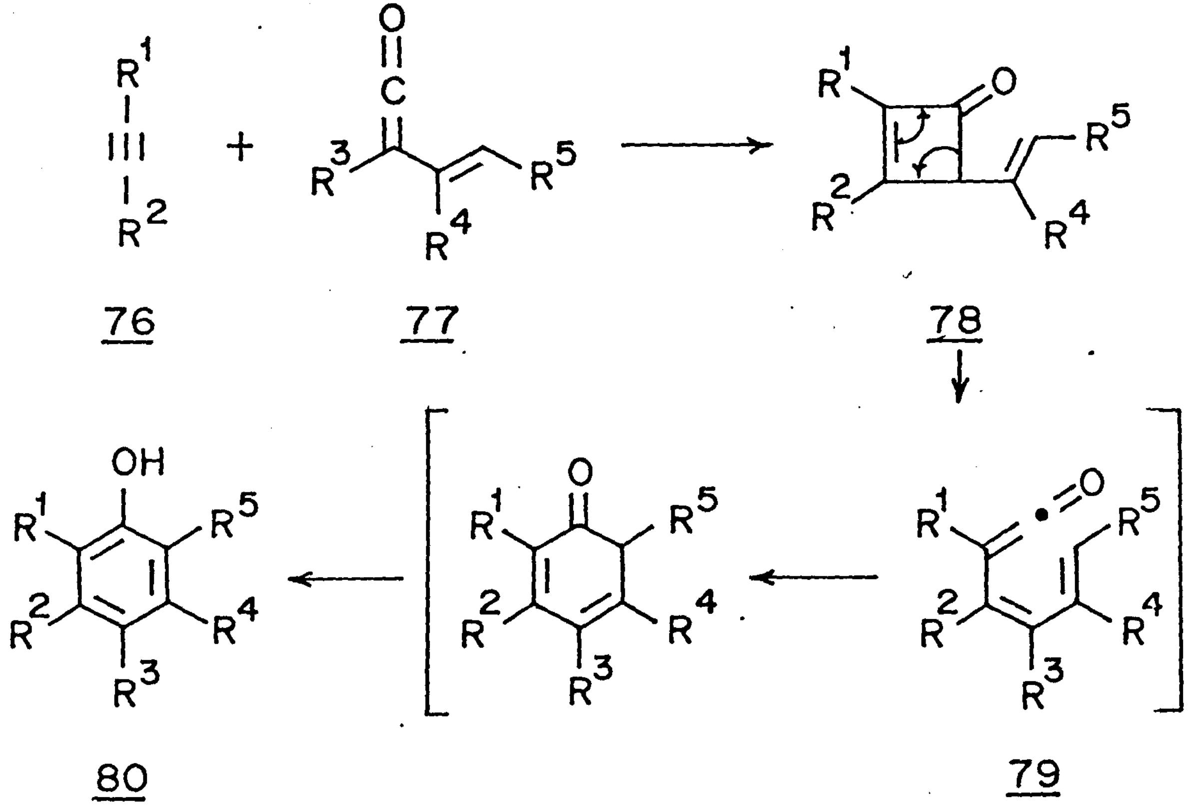
$R^2 = Ph, CH(CO_2Me)CH_2OTBDMS^a, CH(CO_2PNB)CH(CH_3)OH^b,$

$CH_2C_6H_3(OMe)_2\,(2,4), C_6H_4OMe-p, CH(CH_3)Ph, tBu.$

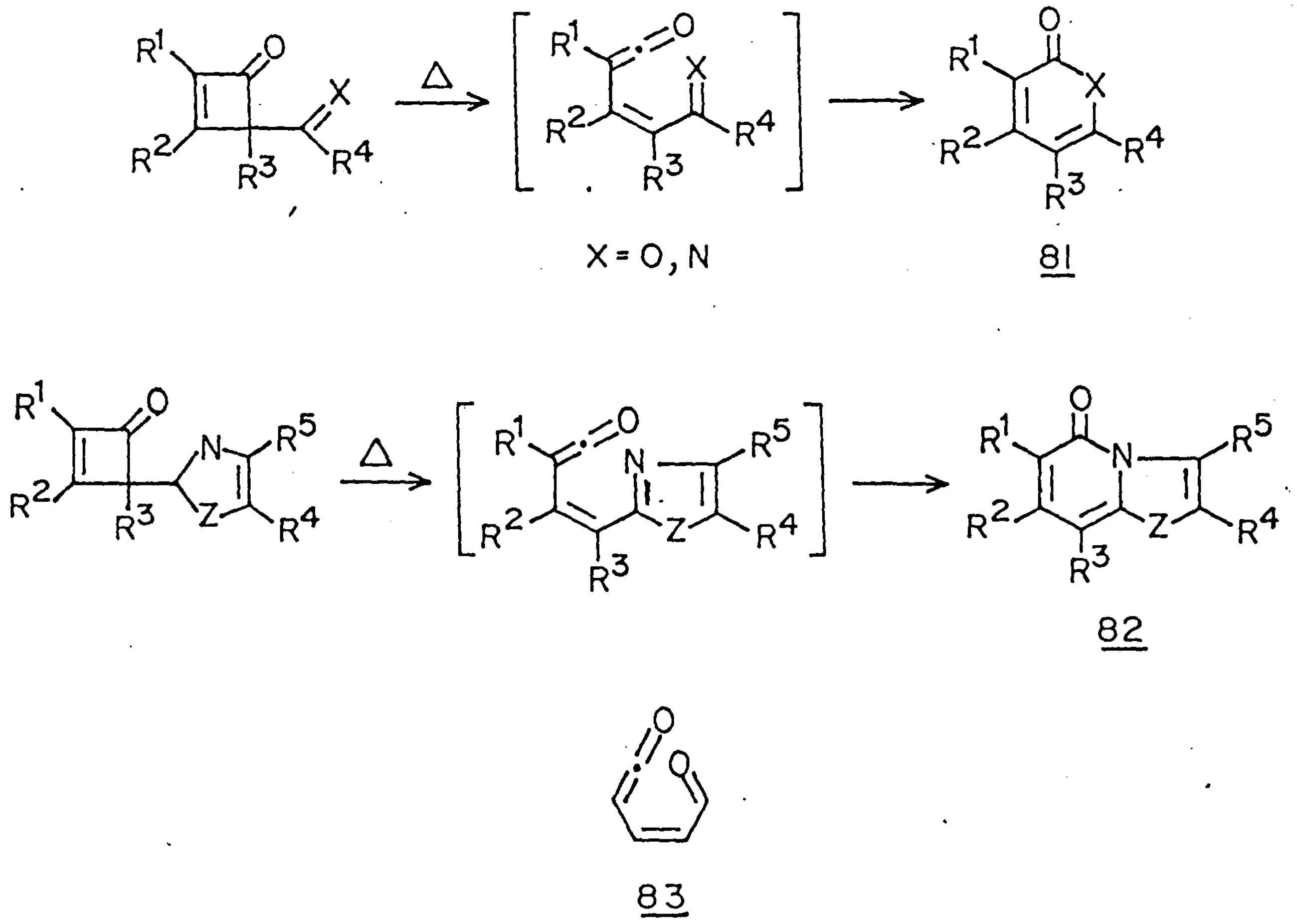
[a] TBDMS = tert-butyldimethylsilyl

[b] PNB = p-nitrobenzyl

Scheme-23



Scheme-24



R^1 = Et, n-Bu, Me, ph, MEM-O-
R^2 = Et, n-Bu, i-PrO, Me, Bu_2N
R^3 = OAc, OH, n-Bu
R^4, R^5 = H, H;
Z = CH = CH, C(OMe) = CH, S, NMe, N-MOM

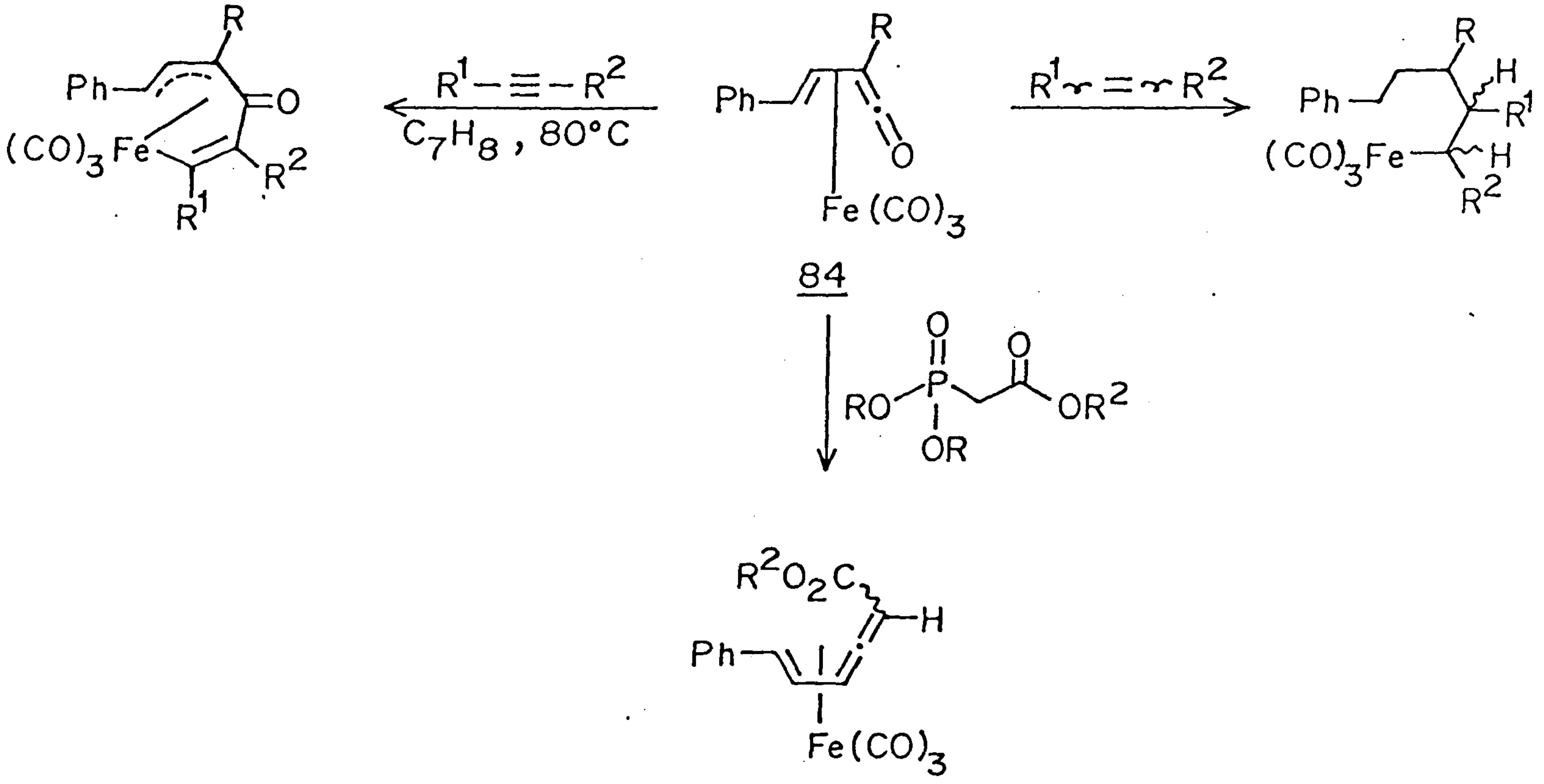
Scheme – 25

have also been carried out on all conformations and several reactions of 5-oxo-2,4-pentadienal **83** vinyllog of formylketene, as well as related systems[100].

The metal bound ketenes and vinylketenes have frequently been postulated as reactive intermediates[101,102] which have created considerable interest towards the reactivity of isolable metal bound ketene and vinyl ketenes[103,104]. Thomas et al extensively studied the fundamental reactivity of easily accessible and highly stable iron centered vinyl ketene complexes **84** and have reported the results of their reactions with isonitriles[105], phosphonoacetate anions[106], nucleophiles[107], alkynes[108] and alkenes[109] (Scheme-26).

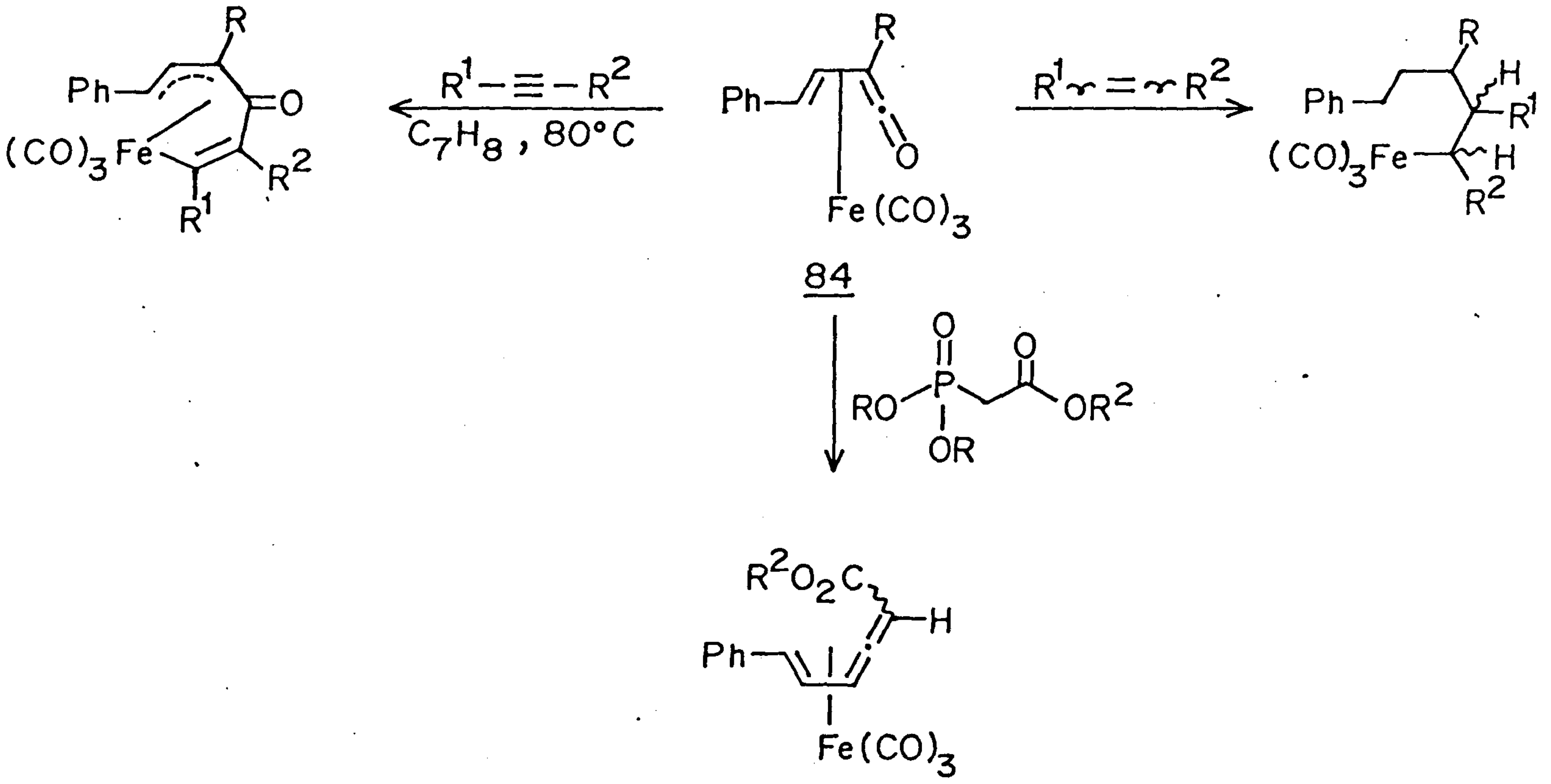
Thus, there are reports of vinylketenes participating either as 2π component in [2+2] cycloaddition with imines/azadienes or as a 4π component in [4+2] cycloadditions reactions. It has recently been reported that vinyl ketenes participated as 2π component in [4+2] cycloaddition reactions with polarised acyclic 1,3-diaza-1,3-butadienes[72]. This perhaps formed the first report concerning the participation of such ketenes as 2π component in [4+2] cycloaddition reactions. Thus, the reactions of 1,3-diaza-1,3-butadienes **25** with isopropenyl/vinylketenes **85** resulted in the formation of previously unknown pyrimidinones **87**. Similarly , the reactions of 1,3-diaza-1,3-butadienes **27** and **28** with vinyl ketenes resulted in the formation of pyrimidinones **89** by the elimination of dimethylamino function from the initially formed [4+2] cycloadducts **88** as intermediates (Scheme-27). The formation of pyrimidinones **87** and **89** in these reactions requires the trans arrangement of H-5/methylthio functions and H-5/dimethylamino functions in the intermediates **86** and **88** respectively. The intermediates **86** and **88**, with the desired stereochemical arrangements, may either be formed through highly stereoselective and concerted [4+2] cycloadditions, or via the equilibration of the intermediates possibly through zwitterionic intermediates[19,54].

Further, the incorporation of an unsaturated side chain (1-propenyl) at C-5 of uridine has recently been reported to increase binding to both single strand RNA and double strand DNA[110]. In continuation of our studies concerning regioselective

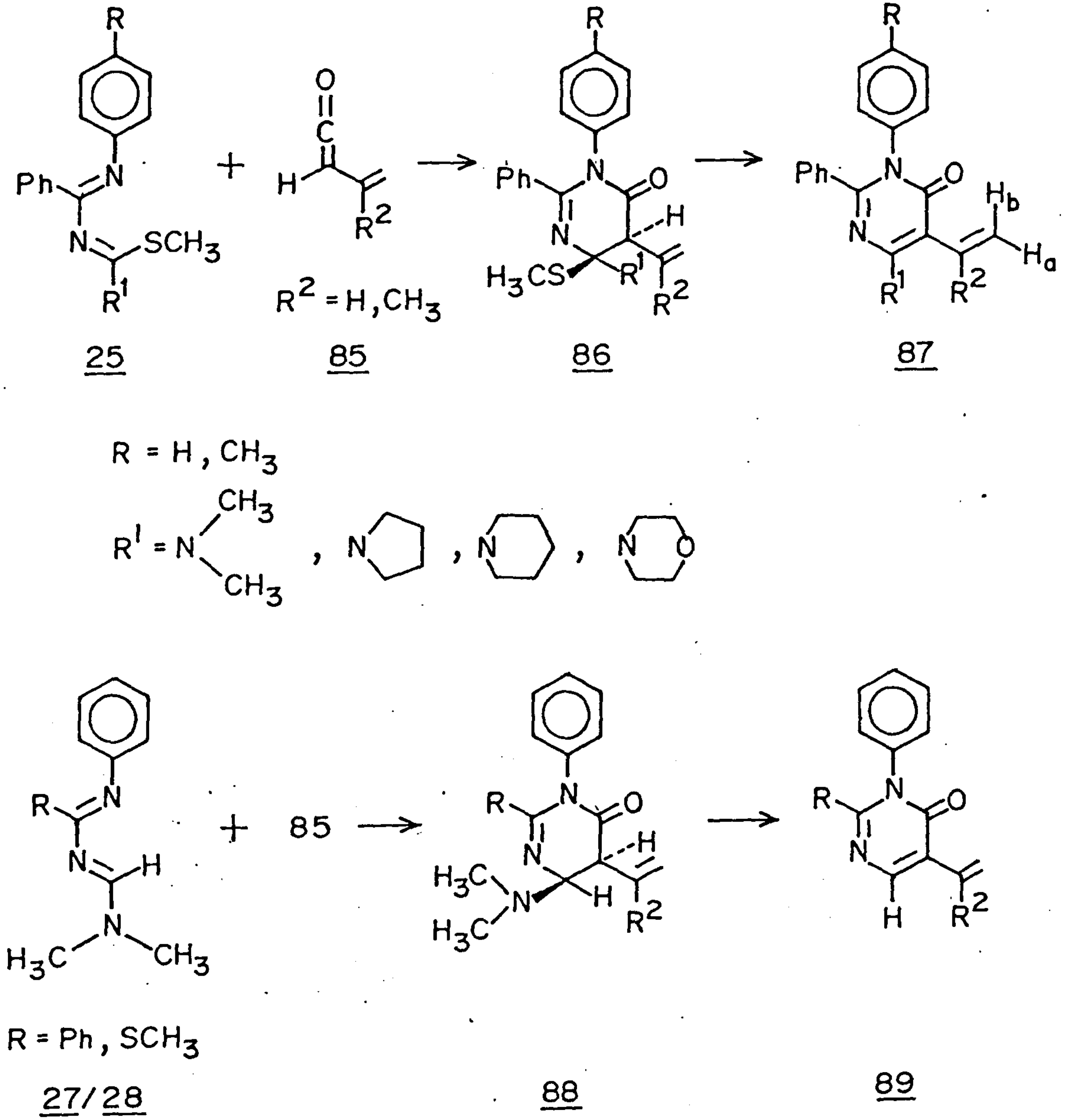


84

Scheme – 26


R
Ph
(CO)$_3$Fe
O
R^2
R^1
$R^1-\equiv-R^2$
C_7H_8, 80°C
84
Fe(CO)$_3$
R^1 = R^2
H
RO
OR
OR^2
R^2O_2C
P

Scheme - 26

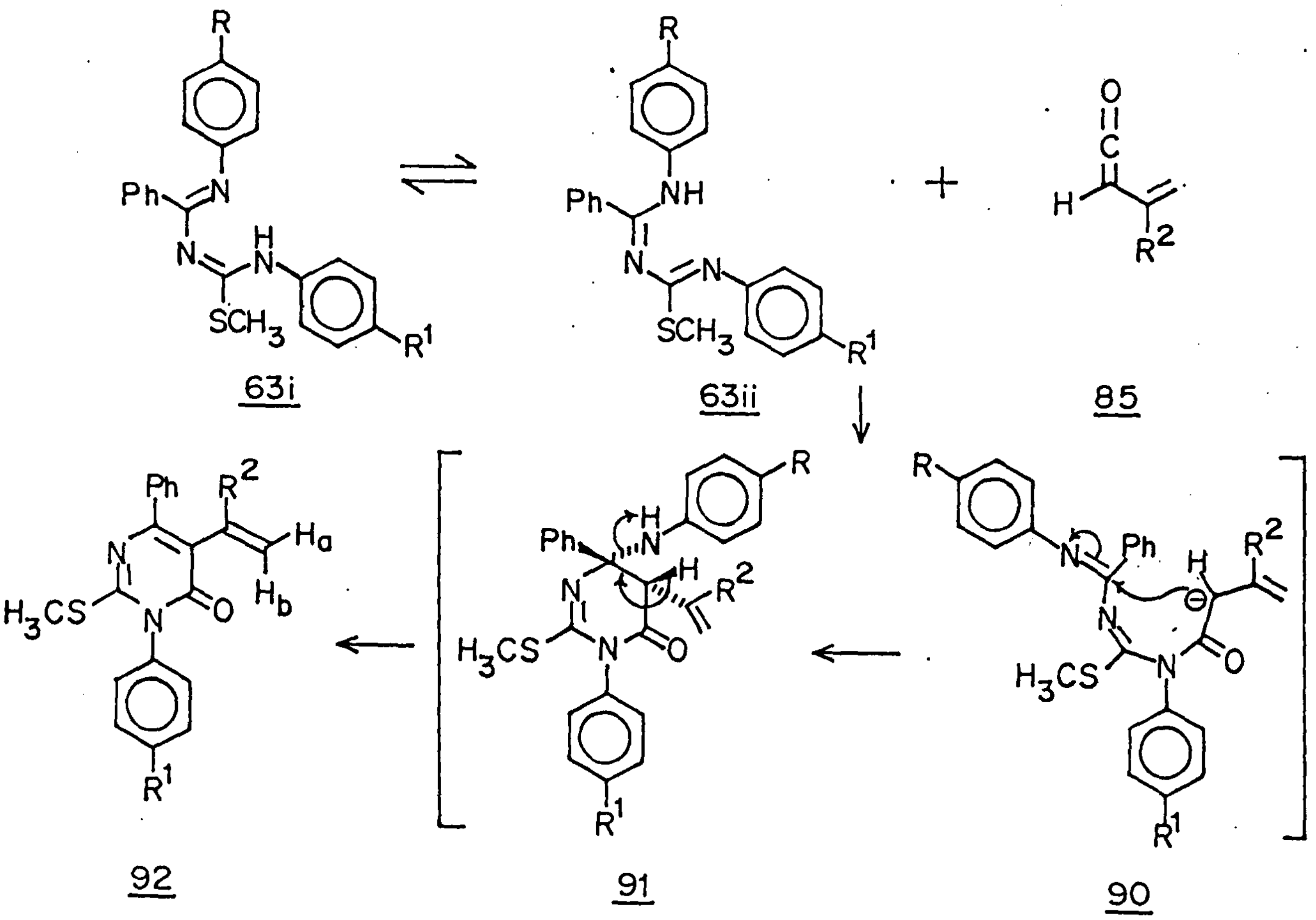

R
Ph
N
N
SCH3
R1
25
O
C
H
R2
R2 = H, CH3
85
R
Ph
N
O
N
N
H
H3CS
R1
R2
86
R
Ph
N
O
N
Hb
Ha
R1
R2
87
R = H, CH3
R1 = N(CH3)2, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl
R
N
N
H
N
H3C
CH3
R = Ph, SCH3
27/28
+ 85
R
N
O
N
H
H3C
N
H3C
H
R2
88
R
N
O
N
H
R2
89

Scheme - 27

reactions of N-arylamino substituted 1,3-diaza-1,3-butadienes with ketenes, and in view of the reported biological significance of vinyl substituted pyrimidinones, we have further examined the reactions of these diazabutadienes with phenyl-, vinyl- and isopropenyl ketenes[75].

Results and Discussion

The treatment of 1-aryl-4(N-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **63** with isopropenyl/ vinylketenes **85**, generated in situ from 3,3-dimethyl acryloyl chloride /crotonyl chloride in presence of triethylamine, in dry methylene chloride at room temperature, afforded good yields (70-75%) of previously unknown 3-aryl-2-methylthio-6-phenyl-5-isopropenyl/vinyl-4(*3H*)- pyrimidinones **92** (Scheme-28). The products were characterised on the basis of analytical results and spectral evidences. Thus, compound **92a**, for example, analysed for $C_{20}H_{18}N_2OS$, showed in its mass spectrum a molecular ion peak at m/z 334. Its **IR** spectrum (KBr) showed a strong absorption peak at 1668 cm^{-1}, assigned to the α,β-unsaturated carbonyl group. Its **^{1}H NMR** (300 MHz) spectrum exhibited the presence of two singlets at ca. δ 2.00 (3H) and 2.46 (3H) assigned to methyl and methylthio groups and also two broad singlets centered at ca. δ 4.87(1H) and 5.17 (1H) assignable to H_a and H_b respectively. It also exhibited the absence of protons due to N-arylamino functions next to the carbon bearing the phenyl group. The compound **92e** in its mass spectrum showed a molecular ion peak at m/z 320 and its **IR** spectrum (KBr) showed a strong absorption peak at 1667 cm^{-1} due to α,β-unsaturated carbonyl group. Its **^{1}H NMR** spepctrum, in addition to other protons exhibited the presence of three doublet of doublets at ca, δ 5.37, 6.17 and 6.59. The probable mechanism for the formation of pyrimidinone derivatives **92**, in these reactions , involves initial nucleophilic attack by the non-bonding electrons of the amino nitrogen of 1-aryl-4-(N-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **63** at the ketene carbonyl, leading to an intermediate **90**, which on ring closure and subsequent elimination of aromatic amines from intermediate **91** results in pyrimidinones **92** (Scheme-28).

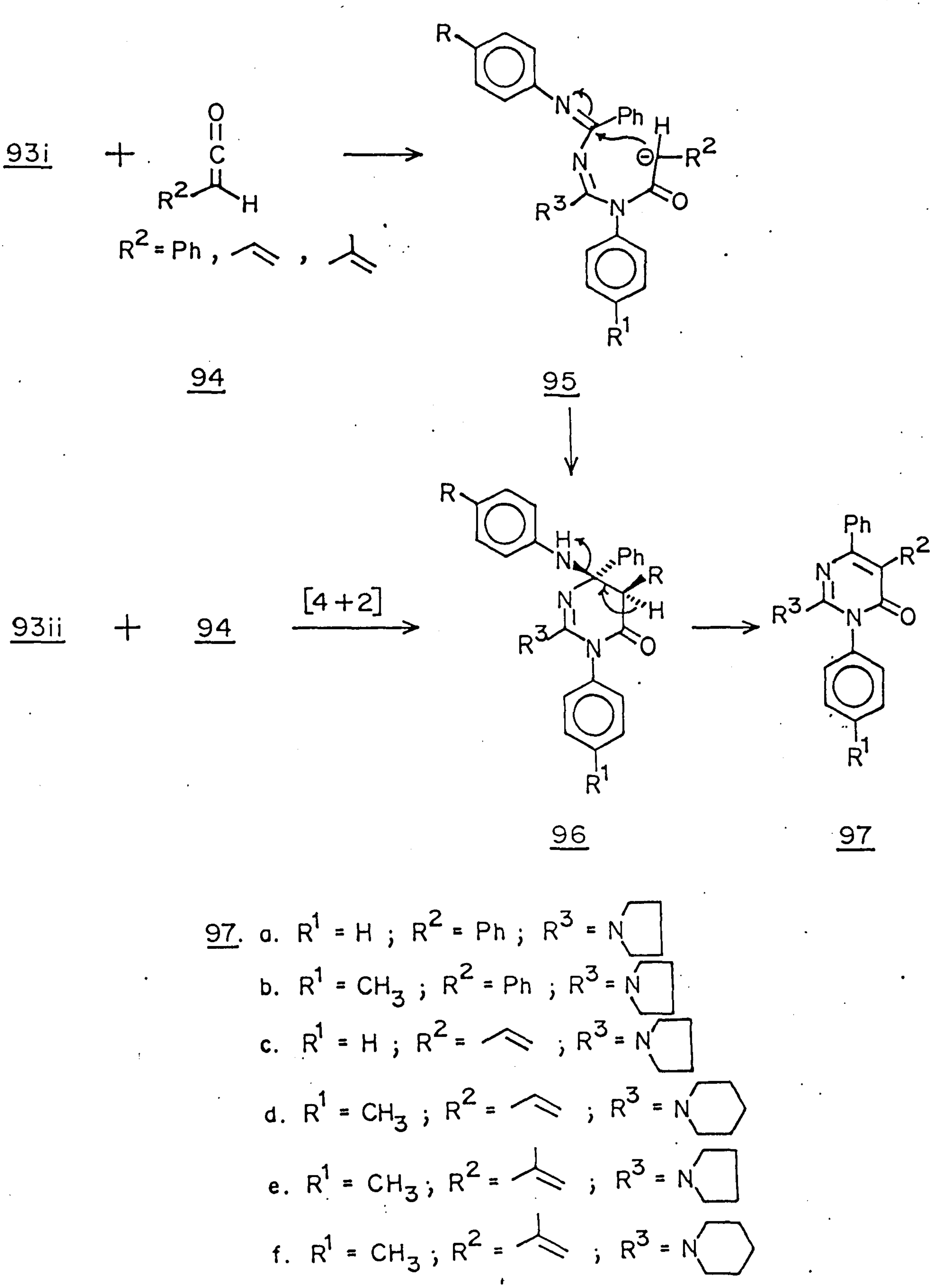


92. a. $R^1 = H$; $R^2 = CH_3$
b. $R^1 = CH_3$; $R^2 = CH_3$
c. $R^1 = OCH_3$; $R^2 = CH_3$
d. $R^1 = Cl$; $R^2 = CH_3$
e. $R^1 = H$; $R^2 = H_c$
f. $R^1 = CH_3$; $R^2 = H_c$
g. $R^1 = OCH_3$; $R^2 = H_c$
h. $R^1 = Cl$; $R^2 = H_c$

Scheme– 28

In continuation of our investigations it was thought worthwhile to examine cycloaddition reactions of 1,3-diaza-1,3-butadienes **93** bearing N-arylamino and secondary amino substituents. The interest in such investigations was stimulated primarily because of the possible dominance of tautomer **93ii**, due to better polarising ability of secondary amino functions, which in comparison to earlier observations[67] may yield products arising from reversed regioselectivity. The required 1,3-diaza-1,3-butadienes **93** were obtained by the replacement of methylthio function of **63** with secondary amine in refluxing benzene (Scheme-29) and the treatment of 1,3-diaza-1,3-butadienes **93** with phenyl-, vinyl- and isopropenyl ketenes resulted in good yields of previously unknown 3-aryl-2-dialkylamino-6-phenyl-5-substituted-4(*3H*)-pyrimidinones. The structure **97** was also assigned to these pyrimidinones on the basis of analytical and spectral evidence. The ^{1}H NMR spectra of **97** showed the absence of N-arylamino groups attached to the carbon bearing phenyl and the presence of secondary amino protons and N-arylamino protons attached to the carbon bearing the secondary amino functions. The formation of pyrimidinones **97** might be following either the [4+2] cycloadditions of tautomer **93ii** with ketenes, or the initial nucleophilic attack by N-arylamino functions of tautomer **93i** on the ketene carbonyl leading to an intermediate **95** which, on subsequent cyclization and elimination of aromatic amine from **96** gave **97** (Scheme-30).

In order to have further insight into the mechanistic paths followed in these reactions, we have performed AM1 calculations[111] on **93**. Complete optimization of **93i** and **93ii** has shown that the N-C-N-C-N frame work prefers to be planar. The energy difference between **93i** and **93ii** is 0.02 k cal/mol in favour of **93ii**. This indicates that the dominance of tautomer **93ii** increases with the secondary amine substituent, which is in accordance with expectations from the polarizing ability considerations. Charge densities and HOMO coefficient of **93** obtained using AM1 method are given in Table II. In both the tautomers of **93**, imino nitrogen is found to be more charged. Similarly, in the HOMO coefficients of **93i** and **93ii**, the p-orbital coefficients on the imino nitrogen are more predominant. This shows that the imino nitrogen is more active in both **93i** and **93ii**, in contrast to the observations


93i
R^2 = Ph ,
94
95
Ph
H
R^2
R
N
R^3
O
R^1
93ii
94
[4+2]
96
97
97. a. R^1 = H ; R^2 = Ph ; R^3 =
b. R^1 = CH$_3$; R^2 = Ph ; R^3 =
c. R^1 = H ; R^2 = ; R^3 =
d. R^1 = CH$_3$; R^2 = ; R^3 =
e. R^1 = CH$_3$; R^2 = ; R^3 =
f. R^1 = CH$_3$; R^2 = ; R^3 =

Scheme- 30

made in **63i** and **63ii**. Thus, based on experimental observations of higher charge densities at imino nitrogen and relative higher stability of **93ii** in solution, it could be concluded that pyrimidinones **97** are formed via [4+2] cycloaddition reactions of **93ii** with various ketenes.

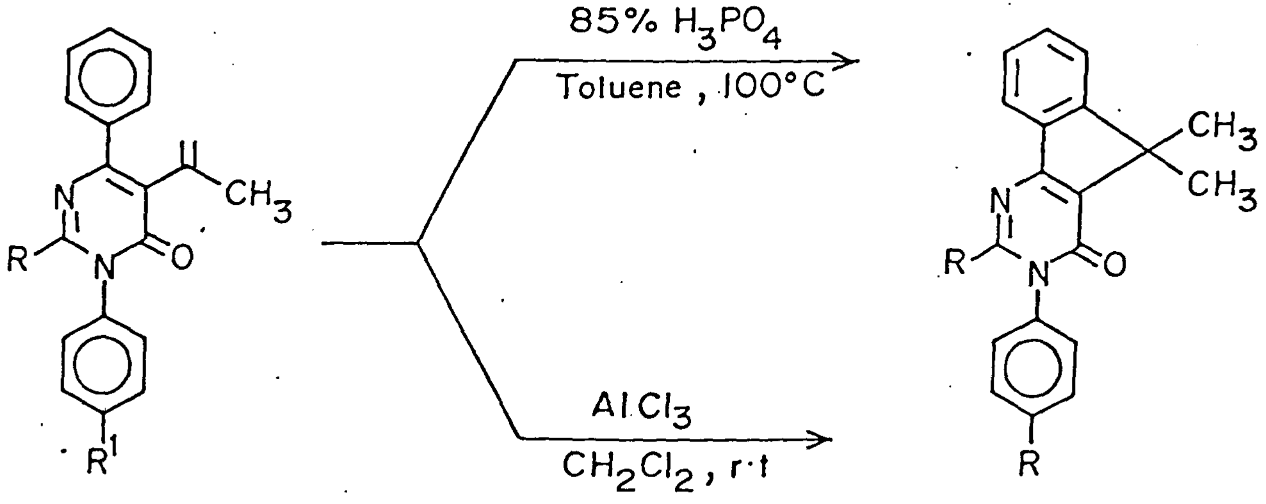
Table II: **Charge Densities and HOMO coefficients of 93 using AM1 method.**

Atoms	Charges		HOMO Coefficients	
	93 i	93 ii	93 i	93 ii
N-1	-0.45	-0.43	0.35	0.37
C-2	0.29	0.36	-0.11	-0.12
N-3	-0.33	-0.35	-0.30	-0.35
C-4	0.26	0.21	0.17	0.18
N-5	-0.30	-0.32	0.30	0.33

The isolated pyrimidinones **92** and **97** having vinyl/isopropenyl functionalities at C-5 might prove to be biologically important, since various pyrimidine nucleosides bearing an unsaturated side chain at C-5 are expected to exhibit biological activity[114].

The pyrimidinones **92(a-d)** and **97(e,f)** appeared to be potential synthons for the synthesis of fused pyrimidinones via annelation reactions. Thus, the treatment of 5-isopropenyl pyrimidinones (R^2 = CH_3) with 85% H_3PO_4 in refluxing toluene resulted in the formation of previously unknown 3-aryl-5,5-dimethyl- 2-methylthio/secondaryamino -3,5-dihydro -4H- indeno[1,2-d] pyrimidin-4-ones **98** (Scheme-31).

A similar reaction in the presence of $AlCl_3$ in methylene chloride resulted in better yields of same indeno [1,2-d] pyrimidinones **98**. However, in case of 5-vinyl pyrimidinones (R^2 = H), the attempted cyclisation with 85% H_3PO_4 or Lewis acid resulted in an intractable mixture from which no pure product could be isolated. The compounds **98** were characterised on the basis of analytical and spectral data. The compound **98a** , for example, got analysed for $C_{20}H_{18}N_2OS$ and showed a molecular ion peak at m/z 334. Its **IR** spectrum showed a sharp band at 1662 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^{1}**H NMR** spectrum showed the

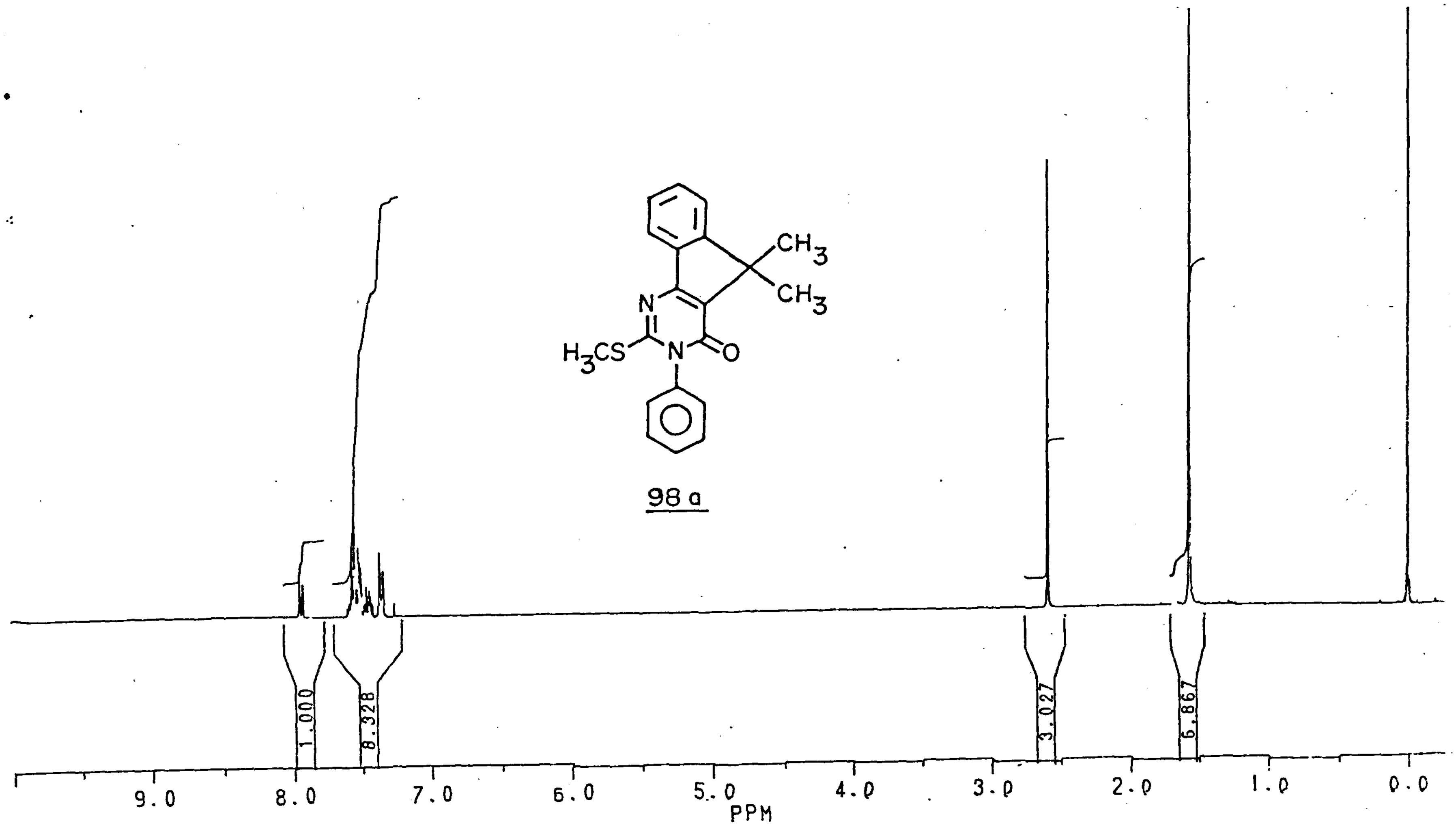


<u>92</u> (a–d)
<u>97</u> (e , f)

<u>98</u>

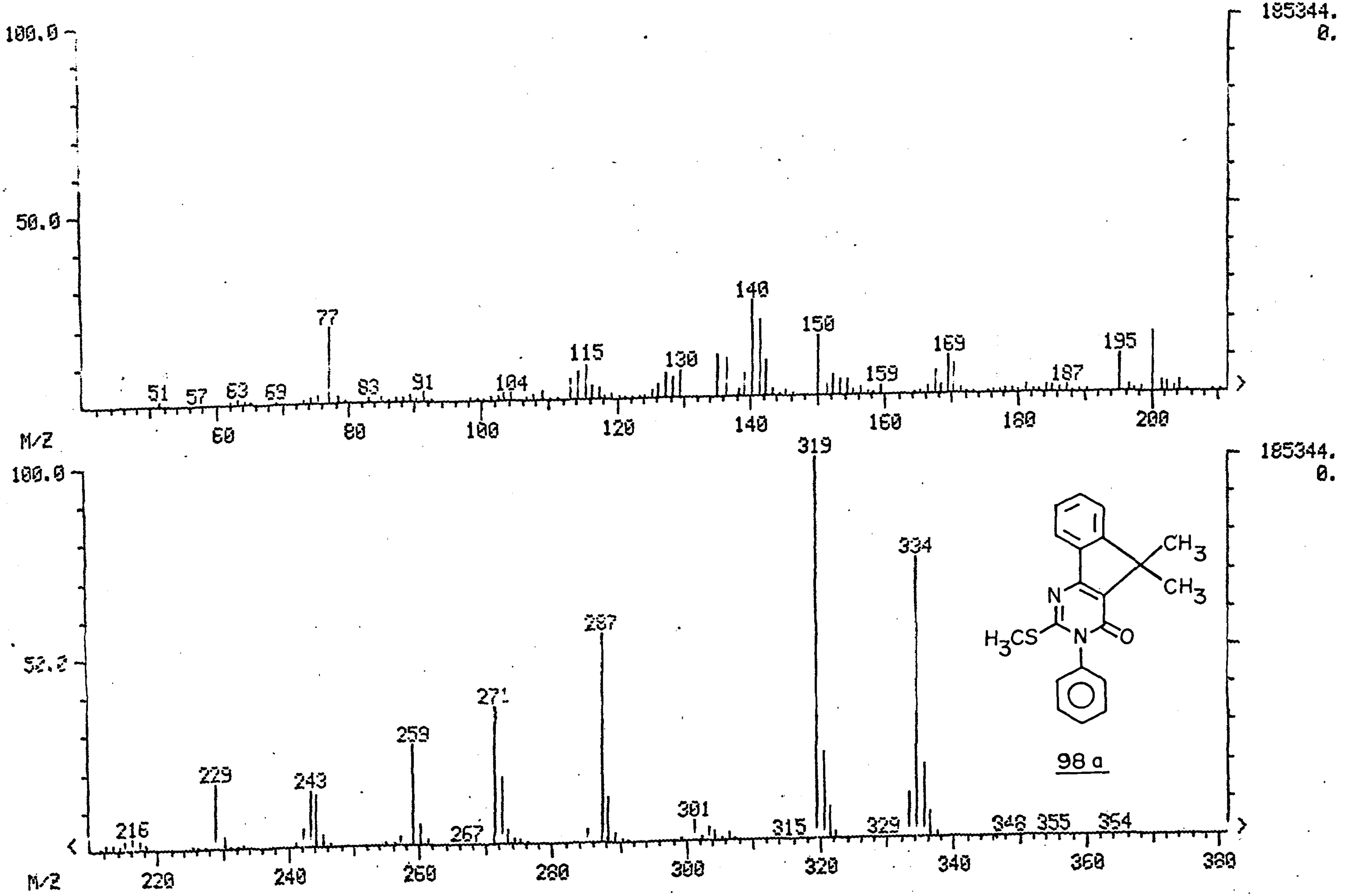
<u>98</u>. a. R^1 = H ; R = SCH_3 d. R^1 = Cl ; R = SCH_3
b. R^1 = CH_3 ; R = SCH_3 e. R^1 = CH_3 ; R = 
c. R^1 = OCH_3 ; R = SCH_3 f. R^1 = CH_3 ; R = 

<u>Scheme – 31</u>



98 a

CH3
CH3
N
H3CS
N
O
1.000
8.328
3.027
6.867
9.0
8.0
7.0
6.0
5.0
PPM
4.0
3.0
2.0
1.0
0.0


100.0
50.0
185344.
0.
51
57
63
69
77
83
91
104
115
130
140
150
159
169
187
195
60
80
100
120
140
160
180
200
M/Z
100.0
52.2
185344.
0.
216
229
243
259
267
271
287
301
315
319
329
334
348
355
364
220
240
260
280
300
320
340
360
380
M/Z
CH3
CH3
N
H3CS
N
O

98 a

absence of isopropenyl functionality and exhibited two sharp singlets due to methylthio (δ 2.59) and the other owing to two methyl (δ 1.57) groups. Its ^{13}C **NMR** spectrum was also in agreement with the assigned structure.

In summary, the [4+2] cycloadditions of various 1,3- diaza-1,3-butadienes with vinyl/isopropenyl ketenes have resulted in a variety of pyrimidinones having an unsaturated side chain at C-5, which might prove to be biologically important. On the other hand, 5- isopropenyl pyrimidinones yielded the fused pyrimidinones via annelation reactions.

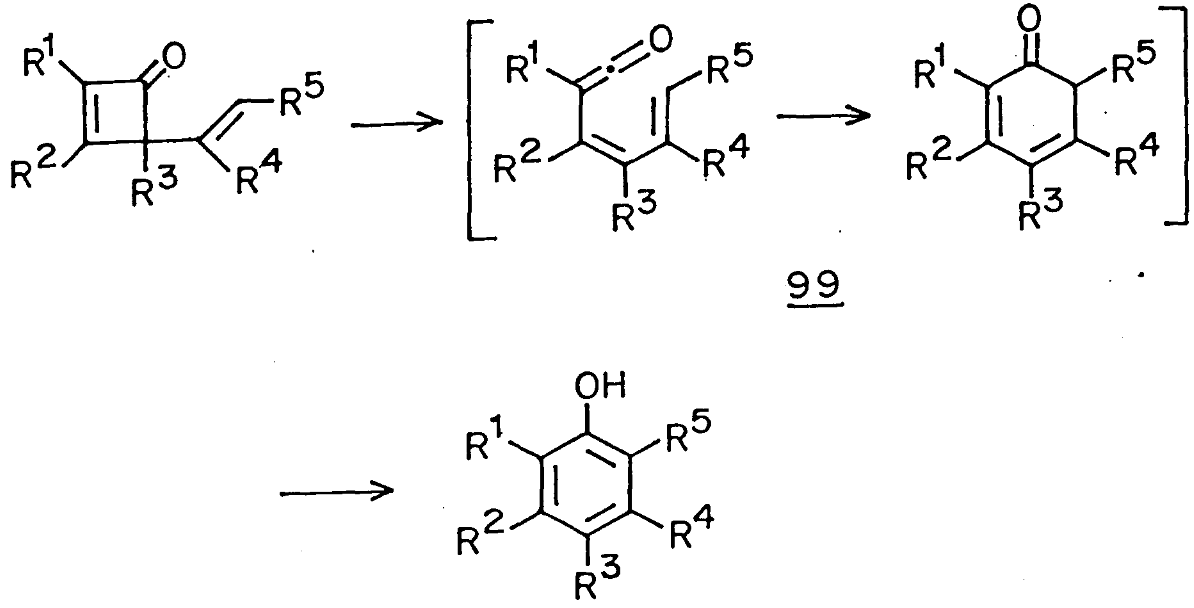
1.4: *REACTIONS OF N-ARYLAMINO-1,3-DIAZA-1,3-BUTADIENES WITH BUTADIENYL KETENES*

The synthetic potential and interesting mechanistic features involving azabutadienes, the synthesis of suitably functionalised 1,3-dienes continue to attract the attention of the synthetic community[115]. Various 1,3- diaza-1,3-butadienes synthesised in our laboratory[44,74] having polarising functions at 2 and / or 4-positions have been found to behave as efficient 4π components in successful [4+2] cycloaddition reactions with a large variety of monosubstituted ketenes[46,54,74]. Subsequently, vinyl/isopropenyl ketenes, consisting of a diene unit were also found to act as 2π component in such cycloadditions with these diaza-butadienes[72,75].

In order to have a further insight into the comparison of the dienic properties of 1,3-diaza-1,3-butadienes and conjugated ketenes, we visualized to investigate the reactions of various 1,3-diaza-1,3-butadienes with butadienyl ketene. To our knowledge, the reports concerning the generation and synthetic utility of dienylketenes are very rare. The only reported methods involve: (i) thermolysis of appropriately substituted cyclobutenones leading to various quinones and catechols **100** formed via dienylketene intermediate **99**[116] (Scheme-32); (ii) photolysis of benzyl phenyl either **101a** and phenylacetate[117] **101b** to give dienic ketenes **103** via transient cyclohexa-2,4-dienone intermediates **102(a,b)** (Scheme-33).

However, the butadienylketene so generated undergoes facile intramolecular processes and hence limits its utility towards intramolecular cycloadditions. Recently, it has been reported that butadienyl ketene **104** could be conveniently generated and successfully utilised in [2+2] cycloaddition reactions with imines **105** and **106** to yield α-dienyl-β-lactams **107**, **108** and **109**[73a] (Scheme-34).

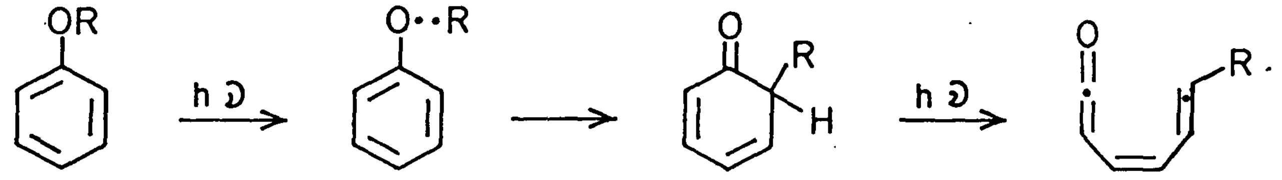
On further exploration, it was observed that the cycloaddition of 1,3-diaza-1,3-butadienes **25** with butadienylketene **104** resulted in pyrimidinones[73b] **111** and **113**, accompanying tandem [1,5] H shift and [1,5] SMe shift (Scheme-35). To our knowledge, this involves the first use of butadienyl ketene as a 2π component in [4+2] cycloaddition reactions.



99

100

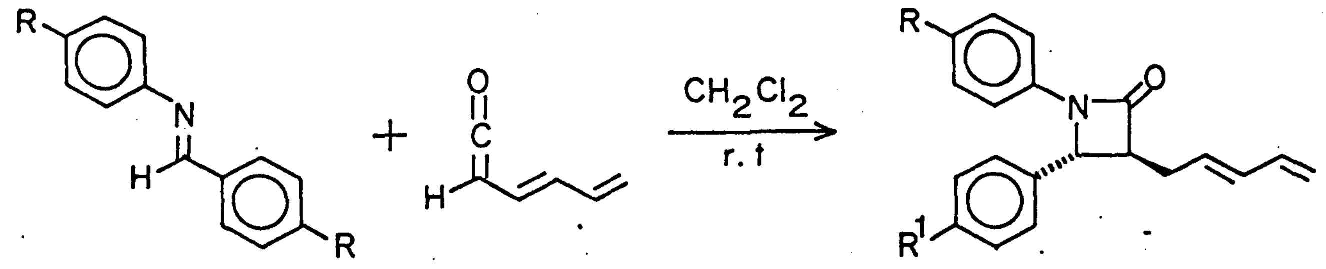
Scheme-32



101 102 103

a. R = Bn
b. R = Ac

Scheme – 33



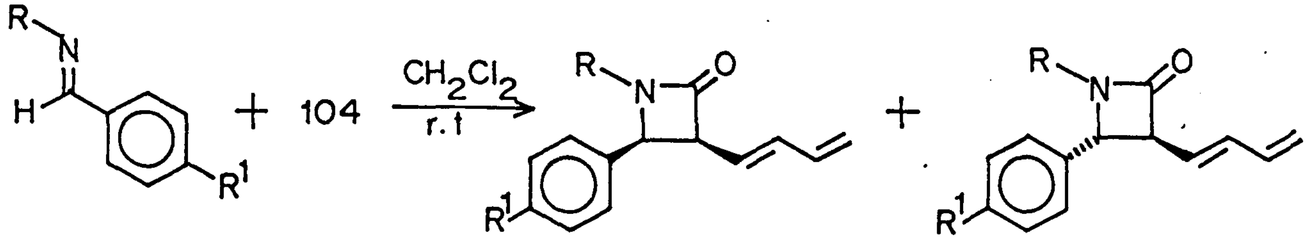
105 104 107

105, 107. a. $R = R^1 = H$

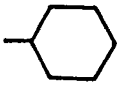
b. $R = H$; $R^1 = OCH_3$

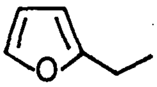
c. $R = CH_3$; $R^1 = H$

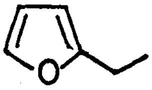
d. $R = CH_3$; $R^1 = OCH_3$



106 108 109

106, 108, 109. a. R =  ; R^1 = Ph

b. R =  ; R^1 = Ph

c. R =  ; $R^1 = C_6H_4OCH_3$-p

d. R = n-Bu ; $R^1 = C_6H_4OCH_3$-p

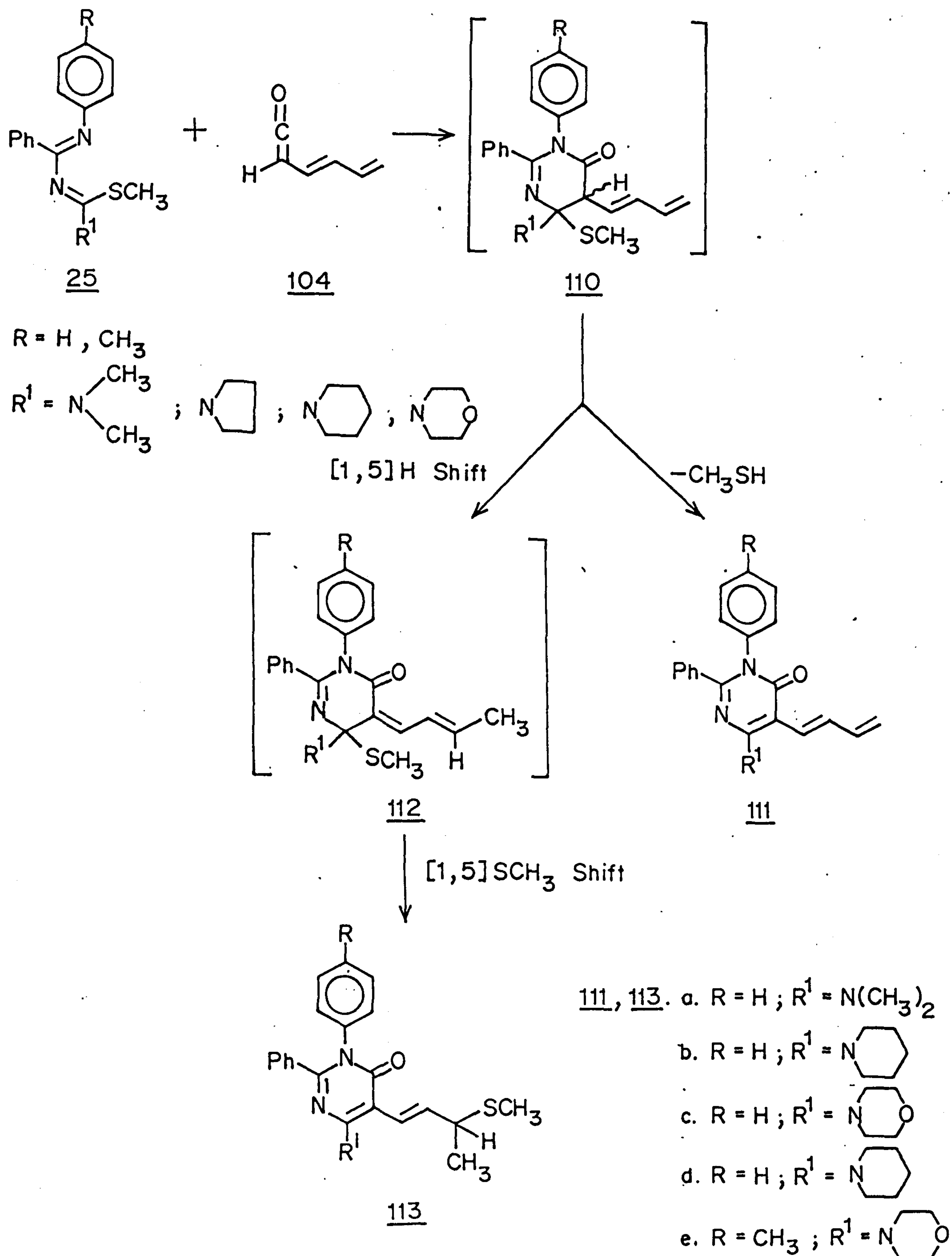
Scheme – 34

In order to understand the mechanistic aspects and to generalise such cycloaddition reactions, it was thought worthwhile to carry out detailed investigations regarding reactions of various N-aryl-1,3-diaza-1,3-butadienes **63** and **93** with butadienyl ketene **104**. Interestingly, these reactions were found to result in a mixture of pyrimidinones **115**, **117**,and **118** respectively.

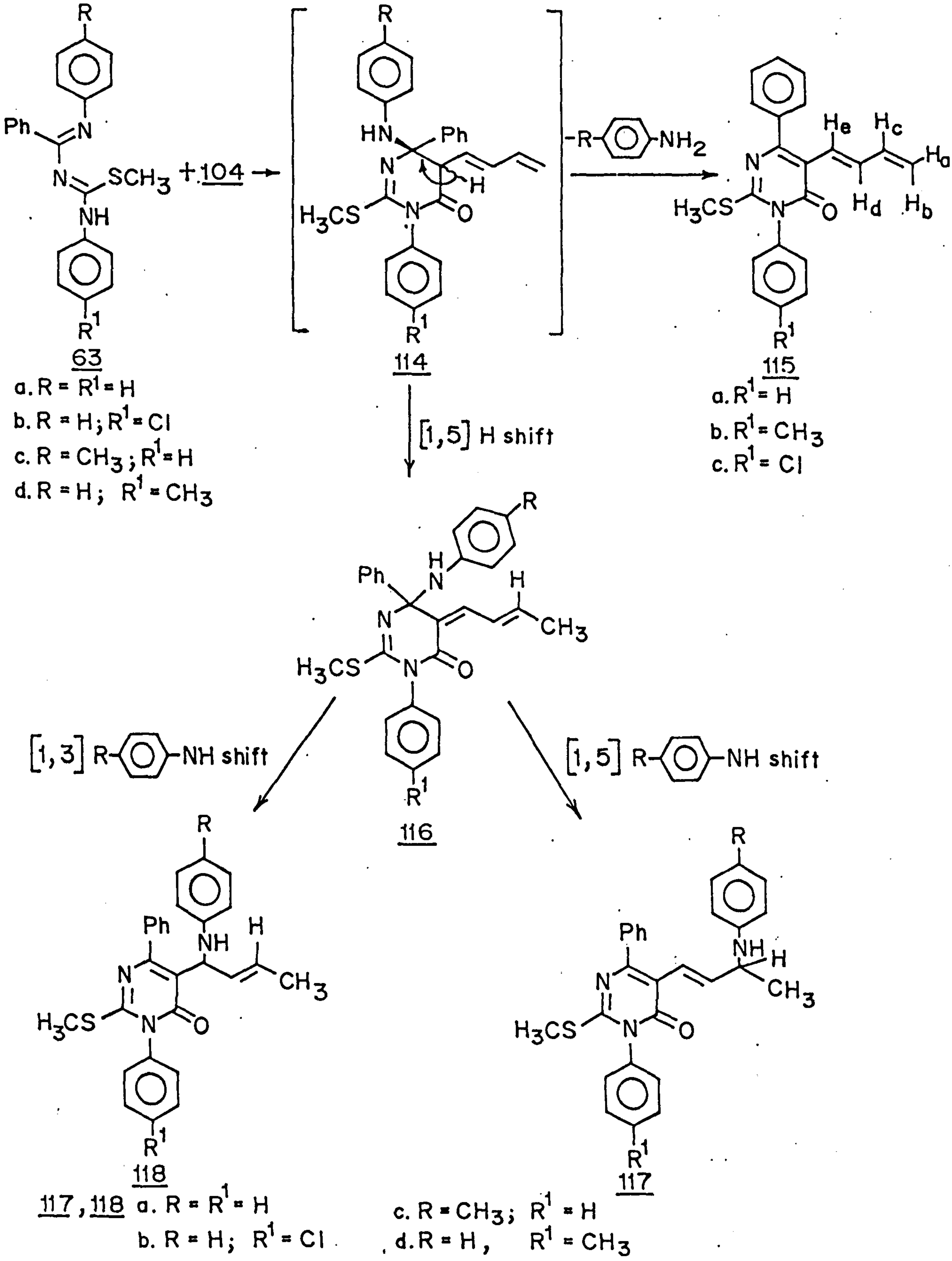
Results and Discussion

The treatment of N-aryl-1,3-diaza-1,3-butadienes **63** with butadienyl ketene **104**, generated in situ from sorbyl chloride and triethylamine in dry methylene chloride, resulted in a mixture of pyrimidinones. The mixture was separated by careful chromatography (silica gel) and resulted in the isolation of three products which were characterised as 5-(1',3'-butadienyl)- pyrimidinones **115** (26 %), 5(1'-butenyl)-pyrimidinones **117** (22 %) and 5-(2'-butenyl)-pyrimidinones **118** (22 %) (Scheme-36).

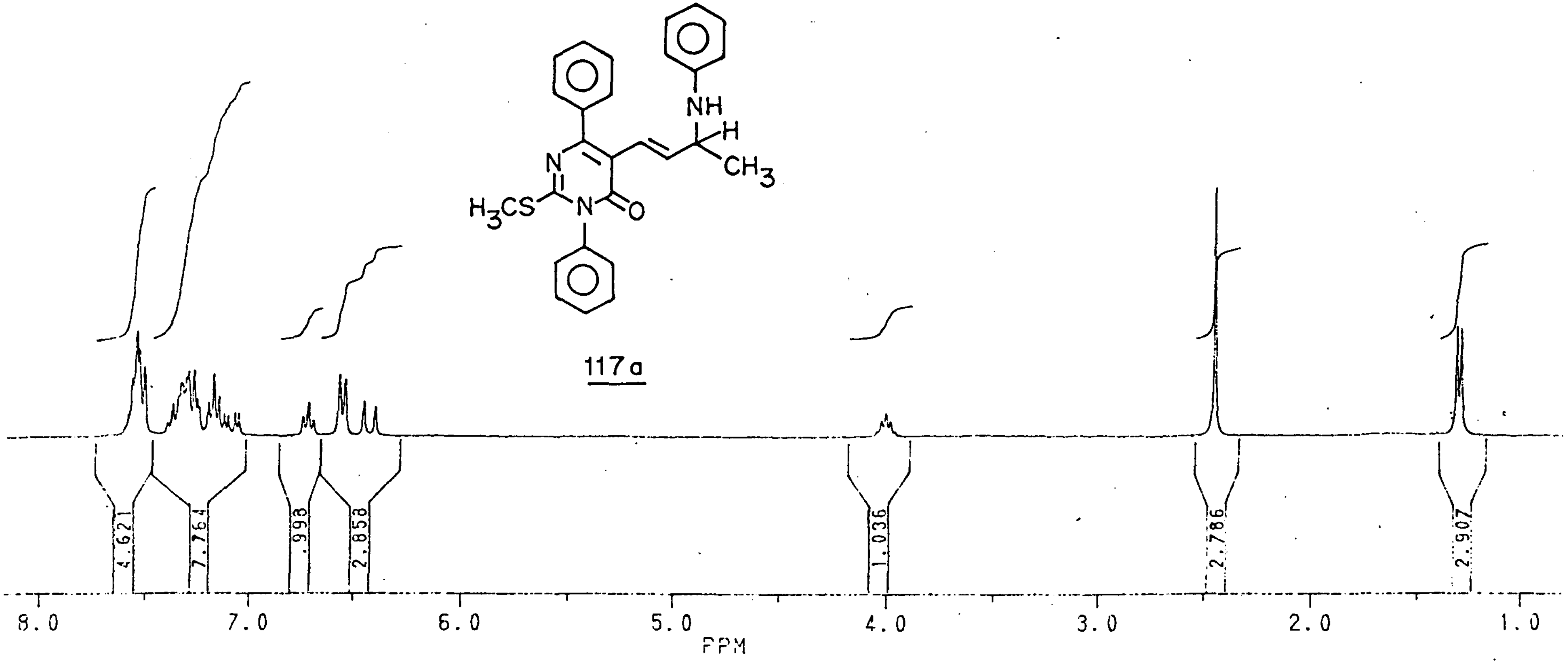
The products were assigned the pyrimidinone structures **115**, **117** and **118** on the basis of their analytical and spectral data. The compound **115a**, for example, analysed for $C_{21}H_{15}N_2OS$, and exhibited in its mass spectrum a molecular ion peak at m/z 346. Its **IR** spectrum showed a sharp peak at 1664 cm^{-1} due to α,β -unsaturated carbonyl group. The ^{1}**H** and ^{13}**C NMR** spectra of **115a** exhibited peaks for methylthio and dineyl functionalities, in agreement with the assigned structure. The product **117a** , on the other hand, analysed for $C_{27}H_{25}N_3OS$, and showed a molecular ion peak at m/z 439 in its mass spectrum, and a sharp band at 1667 cm^{-1} due to α,β-unsaturated carbonyl group in its **IR** spectrum. Its ^{1}**H NMR** spectrum exhibited a doublet at δ 1.31 (J = 6.0 Hz) for methyl protons and a multiplet at δ 3.96-4.03 for methine proton in addition to the signals for methylthio protons (δ 2.45). The product **118a** was analysed for $C_{27}H_{25}N_3OS$, and showed a molecular ion peak at m/z 439 in its mass spectrum, and a sharp band at 1674 cm^{-1} due to α,β-unsaturated carbonyl group in its **IR** spectrum. Its ^{1}**H NMR** spectrum exhibited a doublet at δ 1.69-1.72 due to methyl protons. It also exhibited two double doublets


25
104
110
R = H , CH3
R1 =
[1,5] H Shift
−CH3SH
112
111
[1,5] SCH3 Shift
113
111, 113. a. R = H ; R1 = N(CH3)2
b. R = H ; R1 =
c. R = H ; R1 =
d. R = H ; R1 =
e. R = CH3 ; R1 =

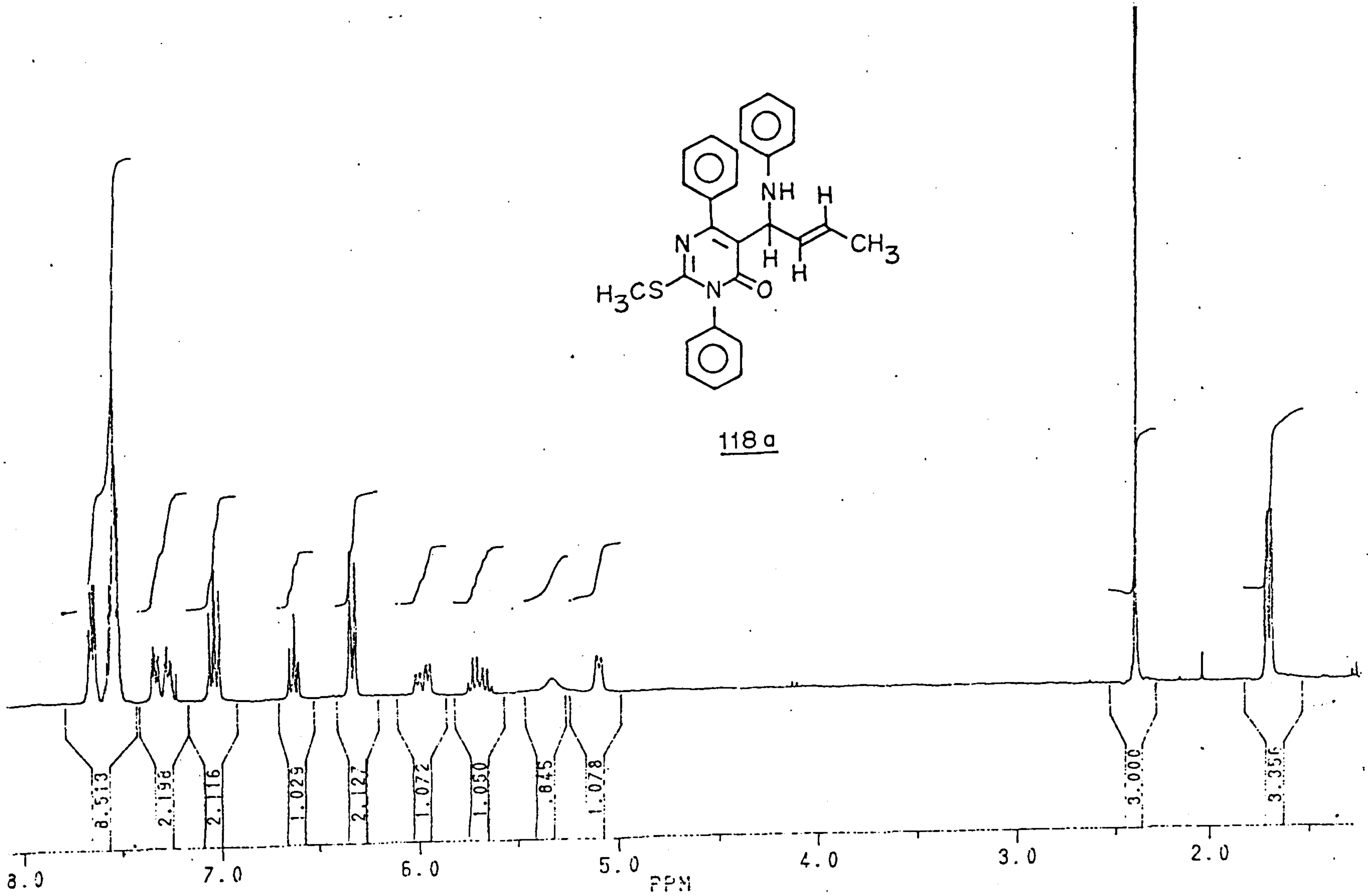
Scheme - 35


R
Ph
N
N
SCH3
NH
R1
+ 104
63
a. R = R1 = H
b. R = H; R1 = Cl
c. R = CH3; R1 = H
d. R = H; R1 = CH3
HN
Ph
H
H3CS
N
O
114
-R-⟨⟩-NH2
He
Hc
Ha
Hd
Hb
115
a. R1 = H
b. R1 = CH3
c. R1 = Cl
[1,5] H shift
CH3
116
[1,3] R-⟨⟩-NH shift
[1,5] R-⟨⟩-NH shift
118
117
117, 118 a. R = R1 = H
b. R = H; R1 = Cl
c. R = CH3; R1 = H
d. R = H, R1 = CH3

Scheme-36


117a

H3CS
N
N
O
NH
H
CH3
4.621
7.764
.993
2.858
1.036
2.786
2.907
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
PPM



118a

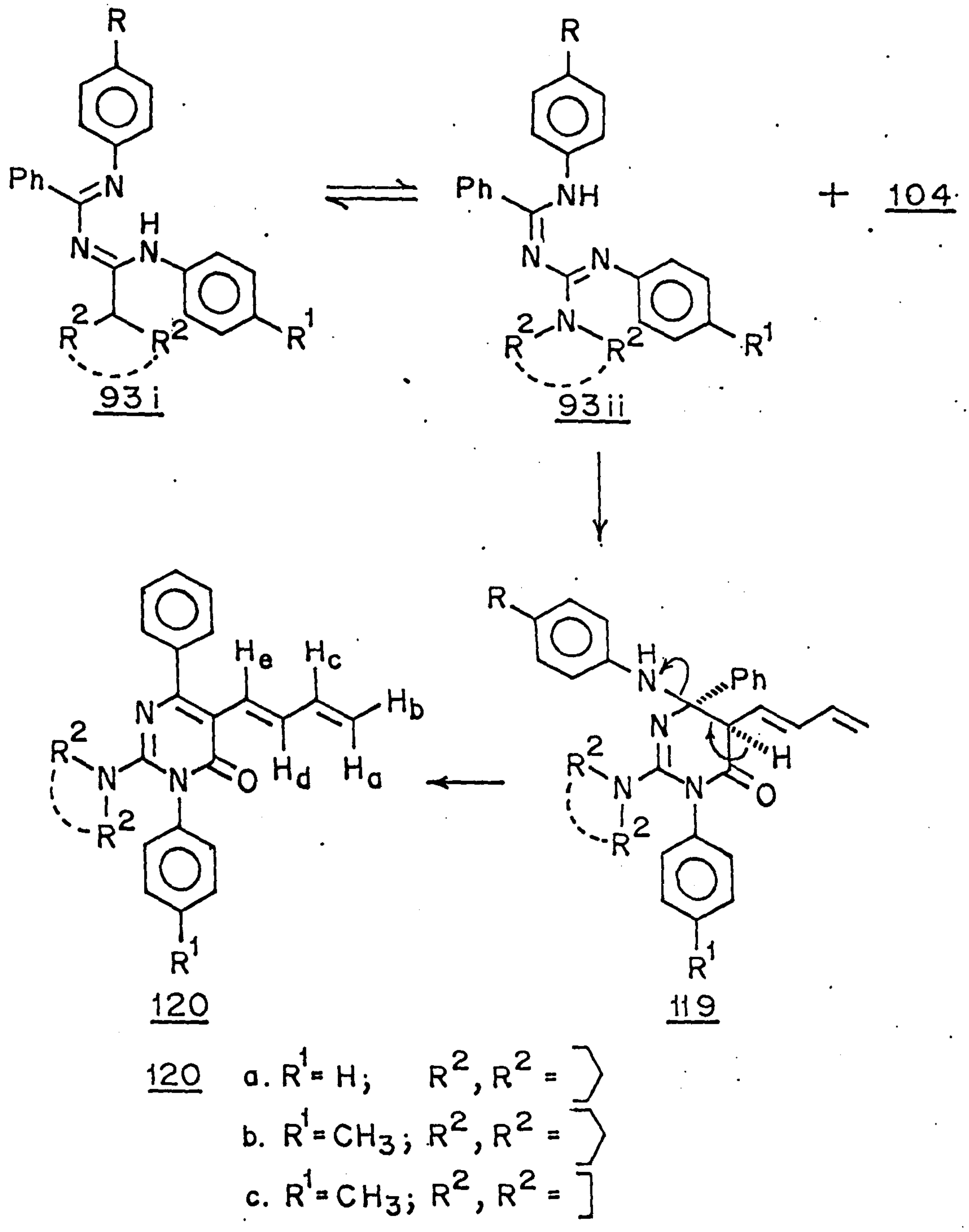
H₃CS
N
NH
H
CH₃
O
8.513
2.198
2.116
1.029
2.127
1.072
1.050
.845
1.078
3.000
3.356
8.0
7.0
6.0
5.0
PPM
4.0
3.0
2.0

at ca. δ 5.08-5.10 and ca. δ 5.94-6.02 due to olefinic protons in addition to a multiplet at ca. δ 5.65-5.74 due to proton H-3'.

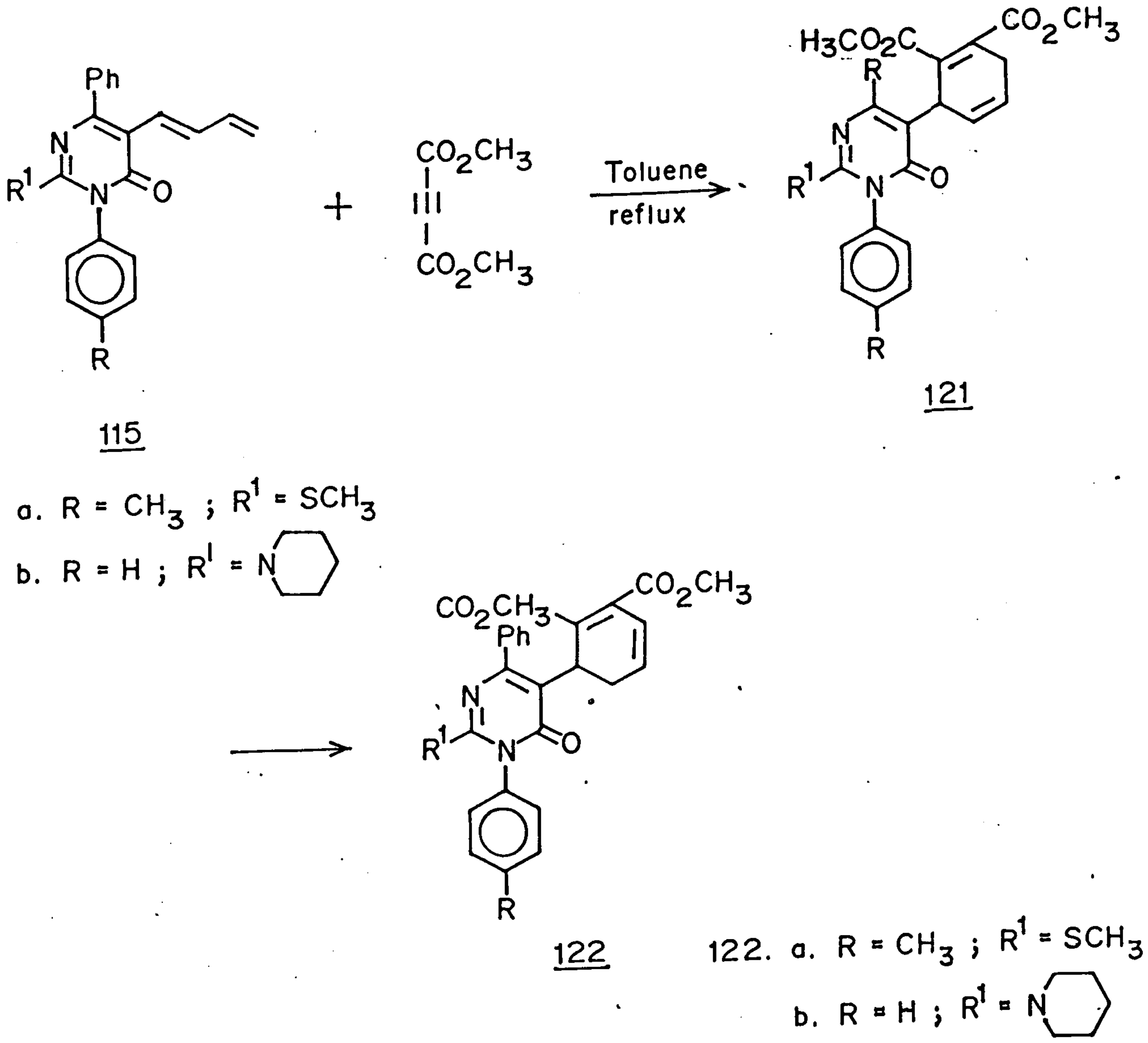
The plausible mechanism leading to the formation of these pyrimidinones is shown in Scheme-36. In this scheme, it is assumed that the reactions of N-aryl-1,3-diaza-1,3-butadienes **63** with butadienyl ketene **104** lead to the initial formation of intermediate **114**. The intermediate presumably consists of a stereoisomeric mixture, with H-5 being cis and trans to the N-aryl group at C-6. This intermediate then undergoes elimination of amine to yield pyrimidinone **115**, when H-5 is *trans* to the N-aryl function. On the other hand, the stereoisomer with *cis* H-5 and N-aryl functions prefer [1,5] H shifts, over equilibration to *trans* stereoisomer, yielding another intermediate **116**, which then undergoes [1,5] HNAr and [1,3] HNAr shifts to yield pyrimidinones **117** and **118**, respectively.

However, the reactions of 1,3-diaza-1,3-butadienes **93** with butadienyl ketene **98** showed the complete absence of rearranged products and led exclusively to the isolation of pyrimidinones **120**. Thus , it seems likely that the reactions of 1,3-diaza-1,3-butadienes **63** and **93** with butadienylketene **104** follow two distinct pathways. Possibly the reactions of **63** with **104** proceed via the initial nucleophilic attack of nitrogen of N-arylamine at ketene carbonyl to yield an intermediate **114** consisting of a stereoisomeric mixture which as indicated, then leads to a mixture of pyrimidinones. The reaction of **93** with **104** probably proceeds through a stereoselective [4+2] cycloaddition of the more likely tautomer **93ii** to yield an intermediate **119**, with *trans* H-5 and N-arylamino functions, which undergoes facile elimination of aromatic amine to exclusively yield pyrimidinone **120** (Scheme-37). This argument is in line with the conclusions drawn earlier in the reactions of **63** and **93** with other ketenes.

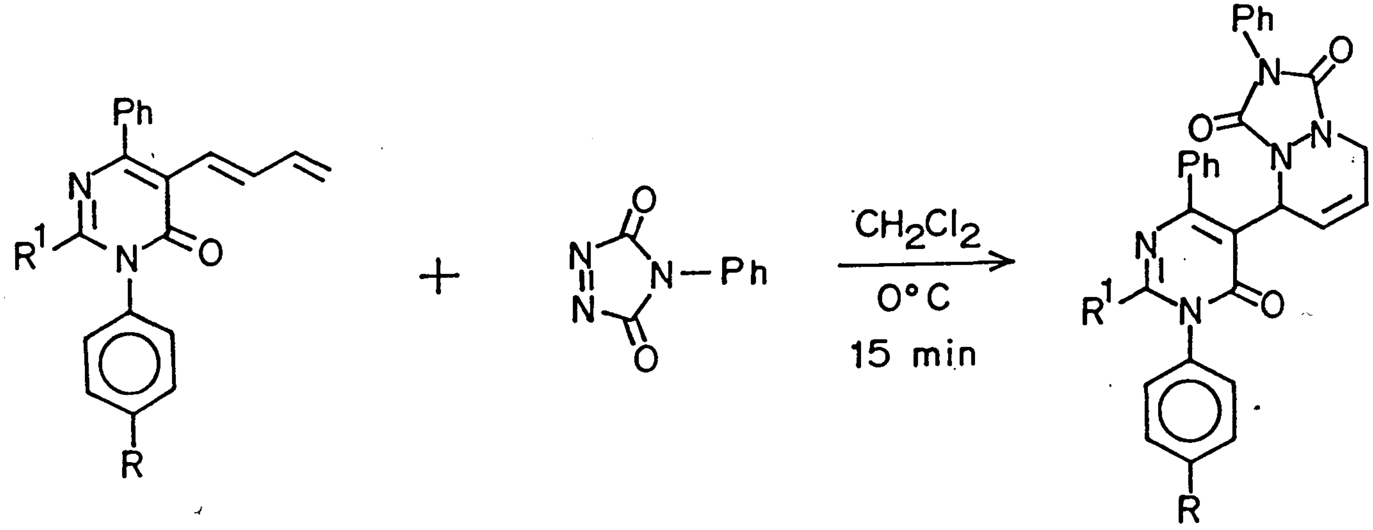
The presence of dienyl functionalities in the case of **115** was established by carrying out their Diels-Alder cycloaddition reactions with a variety of dienophilies. All these reactions resulted in very good yields (86-96%) of corresponding adducts which were unambiguously characterised on the basis of their **IR**, **^{1}H NMR**, **^{13}C NMR** and Mass spectral evidences and analytical data.


93i
93ii
+ 104
119
120
Ph
NH
N
R
R^1
R^2
He
Hc
Hb
Hd
Ha
H
O
120 a. R^1 = H; R^2, R^2 =
b. R^1 = CH_3; R^2, R^2 =
c. R^1 = CH_3; R^2, R^2 =

Scheme-37


115
Toluene
reflux
121
122
a. R = CH3 ; R1 = SCH3
b. R = H ; R1 = N
122. a. R = CH3 ; R1 = SCH3
b. R = H ; R1 = N

Scheme – 38



115

123

123. a. R = Cl ; R^1 = SCH$_3$
b. R = CH$_3$; R^1 = SCH$_3$

Scheme – 39

The reaction of 5-dienyl pyrimidinones **115** with dimethylacetylene dicarboxylate (DMAD) in refluxing toluene resulted in the formation of Diels-Alder adduct **122**, formed presumably by isomerisation of initially formed adduct **121**, as reported recently[73] (Scheme-38). The products were characterised on the basis of their **IR**, ^{1}**H NMR**, ^{13}**C NMR**, mass spectra and analytical evidences.The product **122a**, analysed for $C_{28}H_{26}N_2O_5S$, showed a molecular ion peak at m/z 502 (M^+) in its mass spectrum. Its **IR** spectrum exhibited intense peaks at 1732 and 1640 cm^{-1} due to methoxy carbonyl and α,β-unsaturated carbonyl group of the pyrimidinone ring, respectively. Its ^{1}**H NMR** spectrum, in addition to aromatic protons, exhibited the presence of signals for methyl (s, δ 2.37) thiomethyl (s, δ 2.42), methylene (m, δ 2.84-2.87), methine (m, 4.53-4.55), two methoxy carbonyls (s, δ 3.63 and 3.67) and olefinic protons (m, δ 5.57-5.61 and m, δ 5.76-5.79). The signals observed in ^{13}**C NMR** spectrum also attest to the assigned structure **122**.

The reaction of 115 with 4-phenyl-1,2,4-triazo-3,5-dione (PTAD), in methylene chloride at 0 °C, also resulted in the synthesis of the corresponding Diels-Alder adduct **123**. The compound **123**, for example, exhibited strong absorption peaks at 1660 and 1708 cm^{-1} due to carbonyl groups. Its mass spectrum exhibited a molecular ion peak at m/z 535 (M^+) and a peak at 416 (M -Ph-N=C=O). Its ^{1}**H** and ^{13}**C NMR** spectra were also in agreement with the assigned structures **123** (Scheme-39).

In conclusion, the reactions of N-aryl-1,3-diaza-1,3-butadienes with butadienylketene have led to a convenient route for the synthesis of pyrimidinone substituted 1,3-dienes. Tandem [1,5] H shifts, followed by [1,3] NHAr and [1,5]HNAr shifts, observed in such reactions are unusual and interesting. Subsequently, Diels-Alder cycloadditions of dienyl pyrimidinones with various dienophiles yielded a variety of 5-substituted pyrimidinones.

Experimental Section

Melting points were determined with a Toshniwal melting point apparatus and are uncorrected. **IR** spectra were recorded in a Perkin-Elmer 983 Infrared Spectro-photometer. ^{1}**H NMR** were recorded in deuteriochloroform, with a Varian EM 390 (90 MHz) and Bruker AC-F 300 (300 MHz) Spectrometer using TMS as internal standard. Chemical shifts are expressed as δppm down field from TMS and J values are in Hz. Splitting patterns are indicated as s: singlet., d: doublet, t: triplet, m: multiplet, q: quartet, p: pentet and br: broad peak. ^{13}**C NMR** spectra were also recorded in Bruker Ac-F 300 in deuteriochloroform using TMS as internal standard. Mass spectra were obtained by electron impact at 70 eV.

Starting Materials

Chloroacetyl chloride and iodoacetic acid used were commercially available.

Preparation of Crotonyl chloride/ 3,3-dimethylacryloyl chloride: An equimoloar amount of thionyl chloride was added dropwise at room temperature to the crotonic acid/3,3-dimethylacrylic acid. The acid immediately goes into solution accompanied by strong effervesence. After about 1.5 -2 h, when the effervesence ceased, the reaction mixture was refluxed on a water bath for 5-10 min to ensure complete elimination of HCl. The acid chlorides thus obtained were purified by distillation under reduced pressure.

Preparation of Sorbyl chloride: Equivalent amounts of sorbic acid (5.0g, 45 mmol) and thionyl chloride (5.3g, 3.3 ml, 45 mmol) were refluxed in dry toluene 920 ml) for 2.5-3 h. The solvent was removed under reduced pressure and the sorbyl chloride thus obtained was further purified by distillation under reduced pressure: Yield 4.90 g (84%); bp (observed 75 °C, 20 mm, lit. ref. 75 °C, 20 mm).

Preparation of 1-aryl-4-(N-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes (63): To a stirred solution of N- aryl -benzimidoyl isothiocyanate **60** (2 mmol) in dry acetone (250 ml) was added dropwise a solution of primary amine (1 m mol) in dry acetone (30 ml) and stirring continued for 1 h. To this solution, methyl iodide (1.2 m mol) was added dropwise and stirred for a further period of 3-4 h. The separated hydroiodide salt of **62** was filtered, and washed with anhydrous acetone, basified with 3N aq. KOH (50 ml) and extracted with chloroform (3 x 100ml). The combined extract was washed with water (3 x 50 ml) and dried over anhydrous sodium sulphate. The removal of chloroform under reduced pressure afforded the products **63** which were recrystallised from a mixture (1:1) of benzene and hexane.

1,2-Diphenyl - 4- methylthio- 4- (N-phenylamino) - 1,3-diaza-1,3-butadiene (63a): Yield 90%; m.p. 142-144 °C; IR (KBr) ν 1600 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.51 (s, 3H, $-SCH_3$), 7.08-7.80 (m, 5H, arom) and 8.90-9.68 (brs, 1H, -NH).: Anal. calcd. for $C_{21}H_{19}N_3S$: C, 73.04; H, 5.51; N, 12.17. Found: C, 73.01; H, 5.65; N,12.05. ms m/z: 345 (M^+).

1,2-Diphenyl-4-methylthio-4-{N-(p-chlorophenylamino)}-1,3-diaza-1,3-butadiene (63b):Yield 92%; m.p. 140-142 °C; IR (KBr) ν 1592 cm^{-1} (C=N); ^1H NMR (90 Hz) δ 2.53 (s, 3H,$-SCH_3$), 6.82-7.71 (m, 14H, arom) and 8.88-9.80 (brs, 1H,-NH). Anal. calcd. for $C_{21}H_{18}N_3SCl$: C, 66.39; H, 4.76; N,11.06. Found: C, 66.32; H, 4.77; N, 11.16. ms m/z: 379 (M^+).

1,2-Diphenyl-4-methylthio-4-{N-(p-methylphenylamino)}-1,3-diaza-1,3-butadiene (63c) : Yield 90%; m.p. 135-137°C; IR (KBr) ν 1585 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.31(s, 3H, CH_3), 2.51 (s, 3H, $-SCH_3$), 6.80-7.48 (m, 12H, arom), 7.54-7.70 (m,2H, arom) and 8.87-9.83 (brs,1H, -NH). Anal. calcd. for $C_{22}H_{21}N_3S$: C,73.50; H, 5.89; N,11.69. Found: C,73.60; H, 5.80; N, 11.70. ms m/z: 359(M^+).

1,2-Diphenyl-4-methylthio-4-{N-(p-methoxyphenylamino)}-1,3-diaza-1,3-butadiene (63d) : Yield 96%; m.p. 104-106°C; IR (KBr) ν 1600 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.51 (s, 3H, $-SCH_3$), 3.80 (s,3H, $-OCH_3$), 6.80-7.86 (m,12H, arom), 7.51-7.74 (m, 2H, arom) and 8.70-9.79 (brs, 1H, -NH). Anal. calcd. for $C_{22}H_{21}N_3OS$: C, 70.37; H, 5.64; N, 11.19. Found: C, 70.47; H, 5.55; N, 11.23. ms m/z: 375(M^+).

1-(p-Chlorophenyl) -4-methylthio-4-(N-phenylamino) -2-phenyl- 1,3-diaza-1,3-butadiene (63e): Yield 90%; m.p. 138-140°C; IR (KBr) ν 1539 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.54 (s, 3H,-SCH_3), 6.82-7.72 (m, 14H, arom) and 8.86-9.80 (brs, 1H, -NH) Anal. calcd. for $C_{21}H_{18}N_3SCl$: C, 66.39; H, 4.76; N, 11.06. Found: C, 66.35; H, 4.75; N, 11.16. ms m/z : 379 (M^+).

1-(p-Methylphenyl) -4-methylthio-4-(N-phenylamino) -2-phenyl-1,3-diaza-1,3-butadiene (63f): Yield 94%; m.p. 122-124°C; IR (KBr) ν 1585 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.31 (s, 3H,-CH_3), 2.53 (s, 3H,-SCH_3), 6.80-7.81 (m, 15H, arom) and 8.90-9.82 (brs, 1H,-NH). Anal. calcd. for $C_{22}H_{23}N_3S$: C, 73.61; H, 5.89; N,11.69; Found: C, 73.50; H, 5.80; N, 11.70. ms m/z: 359 (M^+).

1- (p-Methylphenyl) -4-methylthio -4-{N-(p-chlorophenylamino)} -2-phenyl-1,3-diaza -1,3- butadiene (63g): Yield 90%; m.p. 127-129°C; IR (KBr) ν 1599 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.30 (s, 3H,-CH_3), 2.53 (s, 3H, -SCH_3), 6.80- 7.51 (m, 13H, arom) and 8.89-9.97 (brs, 1H, -NH). Anal. calcd. for $C_{22}H_{20}N_3SCl$: C, 67.08; H. 5.12; N, 10.67. Found: C, 67.00; H, 5.22; N. 10.62. ms m/z: 393 (M^+)

1-(p-Methylphenyl) -4-methylthio -4-(p-methoxyphenylamino) -2-phenyl -1,3-diaza-1,3-butadiene (63h): Yield 91%; m.p. 133- 135°C; IR (KBr) ν 1590 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 2.30 (s, 3H,-CH_3), 2.51 (s, 3H, -CH_3), 3.70 (s, 3H,-OCH_3), 6.80-7.12 (m, 9H, arom), 7.28-7.54 (m, 2H, arom), 7.60- 7.90 (m, 2H, arom) and 8.74-9.80 (brs, 1H, -NH). Anal. calcd. for $C_{23}H_{23}N_3OS$: C, 70.92; H, 5.95; N, 10.79. Found: C, 70.82; H, 5.90; N, 10.82. ms m/z.: 389 (M^+).

Reactions of 1,3-Diaza-1,3- Butadienes with ketenes :Method A: To a well stirred solution of 1,3-diaza-1,3-butadiene (4 m mol) and triethylamine (10 m mol) in dry chloroform (30 ml), was added gradually a solution of acid halide (6 m mol) in dry chloroform (30 ml) over a period of 1 h. at room temperature. After completion of the reaction (tlc), it was further diluted with chloroform and washed with water (5 x 50 ml), sodium hydrogen carbonate (2 x 30 ml), water (2 x 50 ml) and finally dried over anhydrous sodium sulfate. Removal of solvent under reduced pressure yielded the crude product, which was purified by silica gel column chromatography.

Method B: A solution of iodoacetic acid (6 m mol) and triethylamine (10 m mol) in dry chloroform (30 ml) was stirred for 10-15 mins. To this solution 1,3-diaza-1,3-butadiene (4 m mol) was added and stirring was continued. A solution of p- toluenesulfonyl chloride (6 m mol) in chloroform (30 ml) was added dropwise over a period of 1 h. After the addition was over, the reaction mixture was further stirred for 4-5 h. On completion of the reaction (tlc) it was successively washed with 5% sodium hydroxide solution (2 x 30 ml) and water (2 x 50 ml). The solution was dried over anhydrous sodium sulfate. The crude product obtained after removal of solvent under reduced pressure was purified by passing it through silica gel column.

5,6-Diphenyl-3-(p-methoxyphenyl)-2-methylthio-4(*3H*)- pyrimidinone (66a): Yield 84%; m.p. 230-232°C; IR (KBr) ν 1680 cm^{-1} (C=O); ^1H NMR (90 MHz) δ 2.54 (s, 3H, $-SCH_3$), 3.89 (s, 3H,$-OCH_3$), and 6.90-7.63 (m, 14H, arom). Anal. calcd. for $C_{24}H_{20}N_2O_2$ S: C, 71.98; H, 5.03; N, 6.99. Found: C, 71.90; H, 5.06; N, 6.91. ms m/z: 400 (M^+).

2-Methylthio-3,5,6-triphenyl-4(*3H*)-pyrimidinone (66b): Yield 80%; m.p. 214-216°C; IR (KBr) ν 1670 cm^{-1} (C=O); ^1H NMR (90 MHz) δ 2.53 (s, 3H, $-SCH_3$) and 6.52-7.68 (m, 15H, arom). Anal. calcd. for $C_{23}H_{18}N_2OS$: C, 74.47; H, 4.90; N, 7.56. Found: C, 74.48; H, 4.93; N, 7.52. ms m/z: 370 (M^+).

5 -Chloro -3- (p-methoxyphenyl) -2-methylthio -6-phenyl-4(*3H*) -pyrimidinone (66c): Yield 72%; m.p. 210-212°C; IR (KBr) ν 1667 cm^{-1} (C=O); ^1H NMR (90 MHz) δ 2.47 (s, 3H, $-SCH_3$), 3.88 (s, 3H, $-OCH_3$), 6.90-7.63 (m, 7H, arom) and 7.83-8.10 (m, 2H, arom). Anal. calcd. for $C_{18}H_{15}N_2O_2SCl$: C, 60.25; H, 4.21; N, 7.81. Found: C, 60.15, H, 4.30; N, 7.76. ms m/z: 358 (M^+).

5-Chloro-3-(p-methylphenyl)-2-methylthio-6-phenyl-4(*3H*)-pyrimidinone (66d): Yield 71%, m.p. 171-173°C; IR(KBr) ν 1664 cm^{-1} (C=O); ^{1}H NMR (90 MHz) δ 2.45 (s, 3H, CH_3), 2.55 (s, 3H, $-SCH_3$), 7.20-7.73 (m, 7H, arom) and 7.81-8.20 (m, 2H, arom). Anal. calcd. for $C_{18}H_{15}N_2OSCl$: C, 63.06; H, 4.41; N, 8.17. Found: C, 63.09; H, 4.41; N, 8.27. ms m/z: 342 (M^+)

5-Chloro-3-(p-chlorophenyl)-2-methylthio-6-phenyl -4(*3H*)-pyrimidinone (66e): Yield 72%; m.p. 222-224°C; IR (KBr) ν 1640 cm^{-1} (C=O); ^{1}H NMR (90 MHz) δ 2.49 (s, 3H,$-SCH_3$), 7.28-7.79 (m, 7H, arom) and 7.82-8.20 (m, 2H, arom). Anal. calcd. for $C_{18}H_{15}N_2O_2SCl$: C, 60.25; H, 4.21; N, 7.81. Found: C, 60.15; H, 4.30; N, 7.80. ms m/z: 363 (M^+).

3,6 - Diphenyl-2-methylthio-5-(N-phenylamino)-4(*3H*)-Pyrimidinone (72a): Yield 87%; m.p. 209-211°C; IR (KBr) ν 1675 cm^{-1} (C=O); 3300 cm^{-1} (-NH). ^{1}H NMR (90 MHz) δ 2.53 (s, 3H, $-SCH_3$), 6.50-6.79 (m, 3H, arom), 7.22-7.68 (m, 10H, arom), 7.28-8.10 (m, 2H, arom) and 9.50-9.80 (brs, 1H, -NH). Anal. calcd. for $C_{20}H_{19}N_3OS$: C, 71.66; H, 4.97; N, 10.90. Found: C, 71.60; H, 4.92; N. 10.90. ms m/z: 385 (M^+).

3-(4-Methylphenyl)-2-methylthio-5-(phenylamino)- 4(*3H*)- pyrimidinone (72b): Yield 88%; m.p. 202-204°C; IR(KBr) ν 1670 cm^{-1} (C=O), 3300 cm^{-1} (-NH); ^{1}H NMR (90 MHz) δ 2.33 (s, 3H, $-CH_3$), 2,50 (s, 3H, $-SCH_3$), 6.29-6.73 (m, 5H, arom), 6.80-7.30 (m, 7H, arom), 7.69-8.10 (m, 2H, arom) and 9.52-9.79 (brs,1H,-NH). Anal. calcd. for $C_{24}H_{12}N_3OS$: C, 72.25; H, 5.34; N, 10.59. Found: C, 72.15; H, 5.30; N, 10.52. ms m/z: 399 (M^+).

3-(p-Methoxyphenyl)-2-methylthio-5-(N-phenylamino)-6-phenyl-4(*3H*)-pyrimid- - inone (72c): Yield 82%; m.p. 189-191°C; IR (KBr) ν 1670 cm^{-1} (C=O); ^{1}H NMR (90 MHz) δ 2.53 (s, 3H, $-SCH_3$), 3.90 (s, 3H, $-OCH_3$), 6.48-7.43 (m, 12H, arom), 7.86-8.19 (m, 2H, arom) and 9.51-9.78 (brs, 1H, -NH). Anal. calcd. for $C_{24}H_{21}N_3O_2S$: C, 69.37; H, 5.09; N, 10.05. Found: C, 69.35; H, 5.03; N, 10.11. ms m/z: 415 (M^+).

3-(4-Chlorophenyl)-2-methylthio-5-(p-methylphenylamino)-6-phenyl-4(*3H*) pyri--midinone (72d): Yield 78%, m.p. 200-202°C; IR (KBr) ν 1680 (C=O) and 3277 cm^{-1} (-NH); ^{1}H NMR (90 MHz) δ 2.12 (s, 3H, -CH$_3$), 2.53 (s, 3H, -SCH$_3$), 6.53 (d, J = 9 Hz, 2H, arom), 6.87 (d, J = 9Hz, 2H, arom), 7.22-7.78 (m, 7H, arom), 7.88-8.10 (m, 2H, arom) and 9.50-9.73 (brs, 1H, -NH). Anal. calcd for $C_{23}H_{20}N_3OSCl$: C, 65.56; H, 4.75; N, 9.98. Found: C, 65.43; H, 4.70, N, 9.99. ms m/z: 421(M$^+$).

Reactions of 1,3-diaza-1,3-butadienes with vinyl/isopropenyl ketene: To a well stirred solution of 1,3-diaza-1,3-butadienes (4 m mol) and triethylamine (10 m mol) in dry methylene chloride (30 ml), was added dropwise a solution of acid chloride (6 m mol) in dry methylene chloride (30 ml) over a period of 1.5-2 h. at room tempeature. After completion of the reaction (tlc), the reaction mixture was washed with water (5 x 50 ml) and the organic layer dried over anhydrous sodium sulfate. Removal of solvent under reduced pressure yielded crude product, which was purified by silica gel column chromatography using 1:10 ethylacetate: hexane mixture.

5-Isopropenyl-2-methylthio-3,6-diphenylpyrimidin-4(*3H*)-one (92a): Yield 70%; m.p. 201-203°C, IR (KBr) ν 1668 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 2.00 (s, 3H, -CH$_3$), 2.46 (s, 3H, -SCH$_3$), 4.87 (brs, 1H, H$_a$), 5.17 (brs, 1H, H$_b$), 7.29-7.37 (m, 5H, arom), 7.51-7.53 (m, 3H, arom), 7.70-7.73 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 15.13 (-SCH$_3$), 22.7 (-CH$_3$), 119.35 (=CH$_2$), 122.19, 127.61, 128.51, 128.72, 128.88, 129.38, 129.60, 135.71, 138.23 (arom), 138.43 (-C=), 156.47 (C-2), 158.69, 161.42 (C-4). Anal. calcd. for $C_{20}H_{18}N_2OS$: C, 71.86; H, 5.39; N, 8.38. Found: C, 71.81; H, 5.32; N, 8.35. ms m/z: 334 (M$^+$).

5- Isopropenyl-3- (p-methylphenyl) -2- methylthio -6- phenylpyrimidin - 4(*3H*) - one (92b): Yield 72%; m.p. 208-210°C; IR (KBr) ν 1669 cm^{-1} (C=O), ^{1}H NMR (300 MHz) δ 2.05 (s, 3H, -CH$_3$), 2.43 (s, 3H, -CH$_3$), 2.51 (s, 3H, -SCH$_3$), 4.88 (brs, 1H, H$_a$), 5.199 (brs, 1H, H$_b$), 7.32-7.60 (m, 7H, arom), 7.69-7.72 (m, 2H, arom);

^{13}C NMR (75 MHz) δ 15.23 (-SCH_3), 21.32 (-CH_3), 22.73 (-CH_3),119.63 (=CH_2), 122.25, 127.71, 128.23, 128.92, 130.20, 133.17, 135.50, 137.57 (arom), 139.79(-C=), 160.11, 161.81 (C-4). Anal. calcd. for $C_{21}H_{20}N_2OS$: C, 72.38; H, 5.79; N, 8.04. Found: C, 72.59; H, 5.90; N, 8.06. ms m/z: 348 (M^+).

5-Isopropenyl -3-(p-methoxyphenyl) -2-methylthio - 6 -phenylpyrimidin -4(*3H*) - one (92c): Yield 72%; m.p. 218-220°C; IR (KBr) ν 1665 cm^{-1} (C=O); ^1H NMR δ 2.03 (s, 3H,-CH_3), 2.50 (s, 3H, -SCH_3), 3.91(s, 3H,-OCH_3), 4.89 (brs, 1H,, H_a), 5.19 (brs, 1H, H_b), 7.17-7.58 (m, 7H, arom), 7.77-7.95 (m, 2H, arom); ^{13}C NMR (300 MHz) δ 15.24 (-SCH_3), 23.19 (-CH_3), 55.20 (-OCH_3), 119.32 (=CH_2), 122.24, 127.60, 128.20, 128.79, 128.94, 130.34, 134.00, 138.64 (arom), 139.84 (-C=), 156.64 (C-2), 160.12, 162.00 (C-4). Anal. calcd. for $C_{21}H_{20}N_2O_2S$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.40; H, 5.61; N. 7.62. ms m/z: 364 (M^+).

3-(p -Chlorophenyl) - 5-isopropeny l - 2-methylthio- 6-phenylpyrimidin-4(*3H*)-one (92d) : Yield 70%; m.p. 225-226°C. IR (KBr) ν 1671 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 2.00 (s, 3H, -CH_3), 2.48 (s, 3H, -SCH_3), 4.89 (brs, 1H, H_a), 5.20 (brs, 1H, H_b), 7.28-7.80 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 15.24 (-SCH_3), 22.74 (-CH_3), 119.56(=CH_2); 122.27, 127.78, 128.81, 129.07, 129.07, 129.85, 130.03, 134.21, 135.95, 138.25 (arom), 138.40 (-C=), 156.73 (C-2), 159.55, 161.48 (C-4). Anal. calcd. for $C_{20}H_{17}N_2OSCl$: C, 65.13; H, 4.65; N, 7.60. Gound: C, 65.08; H, 4.55; N, 7.55. ms m/z: 368 (M^+).

2-Methylthio-3,6-diphenyl-5-vinylpyrimidine-4(*3H*)-one (92e): Yield 70%; m.p. 238-239°C. IR (KBr) ν 1667 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 2.45 (s, 3H, -SCH_3), 5.37 (dd, J= 11.8 and 2.9 Hz, 1H, H_a), 6.17 (dd, J = 17.5 and 2.9 Hz, 1H, H_b); 6.59 (dd, J= 17.5 and 11.8 Hz, 1H, H), 7.25-7.63 (m, 10H, arom); ^{13}C NMR (75 MHz) δ 15.33 (SCH_3), 115.32 (=CH_2), 123.41, 128.06, 128.57, 128.84, 129.33, 129.47 (arom), 139.27 (-C=), 159.23, 161.60 (C-2), 163.36 (C-4). Anal. calcd. for $C_{19}H_{16}N_2OS$: C, 71.22; H, 5.03; N, 8.74. Found: C, 71.24; H, 5.01; N, 8.72. ms m/z: 320(M^+).

3-(p-Methylphenyl)-2-methylthio-6-phenyl-5-vinylpyrimidin-4(*3H*)-one (92f): Yield 72%; m.p. 219-221°C. IR (KBr) ν 1662 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 2.34 (s, 3H, -CH), 2.50 (s,3H, -SCH$_3$), 5.34 (dd, J = 11.8 and 2.9 Hz, 1H, H$_a$); 6.23 (dd, J=1.74 and 2.9 Hz, 1H, H$_b$), 6.54 (dd, J=17.4 and 11.8 Hz, 1H, H), 7.23-7.69 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 15.34 (-SCH$_3$), 21.35 (-CH$_3$), 116.30 (=CH$_2$), 122.23, 128.07, 128.62, 128.89, 129.40, 129.50, 129.82, 129.99, 130.30, 135.00, 138.26 (arom), 139.27 (-C=), 158.92; 161.72 (C-2), 163.40 (C-4). Anal. calcd. for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42; N, 8.38. Found: C, 71.82; H, 5.35; N, 8.33. ms m/z: 334 (M$^+$).

3-(p-Methoxyphenyl)-2-methylthio-6-phenyl-5-vinylpyrimidin-4(*3H*)-one (92g): Yield 75%; m.p. 211-212°C. IR (KBr) ν 1667 cm^{-1} (C=O), ^{1}H NMR (300 MHz) δ 2.51 (s, 3H, -SCH$_3$), 3.71 (s, 3H, -OCH$_3$), 5.36 (dd, J = 11.8 and 2.9 Hz, 1H, H$_a$); 6.18 (dd, J = 17.4 and 11.8 Hz, 1H, H$_b$); 6.54 (dd, J=17.4 and 11.8 Hz, 1H, H); 7.23-7.70 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 15.29 (-SCH$_3$), 50.15 (-OCH$_3$); 115.83 (=CH$_2$), 123.40, 127.80, 128.06, 128.21, 128.21, 128.57, 128.76, 128.99, 129.41, 129.65, 130.60 135.80, 138.30 (arom),158.64, 161.82 (C-2), 164.00 (C-4). Anal. calcd. for $C_{20}H_{18}\,N_2O_2S$ C, 68.56; H, 5.18; N, 8.00. Found: C, 68.51; H, 5.13; N, 7.98. ms m/z: 350 (M$^+$).

3-(p-Chlorophenyl)-2-methylthio-6-phenyl-5-Vinylpyrimidin-4(3H)-one (92h): Yield 71%; m.p. 206-208°C. IR (KBr) ν 1665 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 2.50 (s, 3H, -SCH$_3$), 5.33(dd, J = 11.5 and 2.8 Hz, 1H, H$_b$), 6.58 (dd, J = 17.6 and 11.5 Hz, 1H, H$_b$), 6.58 (dd, J=17.6 and 11.5 Hz, 1H, H), 7.10-7.40 (m, 9H, arom); ^{13}C NMR (300 MHz) δ 15.50 (-SCH$_3$), 115.41 (=CH$_2$), 122.89, 127.90, 128.55, 129.10, 129.17, 129.22, 129.58, 135.15, 137.83 (arom), 139.09 (-C=), 159.03, 161.71 (C-2), 164.22 (C-4). Anal. calcd. for $C_{19}H_{15}N_2OSCl$: C, 64.31; H, 4.26; N, 7.90. Found: C, 64.30; H, 4.28; N, 7.87. ms m/z: 354 (M$^+$).

Preparation of 1-aryl-4-(N-arylamino)-4-phenyl-2-secondaryamino-1,3-diaza-1,3-butadienes: The 1,3-diaza-1,3-butadiene **63** (1 m mol) was refluxed in benzene with secondaryamine (1 m mol) for 5-6 h. It was then washed with water (3 x 50 ml) and dried over anhydrous sodium sulphate. The removal of benzene under reduced pressure afforded the desired product **93**, which was further recrystallised from a mixture 1:1 of benzene and hexane.

1-(p-Methylphenyl)-4-phenyl-4- (N-phenylamino)-2- pyrrolidino -1,3-diaza -1,3-butadiene (93a): Yield 92%; m.p. 162-164°C; IR (KBr) ν 1552 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 1.85 - 1.89 (m, 4H, $-CH_2-CH_2-$), 2.27 (s, 3H, $-CH_3$), 3.42 - 3.46 (m, 4H, $-CH_2$ $-N-CH_2-$), 6.72-7.34 (m, 15H, arom). Anal. calcd. for $C_{25}H_{26}N_4$: C, 78.50; H, 6.85; N, 14.65. Found: C, 78.69; H, 6.89; N, 14.49. ms m/z: 382 (M^+).

1- (p-Methylphenyl) -4-phenyl-4- (N-phenylamino) -4-phenyl -2-pyrrolidino-1,3-diaza -1,3 butadiene (93b): Yield 93%; m.p. 167-169°C; IR (KBr) ν 1555 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 1.82-1.86 (m, 4H, $-CH_2-CH_2-$), 2.26 (s, 3H,$-CH_3-$), 3.38-3.42 (m, 4H, $-CH_2-N-CH_2-$), 6.68-7.34 (m, 13H, arom). Anal. calcd. for $C_{26}H_{28}N_4$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.93; H, 7.07; N, 14.03. ms m/z: 396 (M^+).

1-(p-Methylphenyl)-4-phenyl-4-(N-methylphenylamino) -4-phenyl -2- piperidino - 1,3-diaza-1,3 butadiene (93c): Yield 92%; m.p.175-176°C; IR (KBr) ν 1554 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 1.56-1.68 (m, 6H,$-CH_2-CH_2-CH_2-$), 2.23 (s, 3H, $-CH_3$), 2.24 (s, 3H, $-CH_3$), 3.42-3.45 (m, 4H, $-CH_2-N-CH_2-$), 6.60-7.34 (m, 13H, arom). Anal. calcd. for $C_{27}H_{30}N_4$: C, 78.99; H, 7.37; N, 13.65. Found: C, 79.13; H, 7.45; N, 13.51. ms m/z: 410 (M^+).

3,5,6-Triphenyl-2-pyrrolidonopyrimidine-4(*3H*)-one (97a): Yield *80%*; *m.p. 130-*131°C; IR (KBr) ν 1653 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 1.56-1.68 (m, 4H,-CH_2-N-CH_2-), 7.13-7.25 (m, 8H, arom), 7.38-7.48 (m, 7H, arom); ^{13}C NMR (75 MHz) δ 25.44 ($-CH_2-CH_2-$), 49.99($-CH_2-N-CH_2$), 113.62, 6.38, 127.50, 127.65, 127.75, 128.28, 128.57, 128.91, 129.31, 130.03, 131.50, 135.45, 137.74, 139.29 (arom), 152.91 (C-6), 159.42 (C-2), 163.98 (C-4). Anal. calcd. for $C_{26}H_{23}N_3O$: C, 79.36; H, 5.89; N, 10.68 Found: C, 79.37; H, 5.82; N, 10.68. ms m/z: 393(M^+).

3-(p-Methylphenyl)-5,6-diphenyl-2-pyrrolidinopyrimidine-4(*3H*)-one (97b): Yield 82%; m.p. 204-205°C; IR (KBr) ν 1652 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.73-1.77 (m, 4H, $-CH_2-CH_2-$), 2,37 (s,3H,$-CH_3$), 3.14-3.17 (m, 4H $-CH_2-N-CH_2-$); 7.14 -7.24 (m, 12H, arom), 7.44-7.47 (d, 2H, arom); ^{13}C NMR (75 MHz) δ 21.21 ($-CH_2-CH_2-$), 25.41 ($-CH_3$), 49.95 ($-CH_2-N-CH_2-$), 113.45, 119.81, 126.31, 127.48, 127.61, 128.53, 128.94, 128.13, 129.40, 129.55 130.02, 131.51, 134.95, 135.51, 138.20, 139.32 (arom), 152.98 (C-6), 159.42 (C-2), 164.12 (C-4). Anal. calcd. for $C_{27}H_{25}N_3O$: C, 79.59; H, 6.18; N,10.32. Found: C, 79.58; H, 6.13; N, 10.27. ms m/z: 407 (M^+).

3,6-Diphenyl-3-pyrrolidino-5-vinylpyrimidin-4(*3H*)-one (97c): Yield 76%; m.p. 190-192 °C; IR (KBr) ν 1659 cm^{-1}(C=O); ^{1}H NMR (300 MHz) δ 1.68 - 1.72 (m, 4H, $-CH_2-CH_2-$), 3.07-3.10 (m, 4H, $-CH_2-N-CH_2-$), 5.19 (dd, J= 11.8 and 2.9 Hz, 1H, H_a), 6.29 (dd, J= 17.5 and 2.9 Hz, 1H, H_b), 6.50 (dd, J= 17.5 and 11.7 Hz,1H, H); 7.25-7.68 (m, 10H, arom); ^{13}C NMR (75 MHz) δ 25.38 ($-CH_2-CH_2-$), 49.99 ($-CH_2$ $-N-CH_2-$), 109.12 (C-5), 115.56 ($=CH_2$), 127.91, 128.43, 128.99, 129.07, 129.75, 130.45, 137.64 (arom), 139.27 (-C=), 159.23, 161.64 (C-2), 163.30 (C-4). Anal. calcd. for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.95; H, 6.11; N, 12.21. ms m/z: 343 (M^+).

3-(p-Methylphenyl)-6-phenyl-2-piperidino-5-vinylpyrimidin-4(*3H*) one (97d): Yield 73%; m.p. 188-189°C; IR (KBr) ν 1660 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.65- 1.69 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.28 (s, 3H, $-CH_3$), 3.14-3.17 (m, 4H, $-CH_2-N-CH_2$), 5.33 (dd, J= 11.6 and 2.8 Hz, 1H, H_a), 6.23 (dd, J= 17.5 and 2.8 Hz, 1H, H_b) 6.44 (dd, J= 17.6 and 11.5 Hz, 1H, H); 7.13-7.59 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 21.14 ($-CH_3$), 25.03 ($-CH_2-CH_2-$), 50.1 ($-CH_2-N-CH_2-$), 115.21 ($=CH_2$), 127.70, 127.93, 128.82, 129.33, 129.60, 137.96 (arom), 139.26 (-C=), 158.67, 161.29 (C-2), 163.00 (C-4). Anal. calcd. for $C_{24}H_{25}N_3O$: C, 70.60; H, 6.78; N, 11.31. Found: C, 77.50; H, 6.72; N,11.29. ms m/z: 371 (M^+).

5-Isopropenyl-3- (p-methylphenyl)-6- phenyl-2- pyrrolidinopyrimidin -4(*3H*)-one (97e): Yield 71%; m.p. 210-211°C; IR (KBr) ν 1663 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 1.63-1.66 (m, 4H, $-CH_2-CH_2-$), 2.03 (s, 3H, $-CH_3$), 2.34 (s, 3H, $-CH_3$), 3.14- 3.17 (m, 4H, $-CH_2-N-CH_2-$), 4.85 (brs, 1H, H_a), 5.17 (brs, 1H, H_b),7.34-7.89 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 21.14 ($-CH_3$), 24.22 ($-CH_2-CH_2-$), 25.15 ($-CH_3$), 50.02 ($-CH_2-N-CH_2-$), 118.55 ($=CH_2$), 123.20, 127.34, 127.89, 128.35, 128.63, 128.70, 129.90, 134.88, 138.56 (arom), 139.89 (-C=), 157.43 (C-2), 160.20, 163.50 (C-4). Anal. calcd. for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.60; H, 6.69; N, 11.28. ms m/z: 371 (M^+).

5-Isopropenyl-3-(p-methylphenyl)-6- phenyl-2- pyrrolidinopyrimidin -4(*3H*) -one (97f): Yield 76%; m.p. 204-206°C; IR (KBr) ν 1662 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 1.62-1.65 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.01(s, 3H, $-CH_3$), 2.39 (s, 3H, $-CH_3$), 3.13- 3.16 (m, 4H, $-CH_2-N-CH_2-$), 4.84 (brs, 1H, H_a), 5.11 (brs, 1H, H_b), 7.35-7.76 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 21.21 ($-CH_3$), 24.21 ($-CH_2-CH_2-$), 25.04 ($-CH_3$), 49.59 ($-CH_2-N-CH_2-$), 118.77 ($=CH_2$), 122.23, 127.59, 128.18, 128.92, 130.21, 134.03, 138.27, 138.65, (arom), 139.86 (-C=), 157.43 (C-2), 160.20, 163.49 (C-4). Anal. calcd. for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 77.90; H, 6.98; N, 10.88. ms m/z: 385 (M^+).

Cyclization reactions of pyrimidinones: A solution of pyrimidinone and 85% H_3PO_4 was refluxed in dry tolulene for 8-10 h. After completion of the reaction (tlc), toluene was removed under vacuo and the residue was treated with aqueous sodium bicarbonate solution. The aqueous layer was extracted with chloroform and washed with water (5 x 50 ml). It was then dried over anhydrous sodium sulfate. The removal of solvent under reduced pressure yielded the pure product.

3, 5-Dihydro-5, 5-dimethyl -2-methylthio -3-phenyl -4H-indeno[1,2-d]pyrimidin-4-one (98a): Yield 95%; m.p. 229-231°C; IR (KBr) ν 1662 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 1.57 (s, 6H, 2x-CH_3), 2.59 (s, 3H, $-SCH_3$), 23.58 (2x-CH_3), 2.59 (s, 3H, $-SCH_3$), 23.58 (2x-CH_3), 49.19, 121.70, 122.67, 126.73, 127.07, 129.84, 130.32, 134.34, 135.89 (arom), 137.04, 156.29 (C-6), 159.06, 160.29 (C-

2), 164.01 (C-4). Anal. calcd. for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42; N, 8.38. Found: C, 71.72; H, 5.35; N, 8.33. ms m/z: 334 (M^+).

3,5-Dihydro-5,5-dimethyl-2-methylthio-3-phenyl-4H- indeno [1,2-d] pyrimidin-4-one (98b): Yield 94%; m.p. 262-264°C; IR (KBr) ν 1663 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.55 (s, 6H, 2x-CH_3), 2.44 (s, 3H,-CH_3), 2.58 (s, 3H,-SCH_3), 7.24-7.69 (m, 5H, arom). Anal. calcd. for $C_{21}H_{20}N_2OS$: C, 72.38; H, 5.79; N, 8.04. Found: C, 72.37; H, 5.70; N, 8.00. ms m/z: 348 (M^+).

3,5-Dihydro-3-(p-methyloxyphenyl)-5-5-dimethyl-2-methylthio-4H-indeno[1,2-d] pyrimidin-4-one (98c): Yield 92%; m.p. 228-230°C; IR (KBr) ν 1668 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.56 (s, 6H, 2x-CH_3), 2.58 (s, 3H,-SCH_3), 3.87(S, 3H,-OCH_3), 7.01-7.90 (m, 8H, arom); ^{13}C NMR (75 MHz) δ 15.57 (-SCH_3), 23.53 (2x -CH_3), 46.14 (C-5), 55.25 (-OCH_3), 114.75, 121.61, 122.03, 126.97, 128.34, 129.68, 129.93 (arom), 13701 (C-5), 156.31 (C-6), 159.60, 160.33 (C-2), 164.85 (C-4). Anal. calcd. for $C_{21}H_{20}N_2O_2S$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.30; H, 5.45; N, 7.66. ms m/z: 364 (M^+).

3,5-Dihydro-3-(p-chlorophenyl)-5-5-dimethyl-2-methylthio-4H-indeno[1,2] pyri--midin-4-one (98d): Yield 94%; m.p. 227-228°C; IR (KBr) ν 1660 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.55 (s, 6H, 2x-CH_3), 2.59 (s, 3H, -SCH_3), 7.25-7.90 (m, 8H, arom); ^{13}C NMR (75 MHz) δ 15.50 (-SCH_3), 23.51 (2x-CH_3), 46.19, 121.70, 123.07, 126.73, 129.84, 130.32, 134.34, 135.89 (arom), 137.04, 156.29, (C-6), 159.06, (C-2), 164.01 (C-4). Anal. calcd. for $C_{20}H_{17}N_2OSCl$: C, 65.12; H, 4.65; N, 7.59. Found: C, 65.07; H, 4.56; N, 7.55. ms m/z: 368 (M^+).

3,5-Dihydro-5,5-dimethyl-3-(p-methylphenyl)-2-pyrrolidino-4H-indeno[1,2] pyr--imidin-4-one (98e): Yield 78%, m.p. 236-238°C IR (KBr) ν 1665 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 1.54 (s, 6H, 2x -CH_3), 1.64-1.68 (m, 4H,-CH_2-CH_2), 2.30 (s, 3H,-CH_3), 7.24-7.89 (m, 8H, arom). Anal. calcd. for $C_{24}H_{25}N_3O$: C, 77.63; H, 6.78; N,11.31. Found: C, 77.60; H, 6.71; N, 11.27. ms m/z: 371 (M^+).

3,5 -Dihydro -5,5- dimethyl -3- (p-methylphenyl) -2-piperidino-4H-indeno[1,2-d] pyrimidin-4-one (92f): Yield 79%; m.p. 242-24°C; IR (KBr) ν 1663 cm^{-1} (C=O); ^1H NMR (300 MHz) δ 1.56 (s, 6H, 2x-CH_3), 1.62-1.65 (m, 6H,-CH_2-CH_2-CH_2-), 2.40 (s, 3H,-CH_3), 3.13-3.13 (m, 8H, arom). Anal. calcd. for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N,10.91. Found: C, 77.90; H, 7.00; N, 10.88. ms m/z: 385 (M^+).

Reactions of N-aryl-1,3-diaza-1,3-butadienes 63/93 with butadienyl ketenes (115/117/118 and 120): To a well stirred solution of N-aryl 1,3-diaza-1,3-butadienes **63** (4 m mol) and triethylamine (1g, 10 m mol) in dry dichloromethane (30 ml), was added dropwise a solution of sorbylchloride **104** (6 m mol) in dry dichloromethane over a period of 1.5-2 h at room temperature. After completion of the reaction (tlc), the reaction mixture was washed several times with water and the organic layer dried over anhydrous sodium sulphate. Removal of solvent under reduced pressure yielded the crude product, which was purified by silicagel column chromatography using 1:10 ethylacetate: hexane mixture.

5-(1′,3′-Butadienyl)-3-6-diphenyl-2-methylthiopyrimidin-4(*3H*)-one (115a): Yield 33%; m.p. 162-164°C; IR (KBr) ν 1665 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 2.52 (s, 3H,-SCH_3), 5.06 (d, J=10.3 Hz,^1H, H_b), 5.24 (d, J=16.9 Hz, 1H, H_a), 6.29 (ddd, J=6.4, 10.4 and 16.9 Hz, 1H, H_c), 6.44 (d, J=15.5 Hz,1H,H_e), 7.16-7.66 (m, 11H, arom, H_d); ^{13}C NMR (75 MHz) δ 15.34 (-SCH_3), 115.31 (C-5), 118.00 (C-4), 121.95, 123.43, 124.07, 124.68, 125.76 (C-2), 128.12, 128.48, 128,87, 129.39, 129.51, 129.79, 129.98, 130.37, 135.19(arom); 161.82 (C-4). Anal. calcd. for $C_{21}H_{18}N_2OS$: C, 72.83; H, 5.20; N, 8.09. Found: C, 72.80; H, 5.16; N, 8.07. ms m/z: 346 (M^+).

5-(1′,3′-Butadienyl)-3-(p-methylphenyl)-2-methylthio-6-phenylpyrimidin-4(*3H*)-one (115b): Yield 29%; m.p. 190-192°C; IR (KBr) ν 1664 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 2.32 (s, 3H,-CH_3), 2.53 (s, 3H,-SCH_3), 5.06 (d, J = 10.1 Hz, 1H, H_b), 5.24 (d, J = 16.9 Hz, 1H, H_a), 6.28 (ddd, J= 6.7, 10.7 and 16.9 Hz, 1H, H_c), 6.44 (d,J=15.5,1H, H_e), 7.26-7.29 (d, 2H, arom), 7.45-7.67 (m, 8H, arom, H_d); ^{13}C NMR (75 MHz) δ 15.35 (-SCH_3), 21.39 (-CH_3), 115.30 (C-5), 117.93 (C-4), 125.82 (C-2), 128.11, 128.17, 129.35, 129.80, 130.48, 133.26, 135.19, 138.27 (arom), 138.68 (C-3), 158.81, 159.48 (C-2), 161.95 (C-4). Anal. calcd. for $C_{22}H_{20}N_2OS$: C, 73.33; H, 5.56; N, 7.78. Found: C, 73.29; H, 5.51; N, 7.76. ms m/z: 360 (M^+)

5-(1′,3′-Butadienyl)-3-(p-chlorophenyl)-2-methylthio- 6 -phenylpyrimidin-4(*3H*)-one (115c): Yield 75%; m.p. 209-211°C; IR (KBr) ν 1663 cm^{-1} (C=0); ^{1}H NMR (300 MHz) δ 2.49 (s, 3H-SCH_3), 5.08 (d, J=10.2 Hz, 1H, H_b), 5.25 (d, J= 16.4 Hz, 1H, H_a), 6.30 (ddd, J = 6.6, 10.4 and 16.9 Hz, 1H, H_c), 6.42 (d, J = 15.5 Hz, 1H, H_e), 7.25-7.29 (d, 2H, arom), 7.47-7.68 (m, 8H, arom, H_d); ^{13}C NMR (75 MHz) δ 15.37 (-SCH_3), 115.39 (C-5), 118.23 (C-4), 125.61 (C-2), 128.17, 129.49, 129.81, 130.03, 130.16, 134.36, 135.41, 136.22 (arom); 138.57 (C-3), 159.80, 160.24 (C-2), 162.60 (C-4). Anal. calcd. for $C_{21}H_{17}N_2OSCl$: C, 66.33; H, 4.44; N, 7.86. Found: C, 66.18; H, 4.50; N, 7.23. ms m/z: 380.5 (M^+).

3,6-Diphenyl-2-methylthio-5-{3′-(N-phenylaminobut-1′-en-yl)}-pyrimidin-4(*3H*)-one (117a): Yield 30%; m.p.181-183°C IR (KBr) ν 1667 cm^{-1} (C=0); ^{1}H NMR (300 MHz) δ 1.28-1.32 (d, J = 6.0 Hz, 3H, -CH_3), 2.39 (s, 3H, -SCH_3), 3.96-4.03 (m, 1H, H-3′), 6.40-6.45 (d, J = 15.0 Hz, 1H, H-1′); 6.54-6.57 (d, J = 8 Hz, 2H, arom), 6.69-6.74 (dd, J = 15.6 and 8.7 Hz, 1H, H-2′), 7.04-7.56 (m, 14H, arom, NH); ^{13}C NMR (75 MHz) δ 15.33 (-SCH_3), 22.13 (-CH_3), 51.38 (C-3), 113.36, 114.82 (C-5), 117.05, 121.34 (C-2), 127.91, 128.52, 128.55, 137.89, 138.39, 129.82, 129.97, 136.02 (C-1), 137.89, 138.39, 147.26 (arom); 158.39 (C-6). Anal. calcd. for $C_{27}H_{25}N_2OS$: C, 76.24; H, 5.88; N, 6.59. Found: C, 76.20; H, 5.93; N, 6.81. ms m/z: 425 (M^+).

3,6-Diphenyl-2-methylthio-5-{1′-(N-phenylaminobut-2′-en-yl)}-pyrimidin-4(*3H*)-one (118a): yield 23%; m.p. 160-162°C ; IR (KBr) ν 1674 cm^{-1} (C=0); ^{1}H NMR (300

MHz) δ 1.69-1.72 (d, J = 6.1 Hz, 3H, -CH_3), 2.39 (s, 3H, -SCH_3), 5.08-5.10 (d, J = 6.2 Hz, 1H, H-1′), 5.32 (brs, 1H, NH), 5.65-5.74 (m, 1H, H-3′), 5.94-6.02 (dd, J = 15.6 and 6.0 Hz, 1H, H-2′), 6.31-6.35 (d, 2H, arom), 6.59-6.65 (t, 3H, arom), 7.00-7.05 (t, 3H, arom), 7.24-7.65 (m, 8H, arom); ^{13}C NMR (75 MHz) δ 15.33 (-SCH_3), 17.92 (-CH_3), 54.52 (C-1), 114.16, 117.43, 119.27, 127.57, 128.28, 128.46, 128.55, 128.89, 128.96, 129.53, 129.79, 129.82, 130.04, 130.20, 135.54, 137.96, 146.84 (arom); 159.07 (C-6), 160.48 (C-2), 162.47 (C-4). Anal. calcd. for $C_{27}H_{25}N_2OS$: C, 76.24; H, 5.88; N, 6.59. Found: C, 76.13; H, 5.90; N, 6.75. ms m/z: 425 (M^+).

3- (p-Chlorophenyl)-2 -methylthio -6-phenyl -5{3′-N- phenylaminobut -1′-en-yl}-pyrimidin -4(*3H*)-one (117b): Yield 28%; m.p. 201-203°C; IR (KBr) ν 1667 cm^{-1} (C=0); ^1H NMR (200 MHz) δ 1.28-1.32 (d, J = 6.3 Hz, 3H, -CH_3), 2.44 (s, 3H, -SCH_3), 3.97-4.02 (m, 1H, H-3′), 6.32-6.39 (d, J = 15.3 Hz, 1H, H-1′), 6.47-6.51 (d, J = 8.2 Hz, 2H, arom), 6.66-6.70 (dd, J = 15.8 and 8.4 Hz, 1H, H-2), 6.96-7.52 (m, 13H, arom, NH). Anal. calcd. for $C_{27}H_{24}N_2OSCl$: C, 70.51; H, 5.22; N, 6.09. Found: C, 70.25; H, 5.41; N, 6.17. ms m/z: 459.5 (M^+).

3- (p-Chlorophenyl) -2- methylthio -6- phenyl -5-{1′-(N-phenylaminobut -2′ -en-yl)}-pyrimidin-4(*3H*)-one (118b): Yield 27%; m.p. 213-215°C; IR (Kbr) ν 1676 cm^{-1} (C=0); ^1H NMR (200 MHz) δ 1.69-1.72 (d, J = 6.1 Hz, 3H, -CH_3), 2.43 (S, 3H, -SCH_3), 5.04-5.07 (d, J = 6.0 Hz, 1H, H-1′), 5.03 (brs, 1H, NH), 5.61-5.73 (m, 1H, H-3′), 5.92- 6.02 (dd, J = 15.8 and 6.3 Hz, 1H, H-2′), 6.23-6.28 (d, 2H, arom), 6.82-6.87 (d, 2H, arom), 7.26-7.64 (m, 10H, arom). Anal. calcd. for $C_{27}H_{24}N_2OSCl$: C, 70.51; H, 5.22; N, 6.09. Found: C, 70.55; H, 5.09; N, 6.13. ms m/z: 459.5 (M^+)

3,6-Diphenyl-2-methylthio-5-{3′-(N-p-methylphenylaminobut-1′-en-yl)}-pyrimi-din-4(*3H*)-one (117c): Yield 30%, m.p. 152-154°C; IR (KBr) ν 1666 cm^{-1} (C=0); ^1H NMR (200 MHz) δ 1.29-1.32 (d, J = 6.1 Hz, 3H, -CH_3), 2.43 (s, 3H, -SCH_3), 3.95-4.01 (m, 1H, H-3′), 6.30-6.38 (d, J = 15.2 Hz, 1H, H-1′), 6.45- 6.49 (d, J = 8.5 Hz, 2H, arom), 6.65-6.69 (dd, J = 15.6 and 8.6 Hz, 1H, H-2′), 6.92-7.61 (m, 13H, arom, NH). Anal. calcd. for $C_{28}H_{27}N_2OS$: C, 76.54; H, 6.15; N, 6.38. Found. C, 6.17; H, 6.17; N, 6.21. ms m/z: 439 (M^+)

3,6-Diphenyl-2-methylthio-5{1′-N-(p-methylphenylaminobut-2′-en-yl)}-pyrimidi-n-4(*3H*)-one (118c): Yield 27%; m.p. 175-177 °C; IR (KBr) ν 1667 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 1.59 (s, 3H, -CH_3) (arom), 1.69-1.72 (d, J = 8.3 Hz, 3H, -CH_3), 2.42 (s, 3H, -SCH_3), 5.03-5.06 (d, J = 6.1 Hz, 1H, H-1′); 5.31(brs, 1H, NH); 5.61-5.72 (m, 1H,H-3′) 5.91-6.01 (dd, J = 15.7 and 6.2 Hz, 1H, H-2′), 6.23-6.27 (d, 2H, arom); 6.83-6.87 (d, 2H, arom), 7.25-7.64 (m, 10H, arom). Anal. calcd. for $C_{28}H_{27}N_2OS$: C, 76.54; H, 6.15; N, 6.38. Found: C, 76.50; H, 6.11; N, 6.51. ms m/z: 439 (M^+)

3-(p-Methylphenyl)-2-methylthio-6-phenyl-5-(3′-phenylaminobut-1′-en-yl)-pyri-midin-4(*3H*)-one (117d): Yield 29%; m.p. 150- 152°C; IR (KBr) ν 1666 cm^{-1} (C=0); ^1H NMR (200 MHz) δ 1.28-1.32 (d, J = 6.0 Hz, 3H, -CH_3), 2.19 (s, 3H, -CH_3), 2.41 (s, 3H, -SCH_3), 3.96- 4.02 (m, 1H, H-3′), 6.32-6.39 (d, J = 15.4 Hz, 1H, H-1′), 6.47-6.70 (dd, J = 15.6 and 8.7 Hz, 1H, H-2′), 6.69-7.53 (m, 15H, arom, NH); ^{13}C NMR (75 MHz) δ 15.42 (-SCH_3) 20.44 (-CH_3), 22.40 (-CH_3), 51.54 (C-3′), 113.85, 115.13 (C-5), 117.42, 121.38, 128.02, 129.16, 129.98, 130.13, 130.32, 134.64, 136.29 (C-1′), 138.01; 138.73; 147.31 (arom); 158.52 (C-6); 159.17 (C-2), 162.24 (C-4). Anal. calcd. for $C_{28}H_{27}N_2OS$: C, 76.54; H, 6.15; N, 6.38. Found: C, 76.51; H, 6.12; N, 6.35. ms m/z: 439 (M^+)

3-(p-Methylphenyl)-2-methylthio-6-phenyl-5-{1′-(N-phenylaminobut-2-en-l)}py--rimidin- 4(*3H*)-one (118d): Yield 26%; m.p. 194-196°C; IR (KBr) ν 1676 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 1.69-1.72 (d, J = 6.1 Hz, 3H, $-CH_3$), 2.19 (s, 3H, $-CH_3$), 2.42(s, 3H, $-SCH_3$), 5.04 -5.06 d, J = 6.3 Hz, 1H, H-1′), 5.30 (brs, 1H, NH), 5.62-5.70 (m, 1H, H-3′), 5.91-6.00 (dd, J = 15.7 and 16. 2 Hz, 1H, H-2′), 6.23-6.27 (d, 2H, arom), 6.56-6.59 (t, 3H, arom), 6.92-7.58 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 15.37 ($-SCH_3$), 17.95 ($-CH_3$), 20.42 ($-CH_3$), 54.94 (C-1′), 114.46, 119.53, 126.70, 127.50, 128.29, 128.57, 128.97, 128.52, 129.84, 130.07, 130.45, 135.65, 138.12, 144.58 (arom); 158.02 (C-6), 160.52 (C-2), 163.00 (C-4). Anal. calcd. for $C_{28}H_{27}N_2OS$: C, 76.54; H, 6.15; N, 6.38. Found : C, 76.62; H, 6.09; N, 6.30. ms m/z: 439(M^+)

5-(1′,3′-Butadienyl)-3,6-diphenyl-2-piperidino--pyrimidin-4(*3H*)-one (120a):- Yield 86%; m.p. 214-215°C; IR (KBr) ν 1664 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 1.74-1.77 (m, 6H, $-CH-CH_2-CH_2-$), 3.09-3.11 (m, 4H,$-CH_2-N-CH_2-$), 4.94 (d, J = 10.1 Hz, 1H, H_a), 5.15 (d, J = 16.9 Hz, 1H, H_b), 6.27 (ddd, J = 6.3, 10.6 and 16.9 Hz, 1H, H_c), 6.39 (d, J = 15.4 Hz, 1H, H_e), 7.35-7.68 (m, 11H, arom, H_d); ^{13}C NMR (75 MHz) δ 25.38 ($-CH_2-CH_2-CH_2-$), 50.03 ($-CH_2-N-CH_2-$), 108.99 (C-5), 115.44 (C-4), 127.19, 127.95, 128.46, 129.08, 129.38, 129.76, 130.99, 137.61 (arom), 139.30 (C-3), 151.93; 161.51 (C-2), 163.11 (C-4). Anal. calcd. for $C_{25}H_{25}N_3O$: C, 78.33; H, 6.53; N, 10.97. Found. C, 78.29; H, 6.50; N, 10.95. ms m/z : 383 (M^+)

5-(1′,3′-Butadienyl)-3-(p-methylphenyl)-6-phenyl-2-piperidinopyrimidin -4(*3H*)-one (120b):- Yield 82%; m.p. 160-162°C; IR (KBr) ν 1662 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 1.76-1.79 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.41 (s, 2H, $-SCH_3$), 3.17-3.19 (m, 4H,$-CH_2-N-CH_2-$); 4.99 (d, J = 10.0 Hz, 1H, H_a); 5.18 (d, J = 16.8 Hz, 1H, H_b); 6.28 (ddd,J = 6.5, 10.4, 16.90 Hz, 1H, H_c); 6.40 (d, J = 15.4 Hz, 1H, H_e), 7.25-7.67

(m,10H, arom, H$_d$). Anal. calcd for $C_{25}H_{27}N_3O$: C, 78.59; H, 6.80; N, 10.58. Found: C, 78.54; H, 6.77; N, 0.53. ms m/z: 397(M$^+$).

5-(1′,3′-Butadienyl)-3-(P-methylphenyl)-6-phenyl-2-pyrrolidinopyrimidin-4(*3H*)-one (120c): Yield 80%; m.p. 158-160°C; IR (KBr) ν 1664 cm^{-1}; ^{1}H NMR (300 MHz) 1.67-1.71 (m, 4H, -CH_2-CH_2-), 1.67-1.71 (4H, -CH_2-N-CH_2-), 4.93 (d, J = 10Hz, 1H, H$_a$), 5.12 (d, J = 16.9 Hz,1H, H$_b$), 6.25 (ddd, J = 6.3, 10.5 and 16.9 Hz, 1H, H$_c$), 6.40 (d, J = 15.4 Hz, 1H, H$_e$), 6.53-7.67 (m, 10H, arom, H$_d$); ^{13}C NMR (75 MHz) δ 21.23 (-CH_3), 25.35 (-CH_2-CH_2-), 50.50 (-CH_2-N-CH_2-), 108.85 (C-5), 115.34 (C-4), 127.15, 127.91, 128.23, 128.93, 129.01, 129.60, 130.90, 134.80, 135.08, 138.46, 139.27 (arom), 139.32 (C-3), 151.27, 151.97, 158.78 (C-6), 161.47 (C-2), 163-24 (C-4). Anal. calcd. for $C_{25}H_{25}N_3O$: C, 78.33; H, 6.53; N, 10.97. Found: C, 78.29; H, 6.49; N, 10.94. ms m/z: 383 (M$^+$).

Reactions of butadienyl pyrimidinone (115) with dimethylacetylene dicarboxylate (122): Equimolar amouts of pyrimidinones **115** and DMAD were refluxzed in dry toluene for 7-8 h. The solvent was removed under reduced pressure and the crude product thus obtained was purified from benzene: hexane (3:1) mixture.

6 -Phenyl-5- [(2′,3′-bis(methoxycarbonyl)- 2′,4′-cyclohexadienyl)] -3-(p-ethylphe--nyl) -2-methylthiopyrimidin-4(*3H*)-one (122a): Yield 62%; m.p. 196-198°C; IR (KBr) ν 1732 (-CO_2CH_3), 1709 (-CO_2CH_3) and 1640 cm^{-1} (C=0); ^{1}H NMR (300 MHz) δ 2.37 (s, 3H, -CH_3), 2.42 (s, 3H, -SCH_3), 2.84-2.87 (m, 2H, -CH_2-), 3.63 (s, 3H, -CO_2CH_3), 3.67 (s, 3H, -CO_2CH_3), 4.53-4.55 (m, 1H, H-1′), 5.57-5.61 (m, 1H, olefinic), 5.76-5.79 (m, 1H, olefinic), 7.16-7.19 (m, 2H, arom), 7.25-7.51 (m, 7H, arom); ^{13}C NMR (75 MHz) δ 15.37 (-SCH_3), 21.39 (-CH_3), 26.93 (-CH_2-), 44.98 (C-1′), 51.98 (-CO_2CH_3), 51.99 (-CO_2CH_3), 117.69; 123.61, 124.11, 128.22, 128.31, 129.01, 129.31, 130.36, 130.65, 133.08, 137.48, 138.41, 140.19 (arom); 158.20 (C-

6); 160.68 (C-2), 161.36 (C-4), 167.00 ($-CO_2CH_3$), 168.85 ($-CO_2CH_3$). Anal. calcd. for $C_{28}H_{26}N_2O_5S$: C, 66.98; H, 5.18; N, 5.58. Found: C, 66.91; H, 5.15; N, 5.57. ms m/z : 502 (M^+).

3,6-Dipheyl-5-[2′,3′-bis(methyoxycarbonyl)-2′,4′-cyclohexadienyl) -2- piperidino-pyrimidin-4(*3H*)-one (122b): Yield 62%; m.p. 225-227°C; IR (Kbr) ν 1734 ($-CO_2CH_3$), 1708 ($-CO_2CH_3$) and 1645 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 1.74-1.77 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.85-2.88 (m, 2H, $-CH_2-$), 3.10-3.13 (m, 4H, $-CH_2-N-CH_2-$), 3.64 (s, 3H, $-CO_2CH_3$), 3.68 (s, 3H, $-CO_2CH_3$), 4.52-4.56 (m, 1H, H-1′), 5.57-5.61 (m, 1H, olefinic), 5.75-5.78 (m, 1H, olefinic), 7.29-7.62 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 25.38 ($-CH_2-CH_2-CH_2-$), 26.93 ($-CH_2-$), 45.00 (C-1′), 50.03 ($-CH_2-N-CH_2-$), 52.02 ($-CO_2CH_3$), 52.04 ($-CO_2CH_3$), 117.72, 124.02, 124.12, 128.31, 128.46, 129.05, 129.35, 130.40, 130.69, 137.61, 138.38, 140.21 (arom), 159.20 (C-6), 161.51 (C-2), 162.21 (C-4), 167.00 ($-CO_2CH_3$), 168.89 ($-CO_2CH_3$). Anal. calcd. for $C_{31}H_{31}N_3O_5$: C, 70.86; H, 5.90; N, 8.00. Found: C, 70.91; H, 6.00; N, 7.61. ms m/z: 525(M^+).

Reactions of butadienyl pyrimidinone 115 with 4-phenyl-1,2,4-triazo-3,5-dione (123): Equimolar amounts of butadienyl pyrimidinone **115** and 4-phenyl-1,2,4-triazo-3,5-dione were stirred at 0°C for about 5 min in dry CH_2Cl_2 . The solvent was removed and the crude product thus obtained was purified by recrystallization from a benzene : hexane (3:1) mixture.

3-(p-Chlorophenyl)-2-methylthio-6-phenyl-7′,9′-dioxo-3-[8′-phenyl-1,6,8-triza [4.3.0] bicyclonon-3-en-yl]-pyrimidin-4(*3H*)-one (123a):- Yield 93%; m.p. 258-260°C; IR (KBr) ν 1664 (α,β-unsaturated C=0) and 1704 cm^{-1} (-N-CO-N-); ^1H NMR (300 MHz) δ (s, 3H, $-SCH_3$), 4.25 (m, 2H, $-CH_2-$), 5.60-5.62 (m, 1H, H-2′), 5.81-5.84 (m,1H, olefinic), 6.03-6.07 (m, 1H, olefinic), 7.26-7.66 (m, 14H, arom); ^{13}C NMR (75 MHz) δ 15.44 ($-SCH_3$), 41.49 ($-CH_2$), 52.54 (C-2′), 96.09, 114.53, 120.91, 122.37, 125.51, 127.84, 128.43, 128.63, 129.00, 130.02, 130.30, 131.26, 133.70, 136.39, 137.73, 149.77, 150.18 (arom); 161.72 (C-2), 163.89 (C-4), 171.7, 174.7 (-CO-N-CO-). Anal. calcd. for $C_{29}H_{22}N_5O_3SCl$: C, 62.65; H, 3.96; N, 12.6. Found: C, 62.64; H, 3.93; N, 12.4. ms m/z. 555.5 (M^+).

3-(p-Methylphenyl) -2- methylthio -6-phenyl-7′,9′-dioxo-3- [8′-phenyl -1′,6′,8′-triaza [4.3.0] bicyclonon-3′-en-yl] pyrimidin-4(*3H*)-one (123b): Yield 90%; m.p. 257-259°C; IR (KBr) ν 1661 (C=0) and 1708 cm^{-1} (-CO-N-CO-); ^1H NMR (90 MHz) δ 2.17 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-SCH_3$), 4.26 (m, 2H, $-CH_2-$), 5.60-5.62 (m, 1H, H-2′), 5.79 -5.85 (m, 1H, olefinic), 6.01-6.08 (m, 1H, olefinic), 7.17-7.50 (m, 12H, arom), 7.64-7.68 (m, 2H, arom). Anal. calcd. for $C_{30}H_{25}N_5O_3S$: C, 67.29; H, 4.67; N, 13.08. Found: C, 67.27; H, 4.64; N, 13.04. ms m/z: 535 (M^+).

References

1. J. Sauer; R. Sustmann, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 779. W. Carruthers, *Cycloaddition Reactions in Organic Synthesis*; Pergamon: Oxford, 1990. W. Appolzer, In *Comprehensive Organic Synthesis*; L.A. Paquette. Eds.; Pergamin: Oxford, 1991; Vol-5, P 315. S.M. Weinreb, op.cit., P 401; D.L.Boger, op.cit., P451; W.R. Roush, op.cit., p.513.

2. J. Hammer (ed), *2,4-cycloaddition Reactions*, Acadamic Press, New York, 1967.

3. S.B. Needleman and M.C. Chang-Kuo, *Chem. Rev.*, 1962, **62**, 405.

4. G. Dessimoni and G. Tacconi, *Chem. Rev.*, 1975, **75**, 651.

5. S.M. Weinreb and R.R.Staib, *Tetrahedron*, 1982, **38**, 3087.

6. H. Ulrich (Ed), *Cycloaddition Reactions of Heterocumulenes*, Academic press, New York, 1967.

7. (a) R. Gompper, *Angew. Chem. Int. Ed. Engl*, 1969, **8**, 312. (b) R.R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, 1973, **12**, 212.

8. G. Brieger and J.N. Bannet, *Chem. Rev.*, 1980, **80**, 63.

9. (a) J.L. Ripoll and A. Rouessac, *Tetrahedron*, 1978, **34**, 19. (b) A.R. Katritzky and N. Dennis *Chem. Rev.*, 1989, 827.

10. R.B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*, Academic Press, New York, 1970.

11. K.N. Houk, Acc. Chem. res., 1975,8,361.

12. (a) J.G. Martin and R.H. Hill., *Chem. Rev.*, 1961, **61**, 537. (b) R. Huisgen, *Angew. Chem. Int. Ed. Engl.*, 1963, **2**, 565. (c) J. Sauer, *Angew. Chem. Int. Ed. Engl.*, 1966, **5**, 211.

13. D.L. Boger, *Tetrahedron*, 1983, **39**,2869.

14. (a) O. Tsuge, *Heterocycles*, 1979, **12**, 1067. (b) T.L. Gilchrist, *Chem. Soc. Rev.*, 1983, **12**, 53.

15. (a) D.L. Boger, *Tetrahedron*, 1983, **39**, 2869. (b) D.L. Boger; S.M. Weinreb, *Hetero Diels-Alder Methodology in Organic Synthesis*, Academy press; New York, 1987.

16. (a) D.L. Boger; A.M. Kasper, *J. Am. Chem. Soc.*, 1989, **111**, 1517. (b) D.L. Boger; S. Wakahara, *J. Org. Chem.* 1991, **56**, 880. (c) J. Barluenga; F.O.

Gonzalez; V. Gotor, S. Fustero; *J. Chem. Soc. Perkin Trans. I*, 1988, 1739.
(d) D.L. Boger; S.M. Sakya, *J. Org. Chem.*, 1988, **53**, 1415.

17. M.L. Overman; C.B. Petty; T. Ban and G.T. Huang, *J. Am. Chem. Soc.*, 1983, 105, 6835.

18. R. Alcide; Y.M. Cantalejo; J.Plumet; J.R. Lopez and M.A.Sierra, *Tetrahedron Lett.*,1991, 803.

19. S.N. Mazumdar and M.P. Mahajan, *Tetrahedron*, 1991, **47**, 1473.

20. N. Sewald; J. Riede; P. Bissinger and K. Burger, *J. Chem. Soc. Perkin Trans, I*, 1992, , 267.

21. W. Durckheimer; J. Blumbach; R. Lattrell and K.H. Scheunemann, *Angew. Chem. Int. Ed. Engl.*,1985, **24**, 180.

22. A.K. Bose; J.F. Womelsdorf; L.Krishnan; Z.U. Lipkowska; D.C.Shelly and M.S. Manhas, *Tetrahedron*,1991, **47**, 5379.

23. R. Gomper, *Angew.Chem. Int. Ed. Engl.* 1969, **8**, 312.

24. H.W. Moore and G.M. Huges, *Tetrahedron Lett.*, 1982, 4003.

25. A.O. Eitton; J.R. Frost; P.G. Houghton and H.Suschitzky, *J. Chem. Soc. Perkin Trans. I*, 1977, 1450.
26. T. Kato; T. Chiba and S. Tanaka, *Chem. Pharm. Bull.*, Tokyo, 1974, **22**, 744.

27. R. Gomper, *Angew. Chem.*,1969, **81**, 348.

28. S. Mohon; B. Kumar and J.S. Sandhu, *Chem. and Ind.*, 1971,671.

29. M. Sakamoto; K.Miyazawa; K.Kuwabara and Y.Tomimatsu, *Heterocycles*, 1979, **12**, 231.

30. D.L. Boger, *Tetrahedron*, 1983, **39**, 2869.

31. D.L. Boger and S.M. Weinreb, *Hetero-Diels-Alder Methodology in Organic Synthesis*, Ed. Wasserman, H.W., Academic Press Inc. New York 1987, Chapter-6, P-272.

32. L.S. Povarov and B.M. Mikailov, *Chem. Abstr.*, 1963, **59**, 7489; 1964, **60**, 5451; 1964, **61**, 16057; 1965, **62**, 7723, 14624.

33. I. Arrastica; A. Arrieta; J.M. Ugalde and F.P. Cossio, *Tetrahedron Lett.*, 1994, **35**, 7825.

34. R. Pfleger and A. Jager, *Chem .Ber.*,1957, **90**, 2460.

35. R.D. Burpitt; K.C. Brannock; R.G. Nations and J.C. Martin., *J. Org. Chem.*, 1971, **36**, 2222.

36. M. Sakamoto; K. Miyazawa; Y. Ishihara and Y. Tomimats *U. Chem. Pharm. Bull., Tokyo*, 1974, **22**,1419.

37. W.Friedrichsen and H.G. Oeser, *Chem.Ber.*, 1975, 108,31.

38. (a) M. Sakamoto; K. Miyazawa and Y. Tomimatsu, *Chem. Pharm. Bull.*, Tokyo, 1976, **24**, 2532. (b) M. Sakamoto; M. Shibano; K. Miyazawa; M. Suzuki and Y. Tomimatsu, *Chem. Phar. Bull.* Tokyo, 1976, **24**, 2889

39. M. Sakamoto; K. Miyazawa and Y. Tomimatsu, *Chem. Pharm. Bull.* Tokyo, 1977, **25**, 3360.

40. I. Matsuda; S. Yamamoto and Y. Ishii, *J. Chem. Soc., Perkin Trans I*, 1976, 1523,1528.

41. G. Morel; E. Marchand; A. Foucaud, *J. Org. Chem.*, 1989, **54**, 1185.

42. J. Barluenga; M. Thomas, A. Ballesteros; L.A. Lopez, *Tetrahedron Letr*, 1989, **30**, 4573.

43. P. Luthardt; E.U. Wurthwein, *Tetrahedron Lett*, 1988, **29**, 921.

44. S.N. Mazumdar and M.P. Mahajan, *Synthesis*,1990,417.

45. D.G. Farnum;J.R. Johnson; R.F. Hess; T.B. Marshall and B. Wester, *J. Am. Chem.Soc.*, 1965, **87**, 5791.

46. S.N. Mazumdar and M.P. Mahajan, *Tetrahedron*, 1991, **47**, 1473.

47. S.N. Mazumdar; I. Ibnusaud; M.P. Mahajan, *Tetrahedron Lett.*, 1986, **26**, 5875.

48. W.T. Brady; E.F. Hoff, *J. Am. Chem. Soc.*,1968, **90**, 6256.

49. W.T. Brady; E.D. Dorsey; F.H.Parry, *J. Org. Chem.*, 1969, **34**, 2846.

50. C. Metzger; Kurtz, *J. Chem. Ber.* 1971, **104**, 50.

51. F. Duran; L. Ghosez, *Tetrahedron Lett.*, 1970, 245.

52. R. Huisgen; B.A. Davis; M. Morikawa, *Angew . Chem.*, 1968, **80**, 802; *Angew., Chem. Int. Ed. Engl.*, 1968, 826.

53. W.T. Brady; E.D. Dorsey, *J. Org. Chem.*, 1970, **20**, 2732.

54. S.N. Mazumdar; S. Mukherjee; A.K. Sharma; D. Sengupta; M.P. Mahajan, *Tetrahedron*, 1994, **51**, 7459.

55. F. Duran; L.Ghosez., *Tetrahedron Lett.*, 1970, 245.

56. S.N. Mazumdar, Ph.D. Thesis, North Eastern Hill University, 1989.

57. B.Sain; S.P.Singh and J.S.Sandhu, *Tetrahedron Lett.*,1991, **32**, 5151.

58. B. Sain; S.P. Singh and J.S. Sandhu, *Tetrahedron*, 1992, **48**, 4567.

59. E. Rossi; G. Abbiati and E. Pini, *Tetrahedron*, 1997, **53**, 14107.

60. E. Rossi; D. Calabrese; F. Farma, *Tetrahedron*, 1991, **47**, 5819 and ref cited therein.

61. P. Luthardt; E.U. Wurthwein, *Tetrahedron Lett.*, 1988, **29**, 921.

62. I. Arrastia; A. Arrieta; J.M. Ugalde, F.P. Cossio, *Tetrahedron Lett.*, 1994, **42**, 7425.

63. M.S. Manhas; M. Ghosh; A.K. Bose, *J. Org. Chem.*, 1990, **55**, 575.

64. A.K.Bose; R.Spiegelman; M.S. Manhas, *Tetrahedron Lett.*, 1971, 3167.

65. R. Zamboni; G. Just, *Can. J. Chem*, 1979, **57**, 1945.

66.(a) *Chemistry and Biology of β-Lactam Antibiotics*:,R.S. Morin; M. Gorman, Eds, Academic Press: New York,1982; Vol.1-3. (b) *Recent Advances in the Chemistry of β-lactam Antibiotics* A.G. Brown; S.M. Roberts; Eds; The Royal Soceity of Chemistry: London 1984. (c) A.G. Brownh, *Pure Appl. Chemistry*, 1987, **59**, 475. (d) M.I. Page, *Acc. Chem. Res.*, 1984, **17**,180. (e) G.I. George, Ed: *The Organic Chemistry of β-lactams*, Verlag Chemie, New York, 1992.

67. C. Palomo; F.P. Cassio; A. Arrieta; J.M. Odriozola; M. Oiarbide; J.M. Ontoria, *J. Org, Chem.*, 1989, **54**, 5736.

68. A.K. Bose; B.K. Banik, M.S. Manhas; *Tetrahedron Lett*,; 1995, **36**, 213 and references cited therein.

69. M. Browne, D.A. Burnett, M.A. Caplen; L.Y. Chen; J.W. Cladder; M. Domalski, *Tetrahedron Lett.*, 1995, **36**, 2555.

70. L.S. Liebeskind; J.Y. Wang, *Tetrahedron*, 1993, **49**, 5461.

71. A.G. Birchler; F. Liu; L.S. Liebeskind, *J. Org. Chem.*,1994, **59**, 7737.

72. A.K. Sharma; M.P. Mahajan, *Heterocycles*, 1995, **40**, 787.

73.(a) A.K. Sharma, S.N. Mazumdar; M.P. Mahajan; *J. Org. Chem.*, 1996, **61**, 5506. (b) A.K. Sharma, Ph.D.Thesis, 1997.

74. P.D. Dey ; A. K. Sharma, S.N. Rai; M.P. Mahajan, *Tetrahedron*, 1995, **51**, 7459.

75. P.D. Dey; A.K. Sharma; P.V.Bharatam; M.P. Mahajan, *Tetrahedron*, 1997, **53**, 13829.

76. T.Kametani; S. Hibino, *Advances in Heterocyclic Chemistry*, Academic Press, New York, 1987, **42**, 346.

77. L.E. Overman, C.B. Petly; T. Ban; G.T. Huang, *J. Am. Chem. Soc.*, 1983, **40**,261.

78. M.L. Bremer; S.M. Weinreb, *Tetrahedron*, 1983, **40**, 261.

79. D.L. Boger; J.S. Panek, *J. Org. Chem.*, 1983, **48**, 621.

80. J.C. Brindley; J.M. Coldwell, G.D. Meakins; S.J. Plackett; S.J. Price, *J. Chem. Soc., Perkin Trans. I*, 1987, 1153.

81. M.J.S. Dewar; W. Thiel, *J. Am. Chem. Soc.*, 1977, **99**, 4899.

82. (a) J.J.P. Stewart, QCPE Bull.,1983, **3**, 43. (b) D. Gerson, QCPE. Bull., 1989, **9**, 99.

83.(a) E. Valenti; M.A. Pericas; A. Moyana, *J. Org. Chem.*, 1990, **55**, 3582. (b) B.B. Snider, *Chem. Rev.*, 1988, **88**, 793. (c) W.T. Brady, *Tetrahedron*, 1981, **37**, 2949 (d) *Chemistry of Ketenes, Allenes and related compounds*, Ed. S. Patai, Inter science Publications, New york, 1980, 278 (e) D. Bellus; B. Ernst, *Angew. Chem.* Int. Ed. Engl., 1988, **27**, 797.

84.(a) W. Druckheimer, J. Blumback, R. Lattrel, K.H. Scheunemann, *Angew. Chem.* Int. Ed. Engl., 1985, **24**, 180.(b) W.T. Brady, Y.Q. Gu, *J. Org. Chem.*, 1989, **54**, 2834, 2838.(c) B. Alcaide, Y.M. Camtalego, J.Plumet, J.R.Lopez, M.A. Sierra, *Tetrahedron Lett.*, 1991, **32**, 803.

85. For a detailed account, K.G. Holden, *In Chemistry and Biology of β-lactam Antibiotics*, R.B. Morin, M. Gorman, Eds., Academic Press: New York, 1982, Vol.2, p.101.

86. A.K. Bose, G. Spiegelman, M.S. Manhas, *Tetrahedron Lett.*, 1971, 3167.

87. R. Zamboni, G. Just, *Can. J. Chem* ., 1979, **57**, 1945.

88. A.K. Bose; L. Krishnan; D.R.Wagle; M.S.Manhas; *Tetrahedron Lett.*, 1986, **27**, 5955.

89. (a) M. Sunagawa; H. Matsumua; M.Enaomoto; T. Inoue; A. Sasaki, *Chem. Pharm. Bull.*, 1991, **39**, 1931.(b) M.S. Manhas, M. Ghosh, A.K. Bose, *J. Org. Chem.,* 1990, **55**, 575, and references cited therein. (c) M. Colombo, A. Crugnola; G. Franceschi; P.Lombardi; *U.K. Patent Appl.* GB 2144419, Mar.3, 1985 (Derwent WPI, 85-038254).

90. (a) M. Komatsu; H. Ogawa; M. Mohri; Y. Ohshiro, *Tetrahedron Lett.*, 1990, **31**, 3627 (b)Y. Ohshiro, M.Komatsu, M.Uesaka, T.Agawa, *Heterocycles*, 1984, **2**, 549.

91. R.L. Danheiser, D.D. Cha, *Tetrahedron Lett.*, 1990, **31**, 1527.

92. R.L. Danheiser, A.Nishida, S.Savariar, M.P.Trova, *Tetrahedron Lett.*, 1988, **29**, 4917.

93. C.J. Kowalski, G.S. Lal., *J. Am. Chem. Soc.*, 1988, **110** , 3693.

94. R.L. Danheiser, D.S. Casebier, J.L. Loebach, *Tetrahedron Lett.*, 1992, **33**, 1149.

95. R.L. Danheiser; R.G. Brisbois, J.J. Kowalczyk, R.F. Muller., *J. Am. Chem. Soc.* 1990, **112**, 3093.

96. A. Gurski; L.S. Liebeskind, *J. Am. Chem. Soc.*, 1993, **115**, 6101 and the references therein.

97. B.R.Yerxa, H.W. Moore, *Tetrahedron Lett.*, 1992, **33**, 7811.

98. L.S. Leibeskind; J.Y. Wang, *Tetrahedron.*, 1993, **49**, 5461.

99. A.G. Birchler, F.Liu, L.S. Liebeskind, *J. Org. Chem.*, 1994, **59**, 7737.

100. D.M. Birney, *J. Org. Chem.*, 1996, **61**, 243.

101. (a) L.S. Hegedus, G.de Weck, S. D'Andrea, *J. Am. Chem. Soc.*, 1988, **110**, 2122. (b) S.R. Pulley, L.S. Hegedus, *J. Am. Chem. Soc.*, 1993, **115**, 9037.

102. C.A. Challener, W.D. Wulff, B.A. Anderson, S.Chamberlin, K.L. Faron, O.K. Kim, C.K. Murray, Y.C. Xu, D.C. Yang, S.D. Darling, *J. Am. Chem. Soc.*, 1993, **115**, 1359.

103. B.A. Anderson, J. Bao, T.A. Brandvold, C.A. Challener, W.D. Wulff, Y.C. Xu; A.L. Rheingold, *J. Am. Chem. Soc.* , 1993, **115**, 10671

104. M.A. Huffman, L.S. Leibeskind, W.T. Pennington, *Organometallics*, 1992, **11**, 255.

105. N.W. Alcock, C.J. Richards, S.E. Thomas, *Organometallics*, 1991, **10**, 231.

106. S.P. Saberi, S.E. Thomas, *J. Chem. Soc. Perkin Trans.1*, 1992, 259.

107 L. Hill, C.J. Richards, S.E. Thomas, *J.Chem. Soc., Chem. Commun.*, 1990, 1085.

108. (a) K.G. Morris, S.P. Saberi, A.M.Z. Slawin, S.E.Thomas, D.J. Williams, *J. Chem. Soc. Chem. Commun.*, 1992, 1788. (b) K.G. Morris, S.P. Saberi, S.E. Thomas, *J. Chem.Soc.,Chem. Commun.*; 1993, 209. (c) K.G. Morris, S.P. Saberi, M.M. Salter, S.E. Thomas, M.F. Ward, A.M.Z. Slawin, D.J. Williams, *Tetrahedron*, 1993, **49**, 5617.

109.(a) S.P. Saberi, A.M.Z. Slawin, S.E. Thomas, D.J. Williams, M.F. Ward, P.A. Worthington, *J. Chem. Soc., Chem. Commun.*, 1994, 2169.(b) S.E. Gibson (nee Thomas), S.P. Saberi, A.M.Z. Slawin, P.D. Stanley, M.F. Ward, D.J. Williams, P. Worthington, *J. Chem. Soc., Perkin Trans 1*, 1995, 2147.

110. B.C. Froehler; S. Wadwani, T.J. Terhorst, S.R. Gerrard, *Tetrahedron Lett.*, 1992, **33**,5307.

111. M.J.S. Dewar, E.G. Zoebisch, E.F.Healy, J.P.P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.

112.P. Luthardt, E.U. Wurthwein, *Tetrahedron Lett.*, 1988, **29**, 921.

113. J.S. Binkley, J.A. Pople, W.J. Hehre, *J. Am. Chem. Soc.*, 1980, **102**,939.

114. S. Czernecki, A. Hoang, J.M. Valery, *Tetrahedron Lett*, 1994, **35**, 3539.

115. (a) F. Fringuelli, A. Talicchi, Dienes in Diels-Alder Reactions; Wiley: New York, 1990. (b) W. Carruthers, *Cycloaddition Reactions in Organic synthesis*, pergamon press: oxford, 1990. (c) M.Yoshimatsu, J. Hasegawa, *J. Chem. Soc., Perkin Trans 1*, 1997, 211. (d) J. Maddaluno, O.Gaonac'h, A. Marcual, L. Toupet, C. Giessner-Prettre, *J. Org. Chem.*, 1996, **61**, 5290.

116. (a) M. Taing, H.W. Moore, *J. Org. Chem.*, 1996, **61**, 329. (b) L. Sun, L.S. Liebeskind, *J. Org. Chem.*, 1995, **60**, 8191. (c) A.G. Birchler, H. Liu, L.S. Liebeskind, *J. Org. Chem.*, 1994, **59**, 7737.(d) A. Gurski, L.S. Liebeskind, *J. Am. Chem. Soc.*, 1993, **115**, 6101 and references there in.

117. M. Consuelo; Miguel A. Miranda; J.C. Scaiano and Rosa Tormos, *Chem. Commun.*, 1997, 1487.

CHAPTER-II

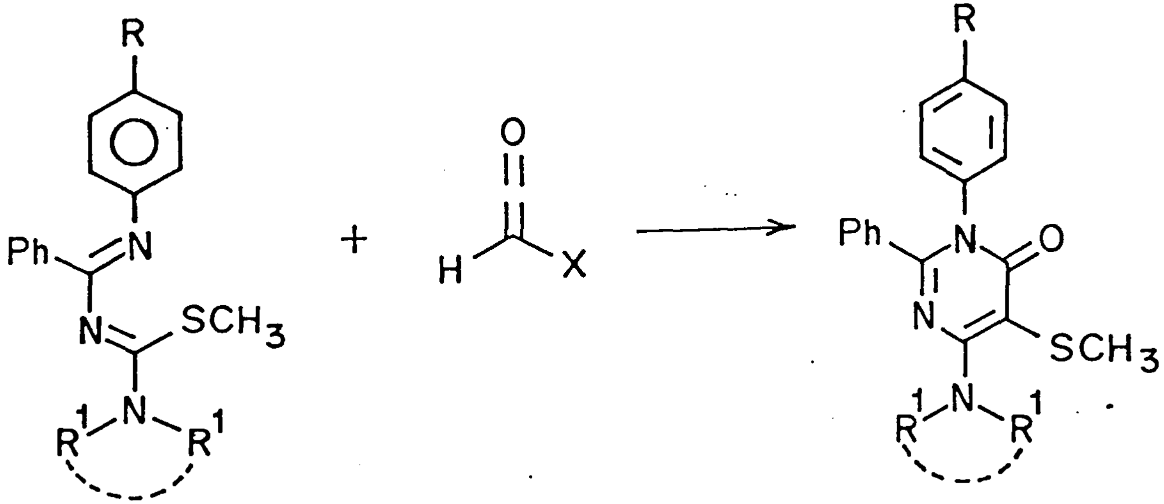
NOVEL SYNTHESIS OF FUSED PYRIMIDINONES VIA 1,3-DIAZA-1,3-BUTADIENES

The compounds comprising a pyrimidinone ring system are of considerable importance because of their incorporation in many natural products[1], antibiotics[2] and drugs[3]. The heterocyclic fused pyrimidine derivatives have also found wide medicinal applications as potent blood sugar lowering activity[4] and antitumor activity[5].

A large variety of substituted pyrimidinones have been synthesised in our laboratory following extensive studies on [4+2] cycloaddition reactions of 1,3-diaza-1,3-butadienes[6,7] with a variety of ketenes[8-10]. An interesting alkylthio shift was found to accompany [4+2] cycloaddition reactions of 1,3`-diazabuta-1,3-dienes **25** with haloketenes leading to pyrimidinones **42**[9]. (Scheme-1).

Also, 1,4- thiazine derivatives have proved to be of great biological importance[11] and have been found to exhibit antimicrobial activity[12,13]. In view of the above, it was thought worthwhile to devise suitable methods for the synthesis of pyrimidinone fused 1,4-thiazine and 1,4 -thiazepine derivatives.

As an entry into this area, we have synthesised various 4-[2-(3-aryl-thiazolidino)-1,3-diaza-1,3-butadienes **3** and 4-[2-(3-aryltetrahydrothiazine)]-1,3-diaza-1,3 butadienes **4** and examined their reactions with chloroketene. It was also conceived that [4+2] cycloaddition reactions of azadienes **63** and **93** (as given in Chapter I) with carbomethoxy methyl ketenes could result in pyrimidinones having an ester function at the C-5 position and such pyrimidinones could then be transformed into fused pyrimidinones.

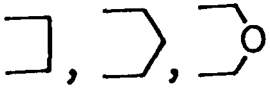


25

X = Cl, Br, I

42

R = H, CH_3, OCH_3, Cl

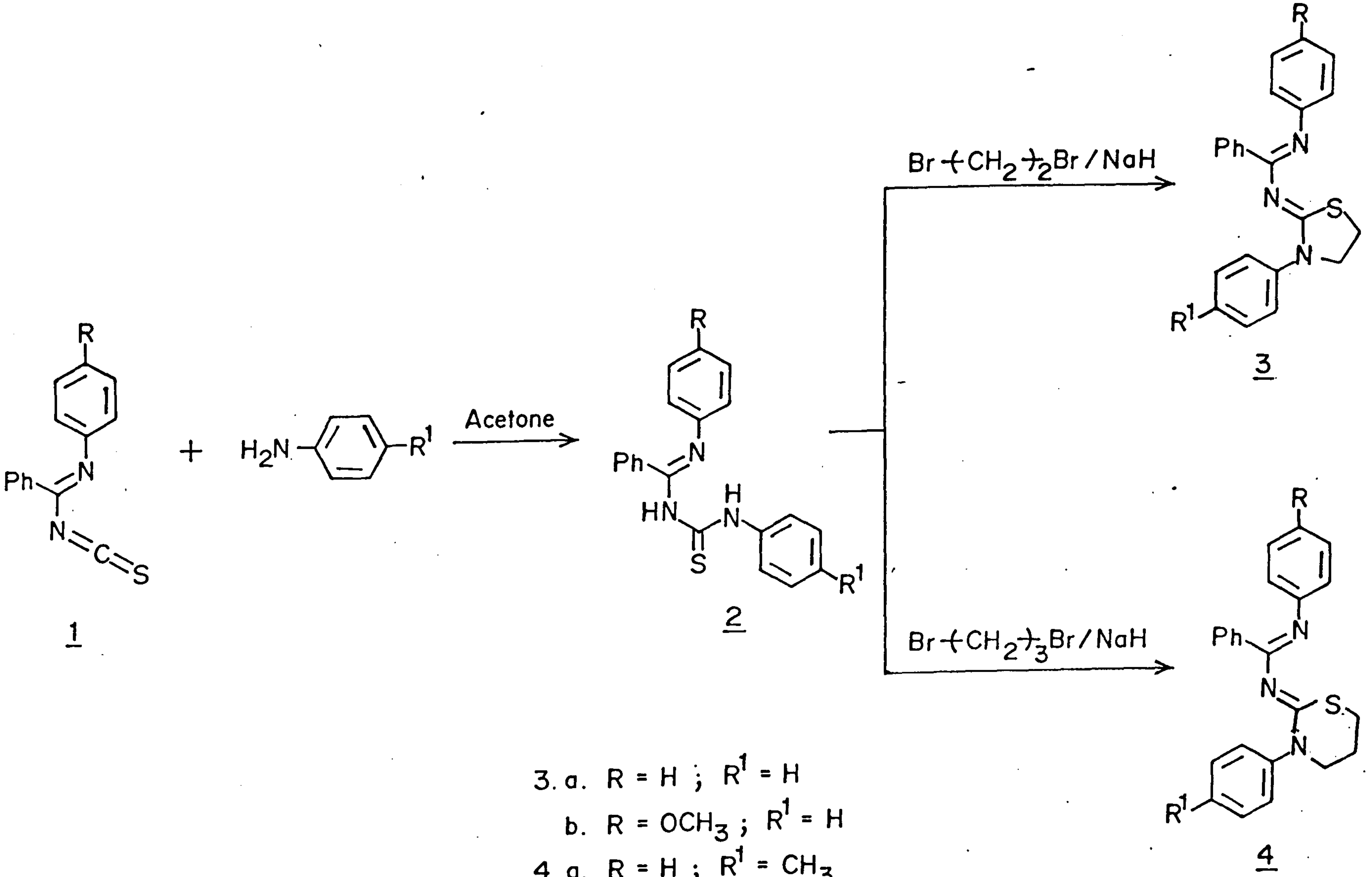
$R^1, R^1, = CH_3, CH_3;$ 

Scheme-1

Results and Discussion

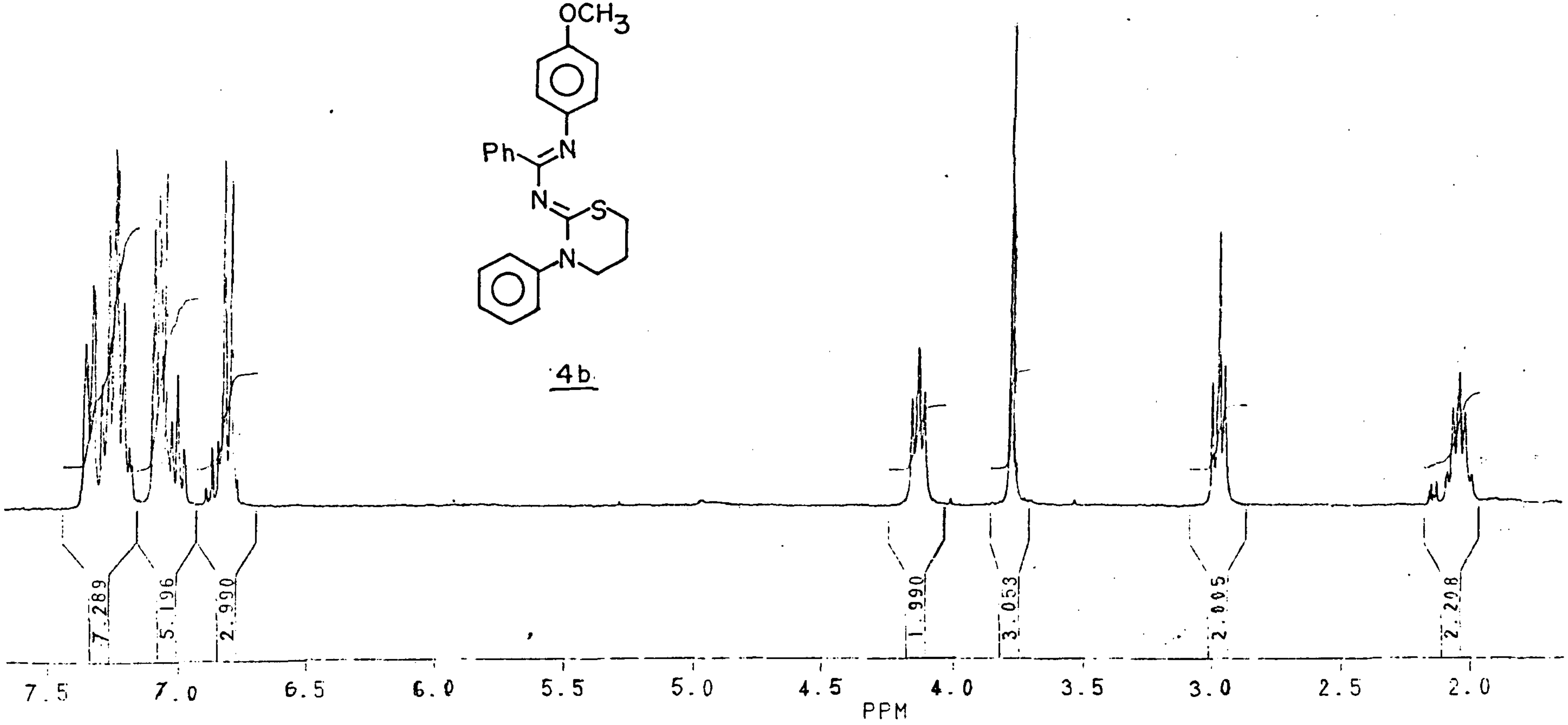
A conceptually attractive strategy to the synthesis of these fused pyrimidinones lies in the initial synthesis of various heterocyclic fused 1,3-diaza-1,3- butadienes. The desired 1,3- diaza- 1,3-butadienes were prepared by the reactions of primary aromatic amines with benzimidoyl isothiocyanates **1**[14] and the treatment of resultant thioureas **2** with 1,2-dibromoethane and 1,3-dibromopropane in the presence of sodium hydride. The 4- [2 (3- arylthiazolidino)]-1,3-diaza-1,3-butadienes and 4-[2-(3-aryltetrahydrothiazino)]-1,3-diaza-1,3-butadienes so obtained as yellow viscous oil (Scheme-2), were assigned structures **3** and **4**, respectively, on the basis of analytical and spectral data. Thus **3a**, for example, in its **IR** (CCl_4) spectrum exhibited carbon- nitrogen double bond stretching at 1555 cm^{-1}. Its ^{1}**H NMR** spectrum exhibited two triplets at δ 3.24 and 3.90, respectively due to $-SCH_2-$ and $-NCH_2-$ protons. The aromatic protons appeared as multiplets at δ 6.70- 7.78 (15H). The compounds **4a**, for example, in addition to $-NCH_2-$, $-SCH_2-$ and aromatic protons exhibited the presence of a quintet due to methylene protons at δ 2.01 . Their ^{13}**C NMR** spectra were also in perfect agreement with the assigned structures **3** and **4**. Attempts were also made to synthesize the heterocyclic fused 1,3- diazabutadienes, of type **5**, by reactions of thioureas **2** with chloroacetylchloride and chloroethylacetate (Scheme-3). Unfortunately, these attempts led to intractable mixtures from which pure **5** could not be isolated.

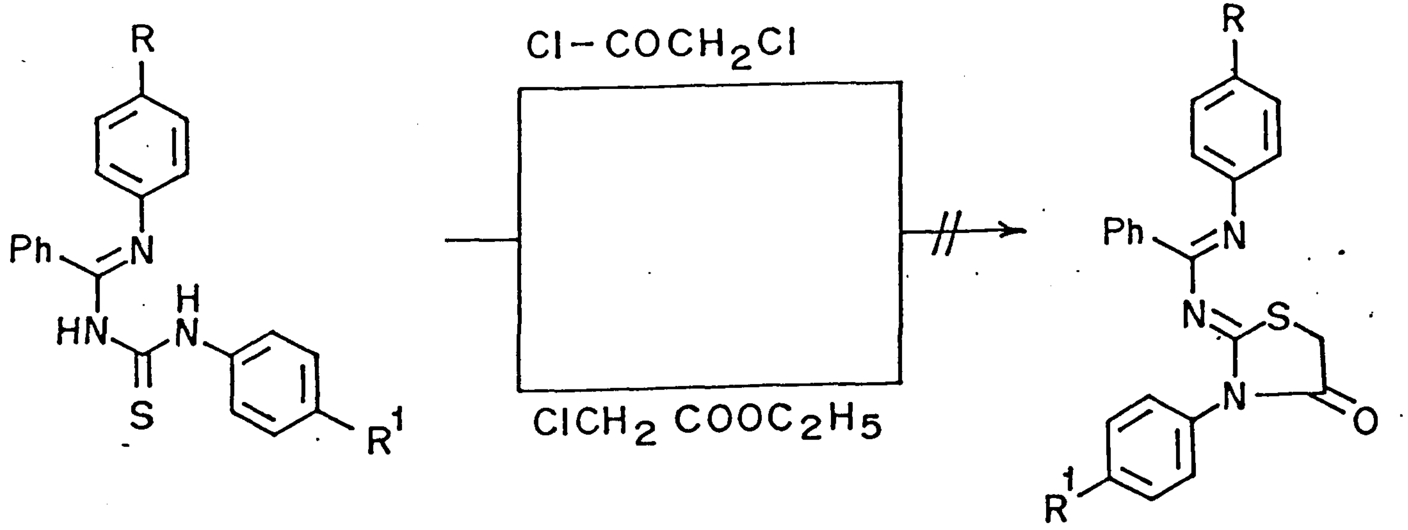
The treatment of 4- [2-(3- arylthiazolidino)] -1,3-diaza-1,3-butadienes **3** with chloroketene, generated in situ from chloroacetylchloride and triethylamine in methylene chloride, resulted in the formation of expected pyrimidinone fused 1,4-thiazines **8**. (Scheme-4).



3. a. $R = H$; $R^1 = H$
b. $R = OCH_3$; $R^1 = H$
4. a. $R = H$; $R^1 = CH_3$
b. $R = OCH_3$; $R^1 = H$

Scheme-2

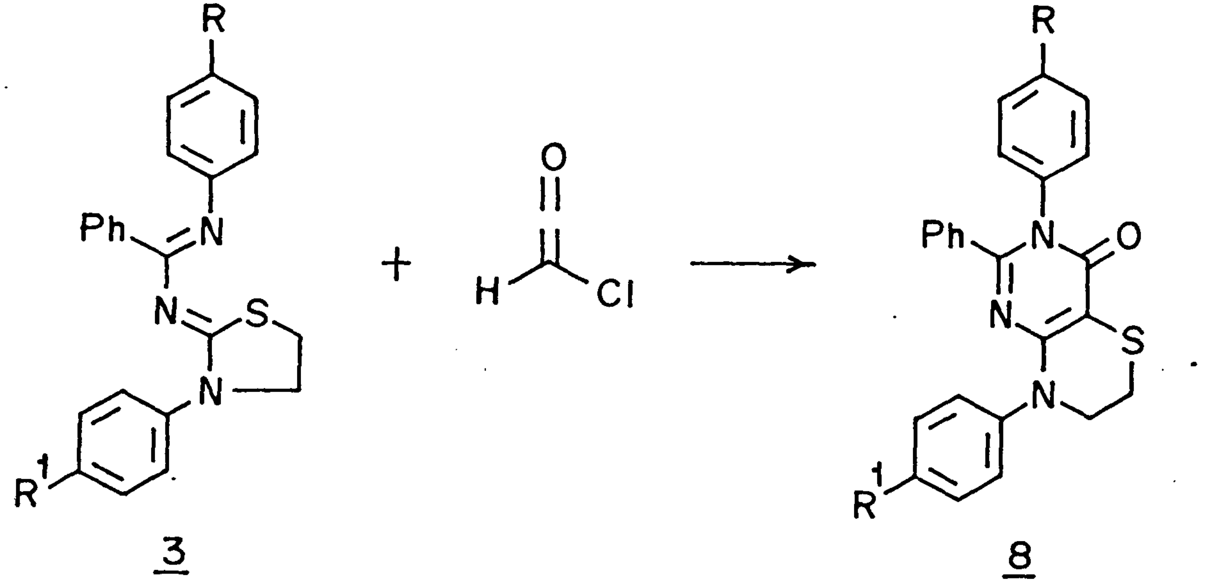

OCH3
Ph
N
N
S
N
4b
7.289
5.196
2.990
1.990
3.053
2.005
2.208
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
PPM



2

5

Scheme – 3



8 a. $R = H$; $R^1 = H$

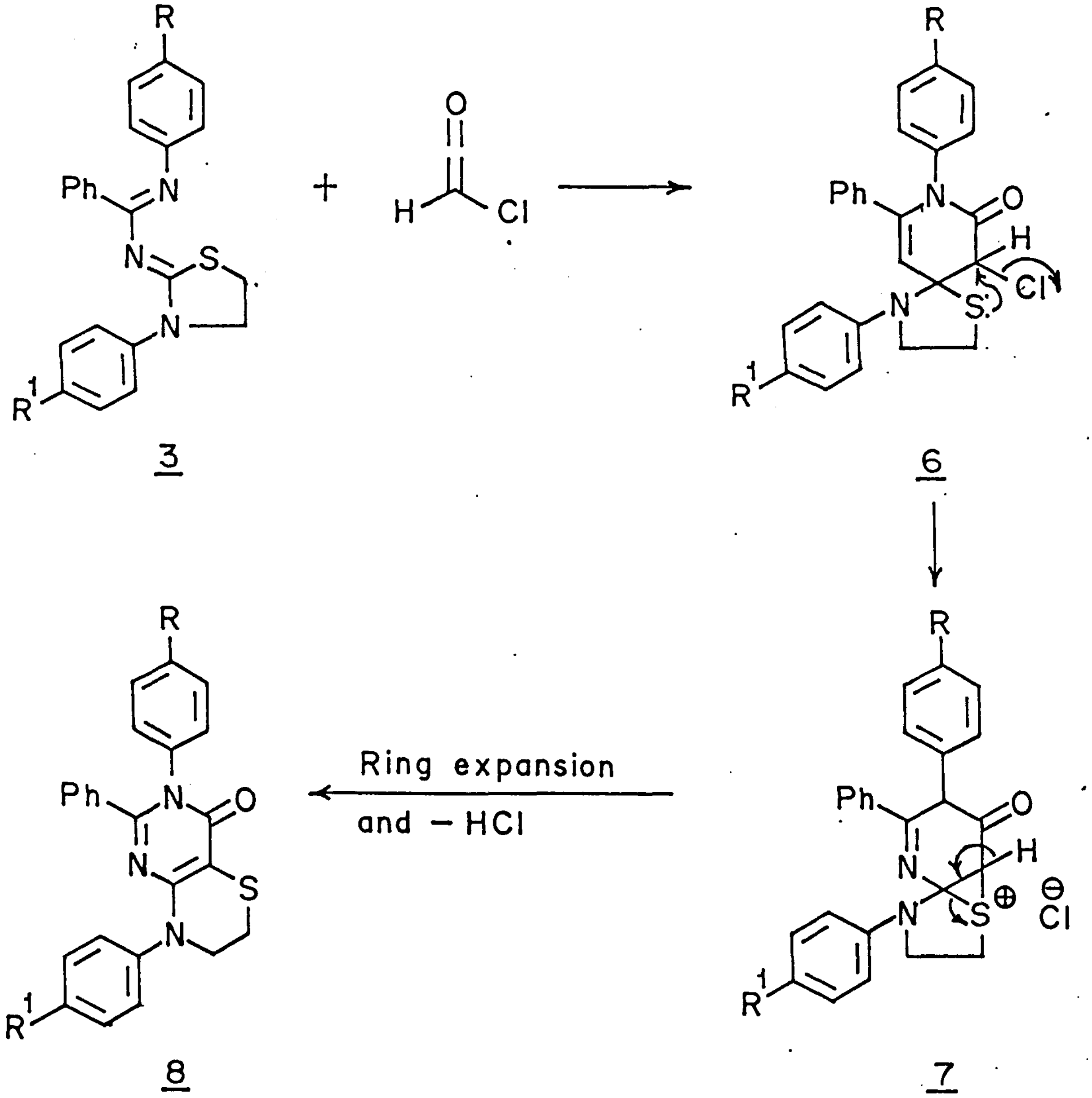
b. $R = OCH_3$; $R^1 = H$

Scheme-4

The formation of pyrimidinones **8** could be explained by the mechanistic pathways as reported in the reactions of 1,3- diaza-1,3-butadienes **25** with haloketenes (as given in Chapter I). It appears that the initially formed [4+2] cycloadduct **6**, as an intermediate transforms into an episulfonium intermediate 7. The intermediate 7, on intramolecular rearrangement, followed by elimination of HCl, leads to the desired ring expansion products **8** (Scheme-5). The products were characterized as 3-aryl-2,8-diphenyl-3,6,7,8-tetrahydropyrimido [5,4-b]1,4-thaizine-4-ones **8**, on the basis of analytical and spectral data. The product **8a**, for example , analysed for $C_{24}H_{19}N_3OS$, showed a molecular ion peak at m/z 397(M^+). Its **IR** (KBr) spectrum exhibited a strong peak at 1671 cm^{-1} assigned to α,β-unsaturated carbonyl group. The ^{1}**H NMR** spectrum in addition to aromatic protons, indicated two triplets at ca. δ 3.25 and 3.94 due to -SCH_2- and -NCH_2- protons, respectively. The aromatic protons appeared as multiplets at δ 6.80-7.99 (15H).

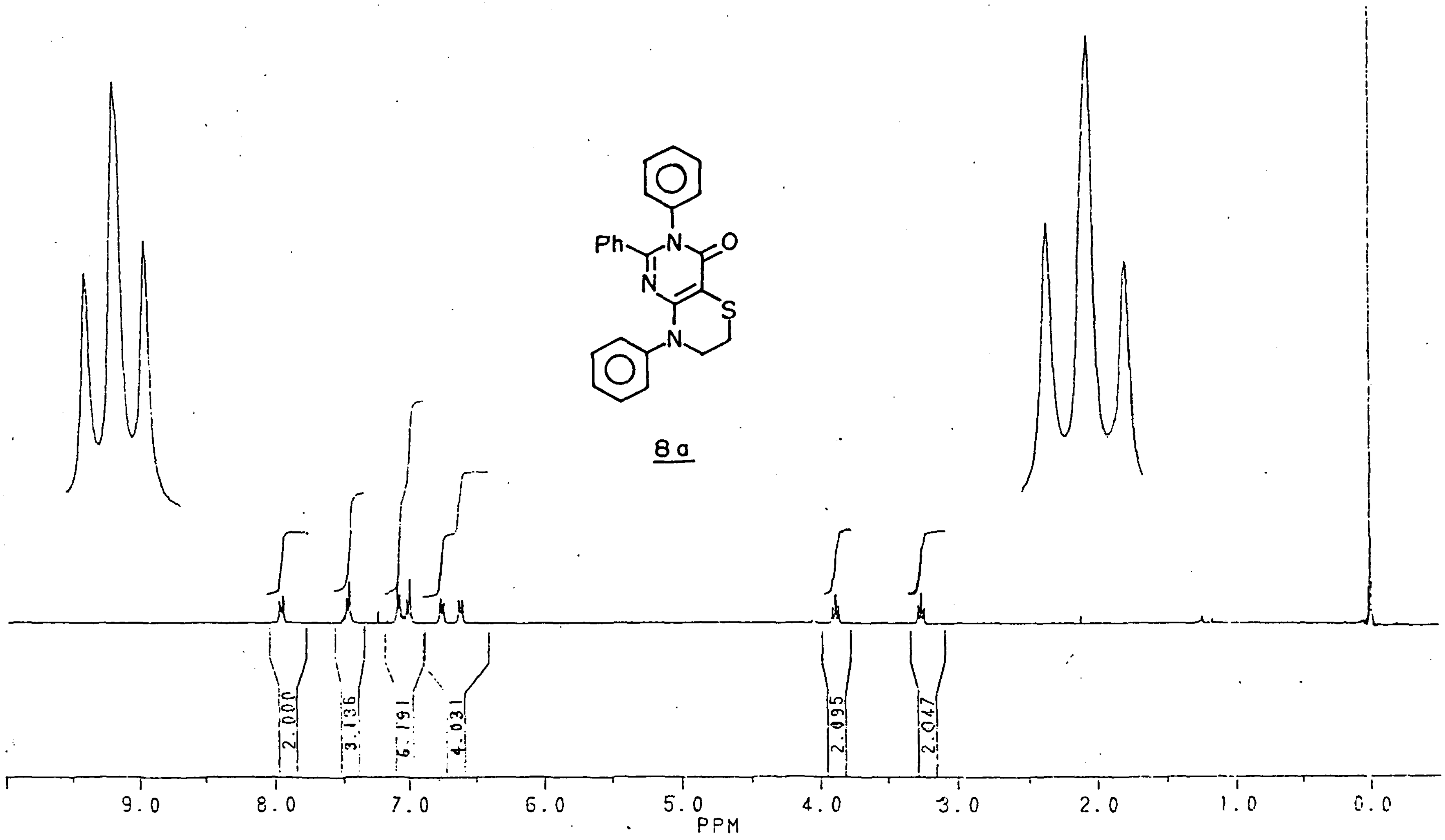
In continuation of the studies in this area, we have carried out the reactions of 4-[2-(3-aryltetrahydrothiazino)]-1,3-diaza-1,3-butadienes **4** with chloroketene and this reaction has also been shown to follow a pathway similar to the one observed in the reactions of **3** with chloroketene. Thus, the formation of the episulfonium intermediate **10**, from the initially formed [4+2] cycloadduct **9** and subsequent ring expansion accompanied by elimination of hydrogen chloride, probably best explains the formation of pyrimidinone fused 1,4-thiazepines **11** (Scheme-6).

The structure **11** for these pyrimidinones was deduced on the basis of analytical and spectral data. Compound **11a**, for example , analysed for $C_{26}H_{23}N_3OS$, showed a molecular ion peak at m/z 425 (M^+) . Its **IR** (KBr) spectrum exhibited a strong band at 1670 cm^{-1}, characteristic of α,β-unsaturated carbonyl group. The ^{1}**H NMR** spectrum of **11a** showed, in addition to other protons, the presence of signals due to -CH_2- (q, δ 2.01), -SCH_2- (t, δ 3.20) and -NCH_2- (t, δ 4.15) functions. Its ^{13}C NMR spectrum was also in agreement with the assigned structures.



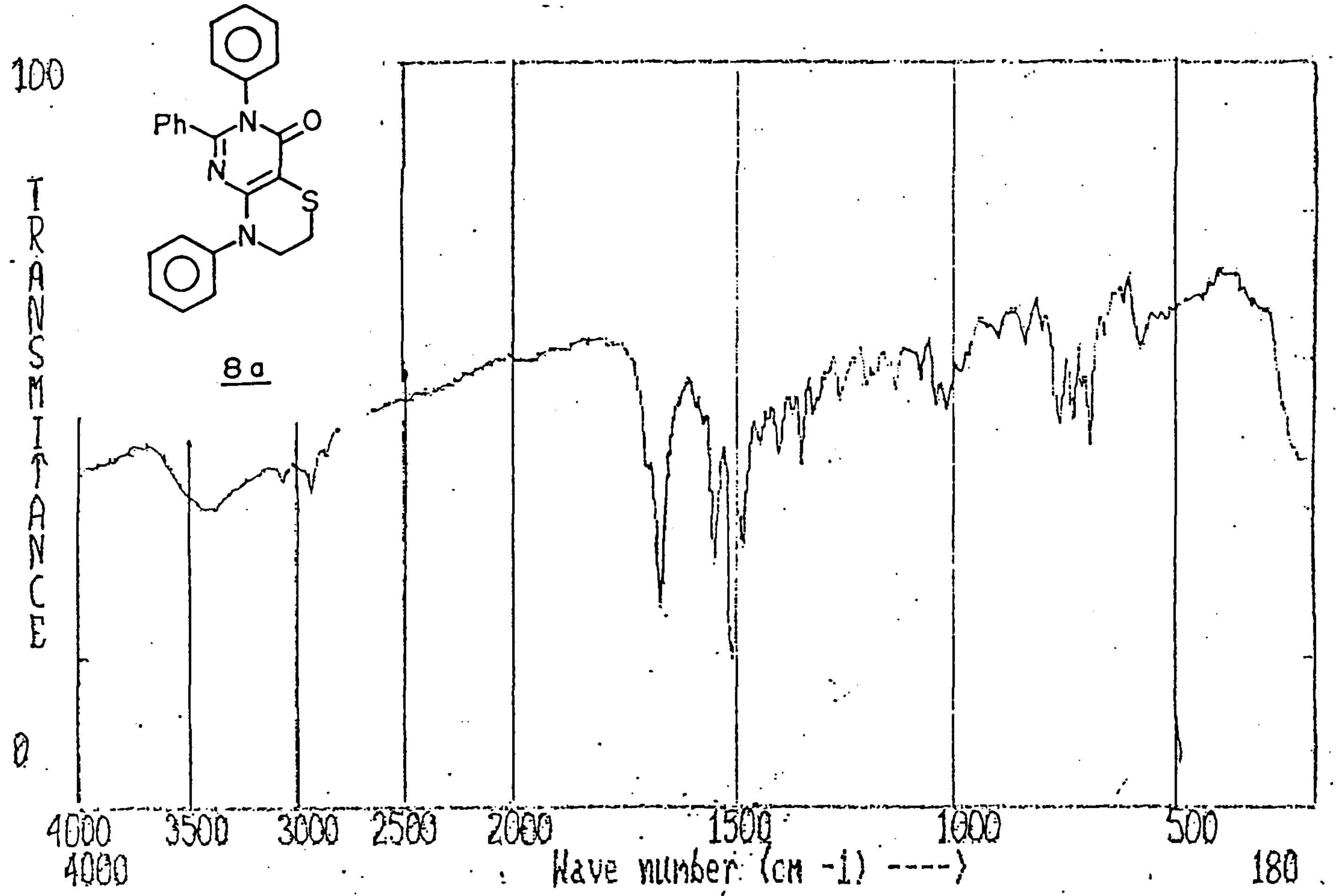
8 a. $R = H$; $R^1 = H$
b. $R = OCH_3$; $R^1 = H$

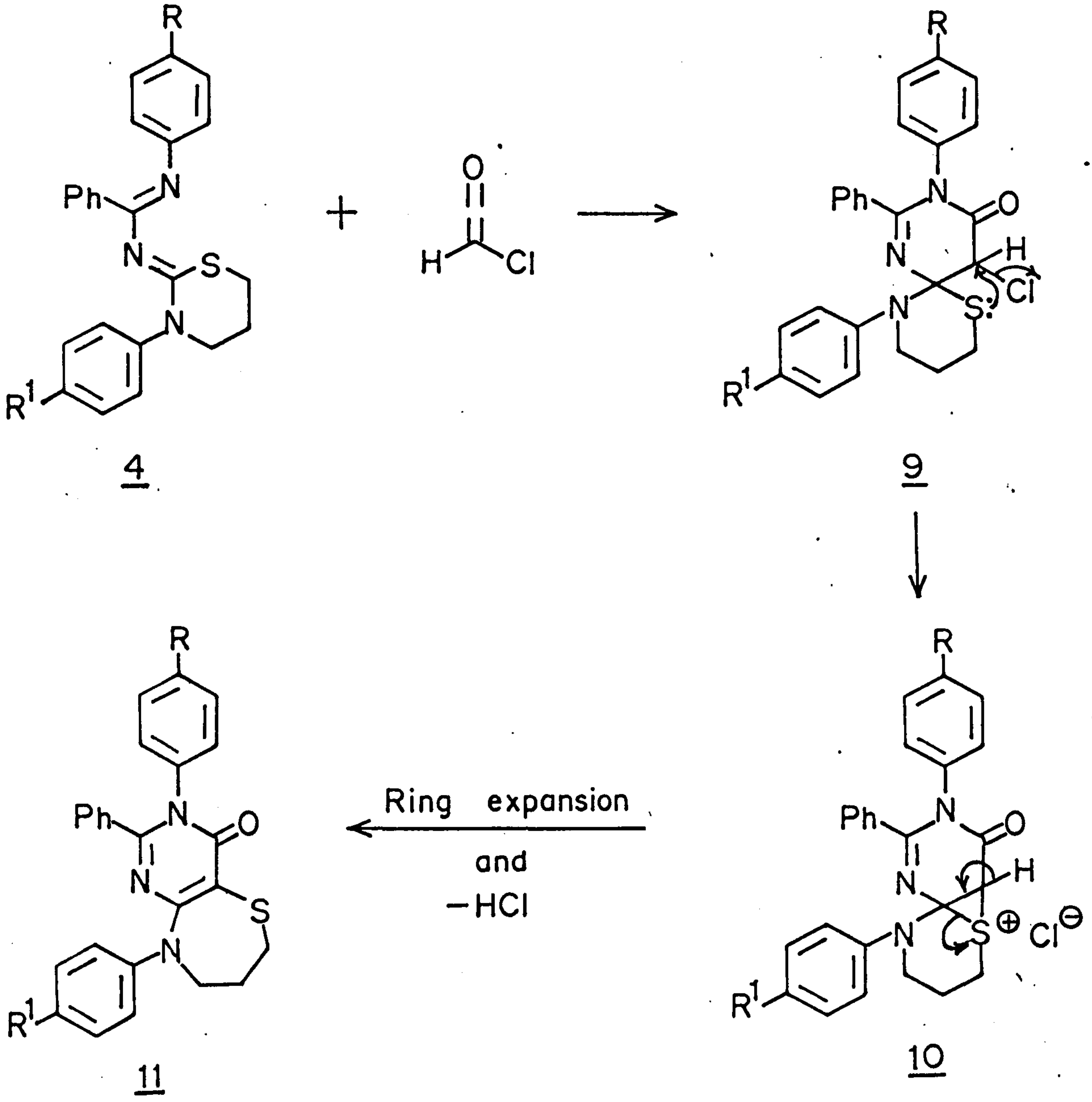
Scheme-5



8a

Ph
N
N
O
S
N
2.000
3.136
6.191
4.031
2.095
2.047
9.0
8.0
7.0
6.0
5.0
PPM
4.0
3.0
2.0
1.0
0.0

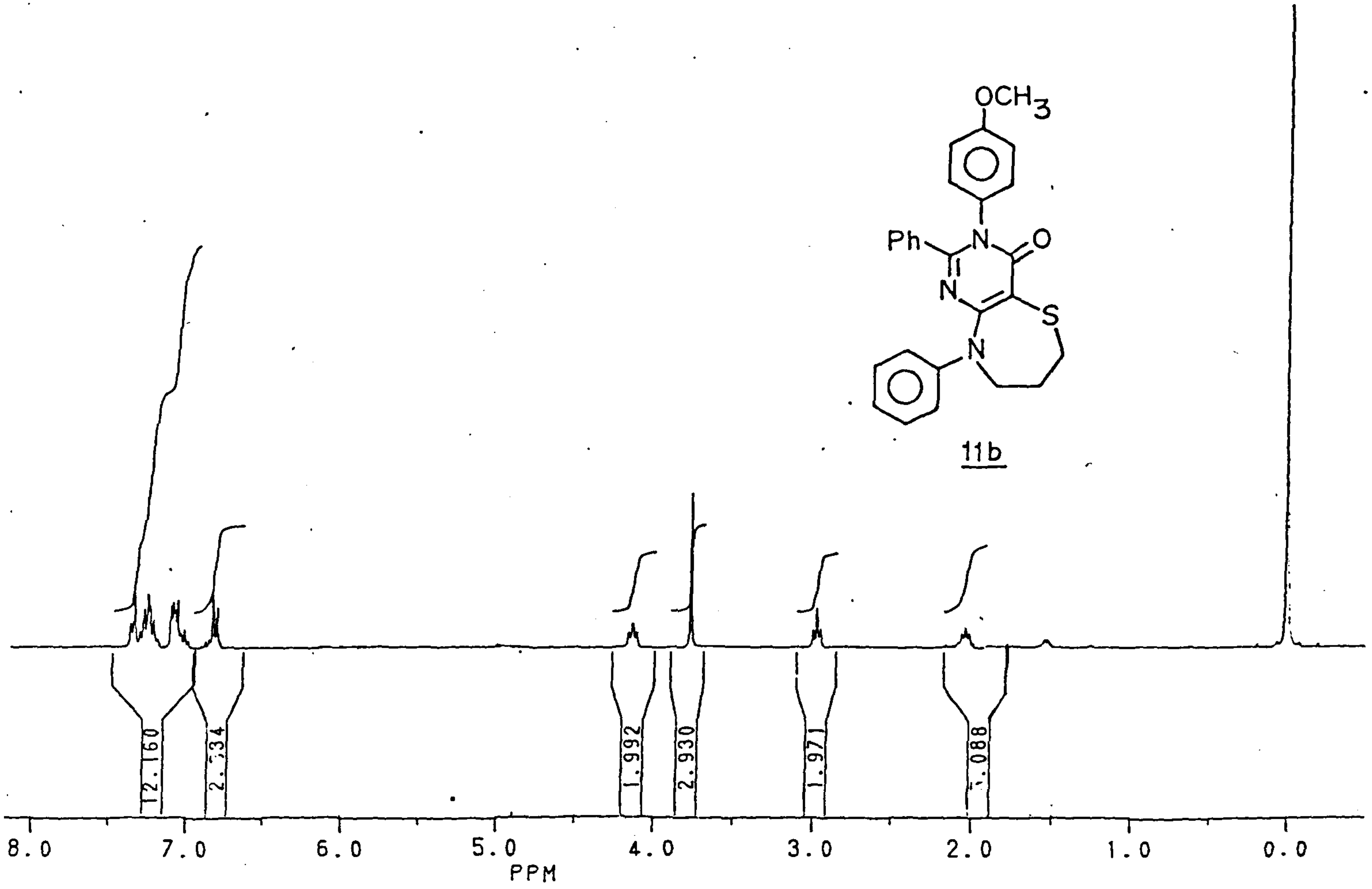

Ph
N
N
O
S
N
8 a
100
TRANSMITANCE
0
4000
3500
3000
2500
2000
1500
1000
500
4000
Wave number (cm -1) ----)
180

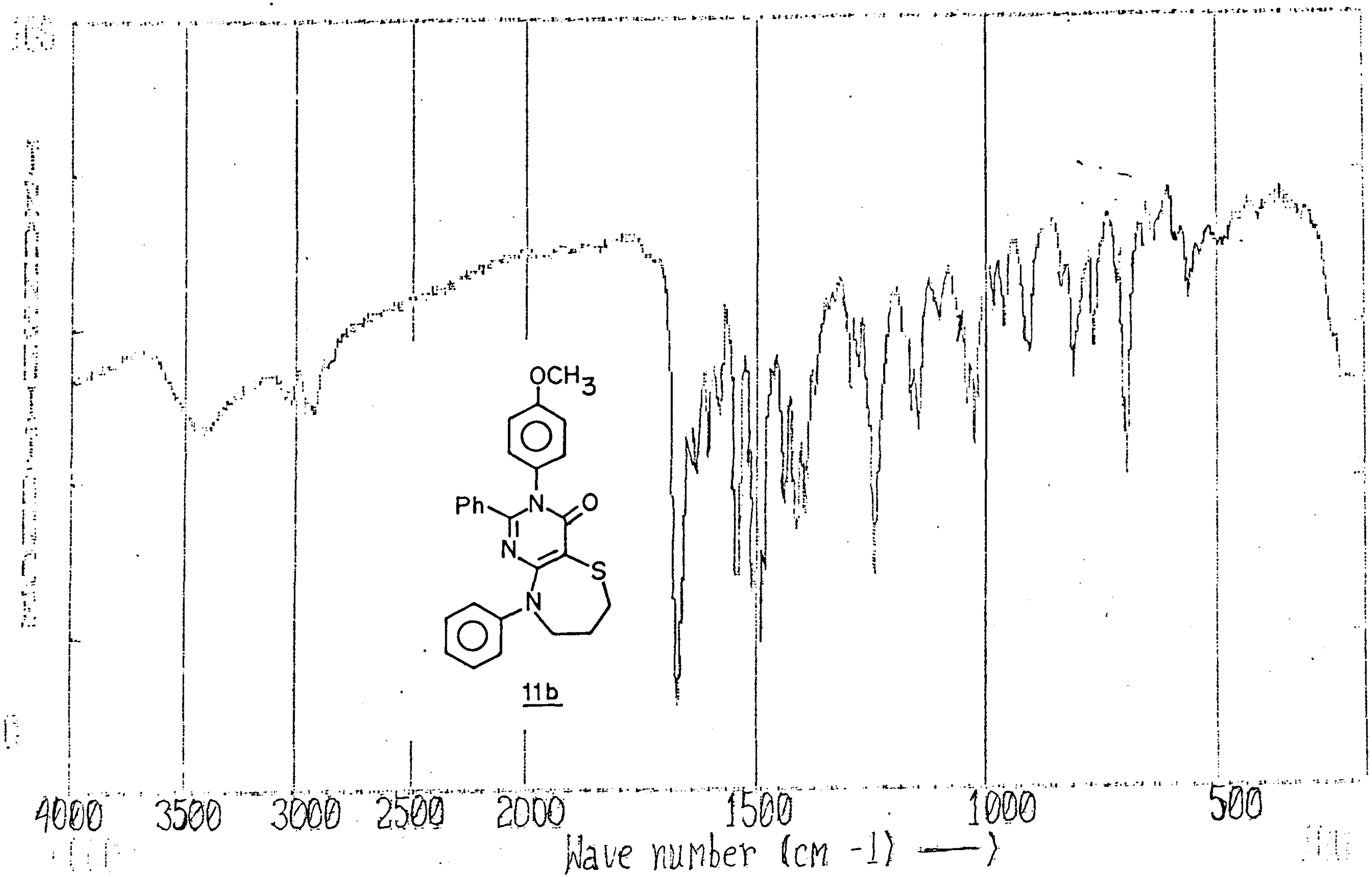


11. a. R = H; $R^1 = CH_3$

b. $R = OCH_3$; $R^1 = H$

Scheme −6

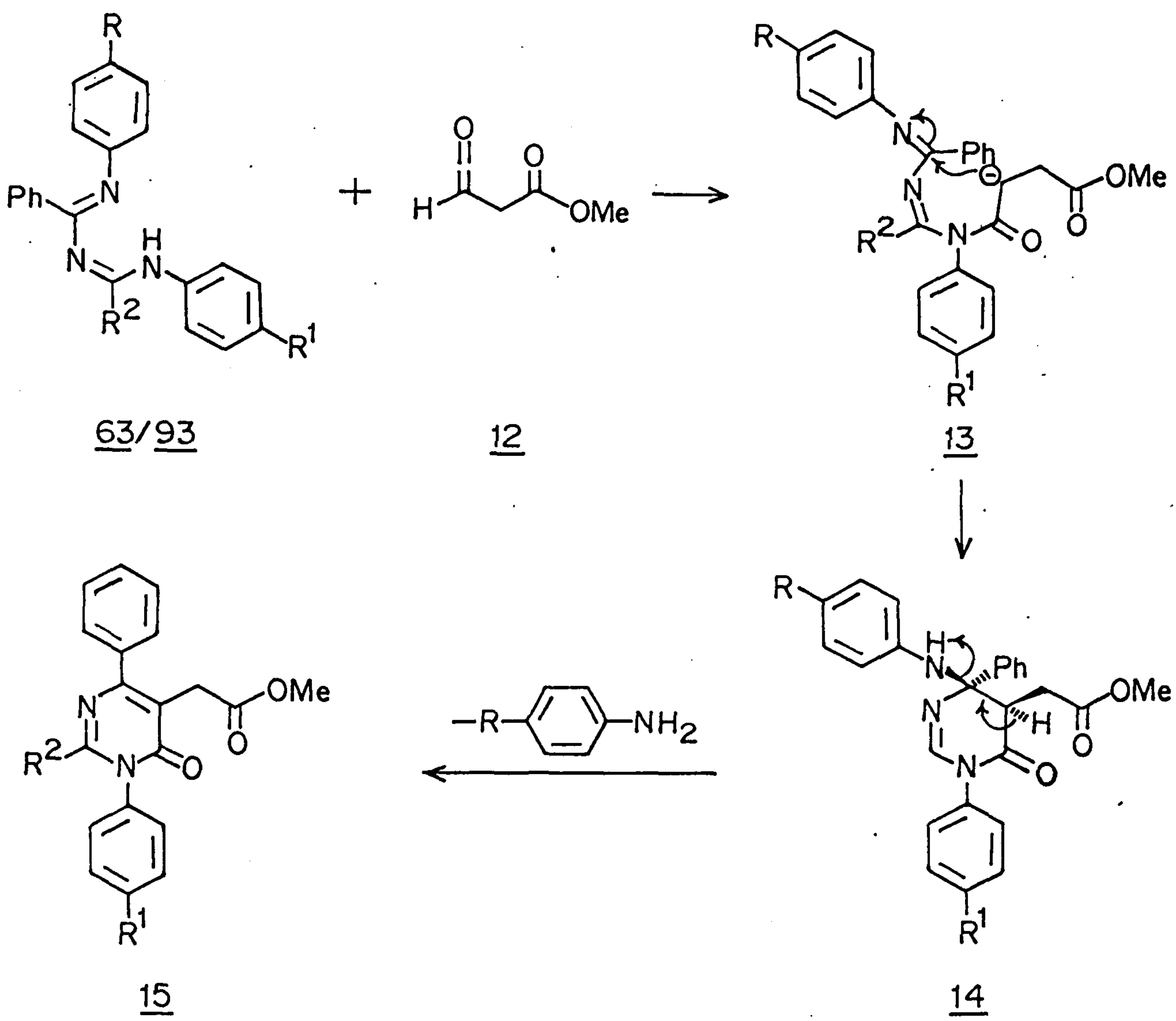

OCH3
Ph
N
N
O
S
N
11b
12.160
2.534
1.992
2.930
1.971
.088
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


OCH3
Ph
N
O
S
4000
3500
3000
2500
2000
1500
1000
500
Wave number (cm -1) ⟶

11b

In continuation of our efforts directed towards the synthesis of fused pyrimidinones, we have examined the reactions of N-arylamino-1,3-diazabutadienes **63** and **93** with carbomethoxymethyl ketene **12**. Thus, N-arylamino-1,3-diaza 1,3-butadienes **63/ 93**, when stirred with the ketene **12**, generated in situ from methoxysuccinyl chloride, in the presence of triethylamine in dry dichloromethane at room temperature, afforded good yields of methyl-4-oxo-pyrimidine-5-acetate **15** (Scheme-7). The products were characterised as methyl-3-aryl-2-methylthio/secondary amine-3-phenyl-4-oxo-3H- pyrimidine-5-acetate, on the basis of analytical data and spectral evidence . In the **IR** spectrum of **15a**, for example, the presence of strong absorption peaks at 1664 and 1734 cm^{-1} indicated the presence of an ester carbonyl group and an α,β-unsaturated carbonyl group respectively. Its **^{1}H NMR** spectrum exhibited the presence of thiomethyl (s, δ 2.46), methylene (s, δ 3.57), methoxy (s, δ 3.68) protons and the loss of protons corresponding to N- arylamino functions next to the carbon bearing the phenyl group. The mechanistic pathway leading to the formation of pyrimidinone **15** probably involves the initial nucleophilic attack by the amino nitrogen of 1-aryl-4(N-arylamino)-4-methylthio/sec.amino-2-phenyl-1,3-diaza-1,3-butadienes **63/93** at the highly electrophilic ketene carbonyl carbon, leading to an intermediate **13**, which upon ring closure and subsequent elimination of aromatic amines from **14**, results in the desired methyl-4-oxo-pyrimidine-5-acetate **15** (Scheme-7). To our knowledge this is the first report concerning the generation and participation of methoxy carbonyl methyl ketene in cycloaddition reactions.

The pyrimidininones **15**, having a methyl acetate function at C-5 appeared to be good candidates for the synthesis of various 5,6- fused pyrimidinones, and this possibility was exploited for the synthesis of desired fused pyrimidinones. Thus, the treatment of pyrimidinones **15** with polyphosphoric acid in refluxing toluene resulted in the formation of 3 aryl-dihydro-2-methylthio/piperideno - naphthaleno [3, 4-d] pyrimidin-4,6- diones **16**, and were isolated as colourless crystals in good yields (Scheme-8).



15. a. R^1 = H ; R^2 = SCH_3

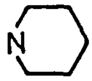
b. R^1 = p-CH_3 ; R^2 = SCH_3

c. R^1 = p-OCH_3 ; R^2 = SCH_3

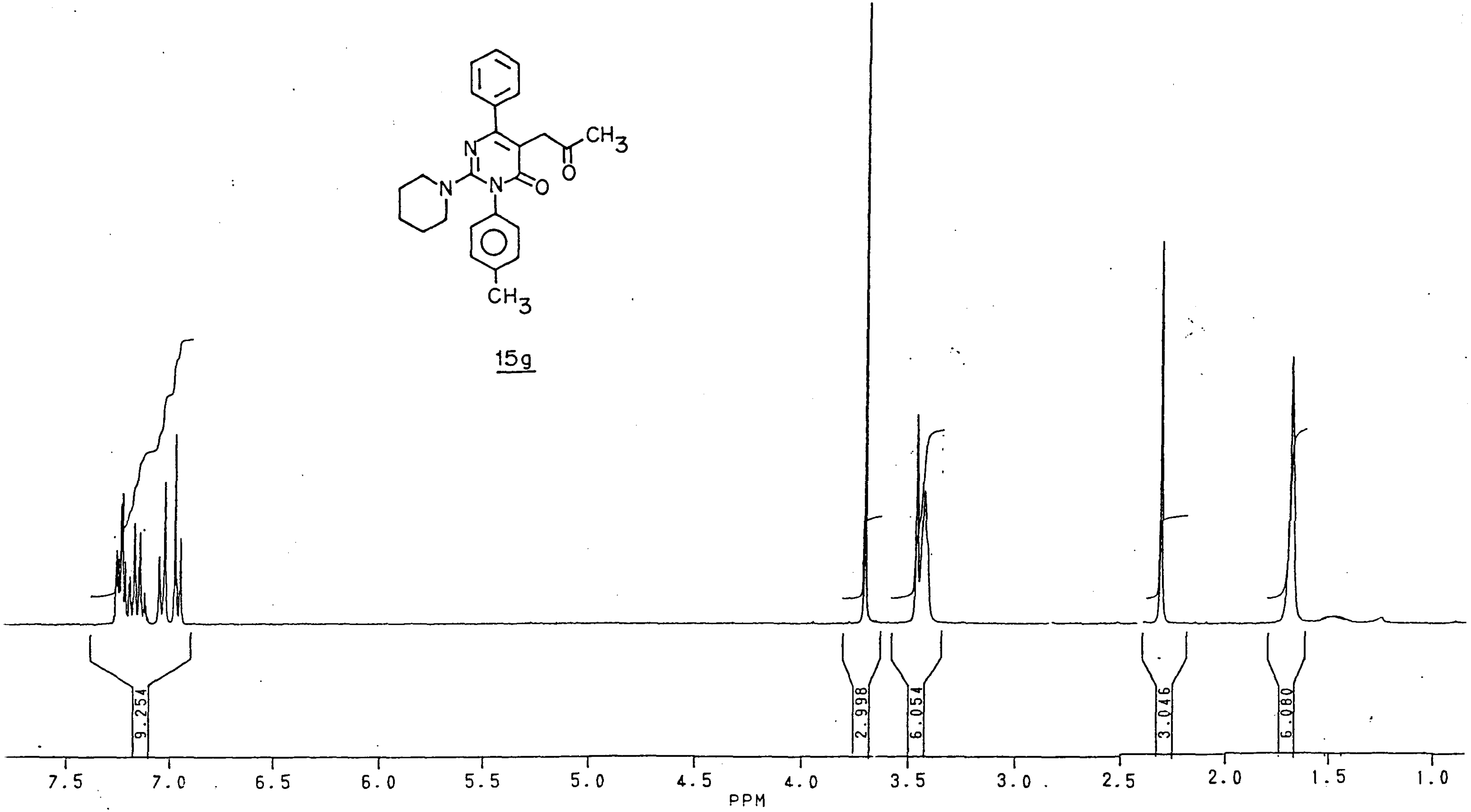
d. R^1 = o-CH_3 ; R^2 = SCH_3

e. R^1 = p-Cl ; R^2 = SCH_3

f. R^1 = H ; R^2 = 

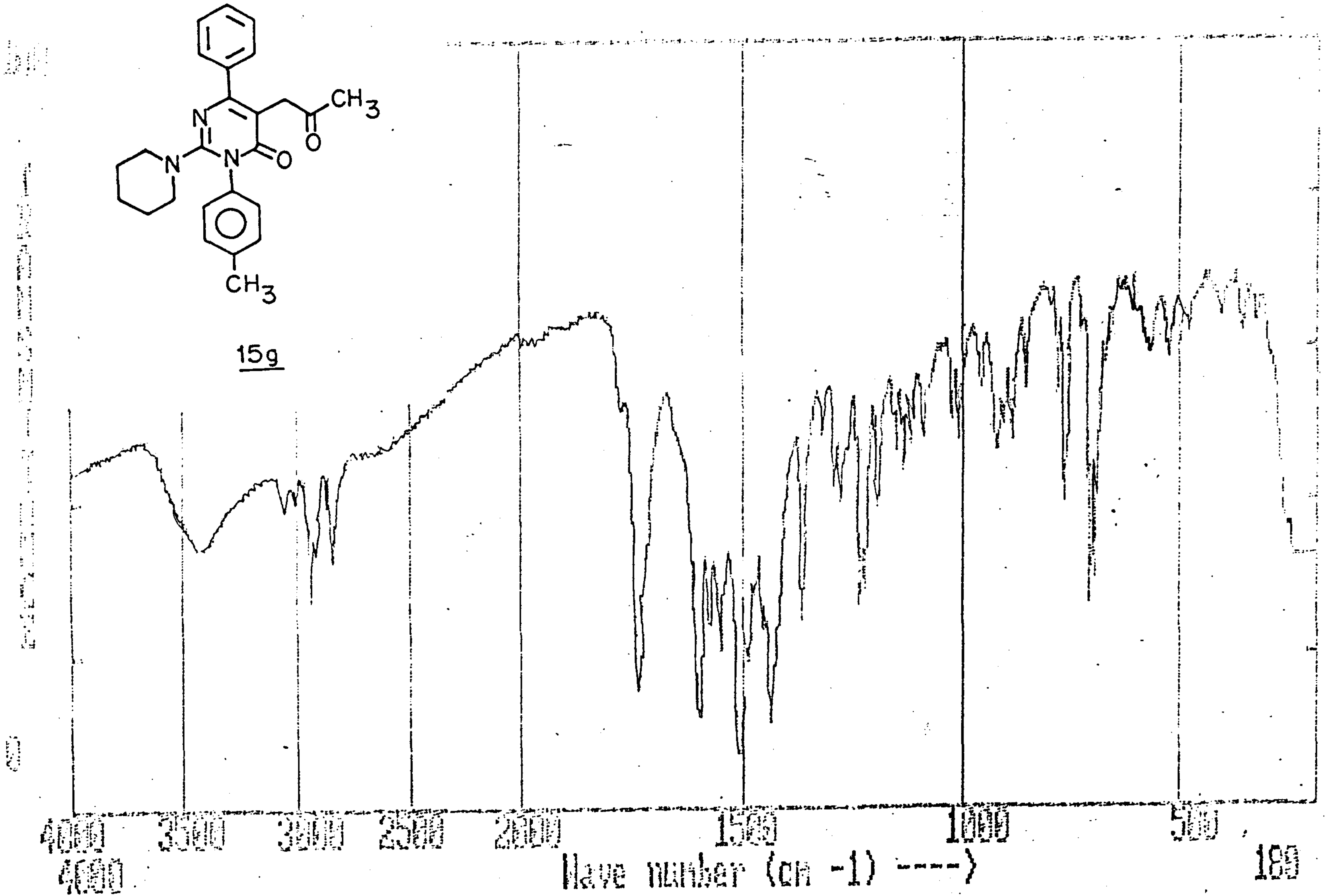
g. R^1 = p-CH_3 ; R^2 = 

Scheme – 7

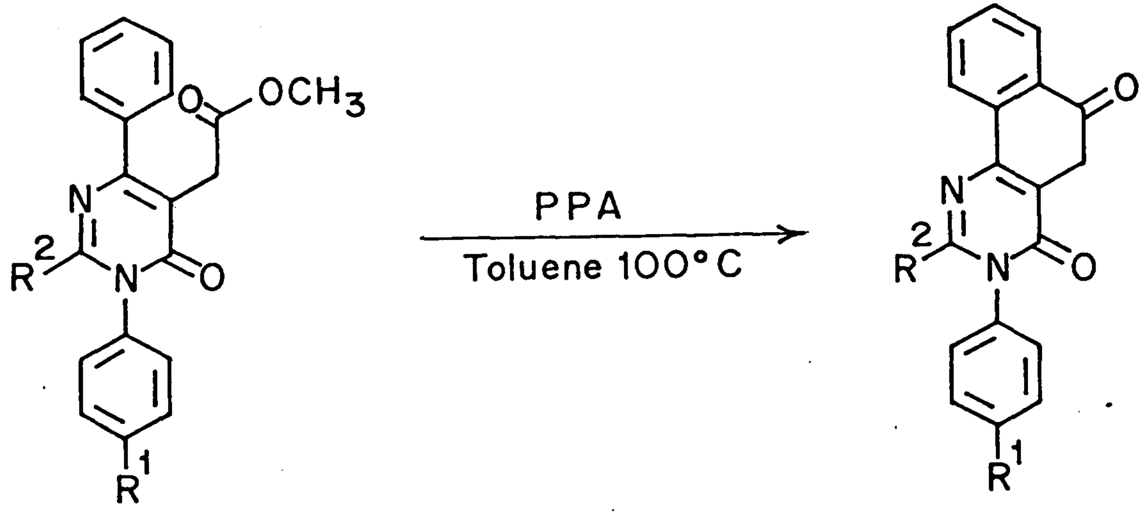


15g

CH3
N
N
O
O
CH3
CH3
9.254
2.998
6.054
3.046
6.080
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
PPM


CH3
O
N
N
O
CH3
4000
3500
3000
2500
2000
1500
1000
500
4000
Wave number (cm -1) ---->
180

15g



15 $\longrightarrow$ 16

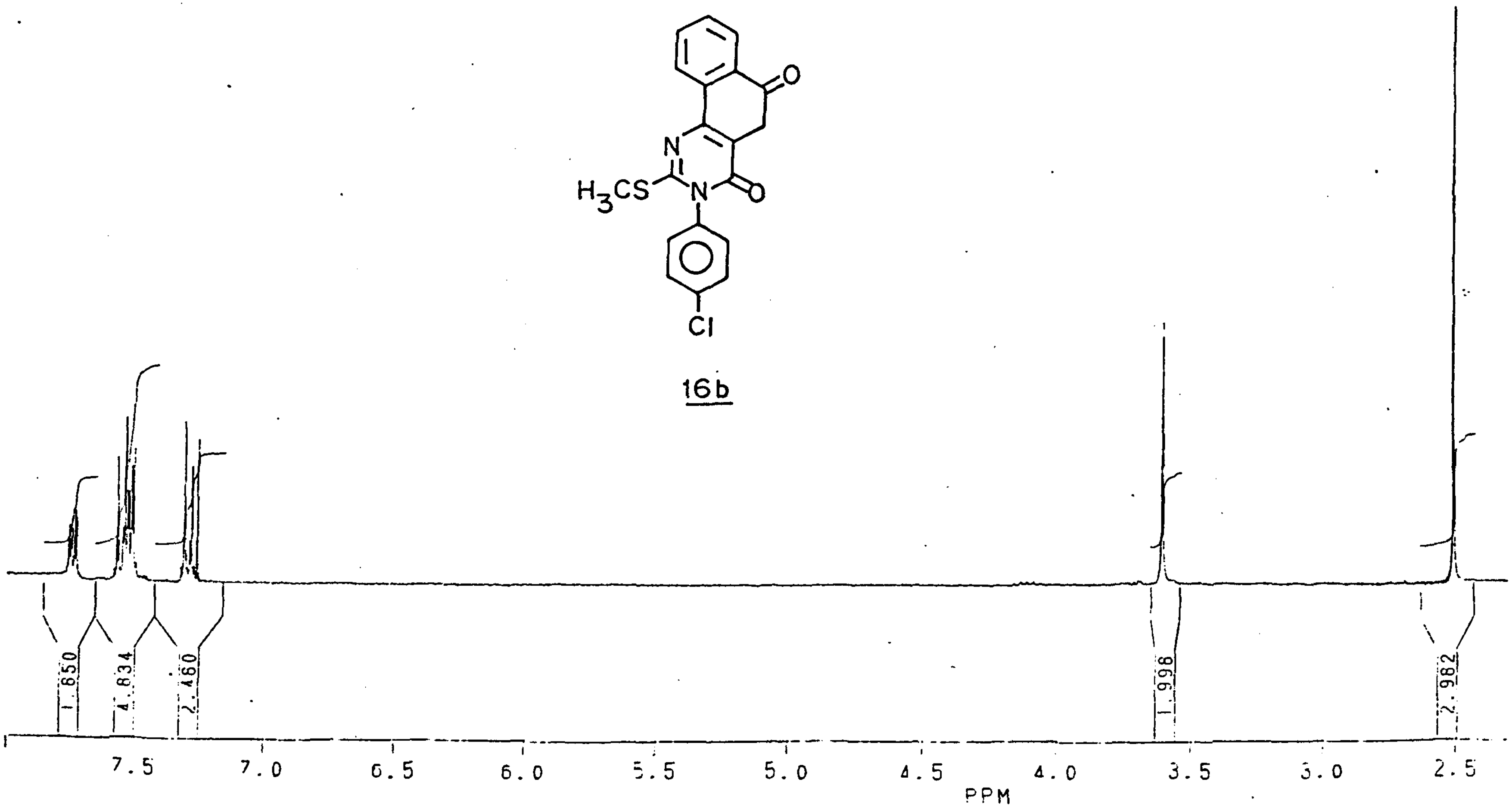
16 a. R^1 = O−CH_3; R^2 = SCH_3

b. R^1 = p−Cl ; R^2 = SCH_3

c. R^1 = p−OCH_3; R^2 = SCH_3

d. R^1 = H ; R^2 =

Scheme-8



16b

H3CS
N
N
O
O
Cl
1.850
4.834
2.460
1.998
2.982
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
PPM

Their **IR**, ^{1}**H NMR** and mass spectral data clearly established the assigned structures **16**. The compound **16a**, for example, showed a strong absorption peak at 1662 cm^{-1} due to the α,β-unsaturated carbonyl group. Its ^{1}**H NMR** spectrum exhibited the presence of methyl (s, δ 2.18), methylthio (s, δ 2.48) and methylene (s, δ 3.58) protons, and the absence of methoxy protons, clearly indicating the formation of the annulated product.

In conclusion, suitable methods have been developed for the synthesis of various 4-[2-(3-arylthiazolidino/ thiazino)]-1,3-diaza-1,3- butadienes **3/4**, and their reactions with chloroketene offer an easy access to various pyrimidinone fused thiazines and thiazepines. The presence of a methoxy carbonyl methyl group in pyrimidinones **15** has led to the development of a convenient route for the synthesis of important naphthaleno- fused pyrimidinones.

Experimental Section

General conditions are the same as described in chapter I. All ^{1}**H NMR** (300 MHz) and ^{13}**C NMR** (75 MHz) spectra were recorded on Bruker ACF-300 Spectrometer. **IR** spectra were recorded on a Perkin-Elmer 983 Infrared Spectrophotometer.

Starting Materials

The 1,3-diaza-1,3-butadienes used were prepared by the reported procedure . Chloroacetyl chloride used was commercially available . All the solvents and triethylamine used were dried before use.

Preparation of Methyl hydrogen succinate: An equimolar mixture of succinic anhydride and absolute methanol was heated on a water bath for 5-6 h. After complete disappearance of the starting material, it was removed from the water bath, and excess methanol was removed under vaccum to give methyl hydrogen succinate.

Preparation of Methoxy succinyl chloride: Equivalent amounts of methyl hydrogen succinate and thionyl chloride were refluxed on a water bath for 3-4 h. The acid chloride thus obtained was used directly for these reactions.

Preparation of 4-[2(3-arylthiazolidino/thiazepino)]-1,3-diazabutadienes (3/4): A suspension of thiourea 2 (1 mol) in DMF (30ml) was treated with NaH (2 mol) under a nitrogen atmosphere. After 30 minutes , 1.5 mol. of 1,2-dibromo ethane/1,3-dibromopropane was added and the mixture stirred for 5-6 hours. After completion of the reaction, the reaction mixture was quenched with water and extracted with dichloromethane. The extracts were washed with dilute base, dried over magnesium sulphate, filtered and the solvent removed at reduced pressure. Column chromatography of the residue gave heterocyclic fused azadienes **3** and **4** as a viscous yellow oil.

1,2-Diphenyl-4-[2-(3-phenylthiazolidino)]-1,3-diaza-1,3-butadiene (3a): Yield 80%; yellow viscous oil; IR (CCl_4) ν 1555 cm^{-1} (C=N) ^1H NMR (90 MHz) δ 3.24 (t, 2H, $-SCH_2-$); 3.90 (t, 2H,$-NCH_2-$); 6.70 - 7.78 (m,15H, arom). Anal. calcd. for $C_{22}H_{19}N_3S$: C, 73.95; H, 5.32; N, 11.76. Found: C, 73.29; H, 5.30; N, 11.84. ms m/z: 357 (M^+).

1-(p-Methoxyphenyl)-2-phenyl-4-[2-(3-phenylthiazolidino)]-1,3-diaza-1,3-butadiene (3b): Yield 81% ; Yellow viscous oil; IR (CCl_4) ν 1557 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 3.25 (t, 2H, $-SCH_2-$); 3.77 (s, 3H, $-OCH_3$); 3.94 (t, 2H, $-NCH_2-$), 6.72- 7.79 (m, 14H, arom). Anal. calcd. for $C_{23}H_{21}N_3OS$: C, 71.32; H, 5.43; N, 10.85. Found: C, 72.00; H, 5.23; N, 10.70. ms m/z: 387 (M^+).

1,2-Diphenyl-4-[2-(3-p-methylphenylthiazolidino]-1,3-diaza-1,3-butadienes (4a): Yield 80% ; yellow viscous oil; IR (CCl_4) ν 1556 cm^{-1} (-C = N); ^1H NMR (90 MHz) δ 1.89 - 2.03 (q, 2H, $-CH_2-$); 2.30 (s, 3H, $-CH_3$); 3.23-3.25 (t, 2H, $-SCH_2-$); 4.10-

4.14 (t, 2H, -NCH$_2$-); 6.70-7.77 (m, 14H, arom). Anal. calcd. for $C_{24}H_{23}N_3S$: C, 74.81; H, 5.97; N, 10.91. Found: C, 73.75; H, 5.80; N, 11.00 ms m/z: 385 (M^+).

1-(p-Methoxyphenyl)-2-phenyl-4-[2(3-phenylthiazolidino)]-1,3-diaza-1,3-butad--ienes (4b): Yield 83% ; yellow viscous oil; IR (CCl_4) ν 1556 cm^{-1} (C=N) ^{1}H NMR (300 MHz) δ 2.01 - 2.06 (q, 2H, -CH$_2$-); 3.23-3.25 (t, 2H, -SCH$_2$-); 3.78 (S, 3H,-OCH$_3$); 4.11-4.15 (t, 2H,-NCH$_2$-); 6.79-6.87 (m, 2H, arom); 7.00-7.10 (m, 5H, arom), 7.21-7.36 (m, 7H, arom); ^{13}C NMR (75 MHz) δ 17.81 (-SCH$_2$-); 25.97 (-CH$_2$-); 50.97 (-NCH$_2$-); 54.98 (-OCH$_3$); 113.87 ; 117.27 ; 122.99; 123.39; 127.65, 128.41, 129.11, 129.22, 129.31, 129.86, 130.08 (arom); 130.19, 134.97, 140.00, 146.18, 156.08 (C-2);159.88 (C-4). Anal. calcd. for $C_{24}H_{23}N_3OS$: C, 71.82; H, 5.74; N, 10.47. Found: C, 72.00; H, 5.80; N, 10.23. ms m/z 401 (M^+).

Reaction of 4-[2-(3-arylthiazolidino/thiazepino)]- 1, 3-diazabutadienes with ketenes (8/11):- A solution of chloroacetic acid (6mmol) and triethylamine (10 ml) in dry dichloromethane (30 ml) was stirred for 10-15 mins. To this solution, 4-[2-(3-arylthiazolidino/thiazepino)]-1,3-diazabutadienes **3/4** (4 mmol) was added, and stirring was continued. A solution of p-toluene sulfonyl chloride (6 mmol) in dichloromethane (30 ml) was added dropwise over a period of 1 h. After the addition was over, the reaction mixture was further stirred for 4-5 h. On completion of the reaction (tlc), it was successively washed with 5% NaOH solution (2 x 30 ml) and water (2 x 50 ml). The solution was dried over anhydrous sodium sulfate . The crude product obtained after removal of solvent under reduced pressure was purified by passing it through silica gel column.

2,3,8 Triphenyl- 3,6,7,8-tetrahydropyrimido [5,4,-b]1,4- thiazine -4-one (8a): Yield 62% m.p.189-191 °C; IR (KBr) ν 1671 cm^{-1} (C=O); ^{1}H NMR (90 MHz) δ 3.23-3.27 (t, 2H, -SCH$_2$-); 3.92-3.95 (t, 2H, -NCH$_2$-); 6.80-7.99 (m, arom, 15H). Anal. calcd. for $C_{24}H_{19}N_3OS$: C,70.75; H, 5.22; N, 9.53. Found : C, 70.12 ; H, 5.00; N, 9.50. ms m/z: 397 (M^+).

3-(p-Methoxyphenyl)-2,8-diphenyl-3,6,7,8 tetrahydropyrimidio[5,4-b]1,4-thiazi--ne -4-one (8b): Yield 61% ; m.p. 206-208 °C; IR (KBr) ν 1669 cm^{-1} (C=0); ^1H NMR (90 MHz) δ 3.26-3.29 (t, 2H, $-SCH_2-$); 3.77 (S, 3H,$-OCH_3$); 3.95-3.99 (t, 2H,$-NCH_2-$); 6.81-7.98 (m, 14H, arom). Anal calcd. for $C_{25}H_{21}N_3OS$: C, 70.26; H, 4.92; N, 7.65. Found: C, 69.82; H, 4.90; N, 7.62. ms m/z 427 (M^+).

2,3-Diphenyl-9-(p-methylphenyl)-3,6,7,8,9pentahydropyrimido-[5,4-b]1,4-thiaz--epine-4 one (11a): yield 65% m.p. 215-217 °C IR (KBr) ν 1670 cm^{-1} (C=0); ^1H NMR (90 MHz) δ 1.89-2.03 (q, 2H,$-CH_2-$); 2.30 (s,3H,$-CH_3$), 3.24-3.28 (t, 2H, $-SCH_2-$); 4.09-4.14 (t, 2H, $-NCH_2-$); 6.83-8.00 (m, 14H, arom). Anal. calcd. for $C_{26}H_{23}N_3OS$: C, 73.41; H, 5.41; N, 9.88. Found: C, 73.62; H, 5.35; N, 9.85. ms m/z: 425 (M^+).

2,9-Diphenyl-3-(p-methoxyphenyl)-3,6,7,8,9-pentahydropyrimido-[5,4-b]-1,4-thiazepine-4-one (11b): Yield 64%; m.p. 245-247 °C; IR (KBr) ν 1662 cm^{-1} (C=0); ^1H NMR (90 MHz) δ 2.01-2.05 (q, 2H,$-CH_2-$); 2.95 - 3.00 (t, 2H, $-SCH_2-$); 3.78 (S, 3H, $-OCH_3$); 4.11 - 4.13 (t, 2H, $-NCH_2-$); 6.80-6.88 (m, 2H, arom); 6.99-7.36 (m, 12H, arom). Anal. calcd. for $C_{26}H_{23}N_3O_2S$: C, 70.75; H, 5.22; N, 9.53. Found: C, 70.62; H, 5.20; N, 9.60. ms m/z: 441 (M^+).

Reactions of N-aryl-1,3-diaza-1,3-butadienes (63/93) with methoxy carbonyl methyl ketene (15): To a well stirred solution of N - aryl - 1,3 - diaza - 1,3 - butadienes **(63/93)** (4 mmol) and triethylamine (1g, 10 m mol) in dry dichloromethane (30 ml), a solution of acid chloride (6 m mol) in dry dichloromethane was added, dropwise, over a period of 1.5 - 2 h at room temperature. After completion of the reaction (tlc), the reaction mixture was washed several times with water and the organic layer dried over anhydrous sodium sulphate. Removal of solvent under reduced pressure yielded the crude product, which was purified by silica gel column chromatography using 1:10 ethyl acetate hexane mixture.

Methyl-3,6-diphenyl-2-methylthio-4-oxo-3H-pyrimidine-5-acetate (15a): Yield 92%; m.p. 115-117 °C; IR (KBr) ν 1663 (α,β-unsaturated C=0 gr), 1734 cm^{-1} (ester C=0 group); ^1H NMR (90 MHz) δ 2.46 (s, 3H,-SCH_3); 3.57 (s, 2H,-CH_2-); 3.68 (S, 3H,-OCH_3); 7.19 7.50 (m, 10H, arom). Anal. calcd. for $C_{20}H_{18}N_2O_3S$: C, 65.57; H, 4.92; N, 7.65. Found: C, 65.55; H, 4.88; N, 7.62. ms m/z: 366 (M^+).

Methyl-3-(p-methylphenyl) -2-methylthio -6-phenyl-4-oxo -3H-pyrimidine-5-acetate (15b): Yield 95% ; m.p.154-156 °C; IR (KBr) ν 1663 (α,β-unsaturated C=O gr); 1735 cm^{-1} (ester C=0 gr); ^1H NMR (90 MHz) δ 2.30 (s, 3H,-CH_3); 2.45 (s, 3H,-SCH_3); 3.58 (s, 2H, -CH_2-); 3.70 (s, 3H, -OCH_3); 7.14- 7.70 (m, 9H, arom). Anal. calcd. for $C_{21}H_{20}N_2O_3S$: C, 66.32; H, 5.26; N. 7.37. Found : C, 66.30; H, 5.22; N, 7.33. ms m/z: 380(M^+).

Methyl -3- (p-methoxyphenyl) -2- methylthio -6- phenyl -4-oxo-3H-pyrimidine-5-acetate (15C): Yield 93% ; m.p. 184-86 °C; IR (KBr) ν 1664 (α,β-unsaturared C=0 gr); 1738 cm^{-1} (ester C=0 gr); ^1H NMR (300 MHz) δ 2.43 (s, 3H, -SCH_3); 3.53 (s, 2H, -CH_2-); 3.69 (s, 3H, -OCH_3); 3.84 (s, 3H, -OCH_3); 6.97-7.00 (d, 2H, arom); 7.19-7.22 (d, 2H, arom); 7.41-7.43 (m, 3H, arom); 7.58- 7.61 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 15.24 (-SCH_3); 32.98 (-CH_2-); 51.79 (ester OMe); 55.14 (aromatic OMe); 96.02 (C-5); 113.80, 114.69, 116.22, 118.20, 127.26,127.62, 128.00, 128.12, 128.32, 128.48, 129.10, 129.55, 137.95, 143.90, 159.45, 160.37 (arom); 160.99 (C-4); 171.41 (ester C=0). Anal calcd. for $C_{21}H_{20}N_2O_4S$: C, 63.64; H, 5.05; N. 7.07. Found : C, 63.61; H, 5.01; N, 7.05. ms m/z: 396 (M^+).

Methyl -3- (*o*-methylphenyl) -2- methylthio -6- phenyl -4- oxo-3H-pyrimidine-5-acetate (15d): Yield 90%; m.p. 141-143 °C; IR (KBr) ν 1665 (α,β-unsaturated C=0 gr); 1735 cm^{-1} (ester C= 0 gr); ^1H NMR (90 MHz) δ 2.19 (s, 3H, -CH_3); 2.46 (s, 3H,- SCH_3); 3.59 (s, 2H, -CH_2-); 3.68 (s, 3H,-OCH_3), 7.15-7.54 (m, 9H, arom). Anal. calcd. for $C_{21}H_{20}N_2O_4S$: C, 66.32; H, 5.26; N, 7.37. Found: C, 66.37; H, 5.21; N, 7.34. ms m/z: 380 (M^+).

Methyl -3- (p-chlorophenyl) -2- methylthio -6- phenyl -4- oxo-3H-pyrimidine-5-acetate (15e): Yield 91%; m.p. 152-154 °C; IR (KBr) ν 1664 (α,β-unsaturated C=0 gr); 1733 cm^{-1} (ester C=0 gr); ^{1}H NMR (300 MHz) δ 2.46 (s, 3H, -SCH$_3$); 3.53 (s, 2H, -CH$_2$-); 3.69 (s, 3H, -OCH$_3$); 7.26-7.29 (d, 2H, arom); 7.44-7.52 (m, 5H, arom); 7.60-7.63 (d, 2H, arom). ^{13}C NMR (75 MHz) δ 15.26 (-SCH$_3$); 32.99 (-CH$_2$-); 51.96 (-OCH$_3$); 96.04 (c-5); 113.00, 128.26, 128.52, 129.36, 129.93, 133.98, 136.07, 137.71, 159.79 (arom); 160.22 (C-2); 162.63 (C-4); 171.51 (ester C=0 gr). Anal. calcd. for $C_{20}H_{17}N_2O_3SCl$: C, 59.93; H, 4.24; N, 6.99. Found: C, 59.90; H, 4.20; N, 6.95. ms m/z: 400.5 (M$^+$).

Methyl-3,6-diphenyl-2-piperidino-4-oxo-3H-pyrimidine-5-acetate (15f): Yield 90%; m.p. 157- 159 °C; IR (KBr) ν 1666 (α,β-unsaturated C=0 gr), 1733 cm^{-1} (ester C=0 gr); ^{1}H NMR (300 MHz) δ 1.65-1.68 (m, 6H, -(CH$_2$)$_3$-); 3.42-3.45 (m, 4H, -CH$_2$-N-CH$_2$-); 3.56 (s, 2H, -CH$_2$-); 3.70 (s, 3H, -OCH$_3$); 7.17-7.53 (m, arom, 10H); ^{13}C NMR (75 MHz) δ 25.00 (-CH$_2$-from piperidine ring) δ 26.17 (2 x -CH$_2$-, from piperidine ring); 32.57 (-CH$_2$-); 51.58 (-OCH$_3$); 97.93 (C-5); 127.41, 127.75, 128.35, 128.93, 129.-03, 129.09, 137.62, 154.91 (arom); 161.81 (C-2); 163.46 (C-4); 171.88, 154.91 (arom), 161.81 (C -2); 163.46 (C-4); 171.88 (ester C=0 gr). Anal. calcd. for $C_{24}H_{25}N_3O_3$: C, 71.46; H, 6.20; N,10.42. Found: C, 71.42; H, 6.17; N, 10.39. ms m/z: 403(M$^+$).

Methyl-3-(p-methylphenyl)-6-phenyl- 2-piperidino - 4-oxo-3H- pyrimidine-5-acetate (15 g): Yield 92%; m.p. 178-80 °C; IR (KBr) ν 1662 (α,β-unsaturated C=O gr); 1738 cm^{-1} (ester C=O gr); ^{1}H NMR (300 MHz) δ 1.64-1.67 (m, 6H, -CH$_2$-CH$_2$-CH$_2$-); 2.30 (s, 3H, -CH$_3$); 3.42-3.46 (m, 14H, -CH$_2$-N-CH$_2$-); 3.57 (s, 2H, -CH$_2$-); 3.71 (s, 3H, -OCH$_3$); 6.95 - 7.06 (m, 4H, arom); 7.12 -7.27 (m, 5H, arom); ^{13}C NMR (75 MHz) δ 21.03 (- CH$_2$-); 24.56 (-CH$_2$-, from piperidine ring); 26.17 (2 x -CH$_2$-); 32.60 (-CH$_2$-, from ester gr); 49.80 (-CH$_2$-N-CH$_2$-); 51.59 (-OCH$_3$); 95.99 (C-5); 127.43, 128.61, 128.98, 129.07, 129.11, 134.99, 135.29, 137.41, 159.61(arom); 161.02 (C-2); 163.22 (C-4); 172.1 (ester -C=0 gr). Anal. calcd. for $C_{25}H_{27}N_3O_3$: C, 71.94; H, 6.47; N, 10.07. Found: C, 71.79; H, 6.45; N, 10.03. ms m/z: 417 (M$^+$).

Cyclization Reactions of 3-aryl-3,5-dihydro-2-methylthio/piperidinonaphthaleno [3,4-d] pyrimidine-4,6-diones (16): A mixture of **15** and polyphosporic acid was heated on a water bath for 5-6 h with stirring from time to time. The reaction mixture was poured into ice water and allowed to stand overnight. After extraction with benzene and removal of acidic material with 5% NaOH, the product was distilled, dried over mangesium sulphate, and obtained as a white crystalline solid. Recrystallization was done from chloroform-hexane mixture.

3,5-diydro-3-(*o*-methylphenyl)-2-methylthionaphthaleno- [3,4-d] pyrimidine 4,6-dione (16a): Yield 70% ; m.p. 169-171 °C; IR (KBr) ν 1662 cm^{-1} (C=0); ^1H NMR (300 MHz) δ 2.18 (s, 3H, $-CH_3$); 2.48 (s, 3H, $-SCH_3$); 3.58 (s, 2H, $-CH_2-$); 7.19-7.25 (m, 1H, arom); 7.34-7.52 (m, 5H, arom); 7.70-7.73 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 15.29 ($-SCH_3$); 17.37 ($-OCH_3$); 34.64 ($-CH_2-$); 112.34 (C-5); 127.56, 128.25, 128.50, 129.29, 130.05, 130.71, 131.62, 134.29, 136.09, 136.94 (arom); 161.22 (C-2); 164.52 (C-4); 173.40 (ester C=0). Anal. calcd. for $C_{20}H_{16}N_2O_2S$: C, 68.97; H, 4.60; N, 8.05. Found: C, 68.95; H, 4.57; N, 8.01. ms m/z: 348 (M^+).

3-(p-Chlorophenyl) -3,5- dihydro - 2 -methylthionapthalene- [3,4-d] pyrimidin - 4,6-dione (16b): Yield 71%; m.p. 170-172 °C; IR (KBr) ν 1664 cm^{-1}; ^1H NMR (90 MHz) δ 2.51 (s, 3H, $-SCH_3$); 3.61 (s, 2H, $-CH_2-$); 7.26 - 7.31 (m, 2H, arom); 7.51-7.57 (m, 4H, arom); 7.73-7.76 (m, 2H, arom). Anal. calcd. for $C_{19}H_{13}N_2O_2$ SCl: C, 61.87; H, 3.53; N, 7.60. Found: C, 61.84; H, 3.50; N, 7.56. ms m/z: 368.5 (M^+).

3,5-Dihydro -3- (p-methoxyphenyl) -2-methylthionaphthaleno-[3,4,-d] pyrimidin 4,6-dione (16c): Yield 73% ;m.p. 206-208 °C; IR (KBr) ν 1663 cm^{-1} (C=0); ^1H NMR (90 MHz) δ 2.44 (s, 3H, $-SCH_3$); 3.54 (s, 2H, $-CH_2-$); 3.78 (s, 3H, $-OCH_3$); 7.23-7.69 (m, 8H, arom). Anal. calcd. for $C_{20}H_{16}N_2O_3S$: C, 65.93; H, 4.40; N, 7.60. Found: C, 65.90; H, 4.37; N, 7.57. ms m/z: 364 (M^+).

3,5 -Dihydro -3- phenyl -2- piperidinonaphthaleno -[3,4-d] pyrimidin -4,6-dione (16d) : Yield 70%; m.p. 172-174 °C; IR (KBr) ν 1667 cm^{-1} (C=0); ^{1}H NMR (90 MHz) δ 1.66-1.69 (m, 6H,-$(CH_2)_3$ -); 3.41-3.45 (m, 4H, -CH_2-N-CH_2-); 3.56 (s, 2H, -CH_2-); 7.22- 7.65 (m, 9H, arom); ^{13}C NMR (75 MHz) δ 24.52 (-CH_2- from pipeiridine ring); 26.48 (2 x -CH_2-, from piperidine ring); 36.04 (-CH_2-, C-5); 127.95, 128.78, 128.85, 129.07, 129.33, 129.97, 134.22, 136.99, 155.33 (arom); 161.73 (C-2); 167.06 (C-4); 172.81 (C-6). Anal. calcd. for $C_{23}H_{21}N_3O_2$: C, 74.39; H, 5.66; N, 11.54. Found: C, 74.36; H, 5.62; N, 11.51. ms m/z: 371 (M^+).

References:

1. (a) W.L.F. Armarego *J . Appl. Chem.*, 1961, **11**, 70, (b) T.J. Schwan, H. Tiecketmann, J.F. Holland, B. Bryant, *J. Med. Chem*, 1965, **8**, 750, (c) C.C. Cheng *Prog. Med. Chem.*, 1969, **6**, 67.

2. (a) D.J. Brown , G.W. Grigg, *Med. Res. Rev.*, 1982, **2**, 191;(b) T. Takia, Y. Muraoka, T. Nakatani, A. Fujii, Y. Umezawa, H. Naganawa, H. Umezawa, *J. Antibiot* 1978, **31**, 801 (c) Ref. 79c (Chap I). (d) S. Onuma, Y. Nawata, Y, Saito, *Bull. Chem. Soc. Japan*, 1966, **39**, 1091, (e) C.L. Stevens, K, Nagarjan, T.H. Hoskell, *J. Org. Chem*, 1962, **27**, 2991.

3. (a) S.C. Harvey in "*The Pharmacological Basis of Therapeutics*" Ed. L.S. Goodman and A.Gilman; Macmillan, New York, 5th Ed., p. 102 and 124, (b) L.Weinstein, ibid, 1975, p. 1113; (c) P.Liberti, B. Stanbury., *Annu. Rev. Pharmacol*, 1971, **11**, 113.

4. A. Ishida, M. Inage, H, Akatsuka, M, Inamasu, T. Mitsui, *Jpn. Kokai Takkyo, Koho Chem. Abs.* p. 06, 220 [94, 220, 059].

5. M. Nomura, Y. Kotake,T. Haneda, T. Okauchi, K. Kito, *Jpn. Kokai Tokkyo Kaho* Chem. Abs. p. 06, 239, 840 (94.239,840].

6. S.N. Mazumdar and M.P. Mahajan, *Synthesis*, 1990, 417.

7. P.D. Dey, A.K. Sharma, S.N. Rai and M.P. Mahajan, *Tetrahedron*, 1995, **51**, 7459.

8. (a) S.N. Mazumdar, I. Ibnusaud and M.P. Mahajan, *Tetrahedron Lett.*, 1986, **27**, 5875.(b) S.N. Mazumdar and M.P.Mahajan, *Tetrahedron*, 1991, **47**, 1473.

9. A.K. Sharma and M.P. Mahajan, *Heterocycles*, 1995, **40**, 787.

10. P.D. Dey, A. K. Sharma, P.V. Bharatam and M.P. Mahajan, *Tetrahedron*, 1997, **53**, 13829.

11. M. Sainsbury, *Compreheisive Heterocyclic Chemistry*, Pergamon; Oxford, 1984, p. 1038.

12. M. Koos, *Monatsh Chem*, 1994, **125**, 101.

13. A. Gupta, S. Prakash, L. Prakash, *Indian J. Heterocycl. Chem.*, 1994, **3** , 261.

14. J.C. Brindley, J.M. Caldwell, G.D. Meakin, S.J. Plackett, S.J. Price, *J. Chem. Soc., Perkin Trans.*, 1987, **1**, 1153.

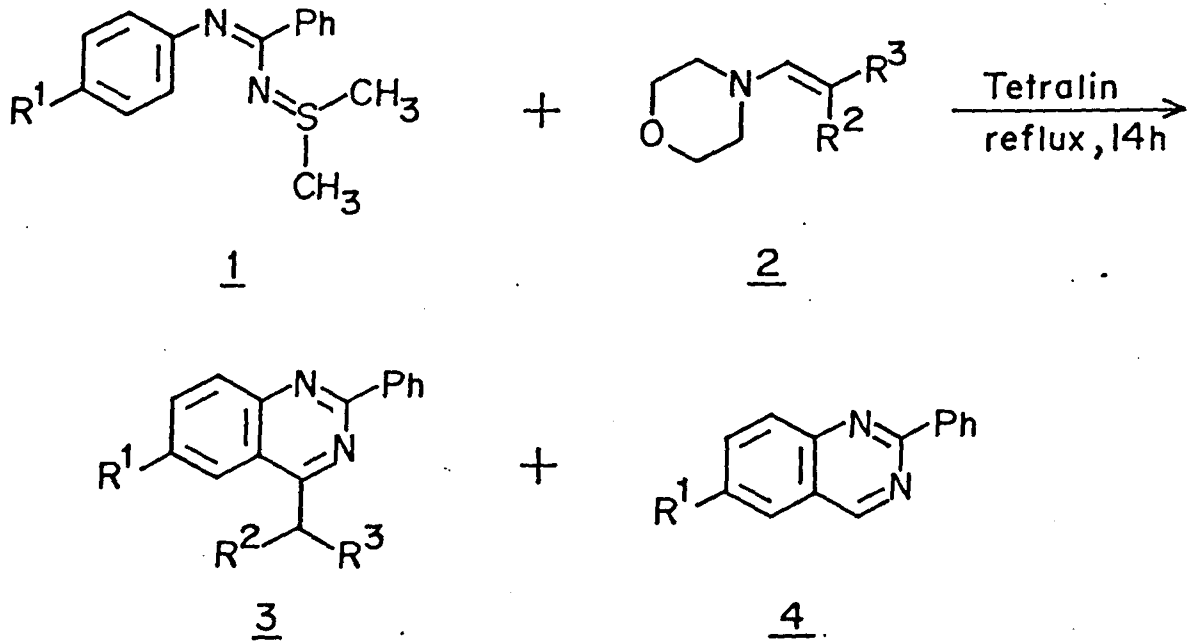
CHAPTER III

CONVENIENT SYNTHESIS OF QUINAZOLINE, THIAZOLE, 1, 2, 4-OXADIAZOLE AND 1,2,4-TRIAZOLE DERIVATIVES USING 1,3-DIAZA-1,3-BUTADIENES.

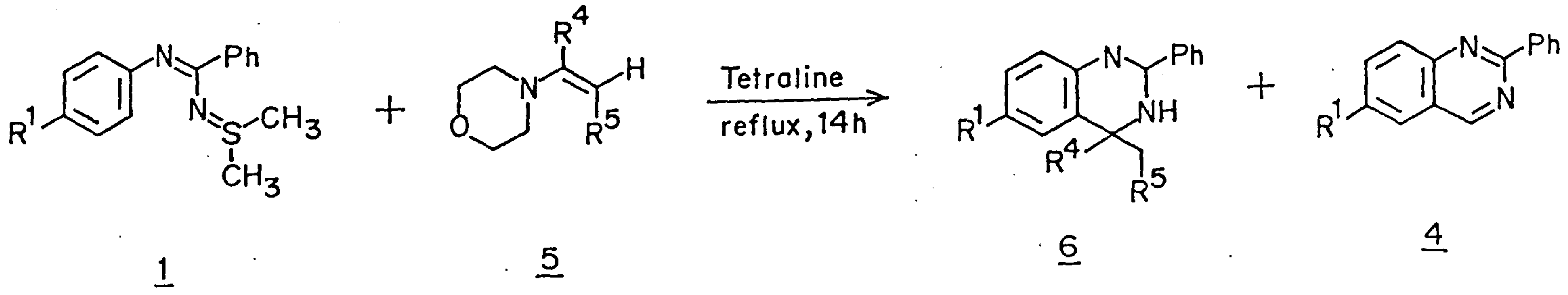
3.1: *SYNTHESIS OF QUINAZOLINE BY ELECTROCYCLISATION OF N-ARYLAMINO-1,3-DIAZA-1,3-BUTADIENES.*

Many quinazolines possessing a wide variety of biological activities are known. However, much attention is being paid towards the synthesis of quinozaline derivatives because of their antimalarial[1], antibacterial[2], antithrombic[3], anticoagulant and other pharmacological properties[4,5]. Quinazoline derivatives have also been found to act as neoplasm inhibitors[6] and are widely used as diuretics[7] and antihypertensive drugs[8]. The growing importance of these heterocyclics continues to provide strong impetus for the development of new synthetic methods for their preparation. Although there are few reported methods[9-11] for the synthesis of quinazolines, the improvements in synthetic methodology and development of new methods are considered to be of great importance due to their biological activity.

Rossi[9] reported a new synthesis of quinazolines **3** and **4** by the reaction of S,S-dimethyl-N-(N-arylbenzimidoyl) sulfimides **1**, with enamines **2** derived from aldehydes (Scheme-1). The formation of 4-alkylquinazolines **3** was explained as involving a thermal cleavage of the imidoylsulfimides **1** into the corresponding imidoylnitrenes and dimethylsulfides. Nitrene insertion on the enamine double bond and subsequent rearrangement of the aziridine intermediate thus formed resulted in the final product **3**. The formation of the by-product **4** involves a known intramolecular rearrangement of the benzimidoylsulfimides.



Scheme - 1



4\. a. $R^1 = CH_3$
b. $R^1 = OCH_3$

6\. a. $R^1 = CH_3$; $R^4 = C_6H_5$; $R^5 = H$
b. $R^1 = CH_3$; $R^4 = C_2H_5$; $R^5 = CH_3$
c. $R^1 = CH_3$; $-(CH_2)_3-$
d. $R^1 = CH_3$; $-(CH_2)_4-$
e. $R^1 = OCH_3$; $R^4 = C_6H_5$; $R^5 = H$
f $R^1 = OCH_3$; $-(CH_2)_4-$

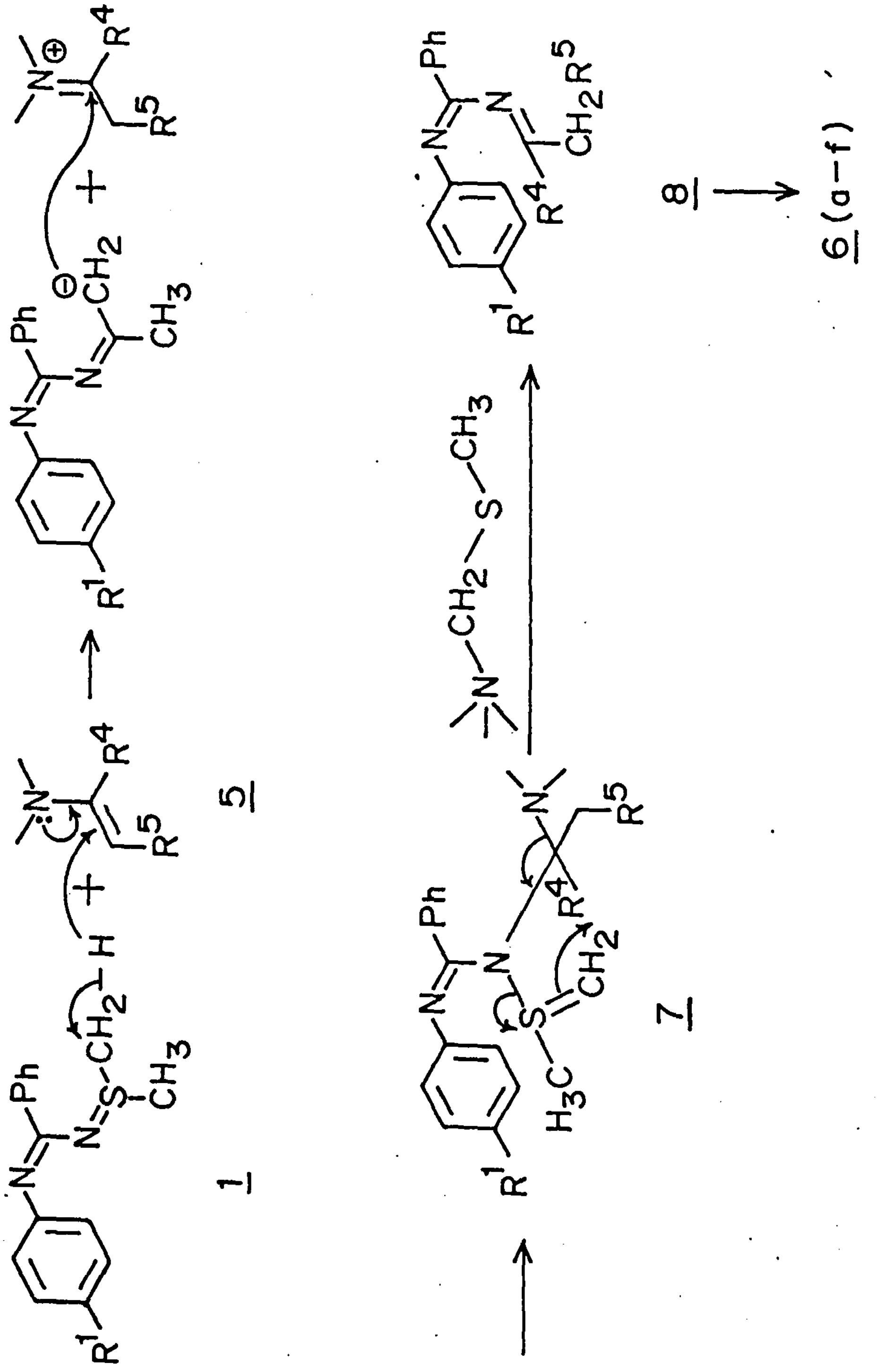
Scheme-2

Later, it was reported[10] that treatment of S,S-dimethyl-N-(N-aryl-benzimidoyl) sulfimides **1** with enamines **5** derived from ketones gave 4,4-disubstituted -2-phenyl-3,4-dihydro quinazolines. The reaction involved a 1,3-diaza-1,3-butadiene intermediate, which underwent electrocyclic ring closure to give the final products **4** and **6** (Scheme-2).

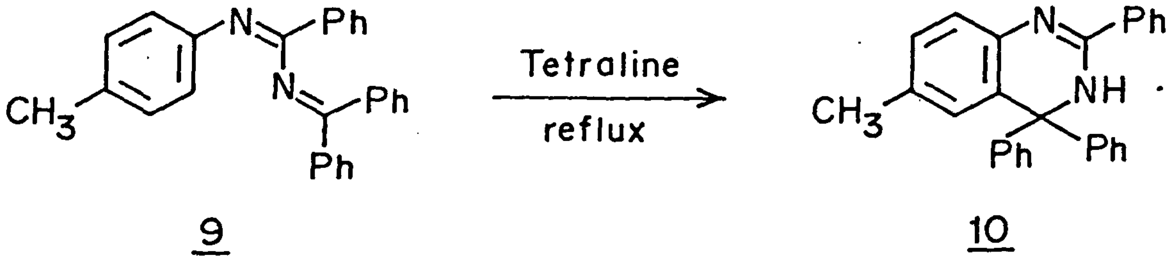
The mechanism proposed for the reaction between S, S-dimethyl-N-(N-aryl-benzimidoyl) sulfimides **1** and enamines **5** is depicted in Scheme-3. In the first step, the enamine **5** removes a proton from the methylthio group of the sulfimide **1**. The iminium salt thus formed underwent a nucleophilic addition reaction that resulted in the formation of the intermediate **7**, which by intramolecular elimination of morpholino-4-[(methylthio)methyl] gave the 1,3-diaza-1,3-butadiene **8**. Quinazoline **6** was formed by electrocyclic ring closure.

The capability of the 1,3-diaza-1,3-butadiene system **8** to undergo electrocyclic ring closure by an alternative synthesis, was shown by the preparation of N-diphenylmethylene-N'-(4-methyl phenyl)-benzamidine **9** which, when heated in tetraline at reflux, yielded 6-methyl-2,4,4-triphenyl-3,4-dihydro quinazoline **10** (Scheme-4).

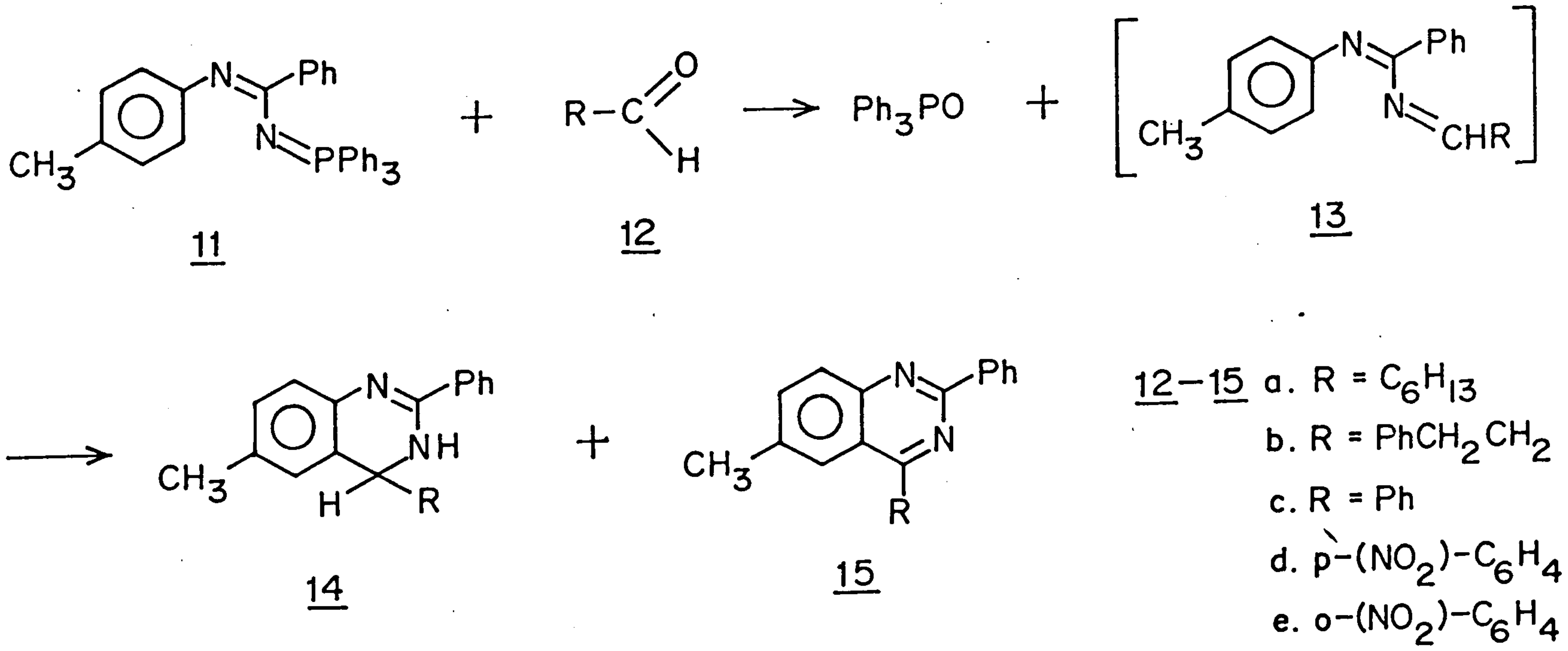
Rossi et al.[11] also found that N-imidoyliminotriphenyl-phosphorane **11** reacted with aromatic and aliphatic aldehydes **12** to give 3,4- dihydroquinazolines **14** and quinazolines **15**, via the 1,3-diaza-1,3-butadiene intermediate **13** (Scheme-5). The 3,4-dihydroquinazoline **14** thus formed could aromatize spontaneously to yield quinazoline **15**. The ratio between compounds **14** and **15** depended probably on the nature of the substituent R. When R was an aliphatic group, an equimolar distribution between compounds **4** and **5** was observed. When the substituent R=C_6H_5 was at C_4, only the 3,4-dihydro derivative **14** was detected. Nevertheless, if an electron withdrawing substituent was present on the aromatic ring, the aromatization process was favoured, and the quinazoline **15** was the sole reaction product. Furthermore , the aromatization seemed to be a temperature- dependent process. A similar behaviour was observed when the



Scheme- 3



Scheme – 4



12–15 a. $R = C_6H_{13}$
b. $R = PhCH_2CH_2$
c. R = Ph
d. p-(NO_2)-C_6H_4
e. o-(NO_2)-C_6H_4

Scheme – 5

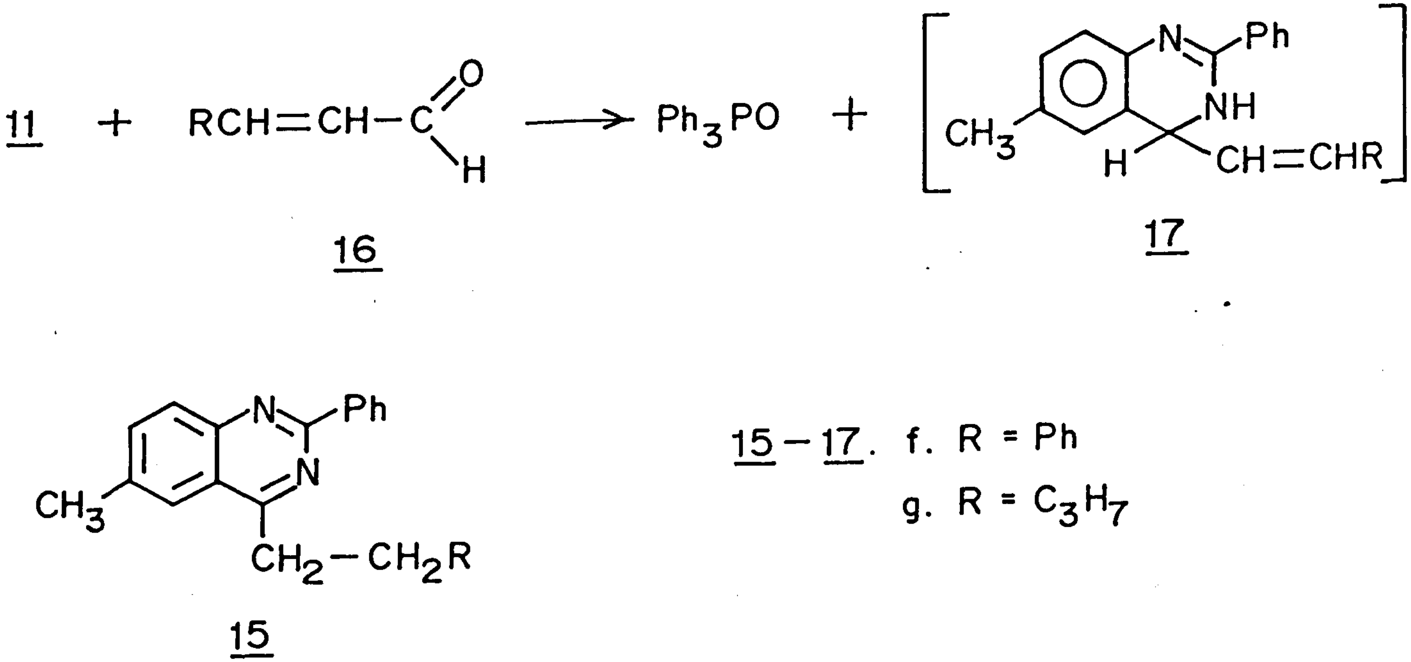
N-imidoyltriphenylphosphorane **11** was reacted with α,β-unsaturated aldehydes **16** (Scheme-6).

Keeping in view the above few reports concerning the generation of quinazoline from compounds such as **1**, **11**, and **17**, where 1,3-diaza-1,3-butadiene occurred as intermediates, we felt that 1,3-diaza-1,3-butadienes bearing polar donating groups at 4-position could perhaps be the better candidates for their electrocyclization to quinazoline derivatives. The object of this investigation was also to understand the nature of reaction pathway followed and the products formed in these reactions.

In this section, we report the synthesis of quinazoline derivatives from N-arylamino,1-3-diaza-1,3-butadienes **63** (as given in Chapter I).

Results and Discussion

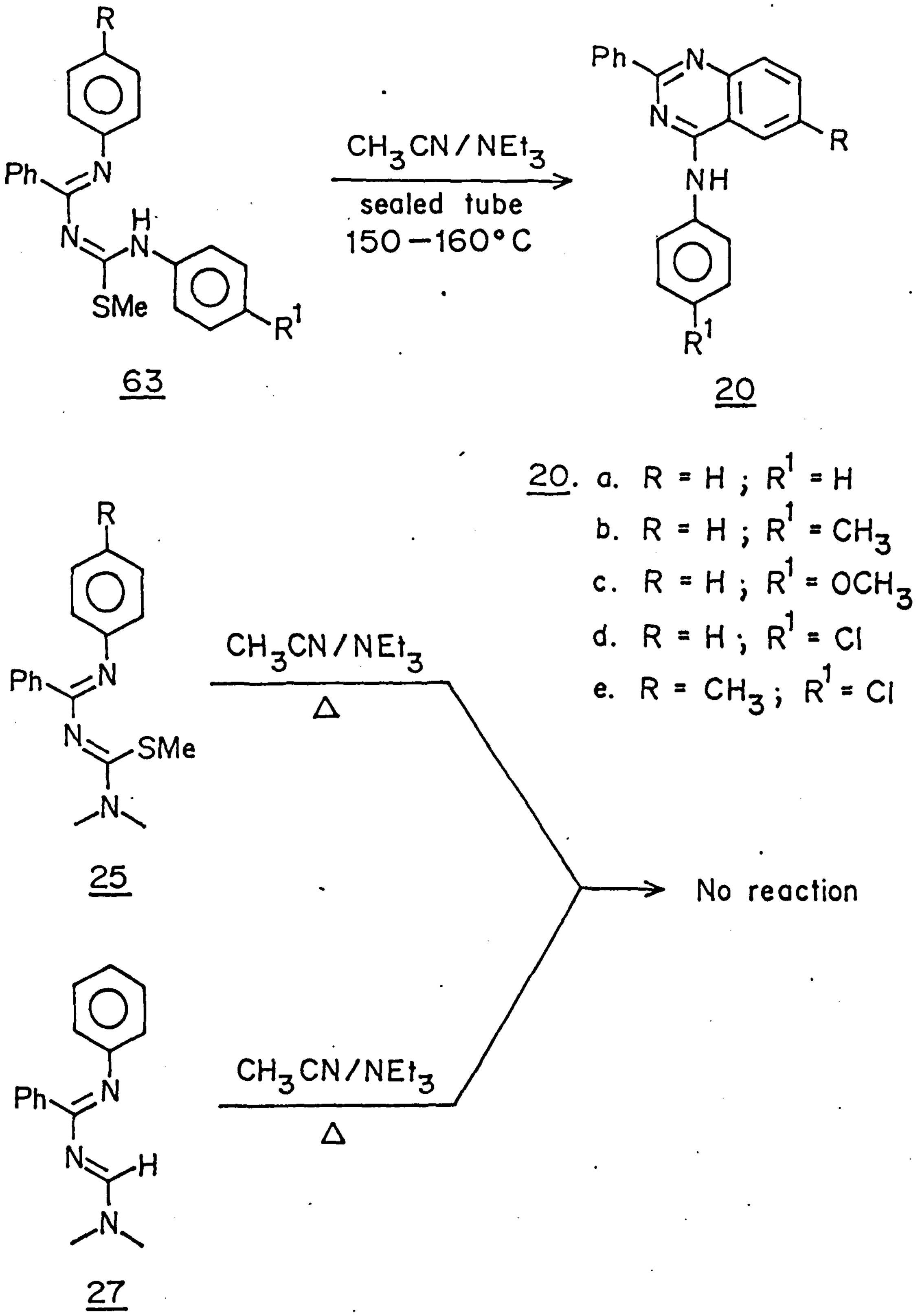
The thermolysis of N-arylamino-1,3-diaza-1,3-butadienes **63** in acetonitrile/triethylamine, in a sealed tube at 140-150°C led to good yields of quinazolines **20** (Scheme-7). Surprisingly, the 1,3-diaza-1,3-butadienes **25** and **27** failed to undergo cyclisations to the desired quinazolines. The possible reasons for the absence of any reactions with diazabutadienes **25**, **27**, and observed cyclisation in thermolysis of **63** are not clearly understood. It was also observed that diazabutadienes **63** failed to undergo any cyclisation in absence of triethylamine as a base. The mechanism of the reaction is depicted in Scheme-8. The most probable mechanism leading to the formation of quinazoline **20**, involves the proton abstraction by triethylamine, followed by cyclisation and subsequent elimination of the methylthio group. The products **20** were characterised on the basis of analytical and spectral evidences. Thus, compound **20a** for example, was analysed for $C_{20}H_{15}N_3$ and its mass spectrum showed a molecular ion peak at m/z 297. Its **IR** spectrum showed strong absorption peaks at 3460 and 1568 cm^{-1} due to -NH and -C=N groups respectively. Its **^{1}H NMR** spectrum exhibited the presence of the N-arylamino group, apart from other aromatic protons and the absence of the methylthio group.



15 − 17. f. R = Ph

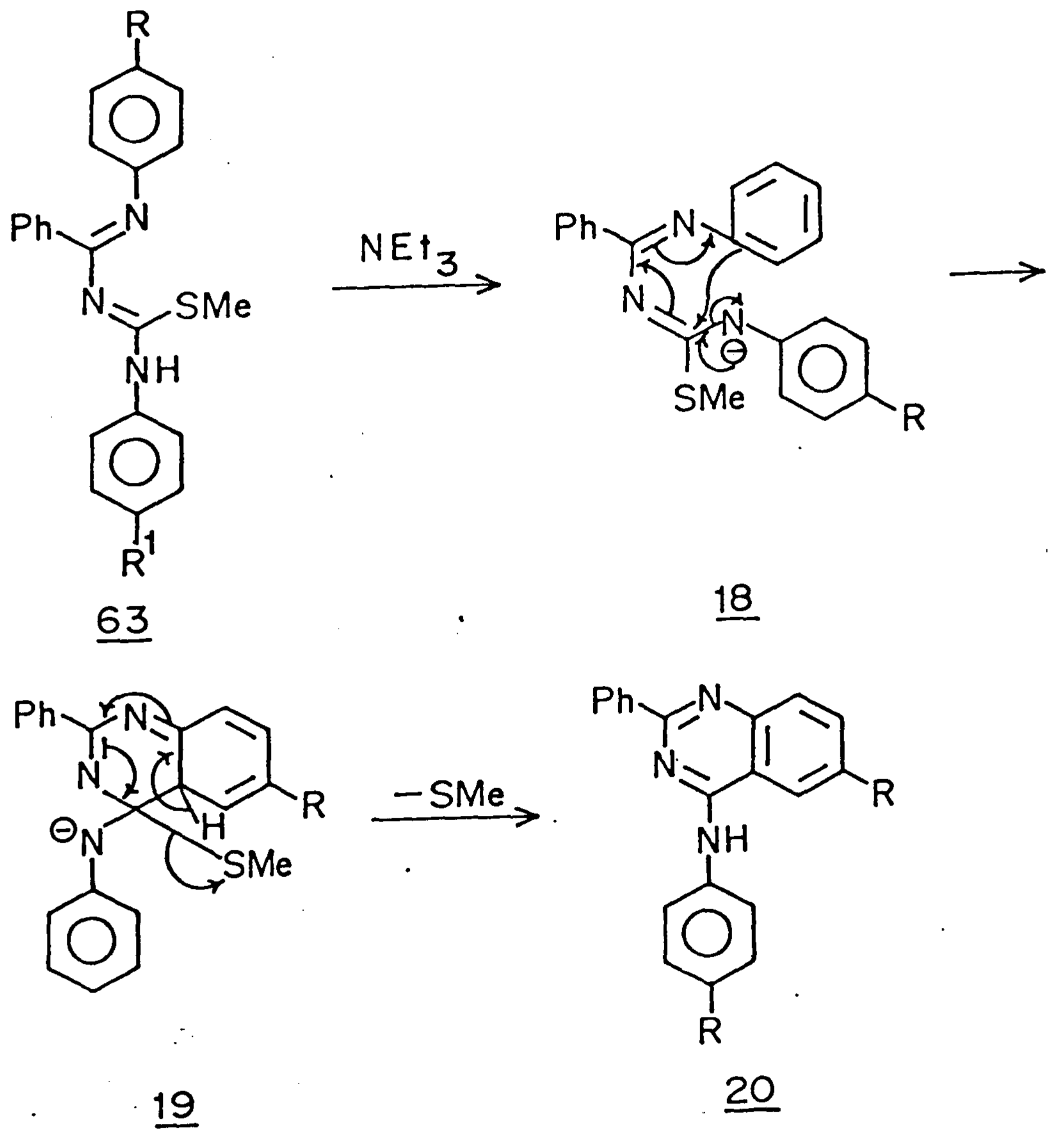
g. R = C_3H_7

Scheme − 6

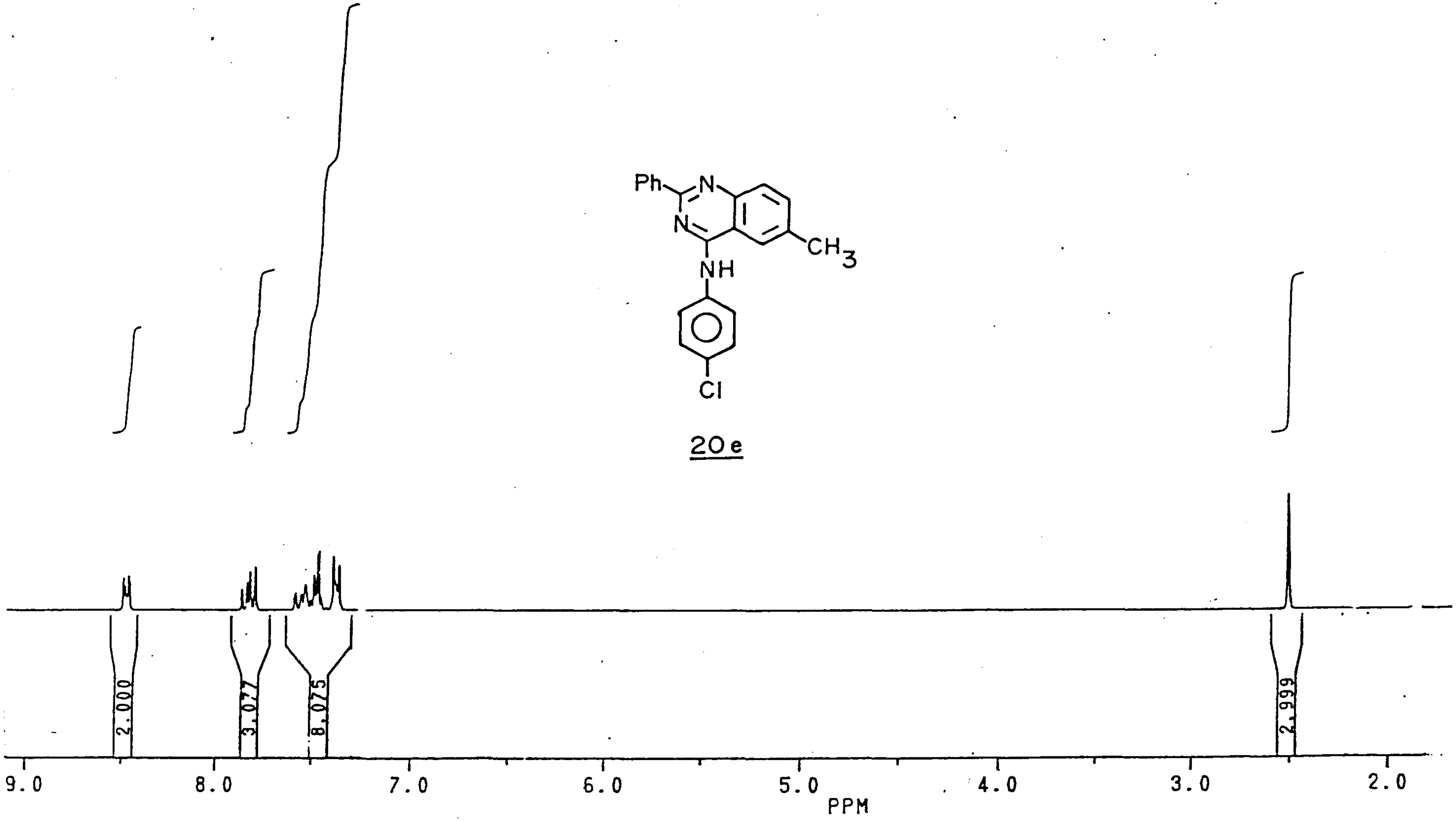


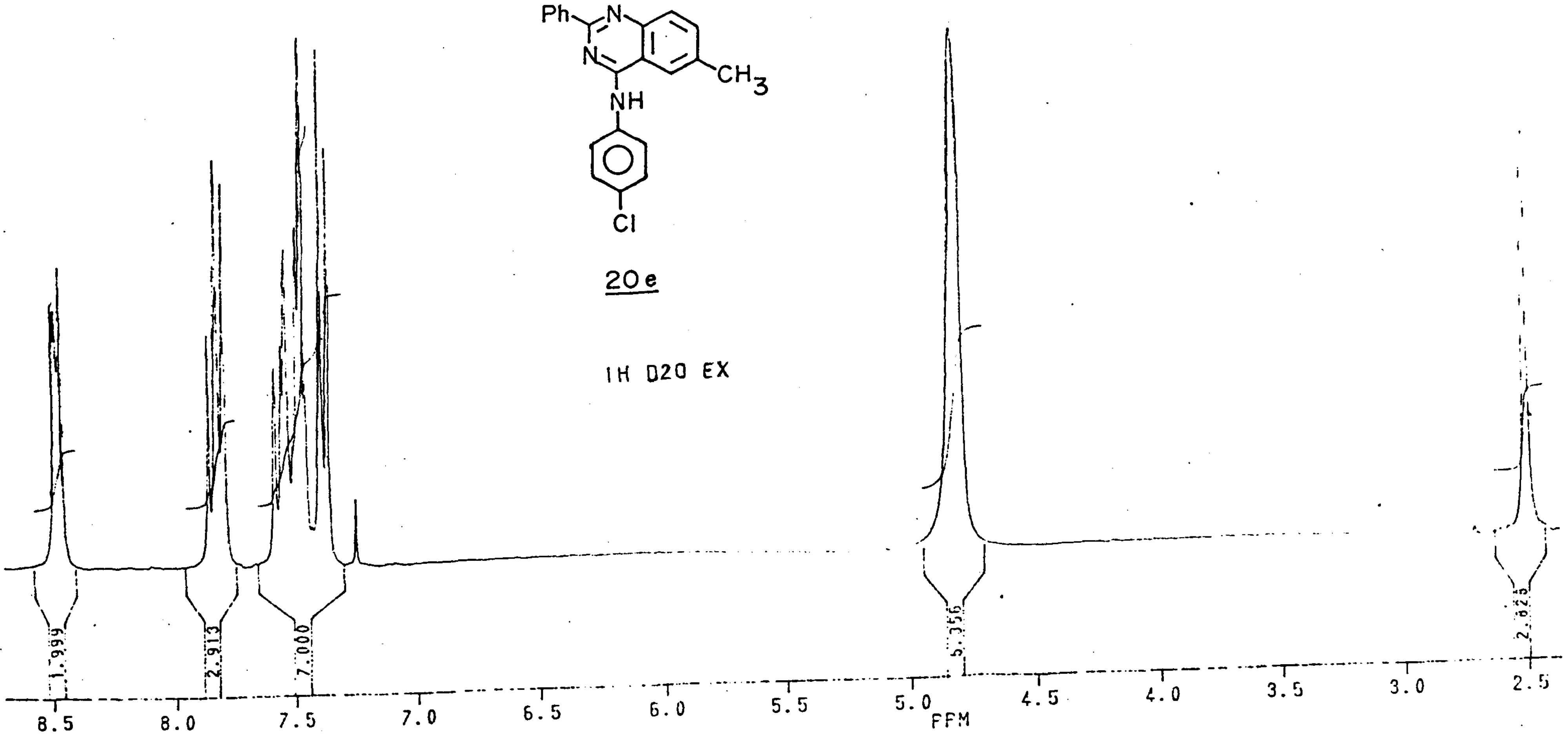
20. a. $R = H ; R^1 = H$
b. $R = H ; R^1 = CH_3$
c. $R = H ; R^1 = OCH_3$
d. $R = H ; R^1 = Cl$
e. $R = CH_3 ; R^1 = Cl$

Scheme – 7


R
Ph
N
N
SMe
NH
R1
63
NEt3
Ph
N
N
N
SMe
R
18
Ph
N
N
N
H
SMe
R
19
—SMe
Ph
N
N
R
NH
R
20

Scheme- 8


20e



20e

Ph
N
N
NH
CH3
Cl
1H D2O EX
1.999
2.913
7.000
5.356
2.625
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
PPM
4.5
4.0
3.5
3.0
2.5

From the results of the reaction, it can be concluded that the reaction profiles depend upon the substituent pattern of amino nitrogen and only the N-arylamino,1-3-diaza-1,3-butadienes underwent electrocyclisation to quinazoline derivatives.

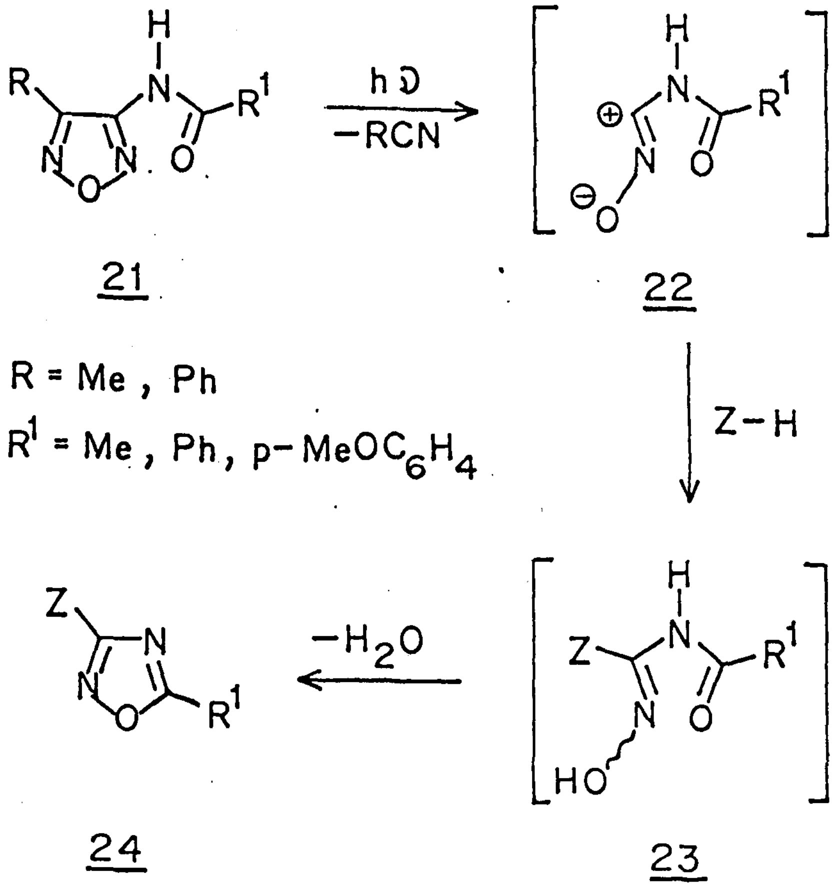
3.2: *SYNTHESIS OF THIAZOLE, 1,2,4-OXADIAZOLE AND 1,2,4-TRIAZOLE DERIVATIVES USING 1, 3-DIAZA-1,3-BUTADIENES.*

Compounds containing a thiazole/triazole ring are widely distributed in nature and have been reported to display significant biological activities.[12-17] Also, the oxadiazole derivatives have gained popularity because they have been reported as therapeutic agents[18], potential muscarinic agonists[19,20] and integral parts of molecules which find their applications in the textile industry.[21] Although there are numerous reported methods for the synthesis of thiazoles[22], 1,2,4-triazoles[23], 1,2,4-oxadiazoles[24], efforts have been directed towards extending the range of reactions available for their synthesis.

Buscemi et al[25] investigated the photochemical behaviour of some 3-acylamino-1,2,5-oxadiazoles. On irradiation at 254 nm, in the presence of nucleophiles (ammonia, primary or secondary amines), the photo reaction produced 3-substituted 1,2,4-oxadiazoles **24** (Scheme-9).

Balsamini et al[26] reported the synthesis of 4,5-dihydro-1,2,4-oxadiazole **27** from 1,1-diphenyl-2-aza-1,3-butadienes **25** and 4-nitrobenzonitrilioxide **26** (Scheme-10).

In recent years, polarised 1,3-diaza-1,3-butadienes have been shown to successfully and effectively participate as 4π component in [4+2] cycloaddition reactions with various ketenes[27], enamines[28], isocyanates[29], oxazolones[30] and dimethyl acetylenedicarboxylate[31] (Schemes-11 and 12). These 1,3-diazabuta-1,3-dienes have also been reported to undergo reactions with isocyanides to yield imidazole and triazine derivatives[32] and undergo electrocyclic ring closure yielding quinazoline derivatives[33]. Surprisingly, 1,3-diaza-1,3-butadienes having more than one apparent electrophilic and nucleophilic sites have not been exploited in heterocyclic synthesis by reactions with suitable electrophiles and nucleophiles.



R = Me , Ph

R^1 = Me , Ph, p−$MeOC_6H_4$

24. a. R^1 = Ph ; Z = NH_2

b. R^1 = Ph ; Z = NHMe

c. R^1 = Ph ; Z = $N(Me)_2$

d. R^1 = Ph ; Z = NC_4H_8

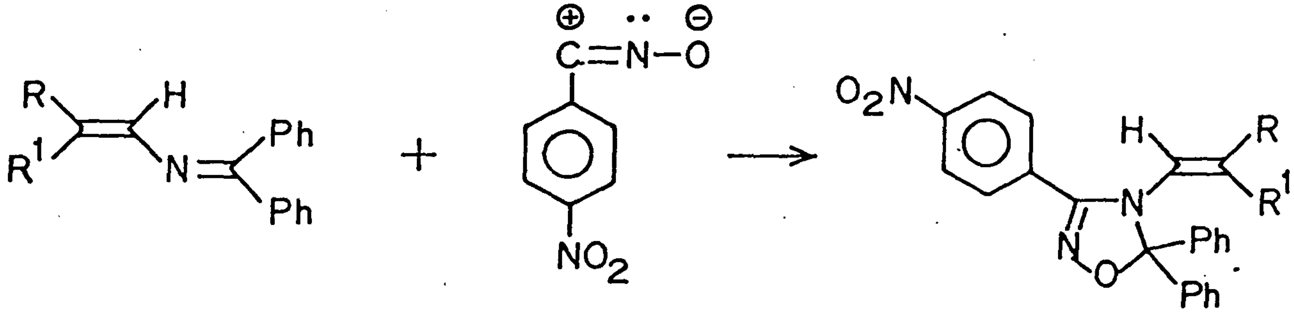
e. R^1 = Ph ; Z = NC_5H_{10}

f. R^1 = Ph ; Z = $NHC_4H_9(n)$

g. R^1 = p−$MeOC_6H_4$; Z = NH_2

h. R^1 = Me ; Z = NH_2

Scheme − 9



25 26 27

$\underline{27}$. a. $R = C_6H_5$; $R^1 = H$

b. $R = R^1 = C_6H_5$

Scheme–10

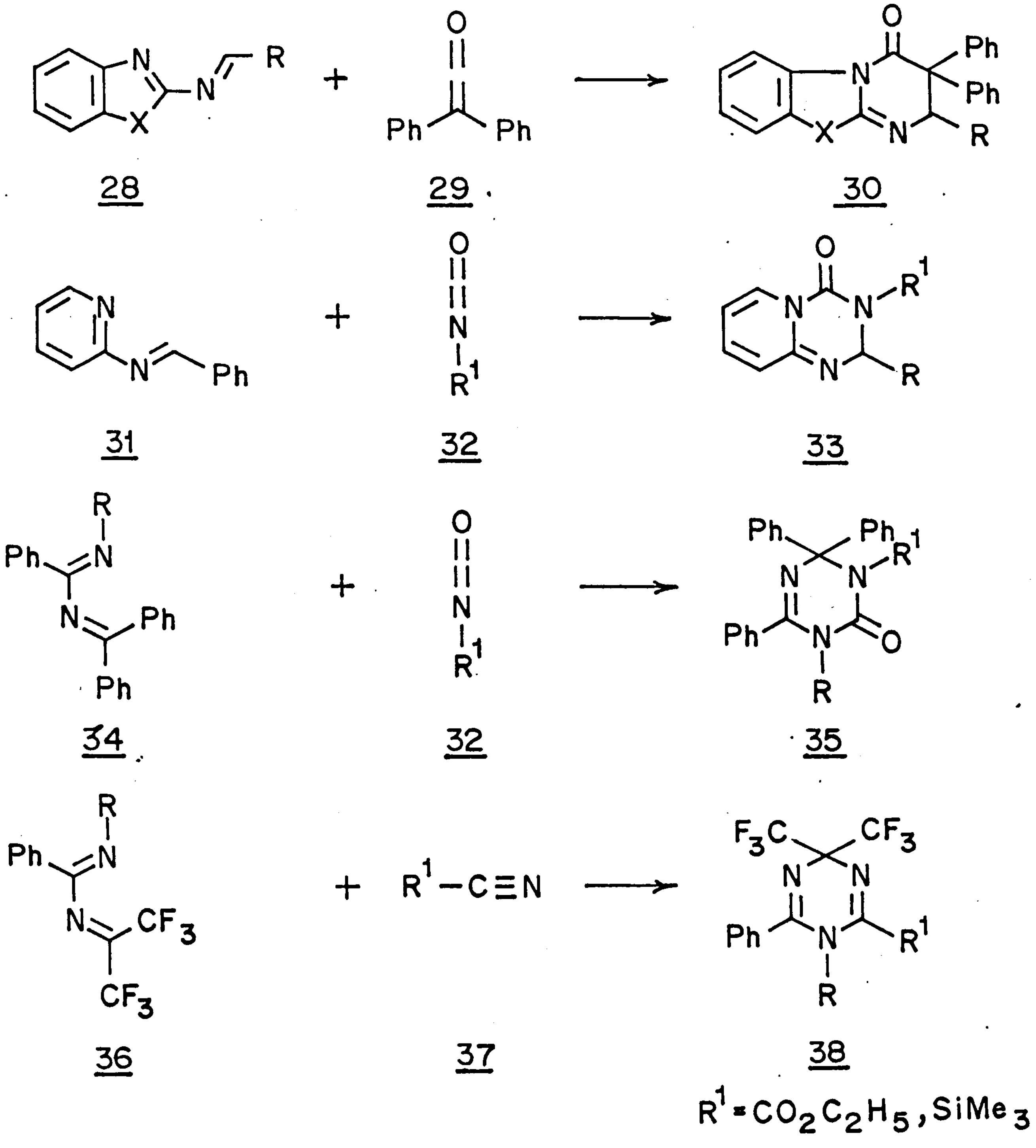
Herein, we report the reactions of few such reagents such as thioglycolic acid, hydroxylamine hydrochloride, sodium azide, hydrazine hydrate, ethyl bromoacetate, with 1,3-diaza-1,3-butadienes leading to the facile synthesis of thiazole,1,2,4-oxadiazole and 1,2,4-triazole derivatives.

Results and Discussions

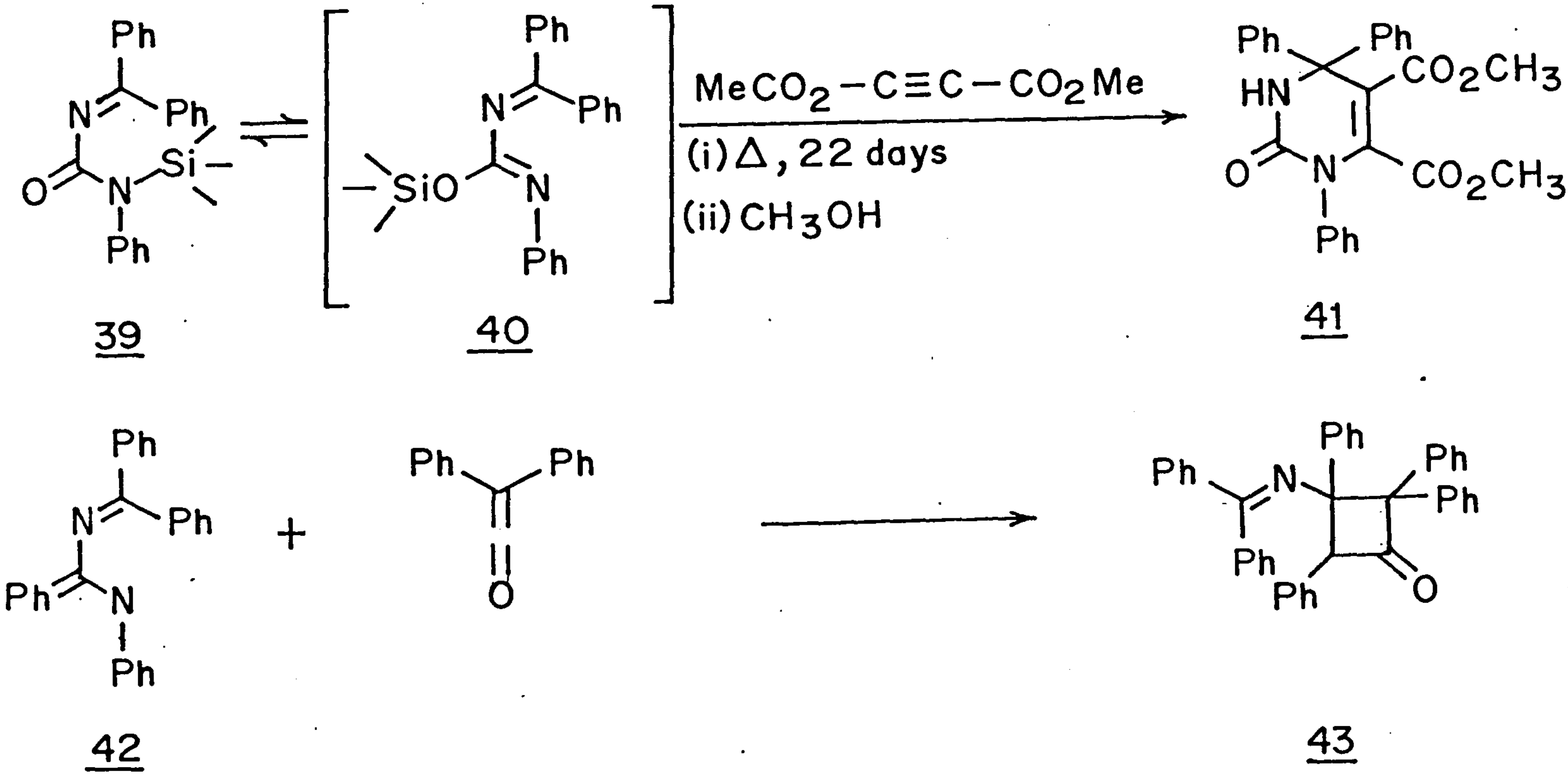
The reactions of 1,3-diaza-1,3-butadienes **25** and **63** with equimolar amounts of thioglycolic acid, in refluxing benzene, resulted in a novel method for good yields of 2-(N-aryl)/secondary amino-5-phenylthiazoles **47**. Thioglycolic acid was also found to undergo similar reactions with 1,3-diaza-1,3-butadienes **25** and **63** , even at room temperature, albeit slowly, to form the desired thiazoles **47**. The formation of thiazoles in these reactions may be explained by the sequence of reaction intermediates shown in Scheme-13. In this scheme, it is assumed that the nucleophilic displacement of methylthio group of 1,3-diaza-1,3-butadines **25/63** by thioglycolic acid yields an intermediate **44**, which on intramolecular proton abstraction, yield another intermediate **45**. This intermediate cyclizes to intermediate **46** which, on decarboxylative deamination, finally yields the desired thiazoles **47**.

The facile decarboxylative deamination of intermediate **46**, under mild reaction conditions, and in the absence of any base is quite interesting. To our knowledge, all known reactions of this type either involve high temperature and /or the presence of a base.

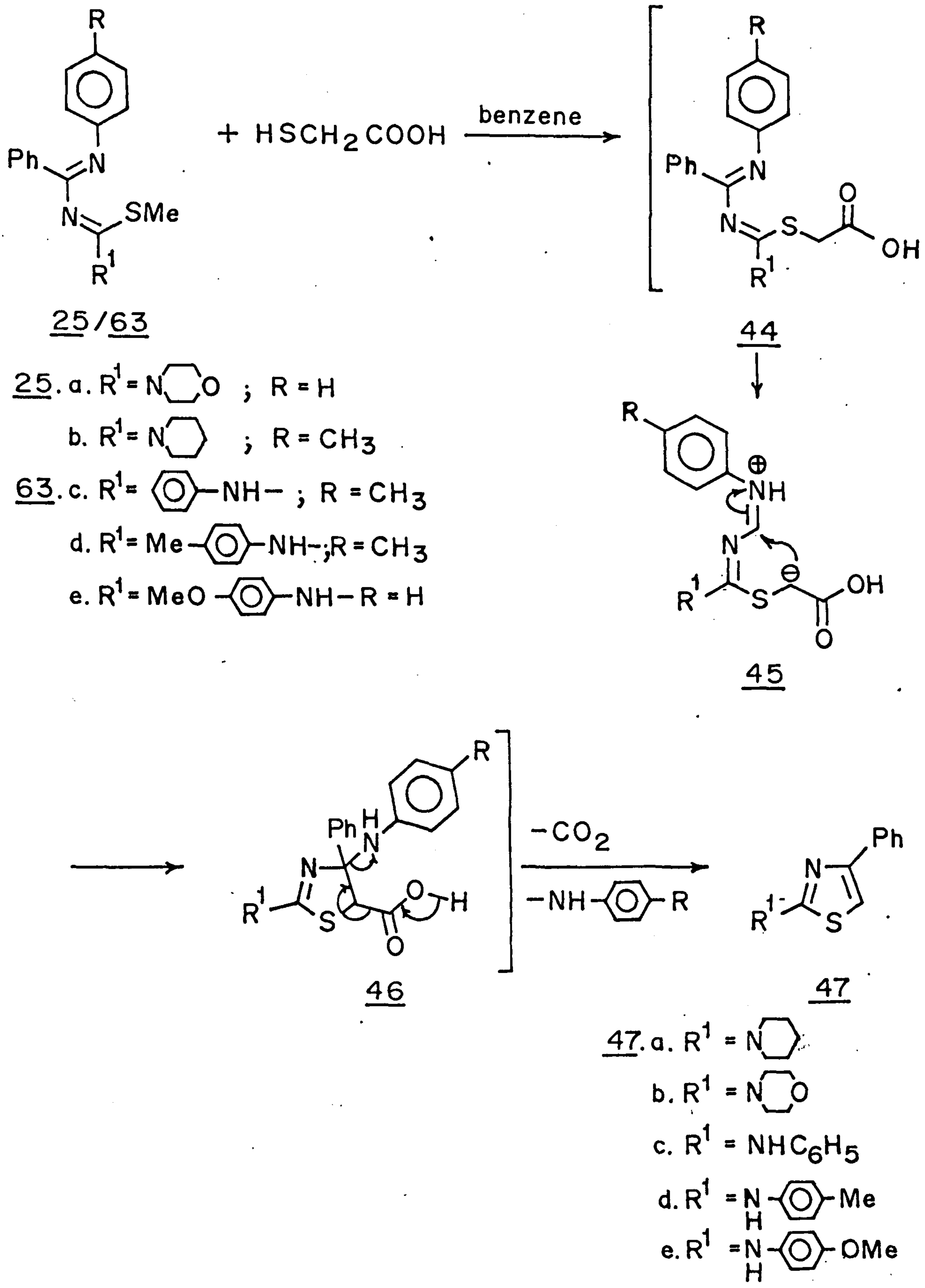
The structure **47** was assigned to these products on the basis of analytical and spectral data. The thiazole **47a**, for example, analysed for $C_{13}H_{14}N_2OS$, showed a molecular ion peak at m/z 246. Its **IR** spectrum exhibited a strong absorption band at 1531 cm^{-1} due to the -C=N group. Its ^{1}**H NMR** spectrum showed the absence of the methylthio group. In addition to aromatic protons, it also exhibited the presence of the vinylic proton around δ 6.78 and the morpholino group. ^{13}**C NMR** signals were also in agreement with the assigned structure **47a**.



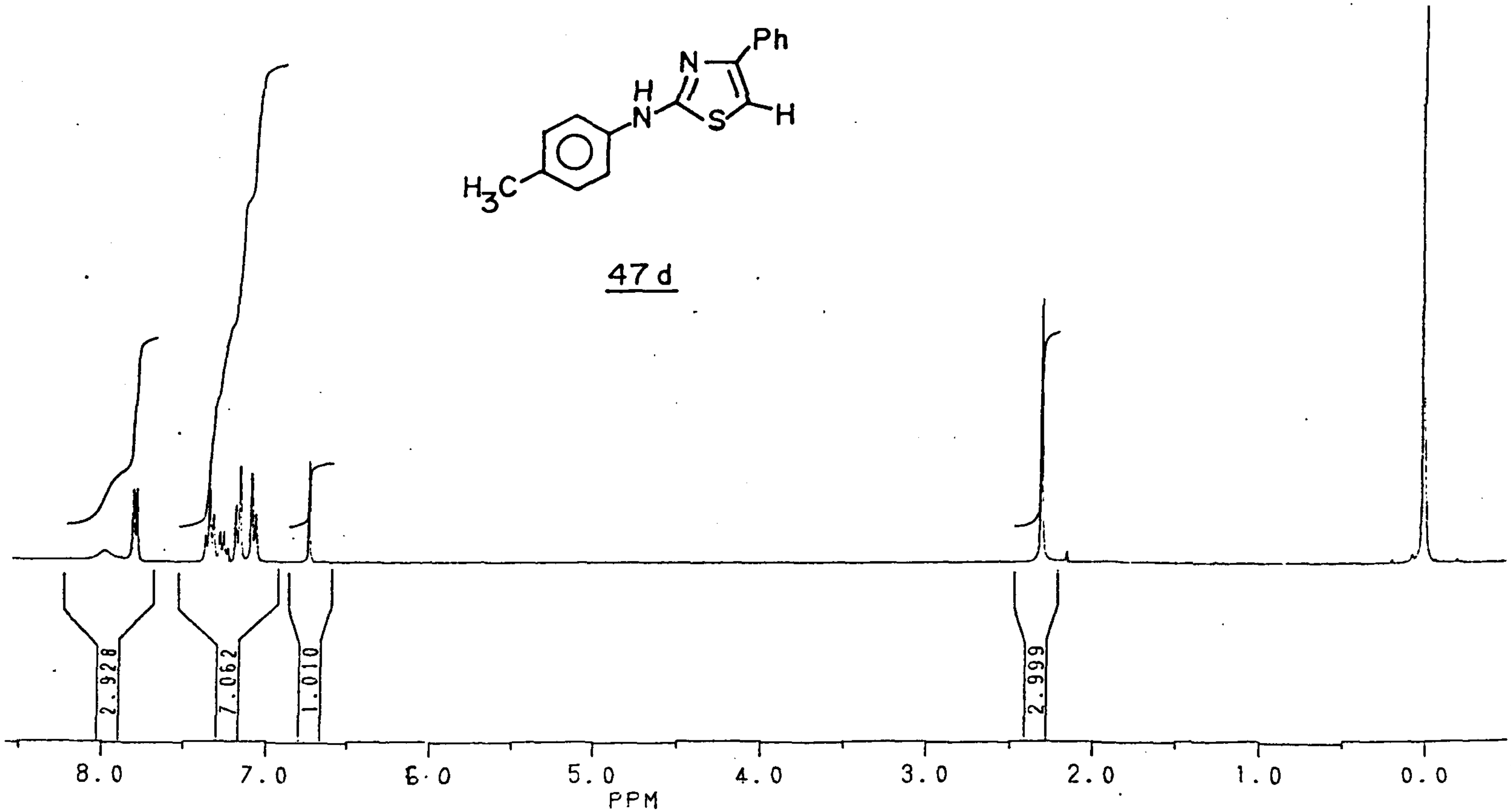
Scheme-11



Scheme -12


+ HSCH2COOH
benzene
25/63
44
45
46
47
−CO2
−NH−⟨◯⟩−R
25. a. R¹ = morpholino ; R = H
b. R¹ = piperidino ; R = CH3
63. c. R¹ = ⟨◯⟩−NH− ; R = CH3
d. R¹ = Me−⟨◯⟩−NH− ; R = CH3
e. R¹ = MeO−⟨◯⟩−NH− R = H
47. a. R¹ = piperidino
b. R¹ = morpholino
c. R¹ = NHC6H5
d. R¹ = NH−⟨◯⟩−Me
e. R¹ = NH−⟨◯⟩−OMe

Scheme -13

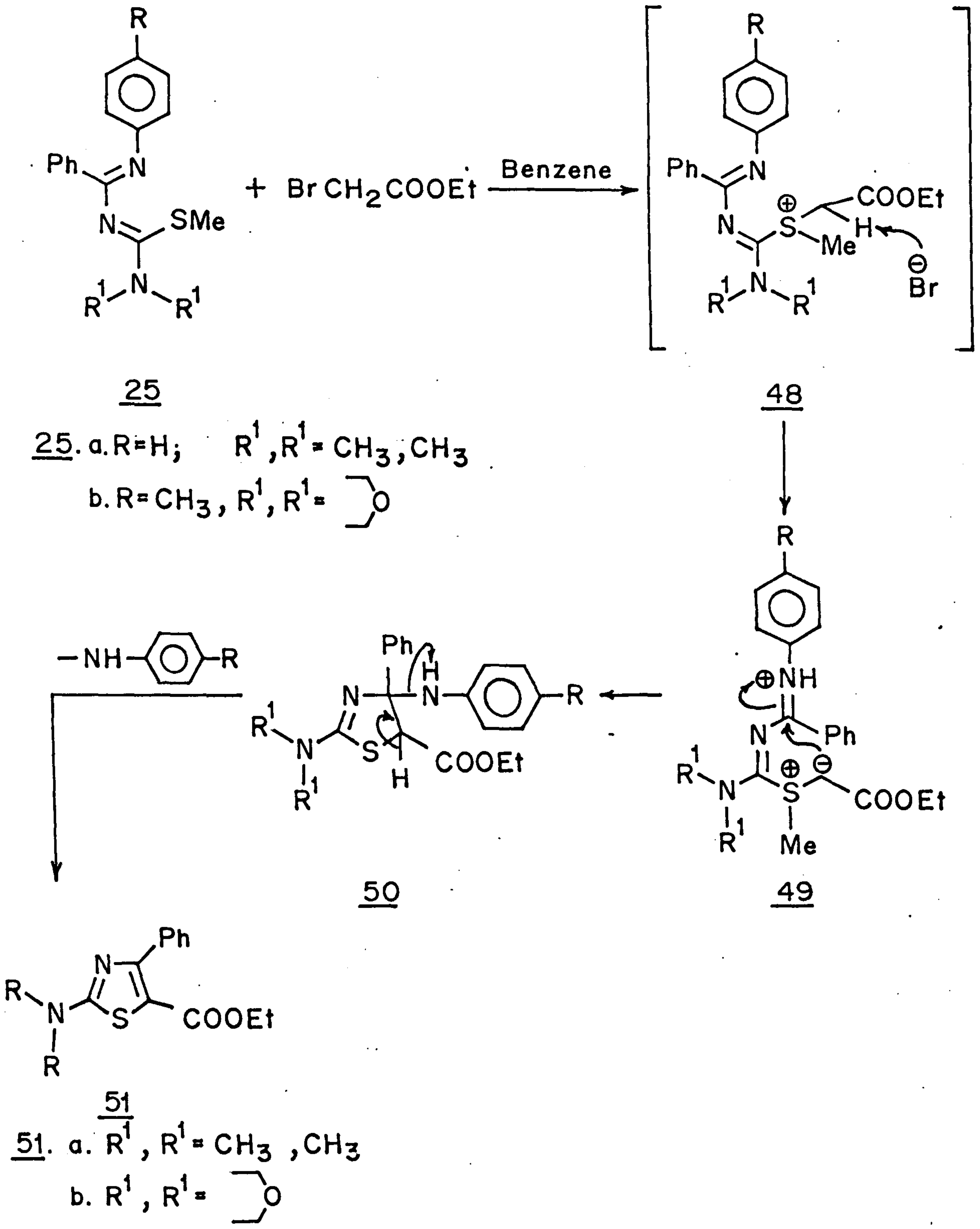


47 d

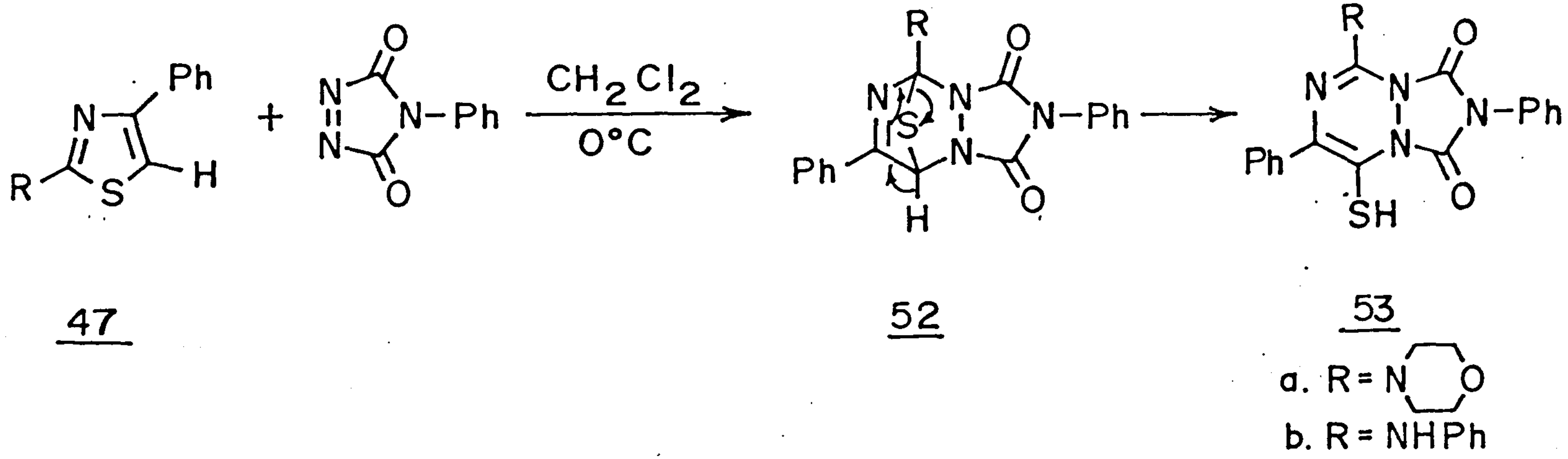
Another convenient method for the synthesis of thiazole derivatives involved the reactions of 1,3-diaza-1,3-butadienes **25** with bromo ethylacetate in refluxing benzene, in the presence of either DBU or few drops of DMF (to impart solubility of the salt formed), resulting in good yield of the thiazoles **51** (Scheme-14). The thiazoles **31** in these reactions are probably obtained via the initial formation of sulfonium salt **48.** The proton abstraction by bromide ion, demethylation of sulfonium salt, followed by cyclisation and deamination finally yields **51** via intermediates **49** and **50** (Scheme-14). Their **IR**, ^{1}**H NMR**, ^{13}**C NMR** and mass spectral data clearly established the assigned structure **51**. The product **51a**, for example, analysed for $C_{14}H_{16}N_2O_2S$, showed a molecular ion peak at m/z 276 in its mass spectrum. Its **IR** spectrum exhibited strong absorption bands at 1699 and 1570 cm^{-1} due to carbonyl and carbon- nitrogen double bonds, respectively. Its ^{1}**H NMR** spectrum in addition to aromatic protons, exhibited the presence of ethoxy group and N,N-dimethyl amino functions. Its ^{13}**C NMR** signals were also in agreement with the assigned structure.

The thiazole **47**, so obtained when reacted with 4-phenyl-1,2,4-thiazole-3,5-dione (PTDA) in methylene chloride at 0 °C, resulted in the synthesis of the corresponding Diels-Alder adduct **53** (Scheme-15).

The probable mechanism leading to the formation of **33** involves the initial [4+2] cycloaddition reaction of **47a** with 4-phenyl-1,2,4-triazolo-3,5-dione, generating the intermediate **52**, which on intramolecular rearrangements leads to the final product **53**. The products were characterised on the basis of analytical and spectral evidences. Thus, compound **53a** , for example, was analysed for $C_{21}H_{19}N_5O_3S$ and its mass spectrum showed a molecular ion peak at m/z 421. Its **IR** spectrum (KBr) showed a strong absorption peak at 1691 cm^{-1} due to the carbonyl group. Its ^{1}**H NMR** spectrum, in addition to aromatic protons, exhibited the presence of morpholino group and -SH group. It also showed the absence of the vinylic proton. Its ^{13}**C NMR** spectra was also in perfect agreement with the assigned structure.

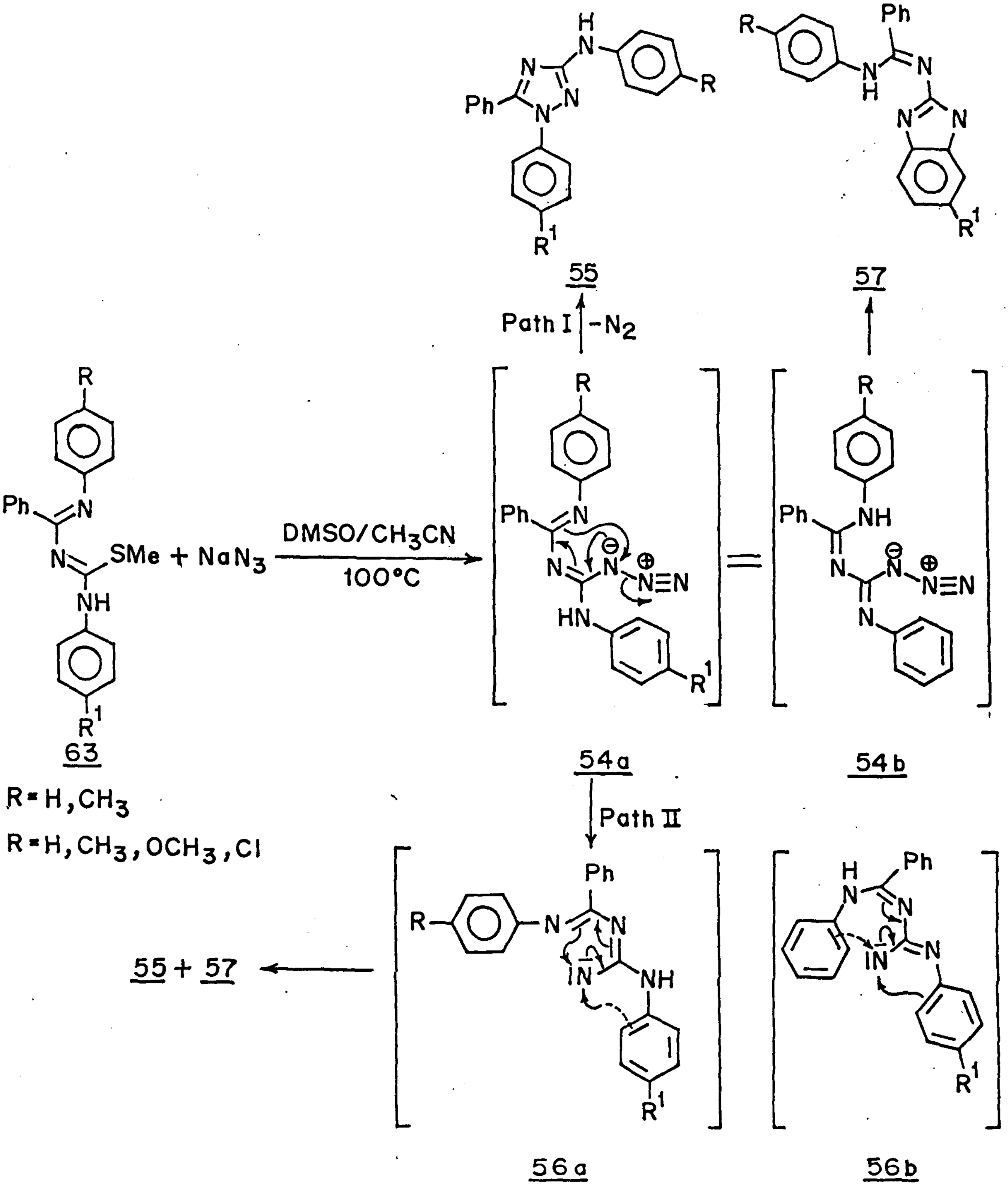

Benzene
BrCH2COOEt
25
48
49
50
51
25. a. R=H; R1,R1 = CH3,CH3
b. R=CH3, R1, R1 = O
51. a. R1, R1 = CH3 ,CH3
b. R1, R1 = O
—NH—C6H4—R
COOEt
Ph
SMe
Me
Br

Scheme-14

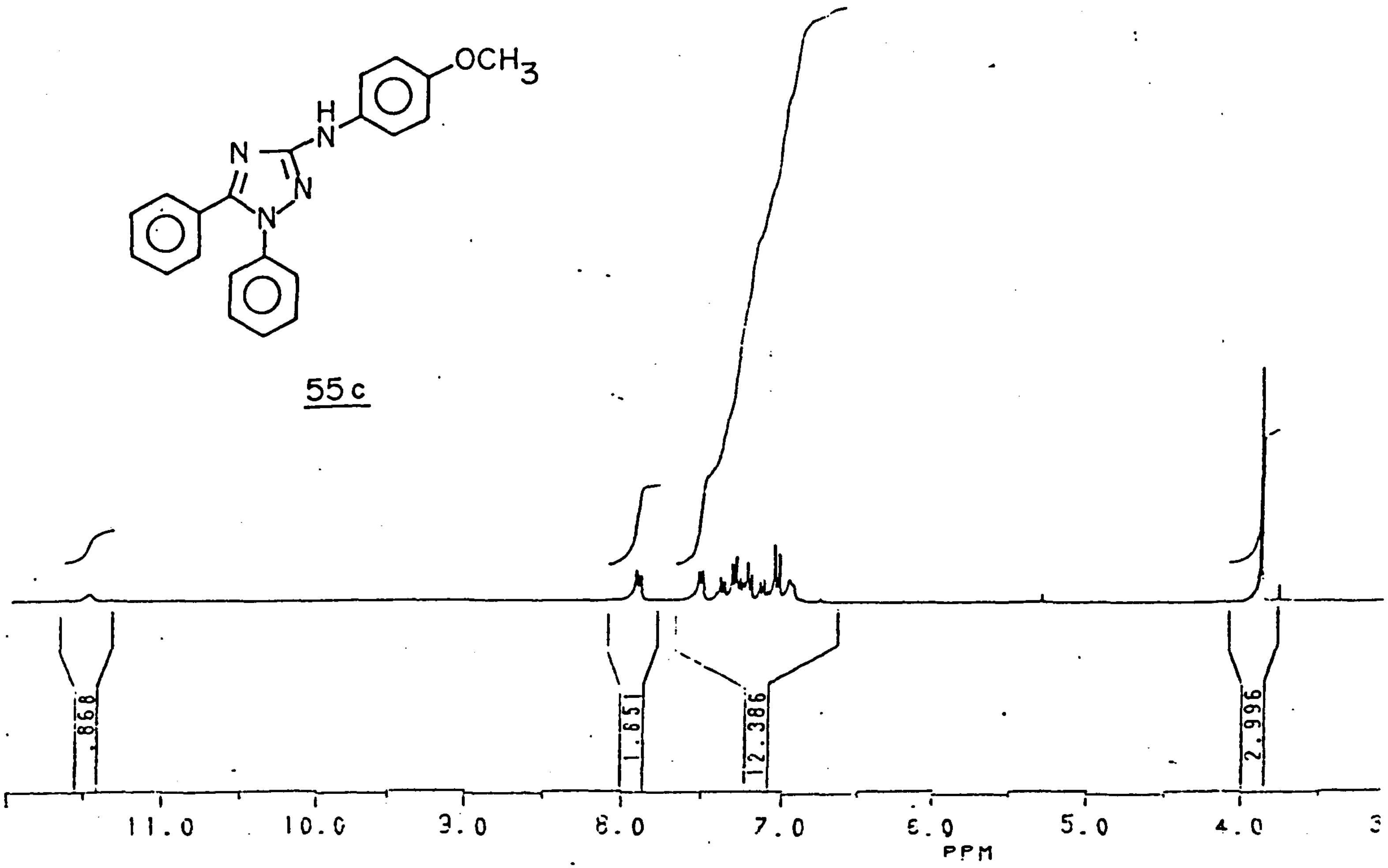


Scheme-15

Since many 1,2,4-triazoles are of biological interest, so much of the activities in the field revolve around improvements in synthetic methodologies and analogue preparations. Although a large number of 1,2,4-triazoles with a variety of substituents and functionalities are reported in the literature[12], there is no report of azide cycloadditions to diazabutadienes to give substituted triazoles. During the course of our studies on the 1,3-diaza-1,3-butadienes, which are shown to be useful precursors for the synthesis of a number of heterocycles, we utilized these dienes for the synthesis of the title 1,2,4-triazoles by their reactions with sodium azide and hydrazine hydrate respectively. Thus, the reactions of 1,3-diaza-1,3-butadienes **63** with sodium azide in dimethylsulfoxide /acetonitrite at 100°C affords good yields (80-85%) of products characterised as 1-aryl-3-arylamino-5-phenyl-1,2,4-triazoles **55** (Scheme-16). The formation of triazoles **55** may be explained by the mechanistic pathways depicted in Scheme-16. In this scheme, it is assumed that the nucleophilic displacement of methylthio group by the azide ion may lead to an intermediate **54a** (Scheme-16), which can also exist in its tautomeric form **54b**, and can follow a number of pathways. The intermediate **54a** may undergo concerted cyclisation and the extrusion of N_2 to yield triazoles **55** (Path I), whereas the tautomeric form **54b** by following a similar route may lead to benzimidazoles **57**. Alternatively, the intermediate **54** may lead to a nitrene intermediate **56a** and /or **56b** (Path.II) which, on electrocyclisation and nitrene insertion reaction, can yield 1,2,4-triazoles **55** and benzimidazoles **57**. The exclusive formation of triazoles **55**, as evidenced by **^{1}H NMR** and other spectral data, clearly indicates the preferential existence of **54a** over **54b**. Thus, it appears that the reaction prefers to follow path I, since the nitrene intermediate **56a** and/or **56b** (Path II) is expected to yield a mixture of triazoles **55** and benzimidazole **57**. The structure **55** was assigned to these products on the basis of analytical and spectral data. The triazole **55a** , for example, analysed for $C_{24}H_{16}N_4$ showed a molecular ion peak at m/z 312. Its **IR** spectrum exhibited strong absorption bands at 3441 and 1618 cm^{-1} due to -NH and -C=N groups, respectively. Its **^{1}H NMR** spectrum showed the presence of aromatic protons and -NH protons and absence of methylthio group. The **^{13}C NMR** signals were also in agreement with the assigned structure.


55
Path I
-N2
57
R
Ph
N
SMe
NaN3
NH
R1
63
R = H, CH3
R = H, CH3, OCH3, Cl
DMSO/CH3CN
100°C
54a
54b
Path II
55 + 57
56a
56b

Scheme -16

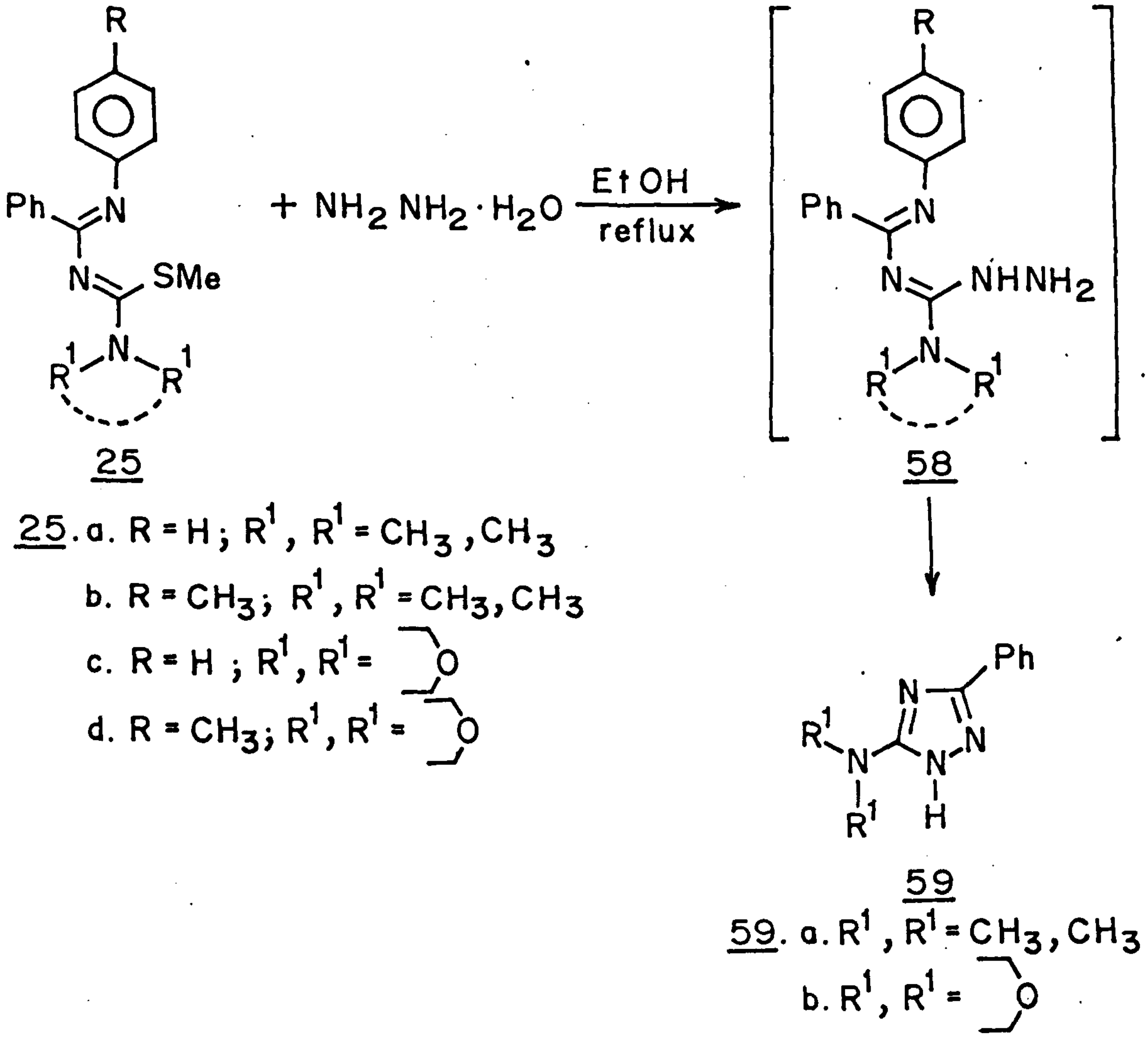


55c

Further, the reactions of 1,3-diaza-1,3-butadienes **25** with hydrazine hydrate in ethanol provided another facile route to good yields of 3-phenyl-5-secondary amino,1,2,4-triazoles **59**. The formation of these triazoles probably involves nucleophilic displacement of methylmercaptan by hydrazine hydrate to yield an intermediate **58**, which then undergoes intramolecular cyclocondensation to yield the desired products **50** (Scheme-17).

The structures of triazoles **59** were deduced on the basis of analytical and spectral data. The compound **59a**, for example, analysed for $C_{10}H_{12}N_4$ showed a molecular ion peak at m/z 188. Its IR spectrum exhibited strong absorption bands at 1611 and 3427 cm^{-1} due to -C=N and -NH groups respectively. The ^{1}**H NMR** spectrum of **59a** showed, in addition to aromatic and -NH protons, the presence of a signal due to the N,N-dimethylamino function. Its ^{13}**C NMR** spectra was also in perfect agreement with the assigned structure **59a**.

Continuing our interest in the preparation of five membered heterocycles, we report here the synthesis of functionalised 1,2,4-oxadiazoles from the corresponding 1,3-diaza-1,3-butadienes **25/63** and hydroxylamine hydrochloride. Thus, the treatment of 1,3-diaza-1,3-butadienes with hydrozylamine hydrochloride in pyridine at room temperature provided an easy route to the formation of substituted oxadiazoles **62** (Scheme-18). The formation of oxadiazoles **62** can be explained by an exchange reaction between the methylthio group of the azabutadiene and hydroxylamine group to give the intermediate **60** which undergoes electrocyclisation to yield another intermediate **61**, followed by deamination finally yields the desired oxadiazoles **62**. The products **62** were characterised on the basis of their mass, **IR**, ^{1}**H NMR** and ^{13}**C NMR** spectral data. The product **62a**, for example analysed for $C_{12}H_{13}N_3O_2$ showed a molecular ion peak at 255. Its **IR** spectrum exhibited strong absorption bands at 1621 and 931 cm^{-1} due to -C=N and N-O groups, respectively. The ^{1}**H NMR** spectrum of **62a**, in addition to aromatic proton signals, exhibited the presence of morpholino function. The structure **62a** was further supported by ^{13}**C NMR** spectral data.



25

58

59

25. a. $R = H$; $R^1, R^1 = CH_3, CH_3$

b. $R = CH_3$; $R^1, R^1 = CH_3, CH_3$

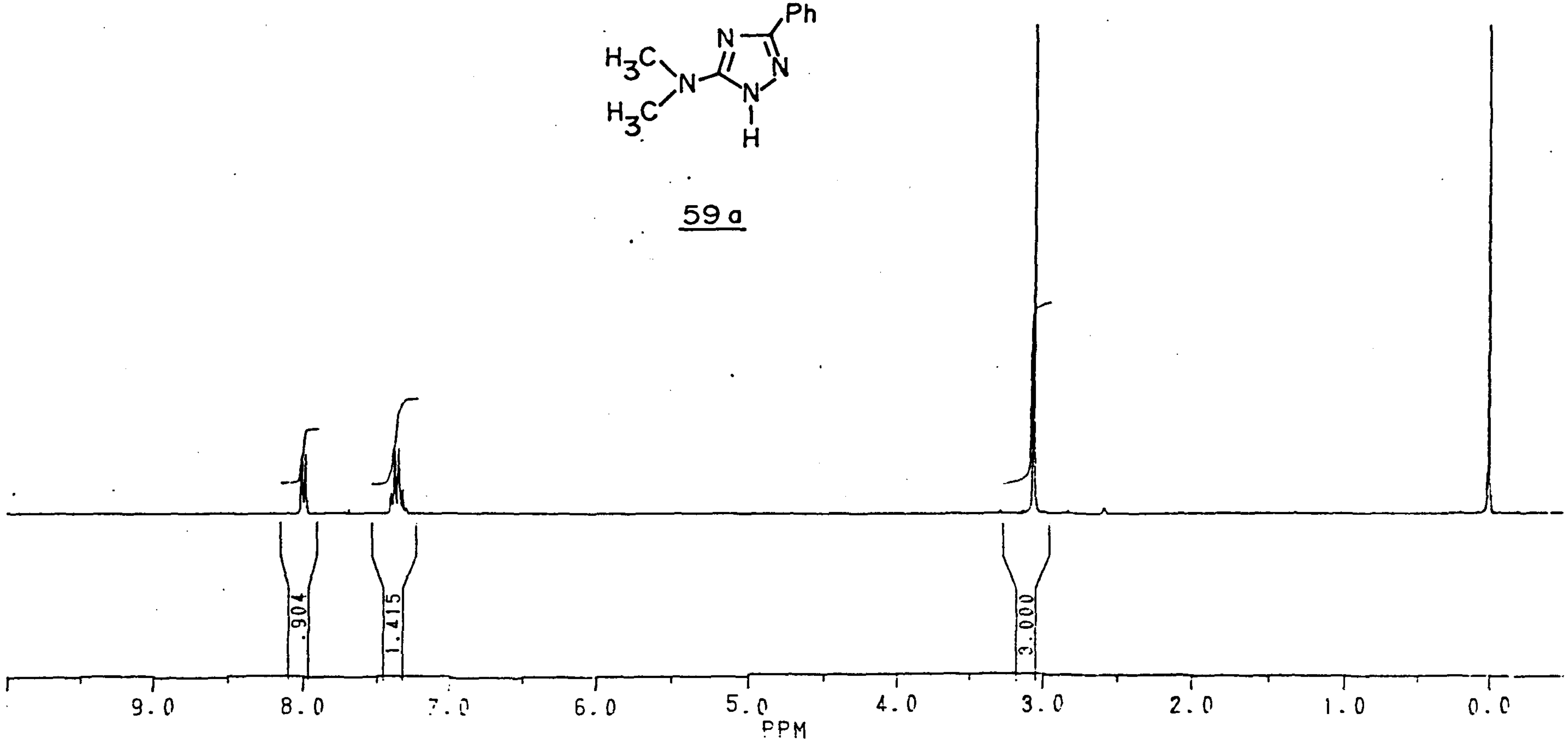
c. $R = H$; $R^1, R^1 =$

d. $R = CH_3$; $R^1, R^1 =$

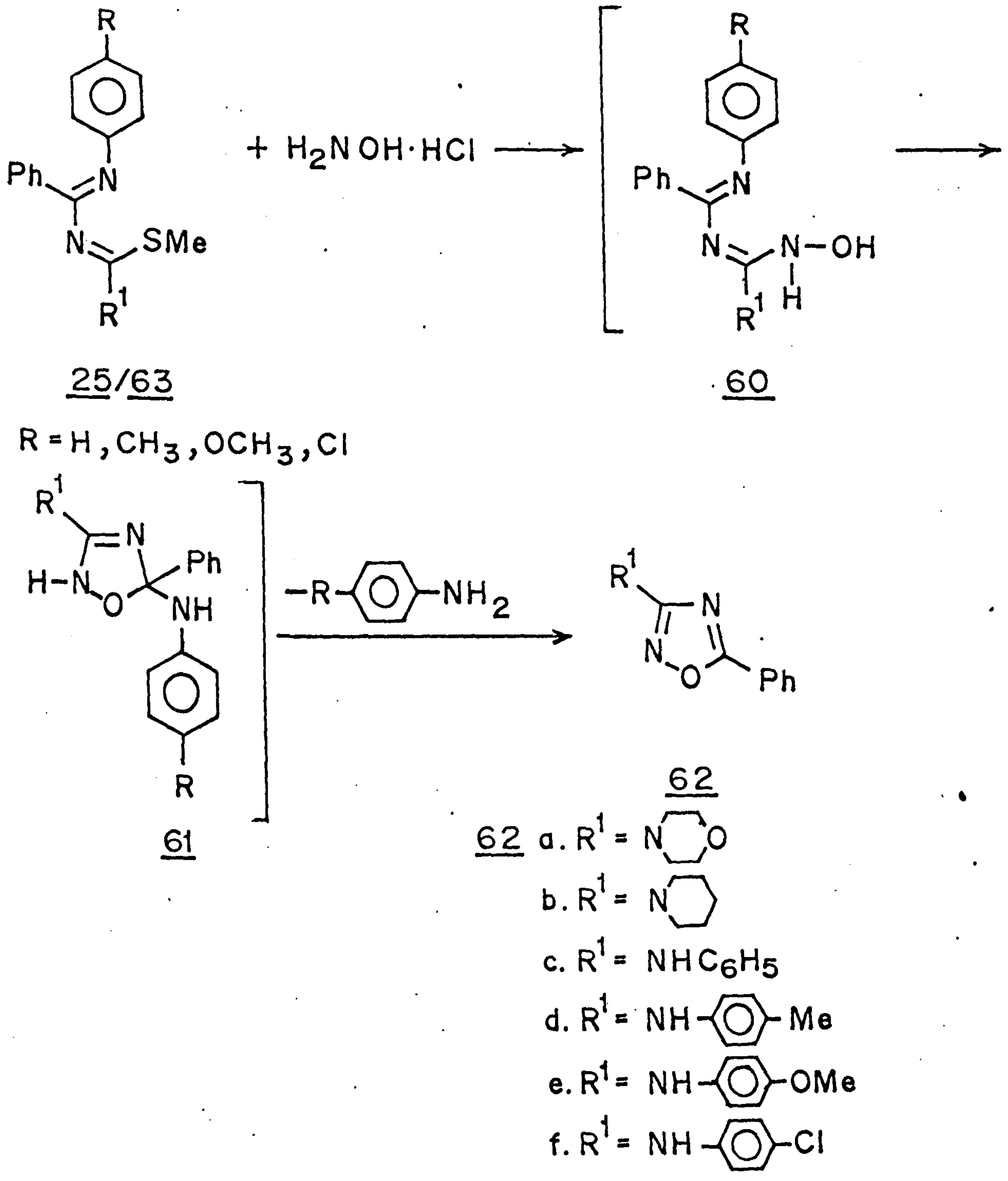
59. a. $R^1, R^1 = CH_3, CH_3$

b. $R^1, R^1 =$

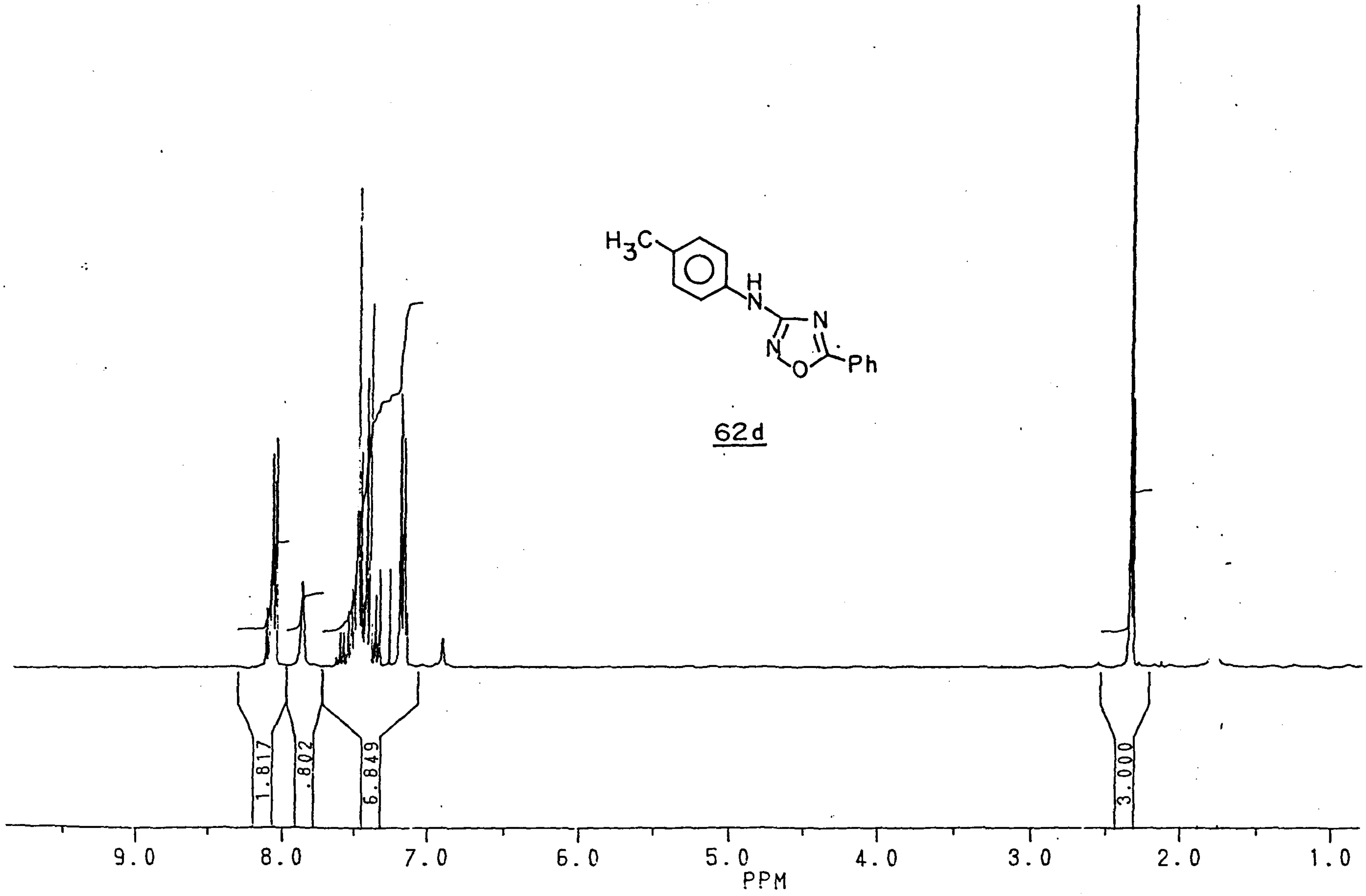
Scheme-17



59a


R
Ph
N
N
SMe
R1
+ H2NOH·HCl
N-OH
H
25/63
60
R = H, CH3, OCH3, Cl
R1
N
Ph
H-N
O
NH
R
61
-R-⟨○⟩-NH2
N
O
Ph
62
62 a. R1 = N⟨ ⟩O
b. R1 = N⟨ ⟩
c. R1 = NHC6H5
d. R1 = NH-⟨○⟩-Me
e. R1 = NH-⟨○⟩-OMe
f. R1 = NH-⟨○⟩-Cl

Scheme-18



62d

Thus, 1,3-diaza-1,3-butadienes have proved extremely useful in the synthesis of various five membered heterocycles. All the methods described herein are simple and regiospecific. The high yields obtained in all the instances and the availability of the starting materials make these syntheses the most convenient methods for their preparations.

Experimental Section

General conditions are the same as described in Chapter-I. All **^{1}H NMR** (300 MHz) and **^{13}C NMR** (75 MHz) spectra were recorded on Bruker ACF-300 spectrometer.

Starting Materials

All 1,3-diazabuta-1,3-dienes were prepared according to the reported procedures[34].

Cyclisation reactions of 1,3-diaza-1,3-butadienes: Triethylamine (0.01 mol) is added to a solution of N-arylamino-1,3-diaza-1,3-butadiene **63** (0.01 mol) in dry acetonitrile in a sealed tube. The mixture is heated to 150-160°C for 48-50 h, then poured into ice cold aqueous sodium bicarbonate (100 ml). This mixture is extracted with chloroform (3 x 20 ml), the extract is dried with sodium-sulfate and evaporated under reduced pressure and the product **20** is purified by recrystsllisation from hexane : chloroform (1:3) mixture.

2-Phenyl-4-(N-phenylamino)-quinazoline (20a): Yield 82%; m.p, 220-222°C; IR (KBr) ν 3460 (C=O), 1595 and 1568 cm^{-1} (C=N); ^{1}H NMR (300 MHz) δ 7.12-7.17 (m, 1H, arom), 7.36-7.49 (m, 7H, arom, NH), 7.66-7.90 (m, 5H, arom), 8.51-8.55 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 113.74, 12-0.21, 121.22, 123.95, 125.96, 128.36, 128.47, 128.91, 129.11, 130.23, 132.78, 138.55, 138.63, 150.94 (arom); 157.23 (C-4); 160.30 (C-2). Anal. calcd. for $C_{20}H_{15}N_3$: C, 80.81; H, 50.51; N, 14.14. Found : C, 80.78; H, 50.50; N, 14.01. ms m/z: 297 (M$^+$).

4-(p-Methoxyphenylamino)-2-phenylquinazoline (20b): yield 81%; m.p. 210-211°C; IR (KBr) ν 3449 (C=0), 1594 and 1554 cm^{-1} (-C=N); ^1H NMR (90 MHz) δ 2.43 (s, 3H, CH_3), 7.25-8.20 (m, 11H, arom, NH), 8.65-8.79 (m, 2H, arom). Anal. calcd. for $C_{21}H_{17}N_3$: C, 81.03; H, 5.47; N, 13.50. Found: C, 80.98; H, 5.42; N, 13.43. ms m/z: 311 (M^+).

4-(p-Methoxyphenylamino)-2-phenylquinazoline (20c): Yield 82%; m.p.250-252°C; IR (KBr) ν 3450 (C=0), 1595 and 1556 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 3.85 (s, 3H, OCH_3), 6.96-6.99 (d, 2H, arom, J = 9.0 Hz), 7.40-7.48 (m, 5H, arom, NH), 7.71-7.82 (m, 4H, arom), 7.95-7.98 (d,1H, arom, J = 9.0Hz), 8.49-8.53 (m, 2H, arom). ^{13}C NMR (75 MHz) δ 55.53 (-OCH_3); 113.72, 114.11, 120.29, 123.35, 125.87, 128.33, 128.45, 129.15, 130.19, 131.57, 132.74, 138.70, 150.95, 156.39 (arom); 157.50 (C-4); 160.41 (C-2). Anal. calcd. for $C_{21}H_{17}N_3O$: C, 77.06; H, 5.20; N, 12.84. Found: C, 77.02; H, 5.17; N, 12.80. ms m/z: 327 (M^+)

4-(p-Chlorophenylamino)-2-phenylquinoazoline (20d): yield 85%; m.p.232-234°C; IR (KBr) ν 3501 (C=0), 1593 and 1563 cm^{-1} (C=N); ^1H NMR (90 MHz) δ 7.15-8.05 (m, 12H, arom, NH), 8.45-8.68 (m, 2H, arom). Anal. calcd. for $C_{20}H_{14}N_3Cl$: C, 72.40; H, 4.22; N, 12.67. Found: C, 72.35; H, 4.19; N, 12.67. ms m/z: 331.5 (M^+).

4-(p-Chlorophenylamino)-6-methyl-2-phenylquinazoline (20e): yield 80%; m.p. 261-263°C; IR (KBr) ν 3451 (C=0), 1600, 1558, 1521 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 2.50 (S, 3H, -CH_3), 7.36-7.54 (m, 8H, arom, NH), 7.79-7.86 (m, 2H, arom); 8.46-8.49 (m, 2H, arom). ^{13}C NMR (75 MHz) δ 21.73 (-CH_3); 113.46, 119.25, 122.32, 128.28, 128.41, 128.66, 128.88, 130.17, 13.94, 136.26, 137.32, 138.55, 149.31 (arom), 156.57 (C-4); 159.41 (C-2). Anal. calcd . for $C_{21}H_{16}N_3Cl$: C , 72.94, H, 4.63; N, 12.16. Found: 72.91; H, 4.60; N, 12.08. ms m/z: 345.5 (M^+).

Reactions of 1,3-diaza-1,3-butadienes with thioglycolic acid: A solution of 1,3-diaza-1,3-butadienes **25** and **63** (10 m mol) in dry benzene was stirred with thioglycolic acid (10 m mol) for 8-10h. The reaction mixture was washed with sodium bicarbonate solution (3 x 50 ml) and then with water (3 x 100 ml), dried over Na_2SO_4 and the solvent removed under vacuo to give the crude product, which was further purified by column chromatography on silica gel (eluent: a mixture of ethylacetate and hexane in a 1:5 ratio) to yield pure thiazoles **47** in high yields.

2-Morpholino-5-phenyl-1,3-thiazole (47a): yield 80%; m.p. 69-70 °C; IR (KBr) ν 1531 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 3.49-3.53 (m, 4H, $-CH_2-N-CH_2-$), δ 3.80-3.83 (m, 4H, $-CH_2-O-CH_2-$), 6.78(s,1H, =CH-); 7.27-7.39 (m, 3H, arom), 7.81-7.84 (m, 2H, arom). ^{13}C NMR (75 MHz) δ 48.5 ($-CH_2-N-CH_2-$); 66.2 ($-CH_2-O-CH_2-$);, 101.7 (C-4), 126.0, 127.6, 128.5, 134.9 (arom); 51.8 (C-5), 172.2 (C-2). Anal,. calcd. for $C_{13}H_{14}N_2OS$: C, 63.39; H, 5.73; N,11.27. Found: C, 63.54; H, 5.69; N, 11.41. ms m/z: 246 (M^+).

2-Piperidino-5-phenyl-1,3-thiazole (47b): yield 83%; m.p. 66-67°C; IR (KBr) ν 1538 cm^{-1} (C=N); ^1H NMR (300 MHz) δ 2.55-2.83 (m, 6H, $-CH_2-CH_2-CH_2-$), 3.45-3.81 (m, 4H, $-CH_2-N-CH_2-$), 6.83 (s, 1H, =CH-), 7.40-7.63 (m, 3H, arom), 7.96-8.13 (m, 2H, arom). ^{13}C NMR (75 MHz) δ 25.1 ($-CH_2-CH_2-CH_2-$), 49.4 ($-CH_2-N-CH_2-$), 100.6 (C-4), 125.9, 127.3, 128.3, 135.1 (arom), 151.7 (C-5); 171.0 (C-2). Anal. calcd. for $C_{14}H_{14}N_2S$: C, 68.82; H, 6.60; N, 11.46. Found: C, 68.69; H, 6.66; N, 11.53. ms m/z: 244 (M^+).

2-(N-Phenylamino)-5-phenyl-1,3-thiazole (47c): yield 82%; m.p.128-130°C; IR (KBr) ν 1565 (C=N), 3481 cm^{-1} (NH); ^1H NMR (300 MHz) δ 6.81 (s, 1H, =CH-), 7.23-7.40 (m, 8H, arom), 7.83-7.86 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 101.7 (C-4), 122.9, 126.1, 127.9, 128.6, 129.4, 134.5 (arom); 1151.2 (C-5); 164.8 (C-2). Anal. calcd. for $C_{15}H_{12}N_2S$: C, 71.40; H, 4.79; N,11.10. Found: C, 71.29; H, 4.72; N, 11.21. ms m/z: 252 (M^+).

2-(p-Methylphenylamino)-5-phenylthiazole (47d): yield 82%; m.p. 110-112°C; IR (KBr) ν 1560 cm^{-1} (C=N); 3378 cm^{-1} (-NH); ^1H NMR (300 MHz) δ 2..31 (s ,3H, $-CH_3$); 6.73 (s, 1H, =CH-), 7.05-7.10 (m, 2H, arom); 7.24-7.37 (m, 3H, arom), 7.19 (m, 2H, arom), 7.24-7.37 (m, 3H, arom), 7.79-7.82 (m, 2H, arom); ^{13}C NMR

(75 MHz) δ 21.9 (-CH$_3$); 101.8 (C-4); 120.3, 127.0, 128.8, 129.0, 130.1, 133.3, 134.6 (arom), 151.3 (C-5); 164.1 (C-2). Anal. calcd. for $C_{16}H_{14}N_4S$: C, 72.15; H, 5.30; N, 12.03. Found : C, 72.29; H, 5.35; N, 11.95. ms m/z: 266 (M^+).

2-(p-Methoxyphenylamino)-5-phenylthiazole (47e): yield 80%; m.p. 159-160°C; IR (KBr) ν 1560 (C=N), 3377 cm^{-1} (-NH); ^{1}H NMR (300 MMz) δ 3.79 (s, 3H, -OCH$_3$); 6.69 (s,1H, =CH-); 6.82-6.86 (m, 2H, arom); 7.25-7.36 (m, 6H, arom). ^{13}C NMR (75 MHz) δ 55.1 (-OCH$_3$); 100.1(C-4); 121.7, 125.9, 127.5, 128.3, 133.4 (arom); 151.3 (C-5); 164.9 (C-2). Anal. calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92. Found: C, 68.18; H, 4.93; N, 10.02. ms m/z: 282 (M^+).

Reactions of 1,3-diaza-1,3-butadienes with bromoethylacetate: Method A: To a solution of 1,3-diaza-1,3-butadiene **25** (10 m mol) in dry benzene (25 ml), was added bromo ethylacetate (10 m mol) in dry benzene and stirred at room temperature for 4-6 h. DBU (12 m mol) was added, the reaction mixture refluxed for 5-6 h (monitored by tlc), cooled to room temperature, poured in water (50 ml), extracted with ethyl acetate (920 ml), washed with water (2 x 20 ml), dried over sodium sulfate and evaporated under reduced pressure to yield the crude product, which was chromatographed on silica gel using a mixture of hexane and ethylacetate (1:6) as eluent.

Method B: To a solution of 1,3-diaza-1,3-butadiene (10 m mol) in dry benzene (20 ml), was added a solution of bromo ethylacetate (10 m mol) in dry benzene (10 ml), and stirred at room temperature for 4-6 h. Few drops of DMF were added just to dissolve the salt formed and the reaction mixture heated at 100°C for 3-4h (monitored by tlc), followed by work-up as described in procedure A.

2-Dimethylamino-5-ethoxycarbonyl-4-phenylthiazole (51a): Yield 86%; m.p. 98-100°C; IR (KBr) ν 1699 (C=0), 1570 cm^{-1} (C=N); ^{1}H NMR (300 MHz) δ 1.23 (t, 3H, CH$_3$, J = 7.1Hz), 3.16 (s, 6H, H$_3$C-N-CH$_3$), 4.17 (q, 2H, -CH$_2$-, J = 7.1 Hz), 7.33-7.38 (m, 3H, arom); 7.69-7.74 (m, 2H, arom). ^{13}C NMR (75 MHz) δ 14.3 (-CH$_3$); 39.9 (-N(CH$_3$)$_2$), 135.0 (arom); 160.1 (C-5); 161.9 (C-2); 170.7 (C=0). Anal.

calcd. for $C_{16}H_{14}N_2O_2S$: C, 60.89; H, 5.81; N. 10.05. Found: C, 60.87; H, 5.82; N, 10.03. ms m/z: 276 (M^+).

5-Ethoxycarbonyl-2-Morpholino-4-phenylthiazole (51b): Yield 881%; m.p. 102-103°C; IR (KBr) ν 1676 (C=O), 1530 cm^{-1} (C=N); ^{1}H NMR (300 MHz) δ 1.24 (t, 3H, CH_3, J = 7.0Hz), 3.53-3.56 (m, 4H, -CH_2-N-CH_2-), 3.75-3.80 (-CH_2-O-CH_2-), 4.18 (q, 2H,-CH_2-, J= 7.0 Hz), 7.32-7.35 (m, 3H, arom), 7.66-7.71 (m, 2H, arom); ^{13}C NMR (75 MHz) δ 14.5(CH_3), 48.2 (-CH_2-N-CH_2-), 60.5 (-CH_2-), 66.1 (-CH_2-O-CH_2-), 127.5, 128.9, 130.1 (arom), 160.2 (C-5), 162.1 (C-2), 170.6 (C=O). Anal. calcd. for $C_{16}H_{18}N_2O_3S$: C, 60.36; H, 5.70, N, 8.80; Found: C, 60.33; H, 5.72; N, 8.73. ms m/z: 318 (M^+).

Reactions of thiazole with 4-phenyl-1,2-4-triazo-3,5-dione (PTAD): To a stirred solution of thiazole (1 m mol) in dry dichloromethane (30 ml) at 0°C was added PTAD (1 m mol) in portions over a period of 5 minutes. The solution was stirred at 0°C for an additional 10-15 minutes. Completion of the reaction was indicated by the decolourisation of the reaction mixture. The solvent was then removed under reduced pressure. The residue was recrystallised from hexane: chloroform (1:3) mixture.

7-Mercapto-4-morpholino-[1,2,4]triazolo[4.3.0] [1,2,4]triazine-2,9-dione (53a): Yield 98%; m.p. 181-183 °C; IR (KBr) ν cm^{-1} 1691(C=O); ^{1}H NMR (300 MHz) δ 2.15 (brs, 1H, SH), 3.49 (brs, 4H, -CH_2-N-CH_2-), 3.78 (brs, 4H, -CH_2-O-CH_2-), 7.35-7.47 (m, 10H, arom); ^{13}C NMR (75 MHz) δ 47.75 (-CH_2-N-CH_2-), 65.99 (-CH_2-O-CH_2-), 113.79, 125.46, 128.10, 128.46, 128.61, 128.98, 129.16, 130.83, 132.73 (arom); 151.93, 152.63, 168.44 (C=O). Anal. calcd. for $C_{21}H_{19}N_5O_3S$: C, 59.85; H, 4.54; N, 16.62. Found: C, 59.92; H, 4.51; N, 16.66. ms m/z: 421 (M^+).

4-(N-arylamino)-7-mercapto-[1,2,4]triazolo[4.3.0] [1,2,4]triazine-2,9-dione (53b): Yield 96% ; m.p. 230-232°C; IR (KBr) ν 1690 cm^{-1} (C=O). ^{1}H NMR (300 MHz) δ 2.14 (brs, 1H, SH), 7.31-7.90 (m, 16H, arom, NH); ^{13}C NMR (75 MHz) δ 114.70, 123.94, 127.40, 127.42, 127.87, 129.01, 129.39, 134.67 (arom), 151.40, 152.09, 166.80. Anal. calcd. for $C_{23}H_{17}N_5O_2S$: C, 64.64; H, 3.98; N, 16.40. Found : C, 64.72; H, 4.06; N, 16.32. ms m/z: 427 (M^+).

Reactions of 1,3-diaza-1,3-butadienes with sodium azide: To a solution of 1,3-diaza-1,3-butadienes (10 m mol) in acctonitrile (30 ml) was added a solution of sodium azide (10 m mol) in DMSO (15 ml) and the mixture was heated for reflux at 100°C for 15-16 h (monitored by tlc). The reaction mixture was then cooled to room temperature, poured into crushed ice (100 g), acidified with 20% acetic acid (15 ml) and extracted with chloroform (3 x 50 ml). The organic layer was washed with water (3 x 100 ml), dried over and anhydrous sodium sulphate and evaporated under reduced pressure to give an oily liquid, which was column chromatographed on silica gel using a mixture of hexane and ethylacetate (1:8) as eluent.

1,5-Diphenyl-3(phenylamino)-1,2-4-triazole (55a): Yield 80%; m.p. 138-140°C; IR (KBr) ν 1618 (C=N) and 3441 cm^{-1} (NH); ^1H NMR (300 MHz) δ 6.80-7.71 (m, 13H, arom), 7.92-8.15 (m, 2H, arom), 11.49 (brs, 1H, NH, exchangable with D_2O); ^{13}C NMR (75 MHz) δ 122.9, 124.3, 125.6, 128.1, 128.9, 129.0, 129.6, 130.6, 134.3, 134.8, 138.5 (arom), 155.9 (C-%), 161.4 (C-3). Anal. calcd. for $C_{20}H_{16}N_4$: C, 76.92; H, 5.13; N, 17.95. Found : C, 76.88; H, 5.08; N, 17.94. ms m/z: 312 (M^+).

1,5-Diphenyl-3-(p-methylphenylamino)-1,2,4-triazole (55b): Yield 83%; m.p. 131-133°C; IR (KBr) ν 1625 (C=N), 3442 cm^{-1} (-NH); ^1H NMR (300 MHz) δ 2.42 (s, 3H, $-CH_3$), 6.93-7.42 (m,10H, arom), 7.52 (d, J=7.3 Hz, 2H, arom), 7.89 (d, J = 8.3 Hz, 2H, arom), 11.47 (brs, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz) δ 21.2 ($-CH_3$); 123.0, 124.39, 125.7, 128.2, 129.1, 129.7, 130.9, 132.3, 134.3, 138.5, 138.6 (arom); 151.6 (C-5); 161.52 (C-3). Anal. calcd . for $C_{21}H_{18}N_4$: C 77.30; H, 5.52; N, 17.18. Found: C, 77.25; H, 5.50; N, 17.11. ms m/z: 326 (M^+).

1,5-Diphenyl-3-(p-methoxyphenylamino)-1,2,4-triazole (55c): yield 82%; m.p. 149-151°C ; IR (KBr) ν 1611 (C=N), 3427 cm^{-1}(-NH). ^1H NMR (300 MHz) δ 3.89 (s, 3H, $-OCH_3$), 6.91-7.64 (m,12H, arom), 7.94-8.06 (m, 2H, arom), 11.60 (brs, 1H, NH- exchangeable with D_2O); ^{13}C NMR (75 MHz) δ 55.5 ($-OCH_3$), 124.4, 124.6, 125.6, 127.8, 128.2, 129.0, 29.7, 130.7, 134.3, 138.6 (arom);156.0 (C-5), 159.6, 161.4 (C-3). Anal. calcd. for $C_{21}H_{18}N_4O$: C, 73.62; H, 5.26; N,16.37. Found: C, 73.62; H, 5.22; N, 16.33. ms m/z: 342 (M^+).

1-(p-Methylphenyl)-3-(p-chlorophenylamino)-5-phenyl-1,2,4-trizole (55d): Yield 80% ; m.p. 143-145°C; IR (KBr) ν 1612 cm^{-1} (C=N), 3431 cm^{-1}(-NH). ^1H NMR (300 MHz) δ 2.29 (s, 3H, $-CH_3$); 7.00-7.52 (m, 11H, arom); 8.03-8.06 (m, 2H, arom); 11.41 (brs, 1H, NH-exchangeable with D_2O). ^{13}C NMR (75 Mhz) δ 20.9 ($-CH_3$); 123.0, 124.1, 124.2, 124.4, 128.3, 128.5, 129.3, 129.6, 129.7,130.8, 134.3, 135.8 (arom); 156.2 (C-5); 161.9 (C-3). Anal. calcd. for $C_{21}H_{17}N_4Cl$: C, 69.90; H, 4.72; N, 15.53; Found: C, 69.87; H, 4.60; N, 15.49. ms m/z : 360 (M^+).

Reactions of 1,3-diaza-1,3-butadienes with hydrazine hydrate: To a solution of 1,3-diaza-1,3-butadienes (10 m mol) in absolute ethanol (25ml) was added hydrazine hydrate (5 ml, 90%) and the reaction mixture was refluxed for 2h, till the starting material disappeared completely (monitored by tlc). The reaction mixture was then poured into water (100 ml), extracted with chloroform (2 x 100 ml), and the combined extracts were washed with water (2 x 70 ml), dried over anhydrous sodium sulphate, and evaporated under reduced pressure to give a viscous oil, which was column chromatographed on silica gel using a mixture of hexane and ethyacetate (5:1) as eluent.

5-(N,N-Dimethylamino)-3-phenyl-1,2,4-trizole (59a): Yields 75%; m.p. 212-214°C; IR (KBr) ν 1611 (-C=N) and 3427 cm^{-1}(-NH); ^1H NMR (300 MHz) δ 3.03 (s, 6H, CH_3-N-CH_3); 7.32-7.41 (m, 3H, arom); 7.98-8.01 (m, 2H, arom);; 11.39 (brs, 1H, -NH). ^{13}C NMR (75 MHz) δ 38.62 (-N $(CH_3)_2$), 125.93, 128.23, 128.23, 128.52, 129.40 (arom), 157.51 (C-3), 162.50 (C-5). Anal. calcd. for $C_{10}H_{12}N_4$: C, 63.81; H, 6.43; N, 29.78. Found: C, 63.79; H, 6.35; N, 29.73. ms m/z: 188 (M^+).

5-Morpholino-3-phenyl-1,2,4-trizole (59b): yield 72%; m.p. 232-233°C; IR (KBr) ν 1624 (-C=N), 3439 cm^{-1} (-NH); ^1H NMR (300 MHz) δ 3.20-3.31 (m, 4H, $-CH_2$-N-CH_2-), 3.62-3.79 (m, 4H, $-CH_2$-O-CH_2-), 7.32-7.40 (m, 3H, arom); ^{13}C NMR (75

MHz) δ 46.59 (-CH_2-N-CH_2), 65.93, (-CH_2-O-CH_2-), 157.69 (C-3), 162.50 (C-5). Anal. calcd. for $C_{12}H_{14}N_4O$: C, 62.59; H, 6.13; N, 24.33. Found: C, 62.58; H, 6.07; N, 24.30. ms m/z : 230 (M^+).

Reactions of 1,3-diaza-1,3-butadienes with hydroxylamine hydrochloride: Hydroxylamine hydrochloride (10 m mol) was added to a solution of 1,3-diaza-1,3-butadienes (10 m mol) in 60 ml of pyridine at room temperature and the mixture was stirred for 5-6 h (monitored by tlc). The reaction mixture was then slowly poured into ice-cooled 4N H_2SO_4 (150 ml) and extracted with ether (2 x 80 ml) . The organic layer was then dried over anhydrous sodium sulphate, filtered and evaporated to yield the crude product which was recrystallised from hexane and ether (1:5) mixture.

3-Morpholino-5-phenyl-1,2,4- oxadiazoles (62a): yield 76% ; m.p. 103-105°C; IR (KBr) ν 1621 (C=N) and 931 cm^{-1}(N-O); ^1H NMR (300 MHz) δ 3.51-3.55 (m, 4H,-CH_2-N-CH_2-), 3.80-3.84 (m, 4H, -CH_2-O-CH_2-), 7.42-8.08 (m, 5H, arom); ^{13}C NMR (75 MHz) δ 46.29 (-CH_2-N-CH_2-), 66.23 (-CH_2-O-CH_2-), 124.56, 127. 118, 127.18, 127.56, 128.94, 132.51(arom), 167.74 (C-5), 169.56 (C-3). Anal. calcd. for $C_{12}H_{13}N_3O$: C, 56.47; H, 5.10; N, 16.47. Found: C, 56.41; H, 5.02; N, 16.43. ms m/z: 255 (M^+).

5-phenyl-3-piperidino-1,2,-4-oxadiazole (62b): Yield 78%; m.p. 78-80°C; IR (KBr) ν 1615 (C=N) and 925 cm^{-1}(N-O). ^1H NMR (300 MHz) δ 1.67 (brs, 6H,-CH_2-CH_2-CH_2-), 3.56-3.70 (m, 4H, -CH_2-N-CH_2-), 7.25-7.43 (m, 5H, arom); ^{13}C NMR (75 MHz) δ 24.62 (-CH_2-), 26.39 (2x-CH_2-), 50.69 (-CH_2-N-CH_2-), 122.50, 128.17, 129.16, 131.97, 137.05 (arom), 166,.73 (C-5), 169.99 (C-3). Anal. calcd. for $C_{13}H_{15}N_3O$: C, 68.12; H, 6.55; N, 18.34. Found: C, 68.10; H, 6.59; N, 18.33 ms m/z: 299 (M^+).

3-(N-phenylamino)-5-phenyl-1,2,4-oxadiazole (62c):-Yield 76%; m.p. 126-128°C; IR (KBr) ν 1659 (C=N), 3407 (-NH) and 927 cm^{-1} (N-O); ^{1} H NMR (300 MHz) δ 7.16-8.12 (m, 10H, arom), 7.95 (brs, 1H, NH); ^{13}C NMR (75 MHz) δ 117.3, 122.1, 124.0, 127.4, 129.1, 132.8, 137.0, 139.0 (arom); 168.1, 168.9. Anal. calcd. for

$C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.82; H, 4.62; N, 17.69 ms m/z: 237 (M^+).

3-(p-Methylphenylamino)-5-phenyl-1,2,4-oxadiazole (62d): Yield 78%; m.p. 141-143°C; IR (KBr) ν 1655 (C=N), 3389 (-NH) and 927 cm^{-1} (N-O); ^1H NMR (300 MHz) δ 2.34 (s, 3H, $-CH_3$), 7.15-7.36 (m, 4H, arom), 7.38-8.07 (m, 5H, arom), 7.86 (brs, 1H, -NH); ^{13}C NMR (75 MHz) δ 20.8 ($-CH_3$), 117.4, 127.4, 128.7, 129.1, 129.9, 131.0, 133.0, 134.4 (arom), 168.2, 168.4. Anal. calcd. for $C_{15}N_{13}N_3O$: C, 71.71; H, 5.18; N, 16.73. Found: C, 71.59; H, 5.11; N, 16.91. ms m/z : 251 (M^+).

3-(p-Methoxy phenylamino)-5-phenyl-1,2,4-oxadiazole (62e): Yield 77%; m.p. 143-144°C; IR (KBr) ν 1653 (C=N), 3389 (NH) and 926 cm^{-1} (N-O); ^1H NMR (300 MHz) δ 3.81 (s, 3H, OCH_3), 6.89-6.94 (m, 2H, arom), 7.36-7.59 (m, 5H, arom), 8.02-8.08 (m,2H,arom), 7.85 (brs , 1H, -NH); ^{13}C NMR (75 MHz) δ 55.5 ($-OCH_3$), 119.13, 120.7, 128.0, 128.7, 129.1, 130.1, 132.7,156.5 (arom), 168.3, 168.5. Anal. calcd. for $C_{15}H_{13}N_3O_2$: C, 67.42; H, 4.87; N, 11.73. Found: C, 67.56; H, 4.81; N, 11.68 ms m/z: 267 (M^+).

3-(4-chlorophenylamino)-5-phenyl-1,24-oxadiazole (62f): Yield 78%; m.p. 185-187°C; IR (KBr) ν 1651 (C=N), 3405 (-NH) and 929 cm^{-1} (N-O); ^1H NMR (90 MHz) δ 7.28-7.61 (m, 7H, arom), 8.04-8.09 (m, 2H, arom), 7.84 (brs, 1H, NH). Anal. calcd. for $C_{14}H_{10}N_3OCl$: C, 61.89; H, 3.71; N, 15.47. Found: C, 61.79; H, 3.77; N, 15.39. ms m/z.: 271 (M^+).

References

1. O.Y. Magidson and Y.K. Lu, *Zhur. Obshcher. Khim.* 1959 **29**, 2843; *Chem. Abstr.* **54**, 12144, 1960.

2. K. Asano and S. Asai, *Yakugaku Zasshi* **78**, 450, 1958 (English summary) and *Chem. Abstr.* 1958, **52**, 18428 ; L. Niepp, W. Kung and R. Meier, *Experientia* **13**, 74,1957.

3. D.A. Cox , *German Patent*, **1**, 918, 514, 1969 (CA, 1970, **72**, 79086,).

4. A.G. Farbwerke Hoechst, *French Patent*, **3**, 806, 1966 (CA, 1969, **71**, 91518,)

5. H.Olt, *Swiss Patent*, 491,134, 1970 (CA, 1970, **73**, 120668,).

6. A.J. Barker, F.T. Boyle, L. Henneguin, A.Francais, *Brit. U.K. Pat. Appl. GB*, **2**, 271, 111 (06 Apr 1994).

7. E. Cohen, B. Klarberg, J.R. Vaugham, *J. Am.Chem.Soc.*, 1960, **82**, 2731.

8. a). G.K. Treleaven, J. Thomas, *`Prescription Proprietaries guide'*, Australian Pharmaceutical Publishing Co., Melbourne, 10th edn., 1981, p. 202.
   b). M.C. Koshy, D. Mickley, J. Bourgoignie, M.D. Blaufox, *Circulation*, 1977, **55**, 533.

9. E.Rossi, R.Stradi, *Synthesis*, 1989, 214.

10. E. Rossi, R. Stradi, P. Visentin, *Tetrahedron*, 1990, **46**, 3581.

11. E. Rossi, G. Celentano, R. Stradi and A. Stradi. *Tet. Lett.*, 1990, **31**, 903.

12. a). H. Erlenmeyer, P. Schmidt, *Helv. Chim. Acta*, 1946, **29**, 1957.
    b). H. Erlenmeyer, K, Degan, *Helv. Chim. Acta.*, 1947, **30**, 592.
    c). H. Gregory, L.F. Wiggins, *J. Chem. Soc.*, 1947, 1400.

13. M. Paetzel, A. Schulz, J. Liebscher, W. Richter, M. Richter, *J. Het. Chem.*, 1992, **29**(5), 1209 (e\Eng).

14. M.T.Cocco, V.Onnis, *Synthesis*, 1993, 199

15. A.S.Patil, G.Bagavant, *J. Ind. Chem. Soc.*, 1994, **71**(4), 205.

16. T. Arulmoli, B.G. Khadsi, *Ind. J. Pharm. Sci.*, 1994, **56**(5), 192.

17. N.M. Shah, V. Joshi, *Ind. J. Het. Chem*, 1994, **4**(1), 59.

18. a) M. De Gregorio, *Penminerva Med.*, 1962, **4**, 90.

b) F. Eloy, R. Lenaers, *Bull. Chem. Therap*, 1966,347.
c) J. Sterne, C, Hirsch, Therapie, 1965, 20, 89.
d) K. Harsanyi, P. Kiss, D. Korbonits, I.R. Malyata, *Arzneim-Forsch*, 1966, **16**, 615. *Chem. Abstr.* 1969, **70**, 37724 .

19. D.J. Triggle, Y.M. Kwon, P. Abraham, M.A. Rahman, F.I. Carroll, *Pharm. Res.*, 1992, **9(11)**, 1474.

20. D. Korbonits, E. Tobias-Heza, K. Simon, G. Kramer, P. Kolonits, *J. Chem. Soc., Perkin Trans.*, 1992, **1**, 3069.

21. M. Patsch, H. Eilingsfeld, Ger. Pat., 1949295, 1971 (*Chem. Abstr.*, 1971, 75, p 7417y).

22. J. Metzger, A.R. Kartitzky, C.W. Rees, *Comprehensive Heterocyclic Chemistry*, Vol. 6, Pergamon Press, New York, 1984, P. 235-333 and references therein.

23. J.B. Polya, A.R. Katritzky, C.W. Rees, *Comprehensive Heterocyclic Chemistry*, Vol. 5, Pergamon Press, New York, 1984, P. 733-790 and references therein.

24. L.B. Clapp, A.R. Katritzky, C.W. Rees, *Comprehensive Heterocyclic Chemistry*, Vol. 6, Pergamon Press, New York, 1984, P. 365-392 and references therein.

25. S. Buscemi, V. Frenna, T. Caronna and N. Vivona, *Heterocyclies*, 1992, **34 (12)**, 2313.

26. C. Balsamini, A. Bedini, G.Spadoni, *Tetrahedron*, 1994, **50**, 3773.

27. a). A.K. Sharma, M.P. Mahajan, *Tetrahedron*, 1997, **53**, 13841 and references therein.
b) E. Rossi, G. Abbiati, E. Pini, *Tetrahedron*, 1997, **53**, 14017 and references therein.

28. a). J. Barluenga, M. Thomas, A. Ballesteros, A. Lopez, *Tetrahedron Lett.*, 1989, **30**, 4573.
b) E. Rossi, R. Stradi, P. Visentin, *Tetrahedron*, 1990, **46**, 3581.

29. J. Barluenga, M. Thomas, A. Ballesteros, L.A. Lopez, Synthesis, 1989, 228.

30. B. Sain, S.P. Singh, J.S. Sandhu, *Tetrahedron*, 1992, **48**, 4567.

31. a). A. Guzman, M. Romero, F.X. Talamas, R. Villena, R. Greenhouse, M. Muchowski, *J. Org. Chem.*, 1996, **61**, 2470.
b). I. Ibnasud, E.J.P. Malar, N. Sundaram, *Tetrahedron Lett.*, 1990, **31**, 7357.

32. G. Morel, E. Marchand, A. Foucaud, L. Toupet, *J. Org. Chem.*, 1989, **54**, 11185.

33. E. Rossi, D. Calabrese, F. Farma, *Tetrahedron*, 1991, **47**, 5819.

34. a). S.N. Mazumdar, M.P. Mahajan, *Synthesis*, 1990, 417.b). P.D. Dey, A.K. Sharma, S.N. Rai, M.P. Mahajan, *Tetrahedron*,1995, **51**, 7459.

List of publications

1. Synthesis and Regioselective[4+2] Cycloaddition/Nucleophilic Reactions of N-Arylamino-1,3-Diaza-1,3-Butadienes with Ketenes and accompanying rearrangements. Part I.

   Paramita D. Dey ,A.K. Sharma, S.N. Rai and M.P. Mahajan. *Tetrahedron*, **1995**, 51, 7459.

2. Regioselective [4+2] Cycloaddition versus Nucleophilic Reactions of N-Arylamino substituted 1,3-Diaza- 1,3- Butadienes with Ketenes : Synthesis of Pyrimidinones and Pyrimidinone Derivatives. Part II.

   Paramita D. Dey, A.K. Sharma, P.V. Bharatam and M.P. Mahajan. *Tetrahedron*, **1997**, 53, 13829.