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PARENTS

CYCLOADDITION REACTIONS OF VARIOUS 1, 3-DIAZA-1, 3-BUTADIENES AND IMINES IN HETEROCYCLIC SYNTHESIS

By

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A THESIS

Submitted in Fulfilment of the Requirements for

The Degree of

Doctor of Philosophy

TO

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I certify that the Thesis entitled ***"Cycloaddition Reactions of Various 1,3-Diaza-1,3-Butadienes and Imines in Heterocyclic Synthesis"*** submitted by Mr. Arun Kumar Sharma for the degree of Doctor of Philosophy of the North-Eastern Hill University, Shillong, embodies the record of original investigation carried out by him under my supervision. He has been 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 : 30 September 1996

Signature of the Supervisor

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This is to certify that Mr. Arun Kumar Sharma has satisfactorily completed the following Pre-Ph.D. Courses prescribed by the University:

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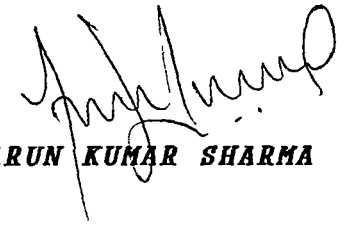

ARUN KUMAR SHARMA

CONTENTS

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CHAPTER—I

Cycloaddition Reactions of various 1,3-Diaza-1,3-Butadienes with Conjugated and Chloroketenes

I.1: *General Introduction*

The Diels-Alder cycloaddition reaction, discovered in 1920s by Otto Diels and Kurt Alder in Germany,[1] is the most widely used and best known pericyclic reaction which turned out to be an important tool in synthetic organic chemistry.[2] It has been the subject of extensive preparative,[3-10] theoretical,[11,12] and mechanistic[13] studies contributing towards the ease and predictability with which these reactions may be carried out. For the recent dramatic advances in organic synthesis which have been accompanied by ever increasing pressures to attain greater levels of stereochemical control, the Diels-Alder cycloaddition has proved to be extremely useful. For many years, the capture of a diene by a dienophile was recognised to be capable of generating as many as four contiguous stereogenic centers in a single

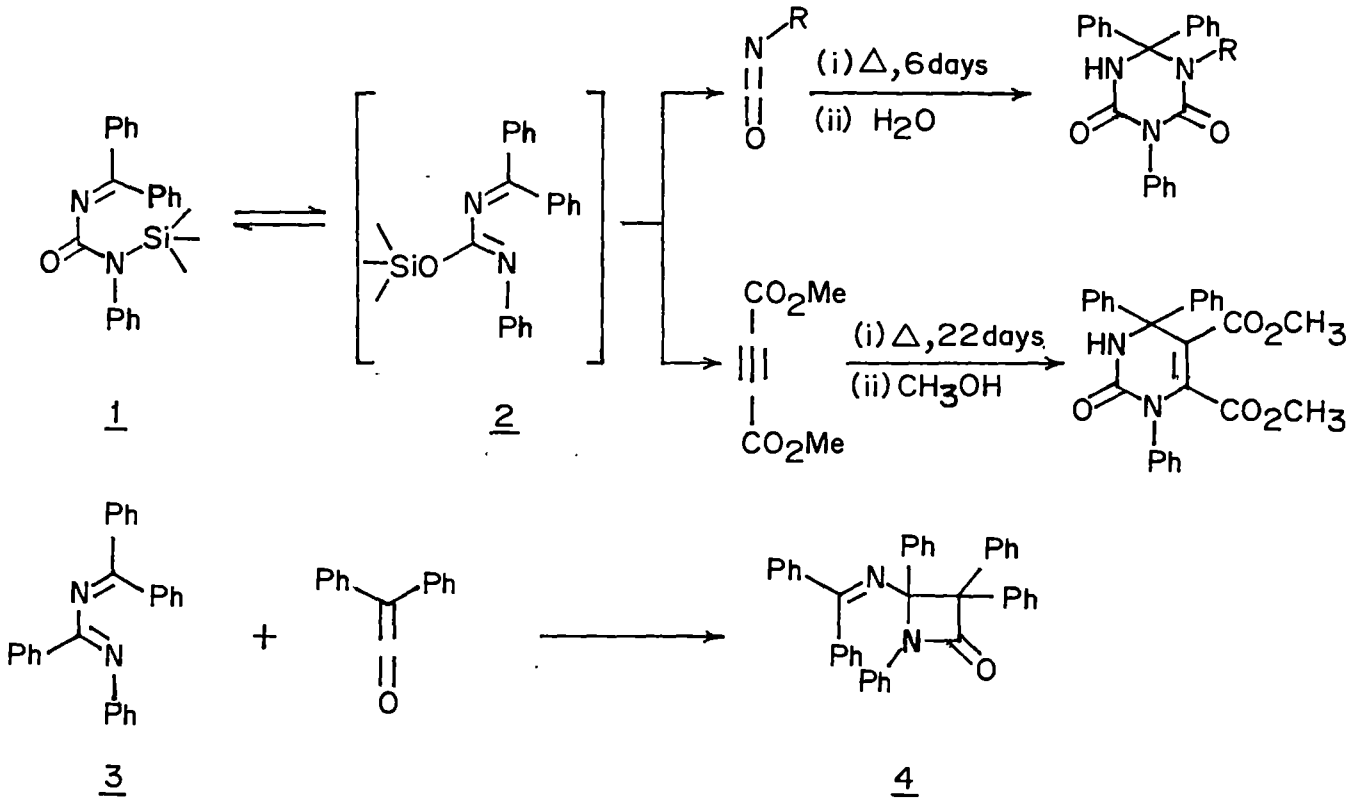
laboratory step.[14-15] Subsequently asymmetric,[16] and intramolecular variants[17] of this process came to the fore and have been accorded widespread attention. To a significant extent the operating controlling factors in these modifications are quite well understood.

Heterodienes have proved to be of great potential in heterocyclic synthesis. Extensive studies have been carried out on the Diels-Alder cycloadditions involving heterodienes containing one or more heteroatoms and some comprehensive reviews have appeared on oxazines,[5] nitrosoalkenes,[18] heterodienophiles[19] and about intra- and intermolecular cycloaddition reactions in the synthesis of heterocyclic natural products.[20] The observation that the azadienes[3,4,6,9,11,18,21,22] show diminished reactivity towards electron deficient dienophiles, lends credence to the electrophilic nature of such systems. These observations together with the recongnised shortcomings in attempting cycloaddition reactions with 2π and 4π components of similar electrophilic nature led to the development of several general approaches for useful azadiene Diels-Alder cycloadditions.

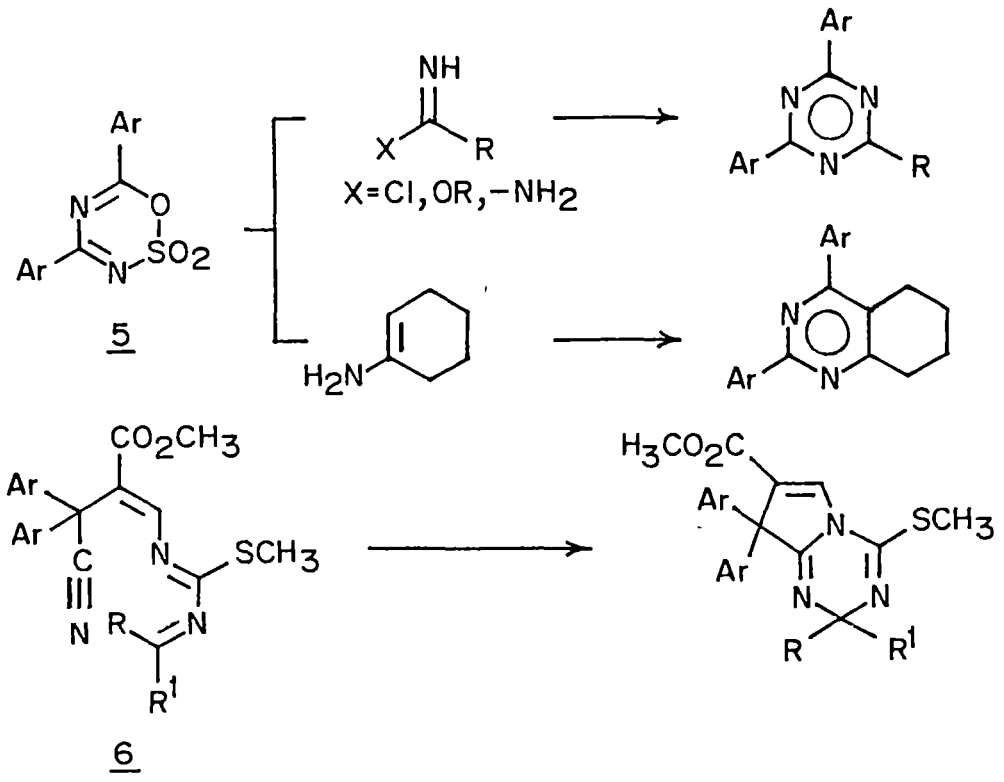
There are numerous reports concerning [4+2] cycloaddition reactions of 1,2- and 1,4-diazabutadienes. In contrast, such cycloaddition reactions with 1,3-diaza-1,3-butadienes, especially, with their acyclic counterparts, are very rare and have not been much exploited in heterocyclic synthesis.[13-15a] This may be atrributed to (i) the lack of suitable methods available for the preparation of stable 1,3-diaza-1,3-butadienes

and (ii) their reluctance to participate in Diels-Alder reaction because of their inverse electron demand tendency due to the unfavourable position of second nitrogen at position 3- of butadiene system. The successful attempts in this direction include the thermal isomerisation of an unsaturated *N*-Silylurea **1** to 2-trimethylsilyloxy-1,3-diaza-1,3-butadiene **2**. and their subsequent Diels-Alder reaction. Their efficiency towards the cycloaddition reactions was soon considered doubtful since such reactions involved long reaction times, poor yields etc.[23] Matsuda *et al.* observed that a similar 1,3-diaza-1,3-butadiene **3**, failed to react with dimethyl acetylene dicarboxylate and formed [2+2] cycloadducts **4** with diphenylketene (Scheme 1).[23] Weidinger *et al.* reported the [4+2] cycloaddition reactions of 4,6-diaryl-1,2,3,5-oxathiadiazine-2,2-dioxides **5** with nucleophilic heterodienophiles[24] and electron-rich olefins[25] (Scheme 2). More *et al.* reported recently, *in situ* generation and subsequent intramolecular Diels-Alder reactions of 2-methylthio-1,3-diaza-1,3-butadienes **6**[26] (Scheme 2).

Few reports of the successful participation of heterocyclic 1,3-diaza-1,3-butadienes as 4π component in Diels-Alder cycloaddition reactions with dienophiles are also available in literature[27-31] (Scheme-3). Recently, there have been reports concerning the [4+2] cycloaddition reactions of simple, yet isolable and stable, 1,3-diaza-1,3-butadienes that concern the reactions of **7** and **8** with isocyanates[32a] substituted nitriles[32b,c] (Scheme-3) and ketenes.[33]


Ph
N
Ph
Si
O
N
Ph
1
SiO
2
R
(i) Δ, 6 days
(ii) H2O
HN
CO2Me
(i) Δ, 22 days
(ii) CH3OH
CO2CH3
3
4

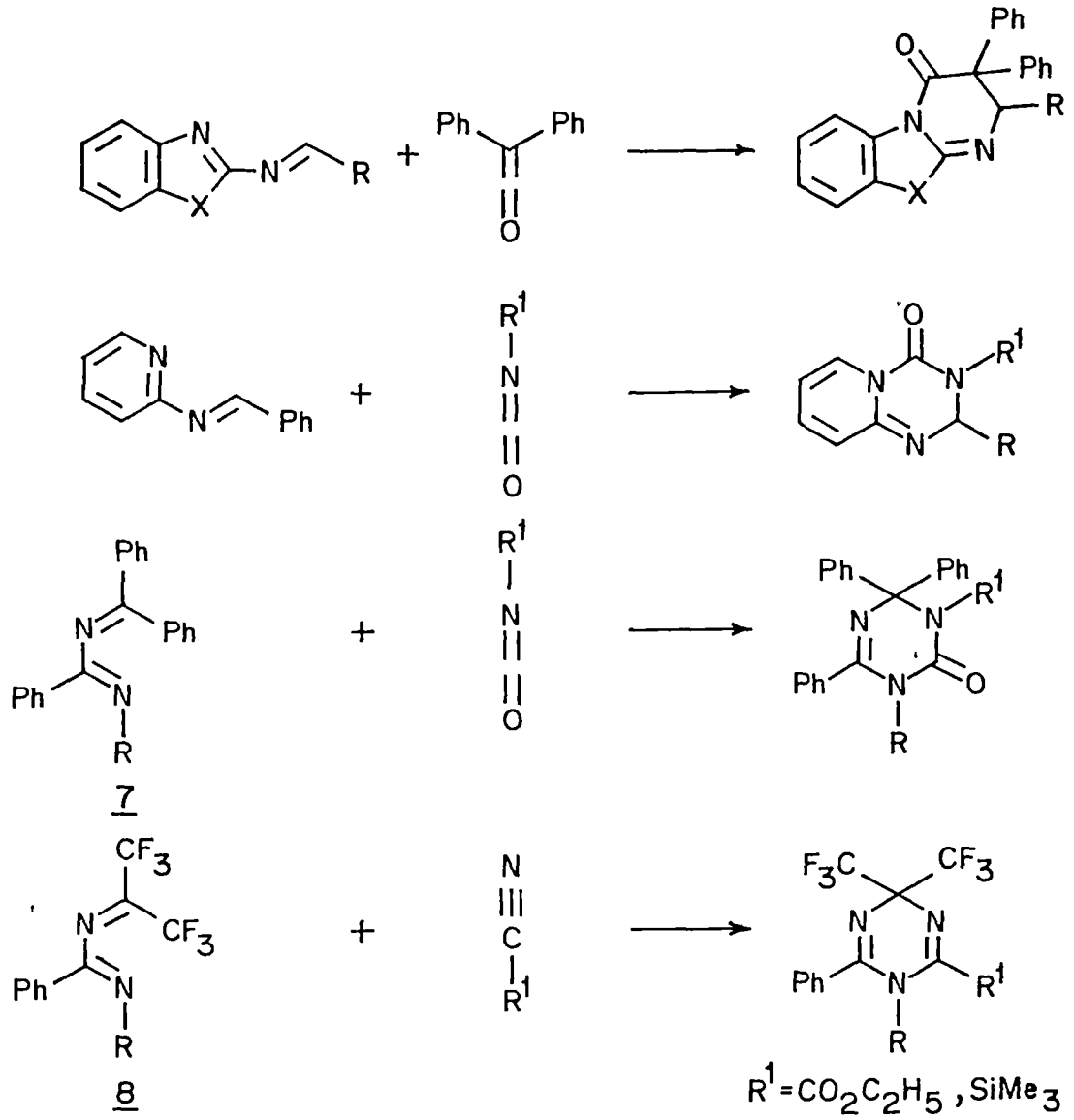
Scheme-1



Scheme - 2

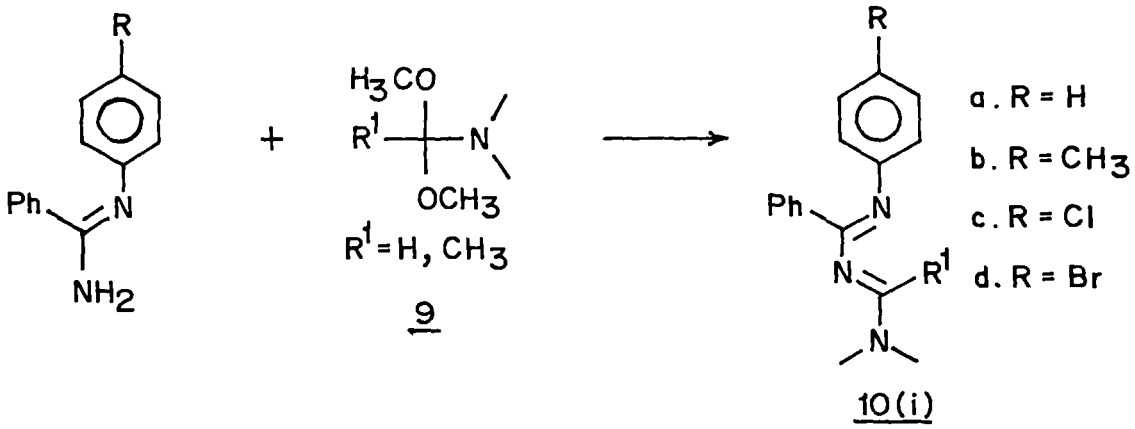
In view of the reported lack of synthetic approaches together with reports of failure of acyclic 1,3-diaza-1,3-butadienes as an effective 4π component in Diels-Alder cycloaddition reactions, we devised simple methods for the preparation of stable acyclic 1,3-diaza-1,3-butadienes.[34] Such 1,3-diazabutadienes with polarising functions at 4 and 2/4-positions (Schemes 4 and 5) were successfully utilised in [4+2] cycloaddition reactions with various ketenes e.g. phenyl-, diphenyl-, chloro-, bromo-, iodo-, chloromethyl-, dichloro- and various other ketenes.

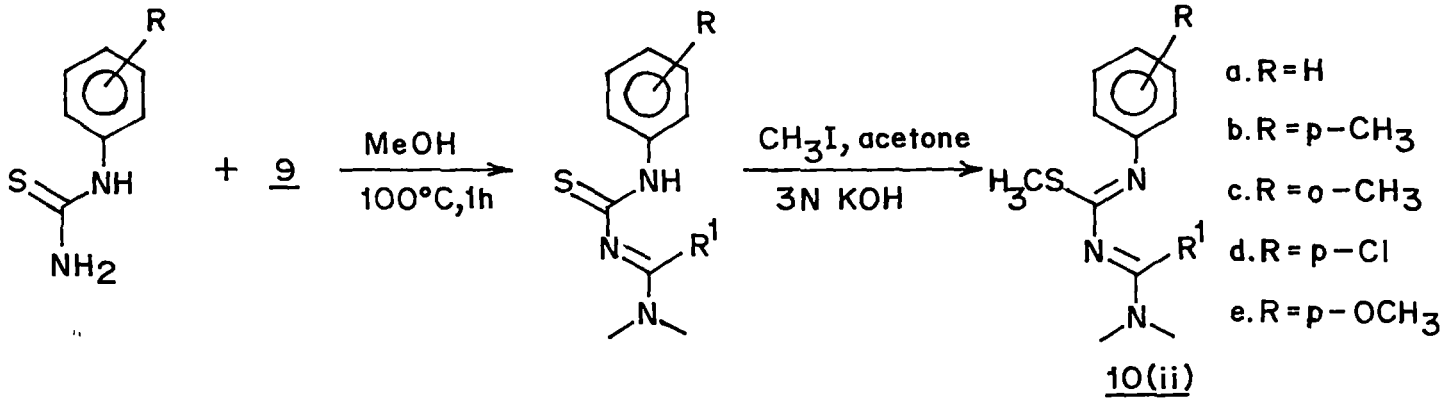
The reaction of 1,3-diaza-1,3-butadienes **10** with monophenyl ketene **13** resulted in the formation of [4+2] cycloadduct 3-aryl-



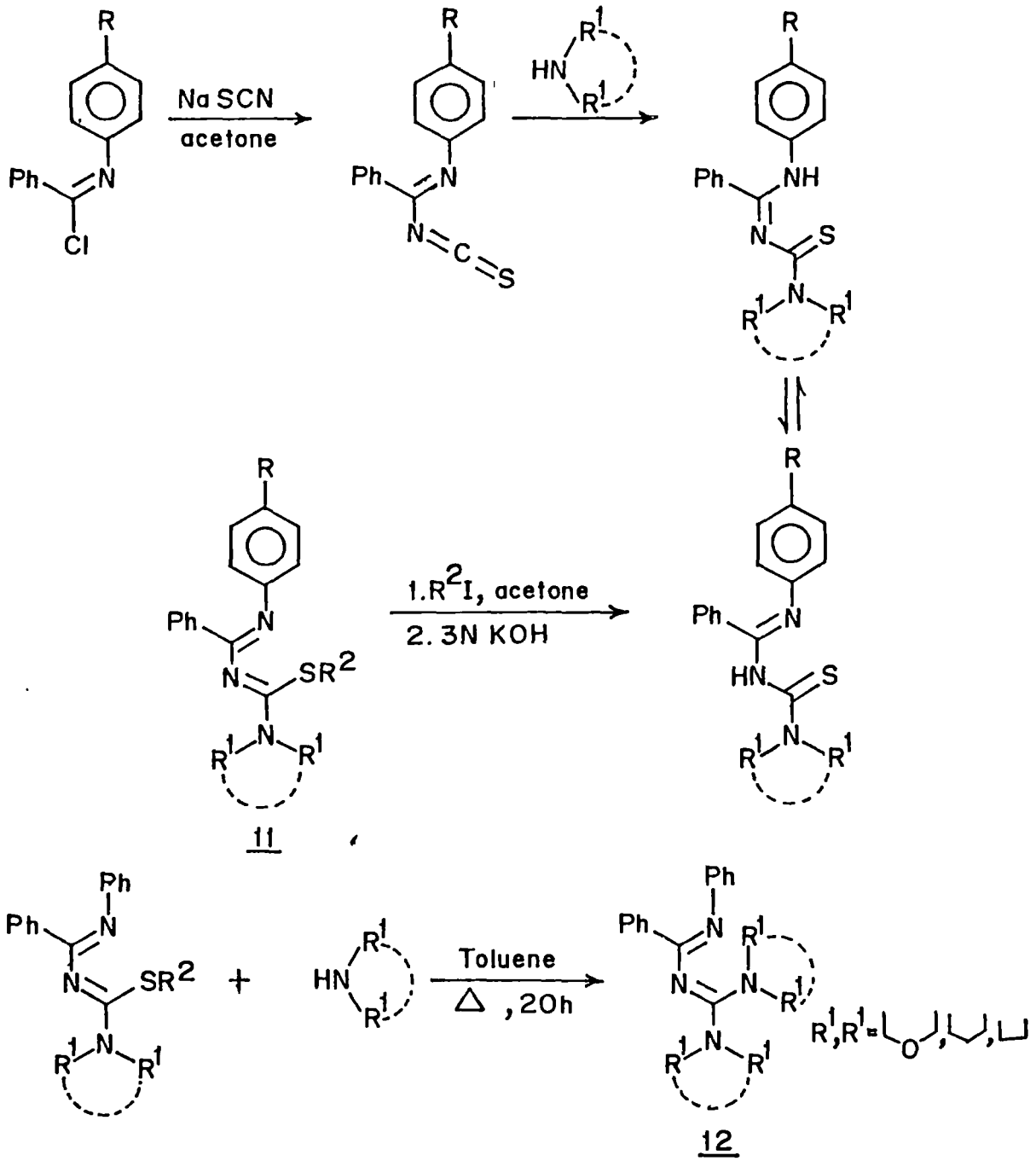
Scheme-3

5-phenyl-2-phenyl/methylthio-4(3*H*)-pyrimidinone **14** *via* the elimination of dimethylamine function. Similar reactions with 1,3-diaza-1,3-butadienes **11** and **12** resulted in the isolation of pyrimidinone **15** and **16** *via* the elimination of methylthio and secondary amine functions respectively[35] (Scheme 6). The


R
Ph
N
NH2
+
H3CO
R1
N
OCH3
R1=H, CH3
9
a. R = H
b. R = CH3
c. R = Cl
d. R = Br
10(i)


R
S
NH
NH2
+ 9
MeOH
100°C, 1h
CH3I, acetone
3N KOH
H3CS
a. R = H
b. R = p-CH3
c. R = o-CH3
d. R = p-Cl
e. R = p-OCH3
10(ii)

Scheme-4

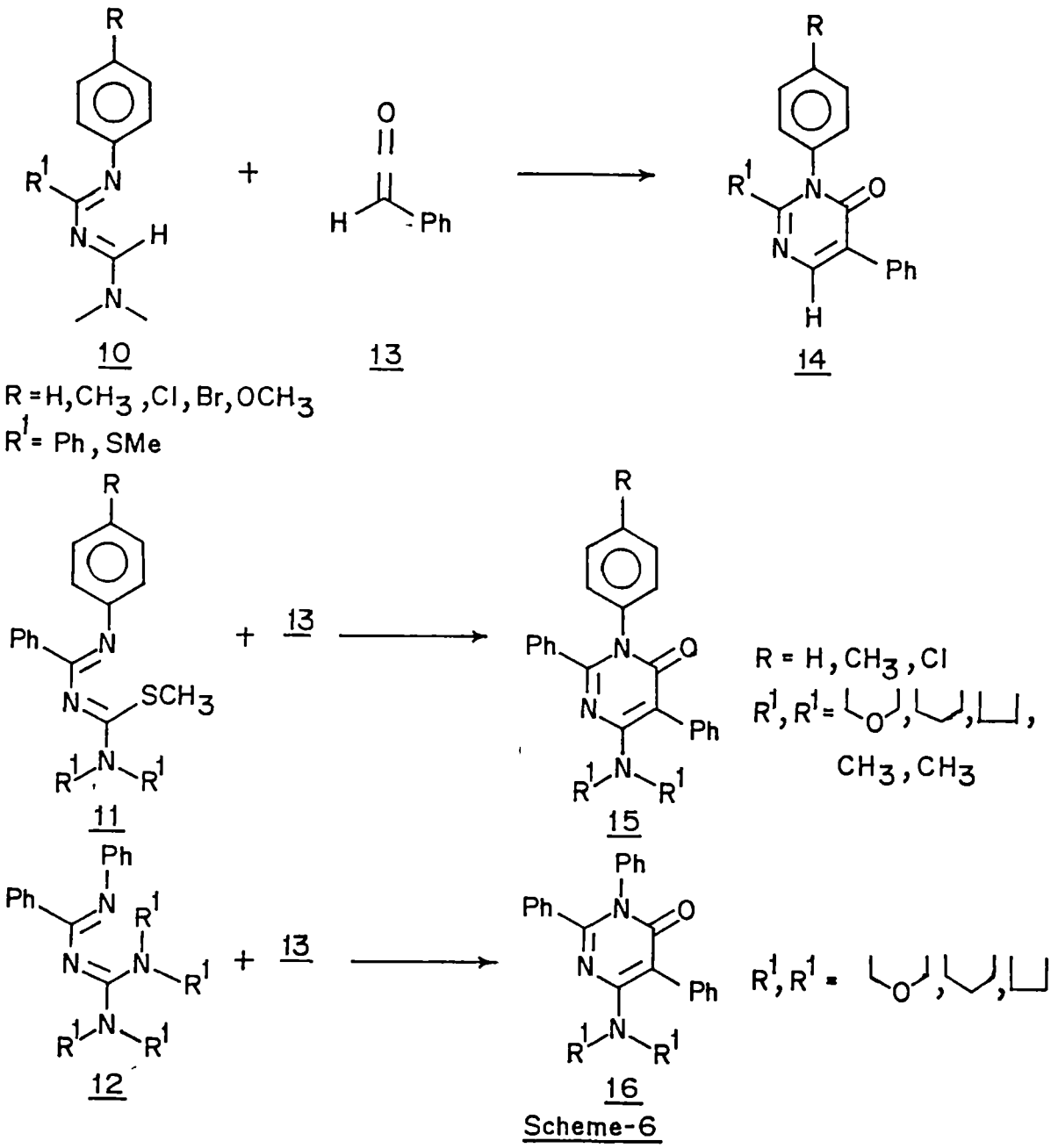


11

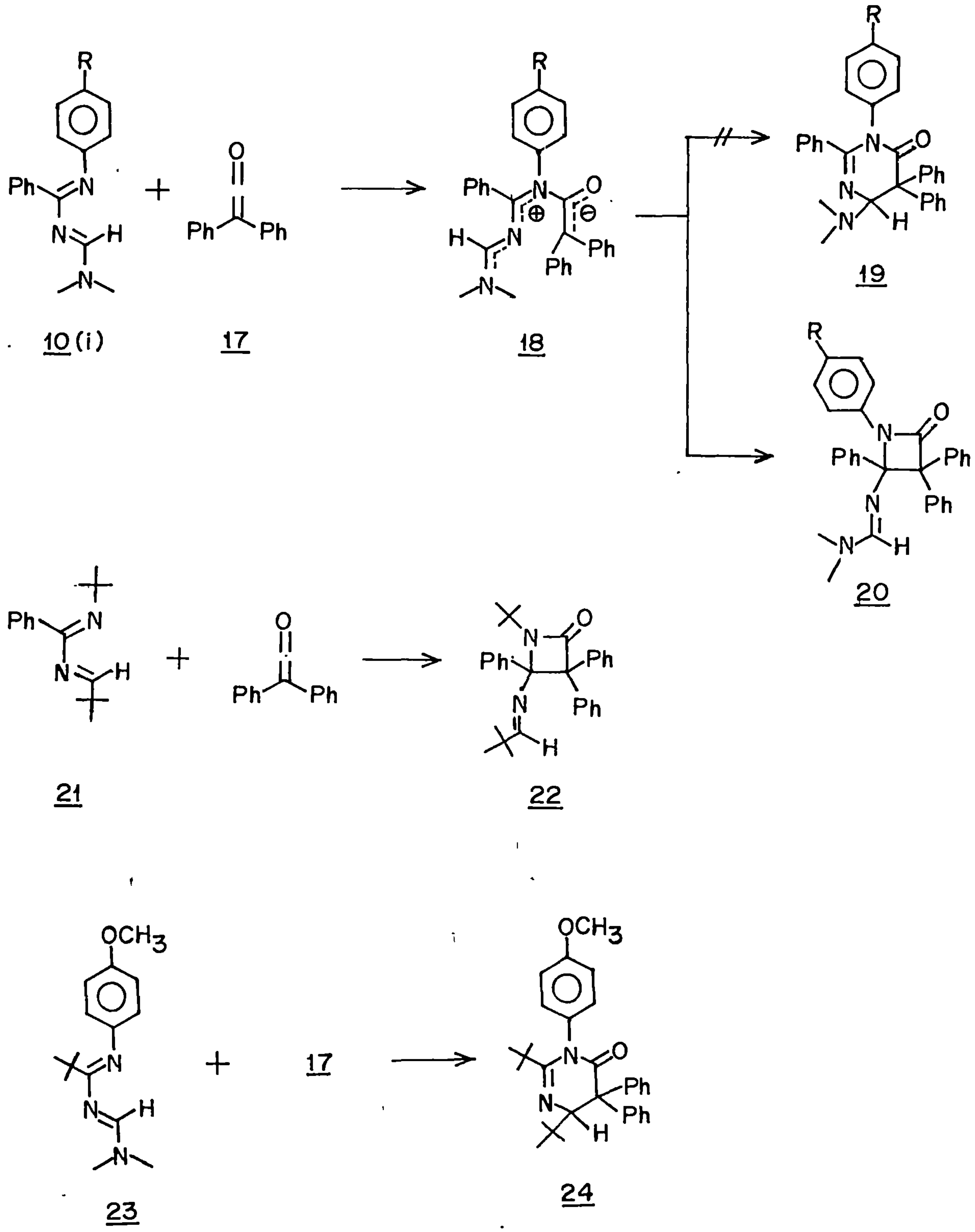
12

Scheme-5

reaction of 1,3-diaza-1,3-butadiene **10** with diphenyl ketene **17** was initially assumed to result in a [4+2] cycloadduct **19**[36] *via* the zwitterrionic intermediate **18**. Luthardt and Wurthwein[37] reported that the intermediate **18** prefers the formation of β-

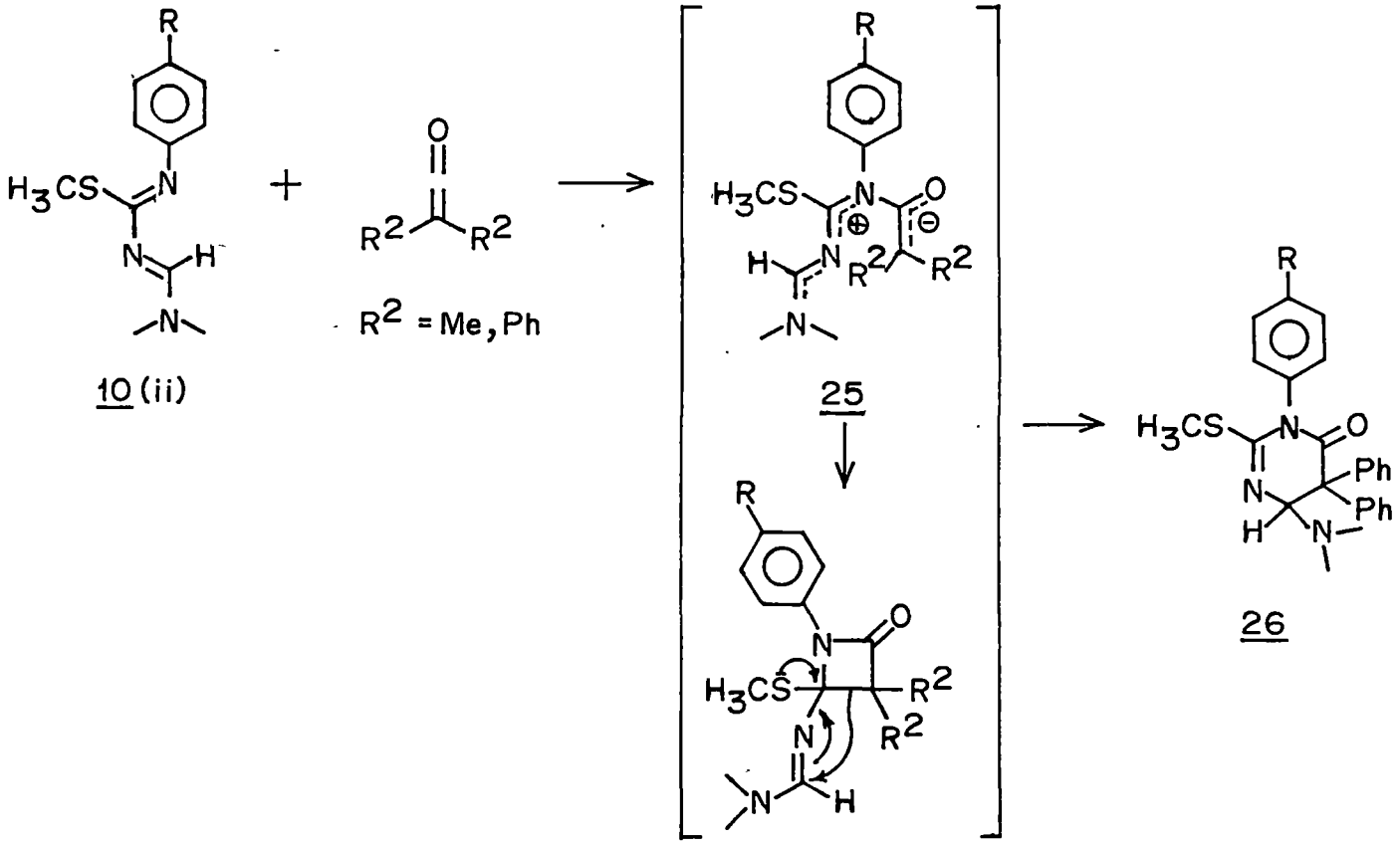


lactam derivative *via* [2+2] cycloaddition due to higher steric hindrance to the approach of two phenyl groups to the dimethylamine function leading to [4+2] cycloadduct **19** as compared to the approach of two phenyl groups to C-2, leading to [2+2] cycloadduct **20** (Scheme-7). They extended the steric arguments to the formation of **22** and **24** in the reaction of diphenylketene **17** with 1,3-diazabutadiene **21** and **23** respectively

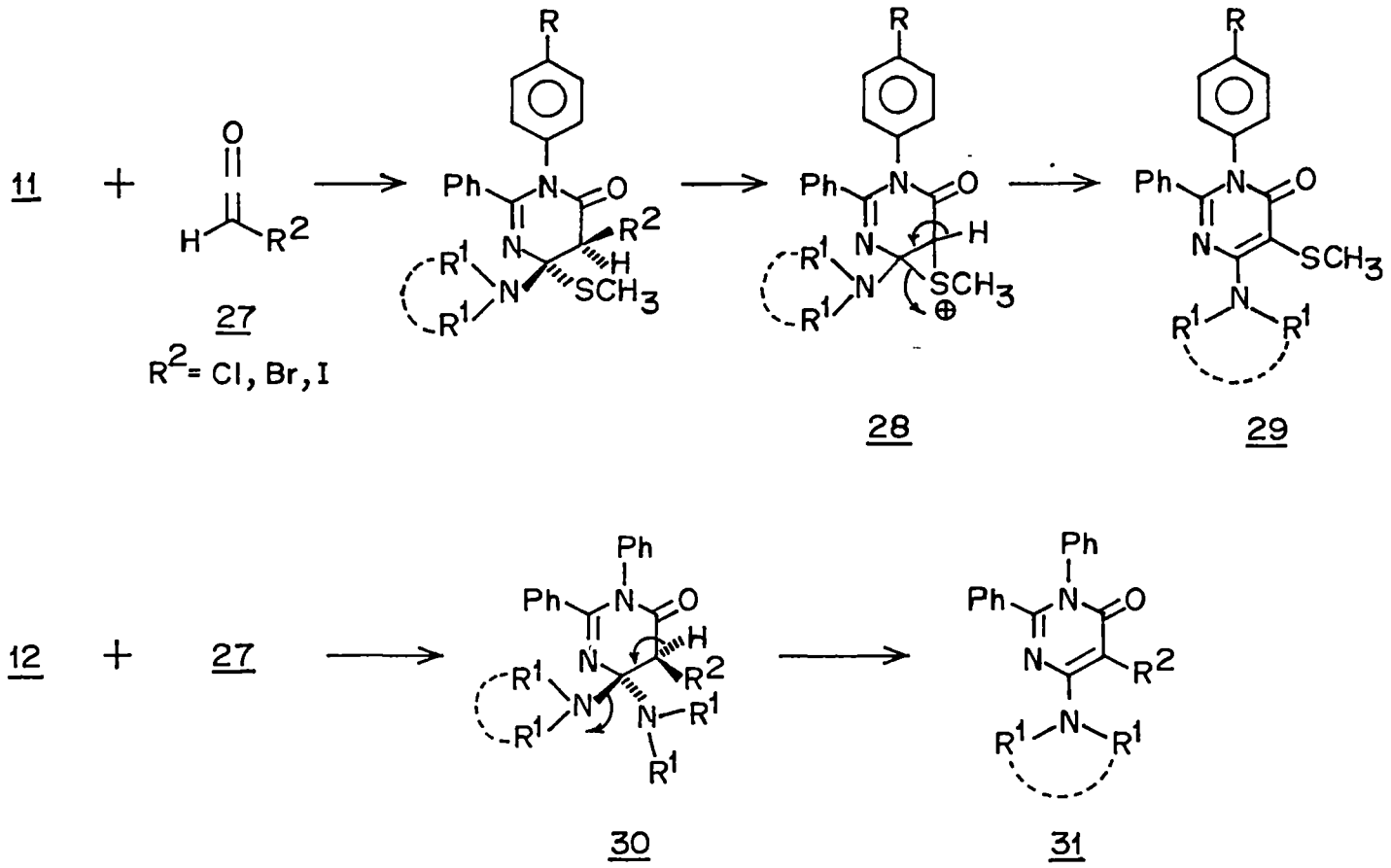


Scheme - 7

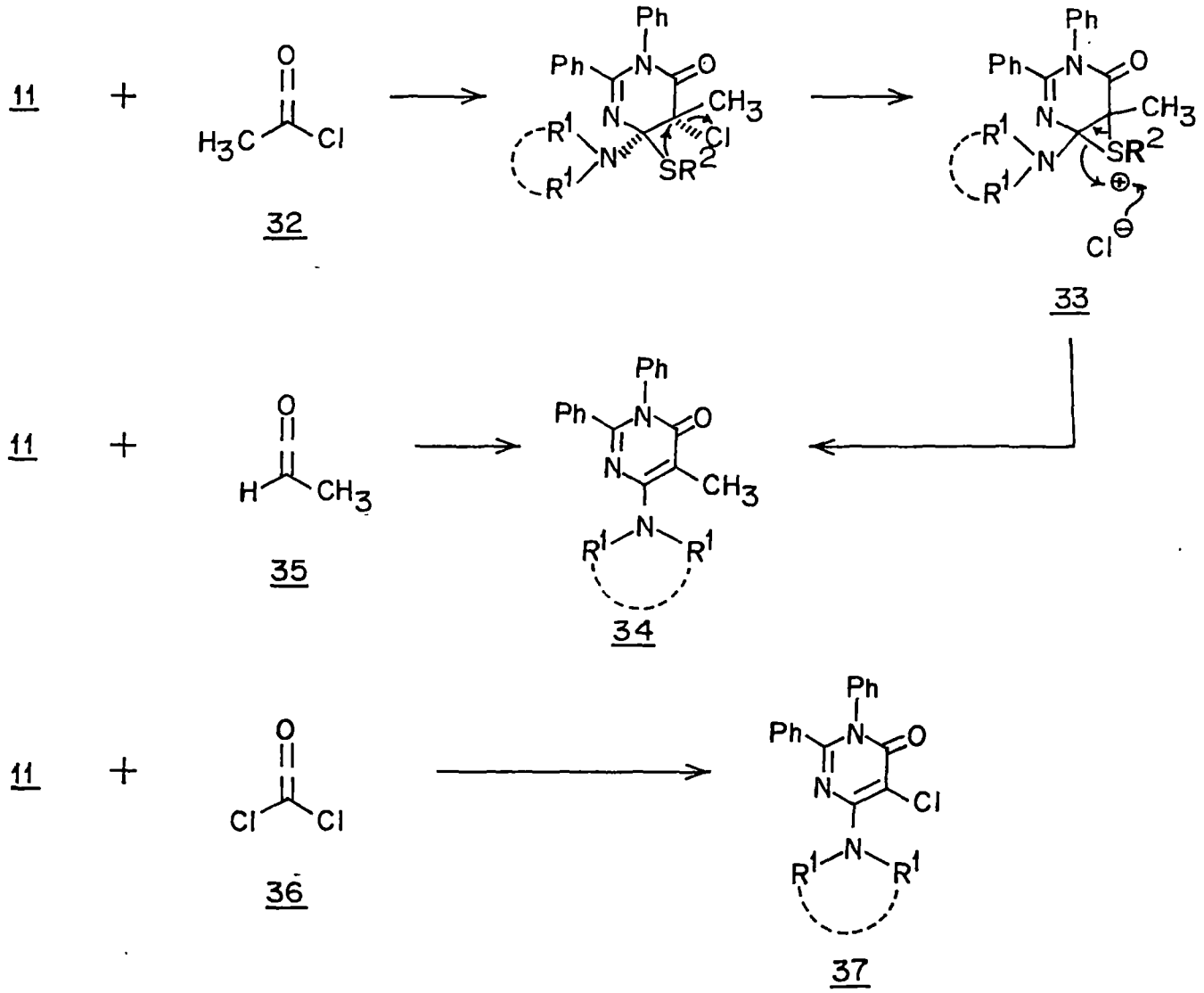
(Scheme 7). Interestingly, the reaction of disubstituted ketenes (diphenyl and dimethylketene), with 1,3-diaza-1,3-butadiene **10ii** having a polarising function at 2-position, which further stabilizes the initially found zwitterionic intermediate **25**, resulted in good yields of [4+2] cycloadducts **26**[38] which have been characterised as 3-aryl-6-dimethylamino-5,5-diphenyl/dimethyl-2-methylthio-3,5,6-trihydropyrimidin-4-ones (Scheme 8). Interesting 1,2-alkylthio shift accompanying [4+2] cycloadditions have been reported in the reactions of 1,3-diaza-1,3-butadienes with halo ketenes. Thus the reaction of 1,3-diazabutadienes **11** with haloketenes (chloro-, bromo-, and iodoketenes) resulted in the formation of pyrimidinones **29** involving 1,2-alkylthio shift in the initially formed [4+2] cycloadduct intermediates. These reactions presumably proceed *via* an episulphonium intermediate **28**.[39] In reactions of 1,3-diaza-1,3-butadienes **12**, having two secondaryamine functions at 4-position, with haloketenes no such rearrangement was observed and these reactions yielded pyrimidinones **31** with the elimination of one of the secondaryamine functions from intermediate **30** (Scheme 9). The treatment of 1,3-diaza-1,3-butadienes **11** with chloromethyl ketene **32** gave another set of rearranged pyrimidinones **34** *via* the esisulphonium intermediate **33**. Further information about structure **34** was derived from the superimposable IR spectra and undepressed mixed melting point with a sample prepared from the reaction of **11** with methylketene **35**. Similar reaction of **11** with dichloroketene **36** resulted in pyrimidinone **37** *via* the loss of



Scheme-8

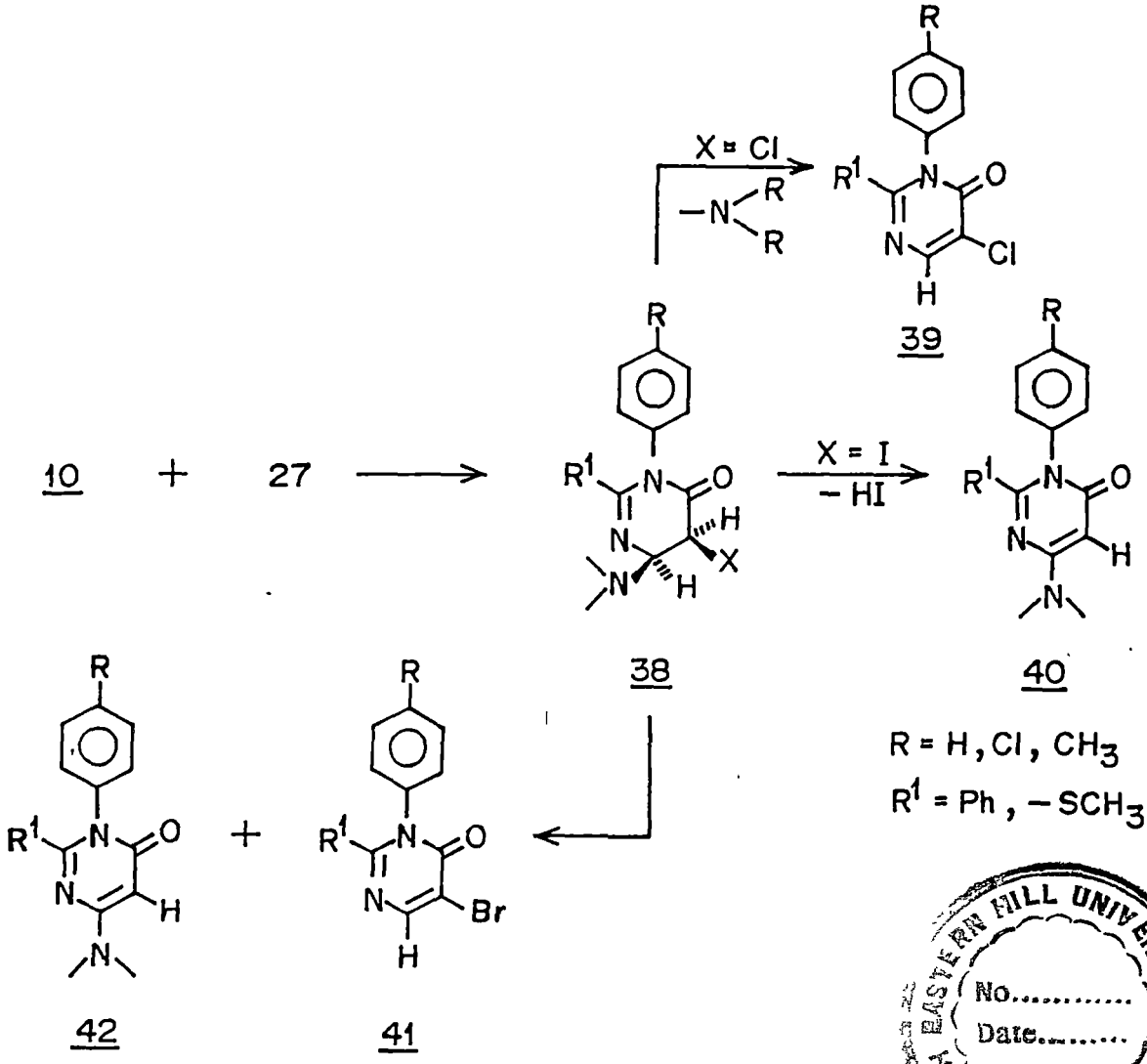


Scheme – 9



Scheme – 10

methyl sulphenyl chloride from an intermediate of the type 33 (Scheme 10). The reactions of 1,3-diaza-1,3-butadienes 10 with various haloketenes were assumed to proceed *via* [4+2] cycloadduct 38 as intermediate, which in case of chloroketene, resulted in pyrimidinones 39 with the exclusive elimination of secondaryamine



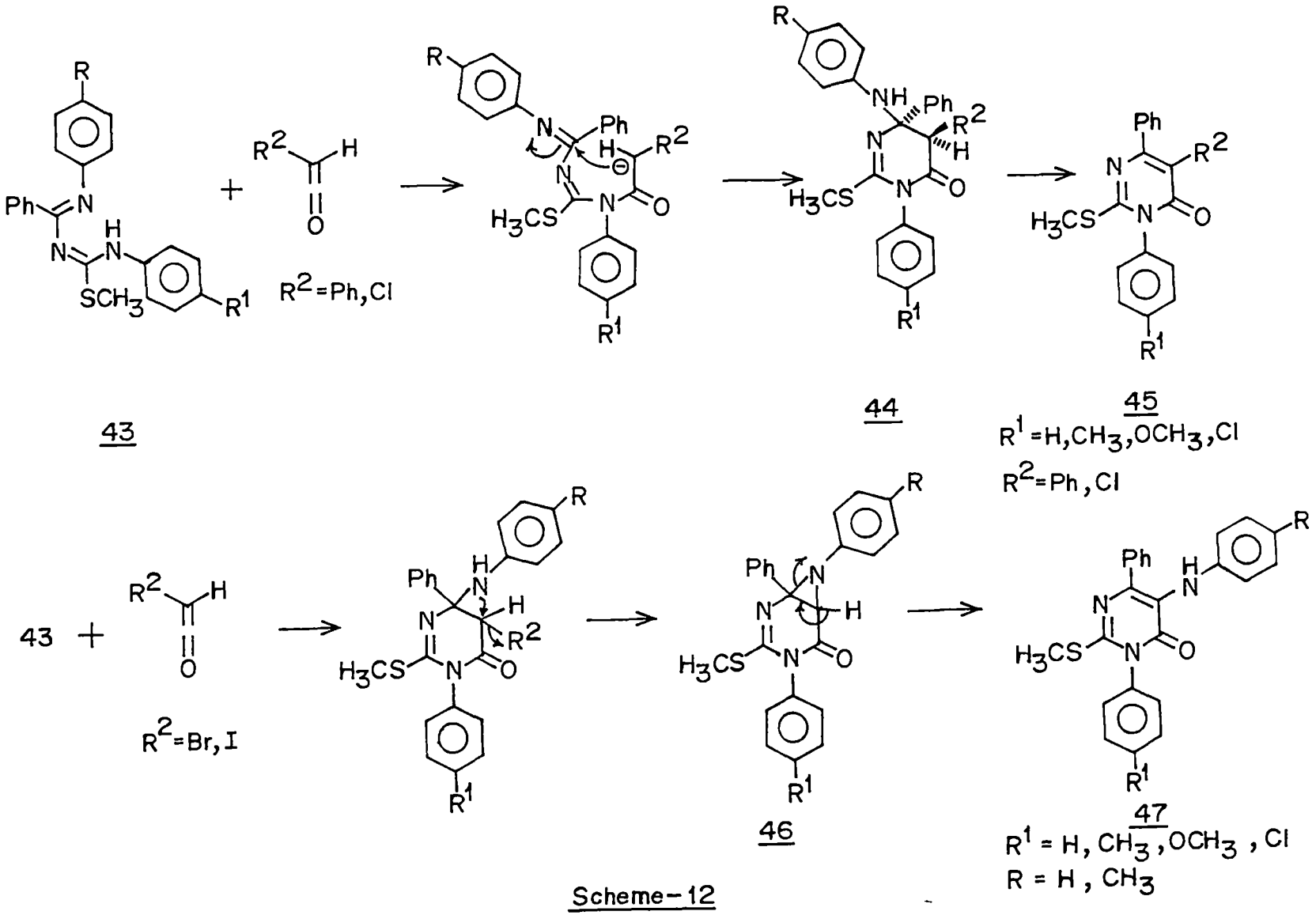
Scheme - 11

functions and pyrimidinones 40 in case of iodoketene with the exclusive elimination of HI. In case of bromoketene, the

intermediate **38** underwent loss, both of dimethylamine and hydrobromic acid resulting in pyrimidinones **41** (34%) and **42** (40%) respectively[39] (Scheme 11).

In continuation of our studies concerning 1,3-diazabutadiene-ketene cycloadditions, we have synthesised various N-aryl-1,3-diaza-1,3-butadienes **43**[40] and carried out their reactions with various ketenes in order to investigate the regiochemical aspects and to understand the nature of the reaction pathway followed in these reactions. The reaction of **43** with phenyl- and chloroketenes underwent nucleophilic reaction followed by cyclisation to yield an intermediate **44** which on elimination of primary aromatic amines gave pyrimidinones **45**. Similar reactions of **43** with bromo- and iodoketenes resulted in rearranged pyrimidinones **47** *via* an aziridinium intermediate **46** followed by 1,2-(N-aryl) shift[40] (Scheme 12).

In view of the interesting results observed in various 1,3-diazabutadiene-ketene cycloadditions and in order to exploit these reaction pathways for the synthesis of various substituted/fused pyrimidinones, we have investigated the reactions of a variety of 1,3-diaza-1,3-butadienes with vinyl-, isopropenyl-, butadienyl and chloroketenes. The results of these reactions are described in Section I.2, I.3 and I.4 of this Chapter.

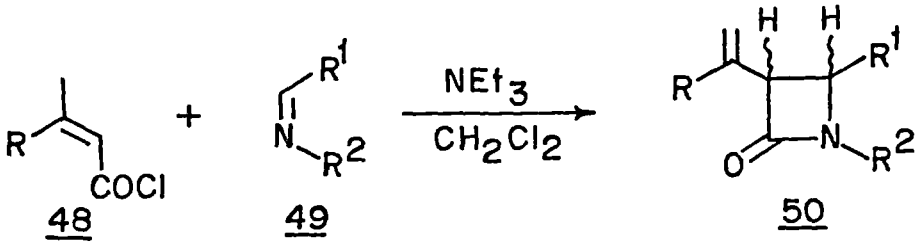

R
Ph
N
H
N
SCH3
R1
R2
H
O
R2=Ph,Cl
Ph
R2
H
H3CS
43
44
45
R1=H,CH3,OCH3,Cl
R2=Ph,Cl
43 +
R2=Br,I
46
47
R1 = H, CH3, OCH3, Cl
R = H, CH3

Scheme-12

I.2: *[4+2] Cycloaddition Reactions of 1,3-Diaza-1,3-Butadienes with Vinyl/Isopropenylketenes*

Introduction

Ketene Chemistry is dominated by [2+2] cycloaddition reactions and such reactions with carbon-nitrogen double bonds of imines, monoaza-, and diazabutadienes have been shown to result in important β-lactam derivatives.[15a,41] However, very few reports describe the synthesis of α-alkyl, α-acyl or α-alkylidene β-lactams based on acid chloride imine cycloadditions.[42] 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/isoprepenylketenes to generate such β-lactams. The reaction of acid chloride **48** with various Schiff bases **49** resulted in the formation of various α-vinyl/isopropenyl azetidinones,[43-46] the



3. R = H, CH_3

R^1 = Ph, furfuryl, Ph−CH=CH_2, CO_2Me, COPh

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

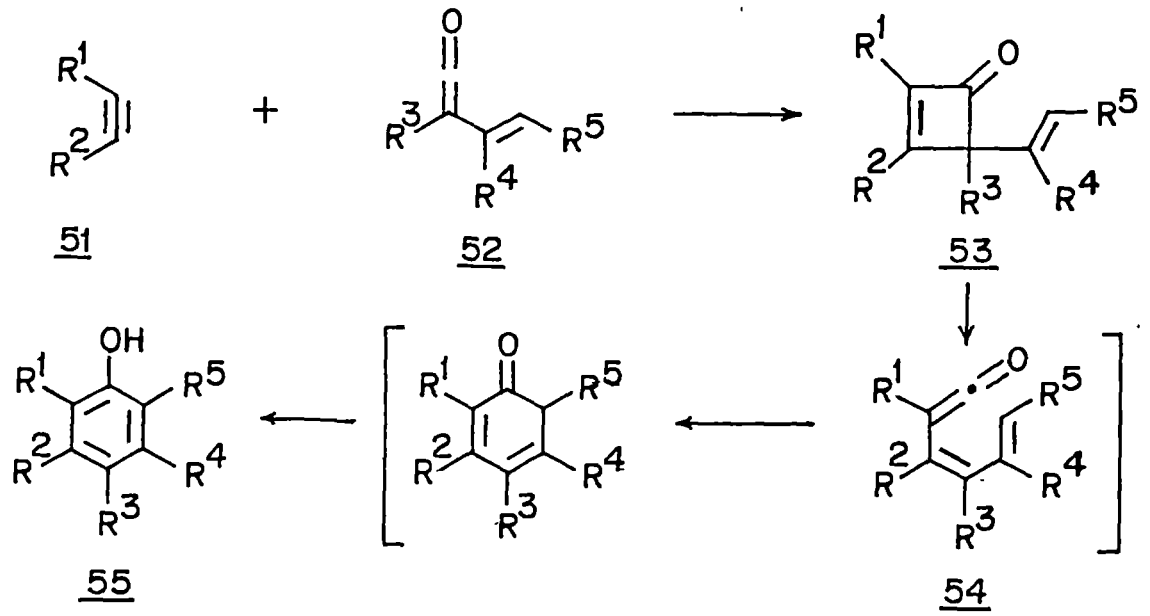
$CH_2C_6H_3(OMe)_2$ (2,4), C_6H_4OMe-p, $CH(CH_3)Ph$, tBu

[a] TBDMS = tert-butyldimethylsilyl [b] PNB = p-nitrobenzyl

Scheme-13

stereochemistry of which was found to depend on the substituents R^1 and R^2 (Scheme 13). This reaction, developed in 1971 by Bose et al[43] was later utilised by Zamboni and Just[44] for preparing various α-vinyl β-lactams, the potential synthones for β-lactam antibiotics. Such α-vinyl azetidinones have been converted to pyrrolidine derivatives,[45] intermediates for carbepenem antibiotics[46] and sulfur containing bicyclic β-lactams.[47]

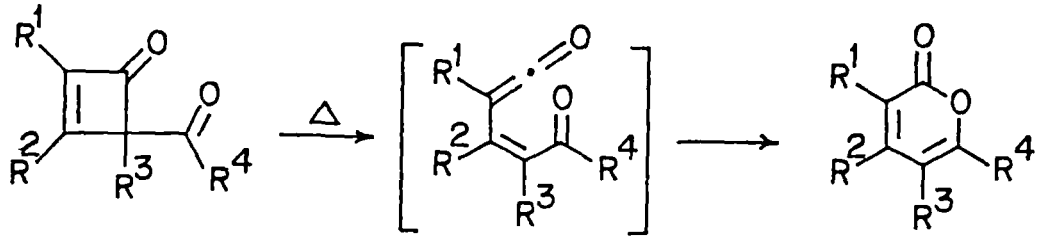
[2+2] cycloaddition reactions of *in situ* generated vinylketenes 52 to electron rich alkynes 51 have also been reported.[48-52] The 4-vinyl cyclobutenones 53 thus obtained were transformed to various catechols[53] 55 through putative



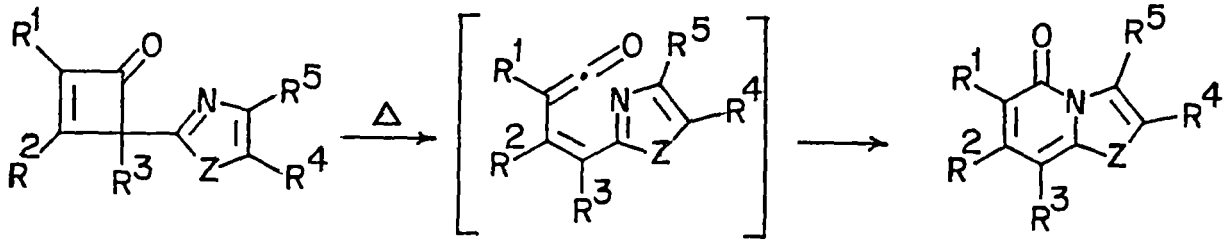
Scheme-14

dienylketene intermediates 54 (Scheme 14). Following the same strategy, the judicious heteroatom permutations of dienylketene provided direct synthetic entry to a variety of valuable

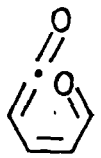
heterocyclic systems *via* intramolecular vinylketene cyclisations on to the C=X (X=N, O) double bonds.[54-56] Using this methodology, a novel approach to indolizine-5,8-dienes[54] was achieved and a new synthesis of α-pyridones 56 has also been developed.[55] Also, a large variety of substituted quinolizin-4-ones 57 and ring fused α-pyridone derivatives have been synthesised by the thermal rearrangements of substituted cyclobutenones *via* vinylketene intermediates[56] (Scheme 15). Ab *initio* calculations have also been carried out on all conformations and several reactions of 5-oxo-2,4-pentadienal 58 vinylog of formylketne, as well as related systems.[57]



56



57



58

R^1 = Et, n-Bu, Me, Ph, MEM-O-

R^2 = Et, n-Bu, i-PrO, Me, Bn_2N

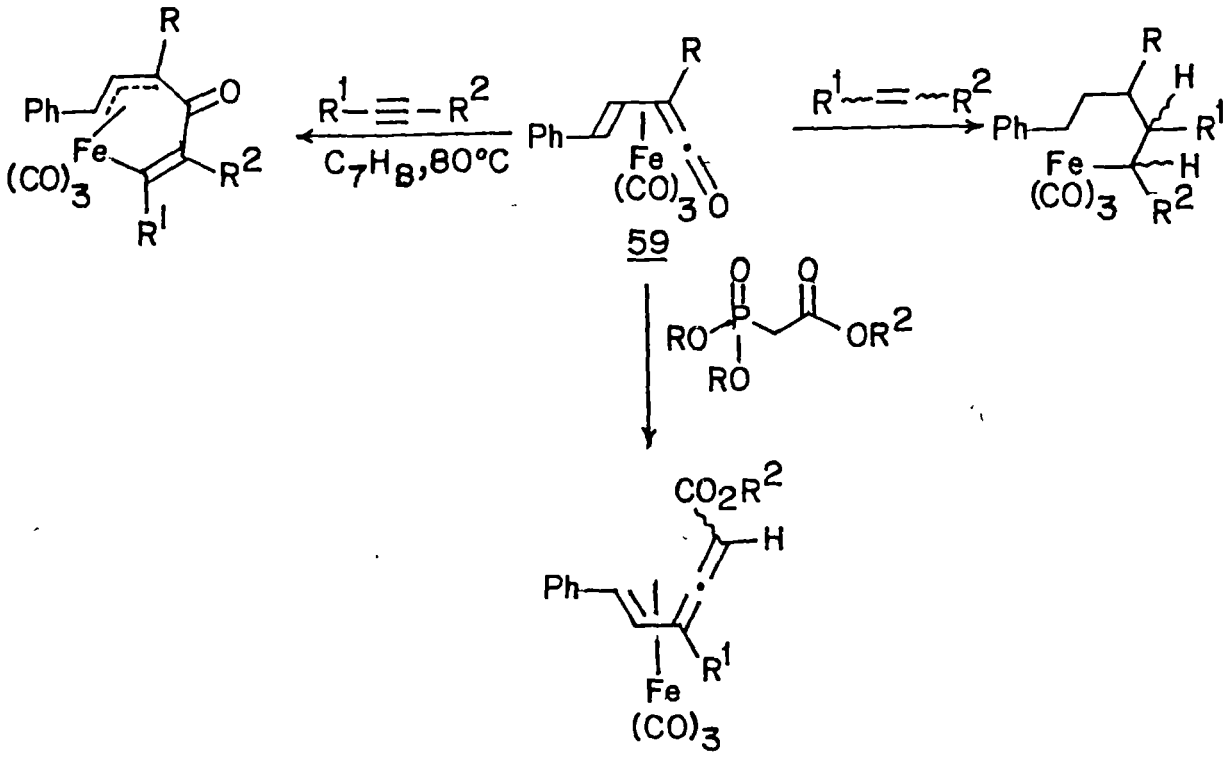
R^3 = OAc, OH, n-Bu

R^4, R^5 = H, H ; benzo

Z = CH=CH, C(OMe)=CH, S, NMe, N-MOM

Scheme-15

The metal bound ketenes and vinylketenes have frequently been postulated as reactive intermediates[58,59] which have created considerable interest towards the reactivity of isolable metal bound ketene and vinylketenes.[60,61] Thomas *et al.* extensively studied the fundamental reactivity of easily accessible and highly stable iron centred vinylketene complexes 59 and have reported the results of their reactions with isonitriles,[62] phosphonoacetate anions,[63] nucleophiles,[64] alkynes[65] and alkenes[66] (Scheme 16). 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. We have recently reported simple methods for the preparation of various acyclic 1,3-diaza-1,3-butadienes[34,40] and

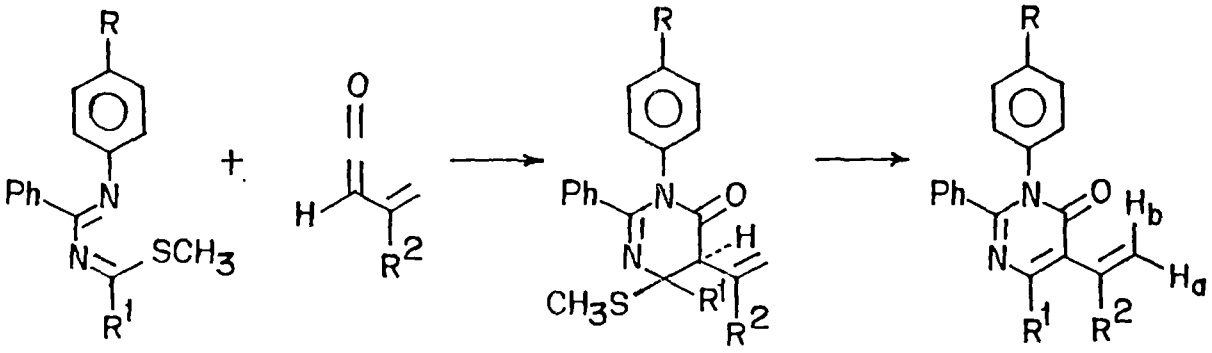


Scheme-16

successfully utilised these in [4+2] cycloaddition reactions with phenyl-, chloro-, bromo-, iodo-, chloromethyl-, dichloro- and various other ketenes.[35,39,40] It was thought that making a comparison of dienic properties between various dienes and/or heterodienes is an interesting scientific enquiry. However, little attention has been paid to such studies by carrying out cycloaddition reactions between such dienes. Accordingly, we got interested in investigating the cycloaddition reactions of 1,3-diazabutadienes with isopropenyl/vinylketenes and these were found to follow [4+2] cycloaddition pathway in which these ketenes behaved as 2π component. To our knowledge, this is the first report concerning the participation of such ketenes as 2π component in [4+2] cycloaddition reactions.

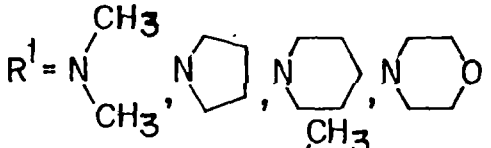
Results & Discussion

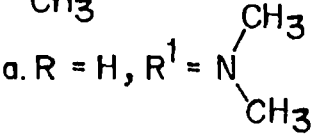
The reactions of 1-aryl-4-dialkylamino-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **11** with isopropenyl/vinylketenes **60**, generated *in situ* from 3,3-dimethylacroyl chloride/crotonyl chloride and excess of triethylamine in dry methylene chloride, resulted in very high yields (89-95%) of 3-aryl-5-isopropenyl/vinyl-2-phenyl-6-dialkylamino pyrimidin-4(3*H*)-ones **62** (Scheme 17). The products were characterised on the basis of analytical and spectral evidences. Thus, compound **62a**, for example, was analysed for $C_{21}H_{21}N_3O$ and its mass spectrum showed a molecular ion peak at *m/z* 331. Its IR spectrum (KBr) showed a strong absorption peak at 1654 cm^{-1} due to α,β-unsaturated carbonyl

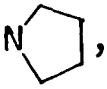


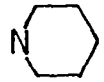
11 60 61 62

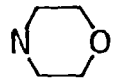
R = H, CH_3 R^2 = H, CH_3

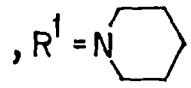
R^1 = 

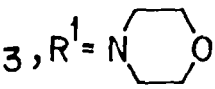
62 a. R = H, R^1 =  , R^2 = CH_3

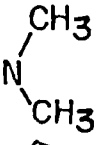
b. R = H, R^1 =  , R^2 = CH_3

c. R = H, R^1 =  , R^2 = CH_3

d. R = H, R^1 =  , R^2 = CH_3

e. R = R^2 = CH_3, R^1 = 

f. R = R^2 = CH_3, R^1 = 

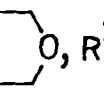
g. R = R^2 = H R^1 = 

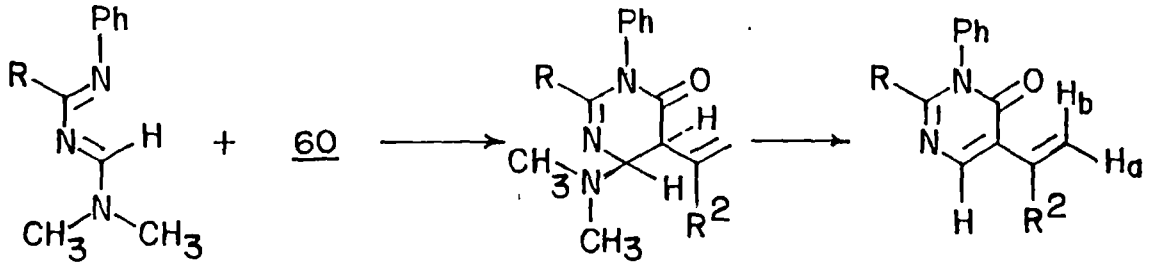
h. R = R^2 = H R^1 = 

i R = R^2 = H R^1 = 

j. R = R^2 = H R^1 = 

k. R = CH_3, R^1 =  , R^2 = H

l. R = CH_3, R^1 =  , R^2 = H



10 63 64

R = Ph, SCH_3

64. a. R = Ph, R^2 = CH_3

b. R = Ph, R^2 = H

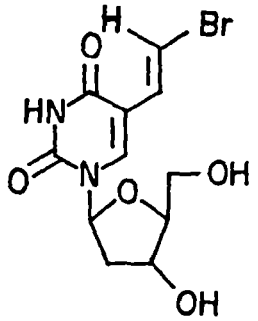
c. R = SCH_3, R^2 = CH_3

Scheme-17

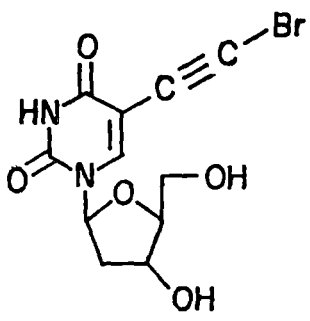
group. The ^1H NMR spectrum of **62a** showed the absence of methylthio and the presence of dialkylamino functions. It also exhibited the presence of $-CH_3$ proton at δ 2.13 and two protons as two broad singlets due to Ha at δ 5.03 and due to Hb at δ 5.33. The ^1H NMR spectrum of pyrimidinone **62g**, in addition to aromatic and dialkyl amino protons showed the presence of three doublet of doublets due to vinylic protons. Ha proton appeared as a doublet of doublet at δ 5.40 (J_{HaH} = 11.4 Hz, J_{HaHb} = 2.5 Hz), Hb exhibited another doublet of doublet at 6.00 (J_{HbH} = 17.5 Hz, J_{HbHa} = 2.5 Hz) and the proton H also appeared as a doublet of doublet at 6.67 (J_{HHb} = 17.5 Hz, J_{HHa} = 11.4Hz). The downfield shift of proton Hb as compared to Ha in the pyrimidinones **62** may be due to the anisotropic deshielding of the carbonyl group. Similarly, the reactions of 4-dimethylamino-2-methylthio/phenyl-1-phenyl-1,3-diaza-1,3-butadienes **10** with vinylketenes resulted in the formation of pyrimidnones **64** by the elimination of dimethylamino function from the initially formed [4+2] cycloadducts **63** as intermediates (Scheme 17). The pyrimidinones **64** were also analysed on the basis of their analytical and spectral data. Compound **64a**, analysed for $C_{19}H_{16}N_2O$ showed the molecular ion peak at *m/z* 288 in its mass spectrum. Its ir spectrum exhibited a strong absorption band at 1668 cm^{-1} due to α,β-unsaturated carbonyl group. The ^1H nmr spectrum showed, in addition to other protons, the presence of an olefinic proton at δ 8.21 and the absence of dimethylamine function. The formation of pyrimidinones **62** and **64** in these

reactions requires the trans arrangement for H-5/methylthio functions and H-5/dimethylamino functions in the intermediates 61 and 63, respectively. The intermediates 61 and 63 with the desired stereochemical arrangements may either be formed through highly stereoselective and concerted [4+2] cycloaddition or *via* the equilibration of the intermediates possibly through zwitterionic intermediate as reported earlier.[35b,39]

The pyrimidinones 62 and 64 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.[67] Uridine, having an unsaturated side chain (1-propenyl) at C-5 was recently shown to increase binding to both single strand RNA and double strand DNA.[68] The antiviral compound bromovinyluridine (A) is known to be one of the most active pyrimidine nucleosides[69] against herpes simplex virus type 1 (HSV-1). 5-Bromoethynyl-deoxyuridine (B) have also been recently tested to be an active compound against HSV-1.[70]



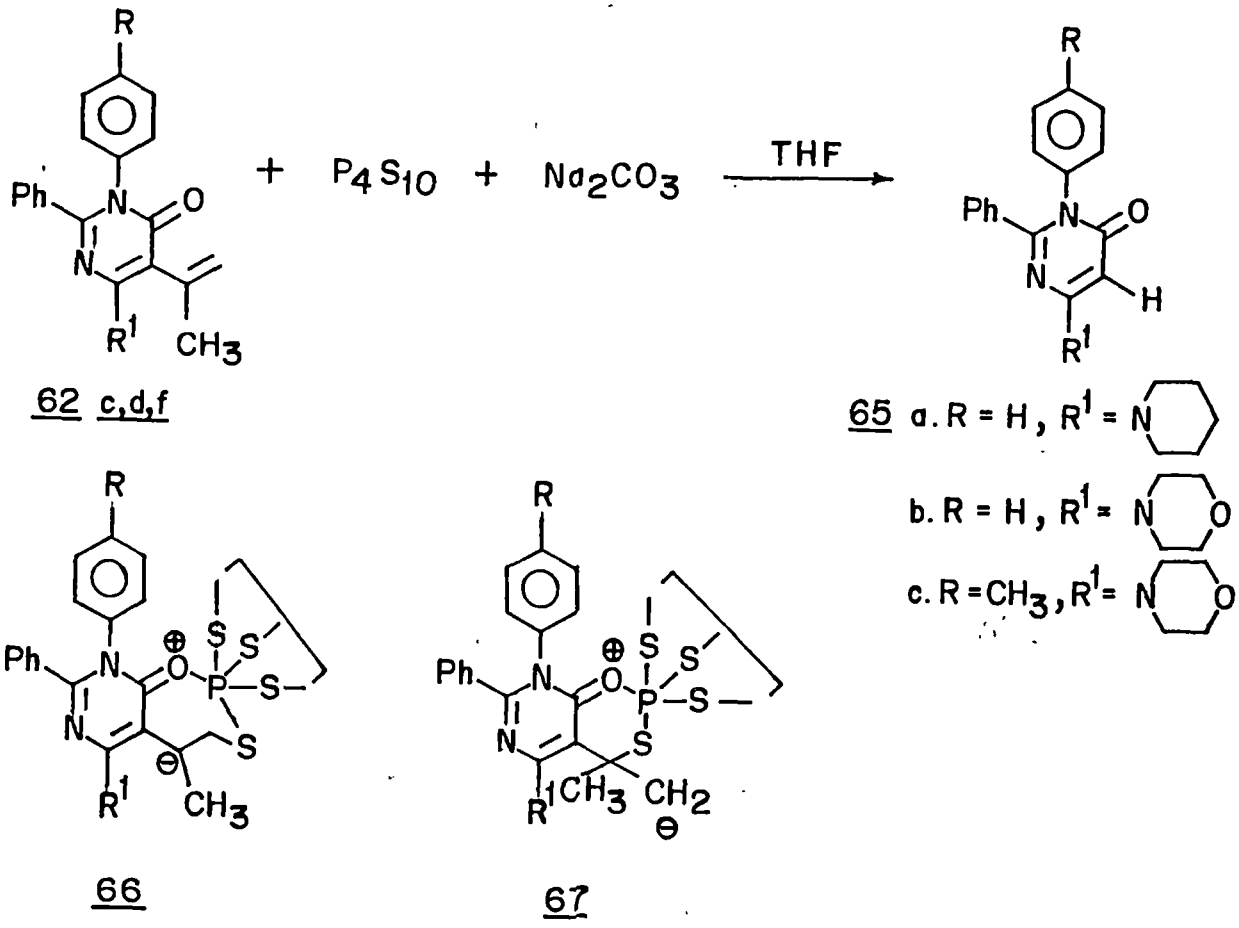
(A)



(B)

The 5-isopropenyl/vinylpyrimidinones 62 and 64 so obtained were treated with phosphorus pentasulfide for their

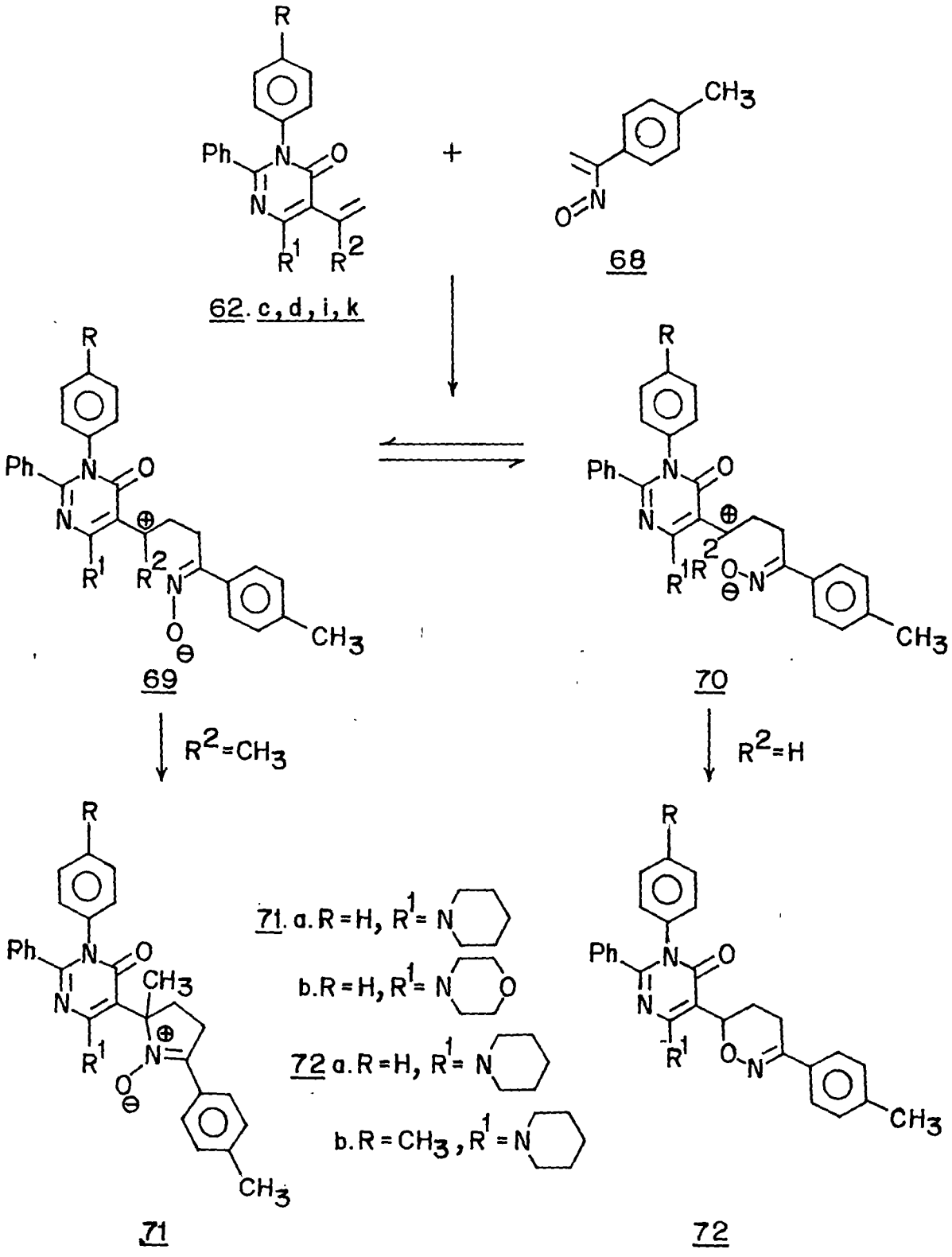
possible conversion into corresponding thiones. But these reactions resulted interestingly in the removal of isopropenyl functionality in case of 5-isopropenylpyrimidinones. Thus, the treatment of 5-isopopenylpyrimidin-4(3*H*)-ones **62c,d,f** with phosphorus pentasulfide in presence of sodium carbonate in dry tetrahydrofuran, followed by washing with aqueous sodium hydrogen *phosphate resulted in very good yields (90-94%) of pyrimidinones* **65** (Scheme 18). The pyrimidinones **65** were also characterised on the basis of analytical and spectral data. The compound **65a**, for example, was analysed for $C_{21}H_{21}N_3O$ and showed the molecular ion



Scheme-18

peak at *m/z* 331. Its IR spectrum showed a sharp band at 1654 cm^{-1} due to α,β-unsaturated carbonyl group and its ^1H NMR spectrum exhibited, in addition to other protons, the 5-H olefinic proton at δ 5.49. The possible mechanism leading to the formation of pyrimidinones **65** is not well understood but it is possible that the starting pyrimidinone first complexes with phosphorus pentasulfide to yield an intermediate of type **66** or **67**, which then decomposes to give the pyrimidinones **65**. However, the reactions of 5-vinylpyrimidin-4(3*H*)-ones **62g-i** with phosphorus pentasulfide resulted in an intractable mixture, from which no pure product could be isolated.

It was thought that the 5-isopropenyl/vinylpyrimidinones **62** can be utilised for the synthesis of a large variety of 5-substituted pyrimidinones by carrying out their reactions with various dienes and 1,3-dipoles. Keeping this in view, we investigated the reactions of pyrimidinones **62** with α-nitrosostyrene **68**, which have been reported to undergo [4+2] cycloadditions with carbon-carbon double bonds of alkenes,[71] allenes,[72] and dienes[73] and unusual [3+2] cycloaddition with cabon-nitrogen double bonds.[74, 75] Thus, the treatment of α-nitrosostyrene **68**, generated *in situ* form α-chlorooximes[76] and sodium carbonate, with 5-isopropenylpyrimidinones (**62c,d**) and 5-vinylpyrimidinones (**62i,k**) resulted in nitrones **71** and oxazines **72** arising from unusual [3+2] cycloadditions and [4+2] cycloadditions, respectively (Scheme 19). To our knowledge, this is the first report of unusual [3+2] cycloaddition of α-


R
Ph
N
O
N
R1
R2
62. c, d, i, k
+
CH3
O=N
68
69
70
R2=CH3
R2=H
71. a. R=H, R1= N
b. R=H, R1= N O
72 a. R=H, R1= N
b. R=CH3, R1= N
71
72

Scheme-19

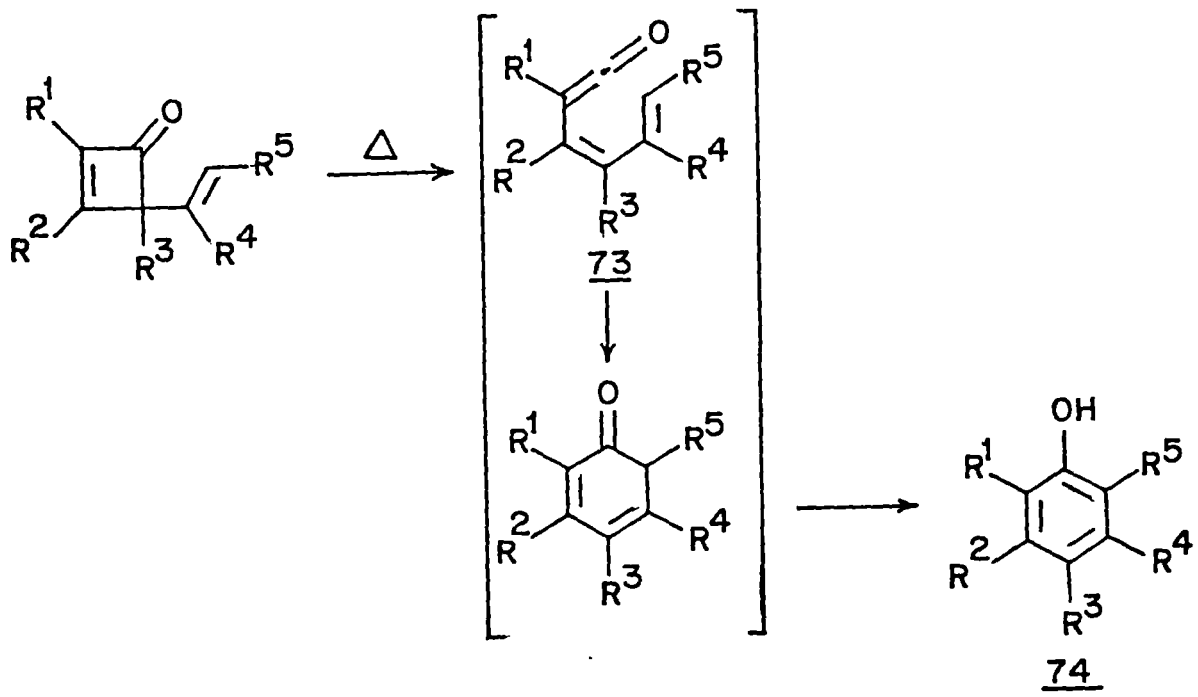
nitrososty renes with carbon-carbon double bonds. The products were characterised as nitrones **71** and oxazine derivative **72** on the basis of their analytical and spectral evidences. The IR spectrum (KBr) for nitrone **71a**, for example, showed strong absorption band around 1662 cm^{-1} due to α,β-unsaturated carbonyl group and 1208 cm^{-1} for N-O of nitrone and its mass spectrum exhibited a weak molecular ion peak at m/z 518. The presence of two downfield protons for the *ortho* protons of 4-methylphenyl group attached to nitrone ring in its ^{1}H NMR spectrum further supported the assigned structure. Similarly, the products **72** were assigned the oxazine structure on the basis of their IR, mass, ^{1}H and ^{13}C NMR spectra and C,H,N analysis. The probable mechanism leading to the formation of these products is outlined in Scheme-19. In this Scheme, it is assumed that the reactions of 5-isopropenyl/vinylpyrimidinones **62** with nitrosoalkene **68** yields interconvertible zwitterionic intermediates **69** and **70** and because of steric reasons, when $R^2 = CH_3$, the tansiod form **69** leads to nitrones **71**, whereas in case $R^2 = H$, the cisoid form **70** gives oxazines **72**.

In summary, the [4+2] cycloadditions of various 1,3-diaza-1,3-butadienes with vinyl/isopropenylketenes has resulted in a variety of pyrimidinones having an unsaturated side chain at C-5, which might prove to be biologically important and promising precurssors for 5-vinyl/isopropenyl pyrimidine nucleosides. The novel deisopropenylisation achieved by treating 5-isopropenyl pyrimidinones with P_4S_{10} may prove to be a general

deisopropenylisation route for any similar system. Unusual [3+2] cycloaddition of nitrosostyrenes with isopropenyl functionality of 5-isopropenyl pyrimidinones, to our knowledge, is perhaps the first such report of nitrosostyrenes addition to any C=C double bond. 5-Vinylpyrimidinones on the other hand yielded the oxazines *via* [4+2] cycloaddition with nitrosostyrenes.

I.3 : [4+2] *Cycloaddition Reactions of various 1,3-Diaza-1,3-Butadienes with Butadienylketene*

Various 1,3-diaza-1,3-butadienes synthesised in our laboratories[34,40] having polarised functions at 2 and/or 4-positions have been found to behave as efficient 4π components in successful [4+2] cycloaddition reactions with large variety of monosubstituted ketenes.[35,39,40] Subsequently vinyl/isopropenyl ketenes, consisting of a diene unit were also found to act as 2π component in such cycloadditions with these diazabutadienes.[77] In continuation of our pursuits in this direction and in order to have a further insight into the comparison of the dienic properties of 1,3-diazabutadienes and conjugated ketenes, we visualised to investigate the reactions of various 1,3-diaza-1,3-butadienes with butadienylketene. To our knowledge, the reports concerning the generation and synthetic utility of dienyl ketene are very rare and the only reported method involves the thermolysis of appropriately substituted cyclobutenones leading to various quinones and catechols 74 formed supposedly through putative dienylketene intermediate 73[78] (Scheme 20).



Scheme-20

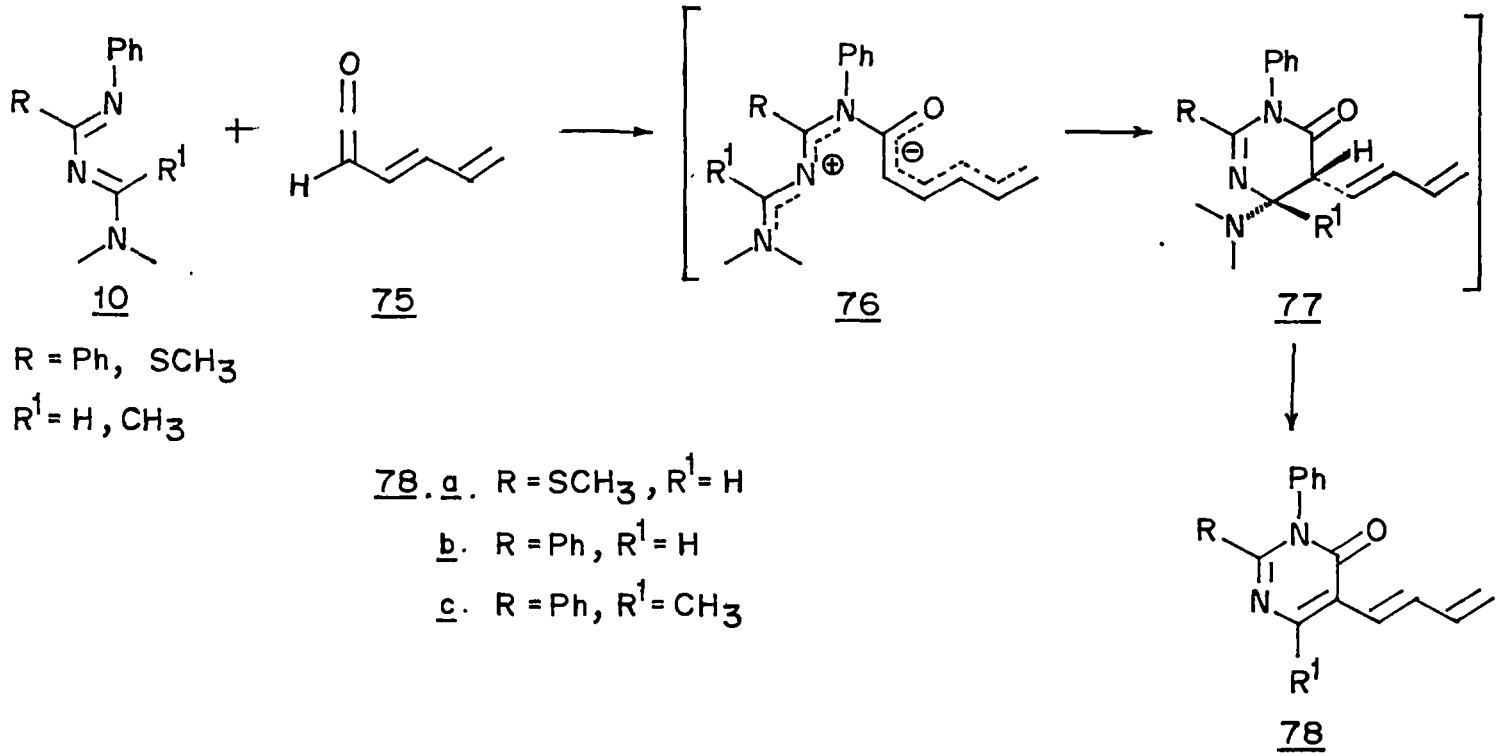
Herein, we report a new method for the *in situ* generation of butadienylketene 75 from sorbyl chloride and successful utilization of this ketene in [4+2] cycloaddition reactions with a variety of 1,3-diaza-1,3-butadienes. To our knowledge, this involves the first use of butadienylketene in cycloadditon reactions.

Results and Discussion

The treatment of 1,3-diaza-1,3-butadienes 10 with butadienylketene 75, generated *in situ* from sorbyl chloride and triethylamine in dry methylene chloride, resulted in the formation of previously unknown 5-(1',3'-butadienyl)pyrimidinones

78 in good yields (60-80%) (Scheme 21). The products were well characterised on the basis of analytical data and spectral evidences. The compound **78a**, for example, analysed for $C_{15}H_{14}N_2OS$ showed a molecular ion peak at *m/z* 270 in its mass spectrum. Its IR spectrum showed a strong absorption peak at 1683 cm^{-1} due to α,β-unsaturated carbonyl group. The absence of *N,N*-dimethylamino function and the presence of an olefinic H at δ 7.90 in the ^1H NMR spectrum of **78a** indicated the elimination of dimethylamine function from the initially formed [4+2] cycloadduct intermediate. In addition, ^1H NMR spectrum showed the presence of all dienyl protons. Its ^{13}C NMR spectrum was also in agreement with the assigned structure **78a**. As in earlier ketene reactions, the pyrimidinones **78** are clearly the result of [4+2] cycloaddition reactions involving 1,3-diaza-1,3-butadienes **10** as 4π component and butadienylketene as 2π component. As proposed earlier, the mechanism involves the initial formation of a [4+2] cycloadduct intermediate **77** *via* a zwitterionic intermediate **76**, followed by the elimination of *N,N*-dimethylamine function from **77** to yield 5-dienyl pyrimidinones **78** (Scheme 21). The formation of 5-dinenyl pyrimidinones **78** requires the *trans* arrangement of H-5/dimethylamino function in the intermediate **77**, which can arise either *via* highly stereoselective [4+2] cycloaddition or more probably through equilibration involving zwitterionic intermediate.

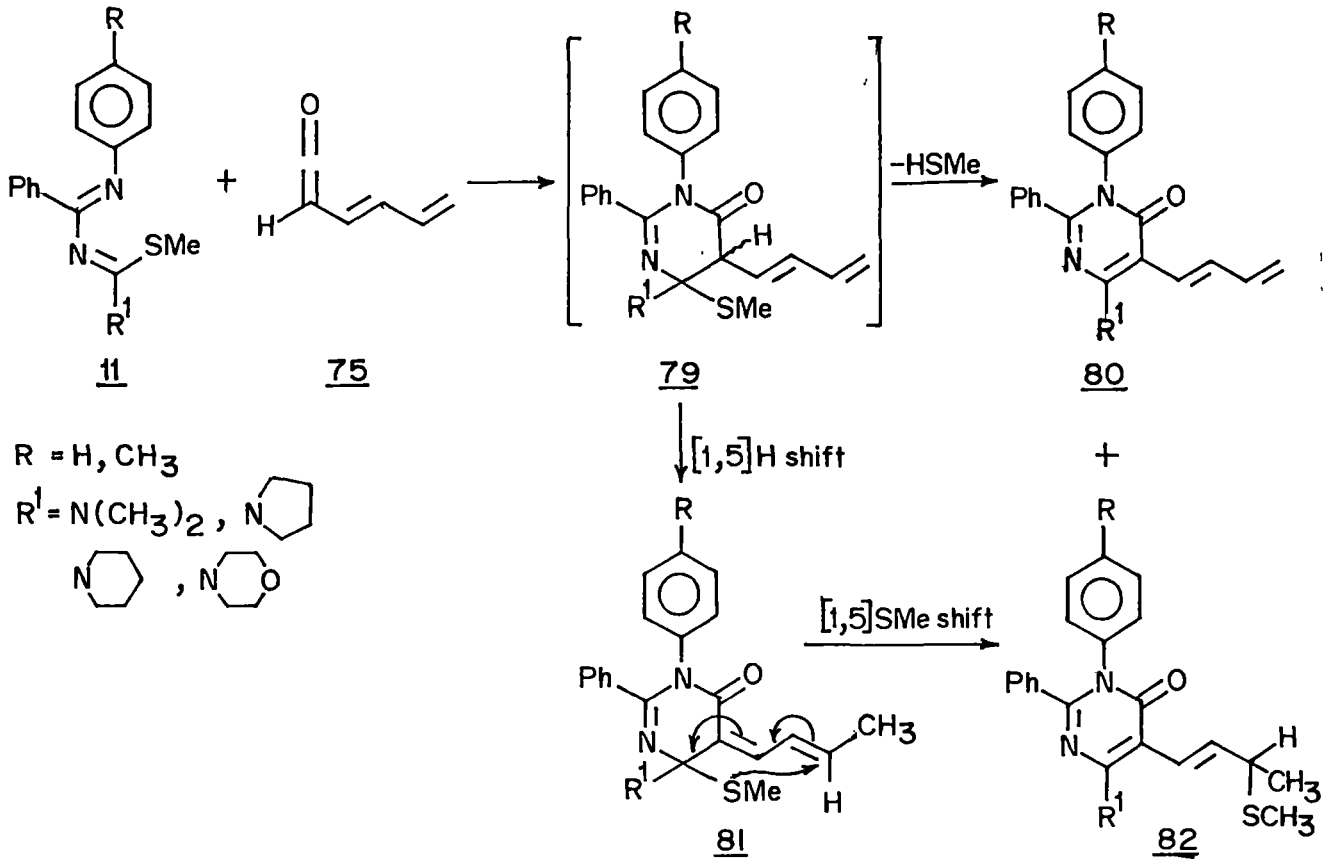
Further to these investigations, we have examined the reactions of butadienylketene **75** with various 1-Aryl-2-


Ph
R
N
N
R1
N
10
O
H
75
R = Ph, SCH3
R1 = H, CH3
76
77
78. a. R = SCH3, R1 = H
b. R = Ph, R1 = H
c. R = Ph, R1 = CH3
78

Scheme-21

phenyl-4-methylthio-4-secondaryamino-1,3-diaza-1,3-butadienes **11**. Interestingly, these reactions were found to result in a mixture (≈1:1) of 5-(1',3'-butadienyl)pyrimidinones **80** and 5-(1'-butenyl)pyrimidinones **82**. The separation of this mixture consisting of **80** and **82** with very close *Rf* values was accomplished by a careful silica gel column chromatography with natural loss of yields. The products were assigned the pyrimidinone structures **80** and **82** on the basis of their analytical and specral data. The compound **80a**, for example, analysed for $C_{22}H_{21}N_3O$ exhibited in its mass spectrum a molecular ion peak at *m/z* 343. Its IR specrum showed a sharp peak at 1649 cm^{-1} due to α,β-unsaturated carbonyl group. The appearance of carbonyl absorption at lower frequency in this case may be due to the weakening of C=O bond due to the possible push-pull mechanism involving secondary amine and carbonyl function. The ^1H and ^{13}C NMR spectra of **80a** exhibited peaks for dimethylamino and dienyl functionalities in agreement with the assigned structure **80a**. The product **82a**, on the other hand, analysed for $C_{23}H_{25}N_3OS$ showed a molecular ion peak at *m/z* 391 in its mass spectrum and a sharp band at 1636 cm^{-1}, due to α,β-unsaturated carbonyl group in its IR spectrum. Its ^1H NMR spectrum exhibited a doublet (J = 6.8 Hz) at δ 1.42 for $-CH_3$ protons and a multiplet at δ 3.36-3.47 for methine proton in addition to the signals for $-SCH_3$ (δ 2.04) and *N,N*-dimethylamine (δ 3.11) functionalities.

The probable mechanism leading to the formation of these pyrimidinones is outlined in Scheme-22. In this scheme it is



R = H, CH_3

R^1 = $N(CH_3)_2$, N , N , N O

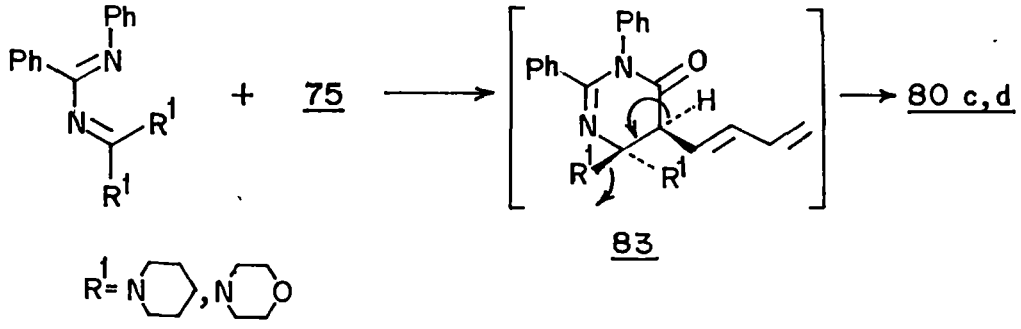
80,82 a. R = H, R^1 = $N(CH_3)_2$

b. R = H, R^1 = N

c. R = H, R^1 = N O

d. R = CH_3, R^1 = N

e. R = CH_3, R^1 = N O



R^1 = N , N O

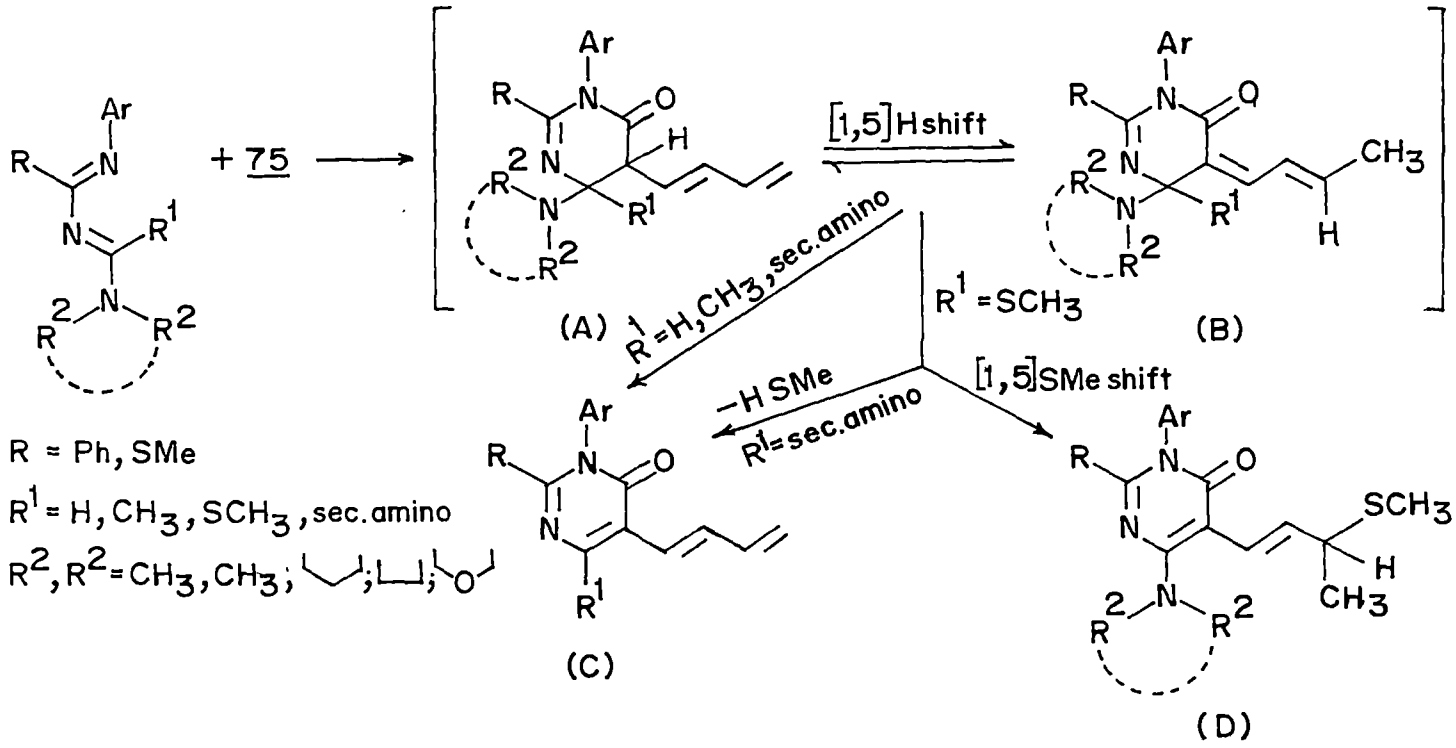
Scheme-22

assumed that the reactions of diazabutadiens **11** with butadienylketene **75** proceeds *via* zwitterionic intermediate of type discussed earlier leading to the initial formation of intermediate **79**. This intermediate persumably consists of a stereoisomeric mixture with H-5 being *cis* and *trans* to the methylthio at C-6. Based on this observations, the earlier assumed highly stereoselective cycloadditon mode for the formation of such an intermediate may clearly be ruled out. This intermediate then undergoes elimination of methanethiol, to yield pyrimidinone **80** when H-5 is *trans* to methylthio function. On the other hand the stereoisomer with *cis* H-5 and methylthio functions prefers [1,5] H shift over equilibration to *trans* stereomer and yields another intermediate **81**, which in turn undergoes [1,5] SMe shift to yield pyrimidinone **82**. Further, the formation of pyrimidinone **82** from intermediate **81** clearly indicates the preference for the methylthio shift over the shift of secondary amine function. A similar preference for [1,2] alkylthio shift has recently been reported in reactions of 1,3-diazabutadienes with haloketenes.[39] In order to further confirm the structure of **82** and to establish the exclusive migration of methylthio in formation of **82**, it was thought worthwhile to investigate the reactions of butadienylketene with 1,3-diaza-1,3-butadienes **12** having two secondaryamino functions at 4-position. But these reactions resulted in the exclusive isolation of pyrimidinones **80**, formed presumably again *via* the elimination of secondary amines from the initially formed intermediate **83**. The absence of

any rearranged product lends further support to the earlier assigned structure for pyrimidinones **82**. The structure **80** was assigned to the products on the basis of undepressed mixed melting points and identical spectral features for the pyrimidinone obtained earlier in reactions of 1,3-diazabutadienes **11** with butadienylketene.

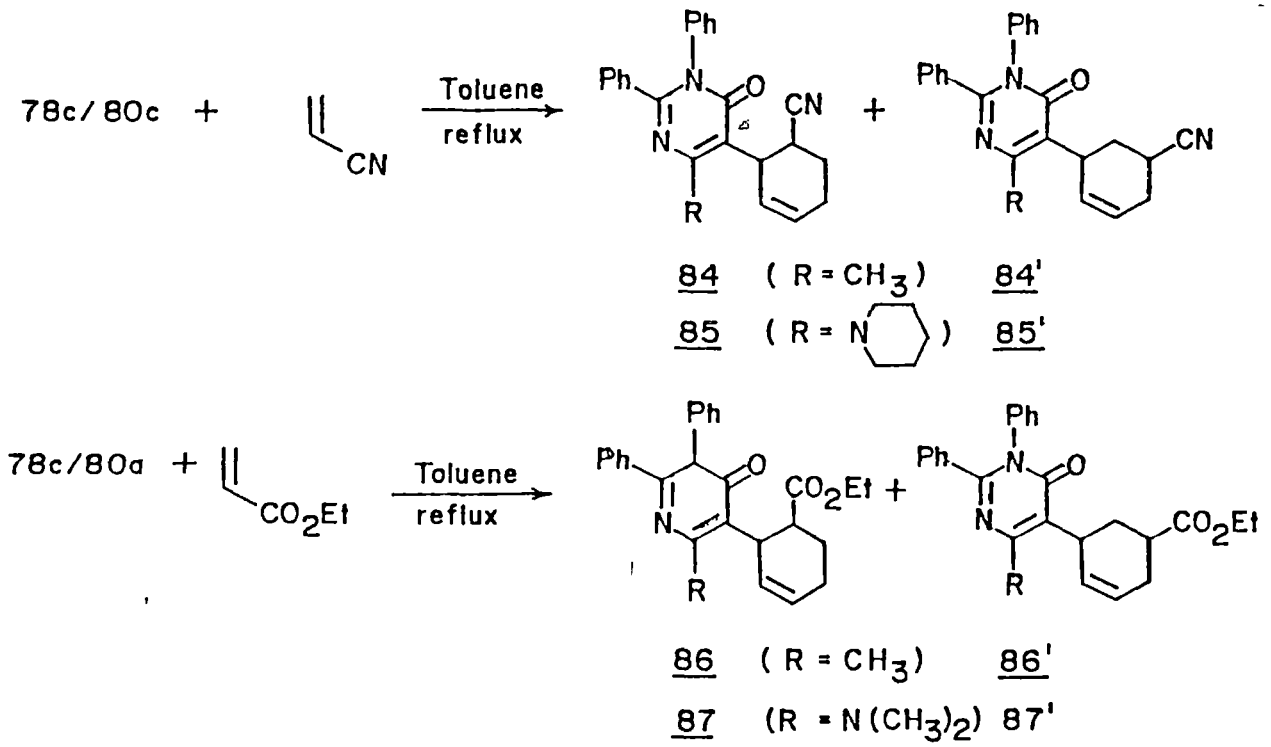
Keeping these observations in view, a generalised mechanistic picture for the formation of pyrimidinones **78**, **80** and **82** is presented in Scheme-23. It is assumed that the treatment of butadienylketene **75** with various 1,3-diaza-1,3-butadienes results in the initial formation of [4+2] cycloadduct (A) as intermediate which is in equilibrium with another intermediate (B) obtained by [1,5] H shift. In case, R^1 = H, CH_3 or secondary amine function, these intermediates (A, B) result in the elimination of secondary amine to yield pyrimidinones C (see reactions with 1,3-diazabutadienes **10** and **12**) and when R^1 = SCH_3, the intermediates (A, B) yield a mixture of C,in case of stereoisomer having *trans* H-5 and methylthio rearrangement via elimination of methylmercaptan (see pyrimidinones **80**) and D, for stereoisomer with *cis* H-5 and methylthio rearrangement *via* [1,5] SCH_3 shift (see pyrimidinones **82**), respectively.

The synthetic potential of 5-dienyl pyrimidinones **78** and **80** was established by carrying out their Diels-Alder cycloaddition reactions with a variety of dienophiles. All these reactions resulted in very good yields (86-96%) of corresponding adducts which were unambiguously characterised on the basis of their IR,


+ 75
[1,5]H shift
R = Ph, SMe
R1 = H, CH3, SCH3, sec.amino
R2, R2 = CH3, CH3;
R1 = H, CH3, sec.amino
R1 = SCH3
-H SMe
R1 = sec.amino
[1,5]SMe shift
(A)
(B)
(C)
(D)

Scheme-23

^{1}H NMR, ^{13}CNMR and mass spectral evidences and analytical data. The reaction of dienyl pyrimidinones **78c** and **80c** with acrylonitrile (AN) in refluxing toluene for 25-26 h resulted in the formation of a mixture of regioisomes **84/84'** (ratio 1:3) and **85/85'** (ratio 1:1.2) (Scheme 24). The individual components of these mixtures could not be separated by silica gel column chromatography because of their almost identical Rf values. The



Scheme-24

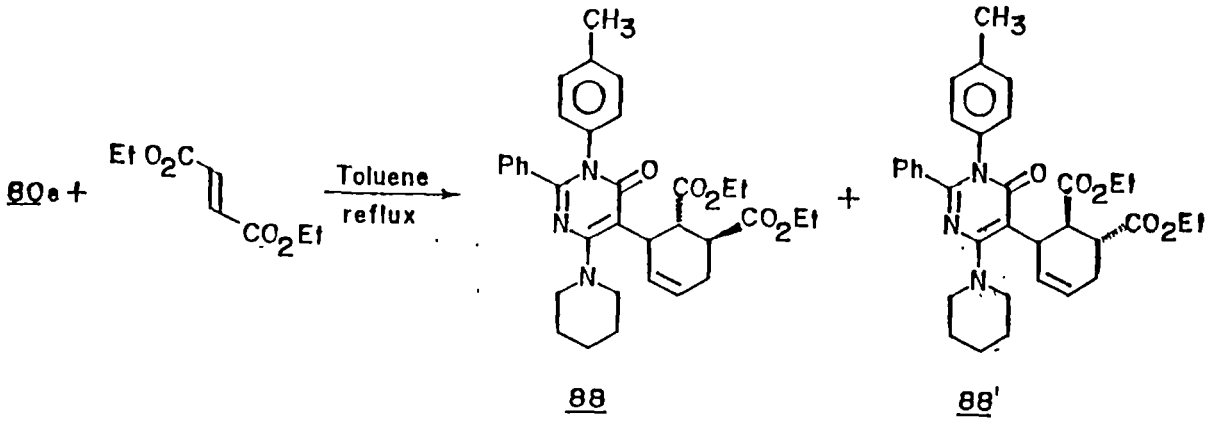
products were analysed as 2,3-diphenyl-5-(6'/5'-cyanocyclohex-2'-en-yl)-6-methyl-pyrimidin-4(3*H*)-ones **84/84'** and 2,3-diphenyl-5-(6'/5'-cyanocyclohex-2'-en-yl)-6-piperidinopyrimidin-4(3*H*)-ones **85/85'** on the basis of their analytical and spectral data. The mixture **84/84'** for example, analysed for $C_{24}H_{21}N_3O$ exhibited a

molecular ion peak at *m/z* 367. Its IR spectrum exhibited a peak of medium intensity at 2234 cm^{-1} and a strong intensity peak at 1659 cm^{-1} due to C= N and α,β-unsaturated carbonyl groups, respectively. Its ^{1}H and ^{13}C NMR spectra displayed spectroscopic signals/features fully compatible with the gross structural features. The ratio (3:1) for the regioisomeric mixture of **84/84'** could be inferred on the basis of the integration values of distinguishable methyl signals (δ 2.58 and 2.65). In addition, the ^{1}H NMR spectrum of **84/84'** showed the presence of all aromatic protons, olefinic protons and a series of multiplets for various methine and methylene protons. The ^{13}C NMR spectrum of this regioisomeric mixture also supported the assigned structures. Though, theoretically and mechanistically, the formation of regioisomers **84** and **85** as major isomers is more probable, but their relative specific regiochemistry in the mixtures could not be assigned on the basis of spectral data.

The Diels-Alder cycloadditions of 5-dienyl-pyrimidinones **78c** and **80a** with ethyl acrylate (EA) in refluxing toluene for 15-16 h yielded a similar inseparable mixture of regioisomers **86/86'** and **87/87'** (Scheme 24). The products were analysed as 2,3-diphenyl-5-(6'/5'-ethoxycarbonylcyclohex-2'-en-yl)]-6-methylpyrimidin-4(3*H*)-ones **86 /86'** and 2,3-diphenyl-6-dimethylamino-5-(6'/5'-ethoxycarbonylcyclohex-2'-en-yl]pyrimidin-4(3*H*)-ones **87 /87'** on the basis of their analytical and spectral data. The mixture **86/86'** analysed for $C_{26}H_{26}N_2O_3$ showed a molecular ion peak at *m/z* 414 in its mass spectrum. Its IR spectrum exhibited strong bands

at 1726 and 1662 cm^{-1} assigned to the ester carbonyl and α,β-unsaturated carbonyl group of pyrimidinone ring, respectively. The ^{1}H NMR spectrum of this regioisomeric mixture showed the presence of two methyl signals (δ 2.50 and 2.52) for 6-methyl group and the integration of these methyl signals indicated the presence of regioisomers **86/86'** in approximately (1:1.2) ratio. However, again the specific structure to the individual regioisomers could not be assigned on the basis of spectral data. The signals observed in ^{13}C NMR spectrum also attest to the gross structural features of the mixture **86/86'**.

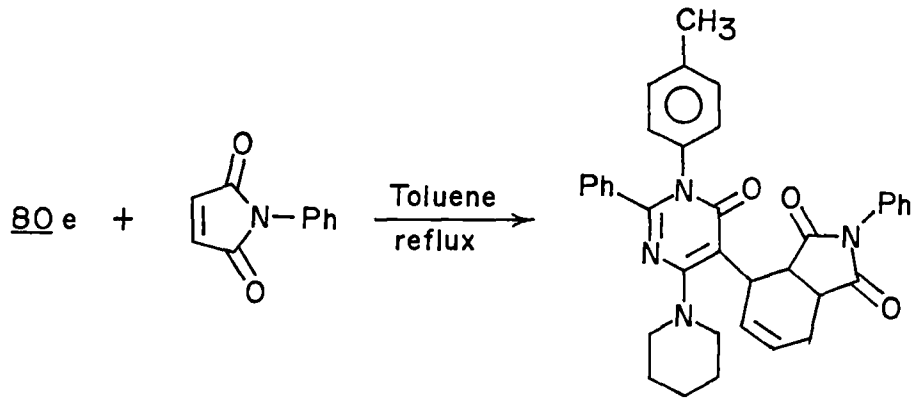
Further, the reaction of **80e** with diethyl fumerate (DEF) in refluxing toluene for 5-6 h also underwent [4+2] cycloaddition reaction to result in an inseparable regio/stereoisomeric mixture of **88/88'** in the ratio (1:1.5) (Scheme 25). The mixture was assigned structures **88/88'** on the basis of analytical data and

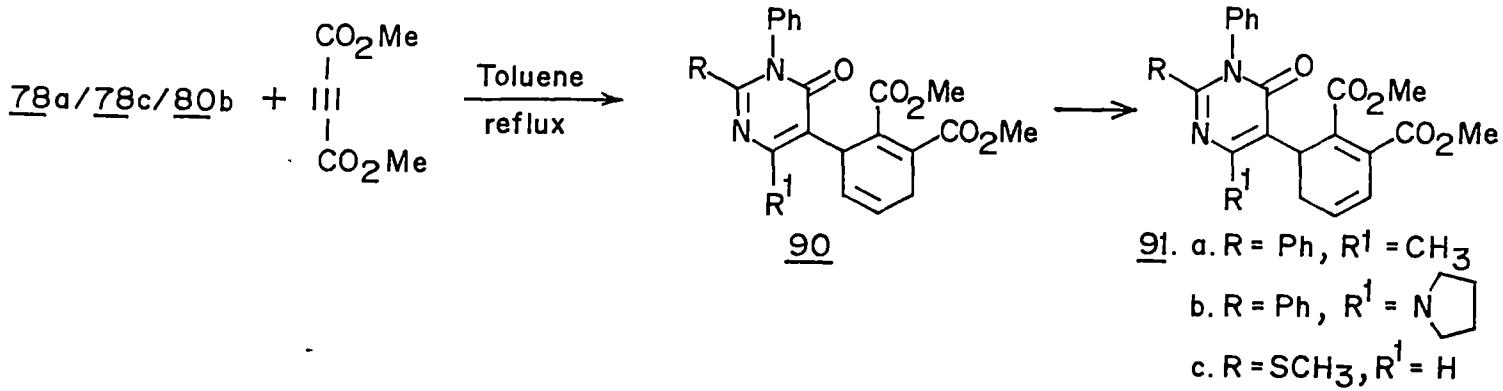


Scheme - 25

spectral evidences. Its mass specrum exhibited a molecular ion peak at *m/z* 569. The IR spectrum of **88/88'** showed strong absorption bands at 1729 and 1661 cm^{-1} due to bis(ethoxycarbonyl) group and α,β-unsaturated carbonyl group of pyrimidinone ring respectively. Its ^{1}H and ^{13}C NMR spectra exhibited spectroscopic parameters fully compatible with the gross structural features of the mixture. The ratio (1:1.2) for this mixture could easily be derived from the integration values of two methyl signals (δ 2.25 and 2.26) in its ^{1}H NMR spectrum. Here again the specific structure to the individual isomers could not be assigned on the basis of the gathered data.

The reactions of 5-dienyl pyrimidinones **78** and **80** with *N*-Phenylmaleimide (NPM) and dimethyl acetylene dicarboxylate (DMAD) resulted in the formation of Diels-Alder adducts which were characterised on the basis of their IR, mass, ^{1}H and ^{13}C NMR spectra and elemental analysis. The treatment of 5-dienyl pyrimidinone **80e** with NPM in refluxing toluene for 1 h gave a single Diels-alder cycloadduct **89** (Scheme 26). The product **89** analysed for $C_{36}H_{34}N_4O_3$ showed peaks at *m/z* 570 (M^+) and 397 (M^+-NPM) in its mass spectrum. Its IR spectrum exhibited intense peaks at 1701 and 1651 cm^{-1} assigned to dicarboximido carbonyls and α,β-unsaturated carbonyl group of pyrimidinone ring respectively. Its ^{1}H NMR spectrum exhibited, in addition to aromatic proton signals, peaks at δ 1.65-1.69 (m, $-CH_2-CH_2-CH_2-$); 2.27-2.31 [m, 4H; consisting in 1H, H-1' and δ 2.30 (s, $-CH_3$)] 2.95-3.02 (m, 1H); 3.29-3.43 (m, consisting of $-CH_2-$ and $-CH_2-N-$


80 e
Toluene
reflux
Ph
CH3
89


78a/78c/80b
CO2Me
CO2Me
Toluene
reflux
Ph
R
R1
90
91. a. R = Ph, R1 = CH3
b. R = Ph, R1 = N
c. R = SCH3, R1 = H

Scheme-26

CH_2-); 3.85 (d, J = 9.0, with fine splitting, 1H) and 5.95-5.98 (m, olefinic). Its ^{13}C NMR spectrum also supported the assigned structure **89**.

The reactions of **78a**, **78c** and **80b** with DMAD, in refluxing toluene for 4-6 h, resulted in the isolation of products which could be assigned structure **91** on the basis of their IR, mass, ^1H and ^{13}C NMR spectra and elemental analysis. The spectral data for **91a**, which was analysed for $C_{27}H_{24}N_2O_5$ includes: molecular ion peak at *m/z* 456 in its mass spectrum; strong peaks at 1719 and 1662 cm^{-1} due to methoxy carbonyl and α,β-unsaturated carbonyl group of pyrimidinone ring, respectively, in its IR spectrum; and the presence, in addition to aromatic protons, of signals for methyl (s, δ 2.41), methylene (m, δ 2.34-2.45), two methoxycarbonyls (s, δ 3.68 and s, δ 3.76), and olefinic protons (m, δ 5.58-5.64 and m, δ 5.83-5.89) in its ^1H NMR spectrum. Surprisingly, the methine protons could not be detected in the ^1H NMR spectrum of **91a** and **91b**. However, their ^{13}C NMR spectra exhibited the presence of all carbons including the methine carbon.

The products **91** presumably arise from the rearrangement of the initially formed nonconjugated 2',5'-cyclohexadienyl Diels-Alder adducts **90**. Any of the structures **90** and **91** may be assigned on the basis of the above mentioned data. However, structure **91** was tentatively assigned on the basis of the observed doublet (J = 9.5 Hz) for H-4' in the ^1H NMR spectrum of **91b**. Also, due to the presence of 6-pyrrolidino functionality in

91b, the downfield shift of methylene (H-4') protons signal (δ 4.33-4.36; m) as compared to that in 91a (δ 2.34-2.45, m) and 91c (δ 2.95-3.20) suggests its close vicinity with the pyrrolidine functionality and hence further supports structure 91. In order to unambiguously assign the structures to these products and to detect the presence of methine proton, it is planned to take help of $\{^1H\}$-$\{^1H\}$ NMR-homonuclear and $\{^1H\}$-$\{^{13}C\}$-NMR heteronuclear spin correlation spectra for these compounds.

In conclusion, the [4+2] cycloaddition reactions of various 1,3-diaza-1,3-butadienes with butadienylketene have proved to be a convenient method for the synthesis of 5-dienyl pyrimidinones. Subsequent Diels-Alder cycloaddition of these pyrimidinones with various dienophiles yielded a variety of 5-substituted pyrimidinones. Further, the cycloadditions of butadienylketene with various heterodienes and imines may, in fact, prove to be a general method for the synthesis of various 1,3-butadiene-substituted heterocyclic systems.

I.4: *Synthesis and [4+2] Cycloaddition Reactions of 4-(N-Allyl/Cinnamoyl-N-Aryl)amino-1,3-Diaza-1,3-Butadienes with Conjugated Ketenes and Chloroketene: Entry to Novel Primidinone/Fused Pyrimidinone Derivatives*

The construction of functionalised nitrogen heterocycles is an important area of recent interest in medicinal and natural product chemistry. In particular, substituted pyrimidinones are attracting the increasing attention of synthetic community

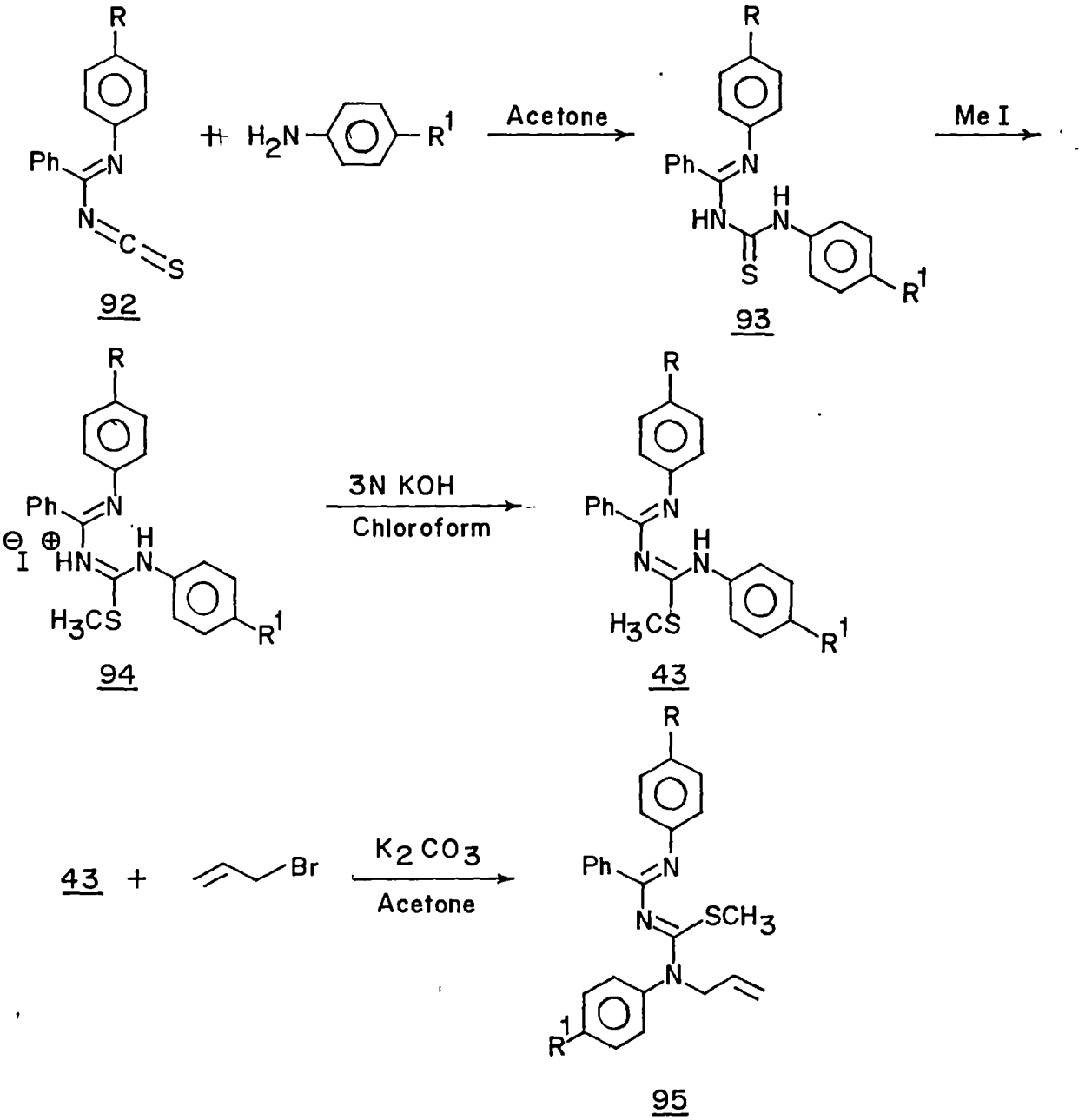
because of the important role played by such systems in many natural products,[79] antibiotics[80] and drugs.[81] The heterocycle-fused pyrimidine derivatives have been shown to exhibit antitumor activity[82] and potent blood sugar lowering activity.[83] Quinazoline derivatives have been found to act as neoplasm inhibitors[84] and are widely used as diuretics[85] and antihypertensive drugs.[86]

A large variety of substituted pyrimidinones have been synthesised in our laboratories following extensive studies on [4+2] cycloaddition reactions of 1,3-diaza-1,3-butadienes with a variety of ketenes. Keeping in view the biological importance of fused pyrimidines, it was thought worthwhile to utilise such [4+2] cycloaddition reactions for the synthesis of heterocycle/benzo fused pyrimidinones. As an entry into this area, we have synthesised 4-(*N*-allyl-*N*-aryl)amino-1,3-diaza-1,3-butadienes **95** and examined their reactions with chloroketene and conjugated ketenes. It was conceived that [4+2] cycloaddition reactions of **95** with such ketenes could result in pyrimidinones having latent functionalities at 5- and 6-position and such pyrimidinones could then be transformed to several useful fused pyrimidinones. The reactions of 1,3-diazabutadienes **95** with various ketenes once again exhibited the preference for **95** to act as 4π-component, as compared to conjugated ketenes, which participate as 2π-component in [4+2] cycloaddition reactions.

Results and Discussion

In continuation of our pursuits to devise methods for the synthesis of newer 1,3-diazabutadienes, we have recently reported the synthesis of various 1-aryl-4-(*N*-aryl)amino-2-phenyl-1,3-diaza-1,3-butadienes **43** which underwent nucleophilic/ cycloaddition reactions with phenyl-, chloro-, bromo- and iodoketenes accompanied at times by interesting rearrangements to yield novel pyrimidinone derivatives.[40] It was felt that the synthesis of targeted benzo/heterocyclic ring(s) fused pyrimidinones could be best realised by the initial [4+2] cycloaddition of 1-aryl-4-(*N*-allyl-*N*-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **95**. The desired 1,3-diazabutadienes **95** were synthesised by the reaction of benzimidoyl isothiocyanates **92**[87] with primary aromatic amines, S-methylation of the resultant thioureas **93** followed by the treatment of hydroiodide salt **92** so obtained with allyl bromide in acetone in the presence of potassium carbonate. The attack of *N*-5 and not *N*-1 or *N*-3 at allyl bromide is in accordance with the earlier observed better nucleophilicity of *N*-5 compared to other nucleophilic sites.[40] Such regiochemical aspects concerning the cycloadditions of **95** with various ketenes have been further investigated.

Thus, the treatment of **95** with isopropenyl/vinylketenes **60**, generated *in situ* from 3,3-dimethylacroyl chloride/crotonyl chloride and triethylamine, in methylene chloride, resulted in good (for vinylketene) to high (for isopropenylketene) yields of

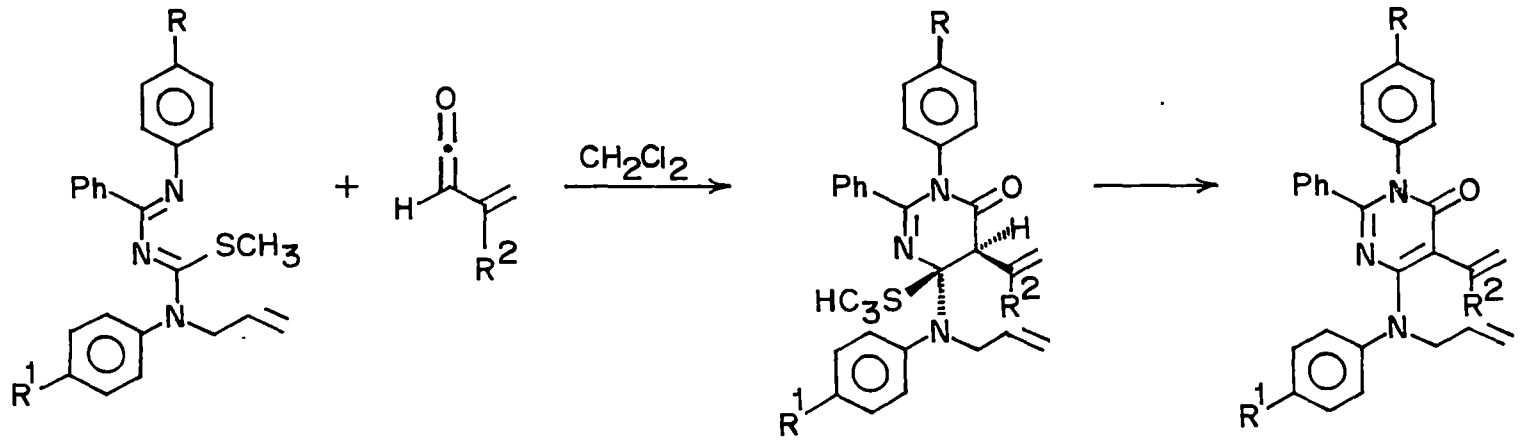


95. a. R = H, R^1 = H
b. R = H, R^1 = CH_3
c. R = H, R^1 = OCH_3
d. R = CH_3, R^1 = H
e R = CH_3, R^1 = CH_3
f. R = CH_3, R^1 = OCH_3

Scheme- 27

3-aryl-6-(*N*-allyl-*N*-aryl)amino-5-isopropenyl/vinyl-2-phenyl-pyrimidin-4(3*H*)-ones **97** (Scheme 28). The pyrimidinones **97** were assumed to be formed *via* the elimination of -HSMe from the initially formed [4+2] cycloadduct **96** as intermediate. The structure **97** was assigned to these products on the basis of analytical and spectral data. The pyrimidinone **97a**, for example, analysed for $C_{28}H_{25}N_3O$ showed a molecular ion peak at *m/z* 419. Its IR spectrum exhibited a strong absorption band at 1651 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^1H NMR spectrum showed in addition to aromatic protons, the signals for methyl (δ 1.64), olefinic and allylic protons (see experimental section). ^{13}C NMR signals were also in agreement with the assigned structure **97a**. The reactions of (*N*-allyl-*N*-aryl)amino-1,3-diaza-1,3-butadienes **95** with isopropenylketene were found to be quite efficient and pyrimidinones (**97a-e**) were isolated in very good yields. However, in reactions of **95** with vinyl ketene, even though the tlc of the reaction mixtures showed complete disappearance of the starting materials, the pure products could usually not be isolated, except pyrimidinone **97f**.

The pyrimidinones **97** having vinyl/isopropenyl function at C-5 and (*N*-allyl-*N*-aryl)amino function at C-6 appeared to be potential auxiliaries for the synthesis of various 5,6-fused pyrimidinones and this possibility was exploited for the synthesis of desired fused pyrimidinones. Thus, the thermolysis of pyrimidinones **97** in refluxing xylene resulted in the formation of 3,9-diaryl-3,5,6,9-tetrahydro-5,5-dimethyl-2-phenylpyrimido-



95 60 96 97

97. a. $R = R^1 = H$; $R^2 = CH_3$

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

c. $R = H$, $R^1 = OCH_3$, $R^2 = CH_3$

d. $R = R^1 = R^2 = CH_3$

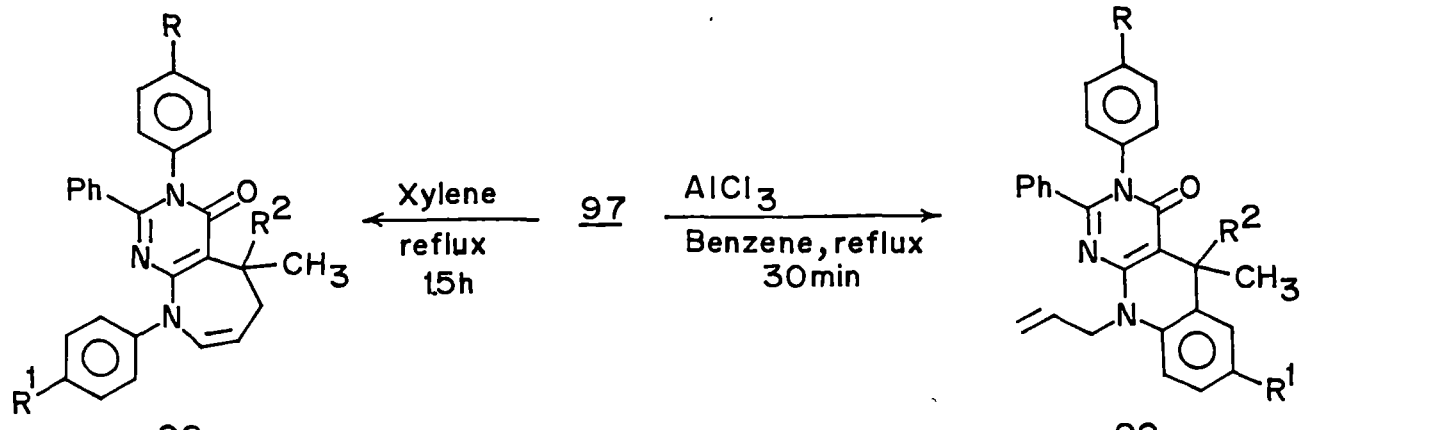
e. $R = CH_3$, $R^1 = OCH_3$, $R^2 = CH_3$

f. $R = H$, $R^1 = OCH_3$, $R^2 = H$

Scheme – 28

[4,5-b]azepin-4-ones **98**, which were isolated in good yields as colorless crystals after purification by silica gel column chromatography. The pyrimido[4,5-b]azepin-4-ones **98**, presumably are the result of an intramolecular ene reaction between *N*-allyl group at 6-positon and isopropenyl group as enophile at 5-position of the starting pyrimidinone **97** (Scheme-29). Their IR, ^{1}H NMR, ^{13}C NMR and mass spectral data clearly established the assigned structures **98**. The compound **98a**, for example, analysed for $C_{29}H_{27}N_3O$, showed a molecular ion peak at *m/z* 433 in its mass spectrum and its IR spectrum (KBr) showed a strong peak at 1645 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^{1}H NMR spectrum showed the presence of three methyl groups (δ 1.59, s, 6H, 2 x $-CH_3$ and δ 2.37, s, $-CH_3$), a methylene group (δ 2.43, d, J = 7.1 Hz) and olefinic protons (δ 5.54 and 6.23). Its ^{13}C NMR spectrum exhibited apart from other carbons, the signals for three methyl carbons (δ_C 21.1, 2 x $-CH_3$ and δ_C 29.2, $-CH_3$) which attest well to the assigned structure **98a**.

Further, the treatment of 5-isopropenyl-6-(*N*-allyl-*N*-aryl) amino-pyrimidinones **97** with aluminium chloride in refluxing benzene for about 30 minutes resulted in annelation reaction to yield novel pyrimidoquinoline derivatives **99** (Scheme 29). The products were characterised as 10-allyl-7-alkyl-3-aryl-2-phenyl-3,5,10-trihydro pyrimido[4,5-b]quinolin-4-ones **99** on the basis of their analytical and spectral data. The IR spectrum of **99a** showed a sharp absorption band at 1652 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^{1}H NMR spectrum exhibited the presence of



98

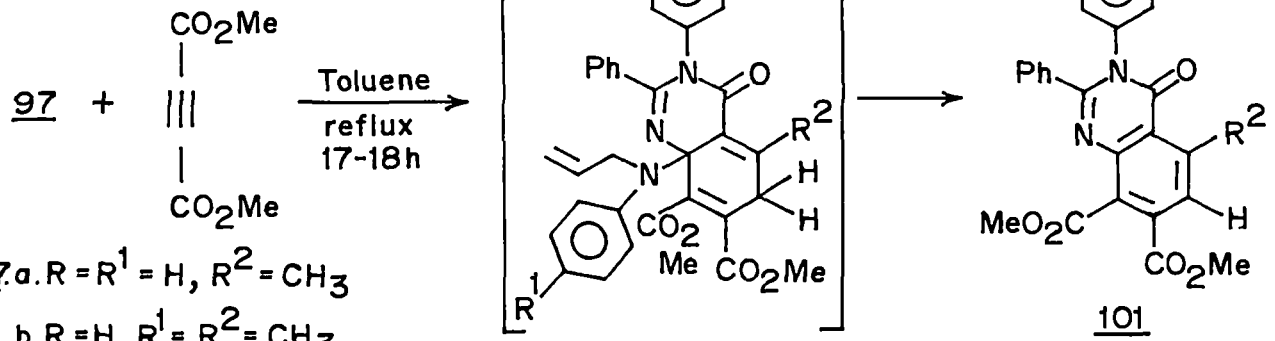
98.a. R = H, $R^1 = R^2 = CH_3$

b. R = CH_3, $R^1 = OCH_3$, $R^2 = CH_3$

99

99.a. R = H, $R^1 = R^2 = CH_3$

b. R = H, $R^1 = OCH_3$, $R^2 = CH_3$



97.a. R = R^1 = H, $R^2 = CH_3$

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

c. R = H, $R^1 = OCH_3$, $R^2 = CH_3$

100

101

R = H, $R^2 = CH_3$

Scheme-29

aromatic protons with expected splittings, three methyl protons (δ 1.87, 2 x $-CH_3$ and δ 2.30, Ar-CH_3) and *N*-allyl protons. Presence of a molecular ion peak at *m/z* 433 in its mass spectrum and three methyl carbons (δ_C 20.7, 2 x $-CH_3$ and δ 30.3, $-CH_3$) along with allyl carbons and quartenary carbons in its ^{13}C NMR spectrum further confirmed the assigned structure **99a**.

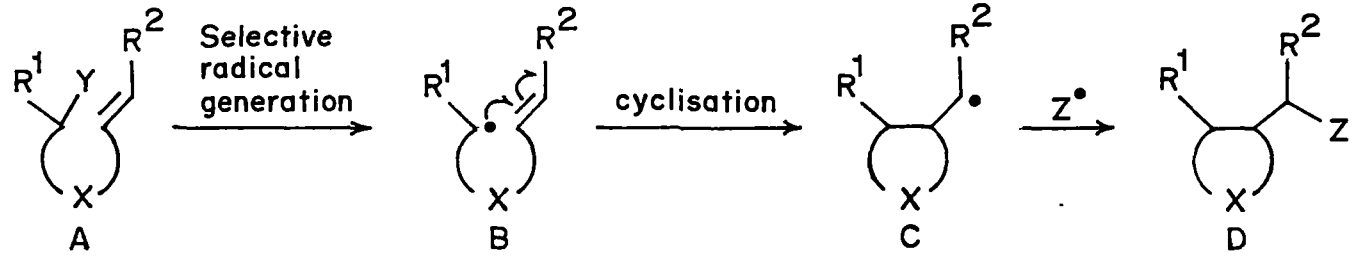
It was felt that the reactions of pyrimidinones **97** with dimethylacetylene dicarboxylate (DMAD) can follow a number of paths leading to the formation of fused pyrimidinones and these reactions were investigated in order to understand the reaction path followed and nature of the products formed in these cases. Thus, the treatment of **97** with DMAD in refluxing toluene for 17-18 h resulted in the good yields of the product which was characterised as 7,8-bis(methoxycarbonyl)-5-methyl-2,3-diphenyl quinazolin-4(3*H*)-one **101**. The quinazolinone **101** was assumed to be formed *via* the elimination of (*N*-allyl-*N*-aryl)amino group from the initially formed [4+2] cycloadduct **100** as intermediate. This was further confirmed experimentally by performing the DMAD cycloaddition under similar conditions by varying the function R^1 (R^1=H, CH_3, OCH_3) in pyrimidinones **97**; all of which were shown to give the same product **101**. The quinazolinone structure **101** could easily be assigned on the basis of analytical data and spectral evidences. The product **101**, analysed for $C_{25}H_{20}N_2O_5$ showed a molecular ion peak at *m/z* 428 in its mass spectrum. Its IR spectrum exhibited strong absorptions for two ester carbonyl groups (1733 cm^{-1}) and a sharp peak at 1674 cm^{-1} due to α,β-

unsaturated carbonyl group. Its ^{1}H NMR spectrum showed peaks for a methyl (δ 2.91), two methoxy (δ 3.97 and 3.99) and an aromatic proton at δ 7.87 (H-6) as sharp singlet, apart from other aromatic protons. The signals observed in its ^{13}C NMR also attest to the assigned structure.

Radicals have recently attracted the attention of synthetic chemists due to their high stereo and regioselectivity in radical cyclisations and because of their potential utility in the synthesis of both carbocyclic and heterocyclic compounds.[88] Radical reactions can be classified into two types, based on the structures of radical initiators[89] (Scheme 30). Type I radical cyclisations proceed by the formation of a carbon centered radical A generated by the homolytic cleavage of a carbon-hetero atom bond, such as C-X, C-S, C-Se etc. The resulting radical B adds to intramolecular multiple bond, generating the exocyclic radical C which is then trapped to form the cyclised product D. Alternatively, the type II radical cyclisation[90] is defined as one in which carbon centered radical F is generated by the addition of a radical Y$^{\bullet}$ to an olefin, which then undergoes the corresponding cyclisation process.

In continuation of our studies on the synthesis of fused pyrimidinones, we have investigated the use of sulfenyl radical in the cyclisation of pyrimidinones **97** having two different double bonds, isopropenyl group at 5-position and *N*-allyl function at 6-position. In order to know the nature of products formed we have carried out the reactions of pyrimidinones **97** with

Type I



X = C, O, N etc

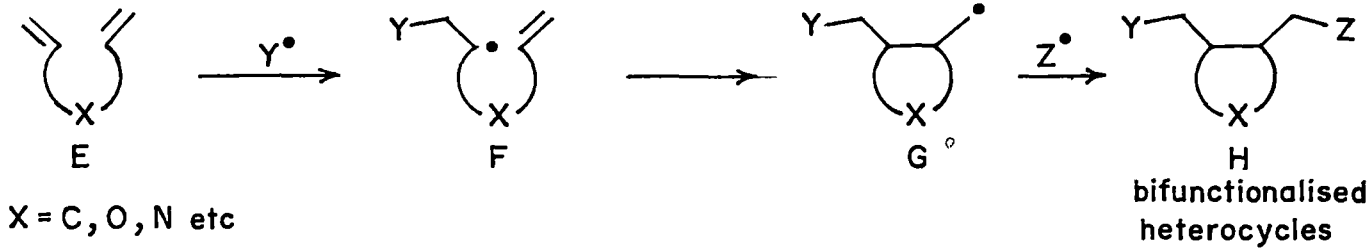
Y = hetero atom

initial radical

cyclic radical

stable product

Type II



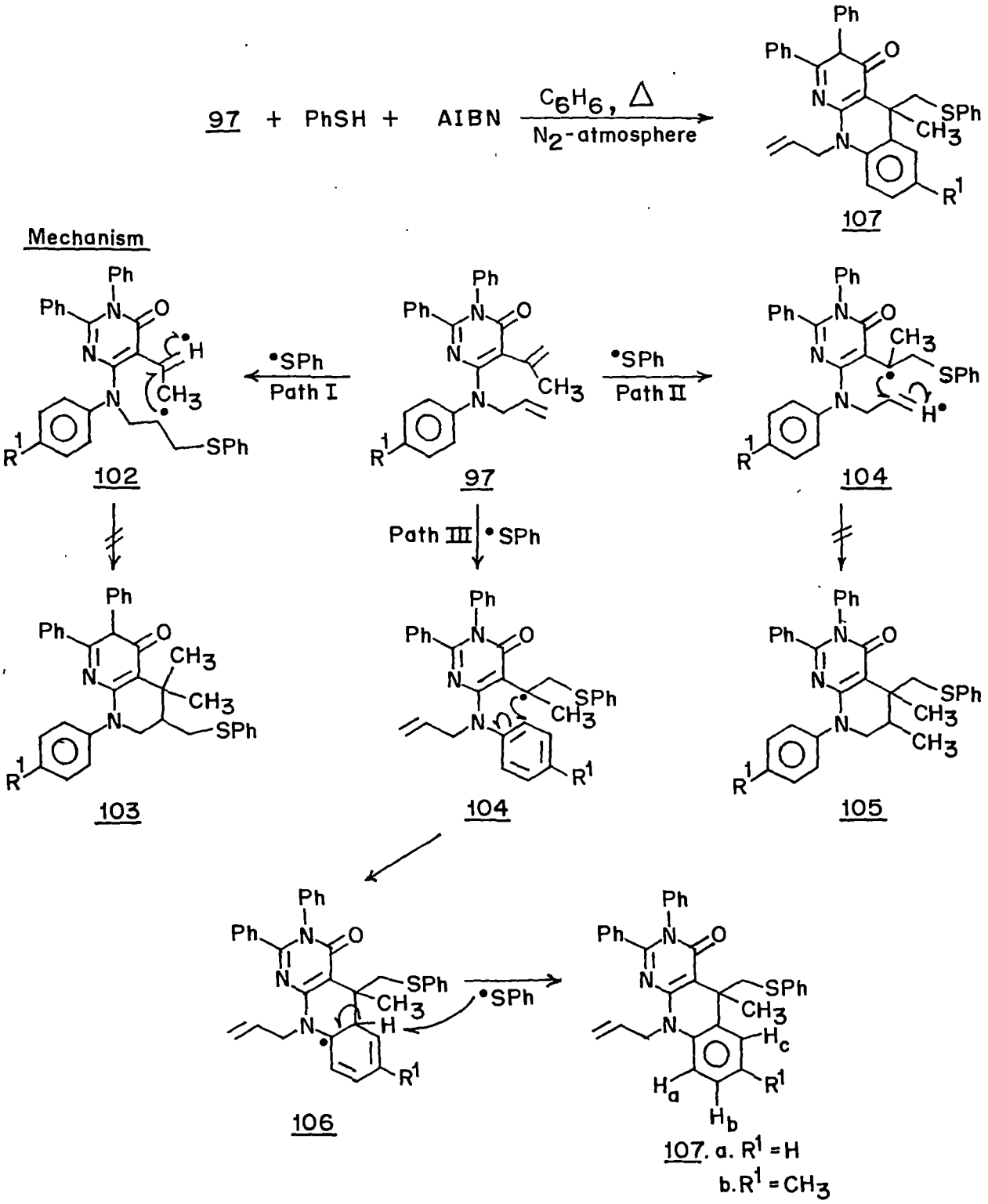
X = C, O, N etc

bifunctionalised heterocycles

Scheme-30

thiophenol in the presence of α,α'-azoisobutyronitrile (AIBN) in refluxing benzene under nitrogen atmosphere. Based on the above mentioned type II radical addition-cyclisation process, the expected products were pyrido pyrimidinones **103**, involving the addition of the sulphenyl radical to the *N*-allyl function resulting in a radical intermediate **102** which on cyclisation can yield **103** (Path I); pyrido pyrimidinones **105**, involving the addition of sulphenyl radical to the isopropenyl function leading to radical intermediate **104**, which on cyclisation with *N*-allyl can yield **105** (Path II). However, Path I may be ruled out on the basis of the better stability of the isopropenyl radical in intermediate **104** as compared to that in intermediate **102**. Further, the spectral data of the isolated products from the above reaction, ruled out the possibility of products **103** or **105**. A careful examination of the spectral data revealed, interestingly, the formation of unusual cyclisation involving the *N*-aryl group in preference to *N*-allyl leading to the formation of 10-allyl-2,3-diphenyl-5-methyl-5-phenylthiomethyl-3,5,10-trihydro-pyrimido[4,5-b]quinolin-4-ones **107** *via* **104** as an intermediate (Scheme 31).

The structure **107** for these products was established on the basis of IR, mass, ^{1}H NMR, ^{13}C NMR and $\{^{1}H\}$-$\{^{1}H\}$-homonuclear correlation spectra (Fig.1). The compound **107a**, for example, analysed for $C_{34}H_{29}N_3OS$ showed a molecular ion peak at *m/z* 527. Its IR spectrum showed a strong absorption band at 1655 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^{1}H NMR spectrum exhibited


97 + PhSH + AIBN
C6H6, Δ
N2-atmosphere
107
Mechanism
•SPh
Path I
•SPh
Path II
102
97
104
Path III •SPh
103
104
105
106
•SPh
107. a. R1 = H
b. R1 = CH3
Scheme-31

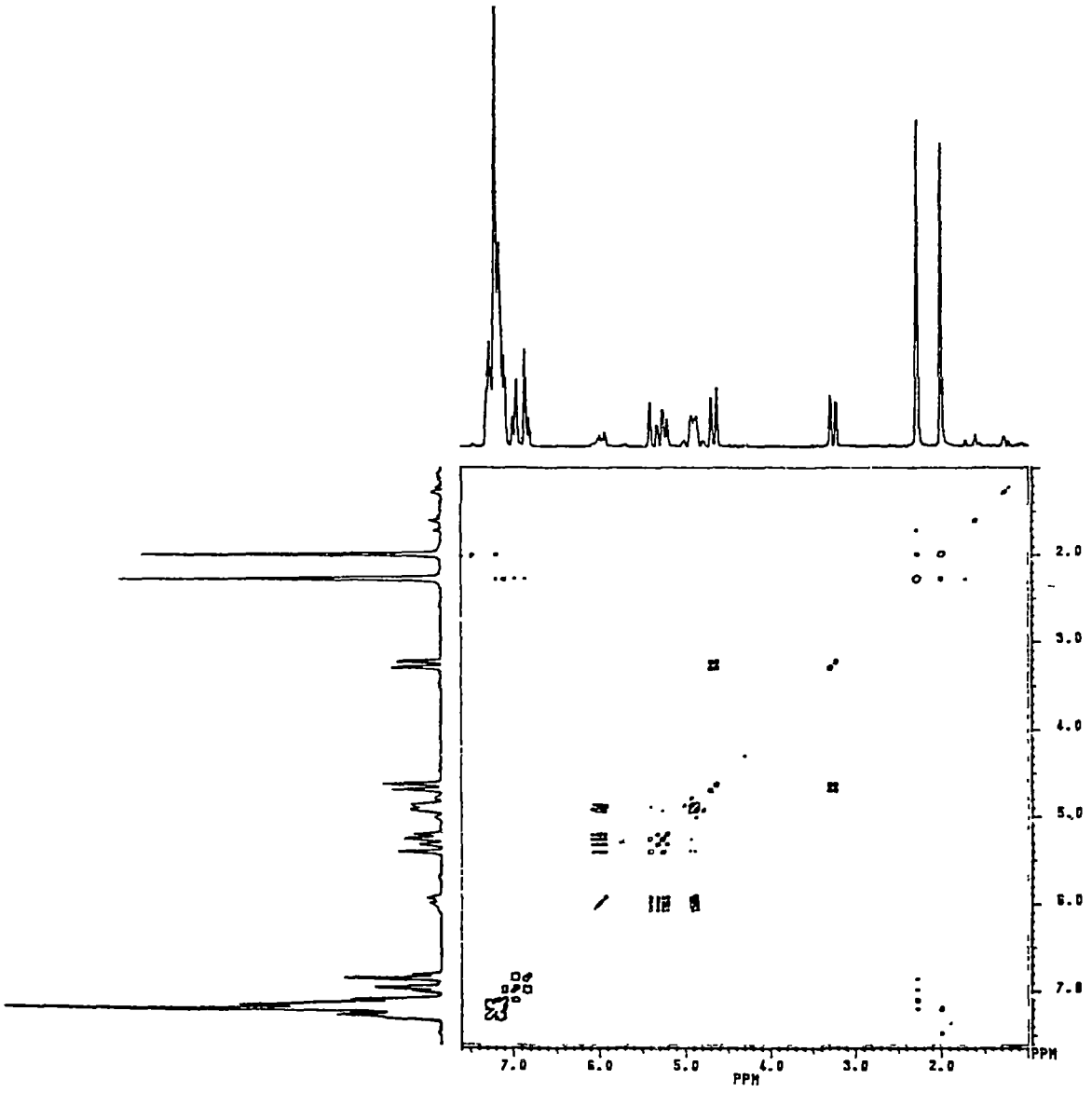


Fig. 1: 200 MHz $\{^1H\}$-$\{^1H\}$-NMR homonuclear spin correlation (COSY) spectrum for **107b** in $CDCl_3$

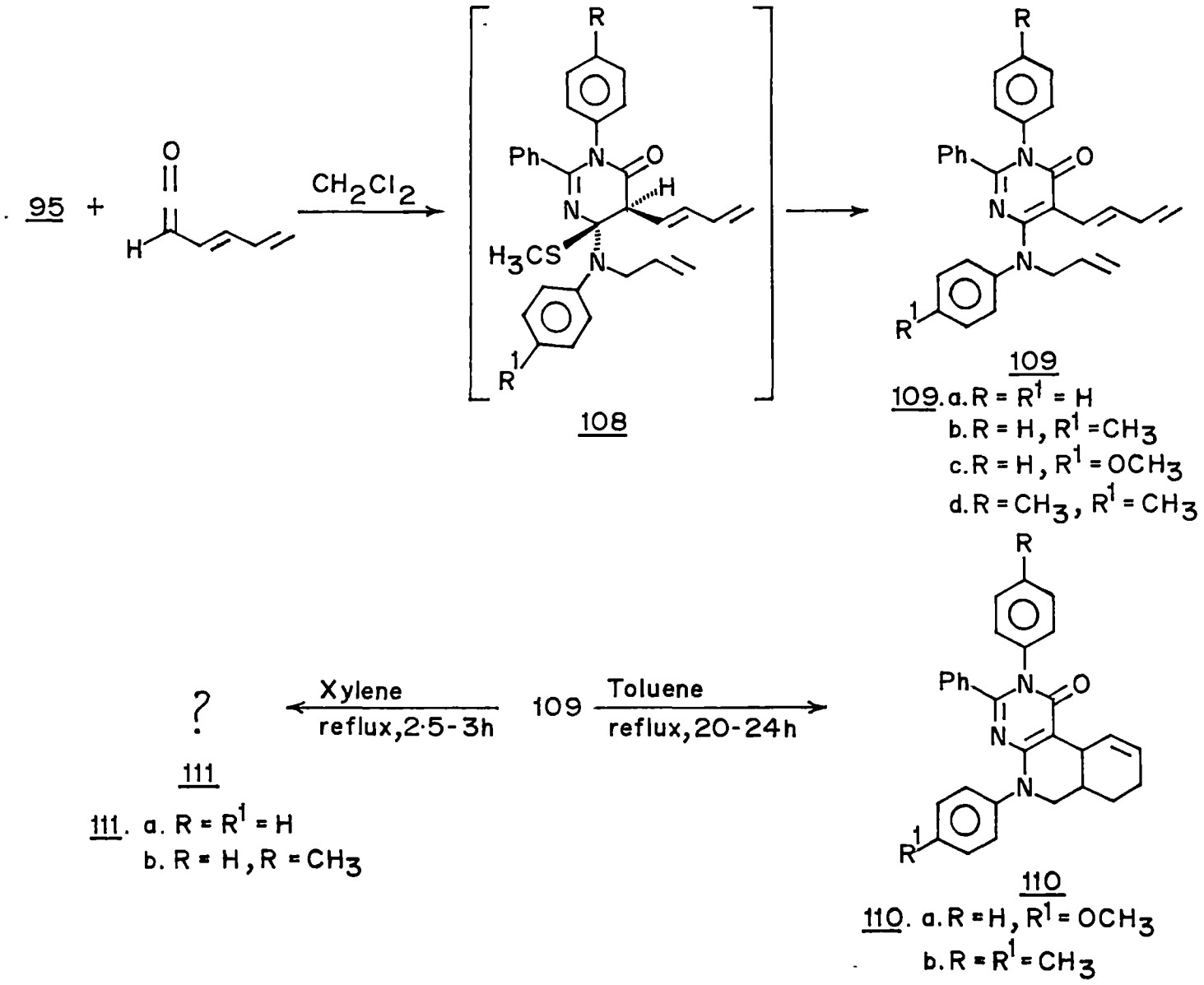
two well separated doublets for $-CH_2-SPh$ methylene protons at δ 3.24 and δ 4.64 with J = 13.2 Hz each. The surprisingly large chemical shift difference between the two methylene protons is in agreement with the literature values[89] for such methylene protons. It also showed the presence of free *N*-allyl functional group including two terminal olefinic protons as doublets (δ 5.22, J = 10.5 Hz and δ 5.36, J = 17.3 Hz), another olefinic proton (δ 5.98, dddd, J = 17.3, 10.5, 4.4 and 4.4) and methylene protons (δ 4.83, m). Further inference for *N*-aryl involvement in cyclisation was drawn from the appearance of two doublets (δ 6.92, J = 8.3 Hz and δ 7.00, J = 8.3 Hz) for the two *ortho* protons of the fused aryl ring. The more conclusive evidence for the assigned structure for **107** was drawn from the ^1H NMR spectrum of **107b** which wxhibited, in addition to other protons, a doublet (δ 6.82, J = 8.4) for Ha, a doublet of doublet (δ 6.96, J = 8.4 and 1.5 Hz) for Hb and another doublet (δ 7.08, J = 1.5) for Hc. The observed splitting patterns for these three aryl protons clearly establish the assigned structure **107** for the radical cyclisation discussed above.

It has been observed earlier that [4+2] cycloaddition reactions of butadienylketene with various 1,3-diazabutadienes resulted in a variety of 5-dienyl/butenyl pyrimidinones (Chapter I, Section I.3). In continuation of our interest concerning the synthesis of fused pyrimidinones, it was thought worthwhile to carry out the cycloaddition reactions of 1-aryl-4-(*N*-allyl-*N*-aryl)amino-4-methylthio-2-phenyl-1,3-diaza-1,3-butadi-

enes 95 with butadienylketene, generated *in situ* from sorbyl chloride and triethylamine in methylene chloride, at room temperature, which resulted in the exclusive isolation of 6-(*N*-allyl-*N*-aryl)amino- 3-aryl-5-(1',3'-butadienyl)-2-phenylpyrimidin 4(3*H*)-ones **109** (Scheme 32). The pyrimidinones **109** were characterised on the basis of IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The compound **109a**, for example, analysed for $C_{29}H_{25}N_3O$ exhibited molecular ion peak at *m/z* 431. Its IR spectrum showed a strong peak at 1644 cm^{-1} due to α,β-unsaturated carbonyl group. Its $^{1}H/^{13}C$ NMR spectra exhibited, apart from aromatic protons/carbon signals, the peaks for all the dienyl and allylic protons/carbons.

As mentioned earlier (Chapter I, Section I.3), in reactions of 1-aryl-4-methylthio-2-phenyl-4-secondaryamino-1,3-diaza-1,3-butadienes **11** with butadienylketene, the tlc of the reaction mixture showed two prominent but very close spots and the mixture was separated by careful column chromatography to yield 5-dienyl pyrimidinones **80** and 5-butenyl pyrimidinones **82** formed *via* the elimination of methylmercaptan and [1,5] SMe shift, respectively. However, reactions of 4-(*N*-allyl-*N*-aryl)amino-1,3-diaza-1,3-butadienes **95** with butadienylketene resulted in the formation of pyrimidinones **109** as the only isolable product formed presumably by the elimination of -HSMe from the initially formed [4+2] cycloadduct **108** as intermediate and no product corresponding to [1,5] SMe shift could be isolated or seen in the tlc.

The 6-(*N*-allyl-*N*-aryl)amino-3-aryl-5-(1',3'-butadienyl)-2-


95
CH2Cl2
Ph
H3CS
108
109
109.a.R = R1 = H
b.R = H, R1 = CH3
c.R = H, R1 = OCH3
d.R = CH3, R1 = CH3
Xylene
reflux,2·5-3h
109
Toluene
reflux,20-24h
?
111
111. a. R = R1 = H
b. R = H, R = CH3
110
110. a.R = H, R1 = OCH3
b.R = R1 = CH3

Scheme-32

phenyl pyrimidin-4(3*H*)-ones **109** appeared to be promising synthons for the synthesis of 5,6-fused pyrimidinones *via* ene/cycloaddition reactions. For this purpose, thermolysis of pyrimidinones **109** was carried out. Thus, on refluxing a solution of **109** in dry toluene for 20-24 h, resulted in the isolation of isoquinolines **110**, which persumably are the result of intramolecular [4+2] cycloaddition reactions involving diene function at C-5 and *N*-allyl double bond as dienophile. The structure **110** for these products was established on the basis of their analytical and spectral data. The compound **110a**, for example, analysed for $C_{30}H_{27}N_3O_2$ exhibited a maolecular ion peak at *m/z* 461. Its IR spectrum showed a strong peak at 1651 cm^{-1} due to α,β-unsaturated carbonyl group. The ^1H NMR spectrum of **110a** showed, apart from aromatic protons, the presence of methoxy proton (δ 3.79), two olefinic protons as multiplets (δ 5.62-5.67 and δ 6.04-6.08) and a series of multiplets for various methine and methylene protons which were assigned on the basis of proton decoupling experiments (see experimental section). Its ^{13}C NMR spectrum also attest to the assigned structure **110**.

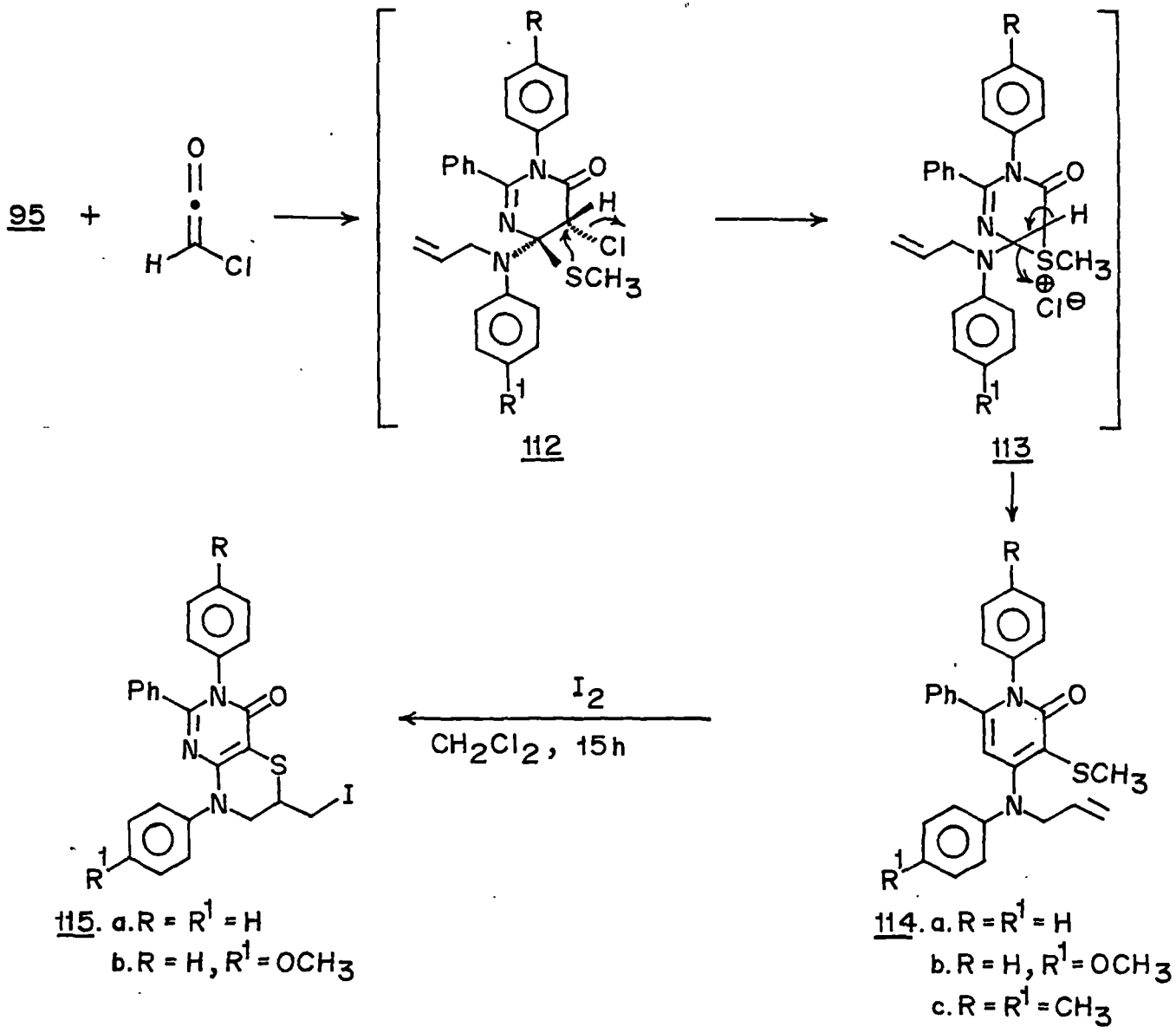
Interestingly, thermolysis of pyrimidinone **109** in refluxing xylene for 2-3 h and subsequent purification by column chromatography resulted in the fromation of crystelline products **111** (Scheme 32), the structures of which could not be established on the basis of available IR, mass, ^1H NMR and ^{13}C NMR spectral data. The IR spectrum of **111a**, for example, showed a strong peak at 1657 cm^{-1} indicating the presence of α,β-unsaturated carbonyl

group of pyrimidinone ring and its mass spectrum exhibited a (M^++1) peak at *m/z* 432. The detailed examination of the ^{1}H NMR spectrum of **111a**, showed the absence of dienyl proton signals, indicating the involvement of 5-dienyl function in the formation of product. Also, the presence of free *N*-allyl group is indicated by the signals for two terminal methylene protons (δ 5.15; *J* = 10.3 Hz, 1H and δ 5.24; d, *J* = 17.2 Hz, with fine splitting), a methine proton (δ 6.06; dddd, *J* = 17.2, 10.3, 5.2 and 5.2 Hz) and two methylene protons (δ 4.72: dq, *J* = 16.5 and 5.2 Hz). This indicated the possible participation of 5-dienyl and 6-(*N*-phenyl) group in the cyclisation. But the presence of all 15 aromatic protons again seem to rule out this possibility. Further, the spectrum indicated the presence of two methyl group signals, a doublet at δ 1.07 (*J* = 6.8 Hz) and a singlet at δ 1.68. The spectrum also exhibited the presence of three more methine protons signals, a multiplet (δ 2.85-2.90), a doublet (δ 5.84, *J* = 15.5 Hz) and a doublet of doublet (δ 6.67, *J* = 15.5 and 8.7 Hz). All these signals taken together were so confusing that none of the possible structures deduced for this transformation could satisfy the observed ^{1}H NMR spectral features. ^{13}C NMR spectra of **111** also could not help in deducing the actual structure. Thus, in order to firmly establish the structure it is planned to have the X-ray crystallography data for these products.

It has recently been reorted that [4+2] cycloaddition reactions of 1-aryl-4-methylthio-2-phenyl-4-secondaryamino-1,3-

diaza-1,3-butadienes **11** with haloketenes accompanied an interesting 1,2-SMe shift to result in various 5-methylthio pyrimidinones[39]. In continuation of our pursuits directed towards the construction of functionalised fused pyrimidinones and to further confirm and exploit this interesting rearrangement, we have carried out the reactions of various (*N*-allyl-*N*-aryl)amino-1,3-diaza-1,3-butadienes **95** with chloroketene. Thus, the reaction of **95** with chloroketene, generated *in situ* from chloroacetyl chloride and triethylamine in methylene chloride, resulted as expected, in various 1-aryl-6-[*N*-allyl-*N*-aryl)amino-5-methylthio-2-phenyl pyrimidin-4(3*H*)-ones **114** (Scheme 33) The formation of pyrimidinones **114** was assumed to follow an identical pathway as observed in the reactions of 1,3-diazabutadienes **11** with haloketenes[39]. Thus, initially formed [4+2] cycloadduct **112**, as an intermediate, is transformed into an episulfonium intermediate **113** followed by the rearrangement of **113** to yield pyrimidinones **114** (Scheme 33). Clearly, the preferential migration of methylthio group requires a *trans* arrangement of chloride and methylthio groups in intermediate **112**. This intermediate with desired stereochemical rearrangement is obtained either through highly stereoselctive [4+2] cycloaddition or more probably *via* the equilibration through a zwitterionic intermediate.

The structures of pyrimidinones **114** were deduced on the basis of analytical and spectral data. Compound **114a**, for example, analysed for $C_{26}H_{23}N_3OS$ showed a molecular ion peak at


95
112
113
114. a. R = R1 = H
b. R = H, R1 = OCH3
c. R = R1 = CH3
I2
CH2Cl2, 15h
115. a. R = R1 = H
b. R = H, R1 = OCH3

Scheme-33

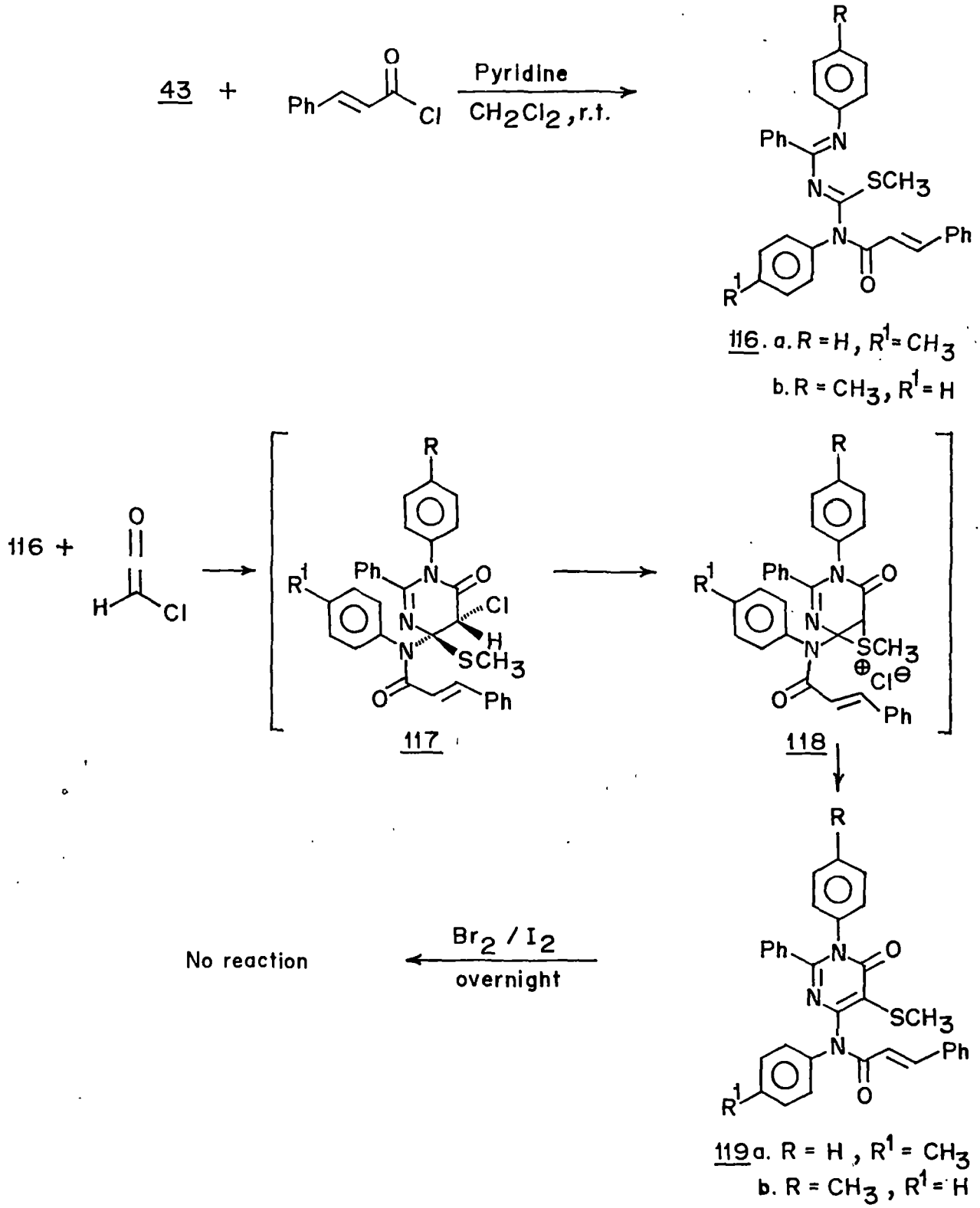
m/z 425. Its IR spectrum exhibited a strong band at 1657 cm^{-1} characteristic of α,β-unsaturated carbonyl group. ^{1}H NMR sectrum of **114a** showed, in addition to aromatic protons, the presence of signals for both methylthio (δ 2.15) and *N*-allyl functions. Its ^{13}C NMR spectrum was also in perfect agreement with the assigned structure **114a**.

It was thought that the pyrimidinones **114** could easily be converted to 1,4-thiazines which over the years have proved to be of great biological importance[91]. Recently, various 1,4-thiazines have been found to exhibit antimicrobial activity[92,93]. In view of the reported biological importance of 1,4-thiazines and especially fused 1,4-thiazines, it was through worthwhile to devise suitable strategies for the synthesis of pyrimidinone fused 1,4-thiazines. Thus, stirring a solution of **114** in methylene chloride with I_2 resulted in the formation of desired pyrimidinone fused 1,4-thiazines **115** (Scheme 33). The products were characterised as 3,8-diaryl-6-iodomethyl-3,7,8-trihydro-2-phenylpyrimido[5,4-b]-1,4-thiazine-4-ones **115** on the basis of their mass, IR, ^{1}H NMR and ^{13}C NMR spectral data. The product **115a**, for example, analysed for $C_{26}H_{22}N_3O_2SI$ showed a molecular ion peak at *m/z* 567. Its IR spectrum exhibited a strong peak at 1649 cm^{-1} due to α,β-unsaturated carbonyl group ^{1}H NMR spectrum of **115a** showed, in addition to aromatic proton signals, a singlet for methoxy protons (δ 3.82), a multiplet (δ 3.53-3.75) comprising of a methine $-CH_2-I$ and a multiplet (δ 4.30-4.34) for $-N-CH_2-$protons. Its ^{13}C NMR spectrum exhibited in addition to

other carbon signals, a signal at δ 7.1 characteristic of methylene attached to Iodo group and further confirmed the assigned structure **115a**.

Continuing this area of study we have synthesised some *N*-cinnamoyl-1,3-diazabutadienes **116** and carried out their reactions with chloroketene. Various 1-aryl-4-(*N*-aryl-*N*-cinnamoyl)amino-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **116** could easily be synthesized by treating *N*-arylamino-1,3-diazabutadienes **43** with cinnamoyl chloride in methylene chloride in the presence of pyridine (Scheme-34) and were well characterised with the help of their analytical and spectral data.

The treatment of **116** with chloroketne followed a reaction route similar to the reaction of **95** with chloroketene i.e. the formation of episulphenium intermediate **118** from the initially fromed [4+2] cycloadduct intermediate **117**, and subsequent elimination of -HCl to give 1-aryl-6-(*N*-aryl-*N*-cinnamoyl)amino-5-methylthio-2-phenylpyrimidin-4(3*H*)-ones **119** (Scheme 34). The pyrimidinone strtucture **119** was deduced on the basis of analytical and spectral evidences. The IR spectrum of **119a** showed sharp absorption bands at 1644 and 1670 cm^{-1} due to α,β-unsaturated carbonyl groups of pyrimidinone ring and cinnamoyl group respectively. Its ^{1}H NMR spectrum showed the presence of signals for aromatic protons, singlets for methyl protons (δ 2.41) and methylthio protons (δ 2.52); and two identical doublets at δ 6.40, J = 15.9 and δ 7.68, J = 15.9 for olefinic protons of


43 +
Pyridine
CH_2Cl_2, r.t.
116. a. R = H, R^1 = CH_3
b. R = CH_3, R^1 = H
116 +
117
118
119a. R = H, R^1 = CH_3
b. R = CH_3, R^1 = H
No reaction
Br_2 / I_2
overnight

Scheme – 34

cinnamoyl group. The structure 119 was further supported by ^{13}C NMR and mass spectral data.

The halo cyclisation of 6-(*N*-aryl-*N*-cinnamoyl)amino-5-methylthiopyrimidinones 119 was attempted with Br_2/I_2 in methylene chloride, but unfortunately the reaction did not take place and hence no product could be isolated from these reactions (*Scheme* 34).

In conclusion, a suitable method was developed for the synthesis of (*N*-allyl-*N*-aryl)amino-1,3-diaza-1,3-butadienes 95 and their reactions with various ketenes offer an easy access to various functionalised pyrimidinones. Careful manipulation of the functionalities present in these pyrimidinones led to the development of convenient routes for the synthesis of possibly biologically and medicinally important, heterocycle/benzo-fused 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 Spectrophotometer. ^1H NMR were recorded in deuteriochloroform, with a Varian 390 (90 MHz) and Burker AC-F 300 (300 MHz) Spectrometer using TMS as internal standard. Chemical shifts are expressed as δ ppm 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 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. Elemental analysis were performed on a Heraeus CHN-O-Rapid Elemental Analyser.

Starting Materials

1,3-Diaza-1,3-butadienes[34] and α-chlorooxime of *p*-methylacetophenone[76] were prepared by the reported procedures. Chloroacetyl chloride used was commercially available.

Preparation of crotonyl chloride/3,3-dimethylacroyl chloride: An equimolar 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 effervesce. After about 1.5-2 h, when the effervesce ceased, the reaction mixture was reluxed on water bath for 5-10 min to ensure complete elimination of HCl. The acid chloride thus obtained were used directly for these reactions.

Preparation of sorbyl chloride: Equivalent amounts of sorbic acid (5.0 g, 45 mmol) and thionyl chloride (5.3 g, 3.3 ml, 45 mmol) were refluxed in dry toluene (20 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.[94] .75 °C, 20 mm).

Reactions of 1,3-Diaza-1,3-butadienes 10 and 11 with Ketenes: General procedure for pyrimidinones (62): To a well stirred solution of 1,3-diaza-1,3-butadiene (4 mmol) and triethylamine (1g, 10 mmol) in dry methylene chloride (30 ml), was added dropwise, a solution of crotonyl chloride/3,3-dimethylacroyl chloride (6 mmol) in dry methylene chloride (30 ml) 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 (5 x 50 ml) and the organic layer dried over anhydrous sodium sulfate. 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.

6-Dimethylamino-2,3-diphenyl-5-isopropenylpyrimidin-4(3*H*)-one (62a): Yield 94%; mp 196-197°C; IR (KBr) ν 1654 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 2.13 (s, 3H, $-CH_3$); 3.13 (s, 6H,$-N(CH_3)_2$); 5.03 (br s, 1H, Ha); 5.33 (br s, 1H, Hb); 7.15-7.41 (m, 10H, arom). ms *m/z*: 331 (M^+). Anal. Calcd for $C_{21}H_{21}N_3O$: C, 76.11; H, 6.39; N, 12.68. Found: C, 76.05; H, 6.34; N, 12.60.

2,3-Diphenyl-5-isopropenyl-6-pyrrolidinopyrimidin-4(3*H*)-one (62b): Yield 93%; mp 221-222°C; IR (KBr) ν 1652 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 1.85-2.05 (m, 4H, $-CH_2-CH_2-$); 2.16 (s, 3H, $-CH_3$); 3.51-3.75 (m, 4H, $-CH_2-N-CH_2-$); 4.91 (br s, 1H, Ha); 5.39 (br s, 1H, Hb); 7.17-7.47 (m, 10H, arom). ms *m/z*: 357 (M^+). Anal. Calcd for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.75. Found: C, 77.15; H, 6.48; N, 11.69.

2,3-Diphenyl-5-isopropenyl-6-piperidinopyrimidin-4(3*H*)-one (62c): Yield 90%; mp 179-180°C. IR (KBr) ν 1649 cm^{-1} (C=O). ^{1}H NMR (300 MHz) δ 1.64 (br s, 6H, $-CH_2-CH_2-CH_2-$); 2.10 (s, 3H, $-CH_3$); 3.56 (br s, 4H, $-CH_2-N-CH_2-$); 5.07 (br s, 1H, Ha); 5.24 (br s, 1H, Hb); 7.10-7.26 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 22.29 ($-CH_3$); 24.70 ($-CH_2-$); 25.88 (2 x $-CH_2-$); 48.27 ($-CH_2-N-CH_2-$), 101.30 (C-5), 116.60 ($=CH_2$), 127.50, 127.65, 128.33, 129.12, 129.15, 135.34, 137.87 (aromatic); 140.02 (-C=); 154.42 (C-6); 158.11 (C-2) and 162.35 (C-4). ms *m/z*:371 (M^+). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.56; H, 6.77; N, 11.22.

2,3-Diphenyl-5-isopropenyl-6-morpholinopyrimidin-4(3*H*)-one (62d): Yield 89%; mp 186-187°C; IR (KBr) ν 1654 cm^{-1} (C=O). ^{1}H NMR (90 MHz) δ 2.13 (s, 3H, $-CH_3$); 3.60-3.88. (br s, 8H, morpholine); 5.18 (br s, 1H, Ha); 5.33 (br s, 1H, Hb); 7.17-7.50 (m, 10H, arom). ms *m/z*: 373 (M^+). Anal. Calcd for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.21; N, 11.25. Found: C, 73.83; H, 6.18; N, 11.23.

5-Isopropenyl-3-(4-methylphenyl)-2-phenyl-6-piperidinopyrimidin-4(3*H*)-one (62e): Yield 93%; mp 199-201 °C; IR (KBr) ν 1645 cm^{-1} (C=O). ^{1}H NMR (90 MHz) δ 1.57-1.73 (br s, 6H, $-CH_2-CH_2-CH_2-$); 2.10 (s, 3H, $-CH_3$); 2.30 (s, 3H, $-CH_3$); 3.50-3.70 (br s, 4H, $-CH_2-N-CH_2-$); 5.13 (br s, 1H, Ha); 5.30 (br s, 1H, Hb); 7.09-7.47 (m, 9H, arom). ms *m/z*: 385 (M^+). Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 77.85; H, 7.06; N, 10.80.

5-Isopropenyl-3-(4-methylphenyl)-6-morpholino-2-phenylpyrimidin-4(3*H*)-one (62f): Yield 91%; mp 198-199.5°C. IR (KBr) ν 1651 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 2.09 [s, 3H, $-CH_3$]; 2.30 (s, 3H,$-CH_3$): 3.50-3.87 (br s, 8H, morpholine); 5.10 (br s, 1H, Ha); 5.30 (br s, 1H, Hb); 6.93-7.47 (m, 9H, arom). ms *m/z*: 387 (M^+). Anal. Calcd for $C_{24}H_{25}N_3O_2$: C, 74.39; H, 6.50; N, 10.84. Found: C, 74.31; H, 6.47; N, 10.71.

6-Dimethylamino-2,3-diphenyl-5-vinylpyrimidin-4(3*H*)-one (62g): Yield 90%; mp 156-157°C; IR (KBr) ν 1658 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 3.17 [S, 6H, $-N(CH_3)_2$]; 5.40 (dd, *J* = 11.4 and 2.5, 1H, Ha); 6.00 (dd, *J* 17.5 and 2.5, 1H, Hb); 6.67 (dd, *J* = 17.5 and 11.4, 1H, H); 7.13-7.47 (m, 10H, arom). ms *m/z*: 317 (M^+). Anal. Calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.51; H, 6.02; N, 13.18.

2,3-Diphenyl-6-pyrrolidino-5-vinylpyrimidin-4(3*H*)-one (62h): Yield 95%; mp 199-200°C. IR (KBr) ν 1653 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 1.83-2.01 (m, 4H, $-CH_2-CH_2-$); 3.53-3.80 (m, 4H, $-CH_2-N-CH_2-$); 5.40 (dd, *J* = 11.4 and 2.3, 1H, Ha); 5.73 (dd, *J* = 17.5 and 2.3; 1H, Hb); 6.77 (dd, *J* = 17.5 and 11.4, 1H, H); 7.12-7.49 (m, 10H, arom). ms *m/z*: 343 (M^+). Anal. Calcd. for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.77; H, 6.14; N, 12.24.

2,3-Diphenyl-6-piperidino-5-vinylpyrimidin-4(3*H*)-one (62i): Yield 88%; mp 163-164°C. IR (KBr) ν 1650cm^{-1} (C=O). ^1H NMR (300 MHz) δ 1.75 (br s, 6H, $-CH_2-CH_2-CH_2-$); 3.55 (br s, 4H, $-CH_2-N-CH_2-$); 5.33 (dd, *J* = 11.5 and 2.8, 1H, Ha); 6.21 (dd *J* = 17.6 and 2.8,

1H, Hb); 6.41 (dd, *J* = 11.5 and 17.6, 1H, H); 7.10-7.23 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 24.65 ($-CH_2-$); 26.27 (2 x $-CH_2-$); 49.99 ($-CH_2-N-CH_2-$); 98.62 (C-5); 115.41 ($=CH_2$); 127.57, 127.90, 128.55, 129.10, 129.17, 129.22, 129.58, 135.15, 137.83 (arom); 129.17 (-C=); 154.39 (C-6); 161.05 (C-2); 162.41 (C-4). ms *m/z*: 357 (M^+). Anal. Calcd for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.75. Found: C, 77.23; H, 6.47; N, 11.69.

2,3-Diphenyl-6-morpholino-5-vinylpyrimidin-4(3*H*)-one (62j): Yield 90%; mp 180-182°C; IR (KBr)ν 1651 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 3.53-3.90 (m, 8H, morpholine); 5.43 (dd *J* = 11.3 and 2.6, 1H, Ha); 6.23 (dd, *J* = 17.6 and 2.6, 1H, Hb); 6.53 (dd, *J* = 17.6 and 11.3 1H, H); 7.13-7.47 (m, 10H, arom). ms *m/z*: 359 (M^+). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.42; H, 5.87; N, 11.63.

3-(4-Methylphenyl)-2-phenyl-6-piperidino-5-vinylpyrimidin-4(3*H*)-one (62k): Yield 93%; mp 177-178°C; IR (KBr)ν 1641 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 1.60-1.77 (br s, 6H, $-CH_2-CH_2-CH_2-$); 2.33 (s, 3H, $-CH_3$); 3.50-3.67 (br s, 4H, $-CH_2-N-CH_2-$); 5.38 (dd, *J* = 11.6 and 2.5, 1H, Ha); 6.23 (dd, *J* = 17.7 and 2.5, 1H, Hb); 6.60 (dd, *J* = 17.7 and 11.6, 1H, H); 7.10-7.47 (m, 9H, arom). ms *m/z*: 371 (M^+). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.49; H, 6.78; N, 11.23.

3-(4-Methylphenyl)-6-morpholino-2-phenyl-5-vinylpyrimidin-4(3*H*)-one (62l): Yield 89%; mp 200-202°C; IR (KBr) ν 1653 cm^{-1} (C=O).

^{1}H NMR (300 MHz) δ 2.30 (s, 3H, $-CH_3$); 3.56-3.59 (br s, 4H, $-CH_2-N-CH_2-$); 3.76-3.79 (br s, 4H, $-CH_2-O-CH_2-$); 5.37 (dd, *J* = 11.6 and 2.4, 1H, Ha); 6.21 (dd, *J* = 17.5 and 2.4, 1H, Hb); 6.42 (dd, *J* = 17.5 and 11.6, 1H, H); 6.99-7.27 (m, 9H, arom). ^{13}C NMR (75.5 MHz) δ 21.08 (CH_3); 49.29 ($-CH_2-N-CH_2-$); 66.90 ($-CH_2-O-CH_2-$); 99.99 (C-5); 116.76 ($=CH_2$); 127.61, 128.66, 128.96, 129.12, 129.32, 134.95, 135.04, 137.84 (arom). 129.12 (-C=); 154.98 (C-6); 160.45 (C-2); 162.38 (C=O). ms *m/z*: 373 (M^+). Anal. Calcd for $C_{23}H_{23}N_3O_2$: C, 73.97; H, 6.20; N, 11.25. Found: C, 73.88; H, 6.18; N, 11.23.

2,3-Diphenyl-5-isopropenylpyrimidin-4(3*H*)-one (64a): Yield 75%; mp 142-143°C; IR (KBr) ν 1668 cm^{-1} (C=O). ^{1}H NMR (90 MHz) δ 2.21 (s, 3H,$-CH_3$); 5.35 (br s, 1H, Ha); 6.05 (br s, 1H, Hb); 7.19-7.55 (m, 10H, arom); 8.21 (s, 1H, olefinic). ms *m/z*: 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.04; H, 5.57; N, 9.69.

2,3-Diphenyl-5-vinylpyrimidin-4(3*H*)-one (64b): Yield 78%; mp 137-139°C; IR (KBr) ν 1661 cm^{-1} (C=O). ^{1}H NMR (300 MHz) δ 5.45 (dd, *J* = 11.4 and 1.7, 1H, Ha); 6.35 (dd, *J* = 17.6 and 1.7, 1H, Hb); 6.66 (dd, *J* = 17.6 and 11.4, 1H, H); 7.09-7.31 (m, 10H, arom); 8.10 (s, 1H, olefinic). ms *m/z*: 274 (M^+). Anal. Calcd. for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.22. Found: C, 78.69; H, 5.14; N, 10.17.

5-Isopropenyl-2-methylthio-3-phenylpyrimidin-4(3*H*)-one (64c): Yield 79%; mp 89-91°C; IR (KBr) ν 1673 cm^{-1} (C=O). ^{1}H NMR (90

MHz) δ 2.13 (s, 3H, $-CH_3$); 2.45 (s, 3H, $-SCH_3$); 5.29 (br s, 1H, Ha); 5.95 (br s, 1H, Hb); 7.30-7.50 (m, 2H, arom); 7.57-7.77 (m, 3H, arom); 8.05 (s, 1H, olefinic). ms *m/z*: 258 (M^+). Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84. Found: C, 64.98; H, 5.45; N, 10.83.

***Reactions of 3-Aryl-5-isopropenyl/vinyl-2-phenyl-6-dialkyl aminopyrimidin-4(3H)-one 62 with Phosphorus Pentasulfide*:**

General Procedure: Phosphorus pentasulfide (2.0 g, 4.5 mmol) and sodium carbonate (0.47 g, 4.5 mmol) were added to dry THF (30 ml) under dry conditions. The mixture was stirred vigorously for 15-25 min till the contents dissolve and then the pyrimidinone **16** (4 mmol) is added. After about 10 min, a 10% aqueous solution of disodium hydrogen phosphate (25 ml), ethyl acetate (20 ml) and hexane (20 ml) are respectively added. The aqueous layer is extracted with ethyl acetate (1 x 10 ml) and the organic layer is dried with magnesium sulfate. The removal of solvent under reduced pressure yielded the crude product, which was recrystallised form chloroform-hexane mixture.

2,3-Diphenyl-6-piperidinopyrimidin-4(3*H*)-one (65a): Yield 91%; mp 184-185°C; IR (KBr) ν 1654 cm^{-1} (C=O). ^1H NMR (300 MHz) δ 1.66 (br s, 6H, $-CH_2-CH_2-CH_2-$); 3.61 (br s, 4H, $-CH_2-N-CH_2-$); 5.49 (s, 1H, olefinic); 7.08-7.25 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 24.56 ($-CH_2-$); 25.41 (2 x $-CH_2-$); 45.45 ($-CH_2-N-CH_2-$); 84.02 (C-5); 127.49, 127.77, 128.46, 128.96, 129.06, 129.12, 135.47, 137.63 (arom); 157.66 (C-6); 160.17 (C-2); 163.25 (C-4). ms *m/z*:

331 (M^+). Anal. Calcd for $C_{21}H_{21}N_3O$: C, 76.11; H, 6.38; N, 12.68. Found: C, 75.97; H, 6.35; N, 12.60.

2,3-Diphenyl-6-morpholinopyrimidin-4(3*H*)-one (65b): Yield 94%; mp 189-191°C; IR (KBr) ν 1657 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 3.43-3.83 (m, 8H, morpholine); 5.49 (s, 1H, olefinic); 7.00-7.38 (m, 10H, arom). ms *m/z*: 333 (M^+). Anal. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.00; H, 5.74; N, 12.56.

3-(4-Methylphenyl)-6-morpholino-2-phenylpyrimidin-4(3*H*)-one (65c): Yield 93%; mp 212-214°C; IR (KBr) ν 1673 cm^{-1} (C=O). ^1H NMR (90 MHz) δ 2.30 (s, 3H,-CH_3); 3.57-4.03 (m, 8H, morpholine); 5.57 (s, 1H, olefinic); 6.97-7.52 (m, 9H, arom). ms *m/z*: 347 (M^+). Anal. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 6.09; N, 12.09. Found: C, 72.47; H, 6.07; N; 11.99.

***Reactions of 3-Aryl-5-isopropenyl/vinyl-2-phenyl-6-dialkyl aminopyrimidin-4(3H)-ones 62 with α-Nitrosostyrene 68*:**

General Procedure: A solution of 3-aryl-5-isopropenyl/vinyl-2-phenyl-6-dialkyl amino-4(3*H*)-pyrimidinone 62 (4 mmol) and α-chlorooxime (4.2 mmol) in dry methylene chloride (40 ml) was stirred at room temperature in the presence of anhydrous sodium carbonate (0.64 g, 6 mmol) for 24-26 h. The separated salt and excess of sodium carbonate were removed by filtration and the residue was extracted with small portions (2x10 ml) of methylene chloride. The combined filtrate was washed with water (3 x 50 ml), dried over anhydrous sodium sulfate and freed from solvent

under reduced pressure. The crude mixture was then chromatographed over silica gel. Elution with ethyl acetate: hexane (1:10) resulted in the isolation of unreacted starting pyrimidinones. Further elution with ethyl acetate:hexane (1.5:10) in case of 5-vinyl substituted and 2.5:10 in case of 5-isopropenyl substituted pyrimidinones resulted in the isolation of oxazine **27** and nitrone **26** derivatives respectively.

3,4-Dihydro-5-methyl-2-(4-methylphenyl)-5-[2',3'-diphenyl-6'-piperidinopyrimidin-4'(3'*H*)-onyl]-5*H*-pyrrole-1-oxide (71a): Yield 21%; mp 210-212°C; IR (KBr) ν 1662 (C=O), 1556, 1208 (N^+-O^-) and 1120 cm^{-1}. ^1H NMR (300 MHz) δ 1.66 (br s, 6H,-CH_2-CH_2-CH_2-); 2.00 (s, 3H,-CH_3); 2.19-2.25 (m, 1H, H-3); 2.36 (s, 3H,-CH_3); 2.71-2.81 (m, 1H, H-3); 3.03-3.33 (m, 2H, H-4); 3.40 (br s, 4H, -CH_2-N-CH_2-); 7.14-7.32 (m, 12H, arom); 8.22-8.25 (d, *J* = 8.3, 2H, arom). ms *m/z*: 518 (M^+). Anal. Calcd for $C_{33}H_{34}N_4O_2$: C, 76.42; H, 6.60; N, 10.80. Found: C, 76.33; H, 6.54; N, 10.76.

3,4-Dihydro-5-methyl-2-(4-methylphenyl)-5-[2',3'-diphenyl-6'-morpholinopyrimidin-4'(3'*H*)-onyl]-5*H*-pyrrole-1-oxide (71b): Yield 23%; mp 205-207°C; IR (KBr) ν 1654 (C=O), 1558, 1204 (N^+-O^-) and 1110 cm^{-1}. ^1H NMR (300 MHz) δ 2.06 (s, 3H, -CH_3); 2.17-2.26 (m, 1H, H-3); 2.35 (s, 3H, -CH_3); 2.71-2.79 (m, 1H, H-3); 3.16-3.29 (m, 2H, H-4); 3.54 (br s, 4H,-CH_2-N-CH_2-); 3.81 (br s, 4H, -CH_2-O-CH_2-); 7.14-7.35 (m, 12H, arom); 8.21-8.24 (d, *J* = 8.3, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.54(-CH_3); 25.91 (-CH_3); 28.38 (C-3); 31.33 (C-4); 51.96 (-CH_2-N-CH_2-); 66.85 (-CH_2-O-CH_2-); 80.43

(C-5); 108.15 (C-5'); 127.37, 127.70, 128.17, 128.25, 128.79, 129.31, 129.67, 134.42, 137.45, 138.05, 139.76 (aromatic); 154-95 (C-2' and C-6'); 163.30 (C-2); 163.51 (C-4'). ms *m/z*: 520 (M^+). Anal. Calcd. for $C_{32}H_{32}N_4O_3$: C, 73.82; H, 6.19; N, 10.76. Found: C, 73.77; H, 6.17; N, 10.68.

5,6-Dihydro-3-(4-methylphenyl)-6-[2',3'-diphenyl-6'-piperidino pyrimidin-4'(3'*H*)-onyl]-4*H*-1,2-oxazine (72a): Yield 30%; mp 209-211°C; IR (KBr) ν 1648 (C=O), 1510, 1407, 1006 and 892 cm^{-1}. ^1H NMR (300 MHz) δ 1.67 (br s, 6H, $-CH_2-CH_2-CH_2-$); 1.98-2.05 (m, 1H, H-4); 2.36 (s, 3H, $-CH_3$); 2.69-2.82 (m, 2H, H-5); 3.33-3.41 (m, 1H, H-4); 3.56-3.70 (m, 4H, $-CH_2-N-CH_2-$); 4.65-4.71 (m, 1H, H-6); 7.14-7.30 (m, 12H, arom); 7.59-7.62 (d, J = 8.3, 2H, arom). ^{13}C NMR (75.5 MHz): 21.24($-CH_3$); 21.69 (C-4); 23.49 (C-5); 24.61 ($-CH_2-$); 26.40 (2 x CH_2-); 50.68 ($-CH_2-N-CH_2-$); 74.31 (C-6); 97.98 (C-5') 125.35, 127.69, 127.95, 128.51, 128.97, 129.23, 129.47, 133.55, 135.14, 137.63, 139.03 (aromatic); 154.98 (C-6); 156.06 (C-2); 163.38 (C-3); 163.75 (C-4'). ms *m/z*: 504 (M^+). Anal. Calcd for $C_{32}H_{32}N_4O_2$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.08; H, 6.37; N, 11.07.

5,6-Dihydro-3-(4-methylphenyl)-6-[3'-(4'-methylphenyl)-2-phenyl-6'-piperidinopyrimidin-4'(3'*H*)-onyl]-4*H*-1,2-oxazine (72b): Yield 32%; mp 208-210°C; IR (KBr) ν 1654 (C=O), 1514, 1418, 1015 and 893 cm^{-1}. ^1H NMR (300 MHz) δ 1.67 (br s, 6H, $-CH_2-CH_2-CH_2-$); 1.97-2.06 (m, 1H, H-4); 2.28 (s, 3H,$-CH_3$); 2.36 (s, 3H, $-CH_3$); 2.69-2.83 (m, 2H, H-5); 3.34-3.43 (m, 1H, H-4); 3.55-3.69 (m, 4H,

$-CH_2-N-CH_2-$); 4.65-4.71 (d, 1H, H-6); 6.99-7.32 (m, 11H, arom); 7.59-7.62 (d, *J* = 8.2, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.10 ($-CH_3$);21.15 ($-CH_3$); 21.67 (C-4); 23.50 (C-5); 24.62 ($-CH_2$); 26.39 ($2-CH_2-$); 50.69($-CH_2-N-CH_2-$); 74.35 (C-6); 98.12 (C-5'); 125.34, 127.68, 128.88, 128.96, 129.20, 129.24, 129.40, 133.56, 134.91, 135.27, 137.76, 139.01 (aromatic); 155.00 (C-6'); 156.17 (C-2'); 163.14 (C-3); 163.79 (C-4'). ms *m/z*: 518 (M^+). Anal. Calcd for $C_{33}H_{34}N_4O_2$: C, 76.42; H, 6.60; N, 10.80. Found: C, 76.33; H, 6.59; N, 10.76.

Reactions of 1,3-diaza-1,3-butadienes 10 with butadienylketene: **General procedure for pyrimidinones (78):** To a well stirred solution of 1,3-diaza-1,3-butadienes **10** (4.0 mmol) and triethylamine (1.0 g, 10 mmol) in dry methylene chloride (30 ml), was added dropwise, a solution of sorbyl chloride (6.0 mmol) in dry methylene chloride (30 ml). A similar workup as employed for pyrimidinones **62** gave the crude products **78** which were purified by column chromatography (eluent: a mixture of EtOAc/hexane in a 1:10 ratio).

5-(1',3'-Butadienyl)-2-methylthio-3-phenylpyrimidin-4(3*H*)-one (78a): Yield 86%; mp 310-312 °C; IR (KBr) ν 1683 (C=O), 1480 cm^{-1}. ^1H NMR (300 MHz) δ 2.44 (s, 3H, $-SCH_3$), 5.15 (d, *J* = 10.2, with fine splitting, 1H, Ha), 5.29 (d, *J* =16.9, with fine splitting, 1H, Hb), 6.37-6.50 [m, 2H; consisting in at 6.40 (d, *J* = 15.6, 1H, He) and 6.44 (ddd, *J* = 16.9, 10.6, 10.2, 1H, Hc)], 7.25-7.28 (m, 2H, arom), 7.39 (dd, *J* = 15.6 and 10.6, 1H, Hd), 7.51-7.56

(m, 3H, arom), 7.90 (s, 1H, olefinic). ^{13}C NMR (75.5 MHz) δ 15.3 ($-SCH_3$), 118.4 (C-4'), 119.6 (C-5), 125.1 (C-2'), 128.4, 129.8, 130.1, 133.3 (C-1'), 135.8, 137.8 (C-3'), 149.7 (C-6), 160.8 (C-2), 161.7 (C-4). ms *m/z*: 270 (M^+). Anal. Calcd for $C_{15}H_{14}N_2OS$: C, 66.64; H, 5.22; N, 10.36. Found: C, 66.73; H, 5.18; N, 10.30.

5-(1',3'-Butadienyl)-1,2-diphenylpyrimidin-4(3*H*)-one (78b): Yield 63%; mp 109-111 °C; IR (KBr) ν 1660 (C=O), 1481 cm^{-1}. ^1H NMR (300 MHz) δ 5.23 (d, *J* = 10.0, 1H, Ha), 6.34-6.46 [m, 2H; consisting in at 5.41 (d, 17.0, 1H, Hb) and 6.43 (ddd, *J* = 17.0, 10.3, 10.0, 1H, Hc)], 6.58 (d, *J* = 15.4, 1H, He), 7.13-7.37 (m, 10H, arom), 7.74 (dd, *J* = 15.4 and 10.3, 1H, Hd), 8.10 (s, 1H, olefinic). ms *m/z*: 300 (M^+). Anal. Calcd for $C_{20}H_{16}N_2O$: C, 79.97; H, 5.36; N, 9.32. Found: C, 79.83; H, 5.41; N, 9.39.

5-(1',3'-Butadienyl)-2,3-diphenyl-6-methylpyrimidin-4(3*H*)-one (78c): Yield 89%; mp 114 °C; IR (KBr) ν 1656 (C=O), 1480 cm^{-1}. ^1H NMR (300 MHz) δ 2.55 (s, 3H, $-CH_3$), 5.18 (d, *J* = 10.1, 1H, Ha), 5.34 (d, *J* = 16.9, 1H, Hb), 6.44-6.60 [m, 2H; consisting in at 6.50 (ddd, *J* = 16.9, 10.5 and 10.1, 1H, Hc) and 6.58 (d, *J* = 15.5, 1H, He)], 7.10-7.35 (m, 10H, arom), 7.73 (dd, *J* = 15.5 and 10.5, 1H, Hd). ^{13}C NMR (75.5 MHz) δ 22.4 ($-CH_3$), 118.6 (C-5), 118.8 (C-4'), 124.4 (C-2'), 127.9, 128.5, 128.7, 129.0, 129.1, 129.5, 134.7, 136.2 (C-1'), 137.4, 138.5 (C-3'), 155.5 (C-6), 159.1 (C-2), 161.0 (C-4). ms *m/z*: 314 (M^+), 271, 196, 180, 77. Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.35; H, 5.72; N, 8.97.

***Reactions of 1,3-diaza-1,3-butadienes 11 with butadienylketene*: General procedure for pyrimidinoes (80/82):** A similar procedure as employed for pyrimidinones **78**, yilded the crude product consisting in a mixture of **80** and **82** which were separated by column chromatography on silica gel. Elution with a mixture of EtOAc/hexane (1:49) for about 5-6 h resulted initially in the separation of pure **80**, then a mixture of **80** and **82**, and finally pure **82**. (The overall yield in these reactions is about 80-90%, but because of very close *Rf* values of the products **80** and **82**, the separation by column chromatography was accompanied by the loss of the individual products.

5-(1',3'-Butadienyl)-6-dimethylamino-2,3-diphenylpyrimidin-4(3*H*)-one (80a): Yield 29%; mp 135-137 °C; IR (KBr) ν 1649 (C=O), 1517, 1473, 1391 cm^{-1}. ^{1}H NMR (300 MHz) δ 3.14 [s, 6H, $N(CH_3)_2$], 5.01 (d, J = 10.1, with fine splitting, 1H, H-4'), 5.22 (d, J = 16.9, with fine splitting, 1H, H-4'), 6.41-6.55 [m, 2H; consisting in at 6.43 (d, J = 15.5, 1H, H-1') and 6.47 (ddd, J = 16.9, 10.5 and 10.1, 1H, H-3')], 7.11-7.31 (m, 11H, H-2' and arom). ^{13}C NMR (75.5 MHz) δ 41.3 [$N(CH_3)_2$], 96.9 C-5), 115.2 (C-4'), 126.6 (C-2'), 127.7, 128.0, 128.7, 129.1, 129.3, 129.5, 130.5 (C-1'), 135.0, 137.8, 139.0 (C-3'), 153.9 (C-6), 161.1 (C-2), 162.5 (C-4). ms *m/z*: 343 (M^+, 17%), 315 (4%), 300 (4%), 271 (2%), 180 (76%), 104 (5%), 77 (98%). Anal. Calcd for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.23. Found: C, 77.05; H, 6.12; N, 12.29.

6-Dimethylamino-2,3-diphenyl-5-(3'-methylthiobut-1'-en-yl) pyrimidin-4(3*H*)-one (82a): Yield 41%; mp 112-113 °C; IR (KBr) ν 1637' (C=O), 1548, 1517, 1473, 1390 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.42 (d, J = 6.8, 3H, $-CH_3$), 2.04 (s, 3H, $-SCH_3$), 3.11 [s, 6H, $-N(CH_3)_2$]; 3.36-3.47 (m, 1H, H-3'); 6.33-6.38 (m, 2H, olefinic); 7.09-7.30 (m, 10H, arom). ^{13}C NMR (75.5 (MHz) δ 14.2 ($-SCH_3$); 20.8 ($-CH_3$); 41.2 [$-N(CH_3)_2$], 45.3 (C-3'), 96.4 (C-5), 122.8 (C-2'), 127.6, 127.9, 128.6, 129.1, 129.2, 129.3, 133.0 (C-1'), 135.0, 137.8, 153.8 (C-6), 160.7 (C-2), 162.7 (C-4). ms *m/z*: 391 (2%), 314 (4%); 180 (45%), 77 (98%). Anal. Calcd for $C_{23}H_{25}N_3OS$: C, 70.55; H, 6.43; N, 10.73. Found: C, 70.70; H, 6.39; H, 10.81.

5-(1',3'-Butadienyl)-2,3-diphenyl-6-piperidinopyrimidin-4(3*H*)-one (80b): Yield 31%; mp 163-164°C; IR (KBr) ν 1651 (C=O), 1545, 1507, 1486, 1428 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.70 (brs, 6H, $-CH_2-CH_2-CH_2-$), 3.57 (br s, 4H, $-CH_2-N-CH_2-$), 5.03 (d, J = 10.1, 1H, H-4'), 5.23 (d, J = 16.9, 1H, H-4'), 6.33 (d, J = 15.5, 1H, H-1'), 6.49 (ddd, J = 16.9, 10.6 and 10.1, 1H, H-3'), 7.12-7.31 (m, 10H, arom), 7.47 (dd, J = 15.5 and 10.6, 1H, H-2'). ^{13}C NMR (75.5 MHz) δ 24.7 ($-CH_2-$), 26.4 (2 x $-CH_2-$), 50.2 ($-CH_2-N-CH_2-$), 98.6 (C-5), 115.5 (C-4'), 126.5 (C-2'), 127.7, 128.1, 128.7, 129.1, 129.3, 129.4, 130.9 (C-1'), 135.1, 137.9, 139.2 (C-3'), 154.2 (C-6), 161.2 (C-2), 162.6 (C-4). ms *m/z*: 383 (M^+). Anal. Calcd for $C_{25}H_{25}N_3O$: C, 78.30; H, 6.57; N, 10.95. Found: C, 78.38; H, 6.55; N, 11.03.

2,3-Diphenyl-5-(3'-methylthiobut-1'-en-yl)-6-piperidino-pyrimidin-4(3*H*)-one (82b): Yield 26%; mp 101-102 °C; IR (KBr) ν 1649 (C=O), 1545, 1518, 1469, 1390 cm^{-1}. ^1H NMR (300 MHz) δ 1.42 (d, *J* = 6.8, 3H, $-CH_3$), 1.69 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.06 (s, 3H, $-SCH_3$), 3.37-3.48 (m, 1H, H-3'), 3.57 (br s, 4H, $-CH_2-N-CH_2-$), 6.24 (d, *J* = 15.7, 1H, H-1'), 6.65 (dd, *J* = 15.7 and 8.5, 1H, H-2'), 7.09-7.33 (m, 10H, arom). ms *m/z*: 431 (M^+). Anal. Calcd for $C_{26}H_{29}N_3OS$: C, 72.35; H, 6.77; N, 9.73. Found: C, 72.42; N, 6.71; N, 9.63.

5-(1',3'-Butadienyl)-2,3-diphenyl-6-morpholinopyrimidin-4(3*H*)-one (80c): Yield 30%; mp 133-134 °C; IR (KBr) ν 1661 (C=O), 1541, 1504, 1484 cm^{-1}. ^1H NMR (300 MHz) δ 3.59-3.62 (m, 4H, $-CH_2-N-CH_2-$), 3.80-3.83 (m, 4H, $-CH_2-O-CH_2-$), 5.07 (d, *J* = 10.0, 1H, H-4'), 5.25 (d, *J* = 16.9, 1H, H-4'), 6.33 (d, *J* = 15.6, 1H, H-1'), 6.48 (ddd, *J* = 16.9, 10.7 and 10.0, 1H, H-3'), 7.12-7.33 (m, 10H, arom), 7.46 (dd, *J* = 15.6 and 10.7, 1H, H-2'). ^{13}C NMR (75.5 MHz) δ 49.4 ($-CH_2-N-CH_2-$), 67.1 ($-CH_2-O-CH_2-$), 99.6 (C-5), 116.5 (C-4'), 125.5 (C-2'), 127.8, 128.3, 128.8, 129.0, 129.3, 129.6, 132.2 (C-1'), 134.8, 137.6, 138.8 (C-3'), 154.2 (C-6), 160.6 (C-2), 162.5 (C-4). ms *m/z*: 385 (M^+). Anal. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.78; H, 6.01; N, 10.90. Found: C, 74.74; H, 6.05; N, 10.85.

2,3-Diphenyl-5-(3'-methylthiobut-1'-en-yl)-6-morpholino-pyrimidin-4(3*H*)-one (82c): Yield 33%; mp 116-117.5 °C; IR (KBr) ν 1660 (C=O), 1548, 1507, 1487 cm^{-1}. ^1H NMR (300 MHz) δ 1.42 (d, *J* = 6.9, 3H, $-CH_3$), 2.05 (s, 3H, $-CH_3$), 3.34-3.45 (m, 1H, H-3'),

3.57-3.60 (m, 4H, $-CH_2-N-CH_2-$), 3.79-3.82 (m, 4H, $-CH_2-O-CH_2-$), 6.26 (d, *J* = 15.8, 1H, H-1'), 6.66 (dd, *J* = 15.8 and 8.5, 1H, H-2'), 7.11-7.33 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 14.1 ($-SCH_3$), 20.7 ($-CH_3$), 45.2 (C-3'), 49 2 ($-CH_2-N-CH_2-$), 67.0 ($-CH_2-O-CH_2-$), 99.8 (C-5), 122.0 (C-2'), 127.8, 128.2, 128.8, 129.0, 129.2, 129.6, 134.6 (C-1'), 134.8, 137.7, 154.7 (C-6), 160.4 (C-2), 162.7 (C-4). ms *m/z*: 433 (M^+, 6%), 386 (98%), 358 (22%), 344 (10%), 326 (5%), 298 (6%), 225 (5%), 180 (100%), 77 (88%). Anal. Calcd for $C_{25}H_{27}N_3O_2S$: C, 69.25; H, 6.27; N, 9.69. Found: C, 69.31; H, 6.24; N, 9.77.

5-(1',3'-Butadienyl)-3-(p-methylphenyl)-2-phenyl-6-piperidino-pyrimidin-4(3*H*)-one (80d): Yield 36%; mp 156-158 °C; IR (KBr) ν 1652 (C=O), 1548, 1507, 1488 cm^{-1}. ^1H NMR (300 MHz) δ 1.69 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.29 (s, 3H, $-CH_3$), 3.55 (br s, 4H, $-CH_2-N-CH_2-$), 5.02 (d, *J* = 10.1, with fine splitting, 1H, H-4'), 5.22 (d, *J* = 16.9, with fine splitting, 1H, H-4'), 6.32 (d, *J* = 15.4, with fine splitting, 1H, H-1'), 6.47 (ddd, *J* = 16.9, 10.7 and 10.1, 1H, H-3'), 7.00 (d, *J* = 8.4, with fine splitting, 2H, arom), 7.08 (d, *J* = 8.4, with fine splitting, 2H, arom), 7.14-7.32 (m, 5H, arom), 7.46 (dd, *J* = 15.5 and 10.7, with fine splitting, 1H, H-2'). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 24.7 ($-CH_2-$), 26.4 (2 x $-CH_2-$), 50.2 ($-CH_2-N-CH_2-$), 98.7 (C-5), 115.4 (C-4'), 126.6 (C-2'), 127.7, 128.8, 129.3, 129.4, 130.8, 132.1 (C-1'), 135.19, 135.22, 138.0, 139.2 (C-3'), 154.3 (C-6), 161.2 (C-2), 162.7 (C-4). ms *m/z*: 397 (M^+). Anal. Calcd for $C_{26}H_{27}N_3O$: C, 78.56; H, 6.84; N, 10.57. Found: C, 78.64; H, 6.82; N, 10.50.

3-(p-Methylphenyl)-5-(3'-methylthiobut-1'-en-yl)-2-phenyl-6-piperidinopyrimidin-4(3*H*)-one (82d): Yield 28%; mp 101-103 °C; IR (KBr) ν 1653 (C=O), 1548, 1515, 1481 cm^{-1}. ^1H NMR (300 MHz) δ 1.41 (d, J = 6.8, 3H, $-CH_3$), 1.70 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.27 (s, 3H, $-CH_3$), 3.36-3.47 (m, 1H, H-3'), 3.56 (br s, 4H, $-CH_2-N-CH_2-$), 6.25 (d, J = 15.8, 1H, H-1'), 6.64 (dd, J = 15.8 and 8.5, 1H, H-2'), 7.04 (d, J = 8.4, with fine splitting, 2H, arom), 7.09 (d, J = 8.4, with fine splitting, 2H, arom), 7.14-7.30 (m, 8H, arom). ms *m/z*: 445 (M^+). Anal. Calcd for $C_{27}H_{31}N_3OS$: C, 72.77; H, 7.01; N, 9.43. Found: C, 72.69; H, 6.98; N, 9.49. **5-(1',3'-5-(1',3'-Butadienyl)-3-(p-methylphenyl)-6-morpholino-2-phenyl-pyrimidin-4(3*H*)-one (80e)**: Yield 39%; mp 180-181 °C; IR (KBr) ν 1652 (C=O), 1550, 1507 cm^{-1}; ^1H NMR (300 MHz) δ 2.29 (s, 3H, $-CH_3$), 3.57-3.61 (m, 4H, $-CH_2-N-CH_2-$), 3.78-3.82 (m, 4H, $-CH_2-O-CH_2-$), 5.06 (d, J = 10.0, 1H, H-4'), 5.24 (d, J =16.8, 1H, H-4'), 6.31 (d, J = 15.6, 1H, H-1'), 6.46 (ddd, J = 16.8, 10.6 and 10.0, 1H, H-3'), 7.00 (d, J = 8.4, 2H, arom), 7.09 (d, J = 8.4, 2H, arom), 7.17-7.30 (m, 5H, arom), 7.45 (dd, J = 15.6 and 10.6, 1H, H-2'). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 49.4 ($-CH_2-N-CH_2-$), 66.9 ($-CH_2-O-CH_2-$), 100.1 (C-5), 116.4 (C-4'), 125.4 (C-2'), 127.7, 128.6, 129.2, 129.4, 132.1 (C-1'), 134.9, 138.1, 138.8 (C-3'), 154.7 (C-6), 160.5 (C-2), 162.5 (C-4). ms *m/z*: 339 (M^+, 6%), 358 (7%), 314 (3%), 225 (7%), 194 (43%), 104 (19%), 91 (99.8%), 77 (32%). Anal. Calcd for $C_{25}H_{25}N_3O_2$: C, 75.16; H, 6.30; N, 10.52. Found: C, 75.07; H, 6.35; N, 10.58.

5-(3'-methylthiobut-1'-en-yl)-3-(p-methylphenyl)-6-morpholino-pyrimidin-4(3*H*)-one (82e): Yield 32%; mp 130-132 °C; IR (KBr) ν 1667 (C=O), 1550, 1512, 1487 cm^{-1}; ^1H NMR (300 MHz) δ 1.41 (d, *J* = 6.8, 3H, $-CH_3$), 2.05 (s, 3H, $-SCH_3$), 2.29 (s, 3H, $-CH_3$), 3.34-3.45 (m, 1H, H-3'), 3.56-3.60 (m, 4H, $-CH_2-N-CH_2-$), 3.79-3.82 (m, 4H, $-CH_2-O-CH_2-$), 6.26 (d, *J* = 15.7, 1H, H-1'), 6.66 (dd, *J* = 15.7 and 8.5, 1H, H-2'), 7.00 (d, *J* = 8.3, 2H, arom), 7.09 (d, *J* = 8.3, 2H, arom), 7.14-7.30 (m, 5H, arom). ^{13}C NMR (75.5 MHz) δ 14.1 ($-SCH_3$), 20.7 ($-CH_3$), 21.1 ($-CH_3$), 45.1 (C-3'), 49.3 ($-CH_2-N-CH_2-$), 67.0 ($-CH_2-O-CH_2-$), 99.9 (C-5), 122.0 (C-2'), 127.7, 128.6, 129.2, 129.5, 134.5 (C-1'), 135.0, 138.2, 154.8 (C-6), 160.4 (C-2), 162.8 (C-4). ms *m/z*: 447 (M^+, 2%), 400 (98%), 372 (10%), 358 (6%), 194 (100%), 91 (80%), 77 (18%). Anal. Calcd for $C_{26}H_{29}N_3O_2S$: C, 69.77; H, 6.53; N, 9.39. Found: C, 69.87; H, 6.59; N, 9.32.

2,3-Dipenyl-5-(6'/5'-cyanocyclohex-2'-en-yl)-6-methylpyrimidin-4(3*H*)-ones (84/84'): To a solution of **78c** (0.5 g, 1.6 mmol) in dry toluene (6 ml) was added excess of acrylonitrile and the mixture was refluxed for 25-26 h. The solvent and excess acrylonitrile were removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent: a mixure of EtOAc/hexane in a 1:4 ratio) affording a colourless solid (0.52 g, 89%) consisting in a mixture of regioisomers **84/84'** in 1:3 ratio. mp 138-140 °C; IR (KBr) ν 2234 (CN), 1659 (C=O), 1584, 1516, 1485 cm^{-1}. ^1H NMR (300 MHz) δ 1.94-2.30 (series of m, 8H, 4 x $-CH_2-$, both isomers), 2.58 (s, 3H, $-CH_3$, major isomer),

2.65 (s, 3H, $-CH_3$, minor isomer), 3.47-3.51 (m, 1H, H-1', minor isomer), 3.66 (dt, *J* = 12.6 and 2.5, 1H, H-6', major isomer), 3.84-3.89 (m, 1H, H-1', major isomer), 4.26-4.30 (m, 1H, H-5' minor isomer), 5.54 (dd, *J* = 10.1 and 1.8, 1H, H-2', major isomer), 5.81-5.86 (m, 2H; H-3', major isomer and H-2', minor isomer), 5.87-5.91 (m, 1H, H-3', minor isomer), 6.97-7.30 (m, 20H, arom, both isomers). ^{13}C NMR (75.5 MHz) δ 22.3, 23.6, 27.5, 39.3 (major isomer); 21.3, 23.9, 25.4, 29.3, 36.1 (minor isomer); 121.2, 121.3, 121.7, 122.5, 126.4, 126.9, 127.6, 128.0, 128.6, 128.9, 129.0, 129.1, 129.7, 134.4, 136.9, 137.3 (both isomers); 156.4 (C-2, minor isomer); 157.3 (C-2, major isomer); 161.2 (C-4, major isomer); 161.4 (CN, major isomer); 161.5 (C-4, minor isomer), 162.9 (CN, minor isomer). ms *m/z* 367 (M^+) Anal. Calcd for $C_{24}H_{21}N_3O$: C, 78.45, H, 5.76; N, 11.43. Found: C, 78.50; H, 5.74; N, 11.37.

2,3-Diphenyl-5-(6'/5'-cyanocyclohex-2'-en-yl)-6-piperidino-pyrimidin-4(3*H*)-ones (85/85'): To a solution of **80c** (0.5g, 1.3 mmol) in dry Toluene (6 ml) was added excess of acrylonitrile and the mixture was refluxed for 25-26 h. A similar work up, as employed above, afforded a colourless solid (0.50 g, 88%) consisting in a mixture of regioisomers **85/85'** in 1:1.2 ratio. mp 169-171 °C; IR (KBr) ν 2228 (CN), 1636 (C=O), 1555, 1508, 1487 cm^{-1}. ^1H NMR (300 MHz) δ 1.66-1.72 (m, 12H, $-CH_2-CH_2-CH_2-$, both isomers); 1.96-2.41 (seris of m, 8H; 2 x $-CH_2-$, both isomers), 3.39-3.43 (m, 8H, $-CH_2-N-CH_2-$, both isomers), 3.66-3.96 (series

of m, 4H, H-1', both isomers; H-6', major isomer; H-5', minor isomer), 5.64 (dd, J = 10.1 and 1.8, 1H, H-2', major isomer); 5.82-5.95 (m, 3H, H-3', both isomers; H-2', minor isomer), 7.08-7.32 (m, 20H, arom, both isomers). ^{13}C NMR (75.5 MHz) δ 22.0, 23.8, 24.4, 24.5, 25.1 (both isomers); 26.0, 26.1 ($-CH_2-CH_2-CH_2-$, both isomers); 27.0, 27.3, 29.2, 35.9, 38.7 (both isomers); 51.2, 51.9 ($-CH_2-N-CH_2-$, both isomers); 103.6, 122.0, 122.7, 125.6, 126.9, 127.1, 127.3, 127.7, 128.2, 128.8, 129.1, 129.2, 129.3, 129.4, 129.5, 134.8, 134.9, 137.4, 137.6 (both isomers); 155.2 (C-2) 163.1 (C-4), 164.5 (CN) (major isomer); 155.8 (C-2), 163.2 (C-4), 164.3 (CN) (minor isomer). ms *m/z* 436 (M^+). Anal. Calcd for $C_{28}H_{28}N_4O$: C, 77.04; H, 6.46; N, 12.83. Found: C, 77.21; H, 6.40; N, 12.91.

2,3-Diphenyl-5-(6'/5'-ethoxycarbonylcyclohex-2'-en-yl)-5-methyl-pyrimidin-4(3*H*)-ones (86/86'): To a solution of **78c** (0.50 g, 1.6 mmol) in dry toluene (6 ml) was added ethyl acrylate (0.40 g, 4.0 mmol) and the reaction mixture was refluxed for 15-16 h. The solvent was removed under reduced pressure and the residue purified by silica gel column chromatagraphy (eluent: EtOAc/hexane, 1:3) affording a viscous liquid (0.57 g, 86%) consisting in a mixture of regioisomers **86/86'** in 1:1.2 ratio. IR (CCl_4) ν 1726 ($-CO_2Et$), 1662 (C=O), 1523 cm^{-1}. ^1H NMR (300 MHz) δ 1.15-1.25 (m, 6H, $-CH_2CH_3$, both isomers), 1.81-2.30 (series of m, 8H, 2 x $-CH_2$, both isomers), 2.50 (s, 3H, $-CH_3$, major isomer), 2.52 (s, 3H, $-CH_3$, minor isomer), 3.14-3.19 (m, 1H, H-5', major isomer), 3.44 (unresolved dt, J = 12.1 and 1.0, 1H, H-6', minor

isomer), 3.92-4.10 (m, 5H; 4H, 2 x -C*H*$_2$CH$_3$, both isomers and 1H, H-1', minor isomer), 4.21-4.24 (m, 1H, H-1', major isomer), 5.24 (d, *J* = 10.0, with fine splitting, 1H, H-2', minor isomer), 5.73-5.92 (m, 3H; H-3', both isomers and H-2', major isomer), 7.09-7.24 (m, 20H, arom, both isomers). ^{13}C NMR (75.5 MHz) δ 14.1 (-CH$_2$*C*H$_3$, minor isomer), 14.2 (-CH$_2$*C*H$_3$, major isomer); 22.2, 22.8, 23.2, 24.4, 26.3, 35.6, 38.2, 41.8, 42.0 (both isomers); 60.0 (-*C*H$_2$CH$_3$, minor isomer), 60.1 (-*C*H$_2$CH$_3$, major isomer); 115.8, 123.0, 123.5, 126.9, 127.0, 127.1, 127.6, 127.9, 128.4, 128.7, 128.9, 129.4, 129.5, 134.6, 137.2, 137.5, 149.6, (both isomers); 156.1, 156.6 (C-6, both isomers); 160.2, 160.3 (C-2, both isomers); 161.4, 162.5 (C-4, both isomers); 174.4 (*C*O$_2$Et, major isomer); 175.9 (*C*O$_2$Et, minor isomer). ms *m/z*: 414 (M$^+$). Anal. Calcd for $C_{26}H_{26}N_2O_3$: C, 75.34; H, 6.32; N, 6.76. Found: C, 74.41; H, 6.39; N, 6.68.

2,3-Diphenyl-6-(*N*,*N*-dimethylamino)-5-(6'/5'-ethoxycarbonyl-cyclohex-2'-en-yl)pyrimidin-4(3*H*)-ones (87/87'): To a solution of **80a** (0.5 g, 1.45 mmol) in dry toluene (6 ml) was added ethyl acrylate (0.36 g, 3.6 mmol) and the mixture was refluxed for 15-16 h. A similar work up, as employed above, afforded a viscous liquid (0.55 g, 87%) consisting in a mixture of regioisomers **87/87'** in 1:1.2 ratio. IR (CCl_4) ν 1724 (CO_2Et), 1660 (C=O), 1531 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.01-1.08 (m, 6H, -CH$_2$C*H*$_3$, both isomers), 1.62-2.30 (series of m, 8H, 2 x -CH$_2$-, both isomers), 2.93-2.96 (m, 1H, H-5', major isomer), 3.47 (dt, *J* = 12.4 and

2.5, 1H, H-6', minor isomer), 3.60-3.66 (m, 1H, H-1', minor isomer), 3.70-3.79(m, 1H, H-1', major isomer), 3.84-4.01 (m, 4H, -C*H*$_2$CH$_3$, both isomers), 5.65-5.85 (m, 4H, olefinic H-2' and H-3', both isomers), 7.02-7.20 (m, 20H, arom, both isomers). ^{13}C NMR (75.5 MHz) δ 13.3, 13.4 (-CH$_2$*C*H$_3$, both isomers); 20.9, 22.8, 23.5, 25.2, 25.9, 34.2, 37.6, 44.1 (both isomers); 40.7, 41.0 [-N(CH$_3$)$_2$, both isomers]; 58.7, 58.8 (-*C*H$_2$-CH$_3$, both isomers); 99.5 (C-5, minor isomer), 100.2 (C-5, major isomer); 125.6, 125.9, 126.59, 126.64, 126.7, 126.8, 126.9, 127.5, 127.6, 128.0, 128.1, 128.2 128.3, 134.1, 136.8, 136.9, 153.3 (both isomers); 161.9 (C-2, major isomer), 162.2 (C-2, minor isomer); 162.4 (C-4, major isomer), 162.7 (C-4, minor isomer); 173.5 (*C*O$_2$Et, minor isomer), 175.2 (*C*O$_2$Et, major isomer). ms *m/z*: 433 (M^+). Anal. Calcd for $C_{27}H_{29}N_3O_3$: C, 74.80; H, 6.74; N, 9.69. Found: C, 74.93; H, 6.69; N, 9.76.

3-(p-Methylphenyl)-6-piperidino-2-phenyl-5-[(5'R, 6'S)/(6'R/5'S)-bis(ethoxycarbonyl)cyclohex-2'-en-yl]pyrimidin-4-(3*H*)-ones (88/88'): To a solution of **80e** (0.5 g, 1.26 mmol) in dry toluene (6 ml) was added DEF (0.24 g, 1.40 mmol) and the mixture was refluxed for 5-6 h. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:3 ratio) affording a viscous liquid (0.61 g, 85%) consisting in a mixture of regio/ stereoisomers **88/88'** in 1:1.5 ratio. IR (CCl_4) ν 1729 (2 x -CO$_2$Et), 1661 (C=O), 1562, 1521 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.01-1.24 (m, 12H, 2 x -CH$_2$C*H*$_3$, both isomers); 1.61-1.76 (m, 12H,

$-CH_2-CH_2-CH_2-$, both isomers), 1.99-2.10 (m, 2H, both isomers), 2.25 (s, 3H, $-CH_3$, major isomer), 2.26 (s, 3H, $-CH_3$, minor isomer), 2.45-2.65 (m, 1H, minor isomer), 2.58-2.68 (m, 1H, major isomer), 3.05-3.14 (m, 1H, minor isomer), 3.23-3.40 (m, 6H; 4H, $-CH_2-N-CH_2-$, both isomers and 2H, both isomers), 3.65-3.73 (m, 1H, minor isomer), 3.76-3.84 (m, 1H, major isomer), 3.95-4.13 (m, 9H; 8H, $-CH_2-N-CH_2-$, both isomers and 1H, major isomer), 5.73 (br d, J = 10.3, olefinic H-2', minor isomer), 5.79-5.94 (m, 3H, olefinic; H-3', minor isomer and H-2', H-3', major isomer), 7.02-7.30 (m, 18H, arom, both isomers). ^{13}C NMR (75.5 MHz) δ 14.1, 14.2, 14.3, 21.1, 24.6, 26.0 26.2, 28.1, 35.0, 38.0, 39.6, 42.7, 43.1, 46.6, 51.1, 51.3, 59.9, 60.1, 60.4 (both isomers); 102.4 (C-5, major isomer), 103.9 (C-5, minor isomer); 125.2, 125.9, 126.2, 127.6, 127.7, 128.6, 128.7, 129.1, 129.2, 129.4, 135.0, 135.1, 135.2, 137.8, 137.9 (both isomers); 155.2 (C-6, major isomer), 155.4 (C-6, minor isomer); 163.2 (C-2, minor isomer), 163.3 (C-2, major isomer); 164.0 (C-4, major isomer), 164.6 (C-4, minor isomer); 173.6, 176.6 (CO_2Et, major isomer); 174.1, 175.1 (CO_2Et, minor isomer). ms *m/z*: 569 (M^+) Anal. Calcd for $C_{34}H_{39}N_3O_5$: C, 71.68; H, 6.90; N, 7.38. Found: C, 71.53; H, 6.98; N, 7.29.

3-(p-Methylphenyl)-6-piperidino-2-phenyl-5-[(*N*-phenyl)cyclohex-2'-ene-5',6'-dicarboximido)pyrimidin-4(3*H*)-one (89): To a solution of **80e** (0.50 g, 1.26 mmol) in dry toluene (8 ml) was added NPM (0.22 g, 1.26 mmol). The mixture was refluxed for 1 h,

whereupon the solvent was removed under reduced pressure. The crude product thus obtained was purified by recrystallisation (solvent: a mixture of EtOAc/hexane in 3:1 ratio) to give 0.66 g (92%) of crystalline adduct **89**. mp 196-197°C; IR (KBr) ν 1701 (-CO-N-CO-), 1651 (C=O), 1567, 1524 cm^{-1}. ^1H NMR (300 MHz) δ 1.65-1.69 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.28-2.31 [m, 4H; 1H, H-1' and at 2.30 (s, 3H, $-CH_3$)], 2.98 (dm, *J* = 16.4, 1H, H-5'), 3.29-3.43 (m, 6H; 4H, $-CH_2-N-CH_2-$ and 2H, $-CH_2-$), 3.85 (br d, *J* = 9.0, 1H, H-6') 5.95-5.98 (m, 2H, olefinic), 6.89 (br d, *J* = 8.2, 2H, arom), 7.03 (d, *J* = 8.2, 2H, arom), 7.13-7.31 (m, 12H, arom). ^{13}C NMR (75.5 Mz) δ 21.2 ($-CH_3$), 22.0 ($-CH_2-$), 24.5, 26.3 ($-CH_2-CH_2-CH_2-$), 33.7, 40.6 ($-CH_2-$), 42.5, 51.4 ($-CH_2-N-CH_2-$), 102.3 (C-5), 125.1, 127.0, 127.7, 127.9, 128.6, 129.2, 129.3, 129.4, 130.9, 132.7, 135.0, 135.2, 137.8, 155.4 (C-6), 163.4 (C-2), 164.2 (C-4), 177.3 (-N-CO-), 178.6 (-CO-N-). ms *m/z* 570 (M^+), 379 (M^+-NPM). Anal. Calcd for $C_{36}H_{34}N_4O_3$: C, 75.77; H, 6.00; N, 9.82. Found: C, 75.70; H, 6.98; N, 9.89.

General procedure for Diels-Alder adducts (91): Equivalent amounts of 5-butadienyl pyrimidinones **78/80** and DMAD were refluxed in dry toluene for 4-6 h. The solvent was removed under reduced pressure and the crude product thus obtained was purified by recrystallisation from a benzene:hexane (3:1) mixture.

2,3-Diphenyl-5-[(2',3'-bis(methoxycarbonyl)-2',4'-cyclohexadienyl]-6-methylpyrimidin-4(3*H*)-one (91a): Yield, 93%; mp 173-174°C; IR (KBr) ν 1719 (CO_2Me), 1662 (C=O), 1524 cm^{-1}. ^1H

NMR (300 MHz) δ 2.41 (s, 3H, $-CH_3$), 2.34-2.45 (m, 2H, $-CH_2-$), 3.68 (s, 3H, $-CO_2CH_3$), 3.76 (s, 3H,$-CO_2CH_3$), 5.58-5.64. (m, 1H, olefinic), 5.83-5.89 (m, 1H, olefinic), 7.05-7.28 (m, 10H arom). ^{13}C NMR (75.5 MHz) δ 21.6 ($-CH_3$), 27.1 ($-CH_2-$), 35.8 (C-1'), 52.1 (CO_2CH_3), 52.1 ($-OCH_3$), 96.1 (C-5), 121.3, 122.8, 123.7, 127.9, 128.4, 128.7, 128.9, 129.0, 129.5, 130.6, 134.6, 136.2, 137.4, 156.8 (C-6), 161.0 (C-2), 162.1 (C-4), 167.3 (CO_2CH_3), 168.1 (CO_2CH_3). ms *m/z* 456 (M^+), 423, 409, 397 (M^+- $-CO_2Me$), 365, 337, 262, 180. Anal. Calcd for $C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14. Found: C, 70.95; H, 5.35; N, 6.20.

2,3-Diphenyl-5-[2',3'-bis(methoxycarbonyl)-2',4'-cyclohexadienyl]-6-pyrrolidinopyrimidin-4(3*H*)-one (91b): Yield 94%; mp 172-173 °C, IR (KBr) ν 1728 (CO_2Me), 1704 (CO_2Me), 1642 (C=O), 1558, 1524 cm^{-1}. ^1H NMR (300 MHz) δ 1.80-1.87 (m, 2H, $-CH_2-$), 1.98-2.03 (m, 2H, $-CH_2-$), 3.44-3.50 (m, 2H, $-N-CH_2-$), 3.61 (s, 3H, $-CO_2CH_3$), 3.70 (s, 3H, $-CO_2CH_3$), 3.72-3.78 (m, 2H, $-CH_2-N-$), 4.33-4.36 (m, 2H, $-CH_2-$), 6.01 (ddd, *J* = 9.5, 5.9 and 2.3, 1H, H-5'), 6.21 (d, *J* = 9.5, 1H, H-4'), 7.07-7.10 (m, 1H, arom), 7.12-7.31 (m, 9H, arom). ^{13}C NMR (75.5 MHz) δ 25.6 ($-CH_2-CH_2-$), 38.0 (C-4'), 45.8 (C-1') 50.5 ($-CH_2-N-CH_2-$), 51.6 ($-OCH_3$), 51.8 ($-OCH_3$), 96.7 (C-5), 120.4, 125.7, 127.7, 127.9, 128.6, 129.3, 129.5, 134.0, 135.1, 137.7, 138.4; 154.9 (C-6), 158.2 (C-2), 163.3 (C-4), 167.1 (CO_2Me), 176.4 (CO_2Me). ms *m/z* 511 (M^+). Anal. Calcd for $C_{30}H_{29}N_3O_5$: C, 70.44; H, 5.71; N, 8.21. Found: C, 70.52, H, 5.69; N, 8.15.

5-[2',3'-Bis(methoxycarbonyl)-2',4'-cyclohexadienyl]-2-methylthio-3-phenylpyrimidin-4(3*H*)-one (91c): Yield, 96%; mp 185-186°C, IR (KBr) ν 1732 (CO_2Me), 1709 (CO_2Me), 1675 (C=O), 1490 cm^{-1}. ^1H NMR (300 MHz) δ 2.40 (s, 3H, $-SCH_3$), 2.95-3.20 [m, 2H, $-CH_2-$; consisting in at 3.01 (ddd, *J* = 23.1, 6.8 and 2.9, 1H) and 3.14 (dddd, *J* = 23.1, 7.5, 2.0 and 2.0, 1H)], 3.72 (s, 3H, $-OCH_3$), 3.78 (s, 3H, $-OCH_3$), 4.55-4.62 (m, 1H, H-1'), 5.77-5.86 (m, 2H, olefinic), 7.24-7.27 (m, 2H, arom), 7.50-7.55 (m, 3H, arom), 7.72 (s, 1H, olefinic H-6). ^{13}C NMR (75.5 MHz,) δ 15.3 ($-SCH_3$), 27.3 ($-CH_2-$), 35.8 (C-1'), 52.3 ($-OCH_3$), 52.4 ($-OCH_3$), 122.7, 123.2, 125.1, 128.4, 129.80, 129.84, 130.1, 132.4, 135.4, 135.8, 150.5 (C-6), 161.4 (C-2), 162.8 (C-4), 167.6 (CO_2Me), 168.0 (CO_2Me). ms *m/z* 412 (M^+). Anal. Calcd for $C_{21}H_{20}N_2O_5S$: C, 61.15; H, 4.89; N, 6.79. Found: C, 61.21; H, 4.81; N, 6.89.

General procedure for the preparation of 4-(N-allyl-N-aryl)amino-1-aryl-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes (95): To a solution of 1-aryl-4-(*N*-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes[40] (5.0 mmol) in acetone (25 ml) was added K_2CO_3 (1.0g, 10.1 mmol). The mixture was refluxed for 2 h and then allowed to reach rt. Allyl bromide (0.91 g, 7.5 mmol) was then added and the reaction mixture stirred at rt for 7-9 h. It was then filtered and the residue washed with acetone (10 ml). The combined filtrate was concentrated under reduced pressure, diluted with CH_2Cl_2 and washed with water (4 x 100 ml). The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product which was purified by column

chromatography on silica gel (Eluent: a mixture of EtOAc/hexane in a 1:10 ratio).

1,2-Diphenyl-4-methylthio-4-(*N*-allyl-*N*-phenyl)amino-1,3-diaza-1,3-butadiene (95a): Yield 83%; Viscous liquid; IR (CCl_4) ν 1603, 1590, 1567, 1490 cm^{-1}. ^1H NMR (90 MHz) δ 1.97 (s, 3H, $-SCH_3$), 4.30 (d, J = 6.0, 2H, $-CH_2-$), 5.07 (dd, J = 17.0 and 9.2, 2H, $=CH_2$), 5.63-6.03 (m, 1H, -CH=), 6.83-7.63 (m, 13H, arom), 8.10-8.33 (m, 2H, arom). ms *m/z*: 385 (M^+). Anal. Calcd for $C_{24}H_{23}N_3S$: C, 74.77; H, 6.01; N, 10.90. Found: C, 74.70; H, 6.03; N, 10.93.

1,2-Diphenyl-4-methylthio-4-[*N*-allyl-*N*-(p-methylphenyl)]amino-1,3-diaza-1,3-butadiene (95b): Yield 79%; viscous liquid; IR (CCl_4) ν 1608, 1596, 1566, 1507 cm^{-1}. ^1H NMR (90 MHz) δ 2.00 (s, 3H, $-SCH_3$), 2.30 (s, 3H, $-CH_3$), 4.30 (d, J = 6.0, 2H, $-CH_2-$), 5.08 (dd, J = 16.5 and 9.0, 2H, $=CH_2$, 5.70-6.15 (m, 1H, -CH=), 6.85 (d, J = 8.5, 2H, arom), 7.03-7.67 (m, 10H, arom), 8.10-8.43 (m, 2H, arom). ms *m/z*: 399 (M^+). Anal. Calcd for $C_{25}H_{25}N_3S$: C, 75.15; H, 6.30; N, 10.52. Found: C, 75.05; H, 6.33; N, 10.58.

1,2-Diphenyl-4-methylthio-4-[*N*-allyl-*N*-(p-methoxyphenyl)]amino-1,3-diaza-1,3-butadiene (95c): Yield 83%; viscous liquid; IR (CCl_4) ν 1601, 1594, 1561, 1498 cm^{-1}. ^1H NMR (90 MHz) δ 2.00 (s, 3H, $-SCH_3$), 3.73 (s, 3H, $-OCH_3$), 4.30 (d, J = 6.0, 2H, $-CH_2-$), 5.07 (dd, J = 17.5 and 9.0, 2H, $=CH_2$), 5.67-6.08 (m, 1H, -CH=), 6.77-6.97 (m, 4H, arom), 7.20 (d, J = 7.5, 2H, arom), 7.33-7.70 (m, 6H, arom), 8.08-8.40 (m, 2H, arom). ms *m/z* : 415

(M^+). Anal. Calcd for $C_{25}H_{25}N_3SO$: C, 72.26; H, 6.06; N, 10.11. Found: C, 72.30; H, 6.03; N, 10.17.

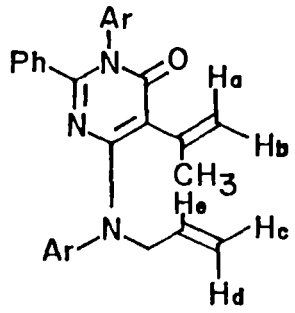
1-(p-Methylphenyl)-4-methylthio-2-phenyl-4-(*N*-allyl-*N*-phenyl) amino-1,3-diaza-1,3-butadiene (95d): Yield 79%; viscous liquid; IR (CCl_4) ν 1608, 1568, 1490 cm^{-1}. ^1H NMR (90 MHz) δ 1.90 (s, 3H, $-SCH_3$), 2.33 (s, 3H, $-CH_3$), 4.33 (d, J = 6.0, 2H, $-CH_2-$), 5.00 (dd, J = 17.5 and 9.0, 2H, $=CH_2$), 5.63-6.17 (m, 1H, -CH=), 6.80-7.53 (m, 12H, arom), 8.07-8.33 (m, 2H, arom). ms *m/z*: 399 (M^+). Anal. Calcd for $C_{25}H_{25}N_3S$: C, 75.15; H, 6.30; N, 10.52. Found: C, 75.20; H, 6.26; N, 10.44.

1-(p-Methylphenyl)-4-methylthio-2-phenyl-4-[*N*-allyl-*N*-(p-methylphenyl)amino-1,3-diaza-1,3-butadiene (95e): Yield 89%; viscous liquid; IR (CCl_4) ν 1609, 1556, 1506 cm^{-1}. ^1H NMR (90 MHz) δ 2.16 (s, 3H, $-SCH_3$), 2.31 (s, 3H, $-CH_3$), 2.36 (s, 3H, $-CH_3$), 4.28 (d, J = 6.0, 2H, $-CH_2-$), 5.15 (dd, J = 17.2 and 9.4, 1H, $=CH_2$), 5.69-6.11 (m, 1H, -CH=), 6.92 (d, J = 7.8, 2H, arom), 7.10-7.53 (m, 9H, arom), 7.64 (d, J = 7.8, 2H, arom). ms *m/z*: 413 (M^+). Anal. Calcd for $C_{26}H_{27}N_3S$: C, 75.51; H, 6.58; N, 10.16. Found: C, 75.45; H, 6.57; N, 10.11.

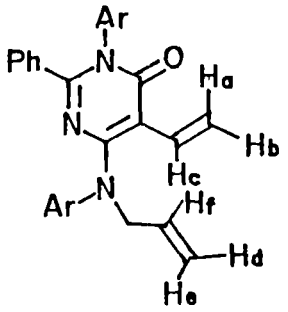
1-(p-Methylphenyl)-4-methylthio-2-phenyl-4-[*N*-allyl-*N*-(p-methoxyphenyl)amino-1,3-diaza-1,3-butadiene (95f): Yield 81%; viscous liquid; IR (CCl_4) ν 1608, 1596, 1558, 1506 cm^{-1}. ^1H NMR (90 MHz) δ 2.00 (s, 3H, $-SCH_3$), 2.37 (s, 3H, $-CH_3$), 3.76 (s, 3H, $-OCH_3$), 4.28 (d, J = 5.5, 2H, $-CH_2-$), 5.23 (dd, J = 17.5 and 9.0 2H, $=CH_2$), 5.67-6.10 (m, 1H, -CH=), 6.80-7.73 (m, 11H, arom),

8.10-8.46 (m, 2H, arom). ms *m/z*: 429 (M^+). Anal. Calcd for $C_{26}H_{27}N_3OS$: C, 72.69; H, 6.33; N, 9.78. Found: C, 72.61; H, 6.30; N, 9.82.

Reactions of (N-allyl-N-aryl)amino-1,3-diaza-1,3-butadienes (95) with vinyl/isopropenylketenes (60): **General procedure for pyrimidinones (97):** Same as employed for pyrimidinones **62**.



97.a-e



97.f

2,3-Diphenyl-5-isopropenyl-6-(*N*-allyl-*N*-phenyl)aminopyrimidin-4(3*H*)-one (97a): Yield 91%; mp 162-163 °C; IR (KBr) ν 1651 (C=O), 1552, 1517, 1490 cm^{-1}. ^1H NMR (300 MHz) δ 1.64 (s, 3H, $-CH_3$), 4.61 (d, J = 5.8, 2H, $-CH_2-$), 4.79 (br s, 1H, Ha), 4.85 (br s, 1H, Hb), 5.15 (unresolved dd, J = 17.3 and 10.3, 2H, Hc and Hd), 6.05 (dddd, J = 17.3, 10.3, 5.8 and 5.8, 1H, He), 7.04-7.33 (m, 15H, arom). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 55.1 ($-CH_2-$), 106.4 (C-5), 116.9 (C-8), 118.4 (C-11), 124.3, 125.3, 127.7, 128.0, 128.6, 128.7, 129.0, 129.2, 129.4 (C-10), 135.0, 135.1, 137.6 (C-7), 138.0, 146.1, 155.2 (C-6), 157.1 (C-2), 162.7 (C-4). ms *m/z*: 419 (M^+). Anal. Calcd for $C_{28}H_{25}N_3O$: C, 80.16; H, 6.00; N, 10.02. Found : C, 80.06, H, 6.03; N, 10.07.

2,3-Diphenyl-5-isopropenyl-6-[*N*-allyl-*N*-(p-methylphenyl)]amino pyrimidin-4(3*H*)-one (97b): Yield 93%; mp 174-175 °C; IR (KBr)ν 1658 (C=O), 1554, 1507, 1485 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.62 (s, 3H, $-CH_3$), 2.32 (s, 3H, $-CH_3$), 4.58 (d, J = 5.8, 2H, $-CH_2-$), 4.77 (br s, with fine splitting, 1H, Ha), 4.85-4.86 (m, 1H Hb), 5.11 (dd, J = 10.0 and 1.5, 1H, Hc), 5.16 (dd, J = 16.9 and 1.5 , 1H, Hd), 6.05 (dddd, J = 16.9, 10.0, 5.8 and 5.8, 1H, He), 6.99 (d, J = 8.5, with fine splitting, 2H, arom), 7.07 (d, J = 8.3, 2H, arom), 7.15-7.34 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 20.9 ($-CH_3$), 21.2 ($-CH_3$), 55.4 ($-CH_2-$), 105.8 (C-5), 116.8 (C-8), 118.4 (C-11), 125.6, 127.7, 128.0, 128.6, 129.1, 129.3, 129.4 (C-10), 134.1, 135.1, 135.3, 137.8 (C-7), 138.2, 143.5, 155.1 (C-6), 157.4 (C-2), 162.8 (C-4). ms *m/z*: 433 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O$: C, 80.34; H, 6.27; N, 9.69. Found: C, 80.43; H, 6.25; N, 9.74.

2,3-Diphenyl-5-isopropenyl-6-[*N*-allyl-*N*-(p-methoxyphenyl)]amino pyrimidin-4(3*H*)-one (97c): Yield 87%; mp 179.5-180.5 °C; IR (KBr) ν 1655 (C=O), 1556, 1508 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.59 (s, 3H, $-CH_3$), 3.78 (s, 3H, $-OCH_3$), 4.54 (d, J = 5.9, 2H, $-CH_2-$), 4.71-4.72 (m, 1H, Ha), 4.85-4.86 (m, 1H, Hb), 5.12 (unresolved dd, J = 17.4 and 10.1, 2H, Hc and Hd), 6.04 (dddd, J = 17.4, 10.1, 5.9 and 5.9, 1H, He), 6.78 (d, J = 8.9, with fine splitting, 2H, arom), 7.03 (d, J = 8.9, with fine splitting, 2H, arom), 7.14-7.32 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 21.3 ($-CH_3$), 55.2 ($-OCH_3$), 55.7 ($-CH_2-$), 104.7 (C-5), 113.8, 116.9 (C-8), 118.2 (C-11), 127.6, 127.8, 127.9, 128.5, 129.1, 129.2,

129.3 (C-10), 135.1, 137.7 (C-7), 138.3, 138.9, 154.9 (C-6), 156.7, 157.3 C-2), 162.5 (C-4). ms *m/z*: 449 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O_2$: C, 77.48; H, 6.05; N, 9.35. Found: C, 77.41; H, 6.05; N, 9.37.

5-Isopropenyl-3-(p-methylphenyl)-2-phenyl-6-[*N*-allyl-*N*-(p-methylphenyl)]aminopyrimidin-4(3*H*)-one (97d): Yield 83%; mp 183-184 °C; IR (KBr) ν 1657 (C=O), 1558, 1528, 1508 cm^{-1}. ^1H NMR (300 MHz) δ 1.62 (s, 3H, $-CH_3$), 2.27 (s, 3H, $-CH_3$), 2.30 (s, 3H, $-CH_3$), 4.57 (d, J = 4.7, 2H, $-CH_2-$), 4.77 (s, 1H, Ha), 4.84 (s, 1H, Hb), 5.14 (unresolved dd, J = 16.9 and 10.1, Hc and Hd), 6.04 (dddd, J = 16.9, 10.1, 5.8, 5.8; 1H, He), 6.98 (d, J = 8.4, 2H, arom), 7.02-7.08 (m, 6H, arom), 7.15-7.24 (m, 3H, arom), 7.34 (d, J = 8.2, with fine splitting, 2H, arom). ^{13}C NMR (75.5 MHz) δ 20.9 ($-CH_3$), 21.1 ($-CH_3$), 21.2 ($-CH_3$), 55.3 ($-CH_2-$), 105.9 (C-5), 116.8 (C-8), 118.3 (C-11), 125.6, 127.8, 128.8, 129.3 (C-10 and one arom C), 134.0, 135.1, 135.3, 135.4, 137.9 (C-7), 138.3, 143.6, 155.2 (C-6), 157.3 (C-2), 163.0 (C-2). ms *m/z*: 447 (M^+). Anal. Calcd for $C_{30}H_{29}N_3O$: C, 80.50; H, 6.53; N, 9.38. Found: C, 80.42; H, 6.50; N, 9.41.

5-Isopropenyl-3-(p-methylphenyl)-2-phenyl-6-[*N*-allyl-*N*-(p-methoxyphenyl)]aminopyrimidin-4(3*H*)-one (97e): Yield 91%; mp 180-181 °C; IR (KBr) ν 1652 (C=O), 1556, 1521, 1506 cm^{-1}. ^1H NMR (300 MHz) δ 1.60 (s, 3H, $-CH_3$), 2.28 (s, 3H, $-CH_3$), 3.79 (s, 3H, $-OCH_3$), 4.55 (d, J = 5.9, 2H, $-CH_2-$), 4.73 (br s, 1H, Ha), 4.85 (br s, 1H, Hb), 5.12 (unresolved dd, J = 17.2 and 9.7, Hc and

Hd), 6.05 (dddd, J = 17.2, 9.7, 5.9 and 5.9, 1H, He), 6.80 (d, J = 8.9, with fine splitting, 2H, arom), 7.02-7.09 (m, 5H, arom), 7.17-7.27 (m, 4H, arom), 7.33-7.36 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 21.3 ($-CH_3$), 55.4 ($-OCH_3$), 55.8 ($-CH_2-$), 106.2 (C-5), 113.9, 116.9 (C-8), 118.2 (C-11), 127.7, 127.8, 128.8, 129.3 (C-7), 129.4 (C-10), 135.3, 137.8, 138.5, 139.2, 155.1 (C-6), 156.7, 157.4 (C-2), 162.9 (C-4). ms *m/z*: 463 (M^+). Anal. Calcd for $C_{30}H_{29}N_3O_2$: C, 77.72; H, 6.30; N, 9.06. Found: C, 77.80; H, 6.29; N, 9.03.

2,3-Diphenyl-5-ethenyl-6-[*N*-allyl-*N*-(p-methoxyphenyl)]amino-pyrimidin-4(3*H*)-one (97f): Yield 63%; mp 66-67 °C; IR (KBr)ν 1638 (C=O), 1548, 1497, 1485 cm^{-1}. ^{1}H NMR (300 MHz) δ 3.78 (s, 3H, $-OCH_3$), 4.67 (d, J = 5.5, 2H, $-CH_2-$), 4.85 (d, J = 9.8, 1H, Ha), 5.05 (d, J = 16.5, 1H, Hb), 5.15 (d, J = 10.3, 1H, He), 5.19 (d, J = 17.3, 1H, Hd), 5.86-6.03 (m, 2H, Hc and Hf), 6.82 (d, J = 8.9, 2H, arom), 7.09 (d, J = 8.9, 2H, arom), 7.16-7.37 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 55.5 ($-OCH_3$), 55.6 ($-CH_2-$), 106.5 (C-5), 114.3, 115.7 (C-11), 116.7 (C-8), 125.4, 125.9, 127.8, 128.3, 128.8, 129.1, 129.4, 129.5, 132.0, 135.2, 137.8, 139.1, 139.8, 155.1 (C-6), 156.3, 157.2 (C-2), 162.6 (C-4). ms *m/z*: 435 (M^+). Anal. Calcd for $C_{28}H_{25}N_3O_2$: C, 77.22; H, 5.79; N, 9.65. Found: C, 77.28; H, 5.79; N, 9.62.

5,5-Dimethyl-2,3-diphenyl-9-(p-methylphenyl)-3,5,6,9-tetrahydro pyrimido[4,5-b]azepin-4-one (98a): A solution of 97b (0.50 g, 1.08 mmol) in xylene (6 ml) was refluxed for 1.5 h. The solvent

was concentrated under *vacuo* and the residue thus obtained was purified by column chromatography (silica gel, EtOAc/hexane, 1:9) to give 0.38 g (76%) of **98a**. mp 182-183 °C; IR (KBr) ν 1645 (C=O), 1560, 1507, 1360 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.59 (s, 6H, 2 x $-CH_3$), 2.37 (s, 3H, $-CH_3$), 2.43 (br d, J = 7.1, 2H, $-CH_2-$), 5.54 (ddd, J = 17.4, 7.4 and 7.4, 1H, H-7), 6.23 (d, J = 7.4, 1H, H-8), 6.99-7.02 (m, 4H, arom), 7.09-7.12 (m, 3H, arom), 7.19-7.28 (m, 7H, arom). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 29.2 ($-CH_3$), 41.1 (C-6), 42.3 (C-5), 108.8 (C-4a), 117.0 (C-7), 127.5, 127.9, 128.0, 128.7 (C-8), 129.1, 129.3, 129.4, 129.5, 133.5, 134.3, 136.0, 138.1, 143.1, 151.6 (C-9a), 155.2 (C-2), 163.3 (C-4). ms *m/z*: 433 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O$: C, 80.34; H, 6.27; N, 9.69. Found: C, 80.25; H,6.27; N, 9.73.

5,5-Dimethyl-9-(p-methoxyphenyl)-3-(p-methylphenyl)-2-phenyl-3,5,6,9-tetrahydropyrimido[4,5-b]azepin-4-one (98b): A solution of **97e** (0.50, 1.08 mmol) in xylene (6 ml) was refluxed for 1.5 h. A similar work up, as employed for **98a**, yielded 0.42 g (82%) of **98b**. mp 185-187 °C; IR (KBr) ν 1645 (C=O), 1558, 1506, 1360 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.58 (s, 6H, 2 x $-CH_3$), 2.26 (s, 3H, $-CH_3$), 2.42 (br d, J = 7.3, 2H, $-CH_2-$), 3.80 (s, 3H, $-OCH_3$), 5.52 (ddd, J = 17.4, 7.3 and 7.3, 1H, H-7), 6.18 (d, J = 7.3, 1H, H-8), 6.91 (d, J = 8.8, with fine splitting, 2H, arom), 6.97-7.11 (m, 9H, arom), 7.21 (d, J = 8.7, with fine splitting, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.1 ($-CH_3$), 29.2 (2 x $-CH_3$), 41.0 (C-6), 42.5 (C-5), 55.4 ($-OCH_3$), 108.5 (C-4a), 113.9, 116.7 (C-7), 127.5, 128.7

(C-8), 129.2, 129.3, 129.5, 133.7, 134.4, 135.3, 137.7, 138.6, 151.6 (C-9a), 155.1 (C-2), 157.8, 163.3 (C-4). ms *m/z*: 463 (M^+). Anal. Calcd for $C_{30}H_{29}N_3O_2$: C, 77.73; H, 6.30; N, 9.06. Found: C, 77.67; H, 6.28; N, 9.11.

10-Allyl-2,3-diphenyl-5,5,7-trimethyl-3,5,10-trihydro pyrimido[4,5-b]quinolin-4-one (99a): To a solution of **97b** (0.50 g, 1.16 mmol) in benzene (10 ml) was added catalytic amount of $AlCl_3$. The mixture was refluxed for 30 min, cooled to rt and diluted with benzene (10 ml). The organic phase was then washed with saturated $NaHCO_3$ and water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:9 ratio) to give 0.47 g (94%) of **99a**. mp 216-217 °C; IR (KBr) ν 1652 (C=O), 1595, 1558, 1525, 1496, 1443 cm^{-1}; ^1H NMR (300 MHz) δ 1.87 (s, 6H, 2 x $-CH_3$), 2.30 (s, 3H, $-CH_3$), 4.83-4.85 (br s, with fine splitting, 2H, $-CH_2-$), 5.18 (d, J = 10.2, with fine splitting, 1H, $=CH_2$), 5.23 (d, J = 17.3, with fine splitting, 1H, $=CH_2$), 5.96 (dddd, J = 17.3, 10.2, 4.5 and 4.5, 1H, -CH=), 6.79 (d, J = 8.4, 1H, H-9), 6.94 (dd, J = 8.4 and 1.8 1H, arom H-8), 7.12-7.30 (m, 11H, arom). ^{13}C NMR (75.5 MHz) δ 20.7 ($-CH_3$), 30.3 (2 x $-CH_3$), 35.4 (C-5), 45.6 ($-CH_2-$), 101.6 (C-4a), 113.9, 116.0 (C-13), 127.4, 127.7, 127.8, 128.1, 128.7, 129.2, 129.3, 129.4 (C-12), 131.7, 133.3, 133.5, 134.2, 137.9, 152.0 (C-10a), 156.2 (C-2), 161.5 (C-4). ms *m/z*: 433 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O$: C, 80.34; H, 6.27; N, 9.69. Found: C, 80.20; H, 6.30; N, 9.75.

10-Allyl-5,5-dimethyl-2,3-diphenyl-7-methoxy-3,5,10-trihydro pyrimido[4,5-b]quinolin-4-one (99b): To a solution of **97c** (0.50 g, 1.12 mmol) in benzene (10 ml) was added catalytic amount of $AlCl_3$. An identical procedure, as employed for **98a**, resulted in the isolation of 0.45 g (90%) of **99b**. mp 205-207 °C; IR (KBr)ν 1650 (C=O), 1603, 1562, 1528, 1494, 1438 cm^{-1}. ^1H NMR (300 MHz) δ 1.88 (s, 6H, 2 x $-CH_3$), 3.80 (s, 3H, $-OCH_3$), 4.84-4.85 (br s, with fine splitting, 2H, $-CH_2-$), 5.19 (d, J = 10.3, with fine splitting, 1H, $=CH_2$), 5.23 (d, J = 17.4, with fine splitting, 1H, $=CH_2$), 5.96 (dddd, J = 17.4, 10.3, 4.5 and 4.4, 1H, -CH=), 6.71 (dd, J = 8.9 and 2.9, with fine splitting, 1H, arom H-8), 6.84 (d, J = 8.9, 1H, H-9), 7.00 (d, J = 2.9, 1H, arom H-6), 7.12-7.30 (m, 10H, arom). ^{13}C NMR (75.5 MHz) δ 30.2 (2 x $-CH_3$), 35.8 (C-5), 45.7 ($-CH_2-$), 55.4 ($-OCH_3$), 100.5 (C-4a), 111.7, 113.3, 114.8, 116.1 (C-13), 127.7, 128.1, 128.7, 129.2, 129.3, 129.4 (C-12), 130.4, 133.6, 135.0, 135.2, 137.9, 152.0 (C-10a), 155.2, 156.2 (C-2), 161.5 (C-4). *m/z*: 449 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O_2$: C, 77.48; H, 6.05; N, 9.35. Found: C, 77.54; H, 6.07; N, 9.31.

7,8-Bis(methoxycarbonyl)-2,3-diphenyl-5-methylquinazolin-4(3*H*)-one (101): Equivalent amounts of **97a/97b/97c** and DMAD were refluxed in dry toluene for 17-18 h. The solvent was removed under reduced pressure and the crude product thus obtained was purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:6 ratio) to give 90-95% of **101a**. mp 192-193 °C; IR (KBr) ν 1733 (2 x $-CO_2Me$), 1674 (C=O), 1588, 1559 cm^{-1}. ^1H NMR (300 MHz) δ 2.91 (s, 3H, $-CH_3$), 3.97 (s, 3H,

$-CO_2CH_3$), 3.99 (s, 3H, $-CO_2CH_3$), 7.13-7.35 (m, 10H, arom), 7.87 (s, 1H, H-6). ^{13}C NMR (75.5 MHz) δ 23.2 ($-CH_3$), 52.8 ($-OCH_3$), 52.9 ($-OCH_3$), 122.2, 127.7, 128.6, 129.0, 129.1, 129.5, 129.6, 129.7, 138.8, 132.7, 134.7, 137.5, 143.2, 146.6, 155.5 (C-2), 162.1 (C-4), 165.1 ($-CO_2Me$), 168.3 ($-CO_2Me$). ms *m/z*: 428 (M^+). Anal. Calcd for $C_{25}H_{20}N_2O_5$: C, 70.08; H, 4.70; N, 6.54. Found: C, 70.15; H, 4.71; N, 6.50.

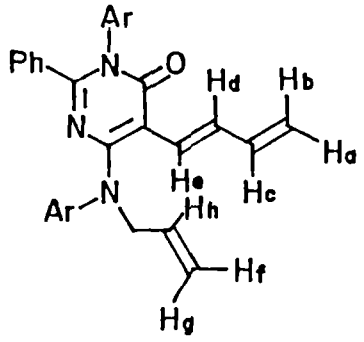
General procedure for pyrimidoquinolines (107): A solution of thiophenol (0.3 g, 2.74 mmol) and AIBN (0.23 g, 1.40 mmol) in dry benzene was added dropwise, over a period of 2 h, to a solution of **97** (2.5 mmol) in boiling benzene while stirring under nitrogen. The solution was further refluxed for 5-6 h and the solvent was removed under *vacuo*. The resulting residue was purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:9 ratio)

10-Allyl-2,3-diphenyl-5-methyl-5-phenylthiomethyl-3,5,10-trihydropyrimido[4,5-b]quinolin-4-one (107a): Yield 61%; mp 161-162°C; IR (KBr) ν 1655 (C=O), 1598, 1563, 1560, 1525 cm^{-1}. ^1H NMR (300 MHz) δ 1.99 (s,3H,$-CH_3$), 3.24 (d, *J* = 13.2, 1H, $-CH_2$-SPh), 4.64 (d, *J* = 13.2, 1H, $-CH_2$-SPh), 4.83-4.95 (m, 2H, $-N-CH_2-$), 5.22 (d, *J* = 10.5, 1H, $=CH_2$), 5.36 (d, *J* = 17.3, 1H, $=CH_2$) 5.98 (dddd, *J* = 17.3, 10.5, 4.4 and 4.4, 1H, -CH=), 6.92 (d, *J* = 8.3, 1H, H-9), 7.00 (d *J* = 8.3, 1H, H-6), 7.09-7.32 (m, 17 H, arom). ^{13}C NMR (75.5 MHz) δ 29.3 ($-CH_3$), 41.6 (C-5), 45.5 ($-CH_2$-SPh), 47.0 ($-N-CH_2-$), 98.5 (C-4a), 114.1, 116.1 (C-13),

119.1, 125.7, 126.9, 127.4, 127.6, 128.1, 128.4, 128.6, 128.7, 129.0, 129.1, 129.3, 129.4 (C-12); 130.9, 133.1, 134.9, 137.5, 138.0, 116.1, 153.2 (C-10a), 156.3 (C-2), 161.1 (C-4). ms *m/z*: 527 (M^+). Anal. Calcd for $C_{34}H_{29}N_3OS$: C, 77.39; H, 5.54; N, 7.96. Found: C, 77.46; H, 5.55; N, 7.98.

10-Allyl-5,7-dimethyl-2,3-diphenyl-5-phenylthiomethyl-3,5,10-trihydropyrimido[4,5-b]quinolin-4-one (107b): Yield 73%; mp 181-183°C; IR (KBr) ν 1652 (C=O), 1598, 1561, 1557, 1530, 1497 cm^{-1}. ^1H NMR (300 MHz) δ 1.98 (s, 3H, $-CH_3$), 2.26 (s, 3H, $-CH_3$); 3.24 (d, *J* = 13.1, 1H, $-CH_2$-SPh), 4.64 (d, *J* = 13.1, 1H, $-CH_2$-SPh), 4.79-4.97 (m, 2H, -N-CH_2-), 5.22 (d, *J* = 10.4, with fine splitting, 1H, $=CH_2$); 5.35 (d, *J* = 17.3, with fine splitting, 1H, $=CH_2$), 5.97 (dddd, *J* = 17.3, 10.4, 4.3 and 4.3, 1H, -CH=), 6.82 (d, *J* = 8.4, 1H, H-9), 6.96 (dd, *J* = 8.4 and 1.5, 1H, H-8), 7.08 (d, *J* = 1.5, 1H, H-6), 7.11-7.29 (m, 15H, arom). ^{13}C NMR (75.5 MHz) δ 20.8 ($-CH_3$), 29.3 ($-CH_3$), 41.7 (C-5), 45.4 ($-CH_2$-SPh), 47.0 (-N-CH_2-), 98.2 (C-4a), 114.1; 116.1 (C-13), 125.6, 127.5, 127.6, 128.0, 128.1, 128.3, 128.6, 128.8, 129.2, 129.4, 129.7 (C-12) 130.9, 131.9, 133.3, 135.0, 135.7, 137.5, 137.6, 153.2 (C-10a), 156.3 (C-2), 161.1 (C-4). ms *m/z* 541 (M^+). Anal. Calcd for $C_{35}H_{31}N_3OS$: C, 77.60; H, 5.77; N, 7.76. Found: C, 77.71; H, 5.77; N, 7.79.

***Reactions of N-allyl-N-aryl-1,3-diaza-1,3-butadienes 95 with butadienylketene*: General Procedure for pyrimidinones (109)**: Same as employed for pyrimidinones 78.



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5-(1',3'-Butadienyl)-2,3-diphenyl-6-(*N*-allyl-*N*-phenyl)amino-pyrimidin-4(3*H*)-one (109a): Yield 73%; viscous liquid; IR (CCl_4) ν 1644 (C=O), 1547, 1488, 1439, 1403 cm^{-1}. ^1H NMR (300 MHz) δ 4.72 (d, J = 5.1, 2H, $-CH_2-$), 4.85 (d, J = 10.0, 1H, Ha), 5.07 (d, J = 16.8, 1H, Hb), 5.14 (dd, J = 10.3 and 1.3, 1H, Hf), 5.23 (dd, J = 17.2 and 1.3, 1H, Hg), 5.85-6.09 (m, 3H, Hc, He and Hh), 6.94-7.01 (m, 1H, arom), 7.10-7.32 (m, 14H, arom), 7.44 (dd, J = 14.9 and 10.2, 1H Hd). ^{13}C NMR (75.5 MHz) δ 54.8 ($-CH_2-$), 102.7 (C-5), 116.1 (C-10), 116.5 (C-13), 122.7, 123.5, 125.8, 127.7, 128.2, 128.3, 128.6, 128.8, 128.9, 129.0, 129.1, 129.3, 129.5, 132.5, 134.7, 135.0, 137.6, 138.8, 146.4, 154.6 (C-6), 157.3 (C-2), 162.5 (C-4). ms *m/z*: 431 (M^+). Anal. Calcd for $C_{29}H_{25}N_3O$: C, 80.71; H, 5.84; N, 9.74. Found: C, 80.65; H, 5.85; N, 9.79.

5-(1',3'-Butadienyl)-2,3-diphenyl-6-[*N*-allyl-*N*-(p-methylphenyl)]-aminopyrimidin-4(3*H*)-one (109b): Yield 63%; viscous liquid; IR (CCl_4) ν 1663 (C=O), 1548, 1504, 1487, 1436, 1398 cm^{-1}. ^1H NMR (300 MHz) δ 2.29 (s, 3H, $-CH_3$), 4.70 (d, J = 5.3, 2H, $-CH_2-$), 4.86 (d, J = 9.9, with fine splitting, 1H, Ha), 5.05 (d, J = 16.9, with fine splitting, 1H, Hb), 5.15 (dd, J = 10.3 and 1.4,

1H, Hf), 5.21 (dd, *J* = 17.2 and 1.4, 1H, Hg), 5.86-6.11 (m, 3H, Hc, He, Hh), 7.02 (d, *J* = 8.7, with fine splitting, 2H, arom), 7.08 (d, *J* = 8.7, with fine splitting, 2H, arom), 7.15-7.37 (m, 10H, arom), 7.41 (dd, *J* = 15.3 and 10.3, partially merged with arom, 1H, Hd). ^{13}C NMR (75.5 MHz) δ 20.8 ($-CH_3$); 55.1 ($-CH_2-$), 101.9 (C-5), 115.9 (C-10), 116.5 (C-13), 123.2, 125.9, 127.7, 128.3, 128.6, 128.8, 129.1, 129.4, 129.5, 129.6, 130.4, 132.1, 133.5, 134.8, 135.2, 137.8, 139.1, 144.0, 154.5 (C-6), 157.7 (C-2), 162.6 (C-4). *ms m/z*: 445 (M^+). Anal. Calcd for $C_{30}H_{27}N_3O$: C, 80.87; H, 6.11; N, 9.43. Found: C, 80.84; H, 6.08; N, 9.45.

5-(1',3'-Butadienyl)-2,3-diphenyl-6-[*N*-allyl-*N*-(p-methoxyphenyl)]aminopyrimidin-4(3*H*)-one (109c): Yield 67%; viscous liquid; IR (CCl_4) ν 1658 (C=O), 1544, 1484, 1432 cm^{-1}. ^1H NMR (300 MHz) δ 3.76 (s, 3H, $-OCH_3$), 4.68 (d, *J* = 5.5, 2H,$-CH_2-$), 4.85 (d, *J* = 9.8, with fine splitting, 1H, Ha), 5.04 (d, *J* = 16.7, with fine splitting, 1H, Hb), 5.14 (dd, *J* = 10.3 and 1.3, 1H, Hf), 5.20 (dd, *J* = 17.3 and 1.3, 1H, Hg), 5.86-6.12 (m, 3H, Hc, He, Hh), 6.82 (d, *J* = 8.7, with fine splitting, 2H, arom), 7.10 (d, *J* = 8.7, with fine splitting, 2H, arom), 7.11-7.38 (m, 10H, arom), 7.45 (dd, *J* = 15.3 and 10.2, 1H, Hd). ms *m/z*: 461 (M^+). Anal. Calcd for $C_{30}H_{27}N_3O_2$: C, 78.07; H, 5.89; N, 9.10. Found: C, 78.11; H, 5.91; N, 9.11.

5-(1',3'-Butadienyl)-3-(p-methylphenyl)-2-phenyl-6-[*N*-allyl-*N*-(*p*-methylphenyl)]aminopyrimidin-4(3*H*)-one (109d): Yield 72%; viscous liquid; IR (CCl_4) ν 1661 (C=O), 1547, 1507, 1488, 1436 cm^{-1}. ^1H

NMR (300 MHz) δ 2.33 (s, 3H, $-CH_3$), 2.38 (s, 3H, $-CH_3$), 4.73 (d, J = 5.2, 2H, $-CH_2$), 4.85 (d, J = 10.1, with fine splitting, 1H, Ha), 5.06 (d, J = 16.9, 1H, Hb), 5.15 (dd, J = 10.2 and 1.3, 1H, Hf), 5.24 (dd, J = 17.1 and 1.3, 1H, Hg), 5.85-6.10 (m, 3H, Hc, He, Hh), 7.00 (d, J = 8.3, 2H, arom), 7.03-7.10 (m, 6H, arom), 7.14-7.22 (m, 3H, arom), 7.36 (d, J = 8.2, with fine splitting, 2H, arom), 7.47 (dd, J = 15.1 and 10.1, 1H, Hd). ms *m/z*: 459 (M^+). Anal. Calcd for $C_{31}H_{29}N_3O$: C, 81.02; H, 6.36; N, 9.14. Found: C, 80.97; H, 6.34; N, 9.17.

2,3-Diphenyl-5-(p-methoxyphenyl)-2,5,6,6a,7,8,10a-heptahydro pyrimido[4,5-c]isoquinolin-1-one (110a): A solution of pyrimidinone **109c** (0.50 g, 1.09 mmol) in dry toluene (6 ml) was refluxed for 20-24 h. The solution was concentrated under *vacuo* and the residue purified by column chromatography (silica gel, EtOAc/hexane, 1:6) to give 0.33 g (66%) of **110a**. mp 194-195 °C; IR (KBr) ν 1651 (C=O), 1566, 1517 cm^{-1}. ^1H NMR (300 MHz) δ 1.76-2.09 (series of m, 4H, 2 x $-CH_2$), 2.38-2.44 (m, 1H, H-6a), 3.47 (dd, J = 11.8 and 3.7, with fine splitting, 1H, H-10a); 3.70-3.74 (m, 1H, $-N-CH_2$), 3.79 (s, 3H, $-OCH_3$), 3.83 (dd, J = 11.5 and 11.5, merged with $-OCH_3$, 1H, $-N-CH_2-$), 5.62-5.67 (m, 1H, H-9), 6.04-6.08 (m, 1H, H-10), 6.87 (d, J = 8.9, with fine splitting, 2H, arom), 7.03-7.14 (m, 7H, arom), 7.22-7.28 (m, 5H, arom). ^{13}C NMR (75.5 MHz) δ 21.1 (C-7), 24.3 (C-8), 29.9 (C-6a), 32.5 (C-10a), 51.8 ($-N-CH_2-$), 55.3 ($-OCH_3$), 97.9 (C-10b), 113.7, 123.6, 127.3, 127.5, 127.9, 128.6, 129.1, 129.2, 129.3, 135.1, 137.8,

138.0, 155.6 (C-4a), 155.7 (C-3), 156.9, 162.1 C-1). ms *m/z* 461 (M^+), 432, 382, 180, 77. Anal. Calcd for $C_{30}H_{27}N_3O_2$: C, 78.06; H, 5.90; N, 9.10. Found: C, 78.15; H, 5.85; N, 9.11.

2,5-Bis(p-methylphenyl)-3-phenyl-2,5,6,6a,7,8,10a-heptahydro-pyrimido[4,5-c]isoquinolin-1-one (110b): A solution of **109d** (0.50 g, 1.09 mmol) in dry toluene (6 ml) was refluxed for 22-24 h. A similar work up (as **110a**) gave 0.36 g, (72%) of **110b**. mp 210-212 °C; IR (KBr) ν 1656 (C=O), 1568, 1526, 1507 cm^{-1}. ^1H NMR (300 MHz) δ 1.76-2.11 (series of m, 4H, 2 x $-CH_2-$), 2.28 (s, 3H, $-CH_3$), 2.30-2.36 [m, 4H; 1H, H-6a and at 2.33 (s, 3H, $-CH_3$)], 3.50 (dd, J = 11.8 and 2.8, with fine splitting, 1H, H-10a), 3.68-3.72 (m, 1H, $-N-CH_2-$), 3.83 (dd, J = 11.4 and 11.4, 1H, $-N-CH_2-$), 5.62-5.67 (m, 1H, olefinic H-9), 6.06 (br d, J = 9.8, 1H, H-10), 6.99 (d, J = 8.1, 2H, arom), 7.05-7.25 (m, 12H, arom). ^{13}C NMR (75.5 MHz) δ 21.0 (C-7), 21.1 ($-CH_3$), 21.2 ($-CH_3$), 24.3 (C-8), 29.9 (C-6a), 32.6 (C-10a), 51.6 ($-N-CH_2-$), 98.4 (C-10b), 123.8, 125.8, 126.0, 126.2, 127.5, 128.3, 128.9, 129.1, 129.3, 129.4, 134.6, 135.3, 137.8, 142.2, 155.5 (C-4a), 155.7 (C-3), 162.4 (C-1). ms *m/z*: 459 (M^+). Anal. Calcd for $C_{31}H_{29}N_3O$: C, 81.01; H, 6.36; N, 9.14. Found: C, 81.14; H, 6.30; N, 9.19.

Procedure and data for (111a): A solution of **109a** (0.50 g, 1.16 mmol) was refluxed in dry xylene (6 ml) for 2.5-3 h. The solvent was removed under reduced pressure and the crude product thus obtained was purified by column chromatography on silica gel (eluent: EtOAc/hexane in 1:6 ratio) to give 0.40 g (80%) of **111a**.

mp 110-111 °C; IR (KBr) ν 1657, 1546, 1507, 1487, 1401 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.07 (d, J = 6.8, 3H), 1.68 (s, 3H), 2.85-2.90 (m, 1H), 4.72 (dq, J = 16.5 and 5.3, 2H), 5.15 (d, J = 10.3, 1H), 5.24 (d, J = 17.2, with fine splitting, 1H), 5.84 (d, J = 15.5, 1H), 6.06 (dddd, J = 17.2, 10.3, 5.2 and 5.2, 1H), 6.67 (dd, J = 15.5 and 8.7, 1H), 6.96-7.01 (m, 1H), 7.09-7.34 (m, 14H). ^{13}C NMR (75.5 MHz) δ 13.8, 20.0, 45.1, 54.8, 103.2, 116.5, 121.8, 122.6, 123.3, 127.8, 128.3, 128.9, 129.0, 129.2, 129.3, 129.5, 134.8, 135.3, 135.4, 137.7, 146.9, 154.8, 157.3, 162.7. ms *m/z* 432 (M^{+}+1, 81%), 404 (11%), 390 (20%), 376 (27%) 259 (5%), 180 (100%), 77 (46%).

Procedure and Data for (111b): A solution of **109b** (0.50 g, 1.13 mmol) was refluxed in dry xylene (6 ml) for 2.5-3 h. A similar procedure, as employed for **111a**, afforded 0.37 g (74%) of **111b**. mp 135 °C; IR (KBr) ν 1664, 1543, 1506, 1486, 1401. ^{1}H NMR (300 MHz) δ 1.09 (d, J = 6.7, 3H), 1.66 (s, 3H), 2.27 (s, 3H), 2.83-2.93 (m, 1H), 4.58-4.78 (m, 2H), 5.14 (dd, J = 10.3 and 1.5, 1H), 5.21 (dd, J = 17.2 and 1.5, 1H), 5.82 (d, J = 15.5, with fine splitting, 1H), 6.05 (dddd, J = 17.2, 10.3, 5.4 and 5.4, 1H), 6.61 (dd, J = 15.5 and 8.8, 1H), 7.01 (d, J = 8.6, 2H), 7.07 (d, J = 8.6, 2H), 7.14-7.32 (m, 10H). ^{13}C NMR (75.5 MHz) δ 13.6, 20.1, 20.7, 45.3, 55.1, 102.1, 116.5, 122.0, 123.2, 127.8, 128.3, 128.8, 129.1, 129.3, 129.5, 129.8, 133.2, 134.9, 135.4, 137.8, 144.5, 154.7, 157.5, 162.7. ms *m/z* 447 (M^{+}+2, 96%), 418 (10%), 404 (25%), 390 (31%), 180 (100%), 91 (15%), 77 (48%).

Reactions of (N-allyl-N-aryl)amino-1,3-diaza-1,3-butadienes 95 with chloroketene: General procedure for pyrimidinones (114): To a well stirred solution of 95 (4.0 mmol) and triethylamine (1 g, 10 mmol) in dry methylene chloride (30 ml), was added dropwise, a solution of chloroacetyl chloride (0.68 g, 6 mmol) in dry methylene chloride (30 ml) over a period of 1.5-2h at rt. A similar workup, as employed for pyrimidinones 62, yielded the crude products 114 which were purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:10 ratio)

2,3-Diphenyl-5-methylthio-6-(*N*-allyl-*N*-phenyl)aminopyrimidin-4(3*H*)-one (114a): Yield 89%; mp 125-126 °C; IR (KBr) ν 1657 (C=O), 1549, 1549, 1484 cm^{-1}. ^1H NMR (300 MHz) δ 2.15 (s, 3H, $-SCH_3$), 4.73 (d, J = 5.1, with fine splitting, 2H, $-CH_2-$), 5.16 (dd, J = 10.3 and 1.6, with fine splitting, 1H, $=CH_2$), 5.28 (dd, J = 17.2 and 1.6, with fine splitting, 1H, $=CH_2$), 6.05 (dddd, J = 17.2, 10.3, 5.1 and 5.1, 1H, -CH=), 7.03-7.34 (m, 15H, arom). ^{13}C NMR (75.5 MHz) δ 16.3 ($-SCH_3$), 55.1 ($-CH_2-$), 100.8 (C-5), 116.5 (C-9), 123.1, 123.9, 127.8, 128.3, 128.8, 129.0, 129.1, 129.3, 129.4, 129.6 (C-8), 134.7, 134.9, 137.7, 146.6, 155.6 (C-6), 160.1 (C-2), 162.6 (C-4). ms *m/z*: 425 (M^+), 378 (M^+-SCH_3). Anal. Calcd for $C_{26}H_{23}N_3OS$: C, 73.38; H, 5.45; N, 9.87. Found: C, 73.33; H, 5.44; N, 9.83.

2,3-Diphenyl-5-methylthio-6-[*N*-allyl-*N*-(p-methoxyphenyl)]amino pyrimidin-4(3*H*)-one (114b): Yield 91%; mp 158-159 °C; IR (KBr) ν 1661 (C=O), 1540, 1506, 1482 cm^{-1}. ^1H NMR (300 MHz) δ 2.11 (s,

3H, $-SCH_3$), 3.79 (s, 3H, $-OCH_3$), 4.65 (d, *J* = 5.4, 2H, $-CH_2-$), 5.14 (dd, *J* = 10.3 and 1.3, 1H, $=CH_2$), 5.20 (dd, *J* = 17.2 and 1.3, 1H, $=CH_2$), 6.04 (dddd, *J* = 17.2, 10.3, 5.5 and 5.5 1H, -CH=), 6.85 (d, *J* = 8.9, with fine splitting, 2H, arom), 7.08-7.32 (m, 12H, arom). ^{13}C NMR (75.5 MHz) δ 16.5 ($-SCH_3$), 55.4 ($-OCH_3$), 55.8 ($-CH_2-$), 98.2 (C-5), 114.2, 116.8 (C-9), 125.7, 127.8, 128.2, 128.7, 129.0, 129.3, 129.6 (C-8), 134.8, 134.9, 137.8, 139.6, 155.5 (C-6), 156.6, 160.4 (C-2), 162.7 (C-4). ms *m/z*: 455 (M^+), 408 (M^+-SCH_3). Anal. Calcd for $C_{27}H_{25}N_3O_2S$: C, 71.18; H, 5.53; N, 9.22. Found: C, 71.24; H, 5.51; N, 9.25.

3-(p-Methylphenyl)-5-methylthio-6-[*N*-allyl-*N*-(p-methylphenyl)]amino-2-phenylpyrimidin-4(3*H*)-one (114c): Yield 86%; mp 154-155 °C; IR (KBr) ν 1652 (C=O), 1550, 1497, 1480 cm^{-1}. ^1H NMR (300 MHz) δ 2.14 (s, 3H, $-SCH_3$), 2.28 (s, 3H, $-CH_3$), 2.31 (s, 3H, $-CH_3$), 4.69 (d, *J* = 5.1, 2H, $-CH_2-$), 5.14 (dd, *J* = 10.3 and 1.1 1H, $=CH_2$), 5.25 (dd, *J* = 17.2 and 1.1 Hz, 1H, $=CH_2$), 6.03 (dddd, *J* = 17.2, 10.3, 5.1 and 5.1, 1H, -CH=), 7.03 (d, *J* = 8.4, 2H, arom), 7.07-7.32 (m, 11H, arom). ^{13}C NMR (75.5 MHz) δ 16.3 ($-SCH_3$), 20.9 ($-CH_3$), 21.1 ($-CH_3$), 55.2 ($-CH_2-$), 99.9 (C-5), 116.4 (C-9), 123.3, 124.6, 127.7, 127.8, 128.6, 128.7, 129.2, 129.3, 129.4, 129.5 (C-8), 129.6, 133.6, 134.6, 134.9, 135.0, 135.1, 138.2, 144.0, 155.6 (C-6), 160.1 (C-2), 162.7 (C-4). ms *m/z*: 453 (M^+), 406 (M^+-SCH_3). Anal. Calcd for $C_{28}H_{27}N_3OS$: C, 74.14; H, 5.99; N, 9.26. Found: C, 74.07; H, 5.97; N, 9.20.

Representative procedure for pyrimidinones (115): To a solution of **114a** (1.18 mmol) in CH_2Cl_2 at rt was added I_2 (0.16 g, 1.27 mmol) and the mixture was allowed to stir for 15h. The reaction mixture was washed with aqueous $NaHSO_3$ solution (50 ml) and then with water (3 x 50 ml). The organic layer was dried over anhydrous $MgSO_4$, evaporated under *vacuo* and the resulting residue purified by column chromatography on silica gel (eluent: mixture of EtOAc/hexane in 1:7 ratio).

6-Iodomethyl-3,7,8-trihydro-2,3,8-triphenylpyrimido[5,4-b]-1,4-thiazine-4-one (115a): Yield 0.48 g (76%) from 0.50 g of **114a**; mp 184-186 °C; IR (KBr) ν 1652 (C=O), 1554, 1499, 1246 cm^{-1}. ^1H NMR (300 MHz) δ 3.49-3.71 (m, 3H; 2H, $-CH_2-I$ and 1H, methine), 4.28-4.32 (m, 2H, $-NCH_2-$), 7.05-7.34 (m, 15H, arom). ms *m/z*: 537 (M^+), 410 (M^+-I). Anal. Calcd for $C_{25}H_{20}N_3OSI$: C, 55.87; H, 3.75; N, 7.82. Found: C, 55.71; H, 3.79; N, 7.89.

2,3-Diphenyl-6-iodomethyl-8-(p-methylphenyl)-3,7,8-trihydropyrimido[5,4-b]-1,4-thiazine-4-one (115b): Yield 0.51 g (81%) from 0.54 g of **114b**; mp 219-221 °C; IR (KBr) ν 1649 (C=O), 1582, 1559, 1507, 1249 cm^{-1}. ^1H NMR (300 MHz) δ 3.53-3.75 (m, 3H; 2H, $-CH_2-I$ and 1H, methine), 3.82 (s, 3H, $-OCH_3$), 4.30-4.34 (m, 2H, $-N-CH_2-$), 6.92 (d, J = 8.9, with fine splitting, 2H, arom), 7.04-7.08 (m, 5H, arom), 7.12-7.17 (m, 2H, arom), 7.26-7.31 (m, 5H, arom). ^{13}C NMR (75.5 MHz) δ 7.1 ($-CH_2-I$), 37.8 (methine C), 54.7 ($-N-CH_2-$), 55.4 ($-OCH_3$), 92.2 (C-4a), 114.1, 127.6, 128.2, 128.4, 128.8, 129.4, 134.2, 137.3, 152.6, 153.3, 157.7, 159.8. ms

m/z: 567 (M^+), 440 (M^+-I). Anal. Calcd for $C_{26}H_{22}N_3O_2SI$: C, 55.03; H, 3.91; N, 7.40. Found: C, 54.89; H, 4.01; N, 7.36.

2,3-Diphenyl-5-methylthio-6-[(*N*-cinnamoyl-*N*-(p-methylphenyl)]-aminopyrimidin-4(3*H*)-one (119a): Yield 83%; mp 186-187 °C; IR (KBr) ν 1670 (C=O), 1644 (C=O), 1517, 1505, 1481 cm^{-1}. ^1H NMR (300 MHz) δ 2.41 (s, 3H, $-CH_3$), 2.52 (s, 3H, $-SCH_3$), 6.40 (d, J = 15.9, 1H, Ph-C*H*=), 6.77 (d, J = 7.9, with fine splitting, 2H, arom), 7.02-7.07 (m, 1H, arom), 7.21-7.35 (m, 11H, arom), 7.45-7.48 (m, 3H, arom), 7.68 (d, J = 15.9, 1H, Ph-CH=C*H*-), 8.11-8.15 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 15.6 ($-SCH_3$), 21.4 ($-CH_3$), 113.3 (C-5), 121.6, 123.5, 127.8, 128.20, 128.24, 128.6, 128.7, 129.6, 129.8, 130.4, 140.7, 147.3, 149.4, 156.5, 157.9, 158.8. ms *m/z*: 529 (M^+), 482 (M^+-SCH_3). Anal. Calcd for $C_{33}H_{27}N_3O_2S$: C, 74.83; H, 5.14; N, 7.93. Found: C, 74.80; H, 4.15, N, 7.91.

2-Phenyl-3-(p-methylphenyl)-5-methylthio-6-(*N*-cinnamoyl-*N*-phenyl)aminopyrimidin-4(3*H*)-one (119b): Yield 76%; mp 195-196°C. IR (KBr) ν 1682 (C=O), 1647 (C=O), 1526, 1499, 1477 cm^{-1}. ^1H NMR (300 MHz) δ 2.29 (s, 3H, $-CH_3$), 2.52 (s, 3H, $-SCH_3$), 6.43 (d, J = 15.9, 1H, Ha), 6.68 (d, J = 8.1, 2H, arom), 7.04 (d, J = 8.1, 2H, arom), 7.23-7.36 (m, 5H, arom), 7.44-7.55 (m, 7H, arom), 7.67 (d, J = 15.9, 1H, Hb), 7.92-7.95 (m, 1H, arom), 8.12-8.15 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 15.5 ($-SCH_3$), 20.8 ($-CH_3$), 113.4, 116.0, 121.5, 127.8, 128.0, 128.2, 128.3, 128.5, 128.6, 128.8, 129.3, 129.4, 129.5, 129.7, 129.8, 129.9, 130.1, 130.3, 132.9, 134.3, 135.3, 135.4, 136.4, 140.5, 144.7, 149.4, 156.6, 157.6,

158.8, 159.5, 160.3. ms *m/z*: 529 (M^+), 482 (M^+-SCH_3). Anal. Calcd for $C_{33}H_{27}N_3O_2S$: C, 74.83; H, 5.14; N, 7.93. Found: C, 74.88; H, 5.14; N, 7.89.

References

1. Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.*, **1928**, *460*, 98. An earlier paper reports a hetero Diels-Alder reaction. A Captivating review of the discovery of Diels-Alder reaction including the fact that von Euler and Thiele earlier observed what we now know as a Diels-Alder reaction, recently appeared: Berson J.A. *Tetrahedron* (Perspective No.1) **1992**, *48*, 3.
2. Sauer, J.; Sustmann, *R. Angew Chem., Int. Ed. Engl.*, **1980**, *19*, 779. Carruthers, W. *Cycloaddition Reactions in Organic Synthesis;* Pergamon: Oxford, 1990. Appolzer W. In *Comprehensive Organic Synthesis*; Trost, B.M.; Fleming, I.; Paquette, L.A. Eds.; Pergamon: Oxford, 1991; Vol. 5, p 315. Weinrelb, S.M., op. cit., p 401; Boger, D.L., op. cit., p 451; Roush, W.R., op., cit., p 513.
3. Hammer J. (Ed), *1,4-Cycloaddition Reactions*, Academic Press, New York, 1967.
4. Needleman, S.B.; Chang Kuo, M.C. *Chem. Rev.*, **1962**, *62*, 405.
5. Dessimoni, G.; Tacconi, G. *Chem. Rev.*, **1975**, *75*, 651.
6. Weinreb, S.M.; Satib, R.R. *Tetrahedron*, **1982**, *38*, 3087.
7. Ulrich, H. (Ed), Cycloaddition *Reactions of Heterocummulenes*, Academic Press, New York, 1967.

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

9. Brieger, G.; Bennet, J.N. *Chem. Rev.*, **1980**, *80*, 63.

10. (a) Ripoll, J.L.; Rouesrac, A. *Tetrahedron*, **1978**, *34*, 19. (b) Katritzky, A.R.; Dennis, N. *Chem. Rev.*, **1989**, 827.

11. Woodward, R.B.; Hoffman, R. *The Conservation of Orbital Symmetry*, Acdemic Press, New York, 1970.

12. (a) Houk, K.N. *Acc. Chem. Res.*, **1975**, *8*, 361. (b) Houk, K.N.; Gonzalez, J.; Li, Y. *Acc. Chem. Res.* **1995**, *28*, 81-90.

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

14. Wasserman, A. *Diels-Alder Reactions*; Elsevier Publishing Co. Amsterdam, 1965 (b) Desimoni, G.; Tacconi. G.; Barco A. Pallini, G.P. *Natural Product Synthesis through Pericyclic Reactions*; ACS monograph 180: American Chemical Society, Washington, DC, 1983.

15 (a) Boger, D.L.; Weinreb, S.M. *Hetero-Diels-Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987 (b) Ho, T.L. *Tactics of Organic Synthesis*; John Wiley and Sons; New York, 1994.

16. (a) Paquette, L.A. In *Assymmetric Synthesis*, Morrison, J.D., Ed. Academic Press: New York, 1984, Vol. 3, Chapter-7 (b) Oppolzer, W. *Angew Chem. Int. Ed. Engl.* **1984**, *23*, 876.

17. Ciganek, E. *Org. React.* (N.Y.) **1984**, *32*, 1.

18. Gilchrist, T.L., *Chem. Soc. Rev.*, **1983**, *12*, 53.

19. Boger, D.L.; Weinreb, S.M. *Hetero Diels-Alder Methodology in Organic Synthesis*, H.H. Wasserman (Ed), Academic Press, New York, 1987, p 239.

20. Kametani, T.; Hibino, S. *Advances in Heterocyclic Chemistry*, Academic Press, New York, **1987**, *42*, 246.

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

22. Truge, O. *Heterocycles*, **1979**, *12*, 1067.

23. Matsuda, I.; Yamamoto, S.; Ishii, Y. *J. Chem. Soc. Perkin Trans. 1*, **1976**, 1523, 1528.

24. Wedinger, H.; Krang, *J. Chem. Ber.*, **1963**, *96*, 2070.

25. Wedinger, H.; Sturm, H.J. *Leibigs Ann. Chem.*, **1968**, *716*, 143.

26. Morel, G.; Marchand, E.; Foucaund, A. *J. Org. Chem.*, **1985**, *50*, 771.

27. Sakamoto, M.; Miyazawa, K.; Tomimatsu, Y. *Chem. Pharm. Bull Tokyo*, **1976**, *24*, 2532.

28. Richter, R.; Ulrich, H. *Chem. Ber.*, **1970**, *103*, 3525.

29. Morimoto, T.; Sekeya, M.; *Chem. Pharm. Bull. Tokyo*, **1974**, *22*, 1607.

30. Kato, T.; Matsuda, S. *Chem. Pharm. Bull. Tokyo*, **1974**, *22*, 1542.

31. Sakamoto, M.; Shibano, M.; Mayazawa, K.; Suzuki, M.; Tomimatsu, *Chem. Pharm. Bull. Tokyo*, **1976**, *24*, 2889.

32. (a) Matsuda, I.; Itoh, K.; Ishii, Y. *J. Chem. Soc. Perkin Trans. 1*, **1972**, 1678. (b) Burger, K.; Peninger, S. *Synthesis*, **1978**, 524. (c) Burger, K.; Huber, E.; Kahl, T.;

Partscht, H.; Ganzer, M. *Synthesis*, **1988**, 44.

33. (a) Barluenga, J.; Thomas, M.; Ballesteros, A.; Lopez, L.A. *Synthesis*, **1989**, 228. (b) Barluenga, J.; Thomas, M.; Ballesteros, A.; Lopez, L.A. *Tetrahedron Lett.*, **1989**, *30*, 4573.
34. Mazumdar, S.N.; Mahajan, M.P. *Synthesis*, **1990**, 417.
35. Mazumdar, S.N.; Mahajan, M.P. *Tetrahedron*, **1991**, *47*, 1473.
36. Mazumdar, S.N.; Ibnusand, I.; Mahajan, M.P. *Tetrahedron Lett.* **1986**, *27*, 5875.
37. Luthardt, P.; Wurthwein, E. *Tetrahedron Lett.*, **1988**, *29*, 921.
38. (a) Mazumdar, S.N.; Ph.D. Thesis, North-Eastern Hill University, Shillong, **1988**, (b) Mukherjee, S. *Ph.D. Thesis*, North-Eastern University, Shillong, **1996**.
39. Mazumdar, S.N.; Mukherjee, S.; Sharma, A.K.; Sengupta, D.; Mahajan, M.P. *Tetrahedron*, *51*, 7459.
40. Dey, P.D.; Sharma, A.K.; Rai, S.N.; Mahajan, M.P. *Tetrahedron*, **1995**, *51* 7459.
41. a) Druckheimer, W.; Blumback, J.; Lattrel, R.; Scheunemann, K.H. *Angew. Chem. Int. Ed. Engl.*, **1985**, *24*, 180. (b) Brady, W.T.; Gu, Y.Q. *J. Org. Chem.*, **1989**, *54*, 2834, 2838 (c) Alcaide, B.; Camtalego, Y.M.; Plumet, J.; Lopez, J.R.; Sierra, M.A. *Tetrahedron Lett.*, **1991**, *32*, 803.
42. For a detailed account, see Holden, K.G. In *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R.B.; Gorman, M., Eds.; Academic Press: New York, **1982**, Vol 2, p.101.

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

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

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

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

47. Komatsu, M.; Ogawa, H.; Mohri, M.; Ohshiro, Y. *Tetrahedron Lett.*, **1990**, *31* 3627. (b) Ohshio, Y.; Komatsu, M.; Uesaka, M.; Agawa, T. *Heterocycles*, **1984**, *22*, 549.

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

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

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

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

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

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

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

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

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

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

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

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

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

61. Huffman, M.A.; Liebeskind, L.S.; Pennington, W.T.; *Organometallics*, **1992**, *11*, 255.

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

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

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

65. a) Morris, K.G.; Saberi, S.P.; Slawin, A.M.Z.; Thomas, S.E.; Williams, D.J. *J. Chem. Soc., Chem. Commun.*, **1992**, 1788. (b) Morris, K.G.; Saberi, S.P.; Thomas, S.E.; *J. Chem. Soc., Chem. Commun.*, **1993**, 209. (c) Morris, K.G.; Saberi,

S.P.; Salter, M.M.; Thomas, S.E.; Ward, M.F.; Slawin, A.M.Z., Williams, D.J. *Tetrahedron*, **1993**, *49*, 5617.

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

67. Czernecki, S.; Hoang, A.; Valery, J.-M. *Tetrahedron Lett.*, **1994**, *35*, 3539.

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

69. De Clercq, E. in *Approaches to Antiviral Agents*; Harnden, M.R. Ed.; VCH Verlagsges. mbH: Weinheim (Ger), 1985; p. 57.

70. Eger, K.; Jalalian, M.; Schmidt, M. *Tetrahedron*, **1994**, *50* 8371.

71. (a) Gilchrist, T.L; *Chem. Soc. Rev.*, **1983**, *12*, 153 (b) Crystal, E.J.T.; Gilchrist, T.L.; Stretch, W. *J. Chem. Res.(s)*, **1987**, 180; *J. Chem. Res. (M)*, **1987**, 1563 and references therein.

72. Zimmer, R.; Reissig, H.U. *Angew. Chem. Int. Ed. Engl.*; **1988**, *27*, 1518.

73. Faragher, R.; Gilchrist, T.L. *J. Chem. Soc., Chem. Commun.*, **1976**, 581.

74. Sharma, A.K.; Mazumdar, S.N.; Mahajan, M.P. *Tetrahedron Lett.* **1993**, *34*, 7961.

75. (a) Mackay, D.; Watson, K.N. *J. Chem. Soc., Chem. Commun*, 1982, 775; 777 (b) Lai, E.C.K.; Mackay, D. Taylor, N.J.; Watson, K.N. *J Chem. Soc., Perkin Trans.1.*; 1990, 1497.

76. Kosten, H.; Scholl, R. *Ber.*; 1901 *34*, 1901.

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

78. (a) Taing, M.; Moore, H.W. *J. Org. Chem.*, 1996, *61*, 329. (b) Sun, L.; Liebeskind, L.S. *J. Org. Chem.*,1995, *60*, 8194. (c) Birchler, A.G.; Liu, F.; Liebeskind, L.S. *J. Org. Chem.*, 1994, *59*, 7737. (d) Gurski, A.; Liebeskind, L.S. *J. Am. Chem. Soc.*, 1993, *115*, 6101 and references therein.

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

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

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

82. a) Nomura, M.; Kotake, Y.; Haneda, T.; Okauchi, T.; Kito, K. Jpn. Kokai Tokkyo Kaho JP 06, 239, 840 [94, 239, 840].

83. Ishida, A.; Inage, M.; Akatsuka, H.; Inamasu, M.; Mitsui, T. Jpn. Kokai Tokkyo Koho JP 06, 220 [94, 220, 059].

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

85. Cohen, E.; Klarberg, B.; Vaughan, J.R., Jr.; *J. Am. Chem. Soc.*, **1960**, *82*, 2731.

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

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

88. For reviews of radical cyclisation see: a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergmon Press, Inc., New York, **1986** (b) Curran, D.P. *Synthesis*, 1988, 417 and 419; (c) Rajan Babu, T.V. *Acc. Chem. Res.*, **1991**, *24*, 139 (d) Jasperse, C.P.; Curran, D.P.; Fevig, T.L. *Chem. Rev.*, **1991**, *91*, 1237. (e) Smadja, W. *Synlett*, 1994, 1.

89. Naito, T.; Honda, Y.; Miyata, O.; Ninomiya, I. *J. Chem. Soc., Perkin Trans 1.*, **1995**, 19.

90. For type II radical addition-cyclisation *via* the route involving the addition of a sulfanyl and related sulfonyl radicals see: sulfanyl radicals: Broka, C.A.; Reichert,

D.E.C. *Tetrahedron Lett.*, 1987, *28*, 1503 (b) Kuehne, M.E.; Damon, R.E. *J. Org. Chem.*, 1977, *42*, 1825 (c) Kuehne, M.E.; Parrons, W.H. *J. org. Chem.*, 1977 *42*, 3408 (d) Padma, A.; Nimmesgern, H.; Wong, G.S.K. *J. Org. Chem.*, 1985, *50*, 5620 (e) Ichinose, Y.; Wakamatsu, K.; Nozaki, K.; Birbaum, J.L.; Oshima, K.; Uchimoto, K. *Chem. Lett.*, 1987, 1647. Sulfonyl radical: (f) Nougier, R.; Lesueur, C.; De Riggi, E.; Bertrand, M.P.; Virgili, A. *Tetrahedron Lett.*, 1990, *31*, 3451 (g) De Riggi, I.; Surjur, J.-M.; Bertrand, M.P.; Archavlis, A.; Faure, R. *Tetrahedron*, 1990, *46*, 5285.

91. Sainsbury, M. *Comprehensive Heterocyclic Chemistry*, Pergamon; Oxford, 1984, p 1038.

92. Koos, M. *Monatsh Chem.* 1994, *125*, 1011.

93. Gupta, A.; Prakash, S.; Prakash, L. *Indian J. Heterocycl. Chem.*, 1994, *3(4)*, 261.

94. MacMillan, J.H.; Washburne, S.S. *J. Org. Chem.* 1973, *38*, 2982.

CHAPTER—II

Diastereoselective Synthesis of α-Butadienyl β-lactams and some Stereochemical Aspects of their Diels-Alder Adducts

Introduction

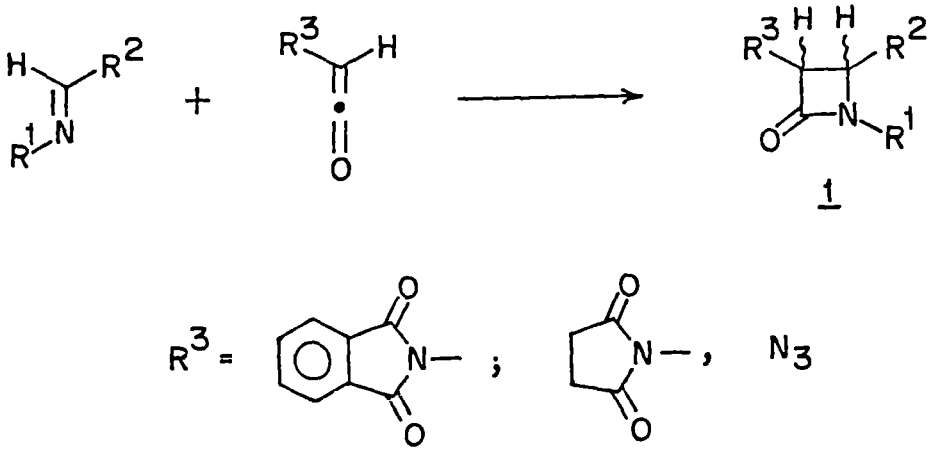
More than 50 years after the discovery of the antibacterial effect of penicillin in man, β-lactam antibiotics are still under active investigations by organic chemists.[1] The importance and structural diversity of biologically active β-lactam antibiotics led to the development of numerous novel methods for the construction of appropriately substituted azetidin-2-ones with attendent control of functional groups and stereochemistry.[2] There is growing demand for selective antibiotics or antibiotics with a broad spectrum of action, since the frequency of the antimicrobial resistant infections has increased in both the hospital and the community.[3] Intense investigations have resulted in the discovery of several natural and synthetic biologically

active substances containing β-lactam ring, including cephalosporins,[4] carbepenems,[5] penems,[6] oxa and carbacephems[7] as well as monolactams,[8] nocardicin derivatives,[9] clavams[10] or other spiranic[11] or multicyclic ring systems.[12] Most of the variations have been introduced by keeping the β-lactam moiety intact but changing the atoms, functional groups and size of the B ring.[13]

In recent years, several natural monocyclic β-lactams have been shown to exhibit high activity against gram-negative organisms[2a,c] and it is felt that suitably substituted monocyclic β-lactam ring might perhaps be the minimum requirement for biological activity.[14] In view of the reported importance of 3-alkyl/3-acetyl β-lactams[15] and 4-vinyl β-lactams[16] as intermediates in the synthesis of β-lactam antibiotics, efforts to devise/improve synthesis of suitably substituted β-lactams is an ongoing challenge and is attracting the increasing attention of synthetic community.

Ketenes have received much wider attention owing to their ability to act as 2π component in cycloaddition reactions.[17] [2+2] cycloaddition reactions of ketenes are most commonly encountered and has become an established synthetic route to the valuable intermediates for various antibiotics and natural products.[18,19] The imine-ketene cycloaddition reaction, referred as Staudinger reaction, was the first method by which an azetidinone was synthesised[20] and was extensively studied after the discovery of penicillin, cephalosporin and later the

carbepenem antibiotics. This reaction is now well established and has proven to be a versatile route to various β-lactam derivatives. Initial studies were directed towards the preparation of intermediates for the synthesis of pencillin and cephalosporin, i.e. 3-amino-2-azetidinones that contain sulfur atom directly attached to the 4-position of the β-lactam ring,[21] and were extended later to constructing intermediates for several other β-lactam antibiotics[21] (Scheme 1). Various azetidinones obtained by the imine-aminoketene cycloaddition e.g. α-azido-β-lactams, were eventually transformed to penicillins,[22,23] cephalosporins,[24-26] nocardicin[27] and a number of their analogues.[28]

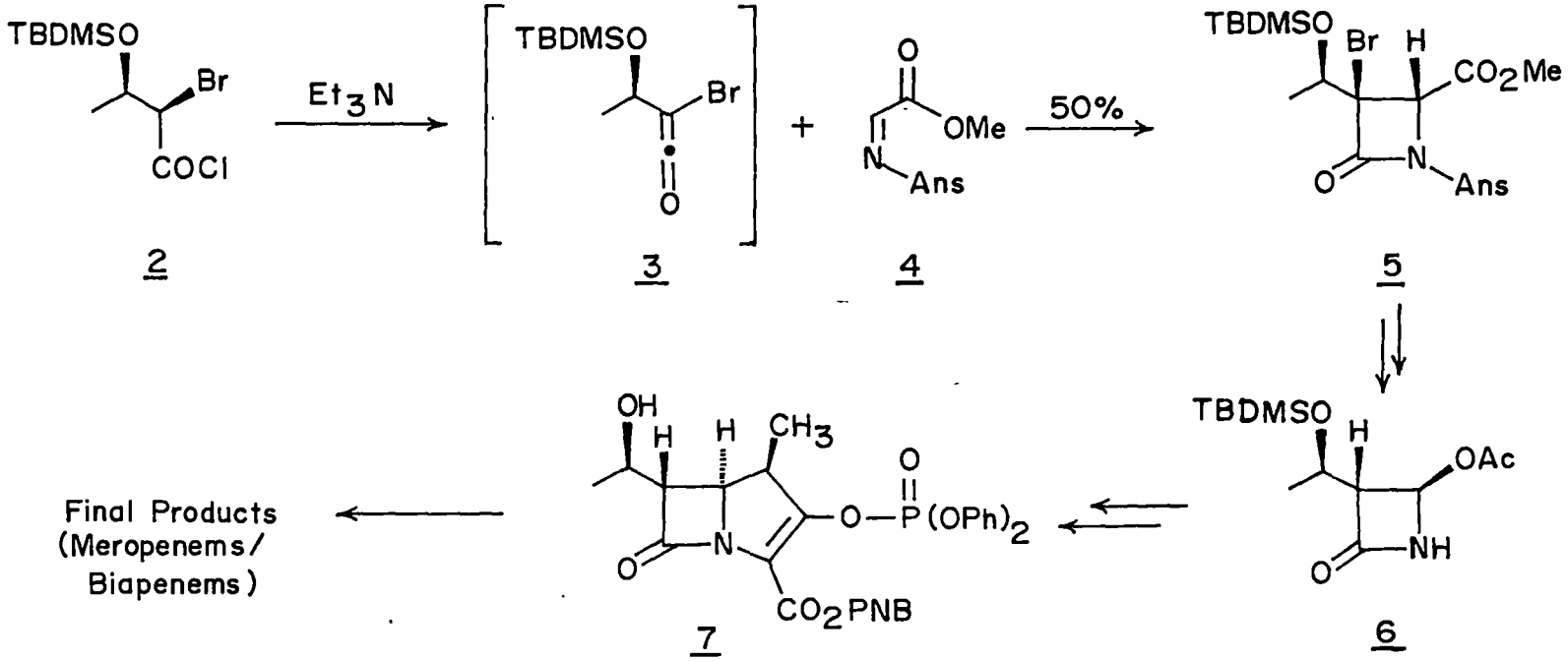


Scheme—1

The carbepenem antibiotics, namely PS-5, PS-6, thienamycin, asparenomycin, meropenem and bipenem constitute an important class of drugs and are the object of ongoing pharmaceutical

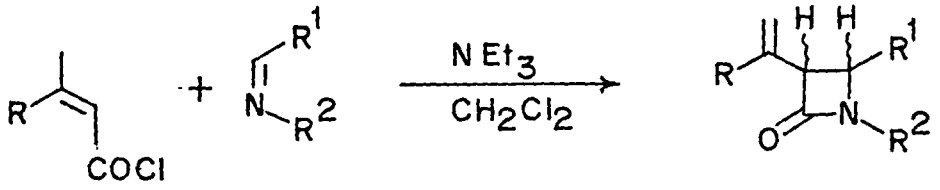
development. The novel chemical features and potent antibacterial properties of these new bicyclic β-lactams together with the reported low yield fermentation processes as compared to those in other β-lactam antibiotics have made carbepenems attractive target molecules for many research groups. Synthesis of α-alkyl, α-acetyl or acetoxy β-lactams became an important target[29] after the discovery of carbepenem antibiotics which possess an alkyl, hydroxyalkyl or acetyl side chain at C-6 position. The main strategies towards carbepenem synthesis usually involves first construction of appropriately substituted monocyclic β-lactams with correct stereochemistry at C-3 and C-4 of β-lactam ring, followed by the chemical manipulation at N-1 and C-3 and subsequent ring closure to form bicyclic ring system.[29-35] However, very few reports describe the synthesis of α-alkyl, α-alkylidene or α-acyl azetidinone based on acid chloride-imine cycloaddition reaction.[28] According to one such example, the acid chloride **2**, derived from D-allothreonine was treated with triethylamine to generate a chiral ketene 3, *in situ*, and subsequent [2+2] cycloaddition reaction with achiral imine 4 afforded azetidinone 5.[36] Known procedures were then employed to carry 5 forward to 6, involving dehalogenation, nitrogen deprotection and transformation of the ester to acetoxy with correct C-4 configuration and subsequently to the meropenems/bipenems[a][31] (Scheme 2).

The reactions of conjugated ketenes *viz.* vinyl/ isopropenylketenes with various Schiff bases continues to be a


TBDMSO
Br
COCl
2
Et3N
TBDMSO
Br
3
OMe
N
Ans
4
50%
TBDMSO
Br
H
CO2Me
N
Ans
5
TBDMSO
H
OAc
NH
6
OH
H
H
CH3
O
O—P(OPh)2
N
CO2PNB
7
Final Products
(Meropenems/
Biapenems)

Scheme-2

subject of intense research owing to (i) the lack of proper generalisation in the formation of *cis/trans* α-vinyl/isopropenyl β-lactams with different substituents and (ii) the conversion of the resulting azetidinones to key intermediates for various carbepenem antibiotics. Bose, Spiegelman and Manhas[37] reported the exclusive formation of *trans* β-lactams from the reactions of *trans* crotonyl chloride and benzylidene aniline at elevated temperatures (Scheme 3). Zamboni and Just treated both crotonyl chloride and dimethylacroyl chloride with various Schiff bases and utilised this reaction for preparing a variety of α-vinyl β-lactams as potential synthons for β-lactam antibiotics. It was observed that all α-vinyl β-lactams, obtainted from Schiff bases derived from aliphatic amines had *cis* stereochemistry whereas when the Schiff base was derived from aniline and cinnamaldehyde, a mixture of *cis* and *trans* β-lactams was obtained (Scheme 3, entry 2, 11 and 12); the relative proportion of isomers appeared to depend on the temperature of the reaction. Other reports of formation of similar *cis* β-lactams involve reactions of vinyl/isopropenyl-ketenes with Schiff base derived from *t*-butylamine.[40] The β-lactams so obtained (Scheme 3, entry 12) was then converted to thiaalkanams and thiaisoalkanams,[41] the compound expected to be of great interest in terms of antibiotics. Also, the β-lactams derived from the reaction of vinyl/isopropenyl ketenes with the Schiff base derived from di-*p*-anisylmethylamine (DAM-NH_2) was smoothly converted to acetoxy azetidinones (Scheme 3, entry 13), which have proven to be potent



Entry	R	R^1	R^2	*cis* 3,%	*trans* 3,%	Ref
1	H	Ph	Ph	-	40-65	37,38,39
2	Me	furfuryl	Ph	-	70	38
3	Me	furfuryl	$CH(CO_2Me)CH_2OTBDMS$[a]	30	-	38
4	H	furfuryl	$CH(CO_2PNB)CH(CH_3)OH$[b]	15	-	39
5	Me	PhCH=CH	$CH(CO_2Me)CH_2OTBDMS$	70	-	38
6	H	PhCH=CH	$CH(CO_2PNB)CH(CH_3)OH$	54	6	39
7	H	CO_2Me	$CH_2C_6H_3(OMe)_2(2,4)$	40	-	38
8	H	COPh	C_6H_4OMe-p	50	30	39
9	H	COPh	$CH(CH_3)Ph$	55	-	39
10	H	PhCH=CH	Ph	7	35	38
11[c]	H	PhCH=CH	Ph	25	5	38
12	H	Ph-CH=CH	^tBu	50	-	40
13	H	CO_2Bu	DAM	94	-	42
14	Me	CO_2Me	C_6H_4OMe-p	68	-	15b

[a] TBDMS = *tert*-butyldimethylsilyl

[b] PNB = p-nitrobenzyl

[c] Reaction conducted at room temperature

Scheme-3

synthons for various antibiotics.[42] In contrast, Bose et al. observed that reactions of Schiff base derived from methyl glyoxalate and p-anisidine with vinylketene led exclusively to *cis* α-vinyl β-lactams,[40] which were further converted to key intermediates for carbapenem antibiotics.[39] Evidently, no clear cut generalisation could be made on the steric composition of α-vinyl β-lactams from a variety of Schiff bases.[39]

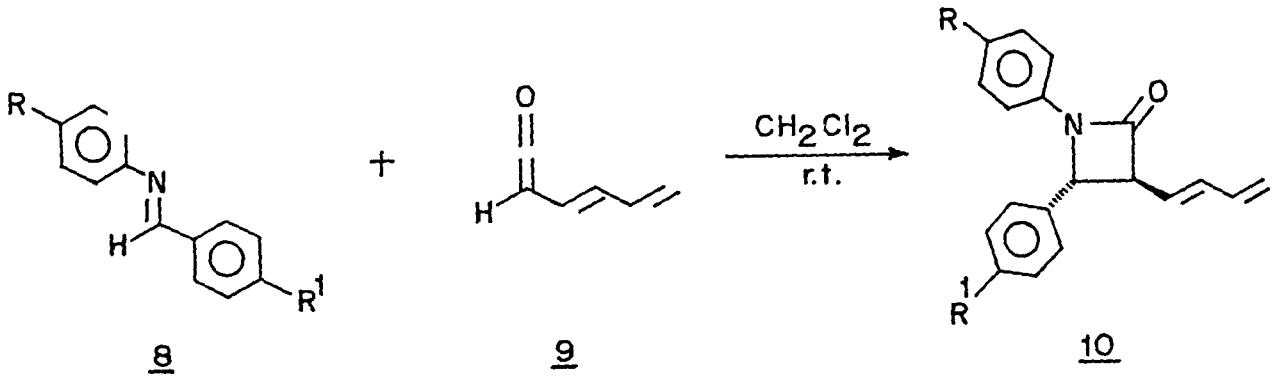
Thus, all proposals to rationalise the steric course and predict the stereochemistry of α-vinyl β-lactam formation seem to be inadequate (see Scheme 3 for summary). Interestingly, the Schiff base derived from furfuraldehyde and aniline produces only *trans* β-lactam on reaction with crotonyl chloride[38] and only a *cis* β-lactam on reactions with azido acetyl chloride. This complete reversal of steric course of annelation is not obvious on the basis of proposed rationalisations concerning β-lactam formations.[38] In such a dilemma of steric routes in these reactions, and in view of synthetic scope of functionalised 1,3-butadienes and biological importance of β-lactams in general and α-substituted β-lactams in particular, we initiated the reactions of various Schiff bases with butadienylketene. To our knowledge this is the first report concerning imine-butadienylketene cycloaddition. During the course of ongoing investigations concerning azadiene-ketene cycloaddition in our laboratory,[43] we have discovered that the use of butadienyl ketene in such cycloadditions proved to be an efficient route to the synthesis of 5-dienyl pyrimidinones (Chapter-I, section I.3). The only

method for the generation of putative and transient dienylketenes reported earlier was in the synthesis of various quinones and catechols by the thermolysis of appropriately substituted cyclobutenones.[44-46] (Scheme 20, Chapter I).

It was thought that the reaction of butadienylketene with a variety of Schiff bases and the study of the stereochemistry of the resulting α-dienyl β-lactams, with different Schiff bases, could be an important scientific enquiry. As an entry into this area we describe here the diastereoselective synthesis of α-butadienyl β-lactams which apparently could prove as versatile synthetic intermediates for the synthesis of a large variety of targeted α-substituted β-lactam derivatives.

Results and Discussion

As mentioned earlier the reactions of various Schiff bases with vinyl/isopropenylketenes were shown to result in *trans, cis* or a mixture of *trans* and *cis* β-lactams.[15b,37,38] Keeping in view the importance of appropriately substituted β-lactams and in order to know the nature of β-lactams formed, we have carried out the reactions of various Schiff bases with butadienylketene. Thus, the treatment of Schiff bases 8, derived from aromatic amines, with butadienyl ketene 9, generated *in situ* from sorbyl chloride in the presence of triethylamine, in methylene chloride at room temperature resulted in good yields (48-63%) of diastereoselective formation of previously unknown *trans*-3-butadienyl β-lactams 10[47] (Scheme 4). The *trans*



8,10 a. $R = R^1 = H$

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

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

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

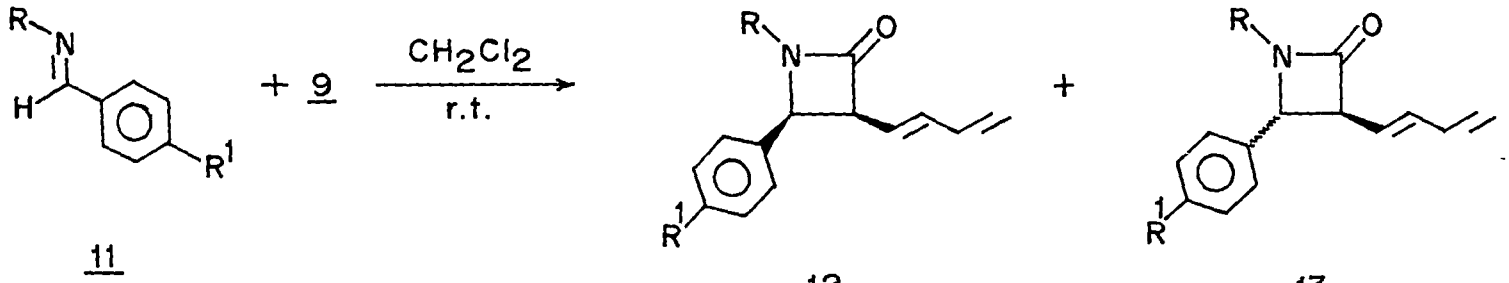
Scheme-4

structure 10 was assigned to these azetidinones on the basis of analytical and spectral data. Their IR spectra exhibited a strong absorption around 1735 cm^{-1} characteristic of the β-lactam ring. Their ^1H NMR spectra showed, in addition to aromatic protons, the presence of two methine protons and olefinic protons. The assignment of *trans* stereochemistry to the β-lactams 10 was based on the observed coupling constant of about 2.4 Hz for methine protons H-3 and H-4.[38,44] Their mass spectra exhibited in addition to the molecular ion peaks, the peaks for $(M^+ - Ph\text{-}N{=}C{=}O)$.

Similar reactions of butadienylketene with the Schiff bases 11 derived from aliphatic amines *viz.* cyclohexylamine, furfurylamine and *n*-butylamine resulted in the formation of either *cis* or a mixture of *cis* and *trans* β-lactams. For example, the reaction of butadienylketene with the Schiff bases derived

from cyclohexylamine/furfurylamine and benzaldelhyde resulted in the exclusive isolation of *cis* β-lactams **12a** and **12b** (Scheme 5). The products **12a,b** were analysed on the basis of their analytical and spectral data. The strong absorption band around 1749 cm^{-1} in the IR spectra of **12a,b** was typical of β-lactam ring. ^{1}H NMR spectrum of **12a** showed, in addition to aromatic protons, a series of multiplets (δ 1.01-1.30, 1.52-1.86 and 2.00-2.05) for cyclohexyl group, the presence of olefinic protons and two methine protons H-3 (δ 4.08) and H-4 (δ 4.85). The assignment of the *cis* stereochemistry to the β-lactam **12a** was based on the observed coupling constant of 5.6 Hz for methine protons H-3 and H-4.[38] ^{1}H NMR spectrum of **12b** (Fig. 1) exhibited, apart from phenyl, furfuryl and olefinic protons, a doublet of doublet for H-3 and a doublet for H-4. The observed coupling constant of 5.3 Hz for H-3 and H-4 protons was again characteristic of *cis* β-lactams.[38]

On the other hand, the reactions of Schiff bases, derived from furfurylamine and p-anisaldehyde, with butadienylketene **9** resulted in the diastereoselective formation of a mixture (6.5:1) of *cis/trans* β-lactam **12c/13c** (Scheme 5). Several attempts at chromatographic separations of these two diastereoisomers failed because of their similar R_f values. The β-lactams **12c/13c** displayed spectroscopic parameters fully compatible with the gross structural features. The relative stereochemistry at C-3 and C-4 in case of **12c/13c** was assigned on the basis of ^{1}H NMR spectrum (Fig. 2). The *cis* and *trans* isomers were identified



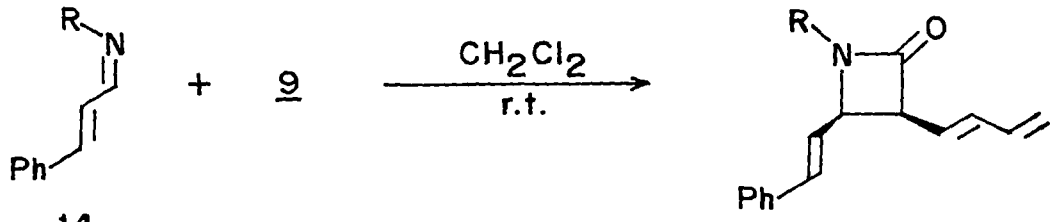
11 12 13

11,12,13, a. R = , R1 = Ph (12 : 13) 100 : 0

b. R = , R1 = Ph 100 : 0

c. R = , R1 = C6H4OCH3-p 6·5 : 1

d. R = n-Bu, R1 = C6H4OCH3-p 4 : 1



14

14,15. a. R = Ph

b. R =

Scheme – 5

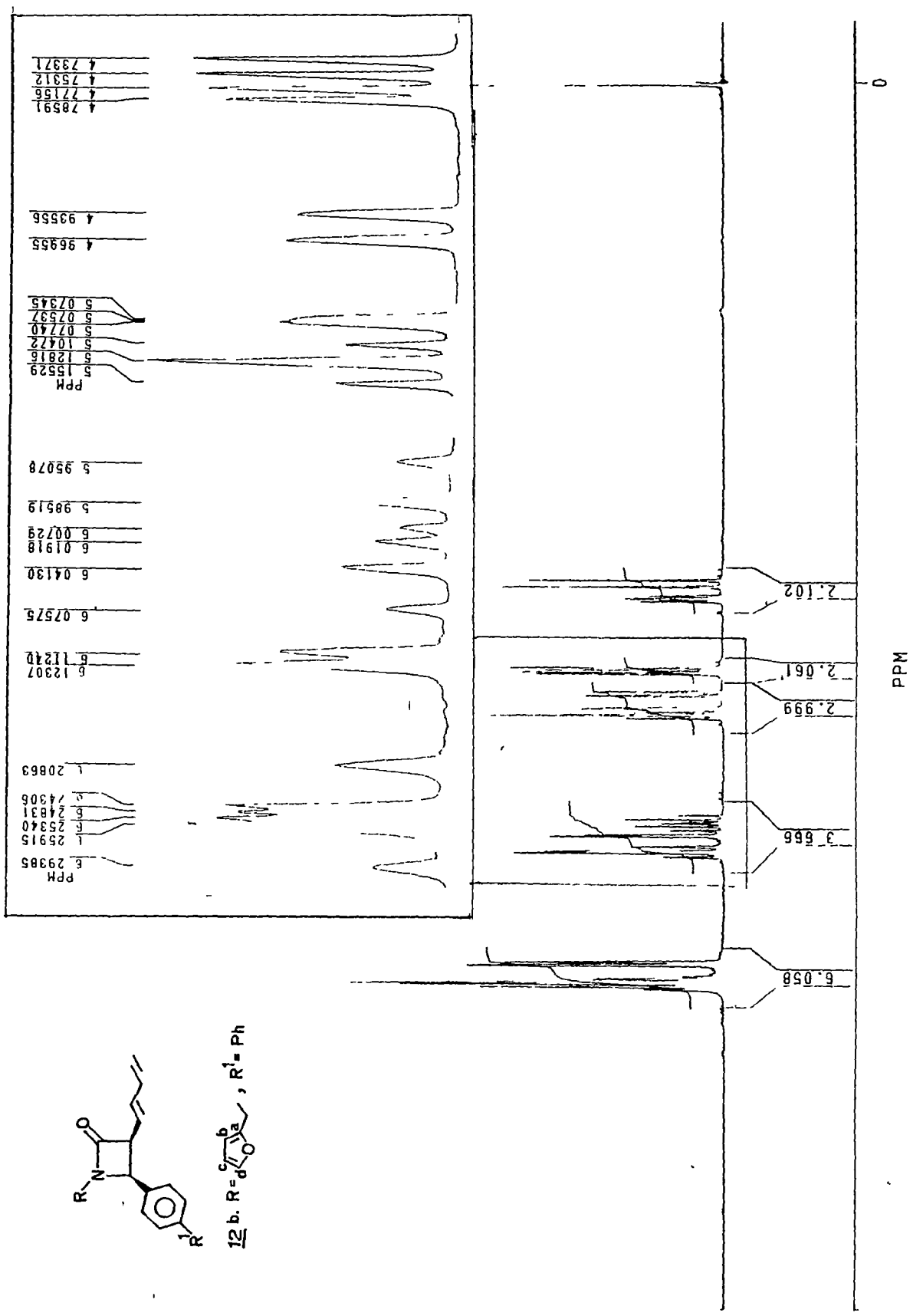


Fig. 1: 300 MHz ^1H NMR spectrum for 12b in $CDCl_3$

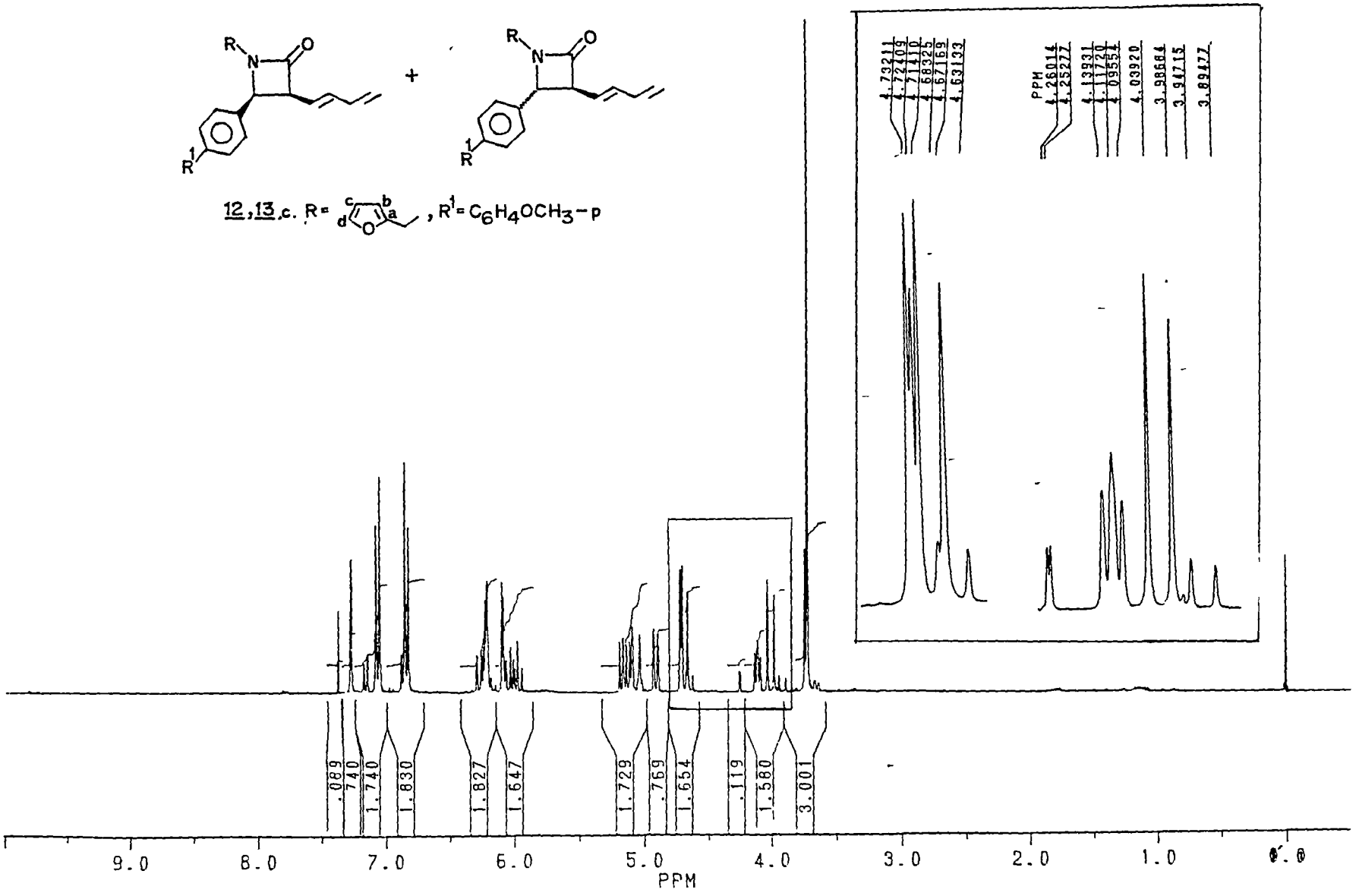


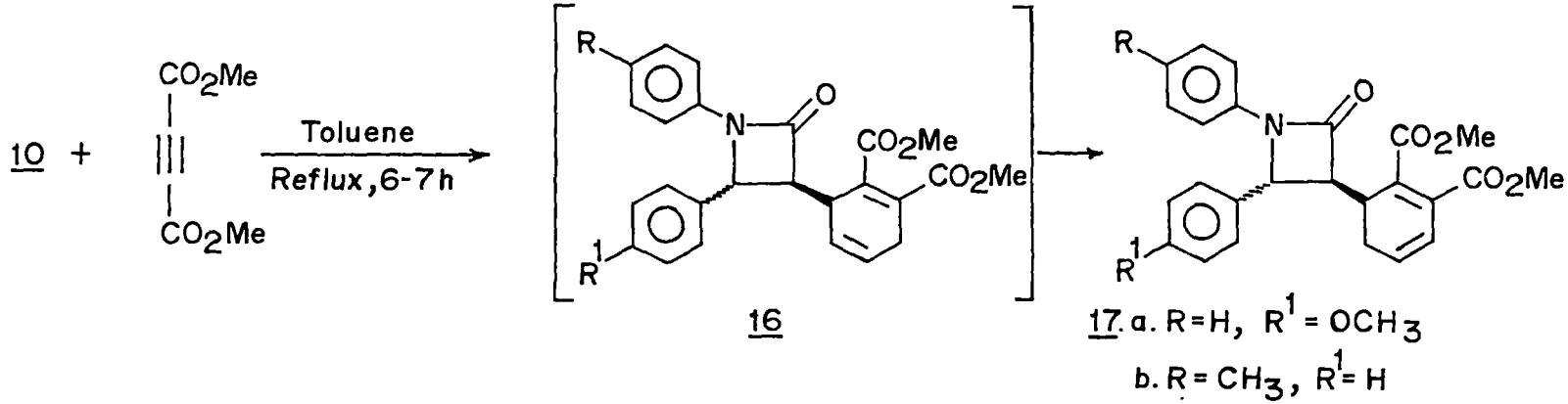
Fig. 2: 300 MHz ^{1}H NMR spectrum for the mixture 12c/13c in $CDCl_3$

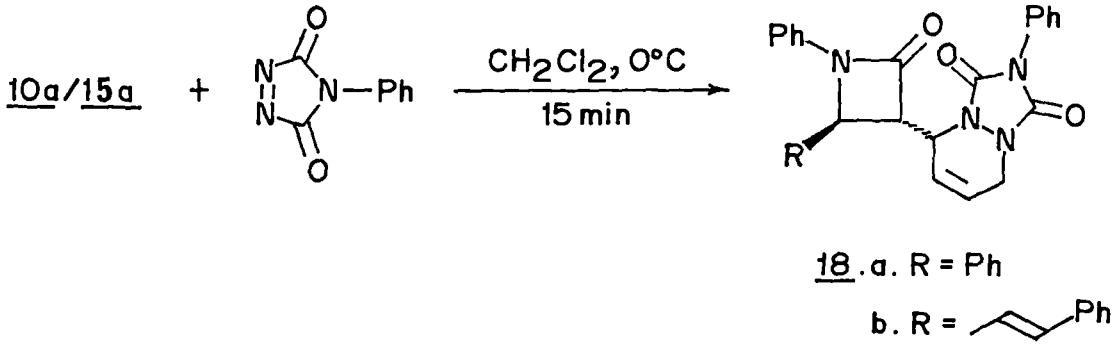
mainly through the observed two signals for H-4 protons; a doublet at δ 4.72 (J = 5.4 Hz) indicated the formation of *cis* β-lactam and another doublet at δ 4.26 (J = 2.2 Hz) showed the presence of *trans* isomer in the mixture. The relative *cis/trans* (6.5:1) ratio was calculated from the integration values of the corresponding two aromatic protons signals of the two isomers and also from the integration values of two signals for one of the furfuryl protons. Further the reaction of butadienylketene with schiff base derived from *n*-butylamine and *p*-anisaldehyde also resulted in the formation of a mixture (4:1) of *cis/trans* β-lactams **12d/13d** (Scheme 5). Thus, it may be inferred that the treatment of butadienylketene with Schiff bases derived from benzaldehyde exclusively yield *cis* β-lactams whereas those derived from *p*-anisaldehyde result in an inseparable mixture of *cis* and *trans* isomers.

In continuation of our studies we have investigated the reactions of various 1-azadienes with butadienylketene. Thus, the treatment of 1-azadienes **14** with butadienylketene **9**, generated *in situ* from sorbyl chloride and triethylamine in methylene chloride, resulted exclusively in the formation of *cis* β-lactams **15** irrespective of the nature of the substituent at 1-position of 1-azadiene (Scheme 5). The products were identified on the basis of IR, mass, ^{1}H and ^{13}C NMR spectra and microanalysis. The β-lactams **15** were assigned *cis* stereochemistry on the basis of the observed coupling constant of about 5.5 Hz between H-3 and H-4 protons.

In order to establish the synthetic potential of the α-dienyl substituted azetidinones, **10**, **12/13** and **15**, we initiated the Diels-Alder cycloaddition reactions of these β-lactams with various dienophiles. All these reactions resulted in very good yields (89-97%) of the corresponding adducts which were well characterised (elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and mass spectral data). The reactions of **10** with dimethylacetylene dicarboxylate (DMAD) in refluxing toluene resulted in the exclusive isolation of the conjugated cyclohexadienyl adducts **17** (Scheme 6). The products could be assigned either structure **16** or **17** on the basis of IR, mass spectra, ^{13}C and simple ^{1}H NMR spectra. However, the adducts were assigned structure **17** on the basis of a $\{^{1}H\}$-$\{^{1}H\}$ NMR homonuclear spin correlation spectrum (Fig. 3) which indicated that both the methylene protons were coupled to H-1', which in turn was coupled with only one of the olefinic protons. Further, the coupling constants observed, in the 300 MHz ^{1}H NMR spectrum between H-1' and the two methylene protons were *ca.* 7.0 Hz and 5.0 Hz. Values such as these are only possible when H-1' is adjacent to the methylene protons; such large coupling constants between the two cannot be anticipated based on structure **16**. The adducts **17** presumably arise from the rearrangement of the initially formed nonconjugated 2',5'-cyclohexadienyl Diels-Alder adducts **16**.

The reaction of **10a** with 4-phenyl-1,2,4-triazo-3,5-dione (PTAD), in methylene chloride at 0°C, also resulted in the diastereoselective synthesis of the corresponding Diels-Alder


10 +
CO2Me
CO2Me
Toluene
Reflux, 6-7h
R
R1
N
O
CO2Me
CO2Me
16
17. a. R=H, R1 = OCH3
b. R = CH3, R1 = H


10a/15a +
N
N
N
O
O
Ph
CH2Cl2, 0°C
15 min
Ph
R
18. a. R = Ph
b. R =
Ph

Scheme-6

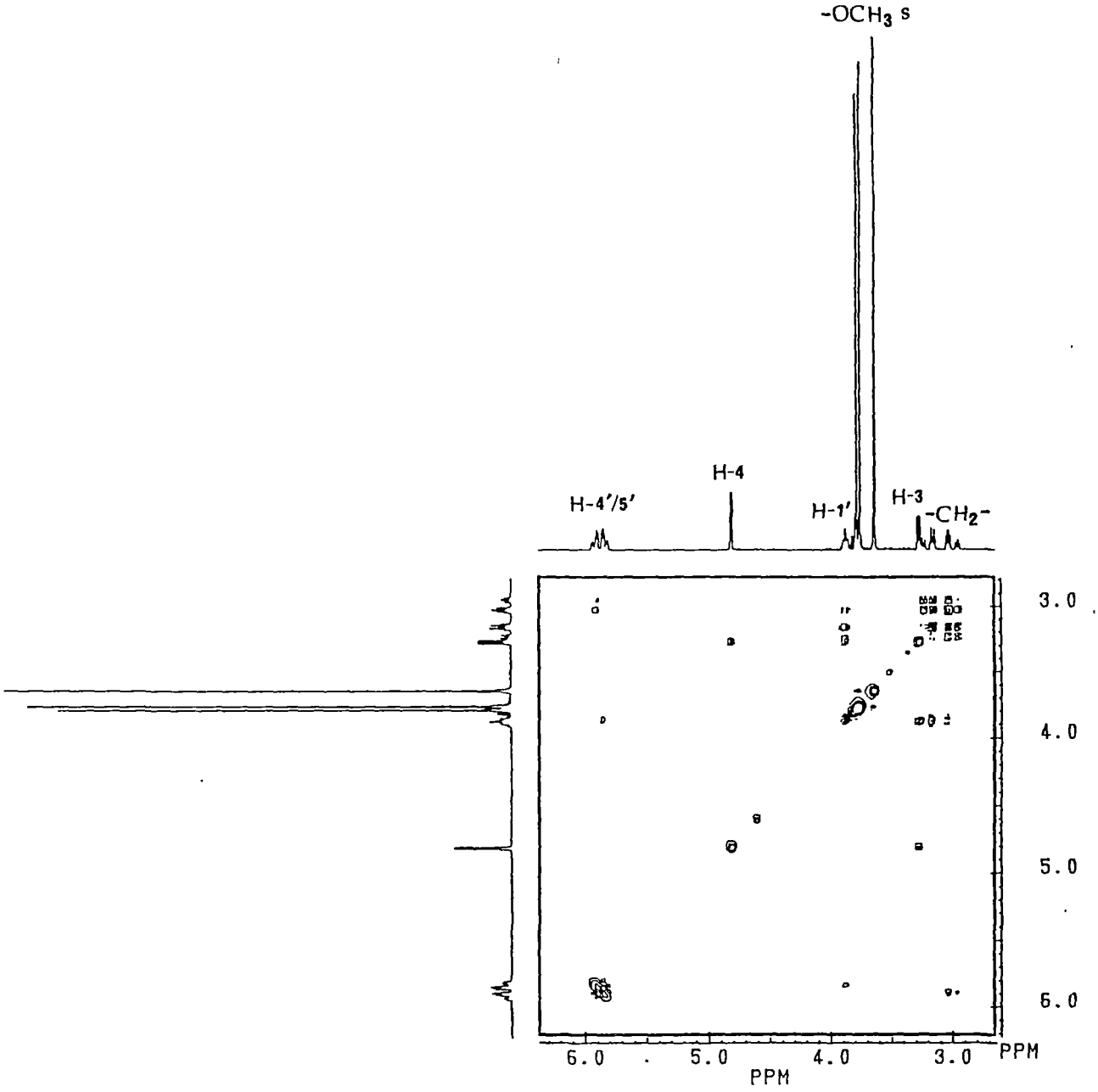
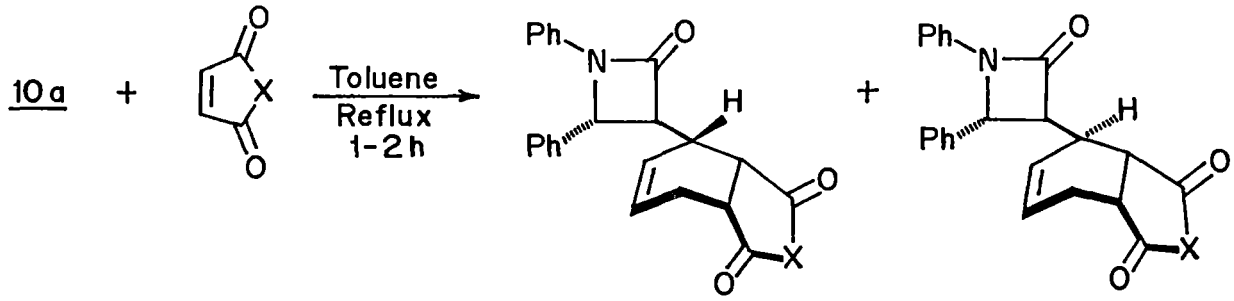


Fig. 3: 300 MHz $\{^1H\}$-$\{^1H\}$-NMR homonuclear spin correlation (COSY) spectrum for 17a in $CDCl_3$

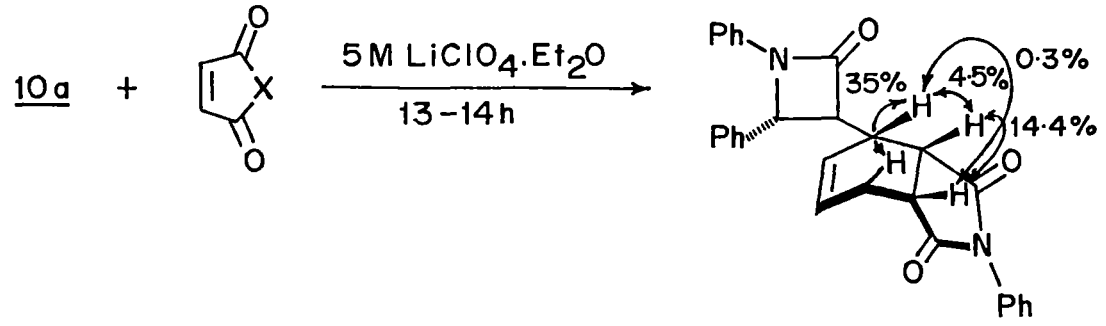
adduct **18** (Scheme 6). Interestingly, the reaction of *cis* β-lactam **15a**, wtih PTAD under similar conditions also resulted in the synthesis of *trans* adducts **18b** (Scheme 6). It is interesting to note that despite severe steric constraints the reaction of 1-azadienes with butadienylketene favours the exclusive formation *cis* β-lactams which on treatment with PTAD led to the thermodynamically more stable *trans* cycloadduct **18b**. The products **18a,b** were purified by silica gel column chromotography and characterised with the help of their analytical and spectral data. The compound **18b** for example, exhibited strong absorption peaks at 1741 and 1704 cm^{-1} due to carbonyl groups. Its mass spectrum exhibited a molecular ion peak at *m/z* 476 (M^+) and a peak at 357 (M^+ - Ph-N=C=O). Its ^1H and ^{13}C NMR spectra were also in agreement with the assigned structure **18b**. The assignment of the *trans* stereochemistry was based on the observed coupling constant of 2.3 Hz for H-3 and H-4 protons.

However, the reactions of **10a** with maleic anhydride (MA) and *N*-phenylmaleimide (NPM) in refluxing toluene yielded a mixture (2:1) as evidenced by ^1H (Fig. 4, 5) and ^{13}C NMR spectra, of diastereoisomers **19/19'** and **20/20'** respectively (Scheme 7). Several attempts at chromotographic separations of the two diastereoisomers **19/19'** and **20/20'** failed because of their similar R_f values. The assignment of the stereochemistry of these adducts by NMR is complicated. Although the mixtures **19/19'** and **20/20'** displayed spectroscopic parameters fully compatible with the gross structural features, but the assignment

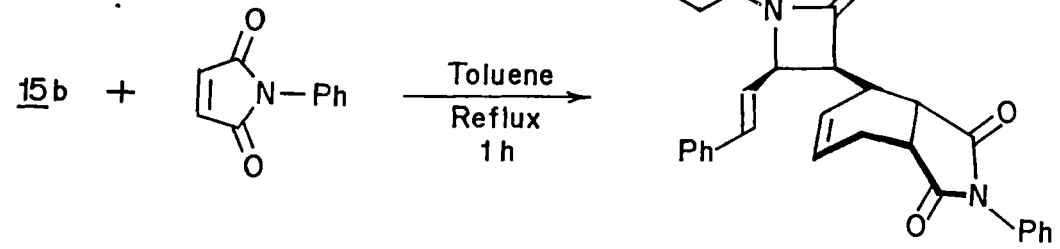


19 (X = O) 19' (X = O)

20 (X = N–Ph) 20' (X = N–Ph)



20



21

Scheme–7

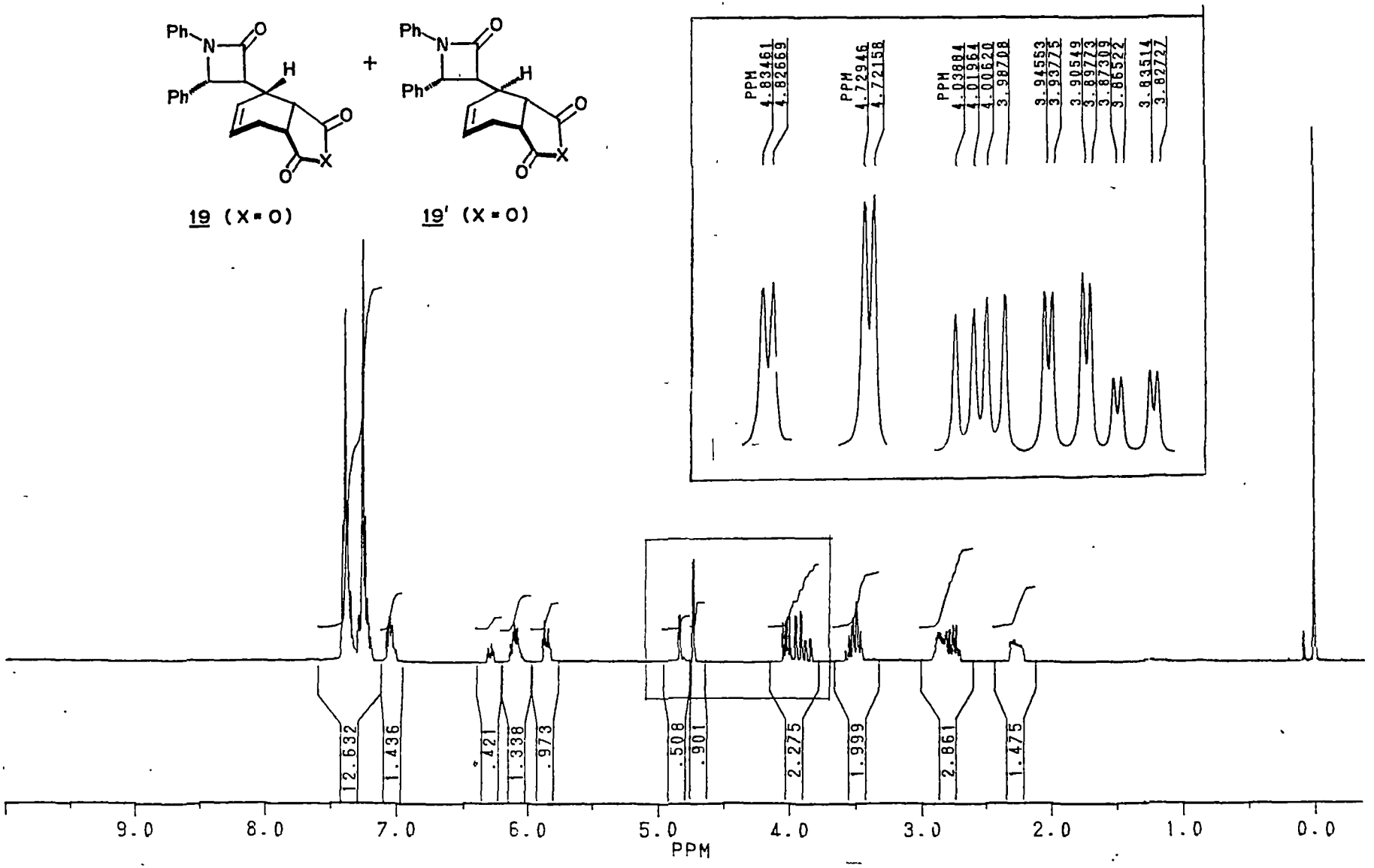


Fig. 4: 300 MHz ^{1}H NMR spectrum for the mixture 19/19' in $CDCl_3$

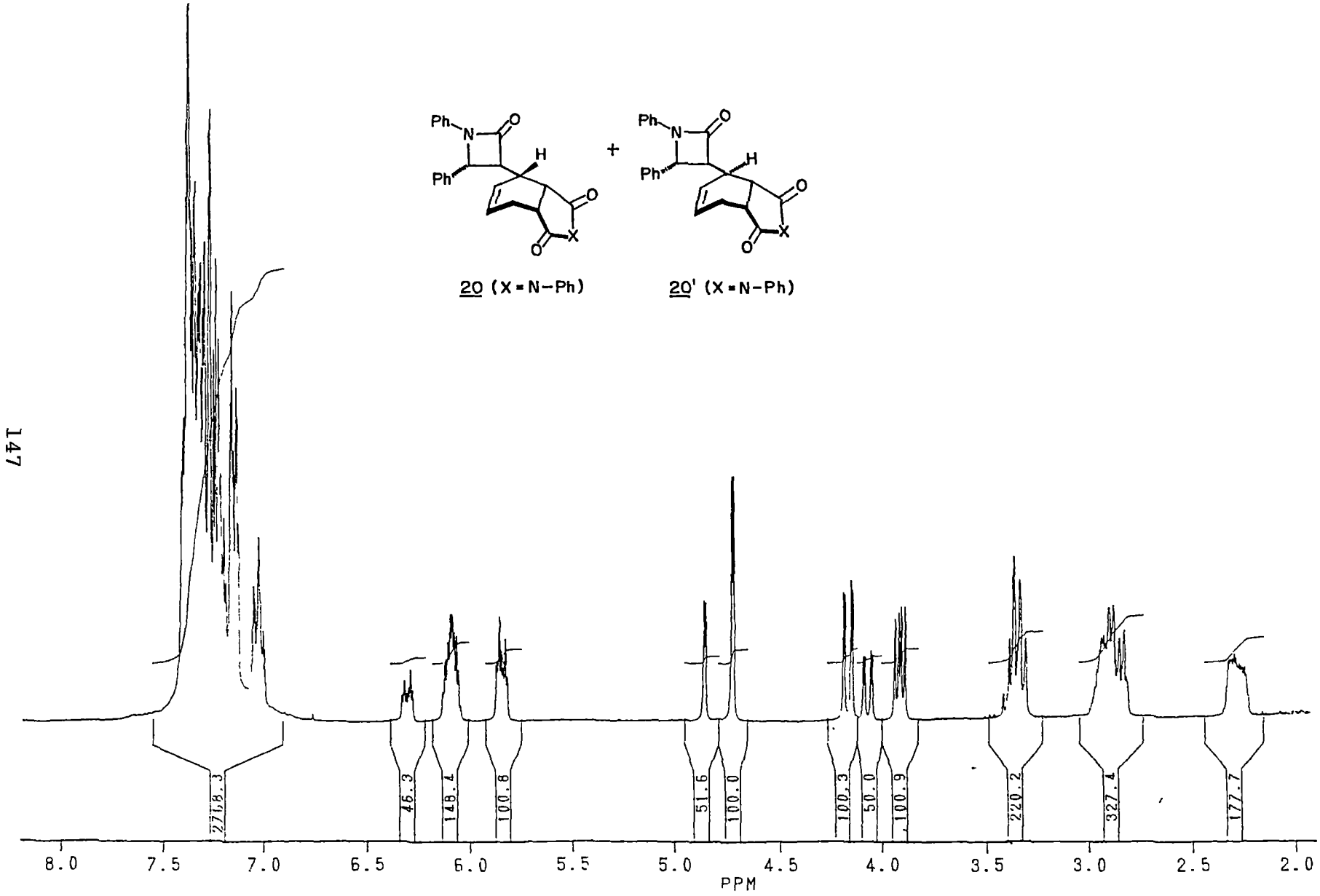


Fig. 5: 300 MHz ^{1}H NMR spectrum for the mixture 20/20' in $CDCl_3$

of specific stereochemistry to the individual isomers of the mixtures is rather difficult. The NOE experiments also proved to be inconclusive and could not help in assigning their specific relative stereochemistry. However, a reaction of **10a** with NPM in 5M lithium perchlorate-ether solution at room temperature, resulted in the isolation of a single diastereoisomer as evidenced by its ^{1}H (Fig. 6) and ^{13}C NMR spectra. The comparison of the ^{1}H and ^{13}C NMR spectra of this single diastereoisomer with that of ^{1}H and ^{13}C NMR spectra of the mixture **20/20'** indicated its identical nature with that of the major isomer **20** in the mixture of **20/20'**. This single diastereoisomer could now be assigned the *endo* configuration on the basis of NOE experiments (Scheme 7). The problem of assigning stereochemistry to the individual isomers in the mixtures, **19/19'** and **20/20'** obtained by the reactions of **10a** with MA and NPM could thus be resolved and the major isomers in these mixtures were assigned the *endo* configuration while the minor isomers were assigned *exo*-configuration.

Unexpectedly, the reaction of **15b** with NPM in refluxing toluene, also resulted in the formation of a single *cis* diastereoisomer **21** (Scheme 7). Also, interestingly, the *cis* stereochemistry at C-3 and C-4 of the starting β-lactam **15b** was retained in the adduct **21** despite steric constraints, unlike the reaction of **15a** with PTAD. The structure **21** was easily established on the basis of its analytical and spectral data. Its mass spectrum exhibited a molecular ion peak at *m/z* 480 and a

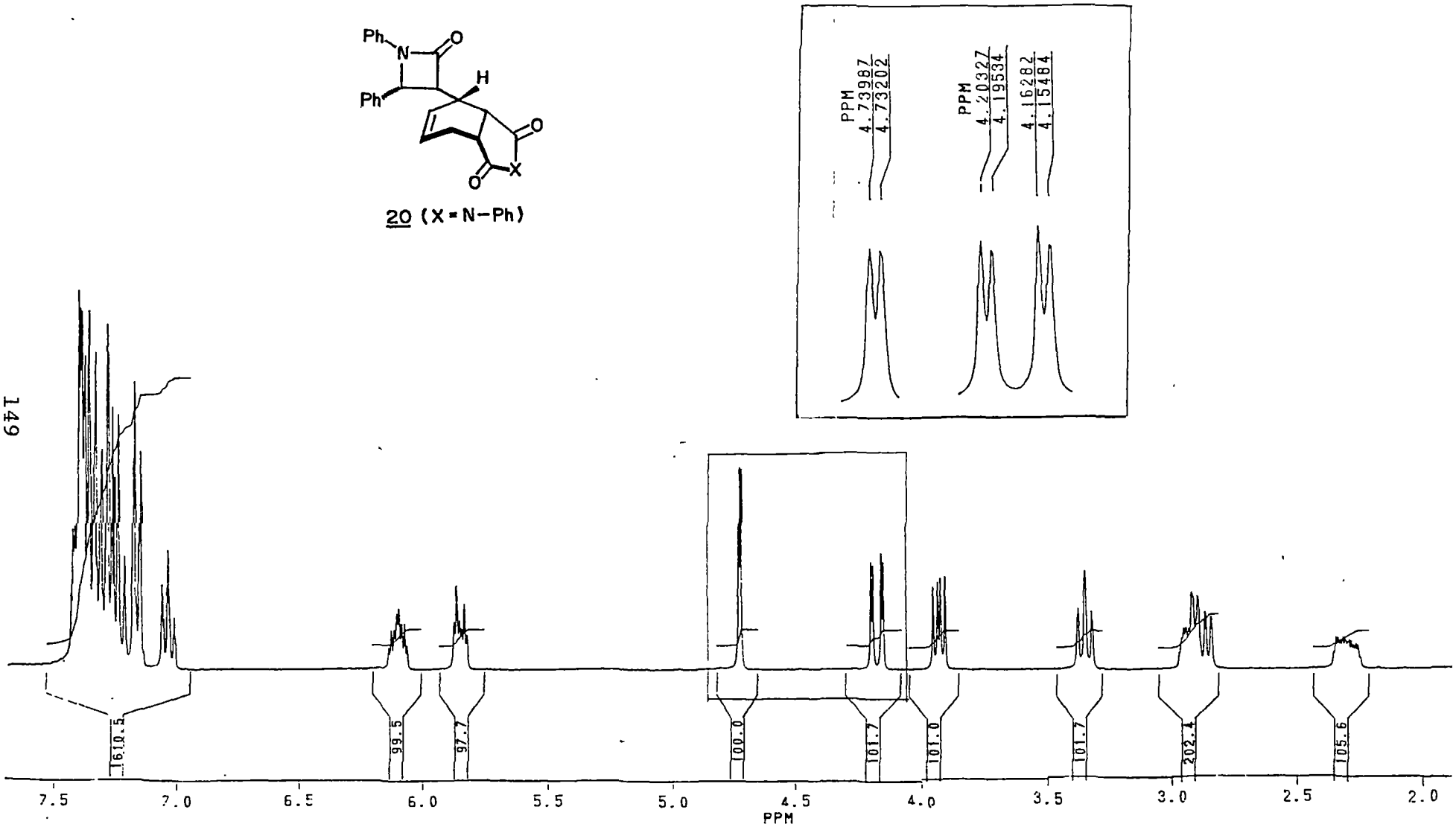


Fig. 6: 300 MHz ^{1}H NMR spectrum for the single isomer **20** in $CDCl_3$

peak at 355. Its IR spectrum showed peaks at 1726 and 1700 cm^{-1} due to β-lactam ring and dicarboximido carbonyls respectively. Its ^{1}H NMR spectrum (Fig. 7) showed all the charactristic proton signals and the *cis* stereochemistry was assigned on the basis of the observed coupling constant of 5.3 Hz between H-3 and H-4. Its ^{13}C NMR spectrum further supported the assigned structure **21**.

Keeping in view the interesting stereochemical observations, in the Diels-Alder reactions of various α-dienyl β-lactams with DMAD, PTAD, MA and NPM, it was thought worthwhile to investigate the reaction of **10** with diethyl fumerate (DEF) and ethyl acrylate (EA). Thus, the reactions of β-lactam **10b** with DEF in refluxing toluene resulted in the isolation of an inseparable mixture (1:1.5) of diastereoisomers **22** and **23** (Scheme 8). The products in the mixture were assigned the structures **22** and **23** on the basis of the ^{1}H and ^{13}C NMR spectra which exhibited signals corresponding to the gross structural features of **22** and **23**. The *trans* stereochemistry was assigned to the β-lactam moiety of isomers **22** and **23** on the basis of the observed coupling constants of about 2.3 Hz between H-3 and H-4 protons. Because of the presence of the complex multiplets in the ^{1}H NMR spectra the exact nature of the individual Diels-Alder cycloadducts **22** and **23** could not be firmly established. Even the NOE experiments in this regard proved to be inconclusive and hence, their specific relative stereochemistry could not be assigned.

Similar reaction of DEF with α-dienyl β-lactam **12/13d** also resulted in a mixture of diastereoisomers **24** and **25**. The

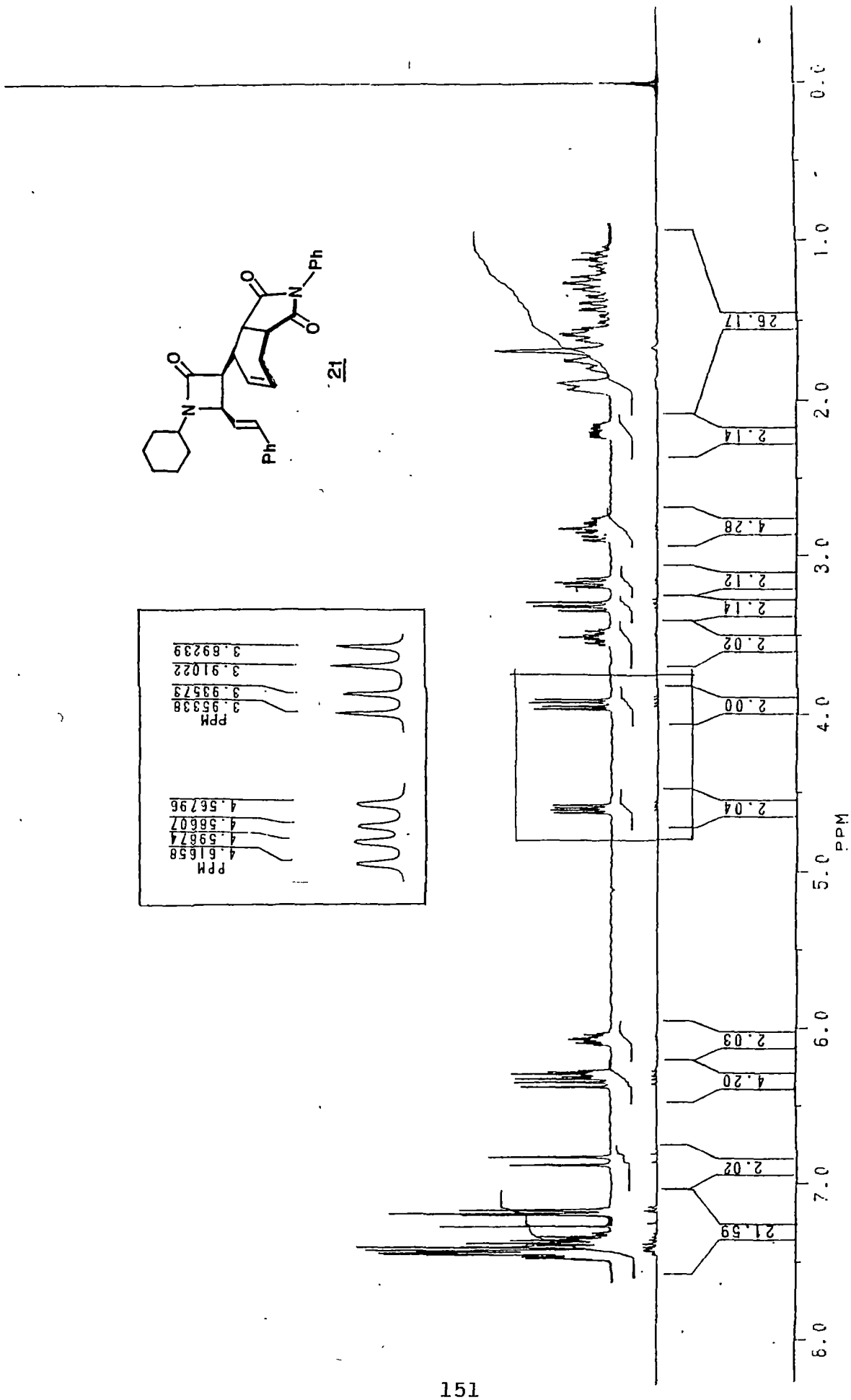
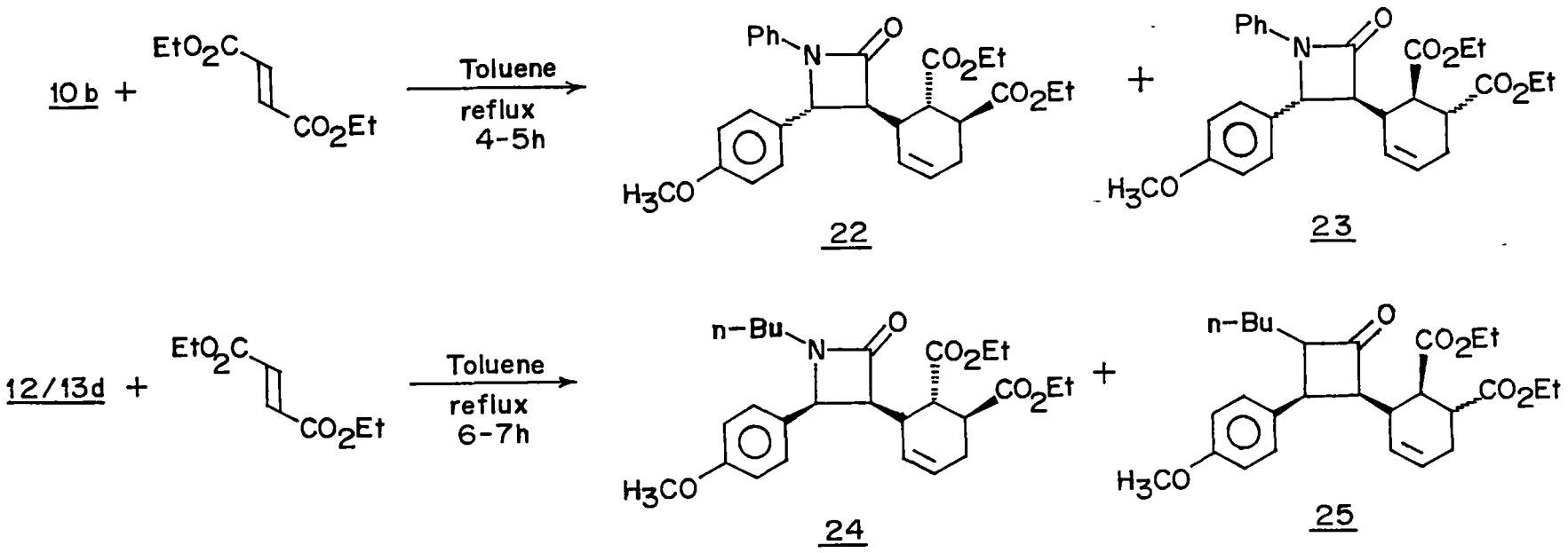


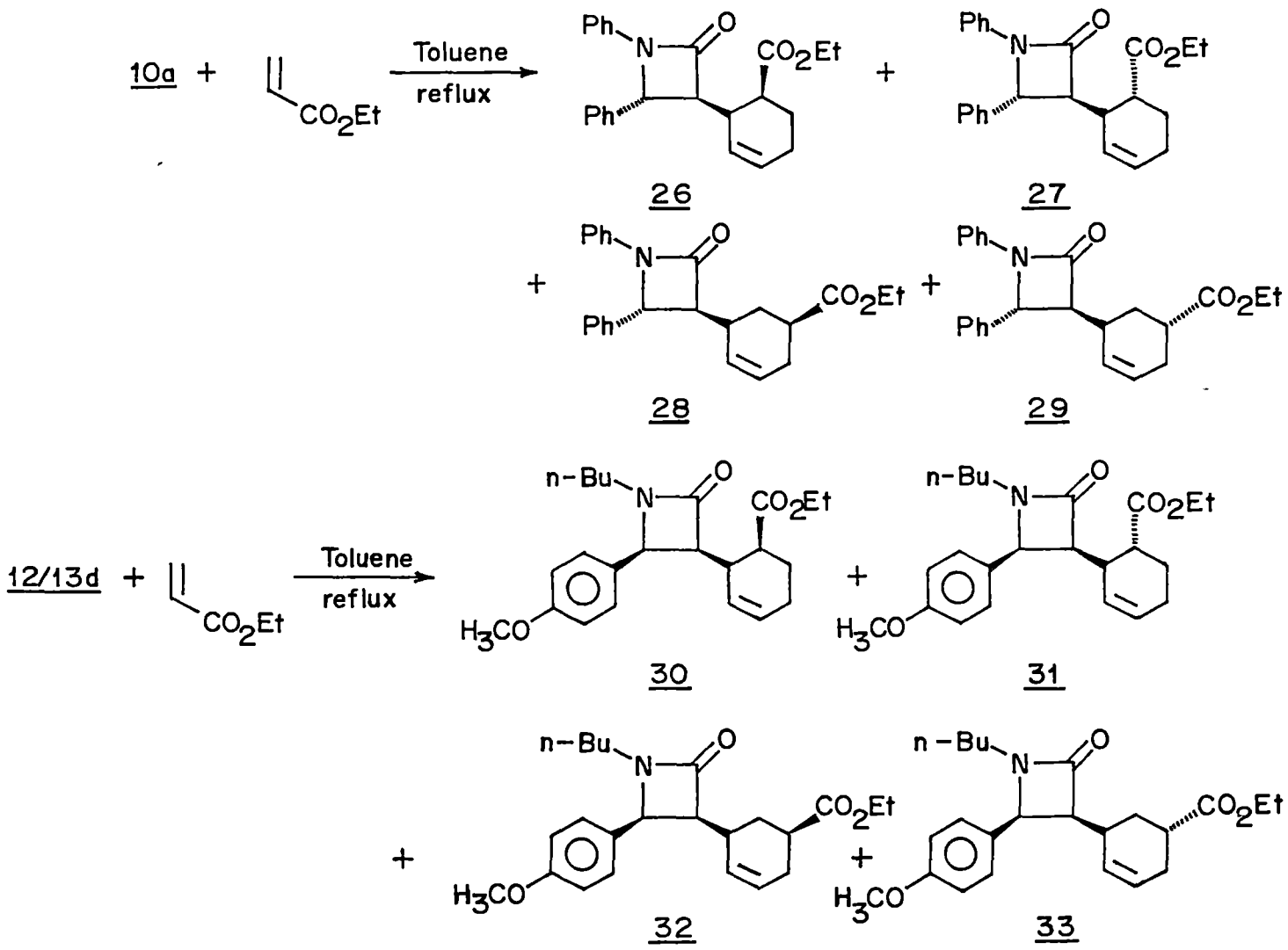
Fig. 7: 300 MHz ^{1}H NMR spectrum for 21 in $CDCl_3$


10b +
EtO2C
CO2Et
Toluene
reflux
4-5h
Ph
N
O
CO2Et
CO2Et
H3CO
22
+
23
12/13d +
n-Bu
24
25

Scheme-8

stereochemistry at C-3 and C-4 in these cases was retained as *cis* in contrast to the reaction of **15a** with PTAD where it changed from *cis* in α-dienyl β-lactam **15a** to *trans* in adduct **18b**. The said *cis* stereochemistry for isomers **24** and **25** was assigned on the observed coupling constant of about 5.3 Hz between H-3 and H-4 protons. In this case also the relative specific stereochemistry could not be assigned to **24** and **25** even with the help of NOE experiments. All efforts at chromatographic separations of the isomers **22/23** and **24/25** also failed because of their close R_f values. In an attempt to isolate a single specific isomer, the reactions of α-dienyl β-lactams with DEF were carried out in 5M $LiClO_4$ solution in ether, but the reactins failed and the starting material was recovered unreacted.

The situation was further complicated in reactions of α-dienyl-β-lactams **10** and **12/13** with ethyl acrylate (EA) which were shown to afford a mixture of stereo as well as regioisomers. For example, the reaction of *trans* β-lactam **10a** with ethyl acrylate afforded an inseparable mixture of products which was characterised mainly on the basis of ^1H NMR specrum and was identified as a mixture (5:4:2:1.2) comprising of **26, 27, 28** and **29**. The formation of these four isomers could be attributed to the four sets of signals observed for H-4 protons and their ratio was based on integration values these signals in the ^1H NMR spectrum of the mixture. The uniform coupling constant value of 1.9-2.5 Hz (between H-3 and H-4 protons) for these four sets of signals for H-4 proton further indicated *trans* relative


10a
Toluene
reflux
Ph
N
O
CO2Et
26
27
28
29
12/13d
n-Bu
H3CO
30
31
32
33

Scheme–9

stereochemistry at C-3 and C-4 in case of these stereo/regioisomers **26/27/28/29** (Fig. 8). Because of the complex nature of ^{1}H and ^{13}C NMR spectra the assignment of exact structure to the individual isomers or the assignment of specific relative regio/stereochemistry is rather difficult.

Similarly, the reaciton of β-lactam **12/13d** with ethyl acrylate also yielded an inseparable mixture (11:4:2.5:1) of four stereo/regioisomers **30**, **31**, **32** and **33**. The formation of these four isomers and their ratio could mainly be inferred from the observed four sets of signals for H-4 proton in its ^{1}H NMR spectrum and from their relative integrations, respectively. The ^{13}C NMR signals also attest to the presence of these four isomers. From the coupling constant value of 5.1-5.3 Hz between H-3 and H-4 protons it was inferred that all these isomers have *cis*-relative stereochemistry at C-3 and C-4. Here again, because of the complex nature of ^{1}H and ^{13}C NMR spectra, the specific relative regio/stereochemistry for the individual isomers in the mxitrue could not be assigned even with the help of NOE experiments. In an attempt to isolate a single diastereoisomer, the reaction of α-dienyl-β-lactams **10** and **12/13** were carried out with EA in 5M $LiClO_4$-Et_2O solution. It was thought that the formation of a single isomer might help, to some extent, in resolving the relative regio/stereochemistry in the above mixture. But these reactions also failed and hence the relative regio/stereochemistry of the individual isomers was not assigned.

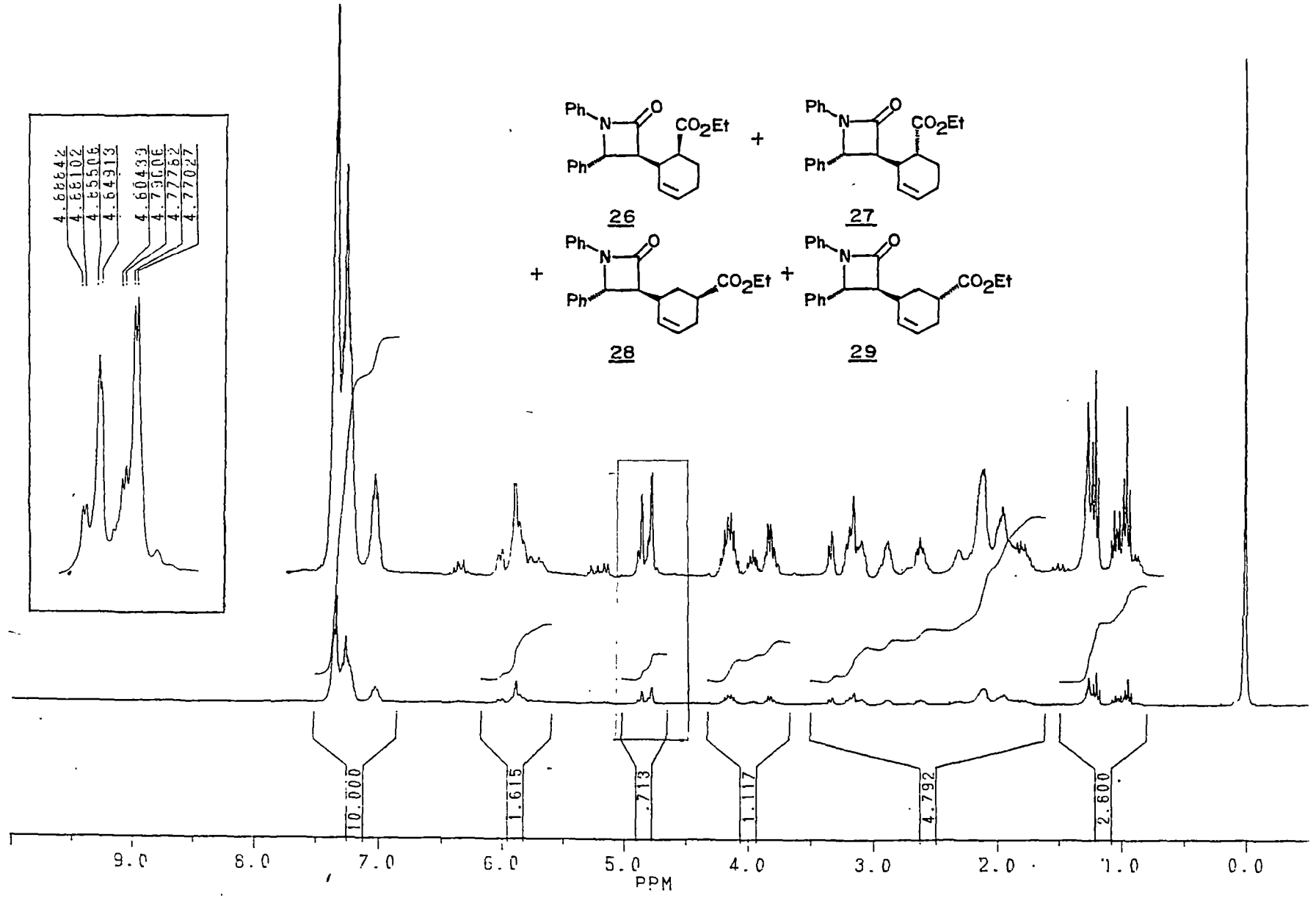


Fig. 8: 300 MHz ^{1}H NMR spectrum for the mixture 26/27/28/29 in $CDCl_3$

In summary, the use of butadienylketene resulted in convenient method for the synthesis of α-butadienyl-β-lactams. Also, the reactions of butadienylketene with 1,3-diazabutadienes resulted in various 5-dienyl pyrimidinones (Chapter I, Section I.3). Thus, the cycloadditions of butadienylketene with various imines and heterodienes appear to be a general method for the synthesis of 1,3-butadiene substituted heterocyclic systems. The reactions of α-butadienyl β-lactams with various dienophiles resulted in stereochemically interesting [4+2] cycloadditions to yield a variety of α-substituted β-lactams.

Experimental Section

General conditions are same as described in chapter I. All ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on Bruker ACF-300 spectrometer.

Starting Materials

Preparation of Schiff bases: A mixture of primary amine (5 mmol) and aldehyde (5 mmol) in CH_2Cl_2 (30 ml) was stirred in the presence of $MgSO_4$ (7.5 mmol) at rt for 3-4 h. The reaction mixture was filtered and the residue washed with CH_2Cl_2 (10 ml). The combined filtrate was then washed with water (3 x 50 ml) and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure and the crude product thus obtained was further purified by silica gel column chromotagraphy (eluent: mixture of EtOAc/hexane in 1:9 ratio).

Preparation of Sorbyl Chloride: See Chapter I, experimental section.

General Procedure for Azetidinones 10, 12/13 and 15: A solution of sorbyl chloride (3 mmol) in dry CH_2Cl_2 (30 ml) was added dropwise to a solution of Schiff base (2 mmol) and triethylamine (6 mmol) in CH_2Cl_2 under stirring at rt. After the addition was complete (*ca* 1.5 h), the solution was stirred for an additional 15 min, washed with water (5 x 50 ml), and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product thus obtained was further purified by column chromatography (silica gel) using a solution of ethyl acetate and hexane (1:9) as eluent.

***trans*-3-(1',3'-Butadienyl)-1,4-diphenylazetidin-2-one (10a):** Yield, 59%; mp 118-119°C; IR (KBr) ν 1734 (C=O), 1596, 1496 cm^{-1}; ^1H NMR δ 3.77 (dd, J = 8.1 and 2.5, 1H, H-3), 4.80 (d, J = 2.5, 1H, H-4), 5.14 (d, J = 9.8, with fine splitting, 1H, H-4'), 5.24 (d, J = 16.2, with fine splitting, 1H, H-4'), 5.88 (dd, J = 14.3 and 8.1, with fine splitting, 1H, H-1'), 6.30-6.39 (m, 2H, H-2' and H-3'), 7.02-7.07 (m, 1H, arom), 7.21-7.38 (m, 9H, arom); ^{13}C NMR δ 61.7 (C-3), 63.3 (C-4), 117.1, 118.5, 124.0, 125.5, 125.8, 128.6, 129.1, 129.2, 135.5, 135.9, 137.2, 137.5 and 165.4 (C-2); ms *m/z*: 275 (M^+), 156 (M^+ - Ph-N=C=O). Anal. Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.08. Found: C, 82.83; H,6.25; N, 5.15.

trans-3-(1',3'-Butadienyl)-4-(p-methoxyphenyl)-1-phenylazetidin-2-one (10b): Yield, 63%; mp 104-105 °C; IR (KBr) ν 1726 (C=O), 1591, 1492 cm^{-1}; ^1H NMR δ 3.71 (dd, J = 8.0 and 1.7, 1H, H-3), 3.78 (s, 3H, $-OCH_3$), 4.75 (d, J = 1.7, 1H, H-4), 5.12 (d, J = 9.5, with fine splitting, 1H, H-4'), 5.22 (d, J = 16.0, with fine splitting, 1H, H-4'), 5.86 (dd, J = 14.0 and 8.0, with fine splitting, 1H, H-1'), 6.25-6.41 (m, 2H, H-2' and H-3'), 6.90 (d, J = 8.5, 2H, arom), 7.00-7.05 (m, 1H, arom), 7.17-7.35 (m, 6H, arom); ^{13}C NMR (one C missing) δ 55.3 ($-OCH_3$), 61.3 (C-3), 63.4 (C-4), 114.5, 117.0, 118.4, 123.9, 125.6, 127.1, 129.0, 135.4, 135.9, 137.5, 159.7, 165.5 (C-2); ms *m/z*: 305 (M^+), 186 (M^+ - Ph-N=C=O). Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.72; H, 6.23; N, 4.49.

trans-3-(1',3'-Butadienyl)-1-(p-methylphenyl)-4-phenylazetidin-2-one (10c): Yield, 59%; viscous oil; IR (CCl_4) ν 1739 (C=O), 1493, 1498 cm^{-1}; ^1H NMR δ 2.25 (s, 3H, $-CH_3$), 3.72 (dd, J = 8.1 and 2.4, 1H, H-3), 4.76 (d, J = 2.4, 1H, H-4), 5.11 (d, J = 10.0, with fine splitting, 1H, H-4'), 5.22 (d, J = 16.3, with fine splitting, 1H, H-4'), 5.84 (dd, J = 14.2 and 8.1, with fine splitting, 1H, H-1'), 6.23-6.39 (m, 2H, H-2' and H-3'), 7.01 (d, J = 8.2, with fine splitting, 2H, arom), 7.19 (d, J = 8.2, with fine splitting, 2H, arom), 7.27-7.39 (m, 5H, arom); ^{13}C NMR δ 20.9 ($-CH_3$), 61.6 (C-3), 63.2 (C-4), 117.0, 118.5, 125.8, 126.9, 128.8, 129.3, 129.7, 133.6, 135.0, 135.5, 135.9, 137.2, 165.2 (C-2); ms *m/z*: 289 (M^+), 170 (M^+ - Ph-N=C=O). Anal. Calcd for

$C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 83.12; H, 6.61; N, 4.76.

***trans*-3-(1',3'-Butadienyl)-4-(p-methoxyphenyl)-1-(p-methylphenyl) azetidin-2-one (10d)**: Yield, 48%; viscous oil; IR (CCl_4) ν 1751 (C=O), 1583, 1511 cm^{-1}; ^1H NMR δ 2.22 (s, 3H, $-CH_3$), 3.70 (dd, J = 8.2 and 2.4, 1H, H-3), 3.74 (s, 3H, $-OCH_3$), 4.71 (d, J = 2.4, 1H, H-4), 5.10 (d, J = 9.3, with fine splitting, 1H, H-4'), 5.20 (d, J = 16.4, with fine splitting, 1H, H-4'), 5.84 (dd, J = 14.1 and 8.2, with fine splitting, 1H, H-1'), 6.23-6.40 (m, 2H, H-2' and H-3'), 6.87 (d, J = 8.7, with fine splitting, 2H, arom), 7.01 (d, J = 8.3, 2H, arom), 7.19 (d, J = 8.3, with fine splitting, 2H, arom), 7.24 (d, J = 8.7, with fine splitting, 2H, arom); ^{13}C NMR δ 20.8 ($-CH_3$), 55.2 ($-OCH_3$), 61.2 (C-3), 63.3 (C-4), 114.5, 117.0, 118.3, 124.2, 125.8, 127.1, 128.2, 129.1, 129.4, 129.6, 133.4, 135.2, 135.8, 135.9, 136.1, 159.7, 165.2 (C-2); ms *m/z*: 319 (M^+), 200 (M^+ - Ph-N=C=O). Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.93; H, 6.59; N, 4.31.

***cis*-3-(1',3'-Butadienyl)-1-cyclohexyl-4-phenylazetidin-2-one (12a)**: Yield 63%; viscous oil; IR (KBr) ν 1746 (C=O), 1489, 1397, 1351 cm^{-1}; ^1H NMR δ 1.01-1.30 (m, 4H, cyclohexyl), 1.52-2.05 (series of m, 6H, cyclohexyl), 3.38-3.46 (m, 1H, cyclohexyl), 4.08 (dd, J = 7.5 and 5.6, 1H, H-3), 4.85 (d, J = 5.6 Hz, 1H, H-4), 4.94 (d, J = 10.0, with fine splitting, 1H, H-4'), 5.08 (d, J = 17.4, with fine splitting, 1H, H-4'), 5.13 (dd, J = 15.3 and 7.5, 1H, H-1'), 6.02 (ddd, J = 17.4, 10.4 and 10.0, 1H, H-3'),

6.25 (dd, J = 15.3 and 10.4, 1H, H-2'), 7.25-7.38 (m, 5H, arom); ^{13}C NMR δ 25.0, 25.2, 30.5, 31.5, 53.0, (cyclohexyl); 57.2 (C-3), 58.3 (C-4), 117.3 (C-4'), 124.8 (C-1'), 127.5, 128.1, 128.3, 135.4 (C-2'), 136.2, (C-3'), 136.6, 168.1 (C-2). ms *m/z*: 265 (M^+), 140 (M^+- 125). Anal. Calcd for $C_{19}H_{23}NO$: C, 85.99; H, 8.73; N, 5.28. Found: C, 85.89; H, 8.74; N, 5.30.

***cis*-3-(1',3'-Butadienyl)-1-furfuryl-4-phenylazetidin-2-one (12b):** Yield 57%; viscous oil; IR (CCl_4) ν 1749 (C=O), 1493, 1397, 1358 cm^{-1}. ^{1}H NMR δ 4.04 (d, J = 15.7, 1H, -CH_2-), 4.17 (dd, J = 7.0 and 5.3, 1H, H-3), 4.76 (d, J = 15.7, 1H, -CH_2-; merged with d, J = 5.3, 1H, H-4), 4.95 (d, J = 10.2, 1H, H-4'), 5.07-5.15 (m, 2H, H-4' and H-1'), 6.01 (ddd, J = 16.9, 10.3 and 10.2, 1H, H-3'), 6.12 (d, J = 3.2, 1H, Hb), 6.20-6.29 (m, 2H, H-2' and Hc), 7.14-7.17 (m, 2H, arom), 7.27-7.36 (m, 4H, arom and Hd). ^{13}C NMR δ 37.2 (-CH_2-), 58.4 (C-3), 59.3 (C-4), 108.7 (C-c), 110.4 (C-b), 117.6 (C-4'), 124.3 (C-1'), 127.2, 128.2, 128.6, 135.0, (arom); 135.6 (C-2'), 136.1 (C-3'), 142.6 (C-d), 148.8 (C-a), 167.9 (C-2). ms *m/z*: 279 (M^+), 156 (M^+- 123). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.48; H, 6.10; N, 5.07.

(*cis/trans*, 6.5:1)-3-(1',3'-Butadienyl)-1-furfuryl-4-(*p*-methoxyphenyl)azetidin-2-one (12/13c): Following the general procedure, a mixture consisting in *cis* and *trans* isomers in 6.5:1 ratio was isolated as viscous oil. Yield, 59%; IR (CCl_4) ν 1745 (C=O), 1491, 1397, 1356 cm^{-1}. ^{1}H NMR δ 3.73 (s, 3H, -CH_3, *cis* isomer), 3.75 (s, 3H, -CH_3, *trans* isomer), 3.92 (d, J = 15.7, 1H, -CH_2-,

trans isomer), 4.01 (d, J = 15.7, 1H, *cis* isomer), 4.09-4.14 (m, 2H, H-3, both isomers), 4.26 (d, J = 2.2, 1H, H-4, *trans* isomer), 4.65 (d, J = 15.7, 1H, $-CH_2-$, *trans* isomer), 4.69 (d, J = 15.7, 1H, $-CH_2-$, *cis* isomer), 4.72 (d, J = 5.4, 1H, H-4, *cis* isomer), 4.92 (d, J_{cis} = 10.1, with *trans* isomer d merged, 2H, H-4', both isomers), 5.07 [d, J_{cis} = 17.0, with *trans* isomer d merged, 2H, H-4', both isomer), 5.16 (dd, J_{cis} = 15.3 and 7.7, with *trans* isomer dd merged, 2H, H-1', both isomers), 6.01 (ddd, J_{cis} = 17.0, 10.3, 10.1, with *trans* isomer ddd merged, 2H, H-3'), 6.10 (d, J_{cis} = 3.1, with trans isomer d merged, 2H, Hb, both isomers), 6.16-6.30 [m 4H; consisting in at 6.23 (dd, J_{cis} = 3.1 and 1.1, with *trans* isomer dd merged, 2H, Hc), 6.26 (dd, J = 15.7 and 10.3, 1H, H-2', *cis* isomer) and 6.20 (merged dd, H-2', *trans* isomer)], 6.85 (d, J = 8.6, with fine splitting, 2H, arom, *cis* isomer; merged with d at 6.88, 2H, arom, *trans* isomer), 7.08 (d, J = 8.6, with fine splitting, 2H, arom, *cis* isomer), 7.17 (d, J = 8.6, with fine splitting, 2H, arom, *trans* isomer), 7.28 (d, J = 1.1, with fine splitting, 1H, Hd, *cis* isomer), 7.38 (d, J = 1.0, 1H, Hd, *trans* isomer). ^{13}C NMR δ 37.0 ($-CH_2-$, *cis* isomer) 37.2 ($-CH_2-$, *trans* isomer), 55.0 ($-OCH_3$, *cis* isomer), 55.1 ($-OCH_3$, *trans* isomer), 58.3 (C-3, *cis* isomer), 58.9 (C-4, *cis* isomer), 61.4 (C-3, *trans* isomer), 63.4 (C-4, *trans* isomer), 108.46 (C-c, *trans* isomer), 108.54 (C-c, *cis* isomer), 110.4 (C-b, both isomers), 113.9 (arom, *cis* isomer), 114.3 (arom, *trans* isomer), 117.4 (C-4', *cis* isomer), 117.9 (C-4', *trans* isomer), 124.8 (C-1', both isomers); 126.3, 127.6, 128.8 (arom, *trans* isomer);

126.8, 128.5 (arom, *cis* isomer), 134.7 (C-2', *trans* isomer), 135.2 (C-2', *cis* isomer), 136.1 (C-3', *trans* isomer), 136.2 (C-3', *cis* isomer), 142.5 (C-d, both isomers), 148.9 (C-a, both isomers), 159.4 (arom, *cis* isomer), 159.8 (arom, *trans* isomer); 167.7 (C-2, *trans* isomer), 167.8 (C-2, *cis* isomer). ms *m/z*: 309 (M^+), 186 (M^+- 123). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.88; H, 6.19; N, 4.46.

***(cis/trans*, 4:1)-3-(1',3'-Butadienyl)-1-(*n*-butyl)-4-(*p*-methoxy phenyl)azetidin-2-one (12/13d):** Following the general procedure a mixture consisting in *cis* and *trans* isomers in the ratio 4:1 was isolated as viscous oil. Yield 67%; IR (CCl_4) ν 1747 (C=O), 1509, 1397, 1249 cm^{-1}; ^1H NMR δ 0.87 (t, J = 7.3, 3H, $-CH_3$, *cis* isomer), 0.93 (t, J = 7.3, 3H, $-CH_3$, *trans* isomer), 1.23-1.36 (m, 2H, $-CH_2-$, *cis* isomer), 1.39-1.52 (m, 4H; $-CH_2-$, both isomers), 1.61-1.68 (m, 2H,$-CH_2-$, *trans* isomer), 3.40-3.62 (m, 4H; $-CH_2-N-$, both isomers), 3.76 (s, 3H, $-OCH_3$, *cis* isomer), 3.78 (s, 3H, $-OCH_3$, *trans* isomer), 4.10-4.15 (m, 2H, H-3, both isomers), 4.31 (d, J = 2.1, H-4, *trans* isomer), 4.80 (d, J = 5.4, 1H, H-4, *cis* isomer), 4.93 (d, J = 10.0, with fine splitting, 1H, H-4', *cis* isomer), 5.05-5.21 [m, 5H; consisting in at 5.08 (d, J = 16.9, with fine splitting, 1H, H-4', *cis* isomer), 5.17 (dd, J = 15.4 and 7.7, 1H, H-1') and merged signals for 2H, H-4', *trans* isomer and 1H, H-1', *trans* isomer], 6.04 (ddd, J = 16.9, 10.3 and 10.0, 1H, H-3', *cis* isomer), 6.22-6.35 (m, 3H; 2H, H-2', both isomers and 1H, H-3', *trans* isomer), 6.87-6.92 [m, 4H; consisting in at 6.89 (d, J = 8.7, with fine splitting, 2H, arom, *cis* isomer, with

(d, 2H, arom) for *trans* isomer merged], 7.13 (d, J = 8.7, 2H, arom, *cis* isomer), 7.19 (d, J = 8.7, 2H, arom, *trans* isomer). ^{13}C NMR δ 13.6 ($-CH_3$, *cis* isomer), 13.9 ($-CH_3$, *trans* isomer), 20.2 ($-CH_2-$, *cis* isomer), 20.4 ($-CH_2-$, *trans* isomer), 29.6 ($-CH_2-$, *cis* isomer), 29.7 ($-CH_2-$ *trans* isomer), 55.1 ($-N-CH_2-$, *cis* isomer), 55.2 ($-N-CH_2-$, *trans* isomer), 58.0 (C-3, *cis* isomer), 58.8 (C-4, *cis* isomer), 61.2 (C-3, *trans* isomer), 63.2 (C-4, *trans* isomer), 117.2 (C-4', *cis* isomer); 117.8 (C-4', *trans* isomer), 125.1 (C-1', both isomers), 126.8, 127.7, 129.3 (arom, *trans* isomer); 127.2, 128.6 (arom, *cis* isomer), 134.6 (C-2', *trans* isomer), 135.2 (C-2', *cis* isomer), 136.2 (C-3', *trans* isomer), 136.3 (C-3', *cis* isomer), 159.6 (arom, *cis* isomer), 159.9 (arom, *trans* isomer), 168.1 (C-2, *trans* isomer), 168.2 (C-2, *cis* isomer). ms *m/z*: 285 (M^+), 186 (M^+ - 99). Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.72; H, 8.14; N, 4.89.

***cis*-3-(1',3'-Butadienyl)-1-phenyl-4-(2"-phenylethenyl)azetidin-2-one (15a):** Yield 67%; viscous oil; IR (CCl_4) ν 1741 (C=O), 1598. 1494, 1380, 1215 cm^{-1}. ^1H NMR δ 4.22 (dd, J = 6.9 and 6.9, 1H, H-3), 4.81 (dd, J =8.0 and 6.1, 1H, H-4), 5.09 (d, J = 9.6, 1H, H-4'), 5.23 (d, J = 16.0, 1H, H-4'), 5.66 (dd, J = 14.5 and 8.0, 1H, H-1'), 6.19 (dd, J = 15.9 and 8.0, 1H, H-1"), 6.25-6.44 (m, 2H, H-2' and H-3'), 6.76 (d, J = 15.9, 1H, H-2"), 7.03-7.08 (m, 1H, arom), 7.22-7.53 (m, 9H, arom). ^{13}C NMR δ 57.0 (C-3); 58.1, (C-4), 114.7, 117.0, 118.4, 124.0, 124.7, 126.6, 126.7, 128.4, 128.5, 128.7, 129.1, 135.4, 135.7, 136.0, 136.3, 137.9 and 165.4

(C-2). ms *m/z*: 301 (M^+), 182 (M^+- Ph-N=C=O). Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.60; H, 6.31; N, 4.69.

***cis*-3-(1',3'-Butadienyl)-1-cyclohexyl-4-(2"-phenylethenyl) azetidin-2-one (15b)** Yield 71%; mp 84-85°C; IR (KBr) ν 1736 (C=O), 1597, 1491, 1444, 1393 cm^{-1}. ^1H NMR δ 1.04-1.92 (series of m, 10H, cyclohexyl), 3.50 (dddd, *J* = 11.7, 11.6, 3.8 and 3.8, 1H, cyclohexyl), 4.01 (dd, *J* = 6.7 and 5.6, with fine splitting, 1H, H-3), 5.07 (d, *J* = 9.3, with fine splitting, 1H, H-4'), 5.19 (d, *J* = 16.9, with fine splitting, 1H, H-4'), 5.63 (dd, *J* = 14.5 and 7.7, 1H, H-1'), 6.10 (dd, *J* = 15.8 and 9.4, 1H, H-1"), 6.23-6.41 (m, 2H, H-2' and H-3'), 6.64 (d, *J* = 15.8, 1H, H-2"), 7.28-7.41 (m, 5H, arom). ^{13}C NMR δ 25.2, 30.6, 32.1, 52.0, (cyclohexyl); 56.4 (C-3), 57.5 (C-4), 117.8, 124.7, 126.6, 126.9, 128.2, 128.7, 134.4, 135.6, 136.0, 136.2, 167.1 (C-2). ms *m/z*: 307 (M^+), 182 (M^+-125). Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 81.95; H, 8.18; N, 4.59.

General Procedure for Diels-Alder Adducts 5: Equivalent amounts of β-lactam **10** and DMAD were refluxed in dry toluene for 6-7 h. The solvent was removed under reduced pressure and the crude product was purified by recrystallisation from benzene:hexane (3:1) mixture.

***trans*-3-[2',3'-Bis(methoxycarbonyl)-2',4'-cyclohexadienyl]-4-(p-methoxyphenyl)-1-phenylazetidin-2-one (17a):** Yield, 95%; mp 178-179 °C; IR (KBr) ν 1733, 1715, 1597, 1497 cm^{-1}; ^1H NMR δ 2.98

(ddd, J = 23.3, 4.9 and 4.9, 1H, $-CH_2-$), 3.19 (dddd, J = 23.3, 6.9, 4.6 and 2.2, 1H, $-CH_2-$), 3.26 (dd, J = 4.7 and 2.6, 1H, H-3), 3.63 (s, 3H, $-CO_2CH_3$), 3.75 (s, 3H, $-CO_2CH_3/-OCH_3$), 3.77 (s, 3H, $-OCH_3/-CO_2CH_3$), 3.87 (m, 1H, H-1'), 4.81 (d, J = 2.3, 1H, H-4), 5.82 (m, 1H, olefinic), 5.91 (m, 1H, olefinic), 6.86 (d, J = 8.4, 2H, arom), 6.98-7.03 (m, 1H, arom), 7.18-7.26 (m, 6H, arom); ^{13}C NMR δ 27.8 ($-CH_2-$), 36.4 (C-1'), 52.3 ($-CO_2CH_3$), 52.4 ($-CO_2CH_3$), 55.2 ($-OCH_3$), 57.6 (C-3), 63.6 (C-4), 114.5, 117.0, 123.8, 124.3, 125.1, 127.3, 128.9, 129.4, 134.2, 134.7, 137.4, 159.7, 164.9 (C-2), 167.4 (CO_2Me), 168.2 (CO_2Me); ms *m/z*: 447 (M^+), 328 (M^+ - Ph-N=C=O). Anal. Calcd for $C_{26}H_{25}NO_6$: C, 69.79; H,5.63; N, 3.13. Found: C, 69.65; H, 5.64; N, 3.19.

***trans*-3-[2',3'-Bis(methoxycarbonyl)-2',4'-cyclohexadienyl]-1-(p-methylphenyl)-4-phenylazetidin-2-one (17b)**: Yield, 97%; mp 182-182.5°C; IR (KBr) ν 1719, 1506, 1431, 1383, 1253 cm^{-1}; ^1H NMR δ 2.25 (s, 3H, $-CH_3$), 2.98 (ddd, J = 23.3, 5.3 and 4.6, 1H, $-CH_2-$), 3.21 (dddd, J = 23.3, 7.0, 5.0 and 2.5, 1H, $-CH_2-$), 3.27 (dd, J = 4.6 and 2.6, 1H, H-3), 3.64 (s, 3H, $-CO_2CH_3$), 3.76 (s, 3H, $-CO_2CH_3$), 3.85-3.91 (m, 1H, H-1'), 4.83 (d, J = 2.3, 1H, H-4), 5.81 (m, 1H, olefinic), 5.91 (m, 1H, olefinic), 7.02 (d, J = 8.3, 2H, arom), 7.20 (d, J = 8.4, with fine splitting, 2H, arom), 7.25-7.36 (m, 5H, arom); ^{13}C NMR (two C missing) δ 20.8 ($-CH_3$), 27.8 ($-CH_2-$), 36.4 (C-1'), 52.3 ($-CO_2CH_3$), 52.4 ($-CO_2CH_3$), 57.8 (C-3), 63.5 (C-4), 116.9, 124.3, 125.2, 126.0, 128.4, 129.0, 129.5, 133.4, 134.9, 137.6, 164.5 (C-2); ms *m/z*: 431 (M^+), 312

(M^+ - Ph-N=C=O). Anal. Calcd for $C_{26}H_{25}NO_5$: C, 72.38; H, 5.84; N, 3.25. Found: C, 72.30; H, 5.91; N, 3.29.

***trans*-4-(p-Methoxyphenyl)-1-phenyl-7',9'-dioxo-3-[8'-phenyl-1',6',8'-triaza[4.3.0]bicyclonon-3'-en-yl]azetidin-2-one (18a):** To a stirred solution of PTAD (0.58 g, 3.3 mmol) in methylene chloride (25 ml) at 0°C was added **10b** (1 g, 3.3 mmol) in portions over a period of 5 min. The solution was stirred at 0°C for an additional 10 min. The crude product obtained after removal of the solvent was purified by column chromatography (silica gel, 60-120 mesh) using a solution of ethyl acetate and hexane (1:3) to yield 1.46 g (92%) of adduct **19a**. mp 200-202 °C; IR (KBr) ν 1744, 1708, 1595, 1493 cm^{-1}. ^1H NMR δ 3.47 (dd, J = 10.3 and 2.3, 1H, H-3), 3.76 (s, 3H, $-OCH_3$), 3.97 (dq, J = 16.7 and 2.4, 1H, $-CH_2-$), 4.30 (dddd, J = 16.7, 4.2, 1.9 and 0.8, 1H, $-CH_2-$), 5.11 (m, 1H, H-2'), 5.46 (d, J = 2.3, 1H, H-4), 6.04 (dddd, J = 10.3, 4.0, 2.0 and 2.0, 1H, olefinic), 6.42 (dddd, J = 10.3, 4.8, 2.4 and 2.4, 1H, olefinic), 6.74 (d, J = 8.7, with fine splitting, 2H, arom), 7.00-7.06 (m, 1H, arom), 7.18-7.31 (m, 8H, arom), 7.39-7.52 (m, 3H, arom); ^{13}C NMR δ 44.5 ($-CH_2-$), 52.9 (C-2'), 55.3 ($-OCH_3$), 58.7 (C-3), 63.7 (C-4), 114.5, 117.2, 121.7, 123.6, 124.2, 125.9, 127.6, 128.5, 129.1, 129.2, 130.7, 137.1, 151.6, 153.6, 159.8, 163.2 (C-2); ms *m/z*: 480 (M^+), 361 (M^+ - Ph-N=C=O). Anal. Calcd for $C_{28}H_{24}N_4O_4$: C, 69.99; H, 5.03; N, 11.66. Found: C, 70.11; H, 5.09; N, 11.59.

trans-1-Phenyl-4-(2"-phenylethenyl)-7',9'-dioxo-3-[8'-phenyl-1',6',8'-triaza[4.3.0]bicyclonon-3'-en-yl]azetidin-2-one (18b): To a stirred solution of PTAD (0.58 g, 3.32 mmol) in CH_2Cl_2 (25 ml) at 0 °C was added 15a (1.0 g, 3.32 mmol) in portions over a period of 5 min. A similar procedure as described above was employed and the crude product thus obtained was purified by recrystallisation from EtOAc to yield 1.50 g (95%) of the adduct 18b. mp 186-187 °C; IR (KBr) ν 1741, 1704, 1596, 1499, 1418 cm^{-1}. ^1H NMR δ 3.49 (dd, J = 10.3 and 2.3, 1H, H-3), 3.98 (dq, J = 16.8 and 2.3, 1H, $-CH_2-$), 4.35 (dm, J = 16.8, 1H, $-CH_2-$), 5.01-5.07 (m, 1H, H-1'), 5.19 (dd, J = 9.0 and 2.3, 1H, H-4), 6.04 (dddd, J = 10.0, 4.1, 2.0 and 2.0, 1H, olefinic), 6.15 (dd, J = 15.9 and 9.0, 1H, H-1"), 6.41 (dddd, J = 10.0, 4.7, 2.3 and 2.3, 1H, olefinic), 6.77 (d, J = 15.9, 1H, H-2"), 7.03-7.09 (m, 1H, arom), 7.15-7.19 (m, 2H, arom), 7.23-7.24 (m, 10H, arom), 7.42 (d, J = 8.5, with fine splitting, 2H, arom). ^{13}C NMR δ 44.4 (C-1'), 52.8 ($-CH_2-$), 58.7 (C-3), 60.6 (C-4), 116.9, 121.8, 123.5, 124.3, 125.4, 125.9, 126.7, 128.4, 128.5, 128.6, 129.1, 130.5, 135.1, 135.6, 137.6, 151.7, 153.5, 162.5 (C-2). ms *m/z*: 476 (M^+), 357 (M^+- Ph-N=C=O). Anal. Calcd for $C_{29}H_{24}N_4O_3$: C, 73.09; H, 5.08; N, 11.76. Found: C, 73.23; H, 4.99; N, 11.68.

Diels-Alder Adduct of 10a and Maleic Anhydride (19/19'): A solution of **10a** (0.30 g, 1.10 mmol) and maleic anhydride (0.11 g, 1.11 mmol) in toluene (4 ml) was refluxed for 1 h. The reaction mixture was then purified by chromatography on 60-120 mesh silica gel column (eluent: mixture of AcOEt/hexane in 1:4 ratio)

affording a colorless solid consisting in a mixture of diastereoisomers in 2:1 ratio (0.38 g, 93%). IR (KBr, mixture of diastereoisomers in 2:1 ratio) ν 1770, 1739, 1596, 1497 cm^{-1}. ^1H NMR (mixture of diastereoisomers in 2:1 ratio) δ 2.21-2.30 (m, 2H, H-1', both isomers), 2.70-2.90 (m, 4H, $-CH_2-$, both isomers), 3.45-3.57 (m, 3H; 2H, H-5' and H-6' for minor isomer and 1H, H-5'/6' for major isomer), 3.84 (dd, J = 11.4 and 2.4, 1H, H-3, minor isomer), 3.92 (dd, J = 12.0 and 2.4, 1H, H-3, major isomer), 4.01 (dd, J = 9.8 and 5.8, 1H, H-6'/5', major isomer), 4.72 (d, J = 2.4, 1H, H-4, major isomer), 4.83 (d, J = 2.4, 1H, H-4, minor isomer), 5.85 (ddd, J = 9.3, 3.2 and 3.2, 1H, olefinic, major isomer), 6.03-6.13 (m, 2H, olefinic, both isomers), 6.29 (ddd, J = 9.4, 3.2 and 3.2, 1H, olefinic, minor isomer), 7.01-7.07 (m, 2H, arom, both isomers), 7.22-7.28 (m, 8H, arom, both isomers), 7.34-7.40 (m, 10H, arom, both isomers); ^{13}C NMR (mixture of diastereoisomers in 2:1 ratio) δ 24.2 (C-1'), 35.6 ($-CH_2-$), 40.2 (C-5'/6'), 42.7 (C-6'/5'), 59.3 (C-3), 60.1 (C-4), (minor isomer); 24.7 (C-1'), 36.4 ($-CH_2-$), 40.5 (C-5'/6'), 42.9 (C-6'/5'), 59.1 (C-3), 61.1 (C-4), (major isomer); 117.0, 124.1, 124.2, 126.1, 126.2, 128.6, 128.8, 128.9, 129.1, 129.2, 129.4, 129.8, 130.4, 130.6, 136.7, 137.0, 137.2, 137.3, 165.9 (C-2), (both isomers); 171.0, 173.7 (-OC-N-CO-, minor isomer); 171.7, 174.0 (-OC-N-CO-, major isomer); ms *m/z*: 373 (M^+), 254 (M^+ - Ph-N=C=O).

Diels-Alder Adduct of 10a and *N*-Phenylmaleimide (20/20'): A solution of **10a** (0.30 g, 1.10 mmol) and *N*-phenylmaleimide (0.19

g, 1.12 mmol) in toluene (4 ml) was refluxed for 2 h. The reaction mixture was then purified by chromatography on 60-120 mesh silica gel column (eluent: mixture of AcOEt/hexane in 1:3 ratio) affording a colorless solid consisting in a mixture of diastereoisomers in 2:1 ratio (0.45g, 92%). IR (KBr) ν 1727, 1702, 1591, 1492, 1379 cm^{-1}; ^{1}H NMR δ 2.25-2.31 (m, 2H, H-1', both isomers), 2.83-2.94 (m, 4H, $-CH_2-$, both isomers), 3.30-3.41 (m, 3H; 2H, H-5' and H-6' for minor isomer and 1H, H-5' for major isomer), 3.91 (dd, J = 8.9 and 5.6, 1H, H-6', major isomer), 4.07 (dd, J = 10.9 and 2.1, 1H, H-3, minor isomer), 4.17 (dd, J = 12.1 and 2.1, 1H, H-3, major isomer), 4.72 (d, J = 2.1, 1H, H-4, major isomer), 4.86 (d, J = 2.1, 1H, H-4, minor isomer), 5.85 (ddd, J = 9.1, 3.2 and 3.2, 1H, olefinic, major isomer), 6.06-6.12 (m, 2H, olefinic, both isomers), 6.30 (ddd, J = 9.3, 3.2 and 3.2, 1H, olefinic, minor isomer), 7.01-7.05 (m, 2H, arom, both isomers), 7.16 (d, J = 7.3, with fine splitting, 4H, arom, both isomers), 7.19-7.41 (m, 24H, arom, both isomers); ^{13}C NMR δ 24.5 (C-1'), 36.8 ($-CH_2-$), 39.8 (C-5'/6'), 42.0 (C-6'/5'), 59.6 (C-3), 60.6 (C-4), (minor isomer); 25.1 (C-1'), 37.3 ($-CH_2-$), 40.0 (C-5'/6'), 42.0 (C-6'/5'), 59.7 (C-3), 61.4 (C-4), (major isomer); 117.0, 124.0, 126.1, 126.3, 126.4, 126.5, 128.6, 128.7, 129.0, 129.1, 129.3, 129.5, 130.0, 130.5, 131.7, 137.4, 137.5 (both isomers); 166.5 '(C-2, minor isomer); 166.6 (C-2, major isomer); 176.0, 178.4 (-OC-N-CO-, minor isomer); 176.7, 178.6 (-OC-N-CO-, major isomer); ms *m/z*: 448 (M^+), 329 (M^+ - Ph-N=C=O).

***trans*-1,4-Diphenyl-3-[(*N*-phenyl)cyclohex-2'-ene-5',6'-dicarboximido]azetidin-2-one (20).** To a 5M Lithium perchlorate-etherate solution (5 ml) were added **10a** (0.3g, 1.10 mmol) and *N*-phenylmalemide (0.19 g, 1.12 mmol). The reaction mixture was stirred at rt for 12 h, the left over solvent was removed and the residue diluted with CH_2Cl_2 (20 ml). The solution was then washed with water (4 x 50 ml), dried over anhydrous Na_2SO_4 and evaporated under *vacuo*. The crude product thus obtained was purified by column chromatography on silica gel (EtOAc/hexane, 1:3) to give 0.42 g (86%) of adduct **20**; mp 250-251°C; IR (KBr)ν 1727, 1702, 1593, 1492, 1379 cm^{-1}; ^1H NMR δ 2.26-2.34 (m, 1H, H-1'), 2.84-2.95 (m, 2H, $-CH_2-$), 3.35 (unresolved dd, *J* = 8.0 and 8.0, 1H, H-5'), 3.93 (dd, *J* = 8.9 and 5.6, 1H, H-6'), 4.18 (dd, *J* = 12.1 and 2.4, 1H, H-3), 4.73 (d, *J* = 2.4, 1H, H-4), 5.96 (ddd, *J* = 9.2, 3.2 and 3.2, 1H, H-3'), 6.11 (dddd, *J* = 9.2, 6.7, 3.1 and 3.1, 1H, H-2'), 7.02-7.07 (m, 1H, arom), 7.15-7.43 (m, 14H, arom). ^{13}C NMR δ 25.1 (C-1'), 37.3 ($-CH_2-$), 40.0 (C-5'/6'), 42.0 (C-6'/5'), 59.7, (C-3) 61.4 (C-4), 117.0, 124.0, 126.1, 126.4, 128.6, 128.7, 129.0, 129.1, 129.3, 129.5, 130.5, 131.7, 137.4, 137.5, 166.6 (C-2), 176.7 (-N-CO-), 178.8 (-OC-N-). ms *m/z* 448 (M^+), 329 (M^+- Ph-N=C=O). Anal. Calcd for $C_{29}H_{24}N_2O_3$: C, 77.66; H, 5.39; N, 6.25. Found: C, 77.57; H, 5.45; N, 6.28.

***cis*-1-Cyclohexyl-4-(2"-phenylethenyl)-3-[(*N*-phenyl)cyclohex-2'-ene-5',6'-dicarboximido]azetidin-2-one (21):** A solution of **15b** (0.30 g, 0.98 mmol) and NPM (0.17 g, 0.98 mmol) in toluene (5 ml) was refluxed for 2 h. The solvent was removed under reduced

pressure and the residue purified by chromatography on silica gel column (eluent: mixture of EtOAc/hexane in 1:3 ratio) affording a colorless solid (0.45 g, 96%). mp 154-155 °C; IR (KBr) ν 1726, 1700, 1494, 1387, 1188 cm^{-1}. ^{1}H NMR δ 1.05-1.92 (series of m, 10H, cyclohexyl), 2.12-2.23 (m, 1H, H-1'), 2.70-2.88 (m, 2H, $-CH_2-$), 3.16 (ddd, *J* = 7.1, 7.1 and 1.6, 1H, H-5'), 3.27 (dd, *J* = 9.1 and 7.1, 1H, H-6'), 3.43-3.53 (m, 1H, cyclohexyl), 3.92 (dd, *J* = 13.0 and 5.3, 1H, H-3), 4.59 (dd, *J* = 9.2 and 5.3, 1H, H-4), 6.05 (dddd, *J* = 9.5, 7.1, 3.0 and 3.0, 1H, H-3'), 6.26-6.36 [m, 2H; consisting in at 6.28 (ddd, *J* = 9.5, 3.1 and 3.1, 1H, H-2') and 6.32 (dd, *J* = 15.9 and 9.2, 1H, H-1")], 6.84 (d, *J* = 15.9, 1H, H-2"), 7.15-7.16 (m, 1H, arom), 7.18-7.19 (m, 1H, arom), 7.32-7.46 (m, 8H, arom). ^{13}C NMR δ 24.0 (C-1'); 25.2, 30.7, 32.1, (cyclohexyl); 40.0 (C-5'/6'), 40.1 (C-6'/5'), 52.0 (cyclohexyl), 54.1 (C-3), 56.4 (C-4), 126.1, 126.4, 126.6, 128.0, 128.5, 128.7, 128.9, 129.1, 131.1, 135.2, 135.9, 168.5 (C-2), 176.6 (-CO-N-), 178.5 (-N-CO-). ms *m/z*: 480 (M^+), 355 (M^+- 125). Anal. Calcd for $C_{31}H_{32}N_2O_3$: C, 77.47; H, 6.71; N, 5.83. Found: C, 77.56; H, 6.73; N, 5.79.

Diels-Alder adduct of 10b with DEF (22/23): A solution of **10b** (0.5 g, 1.64 mmol) and DEF (0.28 g, 1.65 mmol), in toluene (6 ml) was refluxed for 4-5 h, whereupon the solvent was removed under reduced pressure and the resulting residue purified by chromatography on 60-120 mesh silica gel (eluent: mixture of AcOEt/hexane in a 1:5 ratio), affording a viscous liquid (0.70 g,

90%) consisting in a mixture of diastereoisomers in 1:1.5 ratio; IR (KBr) ν 1719, 1590, 1493, 1374 cm^{-1}. ^1H NMR δ 0.95 (t, J = 7.1, 3H, $-CH_3$ minor isomer), 1.10 (t, J = 7.1, 3H, $-CH_3$, major isomer), 1.20-1.28 [m, 6H, consisting in at 1.22 (t, J = 7.1, 3H, $-CH_3$, major isomer) and 1.25 (t, J = 7.1, 3H, $-CH_3$, minor isomer)], 2.14-2.55 (series of m, 3H, two for minor isomer and one for major isomer), 2.90-2.95 (m, 2H, major isomer), 3.08-3.17 (m, 4H, two each for both isomers), 3.26-3.29 (m, 1H, major isomer), 3.35-3.43 (m, 1H, minor isomer), 3.77 (s, 3H, $-OCH_3$, minor isomer), 3.78 (s, 3H, $-OCH_3$, major isomer), 3.77-3.81 (m, merged with $-OCH_3$ peaks, 1H, minor isomer), 3.95-4.15 (m, 8H, 4 x $-CH_2-$, both isomers), 5.76, (br d, 1H, olefinic, major isomer), 5.83-5.91 (m, 2H, olefinic, both isomers), 5.95-6.00 (m, 1H, olefinic, minor isomer), 6.85-6.89 [apparent dd, 4H, consisting in at 6.68 (d, J = 8.7, 2H, arom, minor isomers) and 6.87 (d, J = 8.7, 2H, arom, major isomer)], 6.99-7.03 (m, 2H, arom, both isomers), 7.17-7.27 (m, 12H, both isomers). ^{13}C NMR δ 13.8, 13.9, 14.1, 14.2 (4 x $-CH_3$, both isomers); 27.8, 37.5, 42.8, 45.6, 55.3, 57.5, 60.8, 61.0, 63.0 (major isomer); 28.3, 35.7, 37.8, 44.6, 55.3, 58.9, 60.61, 60.64, 62.2 (minor isomer); 114.4, 114.5, 117.0, 117.1, 123.8, 124.3, 125.1, 127.4, 127.46, 127.50, 127.9, 129.0, 129.4, 137.4, 159.7 (both isomers); 165.5 (C-2, minor isomer); 165.6 (C-2 major isomer); 173.6, 174.2 (2 x $-CO_2Et$, major isomer); 172.5, 175.3 (2 x $-CO_2Et$, minor isomer). ms *m/z*: 477 (M^+), 358 (M^+- Ph-N=C=O). Anal. Calcd for $C_{28}H_{31}NO_6$: C, 70.42; H, 6.54; N, 2.93. Found: C, 70.56; H, 6.44; N, 3.05.

Diels-Alder adducts of 12/13d with DEF (24/25): A solution of 12/13d (0.5 g, 1.75 mmol) and DEF (0.30 g, 1.75 mmol) in toluene (8 ml) was refluxed for 6-7 h. An identical workup as described above afforded 0.69 g (86%) of viscous liquid consisting in a mixture of diastereoisomers 23/24 in 1:1.5 ratio; IR (KBr)ν 1727, 1599, 1501, 1383 cm^{-1}. ^1H NMR δ 0.84-1.41 (series of m, 22H, both isomers), 2.07-2.32 (m, 3H, two for major isomer and one for minor isomer), 2.38-2.85 (series of m, 8H, both isomers), 2.94-3.07 (m, 3H, two for minor isomer and one for major isomer), 3.45-3.56 (m, 4H, both isomers), 3.81 (s, 3H, $-OCH_3$, minor isomers), 3.84 (s, 3H, $-OCH_3$, major isomer), 3.89-4.16 (m, 10H, both isomers), 4.64 (d, J = 5.3, 1H, H-4, major isomer), 4.70 (d, J = 5.0, 1H, H-4, minor isomer), 5.78-6.01 (series of m, 4H, olefinic, both isomers), 6.89-6.96 [m, 4H, arom; consisting in at 6.91 (d, J = 8.7, 2H, minor isomer) and 6.94 (d, J = 8.8, 2H, major isomer)], 7.16-7.20 [m, 4H, arom; consisting in at 7.17 (d, J = 8.8, 2H, major isomer) and 7.18 (d, J = 8.7, 2H, minor isomer)]; ^{13}C NMR δ 13.6, 13.9, 14.1, 14.2, 20.2, 25.6, 27.3, 29.47, 29.50, 31.9, 33.4, 38.4, 39.9, 40.0, 40.6, 43.3, 45.4, 55.26, 55.30, 56.5, 58.1, 58.2, 60.6, 60.8, 114.1, 114.3, 125.8, 126.2, 126.8, 127.0, 127.4, 128.8, 129.1, 159.6 (both isomers); 168.7 (C-2, both isomers); 173.1, 174.6 ($-CO_2Et$, both isomers). ms *m/z*: 457 (M^+), 358 (M^+- 99). Anal. Calcd for $C_{26}H_{35}NO_6$: C, 68.25; H, 7.71; N, 3.06. Found: C, 68.37; H, 7.66; N, 2.99.

Diels-Alder adduct of 10a and EA (26/27/28/29): A solution of 10a (0.50 g, 1.82 mmol) and EA (0.40 g, 4.0 mmol) in toluene (8 ml)

was refluxed for 26 h. The solvent was removed under *vacuo* and the residue purified by column chromatography on silica gel (eluent: EtOAc/hexane, in a 1:4 ratio) affording a viscous liquid consisting in a mixture of *trans* diastereo/regioisomers in 5:4:2:1.2 ratio. IR (CCl_4) ν 1721 (br), 1590, 1493, 1380 cm^{-1}; ^1H NMR δ 0.87-1.07 (m, 9H, 3 x $-CH_3$, three isomers), 1.96 (t, J = 7.1, $-CH_3$, one isomer) 1.22-1.30 (m, 4H, all isomers), 1.76-2.25 (series of m, 16H, all isomers), 2.59-4.22 (series of m, 16H, all isomers), 4.77 (d, J = 2.3, 1H, H-4, one isomer), 4.80 (d, J = 2.5, 1H, H-4, one isomer), 4.85 (d, J = 1.9, 1H, H-4, one isomer), 4.88 (d, J = 2.2, 1H, H-4, one isomer), 5.86-6.03 (series of m, 8H, olefinic, all isomers), 7.00-7.04 (m, 4H, arom, all isomers), 7.22-7.35 (m, 36H, arom, all isomers); ^{13}C NMR δ 13.9, 14.0, 14.1, 14.2, 22.1, 22.3, 23.7, 24.0, 25.3, 27.8, 29.7, 35.3, 36.0, 36.4, 36.5, 37.1, 42.1, 42.3, 43.5, 43.6, 58.5, 59.5, 60.2, 60.6, 60.7, 61.4, 61.7, 62.2, 63.1, 64.0, 64.3, 116.9, 117.0, 117.1, 118.5, 123.7, 123.8, 124.0, 124.9, 125.1, 125.2, 125.5, 125.8, 126.0, 126.2, 126.5, 127.4, 128.4, 128.6, 128.9, 129.0, 129.1, 129.2, 130.0, 135.5, 135.9, 137.5, 137.6, 137.7, 137.8; 166.1, 166.2, 166.38, 166.42, (C-2, all isomers); 173.0, 173.1, 174.4, 175.2 ($-CO_2Et$, all isomers). ms *m/z*: 375 (M^+), 256 (M^+- Ph-N=C=O). Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.60; H, 6.78; N, 3.66.

Diels-Alder adduct of 12/13d with EA (30/31/32/33): A solution of **12/13d** (0.3 g, 1.06 mmol) and EA (0.25 g, 2.50 mmol) in toluene

(5 ml) was refluxed for 30 h. An identical workup as employed above afforded 0.35 g (86%) of a viscous liquid consisting in a mixture of four *cis* diastereo/regioisomers in 11:4:2.5:1 ratio; IR (CCl_4) ν 1725 (br), 1589, 1489, 1381 cm^{-1}. ^1H NMR δ 0.85-1.47 (series of m, 40H, all isomers), 1.71-2.32 (series of m, 16H, all isomers), 2.49-2.90 (series of m, 10H), 3.35-3.57 (m, 7H, all isomers), 3.61 (dd, J = 10.6 and 5.2, 1H, H-3, one isomer), 3.79-3.90 (m, 14H; consisting in 12H for four $-OCH_3$ signals at δ 3.81, 3.82, 3.84, and 3.86 as singlets), 4.02-4.27 (series of m, 8H, all isomers), 4.68 (d, J = 5.2, 1H, H-4, one isomer), 4.72 (d, J = 5.1, 1H, H-4, one isomer), 4.77 (unresolved d, J = 5.2, 1H, H-4, one isomer), 4.79 (unresolved d, J = 5.3, 1H, H-4, one isomer), 5.70-5.75 (m, 4H, olefinic), 5.85-5.95 (m, 4H, olefinic), 6.89-6.94 (m, 8H, arom, merged doublets for all isomers, $J \approx 8.7$), 7.20-7.24 (m, 8H, arom; merged doublets for all isomers, $J \approx 8.7$). ^{13}C NMR δ 13.6, 14.0, 14.1, 14.2, 14.3, 20.1, 20.2, 20.9, 21.7, 21.9, 22.8, 23.2, 24.1, 29.51, 29.55, 29.64, 29.7, 32.1, 33.5, 39.5, 39.6, 39.8, 40.7, 55.2, 55.3, 56.6, 57.5, 57.6, 57.9, 58.0, 58.6, 58.8, 60.0, 60.1, 60.6, 61.3, 113.9, 114.0, 114.1, 114.2, 114.29, 114.34, 117.4, 126.0, 126.3, 127.0, 127.1, 127.4, 127.5, 127.7, 128.1, 128.3, 128.6, 128.9, 132.0, 133.6, 135.4, 136.3, 159.6, 159.7; 169.3, 169.6, (C-2, all isomers); 173.7, 174.5, 174.9, (CO_2Et, all isomers). ms *m/z*: 385 (M^+), 286 (M^+- n-Bu-N=C=O). Anal. Calcd for $C_{23}H_{31}NO_4$: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.57; H, 8.20; N, 3.74.

References

1. Howie, J. *Br. Med. J.* 1986, *293*, 158. Fletcher, C. *Br. Med. J.*, 1990, *300*, 1289. See also : *The Organic Chemistry of β-Lactam Antibiotics*; Georg, G.I., Ed.; VCH : Weinheim, 1993. *Antibiotic and Antiviral Compounds; Chemical Synthesis and Modification*; Krohn, K., Kirst, H.A., Maag, H., Eds VCH : Weinheim, 1994.
2. For reviews on β-lactam antibiotics, see: (a) *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R.B.; Gorman, M. Eds. Academic Press: New York, 1982-1983; Vols. 1-3. (b) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Brown, A.G.; Roberts, S.M. Eds. The Royal Society of Chemistry: Burlington House; London, 1984. (c) *Topics in Antibiotic Chemistry*; Sammes, P.G. Ed. Ellis Horwood: New York, 1980; Vols. 3-4. (d) Southgate, R.; Elson, S. In *Progress in the Chemistry of Organic Natural Products*; Herz, W.; Grisebach, H.; Kirby, G.W.; Tamm, Ch., Eds. Springer-Verlag: New York, 1985; Vol. 47, pp 1-106. (e) Durckheimer, W.; Blumbach, J.; Lattrell, R.; Sheunemann, K.H. *Angew. Chem., Int. Ed. Engl.*, 1985, *24*, 180. (f) Koppel, G.A. In *Small Ring Heterocycles*: Hassner, A. Ed. John Wiley: New York, 1983; Part 2, pp 248-301; Brown, A.G. *Pure Appl. Chemistry*, 1987, *59*, 475.
3. Davies, J. *Science* 1994, *264*, 375. Spratt, B.G. *Science* 1994, *264*, 388. Cohen, M.L. *Science* 1992, 257.

4. Durckheimer, W.; Fischer, G.; Lattrell, R. In *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Bentley, P.H., Southgate, R. Eds.; RSC: Cambridge, 1989, p 49.

5. Palomo, C. In *Recent Advances in the Chemical Synthesis of Antibiotics*; Lukacs, G.; Ohno, M. Eds.; Springer-Verlag: Berlin, 1990; p 567.

6. Wise, R. *Lancet*, 1987, 1251. See also: Perrone, E.; Franceschi, G. Ref 4, p 613.

7. Shibahara, S.; Okonogi, T.; Murai, Y.; Kudo, T.; Yoshida, T.; Kondo, S.; Christrensen, B.G. *J. Antibiot.* 1988, *41*, 1154. Guzzo, P.R.; Miller, M.J. *J. Org. Chem.* 1994, *59*, 4862 and references cited therein.

8. Miller, M.J. *Acc. Chem. Res.* 1986, *19*, 49. Firestone, R.A.; Baker, P.L.; Pisano, M.; Ashe, B.M.; Dahlgreen, M.M.E. *Tetrahedron*, 1990, *46*, 2255. Baker, G.; Giacommini, D.; Panunzio, M.; Martelli, G.; Spunta, G. *Tetrahedron lett.* 1987, *28*, 3593. Baldwin, J.E.; Norriss, W.J.; Freeman, R.T.; Bradley, M.; Adlington, R.M.; Long-Fox, S.; Schofield, C.J. *J. Chem. Soc., Chem. Commun.* 1988, 1128. Marchand-Brynaert, J.; Vanlierde, H.; Ghosez, L. *Bull. Soc. Chim. Belg.* 1988, *97*, 1081. See also: Ren, X-F; Turos, E., *J. Org. Chem.* 1994, *59*, 5858.

9. Aoki, H.; Sakai, H.; Koshaka, M.; Konomi, T.; Hosada, J.; Kobochi, Y.; Iguchi, E.; Imanaka, H. *J. Antibiot.* 1976, *29*, 492. Krook, M.A.; Miller, M.J. *J. Org. Chem.*, 1985, *50*, 1126.

10. Elson, S.W. In *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Bentley, P.H., Southgate, R., Eds.; RSC: London, 1989, p 303.

11. Bateson, J.H.; Guest, A.W. *Tetrahedron Lett.* **1993**, *34*, 1799.

12. Perboni, A.; Tamburini, B.; Rossi, T.; Donati, D.; Tarzia, G.; Gaviraghi, G. In *Recent Advances in the Chemistry of Anti-Infective Agents*; Bentley, P.H., Ponsford, R., Eds.; RSC: Cambridge, 1993; p 21.

13. For some examples of variations on β-lactam ring see: Wojkowski, P.W.; Dolfinji, J.E.; Kocy, O.; Cimarusti, C.M. *J. Am. Chem. Soc.* **1975**, *97*, 5628. Agathocleous, D; Cox, G.; Page, M.I. *Tetrahedron Lett.* **1986**, *27*, 1631. Cainelli, G.; Giacommini, D.; Panunzio, M.; Martelli, G.; Spunta, G. *Tetrahedron lett.* **1987**, *28*, 3593. Baldwin, J.E.; Norriss, W.J.; Freeman, R.T.; Bradley, M.; Adlington, R.M.; Long-Fox, S.; Schofield, C.J. *J. Chem. Soc., Chem. Commun.* **1988**, 1128. Marchand-Brynaert, J.; Vanlierde, H.; Ghosez, L. *Bull. Soc. Chim. Belg.* **1988**, *97*, 1081. See also: Ren, X-F; Turos, E., *J. Org. Chem.* **1994**, *59*, 5858.

14. Page, M.I. *Acc. Chem. Res.*, **1984**, *17*, 144.

15. (a) Palomo, C.; Aizpurua, J.M.; Urchegui, R.; Iturburu, M.; de Retana, A.O.; Cuevas, C. *J. Org. Chem.*, **1991**, *56*, 2244. (b) Manhas, M.S.; Ghosh, M.; Bose, A.K. *J. Org. Chem.*, **1990**, *55*, 575. (c) van der Veen, J.M.; Bari, S.S.; Krishnan, L.; Manhas, M.S.; Bose, A.K. *J. Org. Chem.*, **1989**, *54*, 5758.

(d) Palomo, C.; Cossio, F.P.; Arrieta, A.; Odriozola, J.M.; Oiarbide, M.; Ontoria, J.M. *J. Org. Chem.*, **1989**, *54*, 5736.

16. Arrastia, I.; Arrieta, A.; Ugalde, J.M.; Cossio, F.P.; Lecea, B. *Tetrahedron Lett.*, **1994**, *35*, 7825.

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

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

19. Boger, D.L.; Weinreb, S.M., *"Hetero Diels-Alder Methodology in Organic Synthesis"*, Academic Press, New York, 1987.

20. Staudinger, H. *Liebigs Ann. Chem.* **1907**, *365*, 51.

21. For literature survery on synthesis of 3-amino-2-azetidinones see: van der Steen, F.H.; van Koten, G. *Tetrahedron*, **1991**, *47*, 7503 and references therein.

22. Vanderhaeghe, H.; Thomas, J. *J. Med. Chem.* **1975**, *18*, 486.

23. Bachi, M.D.; Sarron, S.; Vaya, J. *J. Chem. Soc., Perkin Trans.1*, **1980**, 2228.

24. Firestone, R.A.; Maciejewicz, N.S.; Christensen, B.G. *J. Org. Chem.*, **1974**, *39*, 3384.

25. Edwards, J.A.; Guzman, A.; Johnson, R.; Beeby, P.J.; Fried, J.H. *Tetrahedron Lett.* **1974**, 2031.

26. Hashimoto, T.; Watanabe, T.; Kawano, Y.; Tanaka, T.; Miyadera, T. *Chem. Pharm. Bull.* **1980**, *28*, 2980.

27. Kamia, T.; Oku, T.; Nakaguchi, O.; Takeno, H.; Hashimoto, M.; *Tetrahedron Lett.* **1978**, 5119.

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

29. Ishibashi, H.; Kameoka, C.; Kodama, K.; Ikeda, M. *Tetrahedron*, **1996**, *52*, 489 and references therein.

30. For review on the synthesis of PS-5 and related compounds see: Polomo, C. In *Recent Progress in the Chemical Synthesis of Antibiotics*; Lukacs, G.; Ohno, M. Ed.; Springer-Verlag: Berlin-Heidelberg, **1990**; pp 565-612.

31. Berks, A.H. *Tetrahedron*, **1996**, *52*, 331 and references cited therein.

32. (a) Kametani, T.; Honda, T.; Nakayama, A.; Fukumoto, K. *Heterocycles* **1980**, *14*, 1967. (b) Kametani, T.; Fukumoto, K.; Ihara, M. *Heterocycles*, **1982**, *17*, 496.

33. (a) Buynak, J.D.; Rao, M.N.; Pajouhesh, H.; Chandrasekaran, R.Y.; Finn, K.; deMeester, P.; Chu, S.C. *J. Org. Chem.* **1985**, *50*, 4245 (b) Buynak, J.D.; Rao, M.N.; Chandrasekran, R.Y.; Haley, E.; deMeester, P.; Chu, S.C. *Tetrahedron Lett.* **1985**,

26, 5001. (c) Buynak, J.D.; Narayana Rao, M. *J. Org. Chem.* **1986**, *51*, 1571 (d) Buynak, J.D.; Mathew, J.; Narayana Rao, M; Haley, E.; George, C.; Sriwardane, U. *J. Chem. Soc., Chem. Commun.* **1887**, 735.

34. (a) Fetter, J.; Lempert, K.; Gigur, T.; Nyitrai, J.; Kajtar-Peredy, M.; Siming, G.; Hornyak, G.; Doleschall, G. *J. Chem. Soc., Perking Trans.1* **1986**, 221. (b) Fetter, J.; Lempert, K.; Kajtar-Peredy, M.; Simig, G.; Hornyak, G. *J. Chem. Soc., perkin 1*, **1986**, 1453. (c) Fetter, J. Lempert, K.; Horvath, Z.; Kajtar-Peredy, M.; Simig, G.; Hornyak, G. *J. Chem. Res.* **1985** (S), 368.

35. Menard, M.; Banville, J.; Martel, A.; Desiderio, J.; Fung-Tome, J.; Partyaka, R.A. In *Recent Advances in the Chemistry of Anti-Infective Agents*; Bentley, P.H., Ponsford, R.; Eds.; *The royal Society of Chemistry*: Cambridge, **1993**; pp 3-20.

36. Colombo, M.; Crungola, A.; Franceschi, G.; Lombordi, P. U.K. Patent Appl. GB 2144419, Mar. 3, 1985 (Derwent WPI 85-038254).

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

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

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

40. Ohshiro, Y.; Komatsu, M.; Uesaka, M, Agawa, T. *Heterocycles*, **1984**, *22*, 549.

41. Komatsu, M.; Ogawa, H.; Mohri, M.; Ohshiro, Y. *Tetrahedron Lett.* **1990**, *31*, 3627.

42. Sunagawa, M.; Matsumua, H.; Enaomoto, M.; Inoue, T.; Sasaki, A. *Chem. Pharm. Bull.* **1991**, *39*, 1931.

43. (a) Sharma, A.K.; Mahajan, M.P. *Heterocycles*, **1995**, *40*, 787. (b) Dey, P.D.; Sharma, A.K.; Rai, S.N.; Mahajan, M.P. *Tetrahedron*, **1995**, *51*, 7459.

44. (a) Ren, X-F. Turos, E. *J. Org. Chem.* **1994**, *59*, 5858. (b) Ren, X-F.; Turos, E.; Lake, C.H.; Churchill, M.R. *J. Org. Chem.*, **1995**, *60*, 6468.

44. Taing, M.; Moore, H.,W.; *J. Org. Chem.* **1996**, *61*, 329.

45. (a) Sun, L.; Liebeskind, L.S. *J. Org. Chem.* **1995**, *60*, 8194. (b) Birchler, A.G.; Liu, F.; Liebeskind, L.S. *J. Org. Chem.* **1994**, *59*, 7737.

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

47. Sharma, A.K.; Mazumdar, S.N.; Mahajan, M.P. *J. Org. Chem.*, **1996**, *61*, 5506.

CHAPTER—III

Unusual [3+2] Cycloaddition Reactions of α-Nitrosostyrenes with various 1,3-Diaza-1,3-Butadienes and Imines

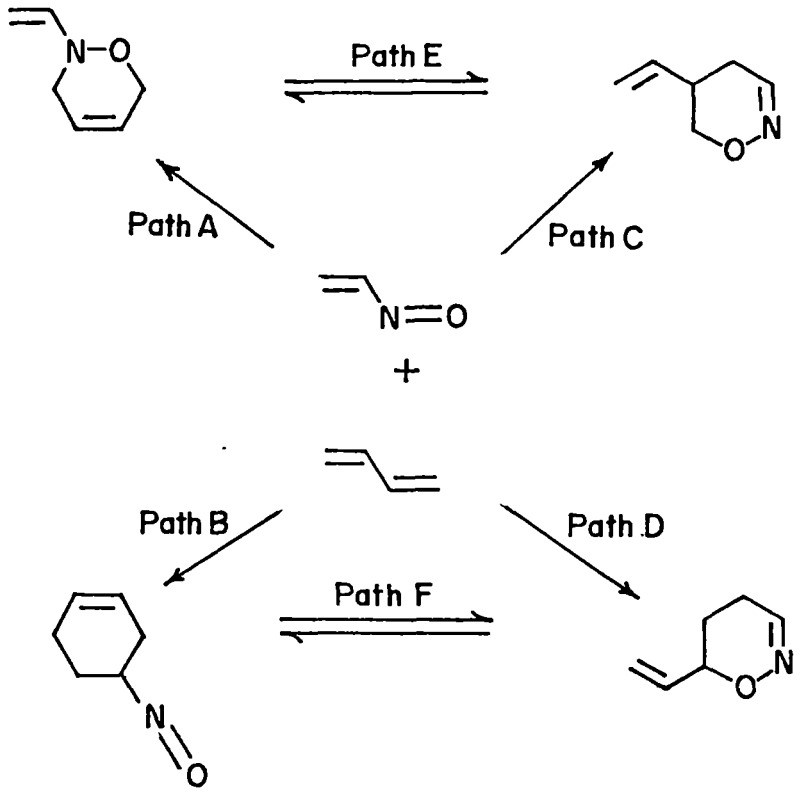
Introduction

Diels-Alder cycloaddition reactions in which a -N=O group participates as a 2π component have been extensively exploited in cycloaddition reactions.[1] The nitrosocarbonyl compounds,[2] nitroso-imines,[3] and nitrosyl cyanide[4] readily undergo Diels-Alder cyloadditions with dienes. The α-nitrosoalkenes form another group of extremely reactive intermediates which have successfully been trapped in Diels-Alder reactions.[5] A number of methods to obtain conjugated nitrosoalkenes are available of which, by far, the most important are the dehydrochlorination of α-chloroaldoximes or ketooximes and the addition of nitrosyl chloride to alkenes.[5-7] The nitrosoalkenes are in general unstable, but can be detected spectroscopically or chemically

trapped in solution and are isolable only if substituted by bulky alkyl[8] or aryl[9] groups. They are synthetically useful species either as a Michael acceptor[5,6] or as one of the components in cycloaddition with an unsaturated substrate[5,6,10] and usually undergo fragmentation through intramolecular condensation in the absence of trapping agents.[5,6]

Although, nitrosoalkenes are capable of acting either as heterodienes or as nitrosodienophiles, their reactivity is critically dependent on their structure. In general, if the nitrosoalkene system contains β-substituents, the compounds react as dienophiles and if there is no β-substituent, the system prefers to act as 4π component in Diels-Alder reactions with dienophiles.[6,11,12] [2+2] Cycloadditions of nitrosoalkenes with alkenes are rare and are usually observed only if both components are highly halogenated or if the alkene is a ketene.[13] The most commonly encountered are [4+2] cycloadditions, especially with dienes. The various possible thermally allowed reactions between α-nitrosoalkene and a diene creating paths (A-D)[14] and interconverting paths (E,F) forming the dihydro-oxazines and cyclohexenes derived from nitrosoethylene and butadiene are shown in Scheme-1. A more complex set of regio- and stereo-isomers arise if either the nitrosoalkene or the diene is substituted.

Path A has been clearly established in the formation of the unstable oxazine **1**, which isomerises to **2**.[11] Path D must be followed to give the oxazines from simple alkenes, e.g. (3) from oct-1-ene;[15] it is likely also followed for the oxazines from a



(3,3) - Sigmatropic rearrangement

Scheme - 1

variety of cyclic dienes and electron rich heterocycles, including furans, pyrroles and indoles,[5,14,15-19] though path B followed by [3,3] sigmatropic rearrangement (path F) cannot be ruled out for some of these reactions. There is no unequivocal evidence for the occurance of path C in any reaction.

In the first reported synthesis of the dihydro-oxazines from furans or cyclopentadiene with nitrosoalkenes the pathway sequence B,F was suggested as plausible, for example, from furan and nitrosostyrene to 4 and finally to 6,[20] though it was later

1

(2)

(3)

(4) R = H
(5) R = Me

(6)

(7) X = NCOR
(8) X = O

(9) X = NCOR
(10) X = O

discounted on the basis of more extensive studies.[5,14] In case of the reaction of cyclopentadiene with azidocarbonyl[21] and nitroso carbonyl compounds,[22] the heterosystem functioned as a dienophile to give the adducts 7 and 8 which could then be thermally isomerized to 9 and 10.

The CNDO/2[23] calculations of nitrosoalkenes and their comparison with butadienes, revealed that major interaction exists between HOMO of butadiene and LUMO of nitrosoethylene i.e. former acts as a donor and later as an acceptor. Thus, the most favourable paths in Scheme-1 appear to be involving an interaction between C-2 of nitrosoethylene and C-1 of butadiene i.e. path B and D.[14] The critical examination of the orbital energies further revealed that nitrosoethylene behaves as an ideal 4π system.[24] This was subsequently experimentally verified

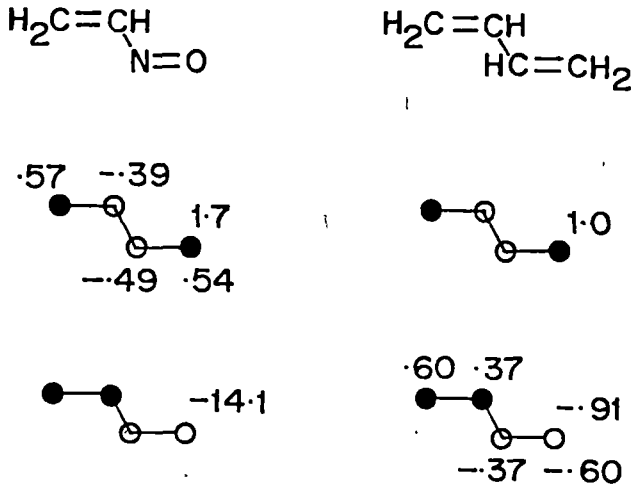
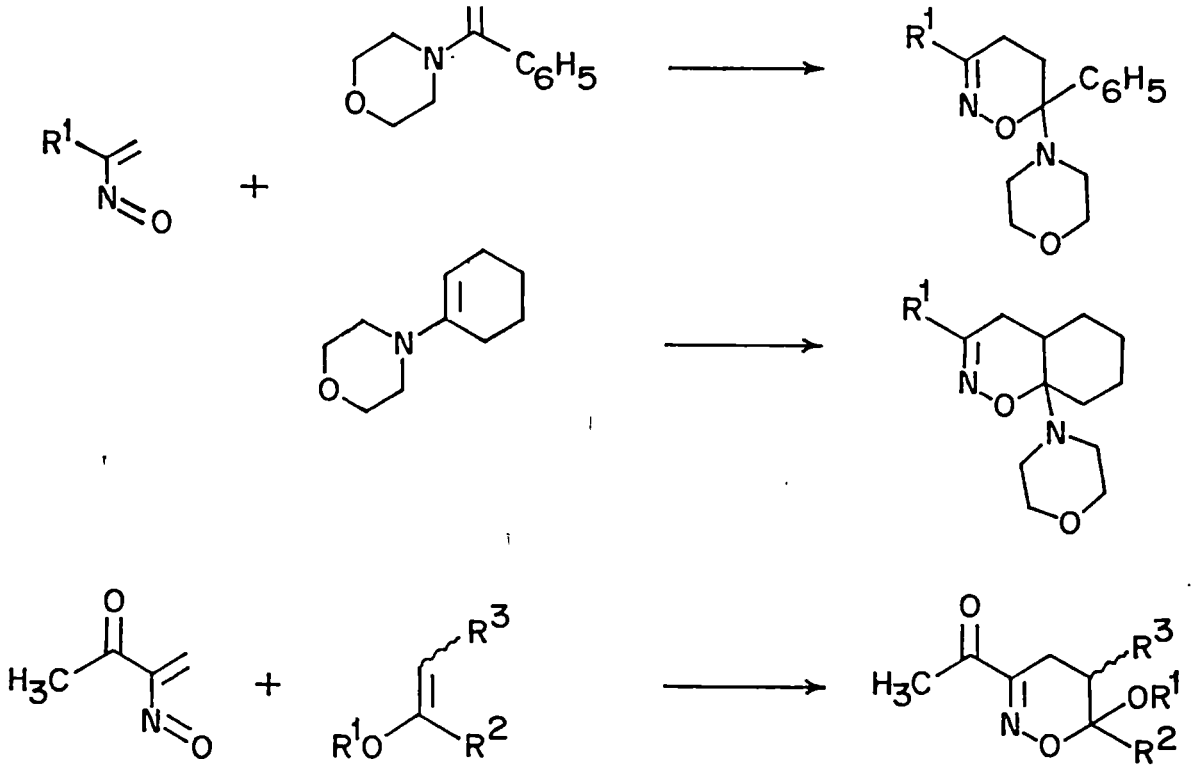


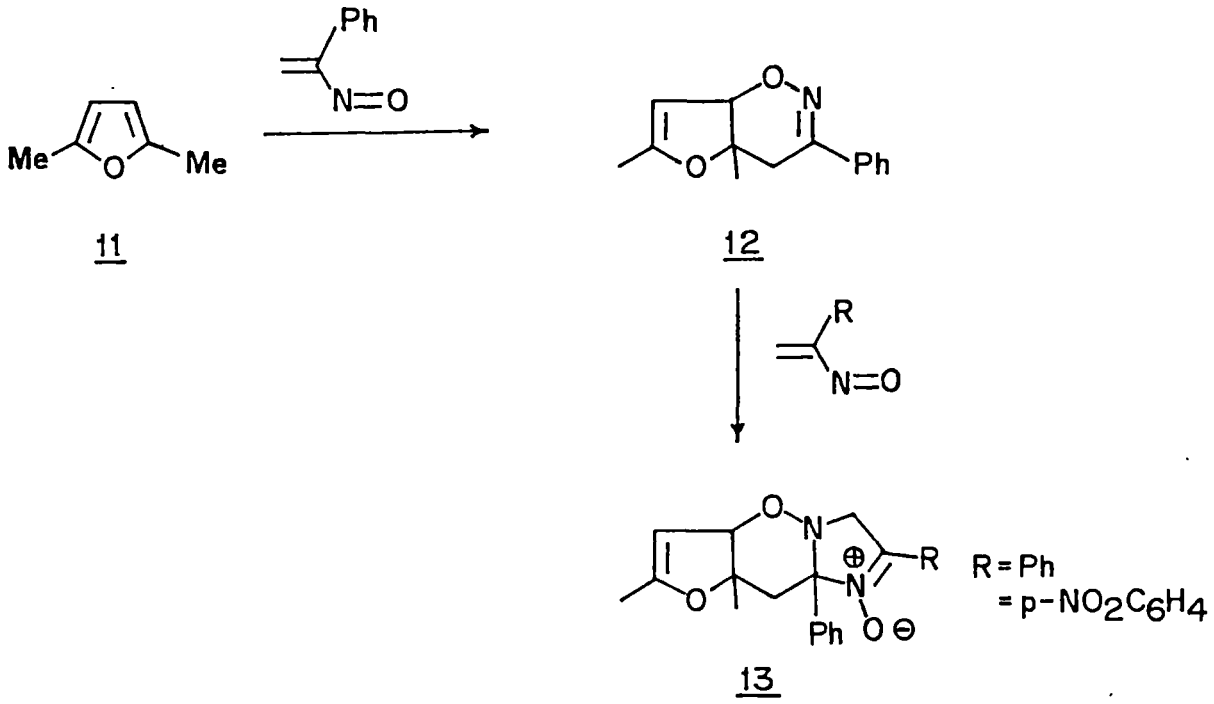
Figure : Frontier Orbital Energies (eV) and coefficients for nitrosoethylene and butadiene

by carrying out the reactions of nitrsoalkenes with carbon-carbon double bonds of alkenes and dienes. It has been observed that the nitrosoalkenes add to simple alkenes in a concerted manner and to electron rich dienophiles e.g. enamines,[12,14,18] enol ethers[25] etc. in a stepwise manner *via* zwitterionic intermediate (Scheme 2).



Scheme-2

The reports concerning the cycloadditions of nitrosoalkenes with carbon-nitrogen double bonds are very rare. Mackay et al.[26-28] investigated the reactions of 2,5-dimethylfuran 11 with 1 equivalent of nitrosostyrene and isolated the oxazine 12 along



Scheme-3

with the minor *bis* adduct the nitrone 13 (Scheme 3). The products 12 and 13 are formed by the successive cycloaddition reactions of nitrosostyrene with C=C and C=N double bond in a [4+2] and [3+2] manner, respectively. They further investigated[28] the reactions of cyclopentoxazine 14 with nitrosoalkenes and reported the formation of oxazine 15 and nitrone 16 *via* a competetion between [4+2] and [3+2] cycloaddition pathways (Scheme 4). The relative proportions of oxazine 15 and nitrone 16 are given in Table-1. The formation of oxazine 16 in higher proportions was explained by the argument that as R gets more electrons withdrawing, the *cisoid* form of nitrosoalkenes was preferred in order to avoid repulsive

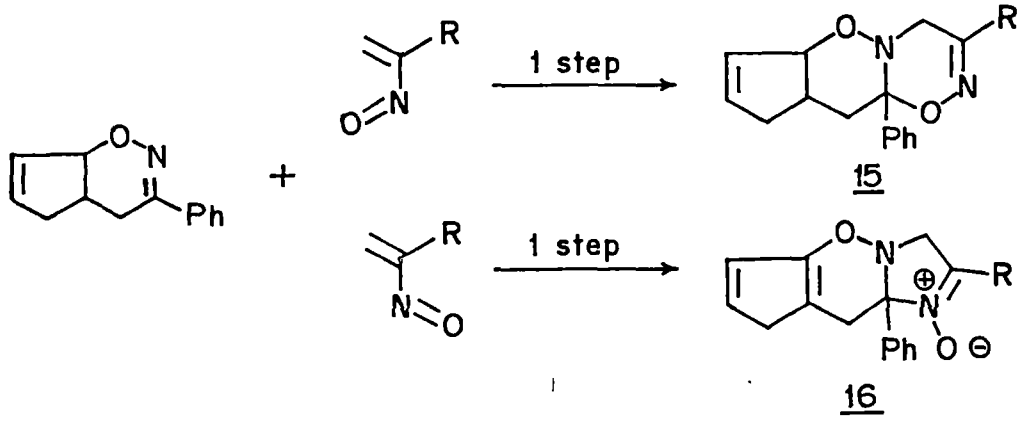


Table-1

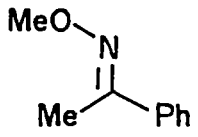
R	Compound	Ratio
Ph	16a : 15a	>10 : 1
p-$NO_2C_6H_4$	16b : 15b	4·1 : 1
CHO	16c : 15c	0·38 : 1
Ac	16d : 15d	<0·1 : 1

Scheme-4

interaction between the strong dipoles of the system. Mackay et al.[28] also reported that the nitrosoalkenes did not react with the carbon-nitrogen double bond of 17, 18, 19, 20, 21 and 22. From the failure of these reactions, it was concluded that the primary requirement for such reactions are (i) oxazines oxygen and (ii) an alkene function allylic to this oxygen in a rigid bicyclic system.

Keeping in view the very few reports concerning the cycloaddition reactions of carbon-nitrogen double bonds with nitrosoalkenes and the reported structural limitations upon the carbon-nitrogen double bond systems for carrying out such

cycloaddition reactions the investigations concerning the cycloaddition reactions of 1,3-diaza-1,3-butadienes with nitrosoalkenes were initiated in our laboratories. The object of these investigations was also to understand the nature of cycloaddition pathway followed, the products formed in these reactions and to compare the dienic properties of 1,3-diaza-1,3-butadienes with those of nitrosoalkenes. Hence, the reactions of nitrosoalkenes with 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes 23 were investigated and unusual [3+2] cycloadducts, the nitrones 24 were isolated in good yields[29] (Scheme 5). In order to generalise these cycloaddition reactions with various carbon-nitrogen double bonds, the reactions of nitrosoalkenes with various 1,3-diaza-1,3-butadienes and polarised imines (amidines) have been investigated and the results of these investigations are discussed in this chapter.



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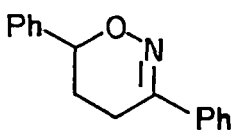

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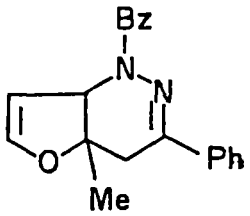

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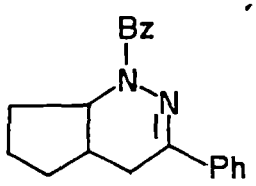

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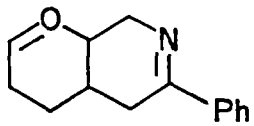

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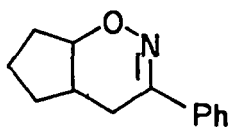

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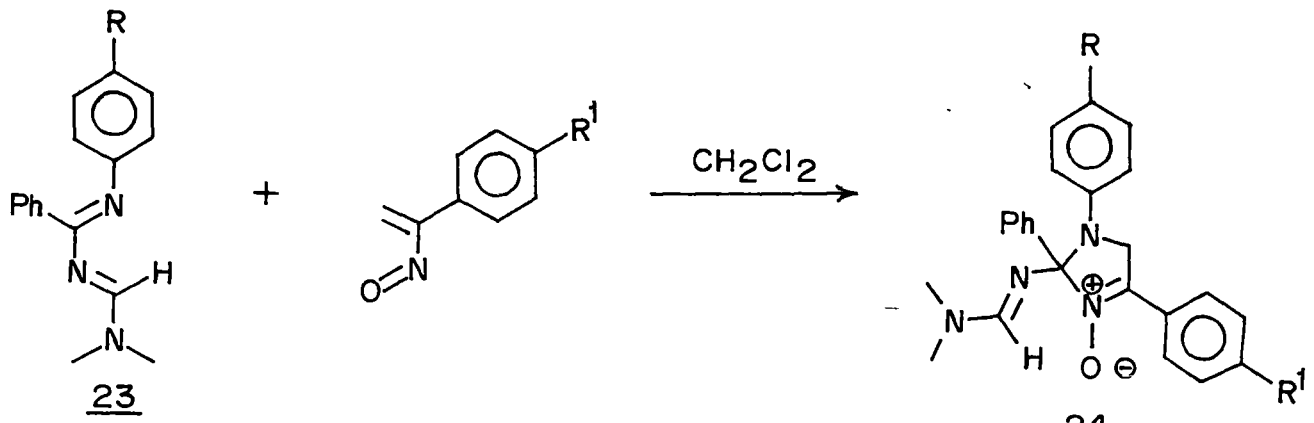


23 + 24

24, a. R = R¹ = H
b. R = CH₃, R¹ = H
c. R = Cl, R¹ = H
d. R = Br, R¹ = H
e. R = H, R¹ = CH₃
f. R = R¹ = CH₃
g. R = Cl, R¹ = CH₃
h. R = Br, R¹ = CH₃

Scheme-5

Results and Discussion

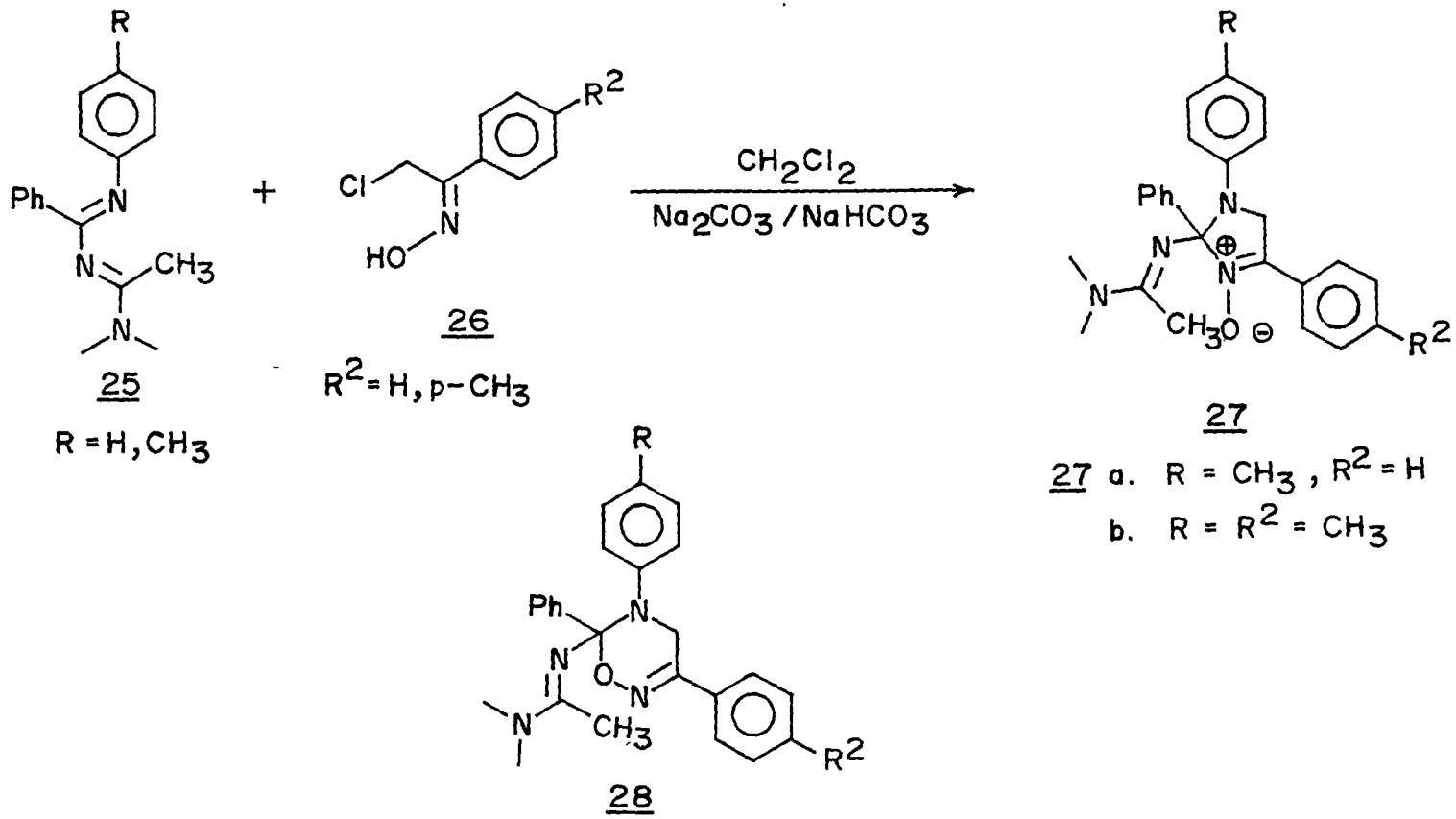
Treatment of 1,3-diaza-1,3-butadienes **23** with α-nitrosostyrenes, generated *in situ* from α-chlorooximes and sodium carbonate, resulted in very good yields (76-90%) of the products which were characterised as 1,4-diaryl-2-*N'*-(*N,N*-dimethyl formamidino)-2-phenyl-Δ^3-imidazoline-3-oxides **24** (Scheme 5) on the basis of analytical data and spectral evidence.[30]

Nitrones have been reported to be highly valuable synthetic intermediates and excellent spin trapping reagents. They have proved to be very useful class of 1,3-dipoles. Since, they are relatively stable and afford synthetically quite flexible nitrogen containing molecular assembles, they have also been utilised for the synthesis of various nitrogen containing biologically active compounds.[31] The isoxazolidine obtained by the 1,3-dipolar cycloaddition of a nitrone to C=C double bond is a versatile precursor for the synthesis of natural products.[31] In a similar fashion, the heterocyclic based nitrones can provide a flexible entry into a range of heterocyclic targets. There are few reports concerning the preparation of such cyclic nitrones [32-35] and all of them have been exploited with a varying degree of success. Keeping in view, the synthetic potential of cyclic nitrones and the observed [3+2] cycloaddition mode in case of 1,3-diaza-1,3-butadienes **23** to yield such nitrones, it was thought worthwhile to explore the reactions of various other 1,3-diaza-1,3-butadienes and amidines with nitrosoalkenes.

Thus, the reactions of 1-aryl-4-dimethylamino-4-methyl-2-

phenyl-1,3-diaza-1,3-butadienes 25 with nitrosoalkenes, generated *in situ* from α-halooximes 26 of acetophenones and sodium carbonate/sodium hydrogen carbonate, in methylene chloride, resulted in very good yields (78-93%) of cyclic nitrones 27 (Scheme 6). The products were characterised as 1,4-diaryl-2-*N*'-(*N*,*N*-dimethylacetamidino)-2-phenyl-Δ^3-imidazoline-3-oxides 27 on the basis of analytical and spectral data. Their IR spectra showed strong absorptions around 1590 and 1521 cm^{-1} and *ca.* 1220 cm^{-1} ascribed to C=N and N-O of a nitrone, respectively. The nitrone 27, as apposed to the oxadiazine 28, structures for the products were supported by the ^1H NMR signals for the methylene and *ortho* phenyl protons of the nitrone ring. The former gave a singlet δ*ca.* 5.00 downfield from the position, δ *ca.* 3.50, typical of oxadiazine.[28] Similarly, the *ortho* protons of the phenyl group attached to nitrone ring resonated at δ *ca* 8.40 downfield from the corresponding signals, δ *ca.* 7.70 of typical oxazines.[36] The peaks around δ 140 and δ 160 in their ^{13}C NMR spectra were assigned to nitrone carbon and amidino carbon, respectively. Their mass spectra exhibited intense M-16 peaks diagnostic of nitrones,[28] in addition to strong M-amidino and imidazole ion peaks. The oxadiazine structure thus was clearly ruled out on the basis of the above spectral informations.

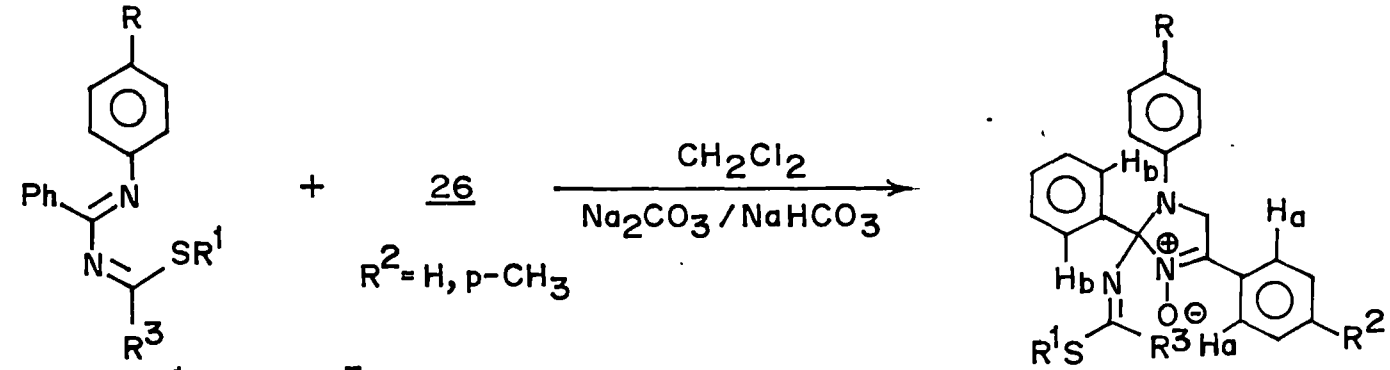
In order to have a deeper insight into such unusual regioselective [3+2] cycloadditions, and to generalise the regioselectivity pattern with polarised 1,3-diazabutadienes, the reactions of α-nitrosostyrenes were also carried out with various


R
Ph
N
N
CH3
N
25
R = H, CH3
+
Cl
R2
N
HO
26
R2 = H, p-CH3
CH2Cl2
Na2CO3 / NaHCO3
R
Ph
N
N
⊕
N
N
CH3
O ⊖
R2
27
27 a. R = CH3 , R2 = H
b. R = R2 = CH3
R
Ph
N
N
O
N
N
CH3
R2
28

Scheme-6

1-aryl-4-secondaryamino-4-alkylthio-2-phenyl-1,3-diaza-1,3-butadienes **29** having two polarising functions at 4-position. The reaction of α-nitrosoalkenes, generated *in situ* from α-halooximes, with **29**, performed under similar conditions, followed the similar regioselective [3+2] cycloaddition pathway to yield nitrones **30** in almost quantitative yields (Scheme 7). The reaction products were characterised as 1,4-diaryl-2-phenyl-2-[N-(2'-methylthio-2'-secondaryamino)imino]imidazoline-3-oxides **30** on the basis of analytical and spectral observations. Their IR spectra (KBr) showed strong absorption peaks around 1595 and 1550 cm^{-1} for -C=N and around 1225 cm^{-1} for N-O of nitrone. ^{1}H NMR spectra (90 MHz) of these nitrones exhibited a two proton multiplet centred around δ 8.50, assigned to two *ortho* phenyl protons Ha characteristic of cyclic nitrones. These spectra also showed another downfield two proton multiplet around δ 7.40 attributed to somehow deshielding of proton Hb by the carbon-nitrogen double bond of the imine functionality. In addition, methylene protons appeared as a singlet at around δ 5.00.

A general mechanism leading to the formation of nitrones **24**, **27** and **30** is outlined in scheme-8. The addition of nitrosoalkenes to C=C has been judged to be a single step[17] reaction, but is less likely to be so for addition to more polar C=N of the 1,3-diazabutadienes. Hence, the possibility of path I in these cases is ruled out. α-Nitrososstyrene has been shown to react with morpholine[37] preferentially in the *transoid* form and may also do so with weakly nucleophilic N-1, which of course is



R = H, CH; R^1 = Me, Et, R^3 = sec. anino

29

30

30. a. $R = R^2 = H, R^1 = CH_3, R^3 =$ 

b. $R = R^2 = H, R^1 = CH_3, R^3 =$ 

c. $R = R^2 = H, R^1 = CH_3, R^3 =$ 

d. $R = R^2 = H, R^1 = CH_3, R^3 =$ 

e. $R = R^1 = CH_3, R^2 = H, R^3 =$ 

f. $R = R^1 = CH_3, R^2 = H, R^3 =$ 

g. $R = R^1 = CH_3, R^2 = H, R^3 =$ 

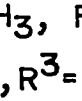
h. $R = R^1 = CH_3, R^2 = H, R^3 =$ 

i. $R = R^2 = H, R^1 = CH_2CH_3, R^3 =$ 

j. $R = R^2 = H, R^1 = CH_2CH_3, R^3 =$ 

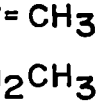
k. $R = H, R^1 = R^2 = CH_3, R^3 =$ 

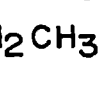
l. $R = R^1 = R^2 = CH_3, R^3 =$ 

m. $R = R^1 = R^2 = CH_3, R^3 =$ 

n. $R = R^1 = R^2 = CH_3, R^3 =$ 

o. $R = R^1 = R^2 = CH_3, R^3 =$ 

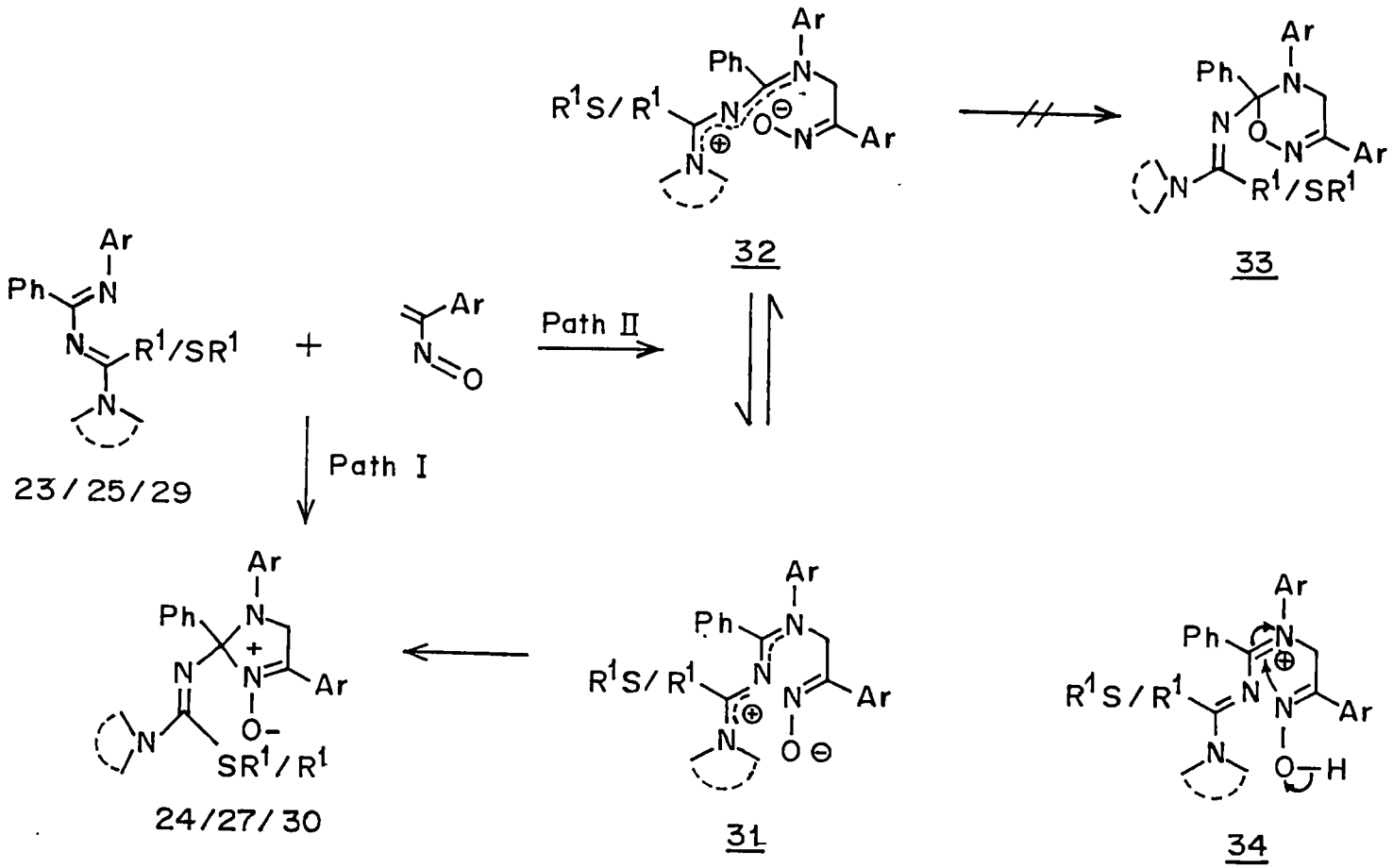
p. $R = Cl, R^1 = CH_3, R^2 = H, R^3 =$ 

q. $R = Cl, R^1 = R^2 = CH_3, R^3 =$ 

r. $R = Cl, R^1 = CH_2CH_3, R^2 = H, R^3 =$

s. $R = Cl, R^1 = CH_2CH_3, R^2 = H, R^3 =$

Scheme-7

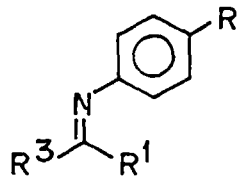


Scheme – 8

more nucleophilic as compared to N-3 of 1,3-diaza-1,3-butadienes. Hence, these reactions may follow path II leading to resonance stabilized zwitterionic intermediate **31** which explain the preferential formation of nitrones **24**, **27** and **30**. Even though, the intermediate **31** is preferred, a crossover mechanism between intermediates **31** and **32** is possible, which can lead to six membered oxadiazine ring structures **33**. The crossing over of the zwitterionic intermediate **31** to **32** perhaps is discouraged due to steric constraints as evidenced by the total absence of oxadiazines **33** as one of the possible products.

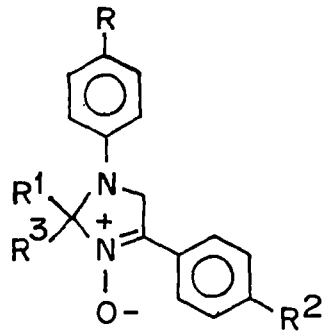
The products, nitrones, are probably the result of the formal [3+2] dipolar addition of free α-nitrostyrene in a 1,3-mode to 1,2-carbon-nitrogen double bond of the polarised 1,3-diaza-1,3-butadienes. The formation of the nitrones may also be explained by the initial formation of resonance stabilised cationic intermediates **34** *via* displacement of halide by N-1 of 1,3-diaza-1,3-butadienes, **23**, **25** and **29** from α-chloroacetophenone oxime. The intermediates **34** after possible deprotonation may cyclise resulting in nitrones **24**, **27**, and **30**. Analogies to such two-step cyclisation of α-chlorooximes are known[38] including ones to *N*-oxides,[39] but in all such cases, recognizably strong nucleophile is involved and it is unlikely that weaker nucleophiles like N-1 of imino nitrogen in present case could behave in a similar fashion. In view of the above observations, it was felt that all polarised carbon-nitrogen double bonds may perhaps behave in a similar fashion and may also add to α-

nitrosoalkenes in a similar [3+2] manner. Hence, in order to generalise the synthetic versatility of this reaction we have investigated the cycloaddition reactions of α-nitrosostyrenes with *N,N,N'*-trisubstituted amidines **35**. As expected, these reactions were also found to follow the unusual and exclusive [3+2] cycloaddition mode resulting in good yields of nitrones **36** (Scheme 9) which were characterised on the basis of analytical and spectral data. The nitrone **36b**, for example, showed a molecular ion peak at *m/z* 281 (42%) and a peak at 264 (M^+ -17, 13%); a sharp IR absorption at 1223 cm^{-1} characteristic of N^+-O^- of a nitrone and its ^1H NMR spectrum (300 MHz, Fig. 1) exhibited peaks at δ 2.66 [s, $-N(CH_3)_2$], 4.50 (dd, *J* = 14.5 and 2.1 Hz, 1H, $-CH_2-$), 4.79 (dd, *J* = 14.5 and 4.5 Hz, 1H, $-CH_2-$), 5.81 (dd, *J* = 4.5 and 2.1 Hz, 1H methine) and it also exhibited two downfield *ortho* phenyl protons (δ 8.32 - 8.35), diagnostic of nitrones. Similarly the spectral data for **36d** was also in confirmity with the assigned structure and the charastristic spectral data includes [*m/z* 397 (M^+), 381 (M^+ - 16); ν_{max} 1223 (N^+-O^-); δ_H (300 MHz, Fig. 2) 4.41 (d, *J* = 14.1 Hz, 1H, $-CH_2-$), 4.59 (d, *J* = 14.1 Hz, 1H, $-CH_2-$), a downfield doublet (δ 8.33, *J* = 8.3 Hz) for two *ortho* phenyl protons]. Their ^{13}C NMR spectra were also in perfect agreement with the assigned structures. Interestingly, ^1H NMR spectrum of **36b** indicates that two methylene protons couple to each other as well as to methine proton and appear as doublet of doublets. The corresponding coupling constants are also exhibited by the methine proton



35

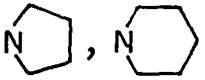
+ 26



36

R = H, CH_3

R^1 = H, Ph

R^3 = $-N(CH_3)_2$; 

35,36 a. R = R^1 = R^2 = H, R^3 = $N(CH_3)_2$

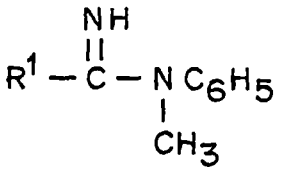
b. R = CH_3, R^1 = R^2 = H, R^3 = $N(CH_3)_2$

c. R = R^1 = H ; R^2 = CH_3, R^3 = $N(CH_3)_2$

d. R = H, R^1 = Ph, R^2 = CH_3, R^3 = 

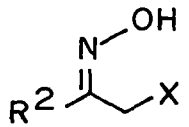
e. R = R^2 = H, R^1 = Ph, R^3 =

f. R = H, R^1 = Ph, R^2 = CH_3, R^3 = 



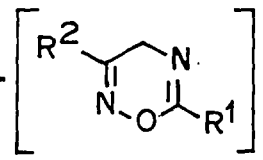
37

+

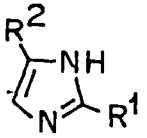


38

Iron carbonyls



39



40

Scheme – 9

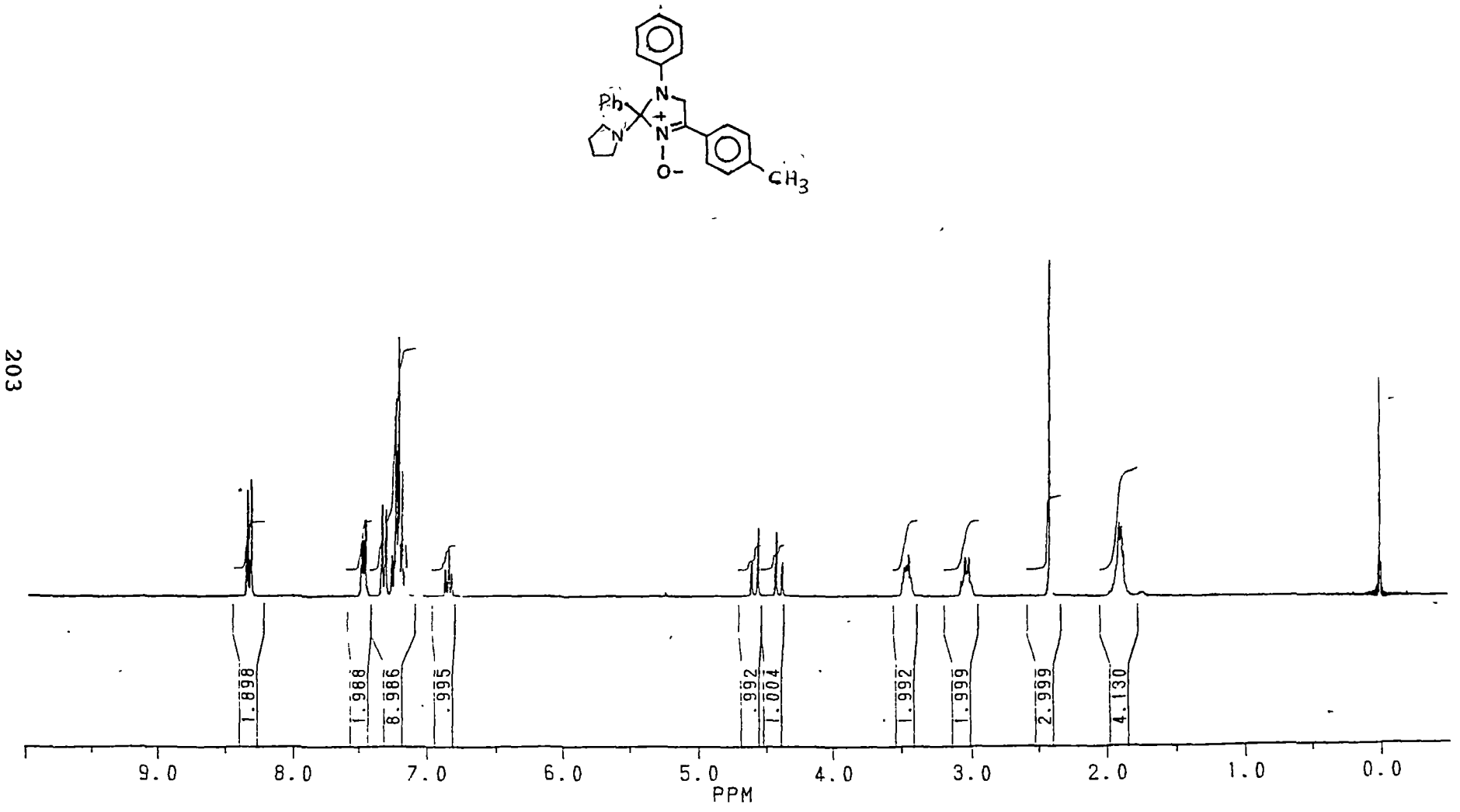


Fig. 2: 300 MHz ^{1}H NMR specturm for **36d** in $CDCl_3$

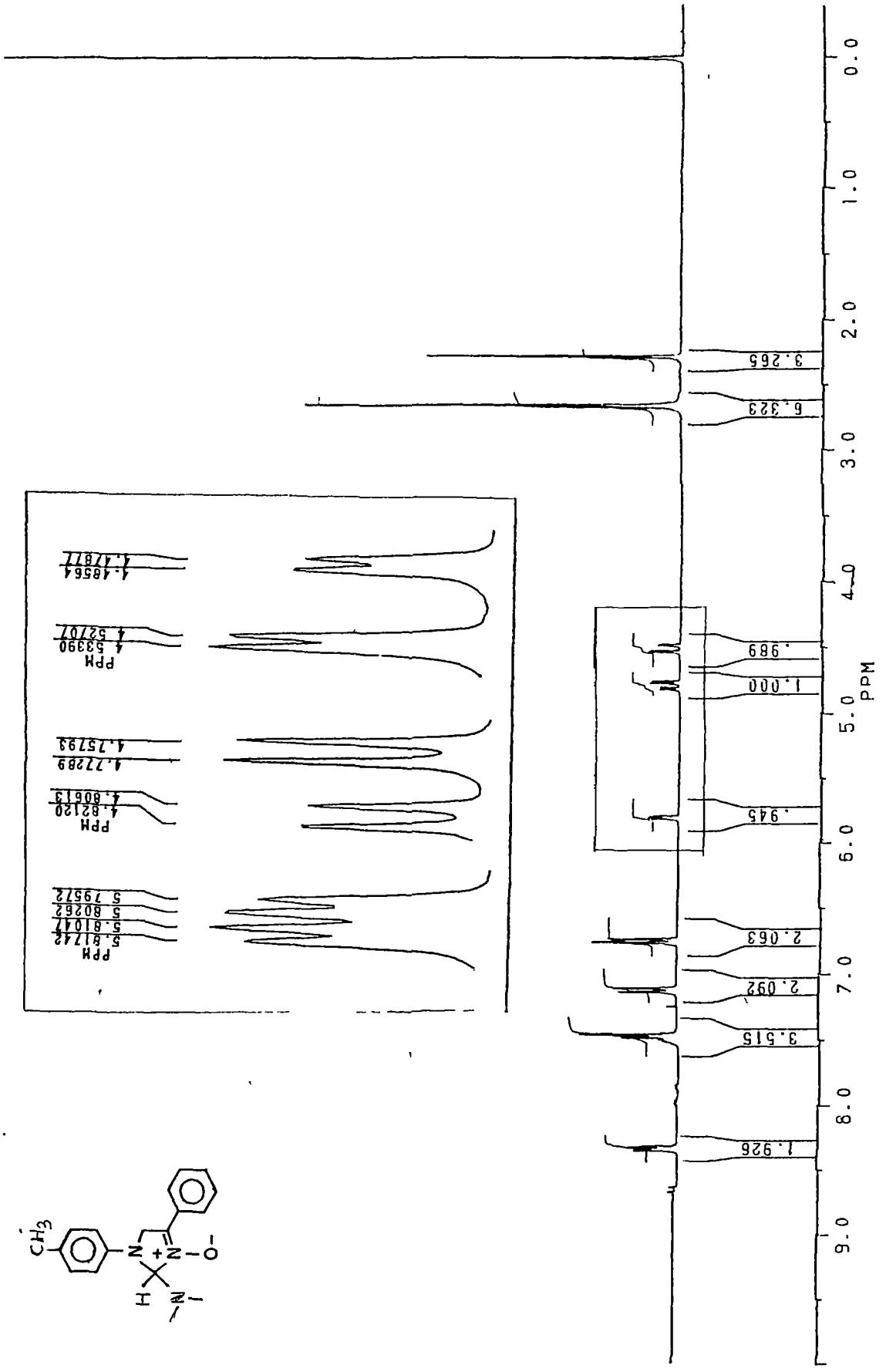


Fig. 1: 300 MHz ^{1}H NMR spectrum for **36b** in $CDCl_3$

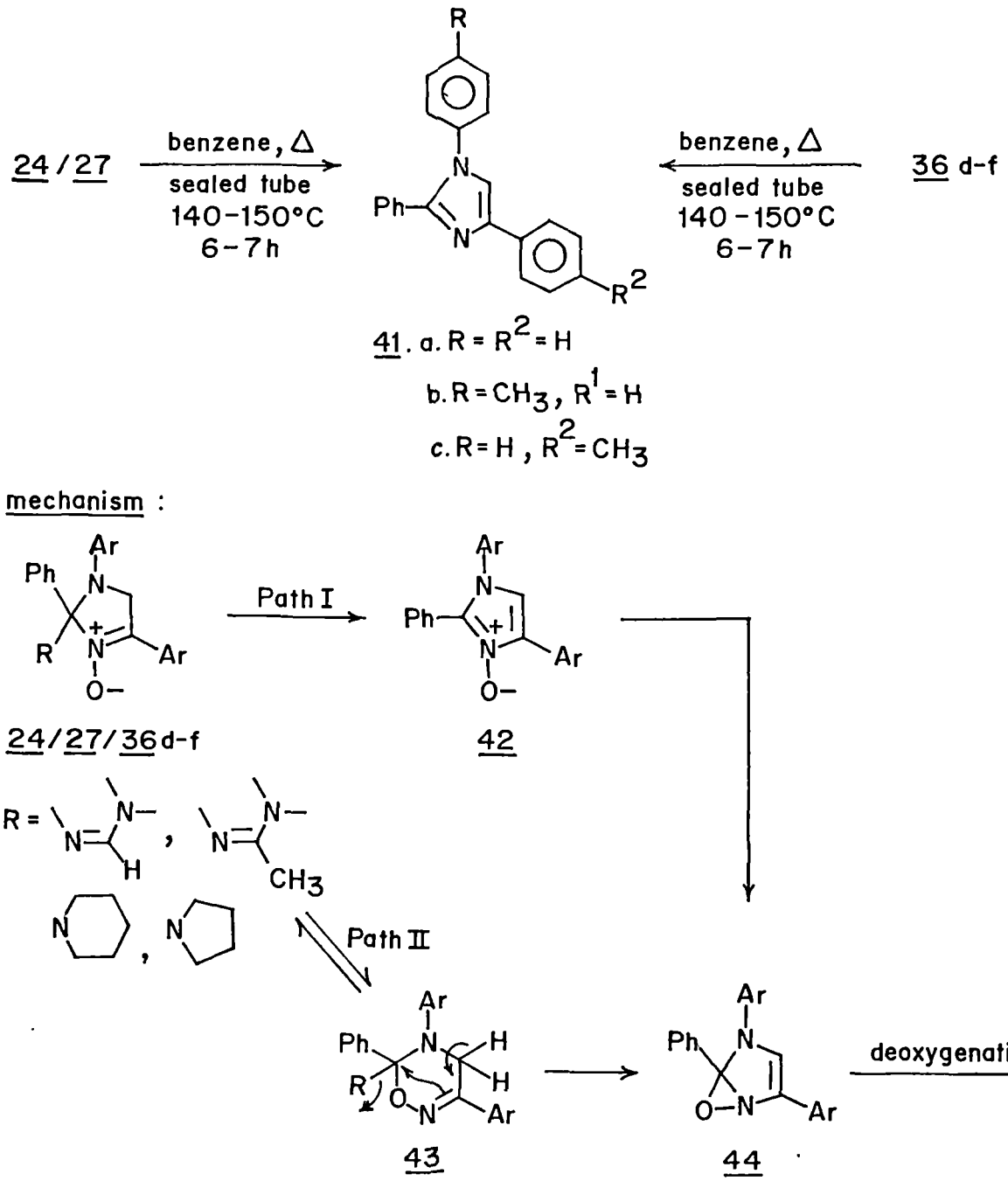
signal which couple with both methylene protons and appear as doublet of doublet. Further support for this is derived from the ^{1}H NMR spectrum of **36d** in which the two methylene protons appear as doublets instead of doublet of doublets. Contrary to the formation of nitrones in the above reactions, Nakanishi et al.[40] have reported the formation of imidazole derivatives **40**, probably *via* oxadiazines **39** in the reactions of α-halooximes **38** with *N*-phenyl-*N*-methyl benzamidines **37** in the presence of iron carbonyls (Scheme 9).

The formation of cyclic nitrones **24**, **27**, **30** and **36** was further confirmed by their thermal degradation studies. Thermolysis of nitrones **24** and **27** in dry benzene in sealed tube at 140-150 °C for 6-7 h resulted in the isolation of products which were chracterised as 1,4-diaryl-2-phenyl imidazoles on the basis of their analytical data and spectral evidences. The compound **41a**, for example, analysed for $C_{21}H_{16}N_2$ exhibited a molecular ion peak at *m/z* 296. Its ^{1}H NMR spectrum showed the absence of formamidino unit and the presence of two downfield (around δ 7.92) *ortho* phenyl protons alongwith a multiplet consisting of other aromatic protons and an olefinic proton. Its ^{13}C NMR spectrum also attest to the imidazole structure **41**.

The formation of imidazoles **41** was initially confused with the corresponding *N*-oxide structures **42**[30] because of (i) expected almost similar spectral features and (ii) the tendency of nitrones to show the absence of molecular ion peak and the presence of intense M^+-16 peak in their mass spectrum. However,

the imidazole structure **41** was assigned to the thermolysis products on the basis of their C, H, N analysis, which indicated the presence of only C, H, N and the absence of oxygen in these compounds. Further evidence for the imidazole structures **41** was derived from their inability to undergo 1,3-dipolar cycloaddition reactions with dienophiles ruling out the formation of *N*-oxide structure **42**.

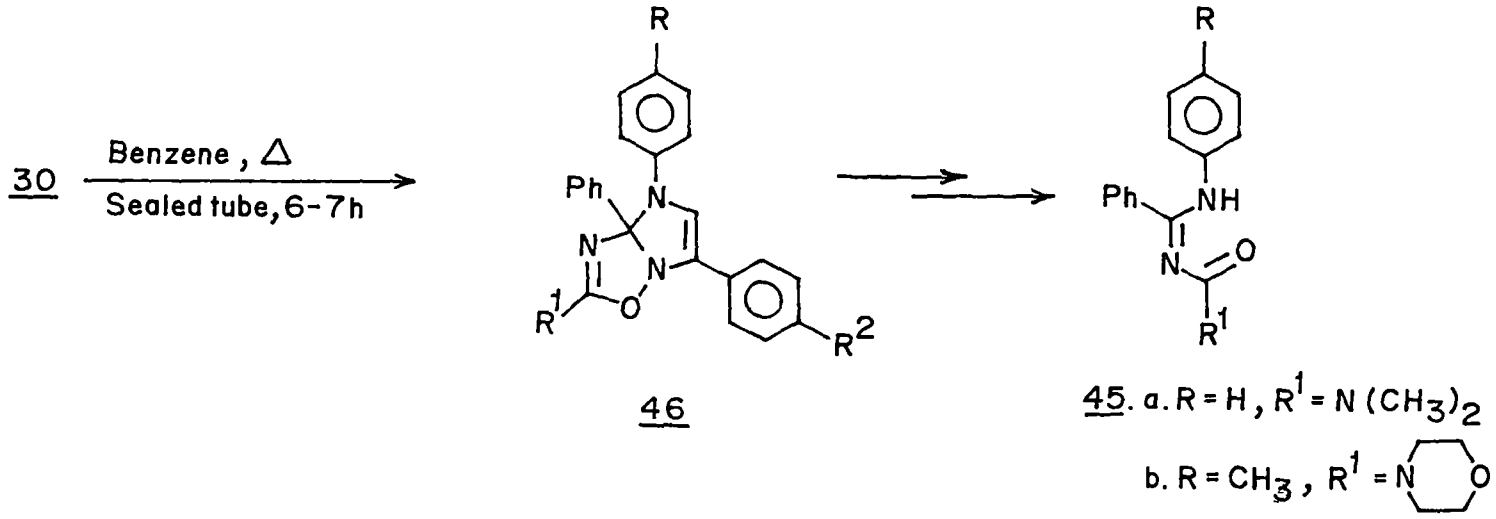
Further, the thermolysis of imidazole-*N*-oxides **36d-f** under similar conditions resulted in the formation of same imidazoles **41** which were chracterised on the basis of their identical spectral spectral features, melting points and undepressed mixed melting points with the samples obtained earlier. The formation of imidazoles **41** by the thermolysis of **24**, **27** and **36d-f** may possibly arise *via* any of the two paths illustrated in Scheme-10. Path-I assumes the initial elimination of formamidino/ acetamidino/secondaryamino moeity to result in *N*-oxide **42**, which under reaction conditions may yield an unstable bicyclic intermediate **44** followed by deoxygenation to yield **41**. Path-II proposes that at elevated tempratures, the nitrones **24**, **27** and **36d-f** are interconvertible with corresponding oxazines **43**. Elimination of formamidino/acetamidino/secondaryamino moeity from this oxazine intermediate **43** yields bicyclic intermediate **44** which as usual undergoes deoxygenation to give **41**. Pathway-II seems to be more probable because such nitrone-oxazine interconversions[41] leading to the formation of imidazoles are known in literature.[40]


24/27
benzene, Δ
sealed tube
140-150°C
6-7h
benzene, Δ
sealed tube
140-150°C
6-7h
36 d-f
41. a. R = R2 = H
b. R = CH3, R1 = H
c. R = H, R2 = CH3
mechanism :
Path I
24/27/36d-f
42
R =
Path II
43
44
deoxygenation
41

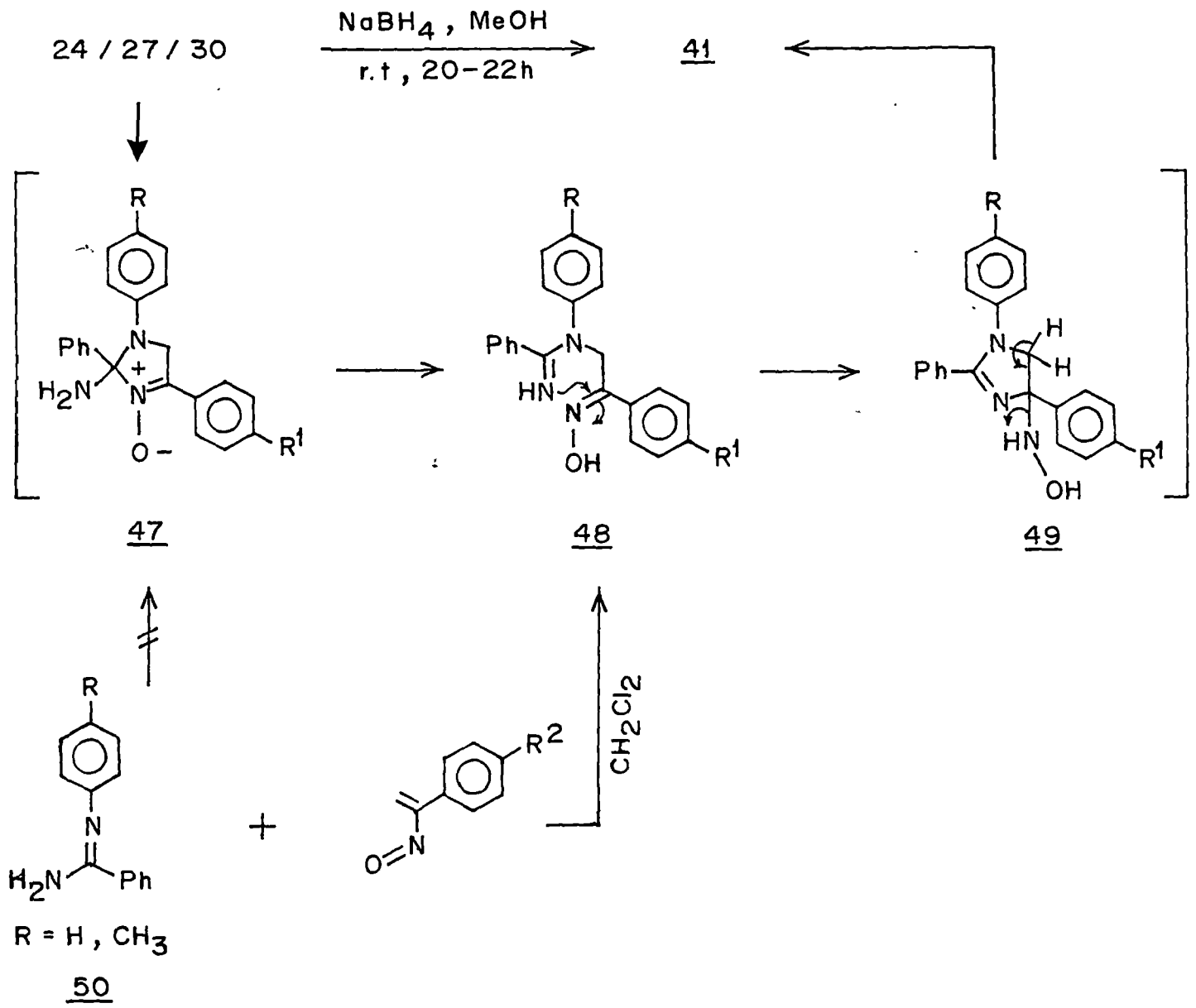
Scheme-10

Thermolysis of nitrones 30, under similar conditions, led interesringly to the formation of amidine derivatives 45 (Scheme 11). The structure 45 could easily be established on the basis of analytical and spectral evidences. The compound 45a, for example, showed a molecular ion peak at *m/z* 267 and IR absorptions at 3063 and 1635 cm^{-1} assigned to -NH and carbonyl groups respectively. Its ^{1}H NMR spectrum exhibited peaks for *N,N*-dimethylamine (δ 3.05, s, 3H and δ 3.32, s, 3H), aromatic (δ 6.80-6.77, m, 10H) and -NH (δ 12.40, br s, exchangable with D_2O) protons. Its ^{13}C NMR spectrum further confirmed the assigned structure 45a. The mechanism involved in the transformation of nitrones 30 to amides 45 could not be clearly visualised. But, it is assumed that there is an initial attack of *N*-oxide oxygen on the imino carbon to give a bicyclic intermediate 46 with the elimination of methyl mercaptan and subsequent decomposition of 46 might lead to the products 45.

Interestingly, the treatment of all the nitrones 24, 27 and also 30 with sodium borohydride in methanol at rt for 22-24 h resulted again in the isolation of imidazoles 41. The products were assigned structure 41 based on their identical spectral patterns, melting points and undepressed mixed melting points with the products obtained on thermolysis of nitrones 24, 27 and 36d-f. The possible mechanism involved in this transformation is outlined in Scheme-12. In this mechanism it is assumed that the reduction of amidino carbon-nitrogen double bond of nitrones 24, 27 and 30 by $NaBH_4$ leads to 2-amino-*N*-oxide intermediate 47. This


30
Benzene , Δ
Sealed tube, 6-7h
R
Ph
N
N
N
O
R1
R2
46
R
Ph
NH
N
O
R1
45. a. R = H , R1 = N (CH3)2
b. R = CH3 , R1 = N O

Scheme – 11



Scheme–12

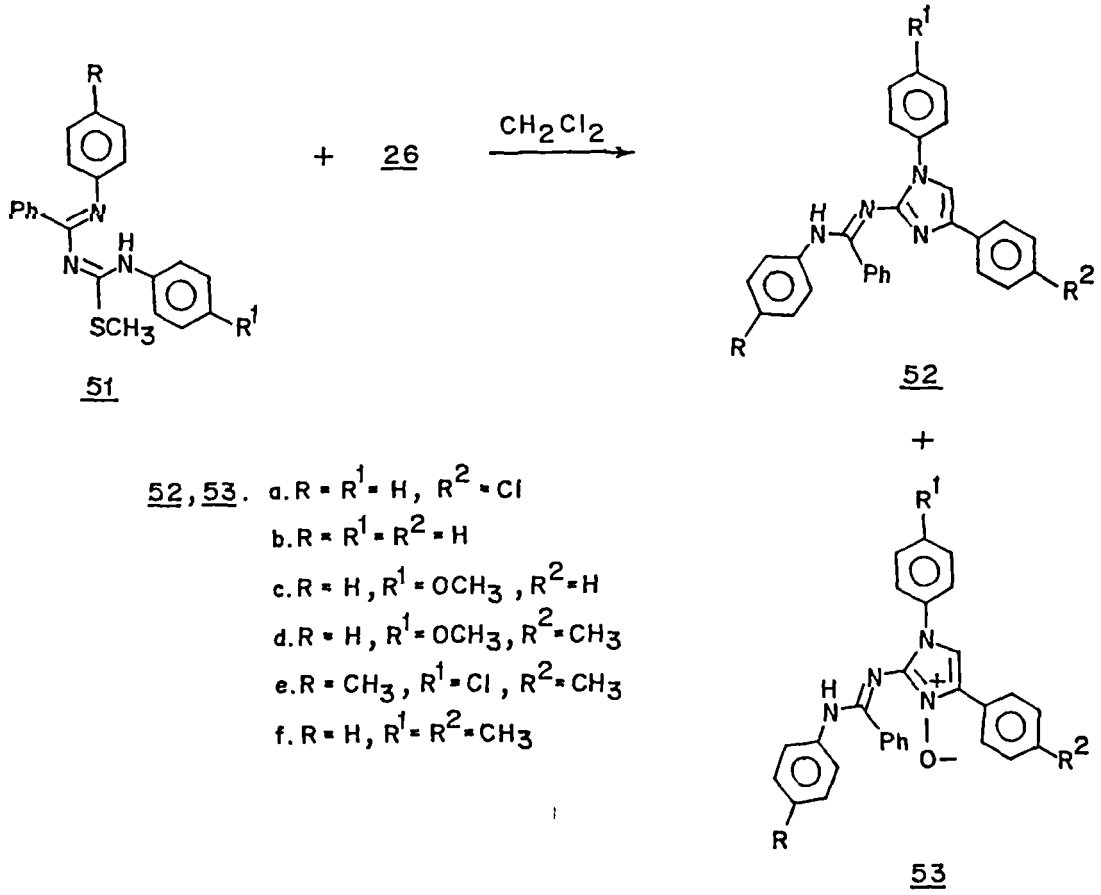
intermediate 47 probably being unstable transforms to intermediate 48. The intermediate 48 then cyclises, as shown, to result in another intermediate 49 which ultimately undergoes elimination of H_2NOH to yield imidazoles 41. The mechanistic paths I and II proposed for thermolysis experiments in Scheme-10 may be ruled out in this case because at room temprature (i) the conversion of *N*-oxide intermediate 42 to bicyclic intermediate 44 (Path-I) and (ii) the interconversion from nitrones to oxazines (Path-II) are less likely.

In order to further confirm this mechanism, we have investigated the reactions of simple *N*-aryl benzamidines 50 with α-nitrosostyrenes. It was thought that the absence of any *N*-oxide 47 should confirm its unstable nature and the formation of imidazoles 41 could further confirm the mechnism proposed in Scheme-12. Thus, the reaction of 50 with α-nitrosostyrenes, generated *in situ* from α-halooximes and sodium carbonate in methylene chloride at room temprature, resulted in the isolation of expected imidazoles 41, probably *via* the intermediates 48 and 49 (Scheme 12).

Cycloaddition reactions of N-arylamino 1,3-diaza-1,3-butadienes with α-nitrosostyrenes

In view of the observed unusual [3+2] cycloadditions of α-nitrosostyrenes with various 1,3-diaza-1,3-butadienses and amidines and interesting mechanistic pathways accompanying the transformations of their products, it was thought worthwhile to

carryout the the reactions of α-nitrosostyrenes with *N*-arylamino-1,3-diaza-1,3-butadienes. Thus, the reactions of 1-aryl-2-phenyl-4-(*N*-arylamino)-4-methylthio-1,3-diaza-1,3-butadienes 51 with α-nitrosostyrenes 26 in methylene chloride resulted in the formation of a mixture of products (Scheme 13). The products were



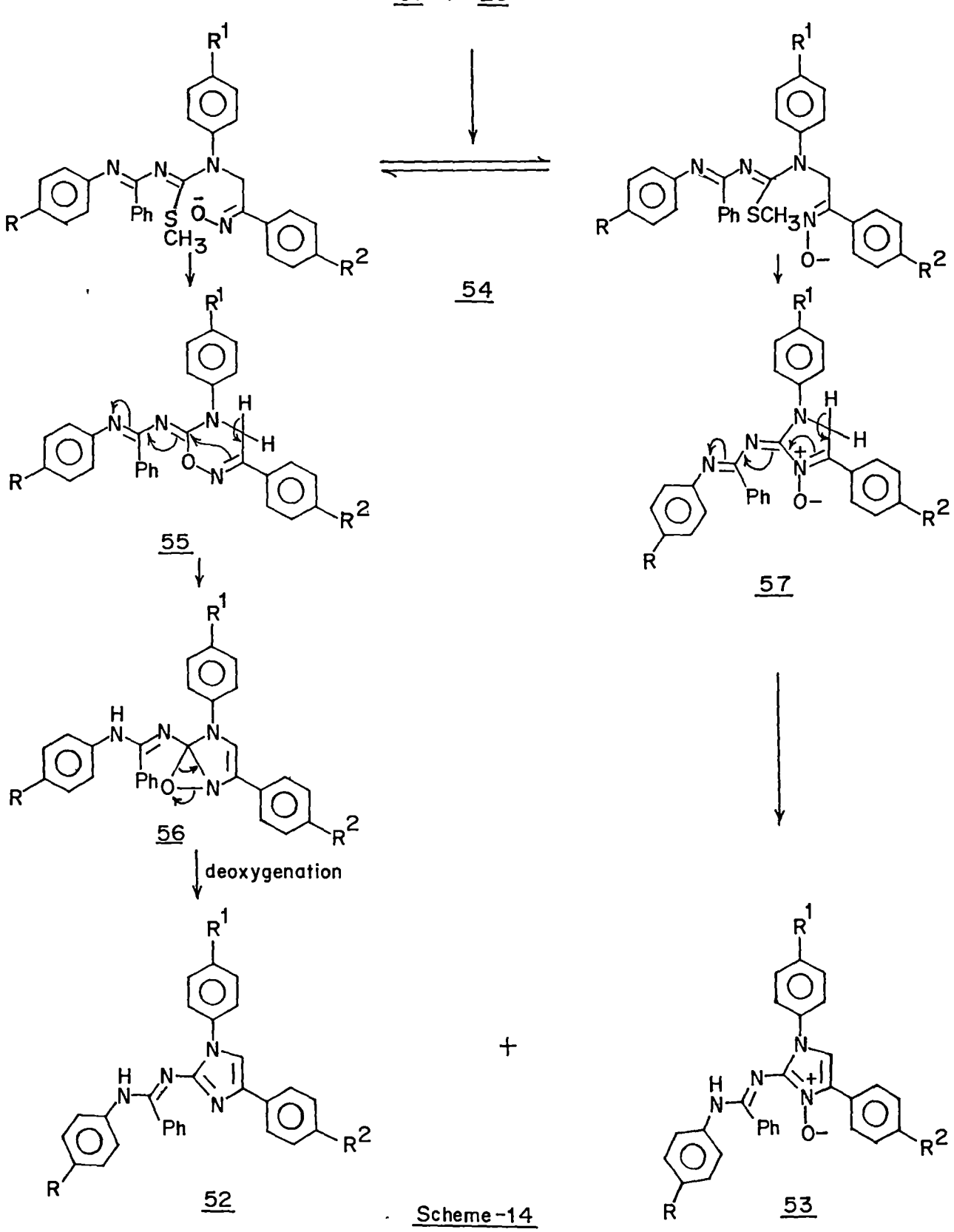
Scheme–13

easily separated by column chromatography and characterised as 1,4-diaryl-2-(*N*-arylbenzamidino)imidazoles 52 and 1,4-diaryl-2-(*N*-arylbenzamidino)imidazole-3-oxides 53 on the basis of their analytical and spectral data. The imidazole 52a, for example, in its IR spectrum showed a broad peak at 3417 cm^{-1} due to -NH group. Its ^1H NMR spectrum exhibited appropriate splittings for

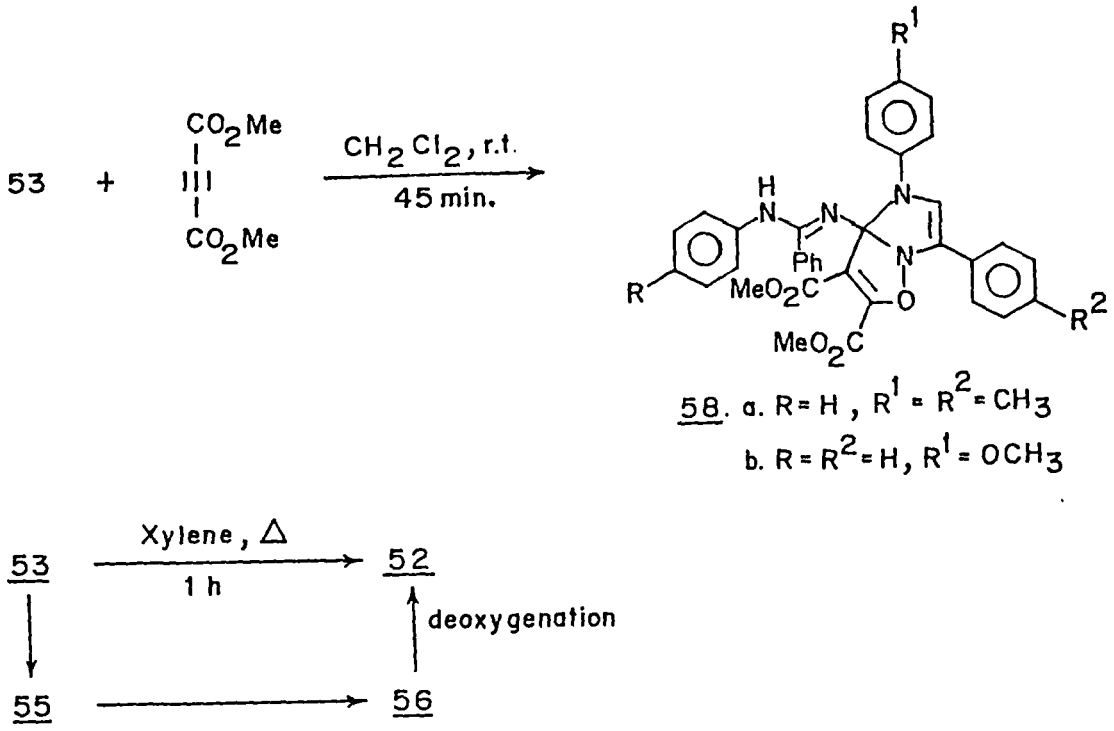
aromatic protons and a broad singlet, exchangable with D_2O at δ 12.70 for -NH proton. Its mass spectrum showed a molecular ion peak at *m/z* 448 (13%). On the other hand, the nitrone 53a showed in its IR spectrum, a broad absorption band at 3430 cm^{-1} for -NH group and a peak at 1251 cm^{-1} characteristic of N^+-O^- of nitrones. Its ^1H NMR spectrum exhibited, in addition to aromatic protons, characteristic downfield shift (δ 8.02, d, *J* = 8.6) for two *ortho* protons of the phenyl group attached to the carbon of nitrone group and a broad singlet at δ 13.27, exchangable with D_2O, for -NH proton. Also the mass spectrum of 53a showed a molecular ion peak at *m/z* 464 (15%) and an intense M^+-16 peak at *m/z* 448 (45%) which further confirmed the assigned structure.

The mechanism leading to the formation of a mixture of imidazoles 52 and nitrones 53 is outlined in scheme-14. It is assumed that nitrosoalkenes 26 add to *N*-aryl-1,3-diaza-1,3-butadienes 51 to give an interconvertible *cisoid* and *transoid* intermediate 54. The *cisoid* form of 54 results in an oxazine intermediate 55 which presumably rearranges under reaction conditions to yield an intermediate 56. The deoxegenation of 56 finally yields imidazoles 52. The *transoid* form of 54, on the other hand leads to intermediate 57 which rearranges, as shown, to yield nitrones 53.

The *N*-oxide structure 53 was further confirmed by carrying out their 1,3-dipolar cycloaddition reactions. Thus, the reaction of 53 with dimethyl acetylene dicarboxylate (DMAD) in methylene chloride at room temperature for 45 mins resulted in



Scheme-14



58. a. R = H, $R^1 = R^2 = CH_3$

b. $R = R^2 = H$, $R^1 = OCH_3$

Scheme – 15

the formation of (Scheme 15) products which were tentatively characterised as 1,3-dipolar adducts 58 on the basis of their IR, mass spec. ^1H and ^{13}C NMR spectra. The product 58a, for example, analysed for $C_{36}H_{32}N_4O_5$ exhibited a molecular ion peak at *m/z* 600. Its IR spectrum showed strong peaks at 1748 and 1723 cm^{-1} due to ester carbonyls. Its ^1H NMR spectrum showed, in addition to aromatic protons, singlets for two methyl protons (δ 2.37 and 2.40), two ester methyl singlets (δ 3.58 and 3.85) and one olefinic proton (δ 5.36). It also exhibited a broad singlet at δ 12.63, exchangable with D_2O, for -NH proton. Its ^{13}C NMR spectrum was also in agreement with the assigned structure 58a.

In order to unambigiously establish the structure of 58 it is proposed to carryout X-ray diffraction studies.

In view of the interesting results observed in the thermolysis of various nitrones 24, 27, 30 and 36, and to have further insight into the mechanistic aspects involved in these transformations, it was thought worthwhile to carry out the thermolysis of nitrones 53 and investigate the products formed. Thus, thermolysis of nitrones 53 in refluxing xylene for 1 h resulted interestingly in the isolation of imadazole derivatives 52 (Scheme 15). It is presumed that, at higher temprature, the nitrone structure 53 is possibly interconvertible with oxazine intermediate 55 which under reaction conditions lead to a bicyclic intermediate 56 and this on subsequent deoxygenation results finally in imidazole 51.

In conclusion, the reactions of various polarised 1,3-diazabutadienes and imines with α-nitrosostyrenes undergo regioselective and unusual [3+2] cycloaddition reactions and offer an interesting route to various substituted cyclic nitrones. Thermolysis of most of these nitrones results in the formation of imidazoles *via* oxazine intermediates.

Experimental Section

General conditions are same as described in Chapter I.

Starting materials

All 1,3-diaza-1,3-butadienes 23, 24, 29;[42] *N*-aryl-1,3-diaza-1,3-butadienes 51,[43] *N*-aryl formamidines 35a-c,[44] *N*-aryl

benzamidines 50,[45] and chlorooximes 26[46] of acetophenone and p-methylacetophenone were prepared by the reported procedures.

General procedure for the preparation of *N*-aryl-2-secondaryamino benzamidines 35d-f: A solution of imidoyl chloride (10 mmol) and secondaryamine (22 mmol) in THF (30 ml) was stirred at rt for 3 h. The reaction mixture was filtered, the residue washed with THF (10 ml) and the combined filterate concentrated under *vacuo*. The residue thus obtained was diluted with CH_2Cl_2 (30 ml), washed with water (3 x 100 ml) and dried over anhydrous Na_2SO_4. The solvent was then removed under reduced pressure and the residue purified by chromatography on silica gel.

***Reactions of 1,3-Diaza-1,3-butadienes 25 and 29 with α-nitrosostyrenes*: General Procedure for nitrones 27 and 30:** A solution of 1,3-diaza-1,3-butadienes 25/29 (4.0 mmol) and α-chlorooxime 26 (4.2 mmol) in dry CH_2Cl_2 (40 ml) was stirred at rt in the presence of anhydrous sodium hydrogen carbonate/sodium carbonate (6 mmol) for 30-32 h. The separated salt and excess of sodium hydrogen carbonate/sodium carbonate were removed by filtration and the residue was washed with small portions (2 x 10 ml) of CH_2Cl_2. The combined filtrate was washed with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The tituration of the residue with ether resulted in the crude product which was recrystallised from a mixture 2:1 of benzene and hexane.

2,4-Diphenyl-1-(p-methylphenyl)-2-*N'*-(*N*,N-dimethylacetamidino)-Δ^3-imidazoline-3-oxide (27a): Yield 86%; mp 140-141 °C; IR (KBr) ν 1580, 1521, 1449, 1399, 1351, 1217, 1187 cm^{-1}. ^1H NMR (90 MHz) δ 1.82 (s, 3H, $-CH_3$), 2.23 (s, 3H, $-CH_3$), 3.17 [s, 6H, $-N(CH_3)_2$], 5.08 (s, 2H, $-CH_2-$), 6.72 (d, J = 8.2, 2H, arom), 7.00 (d, J = 8.2, 2H, arom), 7.25-7.56 (m, 6H, arom), 7.72-7.87 (m, 2H, arom), 8.40-8.56 (m, 2H, arom). ms *m/z*: 412 (M^+), 396 (M^+-16). Anal. Calcd for $C_{26}H_{28}N_4O$: C, 75.70; H, 6.84; N, 13.58. Found: C, 75.81; H, 6.81; N, 13.51.

1,4-Bis(p-methylphenyl)-2-phenyl-2-*N'*-(*N*,*N*-dimethylacetamidino)-Δ^3-imidazoline-3-oxide (27b): Yield 89%; mp 141-143 °C; IR (KBr) ν 1596, 1521, 1451, 1400, 1347, 1221, 1172 cm^{-1}. ^1H NMR (90 MHz) δ 1.75 (s, 3H, $-CH_3$), 2.17 (s, 3H, $-CH_3$), 2.36 (s, 3H, $-CH_3$), 3.05 [s, 6H, $N(CH_3)_2$], 4.88 (s, 2H, $-CH_2-$), 6.62 (d, J = 8.4, 2H, arom), 6.90 (d, J = 8.4, 2H, arom), 7.11-7.28 (m, 5H, arom), 7.56-7.71 (m, 2H, arom), 8.20 (d, J = 8.0, 2H, arom). ^{13}C NMR (75.5 MHz) δ 13.5 ($-CH_3$), 20.1 ($-CH_3$), 21.5 ($-CH_3$), 38.4 [$-N(CH_3)_2$], 50.6 ($-CH_2-$), 101.8 (C-2), 113.2, 124.7, 126.5, 126.6, 127.7, 127.8, 128.2, 129.17, 129.21, 131.3, 140.0, 140.7 (C-4), 142.7, 161.8 (C-acetamidino). ms *m/z*: 426 (M^+), 410 (M^+-16). Anal. Calcd for $C_{27}H_{30}N_4O$: C, 76.03; H, 7.09; N, 13.13. Found: C, 75.94; H, 7.12; N, 13.19.

2-[*N*-(2'-Methylthio-2'-morpholino)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30a): Yield 72%; mp 161.5-162.5 °C; IR (KBr) ν 1599, 1547, 1497, 1353, 1229 cm^{-1}. ^1H NMR (90 MHz) δ 2.06 (s,

3H, $-CH_3$), 3.73 (br s, 8H, morpholine), 5.03 (s, 2H, $-CH_2-$), 6.78 (d, J = 8.5, 2H, arom), 7.18 (d, J = 8.5, 2H, arom), 7.33-7.56 (m, 7H, arom), 7.73-7.90 (m, 2H, arom) and 8.40-8.56 (m, 2H, arom). ms *m/z*: 472 (M^+). Anal. Calcd for $C_{27}H_{28}N_4O_2S$: C, 68.62; H, 5.97; N, 11.85. Found: C, 68.59; H, 5.96; N, 11.87.

2-[*N*-(2'-Methylthio-2'-piperidino)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30b): Yield 88%; mp 145-146.5 °C; IR (KBr) ν 1599, 1553, 1497, 1345, 1222 cm^{-1}. ^1H NMR (90 MHz) δ 1.56-1.75 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.06 (s, 3H, $-SCH_3$), 3.60-3.76 (br s, 4H, $-CH_2-N-CH_2-$), 5.06 (s, 2H, $-CH_2-$), 6.78 (d, 2H, arom), 7.20 (d, 2H, arom), 7.40-7.60 (m, 7H, arom), 7.83-7.95 (m, 2H, arom), 8.35-8.60 (m, 2H, arom). ms *m/z*: 470 (M^+). Anal. Calcd for $C_{28}H_{30}N_4OS$: C, 71.46; H, 6.42; N, 11.90. Found: C, 71.40; H, 6.43; N, 11.97.

2-[*N*-(2'-Methylthio-2'-pyrrolidino)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30c): Yield 79%; mp 143-144.5 °C; IR (KBr)ν 1593, 1548, 1492, 1351, 1225 cm^{-1}. ^1H NMR (90 MHz) δ 1.80-2.00 (m, 4H, $-CH_2-CH_2-$), 2.06 (s, 3H, SCH_3), 3.70-3.83 (d, 4H, $-CH_2-N-CH_2-$), 5.05 (s, 2H, $-CH_2-$), 6.81 (d, J = 8.6, 2H, arom), 7.17 (d, 2H, arom), 7.33-7.56 (m, 7H, arom), 7.80-7.95 (m, 2H, arom), 8.43-8.56 (m, 2H, arom). ms *m/z*: 456 (M^+). Anal. Calcd for $C_{27}H_{28}N_4OS$: C, 71.02; H, 6.18; N, 12.27. Found: C, 71.09; H, 6.18; N, 12.20.

2-[*N*-(2'-Dimethylamino-2'-methylthio)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30d): Yield 75%; mp 149-150 °C; IR (KBr)ν

1596, 1547, 1499, 1347, 1227 cm^{-1}. ^1H NMR (90 MHz) δ 1.96 (s, 3H, $-SCH_3$), 3.20 [s, 6H, $-N(CH_3)_2$], 5.00 (s, 2H, $-CH_2-$), 6.71 (d, *J* = 8.4, 2H, arom), 7.10-7.15 (d, *J* = 8.4, 2H, arom), 7.30-7.50 (m, 7H, arom), 7.80-7-90 (m, 2H, arom), 8.36-8.50 (m, 2H, arom). ms *m/z*: 430 (M^+). Anal. Calcd for $C_{25}H_{26}N_4OS$: C, 69.74; H, 6.09, N, 13.01. Found: C, 69.87; H, 6.15; N, 12.95.

2,4-Diphenyl-1-(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-piperidino)imino]-Δ^3-imidazoline-3-oxide (30e) Yield 82%; mp 147.5-148.5 °C; IR (KBr) ν 1601, 1552, 1493, 1353, 1225 cm^{-1}. ^1H NMR (90 MHz) δ 2.10 (s, 3H, $-SCH_3$), 2.23 (s, 3H, $-CH_3$), 3.73 (s, 8H, mopholine), 5.00 (s, 2H, $-CH_2-$), 6.65 (d, *J* = 8.5, 2H, arom), 7.01 (d, *J* = 8.5, 2H, arom), 7.30-7.56 (m, 6H, arom), 7.73-7.86 (m, 2H, arom), 8.36-8.50 (m, 2H, arom). ms *m/z*: 486 (M^+). Anal. Calcd for $C_{28}H_{30}N_4O_2S$: C, 69.11; H, 6.21; N, 11.51. Found: C, 69.02; H, 6.18; N, 11.58.

2,4-Diphenyl-1-(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-piperidino)imino]-Δ^3-imidazoline-3-oxide (30f): Yield 82%; mp 149-150 °C; IR (KBr) ν 1594, 1551, 1494, 1348, 1226 cm^{-1}. ^1H NMR (90 MHz) δ 1.59 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.03 (s, 3H, $-SCH_3$), 2.16 (s, 3H, $-CH_3$), 3.52 (br s, 4H, $-CH_2-N-CH_2-$), 5.00 (s, 2H, $-CH_2-$), 6.64 (d, 2H, arom), 6.99 (d, *J* = 8.7, 2H, arom), 7.30-7.53 (m, 6H, arom), 7.73-7.86 (m, 2H arom), 8.40-8.53 (m, 2H, arom). ms *m/z*: 484 (M^+). Anal. Calcd for $C_{29}H_{32}N_4OS$: C, 71.87; H, 6.65; N, 11.56. Found: C, 71.80; H, 6.63; N, 11.64.

2,4-Diphenyl-1-(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-pyrrolidino)imino]-Δ^3-imidazoline-3-oxide (30g): Yield 91%; mp 145-146.5°C; IR (KBr) ν 1597, 1549, 1501, 1343, 1229 cm^{-1}. ^1H NMR (90 MHz) δ 1.96-2.00 (m, 4H, 2 x $-CH_2-$), 2.06 (s, 3H, $-SCH_3$), 2.20 (s, 3H, $-CH_3$), 3.70-3.76 (m, 4H, $-CH_2-N-CH_2-$), 5.03 (s, 2H, $-CH_2-$), 6.71 (d, J = 8.8, 2H, arom), 7.01 (d, J = 8.8, 2H, arom), 7.30-7.50 (m, 6H, arom), 7.80-7.90 (m, 2H, arom), 8.43-8.53 (m, 2H, arom). ms *m/z*: 470 (M^+). Anal. Calcd for $C_{28}H_{30}N_4OS$: C, 71.46; H, 6.42; N, 11.90. Found: C, 71.55; H, 6.48; N, 11.82.

2-[*N*-(2'-Dimethylamino-2'-methylthio)imino]-2,4-diphenyl-1-(p-methylphenyl)-Δ^3-imidazoline-3-oxide (30h): Yield 78%; mp 140-141.5°C; IR (KBr) ν 1594, 1548, 1493, 1347, 1222 cm^{-1}. ^1H NMR (90 MHz) δ 2.00 (s, 3H, $-SCH_3$), 2.20 (s, 3H, $-CH_3$), 3.20 [s, 6H, $-N(CH_3)_2$], 5.00 (s, 2H, $-CH_2-$), 6.65 (d, J = 8.5, 2H, arom), 6.98 (d, J = 8.5, 2H, arom), 7.30-7.53 (m, 6H, arom), 7.80-7.93 (m, 2H, arom), 8.40-8.53 (m, 2H, arom). ms *m/z*: 444 (M^+). Anal. Calcd for $C_{26}H_{28}N_4OS$: C, 70.24; H, 6.35; N, 12.60. Found: C, 70.20; H, 6.33; N, 12.67.

2-[*N*-(2'-Ethylthio-2'-pyrrolidino)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30i): Yield 69%; mp 154-155°C; IR (KBr) ν 1597, 1551, 1499, 1351, 1226 cm^{-1}. ^1H NMR (90 MHz) δ 0.88 (t, J = 8.0, 3H, $-CH_3$), 2.53 (q, J = 8.0, 2H, $-SCH_2-$), 3.70 (br s, 8H, morpholine), 5.00 (s, 2H, $-CH_2-$), 6.68 (d, J =8.6, 2H, arom), 7.15 (d, J = 8.6 2H, arom), 7.26-7.50 (m, 7H, arom), 7.73-7.50 (m, 2H, arom), 8.36-8.46 (m, 2H, arom). ms *m/z*: 486 (M^+). Anal.

Calcd for $C_{28}H_{30}N_4O_2S$: C, 69.11; H, 6.21; N, 11.51. Found: C, 69.18; H, 6.15; N, 11.60.

2-[*N*-(2'-Ethylthio-2'-pyrrolidino)imino]-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (30j): Yield 83%; mp 154-155°C; IR (KBr) ν 1599, 1547, 1497, 1349, 1226 cm^{-1}. ^1H NMR (90 MHz) δ 0.86 (t, J = 8.0, 3H, $-CH_3$), 1.86-2.06 (m, 4H, 2 x $-CH_2-$), 2.45 (q, J = 8.0, 2H, $-SCH_2-$), 2.60-2.76 (m, 4H, $-CH_2-N-CH_2-$), 5.13, (s, 2H,$-CH_2-$), 6.88 (d, J = 8.5, 2H, arom), 7.20-7.30 (m, 2H, arom), 7.43-7.66 (m, 7H, arom), 7.93-8.03 (m, 2H, arom), 8.56-8.66 (m, 2H, arom). ms *m/z*: 470 (M^+). Anal. Calcd for $C_{28}H_{30}N_4OS$: C, 71.46; H, 6.42; N, 11.90. Found: C, 71.57; H, 6.37; N, 11.79.

1,2-Diphenyl-4-(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-morpholino)imino]-Δ^3-imidazoline-3-oxide (30k): Yield 75%; mp 149-150°C; IR (KBr) ν 1598, 1548, 1497, 1352, 1228 cm^{-1}. ^1H NMR (90 MHz) δ 2.10 (s, 3H, $-SCH_3$), 2.43 (s, 3H, $-CH_3$), 3.75 (br s, 8H, morpholine), 5.00 (s, 2H, $-CH_2-$), 6.71 (d, J = 8.8, 2H, arom), 7.10-7.46 (m, 6H, arom), 7.73-7.86 (m, 2H, arom), 8.30-8.40 (d, J = 8.4, 2H, arom). ms *m/z*: 486 (M^+). Anal. Calcd for $C_{28}H_{30}N_4O_2S$: C, 69.11; H, 6.21; N, 11.51. Found: C, 69.23; H, 6.16; N, 11.43.

1,4-Bis(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-morpholino)imino]-Δ^3-imidazoline-3-oxide (30l): Yield 88%; mp 154-155°C; IR (KBr) ν 1596, 1552, 1495, 1349, 1227 cm^{-1}. ^1H NMR (90 MHz) δ 2.06 (s, 3H,$-SCH_3$), 2.20 (s, 3H,$-CH_3$), 2.40 (s, 3H, $-CH_3$), 3.70 (br s, 8H, morpholine), 4.96 (s, 2H, $-CH_2-$), 6.59 (d, J = 8.6, 2H,

arom), 6.98 (d, J = 8.6, 2H, arom), 7.26-7.40 (m, 5H, arom), 7.70-7.83 (m, 2H, arom), 8.36 (d, J = 8.3, 2H, arom). ms *m/z* 500 (M^+). Anal. Calcd for $C_{29}H_{32}N_4O_2S$: C, 69.57; H, 6.44; N, 11.19. Found: C, 69.50; H, 6.45; N, 11.28.

1,4-Bis(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-piperidino) imino]-Δ^3-imidazoline-3-oxide (30m): Yield 81%; mp 147-149°C; IR (KBr) ν 1593, 1548, 1493, 1351, 1229 cm^{-1}. ^1H NMR (90 MHz) δ 1.64 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.06 (s, 3H,$-SCH_3$), 2.20 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-CH_3$), 3.63 (br s, 4H, $-CH_2-N-CH_2-$), 4.95 (s, 2H, $-CH_2-$), 6.72 (d, J = 8.6, 2H, arom), 7.00 (d, J = 8.6, 2H, arom), 7.23-7.43 (m, 5H, arom), 7.76-7.96 (m, 2H, arom), 8.30-8.40 (d, J = 8.5, 2H, arom). ms *m/z*: 498 (M^+). Anal. Calcd for $C_{30}H_{34}N_4OS$: C, 72.25; H, 6.87; N, 11.23. Found: C, 72.36; H, 6.84; N, 11.20.

1,4-Bis(p-methylphenyl)-2-[*N*-(2'-methylthio-2'-pyrrolidino) imino]-Δ^3-imidazoline-3-oxide (30n): Yield 93%; mp 158-159 °C; IR (KBr) ν 1595, 1548, 1499, 1353, 1224 cm^{-1}. ^1H (90 MHz) δ 1.90-2.10 (m, 4H, 2 x $-CH_2-$), 2.17 (s, 3H, $-SCH_3$), 2.30 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-CH_3$), 3.60-3.90 (m, 4H, $-CH_2-N-CH_2-$), 5.00 (s, 2H, $-CH_2-$), 6.70 (d, J = 8.8, 2H, arom), 7.00 (d, J = 8.8, 2H, arom), 7.23-7.43 (m, 5H, arom), 7.75-7.97 (m, 2H, arom), 8.38 (d, J = 8.4, 2H, arom). ms *m/z*: 484 (M^+). Anal. Calcd for $C_{29}H_{32}N_4OS$: C, 71.87; H, 6.65; N, 11.56. Found: C, 72.03; H, 6.61; N, 11.48.

2-[*N*-(2'-Dimethylamino-2'-methylthio)imino]-1,4-(p-methylphenyl)-Δ^3-imidazoline-3-oxide (30o): Yield 78%; mp 158.5-159 °C; IR (KBr) ν 1615, 1555, 1513, 1347, 1225 cm^{-1}. ^1H NMR (90 MHz) δ 2.00 (s, 3H, $-SCH_3$), 2.16 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-CH_3$), 3.23 [s, 6H, $-N(CH_3)_2$], 5.03 (s, 2H, $-CH_2-$), 6.71 (d, J = 8.6, 2H, arom), 7.08 (d, J = 8.6, 2H, arom), 7.36-7.50 (m, 5H, arom), 7.90-8.03 (m, 2H, arom), 8.43-8.50 (m, 2H, arom). ms *m/z* 458 (M^+). Anal. Calcd for $C_{27}H_{30}N_4OS$: C, 70.71; H, 6.59; N, 12.22. Found: C, 70.61; H, 6.63; N, 12.18.

1-(p-Chlorophenyl)-2,4-diphenyl-2-[*N*-(2'-methylthio-2'-piperidino)imino]-Δ^3-imidazoline-3-oxide (30p): Yield 88%; mp 161.5-162.5 °C; IR (KBr) ν 1599, 1552, 1498, 1351, 1227 cm^{-1}. ^1H NMR (90 MHz) δ 1.61 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.06 (s, 3H, $-SCH_3$), 3.63 (br s, 4H, $-CH_2-N-CH_2-$), 5.00 (s, 2H, $-CH_2-$), 6.68 (d, J = 8.6, 2H, arom), 7.11 (d, J = 8.6, 2H, arom), 7.30-7.53 (m, 6H, arom), 7.73-7.90 (m, 2H, arom), 8.36-8.53 (m, 2H, arom). ms *m/z*: 517 (M^+). Anal. Calcd for $C_{29}H_{29}N_4OSCl$: C, 67.36; H, 5.65; N, 10.83. Found: C, 67.34; H, 5.62; N, 10.84.

1-(p-Chlorophenyl)-2-[*N*-(2'-dimethylamino-2'-methylthio)imino]-Δ^3-imidazoline-3-oxide (30q): Yield 83%; mp 169-170 °C; IR (KBr) ν 1598, 1552, 1492, 1350, 1226 cm^{-1}. ^1H NMR (300 MHz) δ 2.00 (s, 3H, $-SCH_3$), 2.38 (s, 3H, $-CH_3$), 3.18 [s, 6H, $-N(CH_3)_2$], 4.94 (s, 2H, $-CH_2-$), 6.62 (d, J = 9.0, 2H, arom), 7.06 (d, J = 9.0, 2H, arom), 7.24-7.32 (m, 5H, arom), 7.74-7.78 (m, 2H, arom), 8.26 (d, J = 8.3, 2H, arom). ^{13}C NMR (75.5 MHz) δ 16.2 ($-SCH_3$), 21.7

($-CH_3$)', 40.0 [$-N(CH_3)_2$], 51.4 ($-CH_2-$), 101.0 (C-2), 114.0, 122.6, 124.8, 126.8, 127.9, 128.2, 128.7, 128.9, 129.3, 133.0, 140.4, 141.0, 141.6, 159.0 (C-4). ms *m/z*: 479 (M^+). Anal. Calcd for $C_{26}H_{27}N_4OSCl$: C, 65.19; H, 5.68; N, 11.70. Found: C, 65.31; H, 5.61; N, 11.65.

1-(p-Chlorophenyl)-2,4-diphenyl-2-[*N*-(2'-ethylthio-2'-pyrrolidino)imino]-Δ^3-imidazoline-3-oxide (30r): Yield 89%; mp 163.5-164 °C; IR (KBr) ν 1597, 1551, 1494, 1353, 1225 cm^{-1}. ^1H NMR (90 MHz) δ 0.85 (t, *J* = 8.0, 3H, $-CH_3$), 1.83-2.00 (m, 4H, $-CH_2-CH_2-$), 2.65 (q, *J* = 8.0, 2H, $-SCH_2-$), 3.63-3.90 (m, 4H, $-CH_2-N-CH_2-$), 5.00 (s, 2H, $-CH_2-$), 7.70 (d, *J* = 8.8, 2H, arom), 7.11 (d, *J* = 8.8, 2H, arom), 7.30-7.50 (m, 6H, arom), 7.75-7.85 (m, 2H, arom), 8.36-8.50 (m, 2H, arom). ms *m/z*: 505 (M^+). Anal. Calcd for $C_{28}H_{29}N_4OSCl$: C, 66.58; H, 5.79; N, 11.09. Found: C, 66.53; H, 5.77; N, 11.15.

1-(p-Chlorophenyl)-2-[*N*-(2'-dimethylamino-2'-ethylthio)imino]-2,4-diphenyl-Δ^3-imidazoline-3-oxide (30s): Yield 84%; mp 143.5-145 °C; IR (KBr) ν 1593, 1549, 1495, 1352, 1224 cm^{-1}. ^1H NMR (90 MHz) δ 0.85 (t, *J* = 8.0, 3H, $-CH_3$), 2.56 (q, *J* = 8.0, 2H,$-SCH_2-$), 3.20 [s, 6H, $-N(CH_3)_2$], 5.00 (s, 2H, $-CH_2-$), 6.68 (d, *J* = 8.6, 2H, arom), 7.15 (d, *J* = 8.6, 2H, arom), 7.33-7.53 (m, 6H, arom), 7.76-7.90 (m, 2H, arom), 8.38-8.50 (m, 2H, arom). ms *m/z*: 479 (M^+). Anal. Calcd for $C_{26}H_{27}N_4OSCl$: C, 65.19; H, 5.68; N, 11.70. Found: C, 65.12; H, 5.63; N, 11.81.

***Reactions of amidines 35 with α-nitrosostyrenes*: General procedure for nitrones:** A solution of 35 (4 mmol) and α-chloroacetophenone oxime **26** (4.2 mmol) in dry CH_2Cl_2 (40 ml) was stirred at rt in the presence of sodium carbonate (6 mmol) for 40-52 h. Following an identical workup as employed for nitrones **30**, the crude product obtained was purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:3 ratio).

2-(*N,N*-Dimethylamino)-1,4-diphenyl-Δ^3-imidazoline-3-oxide (36a): Yield 69%; mp 164.5-165.5 °C; IR (KBr) ν 1610, 1591, 1509, 1358, 1220 cm^{-1}. ^1H NMR (90 MHz) δ 2.67 [s, 6H, $-N(CH_3)_2$], 4.52 (dd, *J* = 14.0 and 2.0, 1H, $-CH_2-$), 4.83 (dd, *J* = 14.0 and 4.5, 1H, $-CH_2-$), 5.76-5.88 (m, 1H, H-2), 6.81 (d, *J* = 8.0, 2H, arom), 7.20-7.60 (m, 6H, arom), 8.28-8.50 (m, 2H, arom). ms *m/z*: 281 (M^+), 264 (M^+-17). Anal. Calcd for $C_{17}H_{19}N_3O$: C, 72.57; H, 6.80; N, 14.93. Found: C, 72.64; H, 6.77; N, 14.89.

2-(*N,N*-Dimethylamino)-1-(p-methylphenyl)-4-phenyl-Δ^3-imidazoline-3-oxide (36b): Yield 76%; mp 170-171 °C; IR (KBr) ν 1595, 1579, 1525, 1364, 1223 cm^{-1}. ^1H NMR (300 MHz) δ 2.28 (s, 3H, $-CH_3$), 2.66 [s, 6H, $-N(CH_3)_2$], 4.50 (dd, *J* = 14.5 and 2.1, 1H, $-CH_2-$), 4.79 (dd, *J* = 14.5 and 4.5, 1H, $-CH_2-$), 5.81 (dd, *J* = 4.5 and 2.1, 1H, methine H-2), 6.75 (d, *J* = 8.5, 2H, arom), 7.12 (d, *J* = 8.5, 2H, arom), 7.45-7.52 (m, 3H, arom), 8.32-8.35 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 20.4 ($-CH_3$), 37.1 ($-CH_2-$), 50.8 [$-N(CH_3)_2$], 101.9 (C-2), 112.7, 126.5, 126.7, 128.1, 128.6,

128.7, 129.2, 129.8, 130.7, 133.8, 141.7 (C-4). ms *m/z*: 295 (M^+), 278 (M^+-17). Anal. Calcd for $C_{18}H_{21}N_3O$: C, 73.19; H, 7.16; N, 14.22. Found: C, 73.09; H, 7.21; N, 14.27.

2-(*N,N*-Dimethylamino)-4-(p-methylphenyl)-1-phenyl-Δ^3-imidazoline-3-oxide (36c): Yield 63%; mp 177-178 °C; IR (KBr) ν 1596, 1574, 1499, 1477, 1381, 1360, 1224 cm^{-1}. ^1H NMR (90 MHz) δ 2.41 (s, 3H, $-CH_3$), 2.68 [s, 6H, $-N(CH_3)_2$], 4.52 (dd, *J* = 14.0 and 2.0, 1H, $-CH_2-$), 4.83 (dd, *J* = 14.0 and 4.5, 1H, $-CH_2-$), 5.75-5.83 (m, 1H, H-2), 6.80-7.02 (m, 3H, arom), 7.27-7.50 (m, 4H, arom), 8.33 (d, *J* = 8.2, 2H, arom). ms *m/z*: 285 (M^+), 280 (M^+-17). Anal. Calcd for $C_{18}H_{21}N_3O$: C, 73.19; H, 7.16; N, 14.22. Found: C, 73.05; H, 7.13; N, 14.29.

1,2-Diphenyl-4-(p-methylphenyl)-2-pyrrolidino-Δ^3-imidazoline-3-oxide (36d): Yield 81%; mp 164-165 °C; IR (KBr) ν 1597, 1583, 1495, 1445, 1387, 1329, 1223 cm^{-1}. ^1H NMR (300 MHz) δ 1.88-1.92 (m, 4H, $-CH_2-CH_2-$), 2.42 (s, 3H, $-CH_3$), 3.00-3.08 (m, 2H, $-N-CH_2-$), 3.44-3.49 (m, 2H, $-CH_2-N-$), 4.41 (d, *J* = 14.1, 1H, $-CH_2-$), 4.59 (d, *J* = 14.1, 1H, $-CH_2-$), 6.82-6.87 (m, 1H, arom), 7.16-7.27 (m, 7H, arom), 7.32 (d, *J* = 8.1, 2H, arom), 7.45-7.50 (m, 2H, arom), 8.33 (d, *J* = 8.3, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.7 ($-CH_3$), 25.5 ($-CH_2-CH_2-$), 47.7 ($-CH_2-N-CH_2-$), 48.4 ($-CH_2-$), 107. (C-2), 115.7, 119.7, 124.4, 126.7, 127.3, 128.1, 128.7, 128.9, 129.5, 133.8, 135.6, 141.1, 142.9 (C-4). ms *m/z*: 397 (M^+), 381 (M^+-16). Anal. Calcd for $C_{26}H_{27}N_3O$: C, 78.56; H, 6.85; N, 10.57. Found: C, 78.69; H, 6.81; N, 10.49.

2-Piperidino-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide (36e): Yield 75%; mp 148-149 °C; IR (KBr) ν 1652, 1599, 1499, 1338, 1247, 1219 cm^{-1}. ^1H NMR (90 MHz) δ 1.65 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.83-3.18 (m, 2H, $-N-CH_2-$), 3.27-3.57 (m, 2H, $-CH_2-N-$), 4.63 (br s, 2H, $-CH_2-$), 7.20-7.73 (m, 13H, arom), 8.45-8.65 (m, 2H, arom). ms *m/z*: 397 (M^+), 381 (M^+- 16). Anal. Calcd for $C_{26}H_{27}N_3O$: C, 78.56; H, 6.84; N, 10.57. Found: C, 78.44; H, 6.90; N, 10.62.

1,2-Diphenyl-4-(p-methylphenyl)-2-piperidino-Δ^3-imidazoline-3-oxide (36f): Yield 81%; mp 165-166 °C; IR (KBr) ν 1596, 1580, 1493, 1449, 1389, 1327, 1246, 1226 cm^{-1}. ^1H NMR (90 MHz) δ 1.64 (br s, 6H, $-CH_2-CH_2-CH_2-$), 2.42 (s, 3H, $-CH_3$), 2.81-3.13 (m, 2H, $-N-CH_2-$), 3.27-3.53 (m, 2H, $-CH_2-N-$), 4.55 (s, 2H, $-CH_2-$), 7.13-7.50 (m, 12H, arom), 8.33 (d, J = 8.0, 2H, arom). ms *m/z*: 411 (M^+), 395 (M^+- 16). Anal. Calcd for $C_{27}H_{29}N_3O$: C, 78.80; H, 7.10; N, 10.21. Found: C, 78.69; H, 7.07; N, 10.30.

1,4-Diaryl-2-phenylimidazoles (41):

(i) **Thermolysis of Nitrones 24/27/36d-f:** A solution nitrone **24/27/36d-f** (1.0 mmol) in dry benzene (8 ml) was heated in sealed tube at 140-150 °C for 6-7 h. The solvent was removed under *vacuo* and the residue purified by chromatography on silica gel (eluent: a mixture of EtOAc/hexane in 1:9 ratio) to yield 69-74% of the corresponding imidazoles **41**.

(ii) **Treatment of nitrones 24/27/30 with $NaBH_4$:** To a solution of nitrone **24/27/30** (2.50 mmol) in methanol (50 ml) was added $NaBH_4$

(0.1 g, 2.70 mmol) and the reaction mixture was stirred at rt for 20-24 h. The solvent was removed under *vacuo*, diluted with CH_2Cl_2 (35 ml) and washed with water (4 x 50 ml). The organic layer was dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the residue purified by chromatography on silica gel (eluent: a mixture of EtOAc/hexane in 1:9 ratio) affording 53-66% of products **41**.

(iii) **Reactions of *N*-arylbenzamidine 50 with α-nitrosostyrenes:** A solution of *N*-arylbenzamidine **50** (4.0 mmol) and α-chloro-acetophenone oxime (4.2 mmol) in dry CH_2Cl_2 (20 ml) was stirred at rt in the presence of sodium carbonate for 2-3 h. An identical workup as employed for nitrones **30** was then followed and the crude product thus obtained was further purified by chromatography on silica gel (eluent: A mixture of EtOAc/hexane in a 1:9 ratio) to yield 85-93% of the corresponding products **41**.

1,2,4-Triphenylimidazole (41a): mp 92-94°C; IR (KBr) ν 1591, 1471, 1397, 1205 cm^{-1}. ^1H NMR (90 MHz) δ 7.20-7.61 (m, 14H; 13H, arom and 1H, olefinic), 7.92-8.11 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 118.4 (C-5), 124.9, 125.7, 126.9, 128.1, 128.3, 128.5, 128.7, 129.9, 130.2, 133.8, 138.4, 141.6, 146.9 (C-2). ms *m/z*: 296 (M^+, 100%), 193 (63%), 165 (25%), 116 (3%), 103 (8%), 89 (32%), 77 (28%). Anal Calcd for $C_{21}H_{16}N_2$: C, 85.12; H, 5.44; N, 9.45. Found: C, 85.19; H, 5.41; N, 9.41.

2,4-Diphenyl-1-(p-methylphenyl)imidazole (41b): mp 147-148°C; IR (KBr) ν 1602, 1509, 1399, 1205 cm^{-1}. ^1H NMR (300 MHz) δ 2.35 (s,

3H, $-CH_3$), 7.09 (d, J = 8.4, 2H, arom), 7.15 (d, J = 8.4, 2H, arom), 7.20-7.26 (m, 4H, arom), 7.35-7.40 (m, 3H; 2H, arom and 1H, olefinic), 7.44-7.48 (m, 2H, arom), 7.86-7.90 (m, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.0 ($-CH_3$), 118.5 (C-5), 124.9, 125.4, 126.8, 128.0, 128.2, 128.4, 128.6, 129.9, 130.3, 133.8, 135.8, 138.0, 141.4, 146.8 (C-2). ms *m/z*: 310 (M^+, 89%), 207 (100%), 165 (13%), 116 (10%), 103 (13%), (33%), 65 (13%). Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.84; N, 9.02. Found: C, 85.05; H, 5.86; N, 9.07.

1,2-Diphenyl-4-(p-methylphenyl)imidazole (41c): mp 113.5-114.5 °C; IR (KBr) ν 1600, 1497, 1399, 1204 cm^{-1}. ^1H NMR (90 MHz) δ 2.38 (s, 3H, $-CH_3$), 7.18-7.57 (m, 13H; 12H, arom and 1H, olefinic), 7.83 (d, J = 8.0, 2H, arom). ^{13}C NMR (75.5 MHz) δ 21.2 ($-CH_3$), 118.0 (C-5), 124.9, 125.7, 128.0, 128.1, 128.3, 128.7, 129.2, 129.3, 130.3, 131.0, 136.5, 138.5, 141.7, 146.7. ms *m/z*: 310 (M^+). Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.84; N, 9.02. Found: C, 85.17; H, 5.85; N, 9.07.

***Thermolysis of Nitrones 30* : General procedure for 45:** A solution of 30 (1.0 mmol) in benzene (8 ml) was heated in sealed tube at 140-150 °C for 6-7 h. The solvent was removed under *vacuo* and the residue purified by column chromatography on silica gel (eluent: a mixture of EtOAc/hexane in a 1:6 ratio)

3-(*N,N*-Dimethylformamido)-1'-phenylbenzamidine (45a): Yield 73%; mp 125.5-126.5 °C; IR (KBr) ν 3422 (br), 1635, 1602, 1548, 1490,

1440, 1389, 1346, 1201 cm^{-1}. ^{1}H NMR (90 MHz) δ 3.05 (s, 3H, $-N-CH_3$), 3.32 (s, 3H, $-N-CH_3$), 6.80-6.77 (m, 10H, arom), 12.40 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 35.2 ($-N-CH_3$), 37.3 (CH_3-N-), 123.2, 124.3, 128.0, 128.6, 129.2, 130.2, 135.2, 139.1, 163.0 (C=N), 164.7 (C=O). ms *m/z*: 267 (M^+, 14%), 223 (100%), 180 (22%), 77 (21%). Anal. Calcd for $C_{16}H_{17}N_3O$: *C, 71.89; H, 6.41; N, 15.72. Found: C, 71.78; H, 6.45; N, 15.67.*

***N*-[Phenyl-{*N'*-(p-methylphenyl)imino}methyl]-4-morpholine-carboxamide (45b):** Yield 66%; mp 141-142.5 °C; IR (KBr) ν 3437 (br), 1625, 1590, 1572, 1525, 1447, 1418, 1235 cm^{-1}. ^{1}H NMR (90 MHz) δ 2.30 (s, 3H, $-CH_3$), 3.70 (br s, 8H, morpholino), 6.83 (d, *J* = 8.7, 2H, arom), 7.08 (d, *J* = 8.7, 2H, arom), 7.23-7.67 (m, 5H, arom). 12.43 (br s, exchangable with D_2O, 1H, -NH). ms *m/z*: 323 (M^+). Anal. Calcd for $C_{29}H_{21}N_3O_2$: C, 70.56; H, 6.54; N, 12.99. Found: C, 70.69; H, 6.47; N, 12.91.

***Reactions of N-arylamino 1,3-diaza-1,3-butadienes 51 with α-nitrososty*renes**: General procedure: A solution of *N*-arylamino 1,3-diaza-1,3-butadienes **51** (4 mmol) and α-chloroacetophenone oxime **26** (4.2 mmol) was stirred at rt in the presence of anhydrous sodium carbonate (0.64 g, 6.0 mmol) for 2-3 h. A similar workup as described for nitrones **30** was employed and the crude reaction mixture was chromatographed over a silica gel column. Elution with EtOAc/hexane (1:20) resulted in the isolation of imidazoles **52**. Further elution with EtOAc/hexane (1:5) afforded the nitrones **53**.

4-(p-Chlorophenyl)-1-phenyl-2-[(*N*-phenyl)benzamidino]imidazole (52a): Yield 32%; mp 179-180 °C; IR (KBr) ν 3417 (br), 1625, 1592, 1569, 1493, 1434, 1390, 1197 cm^{-1}. ^1H NMR (300 MHz) δ 6.93 (d, *J* = 7.8, 2H, arom), 7.03-7.07 (m, 1H, arom), 7.18-7.38 (m, 9H; 8H, arom and 1H, olefinic), 7.46-7.54 (m, 4H, arom), 7.68 (d, *J* = 7.8, 2H, arom), 7.75 (d, *J* = 7.3, 2H, arom), 12.70 (br s, exchangable with D_2O, 1H, -NH). ms *m/z*: 448 (M^+, 13%), 356 (15%), 207 (12%), 180 (100%), 77 (63%), 51 (13%). Anal. Calcd for $C_{28}H_{21}N_4Cl$: C, 74.91; H, 4.71; N, 12.48. Found: C, 74.79; H, 4.75; N, 12.54.

4-(p-Chlorophenyl)-1-phenyl-2-[(*N*-phenyl)benzamidino]imidazole-3-oxide (53a): Yield 53%; mp 169-171 °C; IR (KBr) ν 3430 (br), 1626, 1589, 1570, 1491, 1396, 1251 cm^{-1}. ^1H NMR (300 MHz) δ 6.82 (d, *J* = 7.7, 2H, arom), 6.90-6.95 (m, 1H, arom), 7.06-7.62 (m, 15H; 14H, arom and 1H, olefinic), 8.02 (d, *J* = 8.6, with fine splitting, 2H, arom), 13.27 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 111 (C-4), 121.7, 123.0, 125.2, 126.3, 128.0, 128.1, 128.2, 128.7, 128.8, 129.2, 130.2, 130.3, 134.0, 134.7, 136.6, 140.6 (C-2), 158.2 (C-amidino). ms *m/z*: 464 (M^+, 15%), 448 (M^+-16, 45%), 356 (25%), 207 (22%), 180 (100%), 104 (10%), 77 (79%), 51 (17%). Anal. Calcd for $C_{28}H_{21}N_4OCl$: C, 72.33; H, 4.55; N, 12.05. Found: C, 72.41; H, 4.52; N, 12.00.

1,4-Diphenyl-2-[(*N*-phenyl)benzamidino]imidazole (52b): Yield 31%; mp 174-175 °C; IR (KBr) ν 3446 (br), 1623, 1590, 1490, 1399 cm^{-1}. ^1H NMR (300 MHz) δ 6.93 (d, *J* = 7.5, with fine splitting, 2H,

arom), 6.99-7.06 (m, 1H, arom), 7.17-7.55 (m, 14H; 13H, arom and 1H, olefinic), 7.69 (d, J = 7.5, with fine splitting, 2H, arom), 7.83 (d, J = 8.3, with fine splitting, 2H, arom), 12.81 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 112.7 (C-4), 123.4, 124.0, 124.5, 125.1, 126.8, 126.9, 128.0, 128.6, 128.9, 129.6, 129.8, 133.8, 135.5, 137.2, 137.7, 140.1, 150.1 (C-2), 157.1 (C-amidino). ms *m/z*: 414 (M^{+}). Anal. Calcd for $C_{28}H_{22}N_4$: C, 81.13; H, 5.35; N, 13.52. Found: C, 81.04; H, 5.33; N, 13.57.

1,4-Diphenyl-2-[(*N*-phenyl)benzamidino]imidazole-3-oxide (53b): Yield 49%; mp 195-197 °C; IR (KBr) ν 3418 (br), 1636, 1595, 1495, 1395, 1257 cm^{-1}. ^{1}H NMR (300 MHz) δ 6.83 (d, J = 7.7, 2H, arom), 6.88-6.94 (m, 1H, arom), 7.07-7.70 (m, 16H; 15H, arom and 1H, olefinic), 8.05 (d, J = 8.4, with fine spltting, 2H, arom), 13.88 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 111.0 (C-4), 121.8, 123.0, 123.4, 123.9, 124.5, 125.1, 125.2, 126.7, 127.0, 127.8, 128.0, 128.1, 128.3, 128.6, 128.7, 128.8, 129.2, 129.5, 129.8, 129.9, 130.3, 134.9, 136.8, 140.6 (C-2), 140.7, 158.2 (C-amidino). ms *m/z*: 430 (M^{+}), 414 (M^{+}- 16). Anal. Calcd for $C_{28}H_{22}N_4O$: C, 78.12; H, 5.15; N, 13.01. Found: C, 78.03; H, 5.18; N, 13.09.

1-(p-Methoxyphenyl)-4-phenyl-2-[(*N*-phenyl)benzamidino]imidazole (52c): Yield 36%; mp 158-159 °C; IR (KBr) ν 3426 (br), 1622, 1596, 1510, 1248, 1175 cm^{-1}. ^{1}H NMR (300 MHz) δ 3.86 (s, 3H, $-OCH_3$), 6.92 (d, J = 7.7, 2H, arom), 6.98-7.05 [m, 3H, arom; consisting in at 6.99 (d, J = 8.9, 2H)], 7.17-7.34 (m, 8H;

7H, arom and 1H, olefinic), 7.37-7.43 (m, 1H, arom), 7.53 (d, J = 7.7, with fine splitting, 2H, arom), 7.58 (d, J = 8.9, with fine splitting, 2H, arom), 7.82 (d, J = 8.3, with fine splitting, 2H, arom), 12.79 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 55.6 ($-OCH_3$), 113.0 (C-4), 114.0, 123.4, 123.9, 124.4, 126.4, 126.7, 128.0, 128.6, 128.8, 129.5, 129.7, 130.9, 133.9, 135.6, 136.9, 140.2, 150.2 (C-2), 157.0 (C-amidino), 158.4. ms *m/z*: 444 (M^+). Anal. calcd for $C_{29}H_{24}N_4O$: C, 78.36; H, 5.44; N, 12.60. Found: C, 78.28; H, 5.48; N, 12.69.

1-(p-Methoxyphenyl)-4-phenyl-2-[(*N*-phenyl)benzamidino]imidazole-3-oxide (53c): Yield 53%; mp 175-176 °C; IR (KBr) ν 3421 (br), 1618, 1592, 1491, 1571, 1511, 1385, 1250 cm^{-1}. ^1H NMR (300 MHz) δ 3.88 (s, 3H, $-OCH_3$), 6.82 (d, J = 8.0, 2H, arom), 6.88-6.93 (m, 1H, arom), 7.04-7.12 (m, 5H, arom), 7.17-7.24 (m, 2H, arom), 7,28-7.30 (m, 2H, arom), 7.42-7.53 (m, 6H; 5H, arom and 1H, olefinic), 13.42 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 55.6 ($-OCH_3$), 111.3 (C-4), 114.3, 121.8, 122.9, 126.6, 127.0, 128.0, 128.2, 128.5, 128.6, 129.5, 129.8, 130.2, 130.3, 134.9, 140.6 (C-2), 140.8, 158.1 (C-amidino), 159.2. ms *m/z*: 460 (M^+), 444 (M^+- 16). Anal. Calcd for $C_{29}H_{24}N_4O_2$: C, 75.63; H, 5.25; N, 12.17. Found: C, 75.74; H, 5.28; N, 12.15.

1-(p-Methoxyphenyl)-4-(p-methylphenyl)-2-[(*N*-phenyl)benzamidino] imidazole (52d): Yield 38%, mp 165-167 °C; IR (KBr) ν 3447 (br), 1623, 1594, 1510, 1440, 1396, 1242, 1179 cm^{-1}. ^1H NMR (300 MHz) δ 2.37 (s, 3H, $-CH_3$), 3.85 (s, 3H, $-OCH_3$), 6.92 (d, J = 7.7, 2H,

arom), 6.95-7.05 [m, 3H, arom; consisting in at 6.99 (d, J = 8.9)], 7.16-7.32 (m, 8H; 7H, arom and 1H, olefinic), 7.53 (d, J = 6.8, with fine splitting, 2H, arom), 7.57 (d, J = 8.9, with fine splitting, 2H, arom), 7.71 (d, J = 8.1, 2H, arom), 12.82 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 21.3 ($-CH_3$), 55.5 ($-OCH_3$), 112.5 (C-4), 114.0, 123.3, 123.8, 124.3, 126.3, 128.0, 128.8, 129.3, 129.5, 129.7, 131.1, 135.6, 136.3, 136.9, 140.2, 150.0 (C-2), 156.8 (C-amidino), 158.3. ms *m/z*: 458 (M^+, 46%), 366 (12%), 260 (17%), 229 (12%), 210 (12%), 180 (100%), 104 (11%), 77 (67%), 51 (9%). Anal. Calcd for $C_{30}H_{26}N_4O_2$: C, 78.58; H, 5.71; N, 12.22. Found: C, 78.66; H, 5.69; N, 12.17.

1-(p-Methoxyphenyl)-4-(p-methylphenyl)-2-[(*N*-phenyl)benzamidino] imidazole-3-oxide (53d): Yield 44%; mp 170-171 °C; IR (KBr) ν 3423 (br), 1625, 1592, 1512, 1384, 1250 cm^{-1}. ^1H NMR (300 MHz) δ 2.40 (s, 3H, $-CH_3$), 3.90 (s, 3H, $-OCH_2$), 6.82 (d, J = 8.1, 2H, arom), 6.88-6.94 (m, 1H, arom), 7.05-7.31 (m, 10H; 9H, arom and 1H, olefinic), 7.46 (d, J = 8.4, 2H, arom), 7.53 (d, J = 8.8, 2H, arom), 7.93 (d, J = 8.1, 2H, arom), 13.43 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 21.4 ($-CH_3$), 55.6 ($-OCH_3$), 110.9 (C-4), 114.3, 121.8, 122.8, 125.0, 126.6, 127.0, 128.0, 128.6, 129.3, 129.9, 130.2, 130.3, 134.9, 138.2, 140.8 (C-2), 158.0 (C-amidino), 159.2. ms *m/z*: 474 (M^+), 458 (M^+- 16). Anal. Calcd for $C_{30}H_{26}N_4O_2$: C, 75.93; H, 5.52; N, 11.80. Found: C, 75.85; H, 5.50; N, 11.86.

1-(p-Chlorophenyl)-4-(p-methylphenyl)-2-[*N*-(p-methylphenyl) benzamidino]imidazole (52e): Yield 37%; mp 171-172 °C; IR (KBr) ν 3437 (br), 1623, 1588, 1511, 1395, 1239 cm^{-1}. ^1H NMR (90 MHz) δ 2.24 (s, 3H, $-CH_3$), 2.35 (s, 3H, $-CH_3$), 6.88 (d, J = 8.5, 2H arom), 7.07 (d, J = 8.5, 2H, arom), 7.21-7.81 (m, 14H; 13H, arom and 1H, olefinic), 12.71 (br s, exchangable with D_2O, 1H -NH). ms *m/z*: 477 (M^+). Anal. Calcd for $C_{30}H_{25}N_4Cl$: C, 75.54; H, 5.28; N, 11.75. Found: C, 75.43; H, 5.31; H, 11.81.

1-(p-Chlorophenyl)-4-(p-methylphenyl)-2-[*N*-(p-methylphenyl) benzamidino]imidazole-3-oxide (53e): Yield 51%; mp 151-152 °C; IR (KBr) ν 3427 (br), 1618, 1594, 1391, 1249 cm^{-1}. ^1H NMR (90 MHz) δ 2.22 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-CH_3$), 6.73-7.00 (m, 4H, arom), 7.07-7.70 (m, 12H; 11H, arom and 1H, olefinic), 7.98 (d, J = 8.8, 2H, arom), 13.34 (br s, exchangable with D_2O, 1H, -NH). ms *m/z*: 493 (M^+), 477 (M^+- 16). Anal. Calcd for $C_{30}H_{25}N_4OCl$: C, 73.09; H, 5.11; N, 11.36. Found: C, 73.17; H, 5.08; N, 11.44.

1,4-Bis(p-methylphenyl)-2-[(*N*-phenyl)benzamidino]imidazole (52f): Yield 32%; mp 156-157 °C; IR (KBr) ν 3427 (br), 1623, 1593, 1573, 1494, 1434, 1396 cm^{-1}. ^1H NMR (90 MHz) δ 2.40 (s, 3H, $-CH_3$), 2.43 (s, 3H, $-CH_3$), 6.77-7.73 (m, 19H; 18H, arom and 1H, olefinic), 12.75 (br s, exchangable with D_2O, 1H, -NH). ms *m/z*: 442 (M^+). Anal. Calcd for $C_{30}H_{26}N_4$: C, 81.42; H, 5.92; N, 12.66. Found: C, 81.51; H, 5.90; N, 12.59.

1,4-Bis(p-methylphenyl)-2-[(*N*-phenyl)benzamidino]imidazole-3-oxide (53f): Yield 51%; mp 193-194 °C; IR (KBr) ν 3433 (br),

1621, 1596, 1491, 1393, 1248 cm^{-1}. ^1H NMR (90 MHz) δ 2.40 (s, 3H, $-CH_3$), 2.47 (s, 3H, $-CH_3$), 6.83-7.64 (m, 17H; 16H, arom and 1H, olefinic), 8.03 (d, *J* = 8.5, 2H, arom), 13.29 (br s, exchangable with D_2O, 1H, -NH). ms *m/z*: 458 (M^+), 442 (M^+- 16). Anal. Calcd for $C_{30}H_{26}N_4O$: C, 78.58; H, 5.71; N, 12.22. Found: C, 78.69; H, 5.73; N, 12.18.

Diels-Alder adducts of 53 and DMAD: A solution of nitrone **53c/f** (0.30 g, 0.50 mmol) and DMAD (0.06 g, 0.50 mol) in CH_2Cl_2 was stirred at rt for 45 min. The solvent was removed under reduced pressure and the residue chromatographed over a silica gel column (eluent: a mixture of EtOAc/hexane in 1:3 ratio).

2,3-Bis(methoxycarbonyl)-4,6-bis(p-methylphenyl)-3a-[(*N*-phenyl) benzamidino]imidazo[1,2-b]isoxazole (58a): Yield 96%; mp 196-197 °C; IR (KBr) ν 1748, 1723, 1644, 1622, 1592, 1507, 1494, 1480, 1437, 1356, 1204, 1166, 1117 cm^{-1}. ^1H NMR (300 MHz) δ 2.37 (s, 3H, $-CH_3$), 2.40 (s, 3H, $-CH_3$), 3.58 (s, 3H, $-CO_2CH_3$), 3.85 (s, 3H, $-CO_2CH_3$), 5.36 (s, 1H, olefinic), 6.93 (d, *J* = 7.7, 2H, arom), 7.02-7.07 (m, 1H, arom), 7.18-7.32 (m, 9H, arom), 7.39 (d, *J* = 8.2, 2H, arom), 7.47 (d, *J* = 7.7, 2H, arom), 7.55 (d, *J* = 8.1, 2H, arom), 12.63 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 21.25 ($-CH_3$), 21.28 ($-CH_3$), 51.8 ($-CO_2CH_3$), 53.1 ($-CO_2CH_3$), 100.1, 122.2, 123.4, 124.2, 125.2, 126.7, 127.9, 128.9, 129.4, 129.5, 129.8, 130.7, 135.2, 136.6, 137.9, 139.9, 146.6, 157.8, 158.2, 162.2 (CO_2CH_3), 165.1 (CO_2CH_3). ms *m/z*: 600 (M^+). Anal. Calcd for $C_{36}H_{32}N_4O_5$: C, 71.98; H, 5.37; N, 9.33.

Found: C, 72.07; H, 5.37; N, 9.27.

2,3-Bis(methoxycarbonyl)-4-(p-methoxyphenyl)-6-phenyl-3a-[(*N*-phenyl)benzamidino]imidazo[1,2-b]isoxazole (58b): Yield 94%; mp 177-179 °C; IR (KBr) ν 1745, 1717, 1641, 1613, 1588, 1511, 1487, 1355, 1253, 1167, 1107 cm^{-1}. ^{1}H NMR (300 MHz) δ 3.60 (s, 3H, $-CO_2CH_3$), 3.86 (s, 6H, $-CO_2CH_3$ and $-OCH_3$), 5.38 (s, 1H, olefinic), 6.93 (d, J = 7.5, 2H, arom), 7.00 (d, J = 9.0, with fine splitting, 2H, arom), 7.04-7.08 (m, 1H, arom), 7.19-7.31 (m, 6H, arom), 7.40-7.48 (m, 6H, arom), 7.86 (d, J = 8.5, with fine splitting, 2H, arom), 12.61 (br s, exchangable with D_2O, 1H, -NH). ^{13}C NMR (75.5 MHz) δ 51.9 ($-CO_2CH_3$), 53.2 ($-CO_2CH_3$), 55.5 ($-OCH_3$), 100.1, 114.1, 122.0, 123.5, 124.2, 125.2, 126.0, 126.9, 128.0, 128.2, 128.7, 128.9, 129.6, 129.9, 131.7, 135.1, 139.8, 146.8, 157.9, 158.1, 159.1, 162.2 ($-CO_2CH_3$), 165.1 ($-CO_2CH_3$). ms *m/z*: 602 (M^+). Anal. Calcd for $C_{35}H_{30}N_4O_6$: C, 69.75; H, 5.02; N, 9.29. Found: C, 69.87; H, 4.97; N, 9.21.

References

1. Hamer, J.; Ahmed, M. in *1,4-Cycloaddition Reactions*, ed. J Hamer, Academic Press, New York, 1967, p 419 and Cullis, B.T. *ibid.*, p 143 (b) Kirby, G.W.; Sweeny, J.G. *J. Chem. Soc., Perkin Trans. 1*, 1981, 3250 (c) Kirby, G.W.; McGuigan, H.; Mclean, D. *J. Chem. Soc., Perkin Trans. 1*, 1985, 1961. (d) Christie, C.C.; Kirby, G.W.; McGuigan, H.; Mackinnon, J.W.M. *J. Chem. Soc., Perkin Trans 1*, 1985, 2469. (e) Kirby,

G.W.; Nazeer, M. *Tetrahedron*, **1988**, *29*, 6173. (f) McClure, K.F.; Danishefsky, S.J. *J. Am. Chem. Soc.*, **1993**, *115*, 6094. (g) Meekel, A.A.P.; Resmini, M.; Pandit, U.K. *J. Chem. Soc., Chem. Commun.*, **1995**, 571.

2. a) Kirby, G.W.; Sweeny, J.G. *J. Chem. Soc., Chem. Commun.*, **1973**, 704. (b) Kirby, G.W.; Mackinnon, J.W.M. *J. Chem. Soc., Chem. commun.*, **1977**, 23.
3. a) Gilchrist, T.L.; Peek, M.E.; Rees, C.W. *J. Chem. Soc., Chem. Commun.*, **1975**, 913, 914. (b) Gilchrist, T.L.; Harris, C.J.; King, F.D.; Peek, M.E.; Rees, C.W. *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2161.
4. a) Horsewood, P.; Kirby, G.W. *J. Chem. Soc., Chem. Commun.*, **1971**, 1139. (b) Kirby, G.W. *Chem. Soc. Rev.*, **1977**, *6*, 1.
5. Gilchrist, T.L. *Chem. Soc. Rev.*, **1983**, *12*, 53.
6. Francotte, E.; Merenyi, R.; Vandenbulcke-Loyette, B; Viehe, H.-G. *Helv. Chim. Acta*, **1981**, *64*, 1208 and references therein.
7. Denmark, S.E.; Dappen, M.S. *J. Org. Chem.* **1984**, *49*, 798.
8. Wieser, K,; Berndt, A. *Angew Chem., Int. Ed. Engl.*, **1975**, *14*, 70.
9. Hobold, W.; Prietz, U.; Pritzkow, W. *J. Prakt. Chem.*, **1969**, *311*, 260.
10. Denmark, S.E.; Dappen, M.S. *J. Org. Chem.*, **1984**, *49*, 4741.
11. Viehe, H.-G., Merenyi, R.; Francotte, E.; Van Meerssche, M.; Germain, G.; Reclercq, J.P.; Bodart-Filmont, J. *J. Am. Chem. Soc.*, **1977**, *99*, 2340.

12. Faragher, R.; Gilchrist, T.L. *J. Chem. Soc., Perkin Trans. 1*, 1979, 258.

13. Muller, L.L.; Hamer, *J. '1,2-Cycloaddition Reactions,'* Interscience Publ., New York, 1967, p 257.

14. Faragher, R.; Gilchrist, T.L. *J. Chem. Soc., Perkin Trans 1.*, 1979, 249.

15. Gilchrist, T.L.; Roberts, T.G. *J. Chem. Soc., Perkin Trans. 1*, 1983, 1283.

16. Faragher, R.; Gilchrist, T.L. *J. Chem. Soc., Chem. Commun.*, 1978, 847.

17. Davis, D.E.; Gilchrist, T.L.; Roberts, T.G. *J. Chem. Soc., Perkin Trans. 1*, 1983, 1275.

18. Gilchrist, T.L.; Lingham, D.A.; Roberts, T.G. *J. Chem. Soc., Chem. Commun.*, 1979, 1089.

19. Iskander, G.M.; Gulta, V.S., *J. Chem. Soc., Perkin Trans. 1*, 1982, 1891.

20. Faragher, R.; Gilchrist, T.L. *J. Chem. Soc., Chem. Commun.*, 1976, 581.

21. Campbell, J.A.; Harris, I.; Mackay, D.; Sauer, T.D. *Can. J. Chem.*, 1975, *53*, 535.

22. Dao, L.H.; Dust, J.M.; Mackay, D.; Watson, K.N. *Can. J. Chem.*, 1979, *57*, 1712.

23. Pople, J.A.; Beveridge, D.L. "*Approximate Molecular Orbital Theory*", McGraw-Hill, New York, 1970.

24. Curtin, D.Y.; Tristram, E.W. *J. Am. Chem. Soc.*, 1950, *72*, 5238.

Wrong reference!

25. Gilchrist, T.L.; Iskander, G.M.; Yagoub, A.K. *J. Chem. Soc., Chem. Commun.*, **1981**, 696.

26. Mackay, D.; Watson, K.N. *J. Chem. Soc., Chem. Commun.*, **1982**, 775.

27. Mackay, D.; Watson, K.N. *J. Chem. Soc., Chem. Commun.*, **1982**, 777.

28. Lai, E.C.K.; Mackay, D.; Taylor, N.J.; Watson, K.N. *J. Chem. Soc., Perkin Trans. 1*, **1990**, 1497.

29. Mazumdar, S.N.; Mahajan, M.P. *Ph.D. Thesis*, **1988**, North-Eastern Hill University, Shillong-793 003.

30. Sharma, A.K.; Mazumdar, S.N.; Mahajan, M.P. *Tetrahedron Lett.*, **1993**, *34*, 7961.

31. (a) Tufariello, J.J. *Acc. Chem. Res.*, **1979**, *12*, 396. (b) Confalone, P.N.; Huie, E.M. *Organic Reactions*; John Wiley and Sons, Inc.: New York, **1988**, Vol 36, p 1. (c) DeShong, P.; Lander, S.W., Jr.; Leginus, J.M. Dicken, C.M. *Advances in Cycloaddition*, Curran, D.P., Ed.; JAI Press : Greenwich and London, **1988**; Vol. 1, p 87. (d) Breuer, E. *Nitrones, Nitronates and Nitroxides*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons Ltd.; New York, **1989**; p 139. (e) Mulzer, J.; Altenbach, H.-J.; Braun, M; Krohn, K.; Reissig, H.-U. *Organic synthesis Highlights*; VCH : Weinheim, **1991**; p 77.

32. Murahashi, S.I.; Mitsui, H.; Shiota, T.; Tsuda, T. Watanabe, S. *J. Org. Chem.*, **1990**, *55*, 1736 and references therein.

33. Lathbury, D.C.; Shaw, R.W.; Bates, P.A., Hursthouse, M.B.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1*, 1989, 2415 and references therein.

34. Katagiri, N.; Sato H.; Kurimoto, A. Okada, M.; Yamada, A.; Kaneko, C. *J. Org. Chem.*, 1994, *59*, 8101.

35. Cicchi, S.; Goti, A.; Brandi, A. *J. Org. Chem.*, 1995, *60*, 4743 (b) Verboom, W.; Reinhoudt, D.N. *Bull. Soc. Chim. Fr.*, 1990, *127*, 704.

36. Crystal, E.J.T.; Gilchrist, T.L.; Stretch, W. *J. Chem. Res.(s)*, 1987, 180; *J. Chem. Res. (M).*, 1987, 1563.

37. Smith, J.H.; Heidema, J.H.; Kaiser, E.T. *J. Am. Chem. Soc.*, 1972, *94*, 9276.

38. Bravo, P.; Gaudiano, G.; Panti, P.P.; Umani-Ronchi, A.; *Tetrahedron*, 1970, *26*, 1315 and references therein.

39. Dornow, A.; Marquardt, H.H.; Paycksch, H. *Chem. Ber.*, 1964, *97*, 2165.

40. Nakanishi, S.; Nantaku, J.; Otsuji, Y. *Chemistry Letters*, 1983, 341.

41. Delpierre, G.R.; Lamchen, M. *Q. Rev.*, 1965, *19*, 329.

42. Mazumdar, S.N.; Mahajan, M.P. *Synthesis*, 1990, 417.

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

44. Bredereck, H.; Gompper, R.; Klemns, K.; Rampfer, H. *Chem. Ber.*, 1959, *29*, 837.

45. *Org. Synthesis* Coll. Vol. IV, 1963, 769.

46. Korter, H.; Scholl, R. *Ber.*, 1901, *34*, 1901.

Appendix

List of Publications:

1. Regioselective and Unusual [3+2] Cycloadditions of α-Nitrosostyrenes with 1,3-Diaza-1,3-Butadienes
A.K. Sharma, S.N. Mazumdar and M.P. Mahajan
Tetrahedron Lett., **1993**, *34*, 7961.

2. Reactions of 1,3 diaza-1,3-Butadienes with Haloketenes - Rearrangements accompanying [4+2] Cycloaddition Reactions
S.M. Mazumdar, S. Mukherji, **A.K. Sharma**, D. Sengupta and M.P. Mahajan
Tetrahedron, **1994**, *50*, 7579.

3. Synthesis of 5-Isopropenyl/Vinyl Substituted Pyrimidinones via [4+2] Cycloaddition Reactions of 1,3-Diaza-1,3-Butadienes with Isopropenyl/Vinylketenes and their further Transformations: [4+2] and Unusual [3+2] Cycloadditions with α-Nitrosostyrenes
A.K. Sharma and M.P. Mahajan
Heterocycles, **1995**, *40*, 787.

4. Synthesis and Regioselective [4+2] Cycloaddition/ Nucleophilic Reactions of *N*-Arylamino-1,3-Diaza-1,3-Butadienes with Ketenes and accompanying Rearrangements
P.D. Dey, **A.K. Sharma**, S.N. Rai and M.P. Mahajan
Tetrahedron, **1995**, *51*, 7459.

5. A Convenient *Trans* Diastereoselective Synthesis of 3-Butadienyl Azetidinones and their Diels-Alder Cycloaddition Reactions
A.K. Sharma, S.N. Mazumdar and M.P. Mahajan
J. Org. Chem., **1996**, *61*, 5506.