CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES

ABSTRACT

By

SUJIT NANDY MAZUMDAR

DEPARTMENT OF CHEMISTRY

SCHOOL OF PHYSICAL SCIENCES

A THESIS

SUBMITTED

IN

FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

To

THE NORTH-EASTERN HILL UNIVERSITY

SHILLONG-793 001

MEGHALAYA (INDIA)

OCTOBER, 1989

Chemistry

ABSTRACT

Hetero Diels-Alder cycloaddition reactions have been shown to be of great potential for the synthesis in heterocyclic chemistry and hence continue to be the focal point of attention of an increasing number of synthetic organic chemists[1-4]. Dienes containing two nitrogen atoms have attracted the attention of chemists in recent years because of their importance in natural product synthesis[5-8]. Though there are numerous reports concerning the participation of 1,2-diaza-1,3-butadienes as 4π components in Diels-Alder reactions but in the contrary reports on 1,3-diaza-1,3-butadienes were found to be rare, and remained unexploited for the syntheses of heterocyclic compounds. This may be

due to the lack of facile synthetic route for the preparation of stable 1,3-diaza-1,3-butadienes and as well as for the unfavourable position of nitrogen (N-2) in the butadiene system[2]. Taking into consideration of all these, it was thought worthwhile, to develop general methods for the syntheses of simple, yet reactive 1,3-diaza-1,3-butadienes and to study their role in cycloaddition reactions.

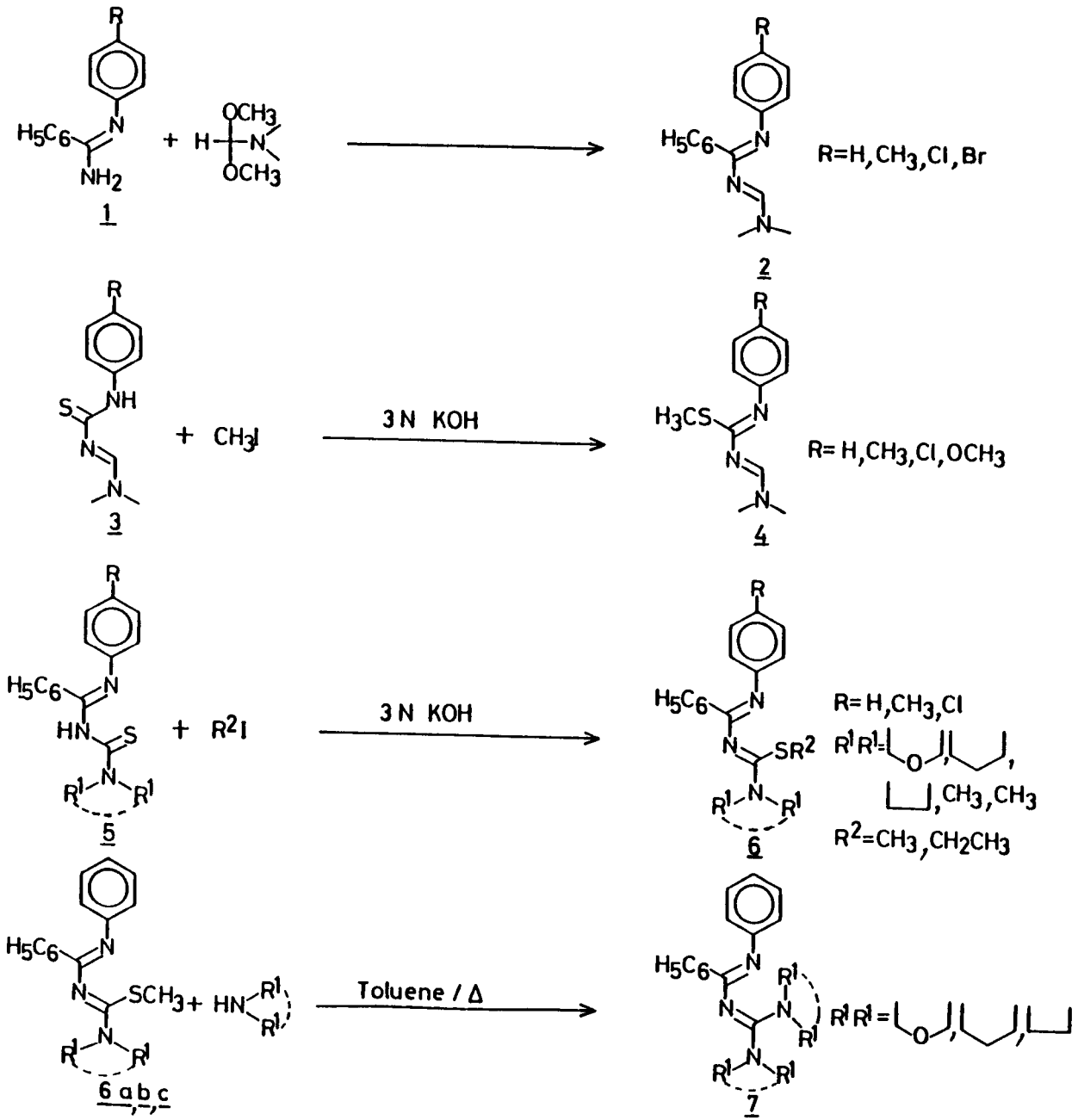
The thesis is divided into five chapters. The first chapter deals with an uptodate literature survey concerning Diels-Alder cycloaddition reactions of various mono- and diazabutadienes.

The lack of reactivity of 1,3-diaza-1,3-butadienes in Diels-Alder cycloaddition reactions has been ascribed to a considerable extent, to the inverse electron demand nature of the system. It was thought, it could perhaps be overcome by devising syntheses of 1,3-diaza-1,3-butadienes having polarising functions at position 4- of this system. The syntheses and reactions of such 1,3-diaza-1,3-butadienes with monophenylketene, monochloroketene, diphenylketene and zinc enolates (derived from ethylbromacetate) are described in chapter II of the thesis Thus, condensation of the appropriate N-arylbenzamidines(1) with N,N-dimethylformamide dimethylacetal resulted in 1-aryl-4-dimethylamino-

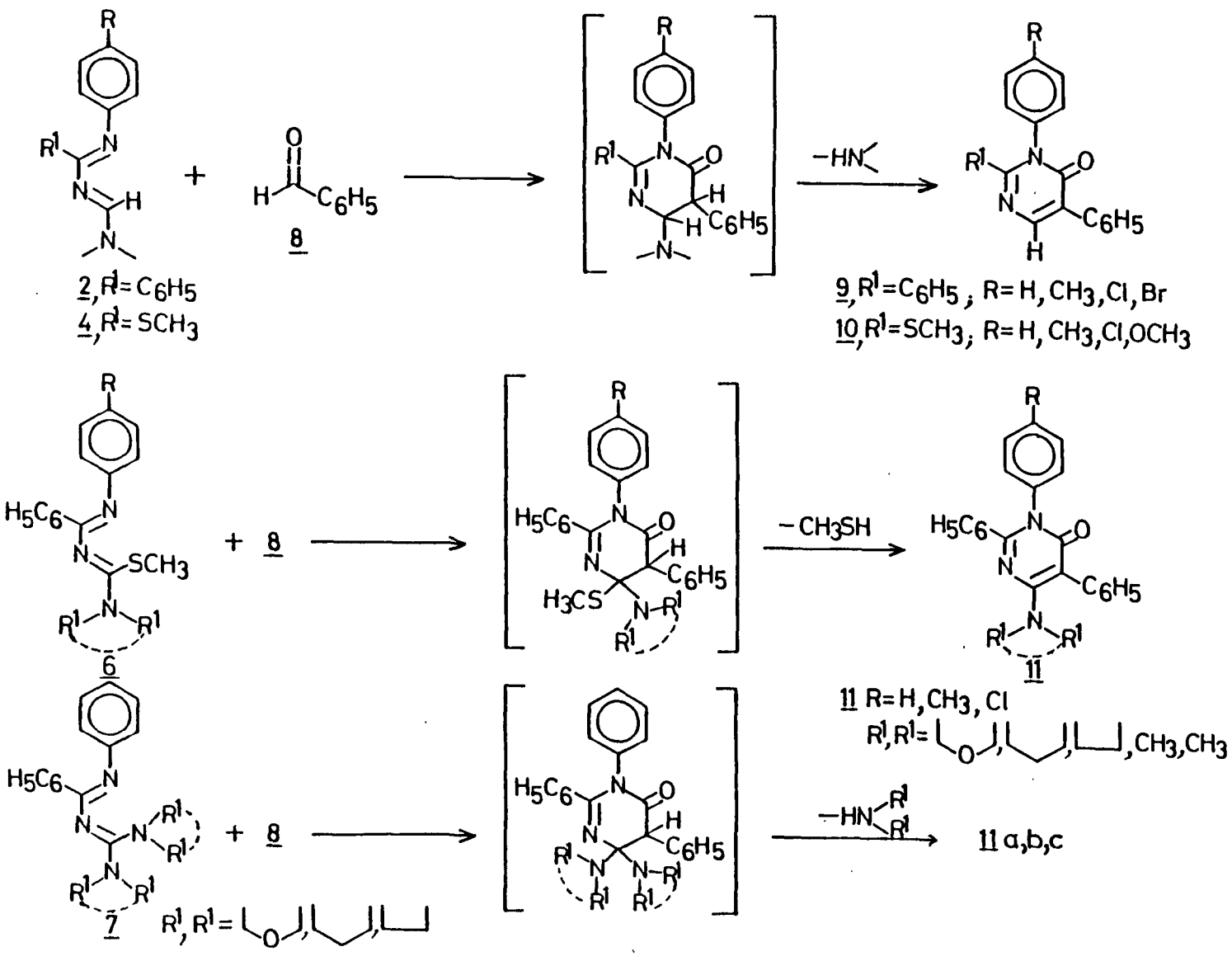
2-phenyl-1,3-diaza-1,3-butadienes(2).

The thiomethylation of N'-aryl-N-thiocarbamoyl formamidines(3) with methyl iodide gave excellent yields of 1-aryl- 4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadienes(4). Similarly, alkylation of 4-[(α-arylamino)benzylidenethiocarbamoyl]sec.amine(5) afforded very good yields of previously unknwon 1-aryl-4-sec. amino-2-phenyl-4-thioalkyl-1,3- diaza-1,3-butadienes(6). The treatment of 6a,b,c with sec. amines in refluxing dry toluene yielded another set of new 1,3-diaza-1,3-butadienes(7)(Scheme-1).

The reactions of 1,3-diaza-1,3-butadienes(2) with monophenylketene(8), generated in situ from phenylacetylchloride and triethylamine, afforded very good yields of previously unknown 1-aryl-2,5-diphenyl-1,6-dihydropyrimidin-6-ones(9)[9]. The pyrimidin-6-ones(9) were formed by the elimination of dimethylamine from the initially formed (4+2) cycloadducts of 2 and 8. In order to observe the effect of polarising function at positions 2- and 4- of 4 and electronic/steric effect of two polarising functions at positions 4- of 1,3-diaza-1,3-butadienes (6 and 7) with monophenylketene(8) their reactions were carried out. The formation of (4+2) cycloadducts 10 and 11 clearly established the general nature of the 1,3-diaza-1,3-butadienes


R
H_5C_6
N
NH_2
1
+ H
OCH_3
N
OCH_3
R=H, CH_3, Cl, Br
2
NH
S
3
+ CH_3I
3 N KOH
H_3CS
R= H, CH_3, Cl, OCH_3
4
HN
SR^2
5
+ R^2I
3 N KOH
R= H, CH_3, Cl
R^1R^1=
O
CH_3, CH_3
R^2=CH_3, CH_2CH_3
6
SCH_3+ HN
6 a b c
Toluene / Δ
R^1R^1=
7

Scheme 1

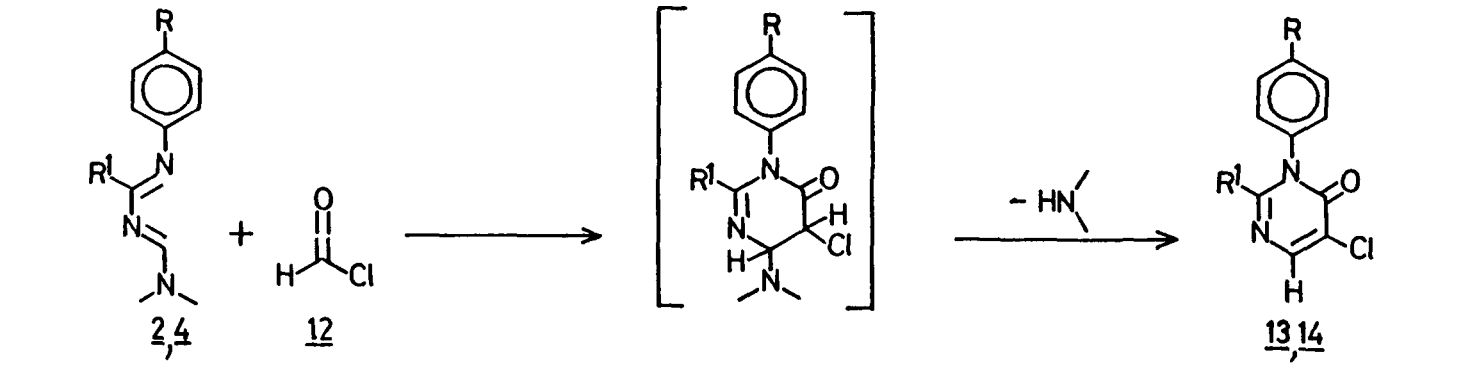

2, R1 = C6H5
4, R1 = SCH3
8
9, R1 = C6H5 ; R = H, CH3, Cl, Br
10, R1 = SCH3; R = H, CH3, Cl, OCH3
6
7
11
11 R = H, CH3, Cl
11 a,b,c

Scheme 2

towards cycloaddition reactions with monophenylketene (Scheme-2).

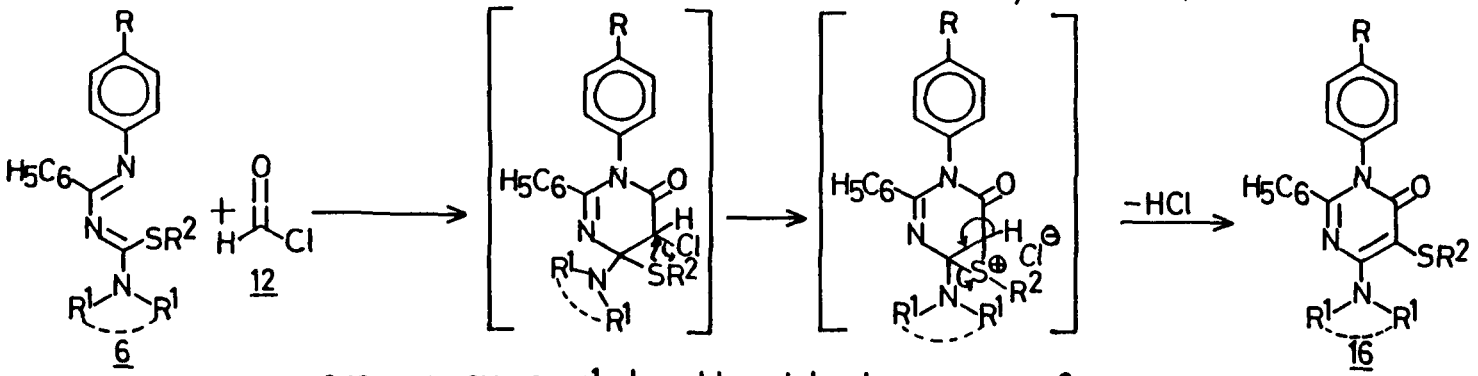
The reactions of 1,3-diaza-1,3-butadienes, 2 and 4 with monochloroketene (12) yielded 1-aryl-5-chloro-2-phenyl-1,6-dihydropyrimidin-6-ones and 1-aryl-5-chloro-2-thiomethyl-1,6-dihydropyrimidin-6-ones, respectively. In these reactions also, the substituted 5-chloropyrimidin-6-ones (13) were formed by the elimination of dimethylamine molecule from initially formed (4+2) cycloadducts. Interestingly, the treatment of 1,3-diaza-1,3-butadienes(6) resulted in 1-aryl-2-phenyl-4-sec.amino-5-thioalkyl-1,6-dihydropyrimidin-6-ones (16). The pyrimidones 16, were probably formed by expulsion of a molecule of hydrogen chloride accompanied by the migration of thioalkyl group via episulphoniumion intermediate. The mechanism is supported by absence of such rearrangement in case of the reactions of 4,4-bis(sec. amino)1,2- diphenyl-1,3-diaza-1,3-butadienes (7) with 12, which selectively gave 5-chloro-1,2-diphenyl-4-sec.amino-1,6-dihydropyrimidin-6-ones (17) (Scheme-3).

The reactions of 1,3-diaza-1,3-butadienes (2) with diphenylketene (18) followed (2+2) cycloaddition pathway and gave β-lactam derivatives(19). The failure of this reaction to undergo (4+2) cycloaddition has been attributed

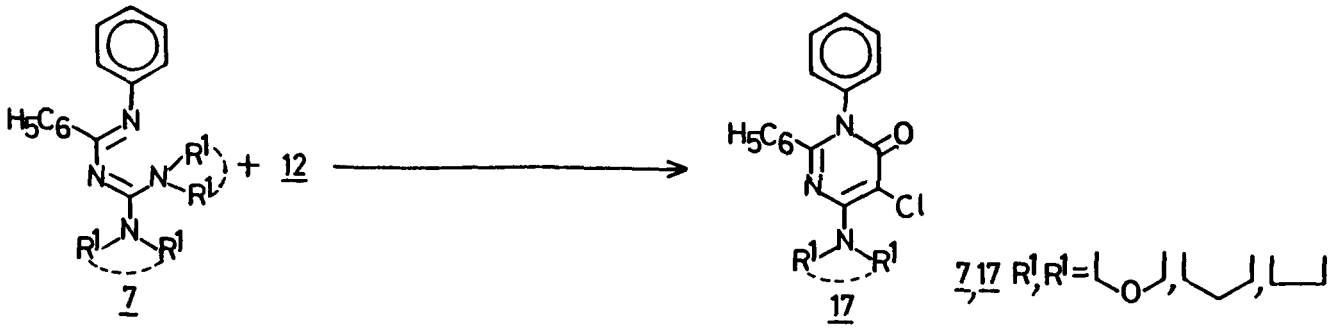


2,4 12 13,14

2,13 $R^1=C_6H_5$; R=H,CH_3,Cl,Br
4,14 $R^1=SCH_3$; R=H,CH_3,Cl,OCH_3



6,16 R=H,CH_3,Cl; R^1= O, $CH_2CH_2CH_2$, CH_2CH_2, CH_3,CH_3; R^2=CH_3, C_2H_5



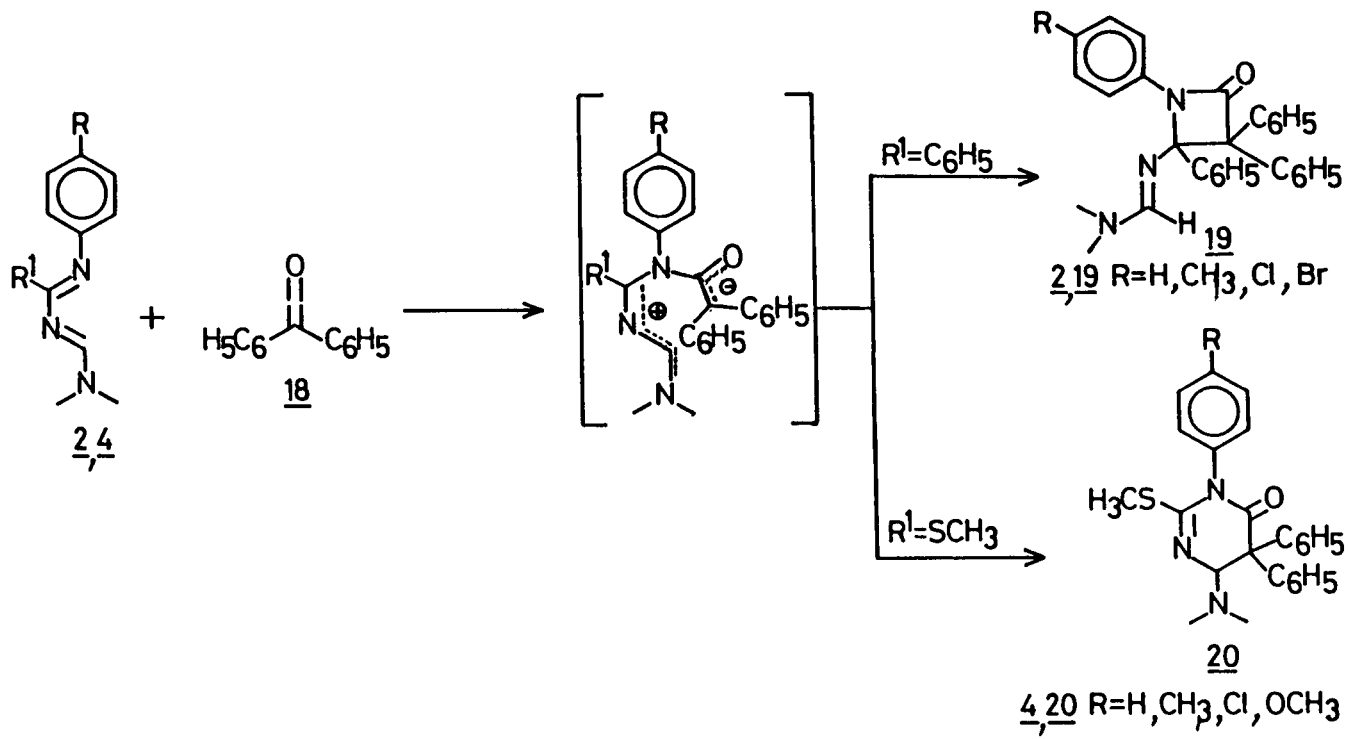
7 12 17 7,17 R^1,R^1= O, $CH_2CH_2CH_2$, CH_2CH_2

Scheme 3

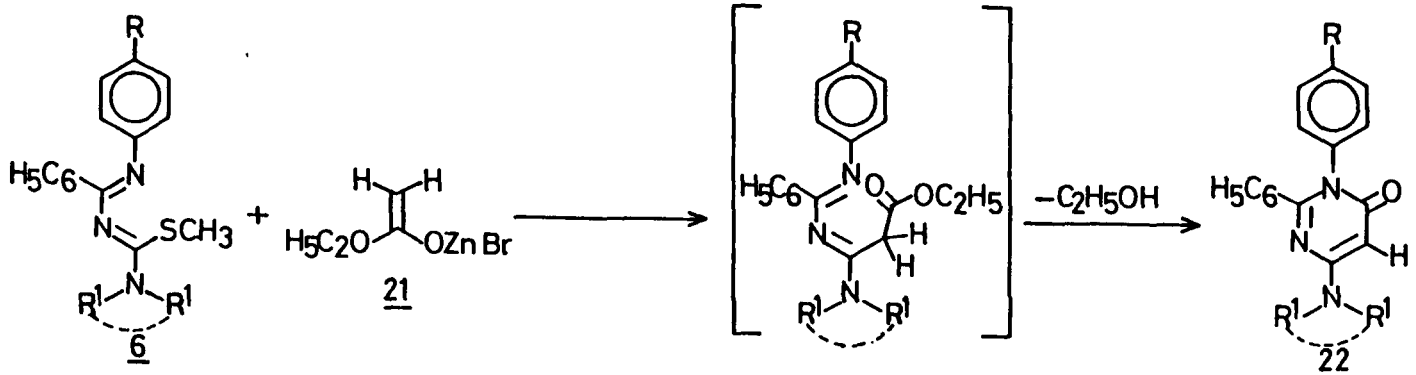
to the steric reasons. However, similar reactions of diphenylketene with 4, gave excellent yields of (4+2) cycloadducts, characterised as 1-aryl-4-dimethylamino-5,5-diphenyl-2-thiomethyl-1,4,5,6-tetrahydropyrimidin-6-ones (Scheme-4). Thus, the cycloaddition pathway followed by 1,3-diaza-1,3-butadienes (2 and 4) with diphenylketene perhaps depends upon the combination of steric and electronic factors.

The reactions of 1,3-diaza-1,3-butadienes (6) with zinc enolate derived from ethylbromoacetate, referred to as Reformatsky reagent (21), in refluxing dry toluene afforded good yields of 1-aryl-2-phenyl-4-sec.amino-1,6-dihydropyrimidin-6-ones (22) (Scheme-5). This constitutes the first report of conjugated 1,4-addition of any Reformatsky reagent to the substrates having carbon-nitrogen double bond. The Reformatsky reagent 21, in this case may be considered equivalent to simple unsubstituted ketene since same product 22, is expected from the reaction of 6 with ketene.

Third chapter of this thesis describes the Diels-Alder cycloaddition reactions of 1,3-diaza-1,3-butadienes (2 and 4) with simple sulphene(23). The reactions of 2 with methanesulphonyl chloride in presence of triethylamine yielded hitherto unknown 2-aryl-5-dimethylamino-3-phenyl-1,2,4-thiadiazin-1,1-dioxide (24) (Scheme-6). Similar reac-


R
R1
N
N
2,4
+
O
H5C6
C6H5
18
R1=C6H5
R1=SCH3
C6H5
C6H5
C6H5
C6H5
19
2,19 R=H,CH3,Cl,Br
H3CS
20
4,20 R=H,CH3,Cl,OCH3

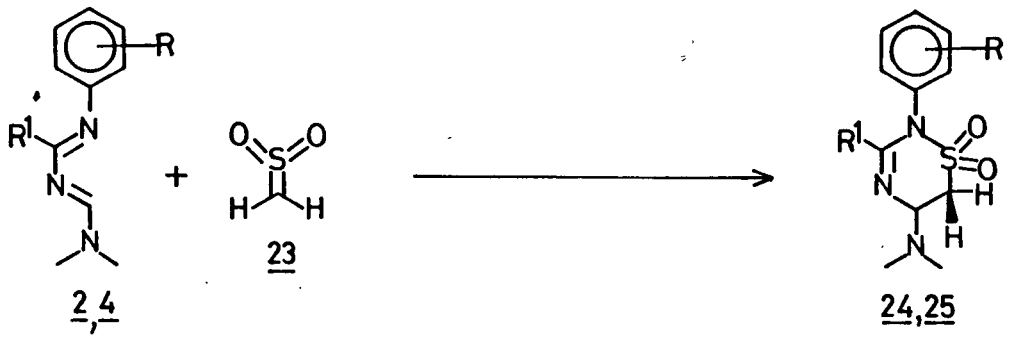
Scheme 4



6,22 R=H, CH_3, Cl

R^1, R^1 = 

Scheme 5



2,24 $R^1=C_6H_5$; R=H, p-CH_3, p-Cl

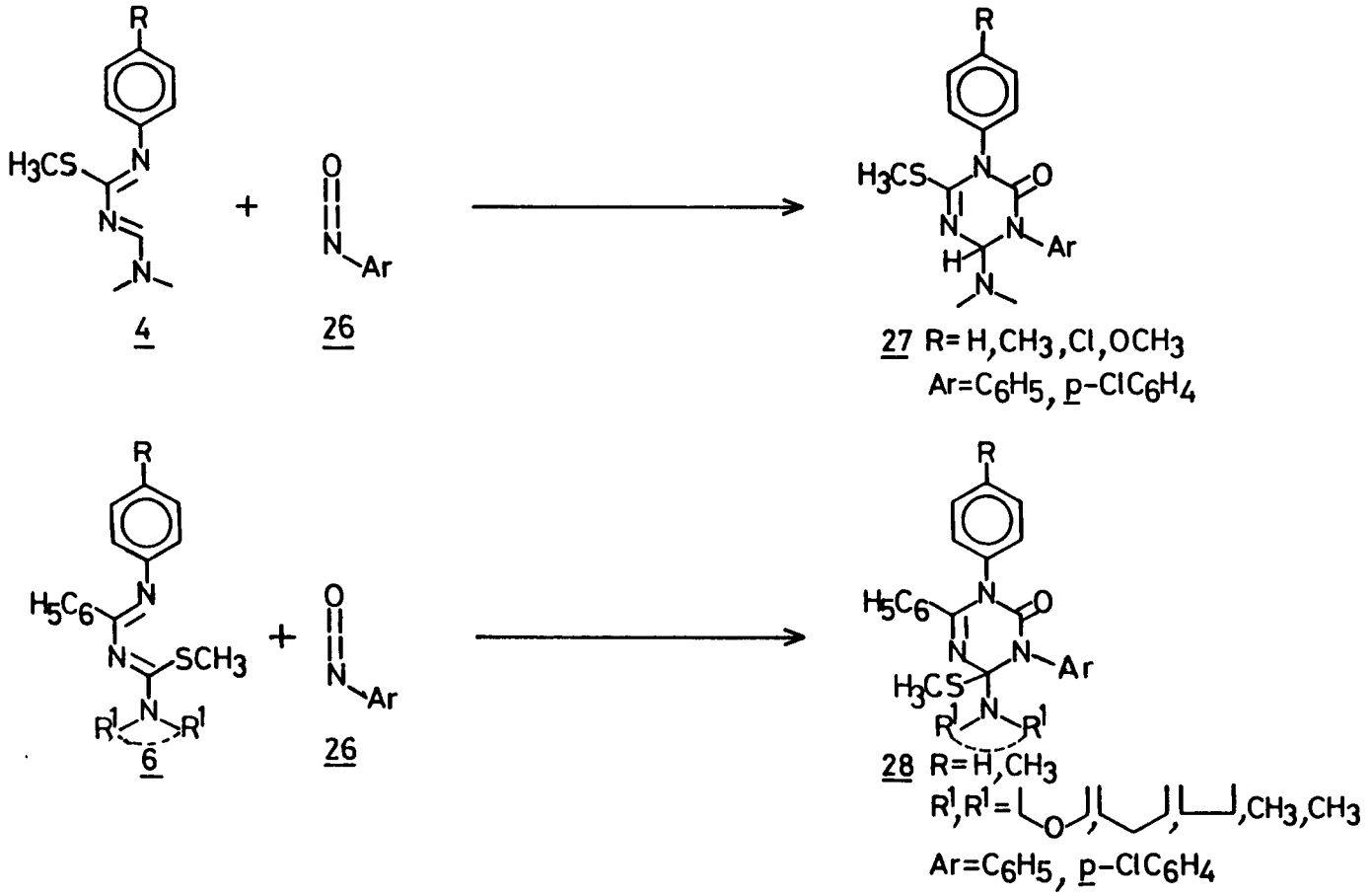
4,25 $R^1=SCH_3$; R=H, p-CH_3, o-CH_3, p-Cl, p-OCH_3

Scheme 6

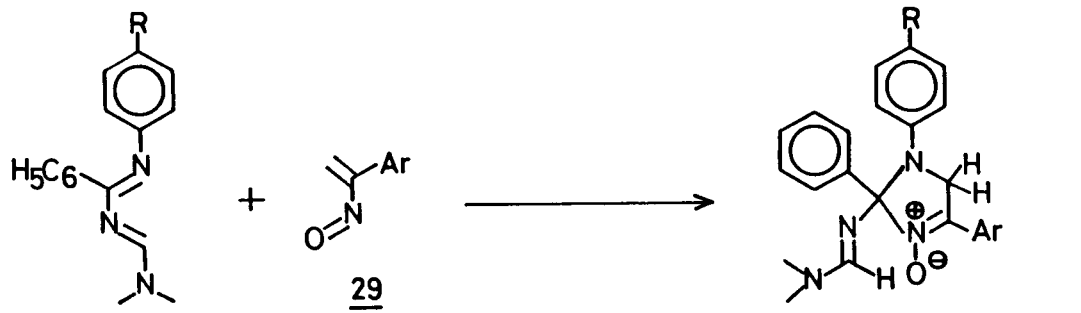
tions of 4 with sulphene resulted in 2-aryl-5-dimetnylamino -3-thiomethyl-1,2,4-thıadiazin-1,1-dioxide (25)[10]. This is the first report of (4+2) cycloaddition of simple sulphene to any substrates having carbon-nitrogen double bond.

Efficient (4+2) cycloaddition reactions of 1,3-diaza -1,3-butadienes (4 and 6) with aryl isocyanate (26) are described in fourth chapter of the thesis. The treatment of 1,3-diaza-1,3-butadienes (4 and 6) with 26 for 10-20 minutes at room temperature in minimum amount of solvent gave good yields of 3,4-dihydro-1,3,5-triazin-2(1H)-ones (27 and 28) (Scheme-7). The earlier reported reactions of 1,3-diaza- 1,3-butadienes with isocyanates have been shown to be much slower possibly because of the pronounced ınverse electron demand nature of 1,3-diaza-1,3-butadienes which makes N-1 of those dienes less nucleophilic[11-13].

The last chapter of the thesis deals with the regioselctive cycloaddition reactions of 1,3-diaza-1,3-butadienes(2) with nitrosoalkenes which interestingly resulted in 1,4-diaryl-2-N'-(N,N-dimethylformamidino)-2-phenyl-Δ^3-imidazolıne-3-oxide (30) (Scheme-8). The nitrones (30) are probably formed by an unusual (3+2) dipolar addition of α-nitrosostryene in a 1,3-mode to 1,2-carbon-nitrogen double bond of 1,3-diaza-1,3-butadienes(2).


R
H3CS
N
N
N
4
+
O
N
Ar
26
27 R= H, CH3, Cl, OCH3
Ar= C6H5, p-ClC6H4
H5C6
SCH3
R1
R1
6
28 R= H, CH3
R1, R1 = O, CH3, CH3

Scheme 7



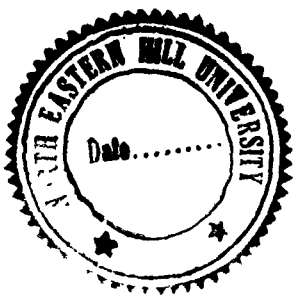
2 + 29 → 30

R=H, CH_3, Cl, Br

Ar=C_6H_5, p-$CH_3C_6H_4$

Scheme 8

All the products mentioned in this thesis have been well characterised on the basis of analytical data and spectral evidences.



REFERENCES

1. D.L. Boger, **Tetrahedron**, 1983, **39**, 2869.
2. D.L. Boger and S.M. Weinreb, **Hetero Diels-Alder Methodology in Organic Synthesis**, Ed. H.H. Wasserman, Academic Press, 1987, 239.
3. D.L. Boger, **Chem. Rev.**, 1986, **86**, 781.
4. A.R. Katritzky and N. Dennis, **Chem. Rev.**, 1989, **89**, 827.
5. L.E. Overman, C.B. Petty, T. Ban, and G.T. Huang, **J. Am. Chem. Soc.**, 1983, **105**, 6335.
6. M.L. Bremmer and S.M. Weinreb, **Tetrahedron Lett.**, 1983, 261.
7. D.L. Boger and J.S. Panek, **J. Org. Chem.**, 1983, **48**, 621.
8. T. Kametini and S. Hibino, The synthesis of Natural Products by Hetero Diels-Alder Cycloaddition Reactions. **Advances in Heterocyclic Chemistry**, 1987, **42**, 246.
9. S.N. Mazmumdar, I. Ibnusand, and M.P. Mahajan, **Tetrahedron Lett.**, 1986, 921.
10. S.N. Mazumdar, M. Sharma, and M.P. Mahajan, **Tetrahedron Lett.**, 1987, 2641.
11. I. Matsuda, Y. Yamamoto, and Y. Ishii, **J. Chem. Soc. Perkin Trans. I**, 1976, 1523.
12. I. Matsuda, Y. Yamamoto, and Y. Ishii, **J. Chem. Soc. Perkin Trans.I**, 1976, 1528.
13. J. Barluenga, M. Tomas, A. Ballesteros, and L.A. Lopez, **Synthesis**, 1989, 228.

CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES

By

SUJIT NANDY MAZUMDAR Majumdar

DEPARTMENT OF CHEMISTRY

SCHOOL OF PHYSICAL SCIENCES

A THESIS

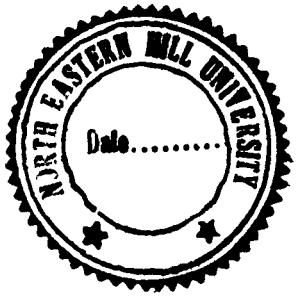
SUBMITTED

IN

FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

To



THE NORTH-EASTERN HILL UNIVERSITY

SHILLONG-793 001

MEGHALAYA (INDIA)

OCTOBER, 1989

Dedicated to my Parents

Phone :
Grams : NEHU

North-Eastern Hill University

Bijni Complex
Bhagyakul, Shillong - 793003 (Meghalaya)

Dr. M.P. Mahajan
Reader
Department of Chemistry

CERTIFICATE

This is to certify that the work desceribed in this thesis has been carried out by Mr. Sujit Nandy Mazumdar under my supervision. He has satisfactorily completed the Pre-Ph.D. courses prescribed and the period of two years of investigational work for the award of Ph.D. degree in Chemistry.

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

(M.P. Mahajan)
Supervisor

Phone :
Grams : NEHU

North-Eastern Hill University

Bijni Complex
Bhagyakul, Shillong - 793003 (Meghalaya)

HEAD
DEPARTMENT OF CHEMISTRY

.....10/12/...1989

This is to certify that Mr. Sujit Nandy Mazumdar, a Ph.D. student of the Department of Chemistry has satisfactorily completed the following courses as a part of his Ph.D. course programme:

Courses No	Title
1. Chem-631	Medicinal Chemistry
2. SPS-632	Magnetic Resonance

(H. Ila)

ACKNOWLEDGEMENT

It gives me immense pleasure to express my deep sense of gratitude to Dr. ***M.P. Mahajan****, Reader, Department of Chemistry, North-Eastern Hill University, my research supervisor, for his keen interest, untiring guidance, and encouragement throughout the course of my Ph.D. research.*

I am very much thankful to the Head of the Department of Chemistry, NEHU for providing me all the required help. I am also indebted to all the faculty members who have been extremely helpful during my stay. I wish to thank in particular, Prof. ***M.K. Chaudhuri*** *and Dr.* ***R.K. Poddar*** *who took care of the day-to-day problems concerning my work during the absence of Dr. M.P. Mahajan.*

I am grately indebted to Rev. Br. ***M.G. Shannon****, Ex-Principal and Rev. Br.* ***W.A. Desouza****, present Principal of my Institution, St. Edmund's College, Shillong and to my colleagues,* ***B.Das Purkayastha, M.P. Kalita,*** *Dr.* ***S.B. Paul, M.L. Purkayastha, A. Debroy,*** *and* ***S. Purkayastha*** *for their active co-operation and constant inspiration over all these years.*

I am extremely grateful to Dr. ***P.D. Baruah*** *and Miss.* ***S. Mukherjee*** *of our laboratory for their constant help and advice throughout the course of my research work.*

I wish to acknowledge with thanks the co-operation and help rendered by ***C.R. Bhattacharjee, P. Paul, A.K. Deb, B. Deb, A. Thomas, F. Mathew,*** *Dr.* ***M. Bhattacharjee,*** *Dr.* ***M.N. Bhattacharjee,*** *Dr.* ***R. Bhattacharjee,*** *Dr.* ***R.N.D. Purkayastha*** *and Dr.* ***U.C. Sharma****. I am also thankful to all other research scholars of our Department who made my stay in the Department extremely pleasant.*

Thanks are also due to Dr. ***J.P. Pradere, Nantes, CEDEX,*** *France, Directors and Technicians and Regional Sophisticated Instrumentation Centres, Central Drug Research Institute, Lucknow and North Eastern Hill UNiversity, Shillong for providing the elemental analyses and spectral data of the compounds described in this thesis.*

I also take this opportunity to thank the non-teaching staff members of this Department, Library and RSIC who have helped me in so many ways during the period of my research.

Thanks are also due to Mr. N.K.Paul Choudhury for neatly typing and Shivaprasan C.V. for xeroxing the thesis.

I am extremely grateful to Mr. ***Prabir Nandy Mazumdar****, my younger brother, who has taken enough pain in drawing the schemes of the thesis so neatly. I have no words to express my gratitude to my parents, brothers, sister and the relatives for their continuous inspiration and encouragement. Lastly, the encouragement and moral support provided by my wife,* ***Mita****, are unforgettable.*

SUJIT NANDY MAZUMDAR

CONTENTS

		Page
	Acknowledgement	
	Preface	
CHAPTER-I	**INTRODUCTION**	1
CHAPTER-II	**SYNTHESES OF 1,3-DIAZA-1,3-BUTADIENES AND THEIR CYCLOADDITION REACTIONS WITH KETENES AND REFORMATSKY REAGENT.**	
	II.1 Syntheses of 1,3-Diaza-1,3-Butadienes	59
	II.2 Cycloaddition Reactions of 1,3-Diaza-1,3-Butadienes with Ketenes	69
	II.3 Reactions of 1,3-Diaza-1,3-Butadienes with Reformatsky Reagent	106
CHAPTER-III	**CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH SULPHENE**	153
CHAPTER-IV	**CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH ISOCYANATES**	175
CHAPTER-V	**CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH NITROSOALKENES**	207

PREFACE

Hetero Diels-Alder cycloaddition reactions have been shown to be of great potential for the synthesis in heterocyclic chemistry. Their study has illuminated many aspects of synthetic and mechanistic chemistry. Dienes containing two nitrogen atoms have attracted the attention of chemists in recent years because of their importance in natural product synthesis though there are numerous reports concerning the participation of 1,2-diaza-1,3-butadienes in Diels-Alder cycloaddition reaction but on the contrary reports of 1,3-diaza-1,3-butadienes were found to be rare, and remained unexploited for the syntheses of heterocyclic compounds. In view of this, studies were undertaken, to develop general methods for the syntheses of reactive 1,3-diaza-1,3-butadienes and to investigate their cycloaddition reactions with different heterodienophiles. The results of these investigations have been embodied in the present thesis.

The thesis is divided into five chapters. The first chapter give a brief review of the cycloaddition reactions of different mono- and diaza-1,3-butadienes. The second chapter details the syntheses of different reactive 1,3-diaza,1,3-butadienes and their (4+2) cycloaddition reaction with monophenyl and monochloroketene. In case of diphenylketene, cycloaddition reactions were found to be sterically controlled. The 1,4-conjugated addition of Reformatsky reagent on the 1,3-diaza-1,3-butadienes is also included in this chapter. Surprisingly simple sulphene, one of the most reactive heterodienophile had not been used much in hetero Diels-Alder reaction. Thus, the cycloaddition reaction of 1,3-diaza-1,3-butadines with sulphene were carried out and results obtained thereof were incorporated in the third chapter. The fourth chapter deals with the cycloadditions of these with arylisocyanates. The unusual (3+2) cycloaddition reactions of α -nitrosostyrene with 1,3-diazabutadines resulting in their nitrone derivatives forms the subject matter of the fifth chapter.

The entire documentation in this thesis is supported by appropriate references.

CHAPTER - I

CHAPTER-I

INTRODUCTION

The Diels-Alder cycloaddition reaction is one of the most common, powerful and elegant tools for the construction of carbocyclic six-membered ring system. It has been the subject of extensive preperative[1-8], theoretical[9,10], and mechanistic[11] studies contributing towards the ease and predictability with which this reaction may be carried out. For the synthesis of polycyclic natural products, it provided an unique opportunity for regioselective and stereospecific introduction of multiple centres of configuration. Moreover, it has been known

that reactive species can be generated in which one or more carbon atoms of diene and/or dienophile have been replaced by heteroatoms, and that cycloadditions of these systems with dienophiles or conjugated dienes can yield a variety of heterocyclic compounds. But much less attention has been paid to the cycloaddition of such systems, which may probably be due to (i) uncertainity in the question of concerted versus polarstepwise nature of cycloaddition, (ii) ambiguities surrounding the observed or predicted regio/stereoselectivity, and (iii) the relative lack of methods concerning the preparation of starting materials.

The observation that the conjugated systems containing nitrogen i.e. azabutadienes[1,2,4,7,9,11,12,13] show diminished reactivity towards electron-deficient dienophiles, lends credence to the electrophilic character of such systems. These observations together with the recognised shortcomings in attempting cycloaddition reactions with 2π and 4π components of a similar electrophilic nature led to the development of several general approaches for useful azadiene Diels-Alder reactions.

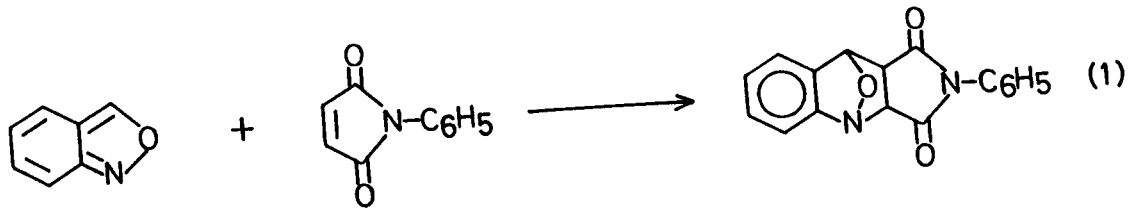
The comprehensive reviews of Diels-Alder cycloaddition reaction involving heterodienes containing one or more heteroatoms appeared in 1975 (oxagines)[3], 1983

(azadienes)[11], and 1983 (nitrosoalkenes)[13b]. In a recent review (1987), Boger and Weinreb[14a] described the cycloaddition reactions of azabutadienes and heterodienophiles for the syntheses of a variety of heterocyclic compounds, and Kametani and Hibino[14b] highlighted the utility of intra- and inter-molecular cycloaddition reactions towards the syntheses of heterocyclic natural products. A comprehensive and uptodate literature survey concerning the cycloaddition reactions of azabutadienes, excluding hetero-azabutadienes, is presented in this chapter.

1-Aza-1,3-Butadienes

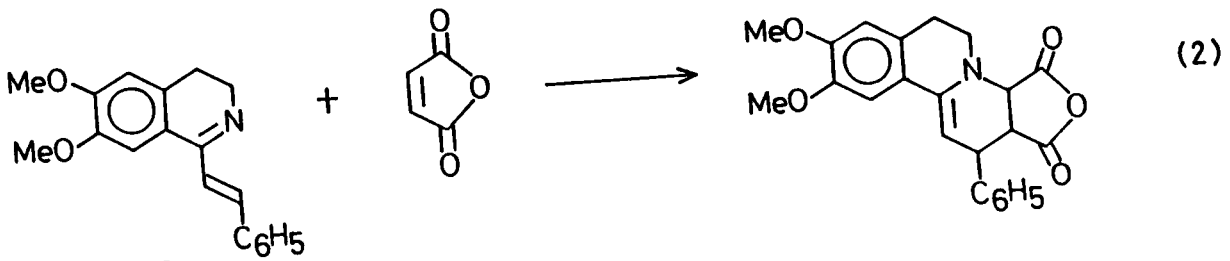
The first few reports, on the successful participation of 1-aza-1,3-butadienes in Diels-Alder reactions, is concerned with the reactions of benzisoxazole(1)[15] and unsaturated 3,4-dihydro isoquinolines (2 and 3)[16] [Eq(1)-(3)]. These reports, contrary to the earlier observations, clearly established that such systems undergo (4+2) reactions. The recent works utilising selected 1-aza-1,3-butadienes, incorporated into unsaturated heterocyclic systems,[15,16] are summarised in scheme-1.

Unsaturated imine(4), simple 1-aza-1,3-butadienes, participate in Diels-Alder reactions with typical electron deficient dienophiles preferably through their enamine tautomer [Eq-(4)][17]. The (2+2) cycloaddition reactions



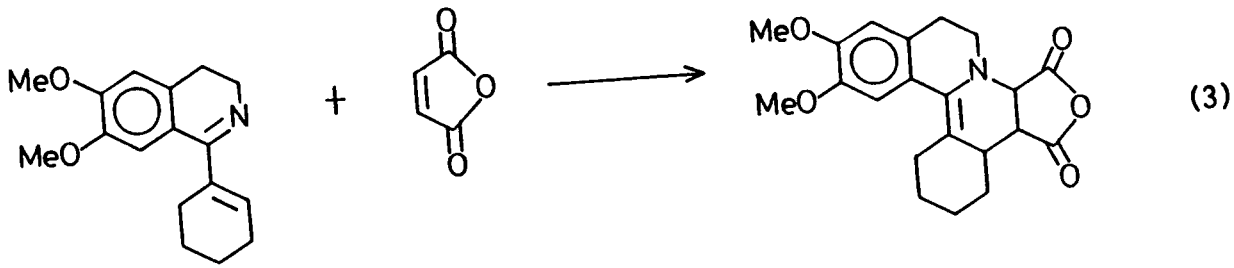
1

(1)



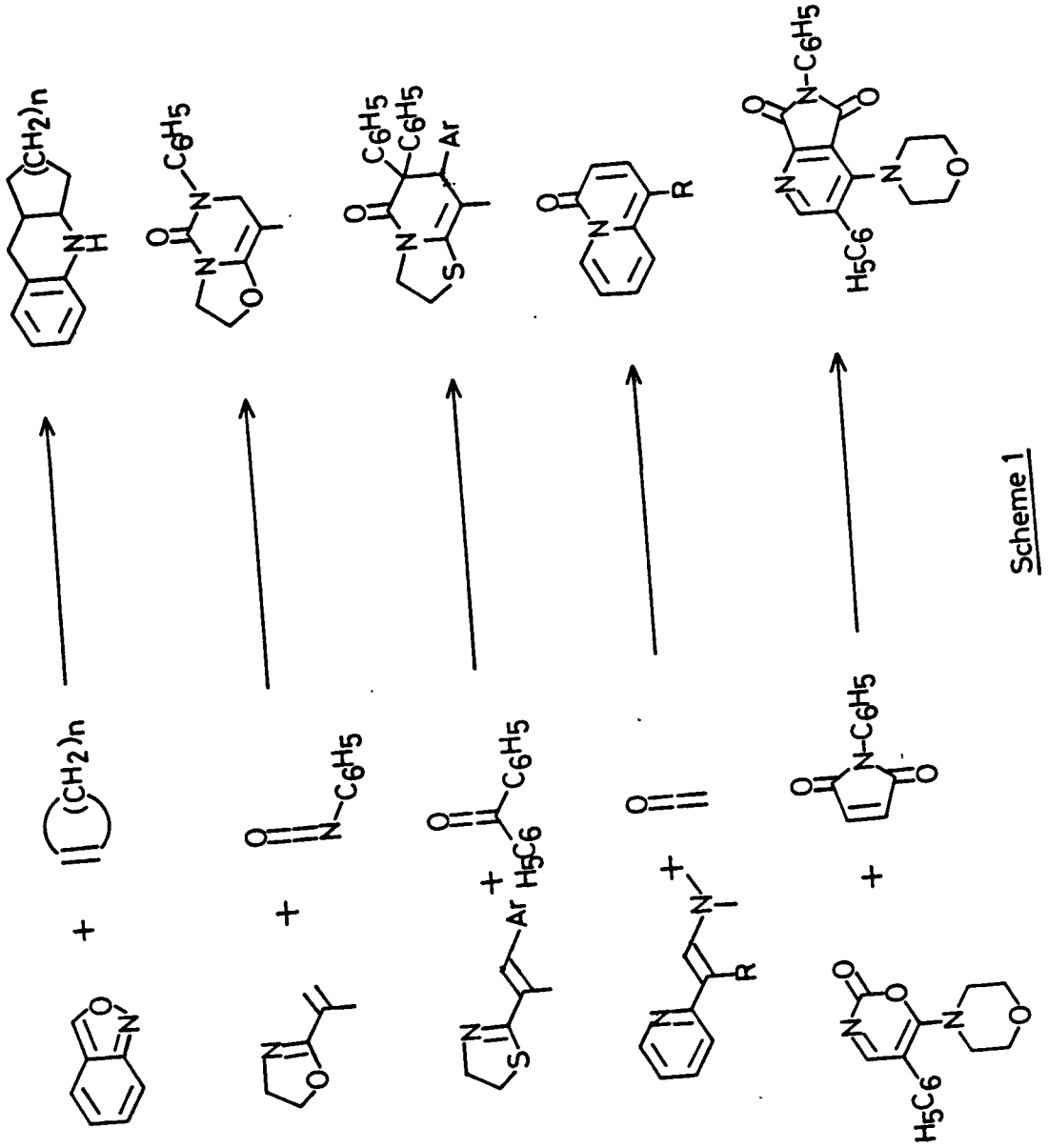
2

(2)

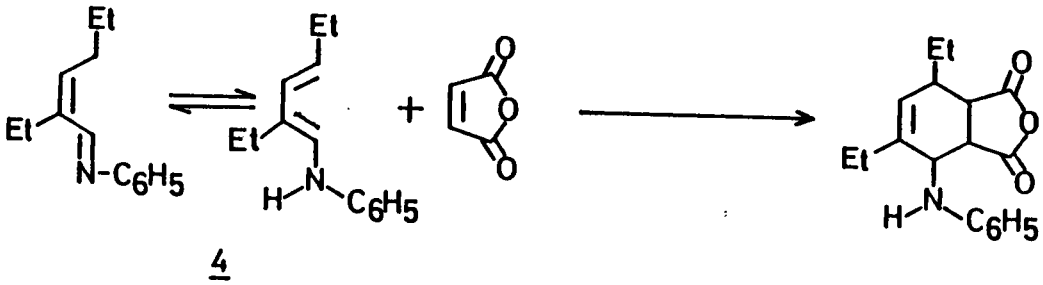


3

(3)

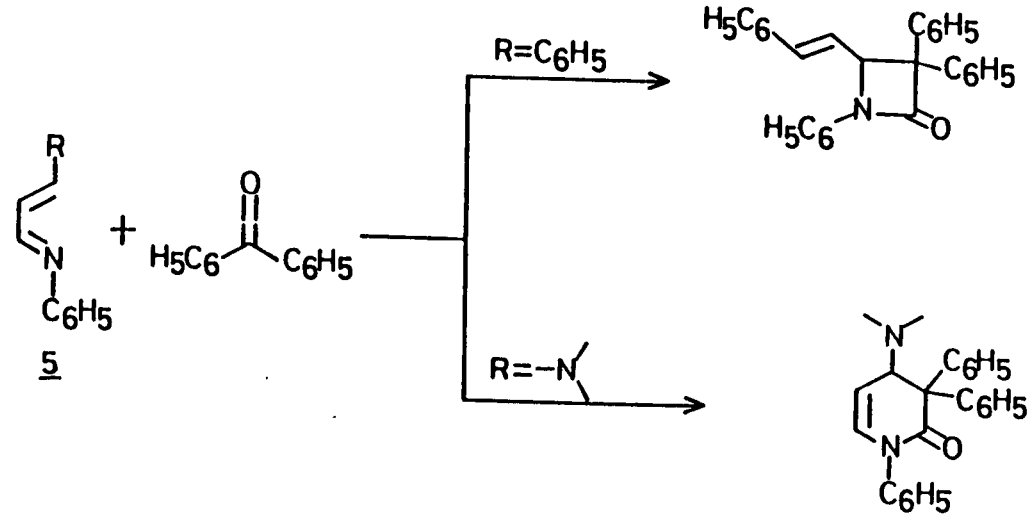


Scheme 1



4

(4)



5

(5)

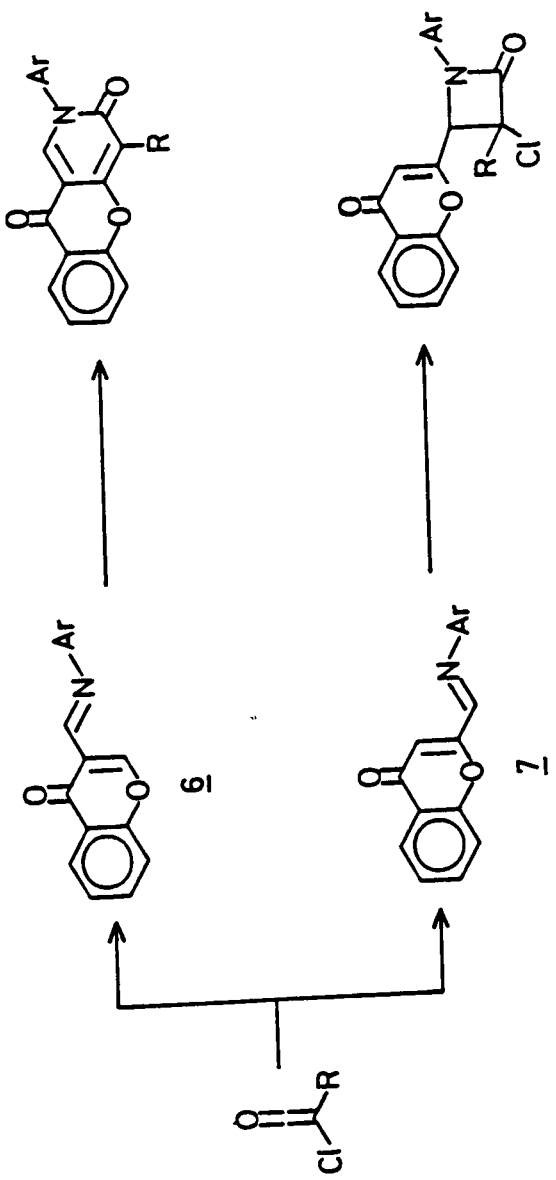
were observed in cases of the α,β-unsaturated imines (5,6 and 1) where the isomersation was prevented, but (4+2) cycloaddition path was followed in cases of delocalised unsaturated imines [Eq-(5) and Eq-(6)][18,19].

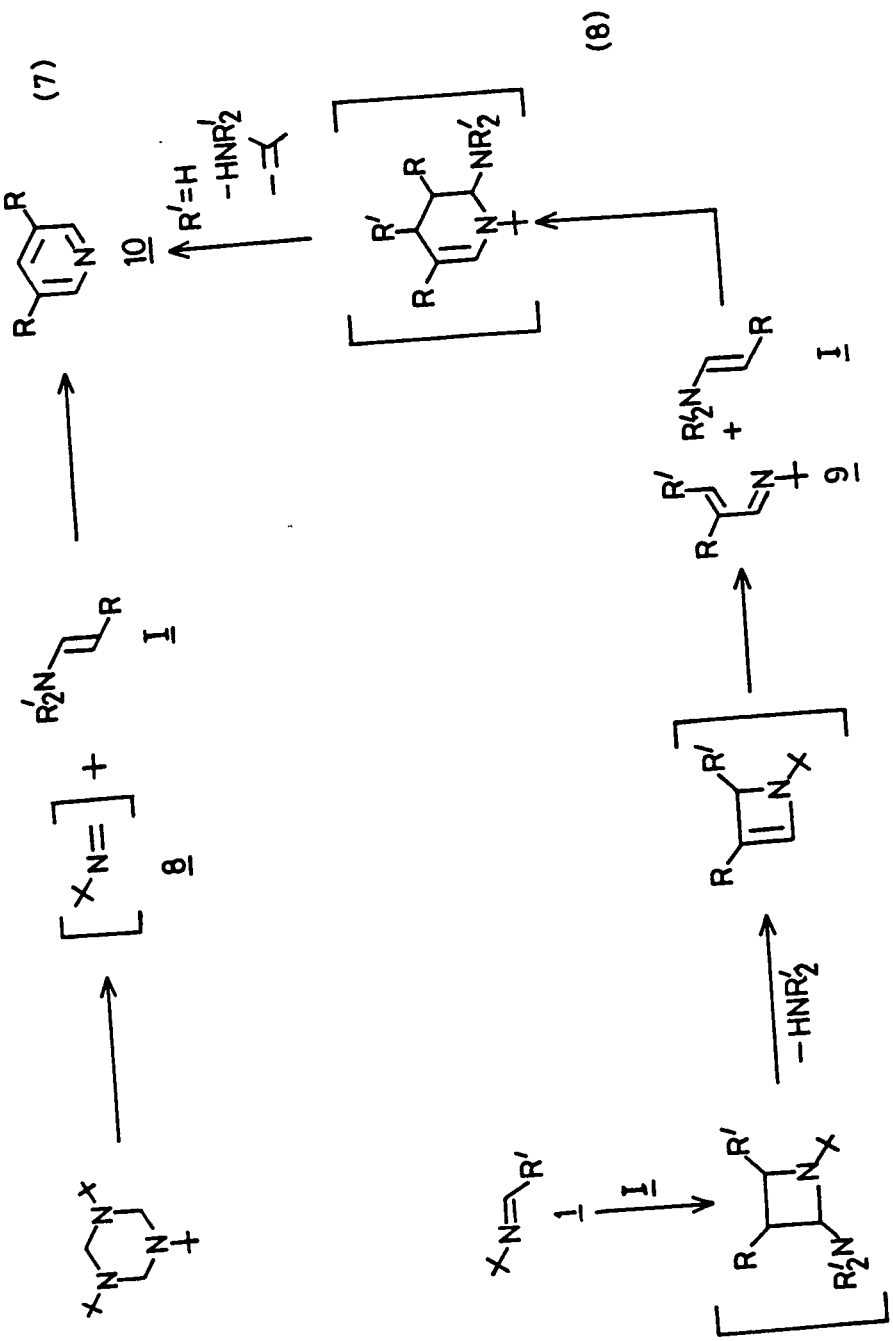
The acid catalysed reaction of methamines(8) with substituted enamines leading to the formation of 3,5-disubstituted pyridines (10)[20] [Eq-(7)], had been carefully reinvestigated. It was shown to proceed by in situ generation, followed by subsequent (4+2) cycloaddition of electrophilic 1-aza-1,3-butadienes (9) with electron rich enamines[21][Eq-(8)].

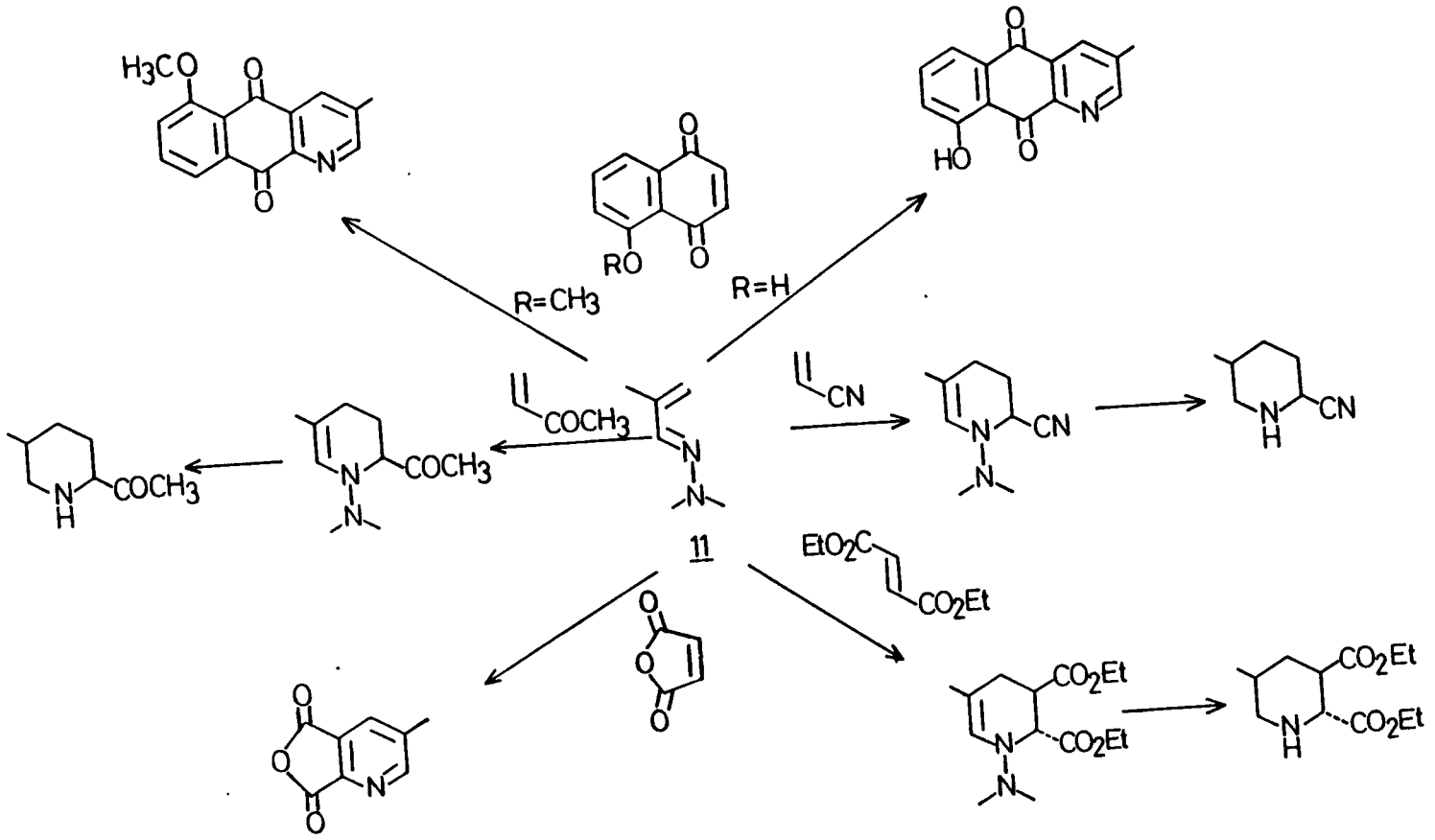
In an effort to increase the reactivity of simple 1-aza-1,3-butadienes toward typical electron-deficient dienophiles, Ghosez and co-workers found that α,β-unsaturated hydrazone (11) behaved as an electron-rich diene in regioselective Diels-Alder reactions with a member of representative dienophiles[22](Scheme-2). Reductive cleavage of the nitrogen-nitrogen bond provided substituted piperidines and aromatisation with elimination of dimethylamine led to substituted pyridines[22].

The successful efforts toward important synthetic implications of 1-aza-1,3-butadienes have recently been reported. Fowler et al[23] have shown that the gas phase

(6)




(7)
(8)
R'=H
-HNR'2
-HNR'2
10
I
I
I
8
9
6
1

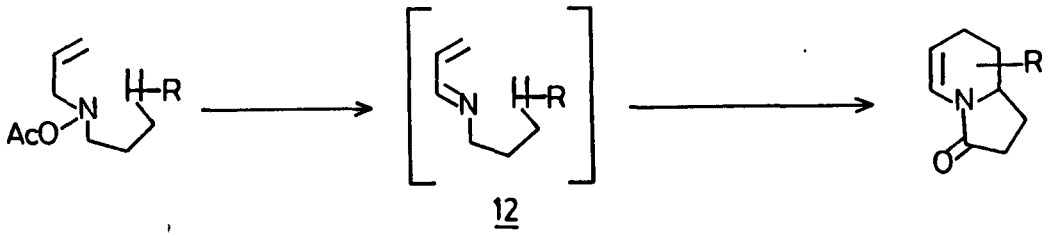

H3CO
O
N
O
RO
O
R=CH3
R=H
HO
O
N
O
COCH3
CN
N
CN
N
H
CN
N
H
COCH3
N
COCH3
N
11
EtO2C
CO2Et
O
O
O
O
O
N
CO2Et
CO2Et
N
CO2Et
N
H
CO2Et

Scheme 2

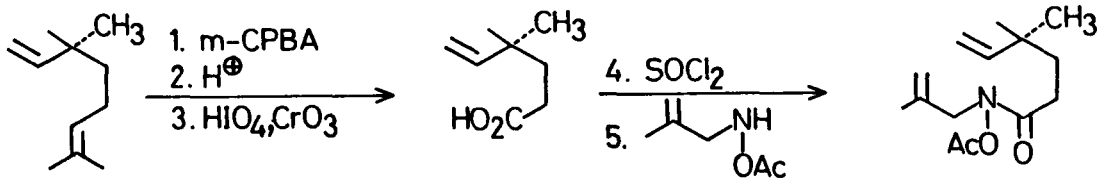
pyrolysis of N-acyl-O-acetyl-N-allylhydroxy lamines generates N-acyl-1-aza-1,3-butadienes (12), which is capable of participating in intramolecular Diels-Alder reactions [Eq-(9)]. The entropic assistance provided by the intramolecular cycloaddition, the inability of the diene to tautomerise and the relative stability of the product (aryl versus alkyl enamine) contribute to the success of this reaction. Thus, the total synthesis of (-) deoxymipharidiene (13) was achieved by the in situ generation and subsequent intramolecular Diels-Alder reaction of an N-aryl-1-aza-1,3-butadienes [Eq-(10)][24].

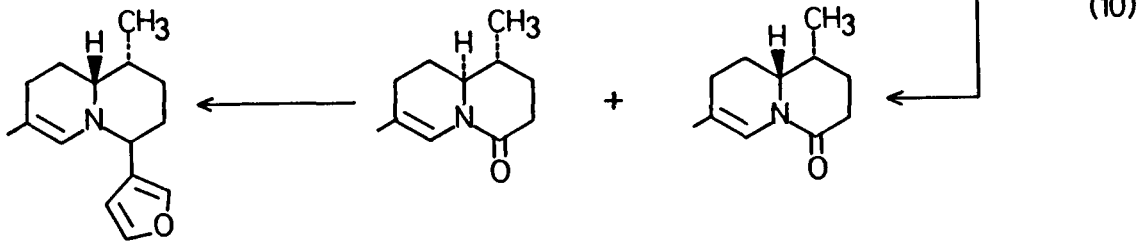
Studies on the generation and properties of O-quinone methide imines (14), suggest them to be useful synthetic intermediate, and comparable to the O-xylenes and O-quinone methides[25]. N-Phenylbenzoazetene (15) upon thermal or photochemical excitation is rapidly converted to reactive O-quinone methide imines (14) which rapidly undergo (4+2) cycloaddition with N-phenylmaleiimide[26] Few notable examples of intermolecular (4+2) cycloaddition reaction of the unstable O-quinone methide imines have been described in scheme-3.

There are a number of reports concerning the intramolecular Diels-Alder cycloaddition reactions of O-quinone methide imines[30-33]. A mild fluoride anion

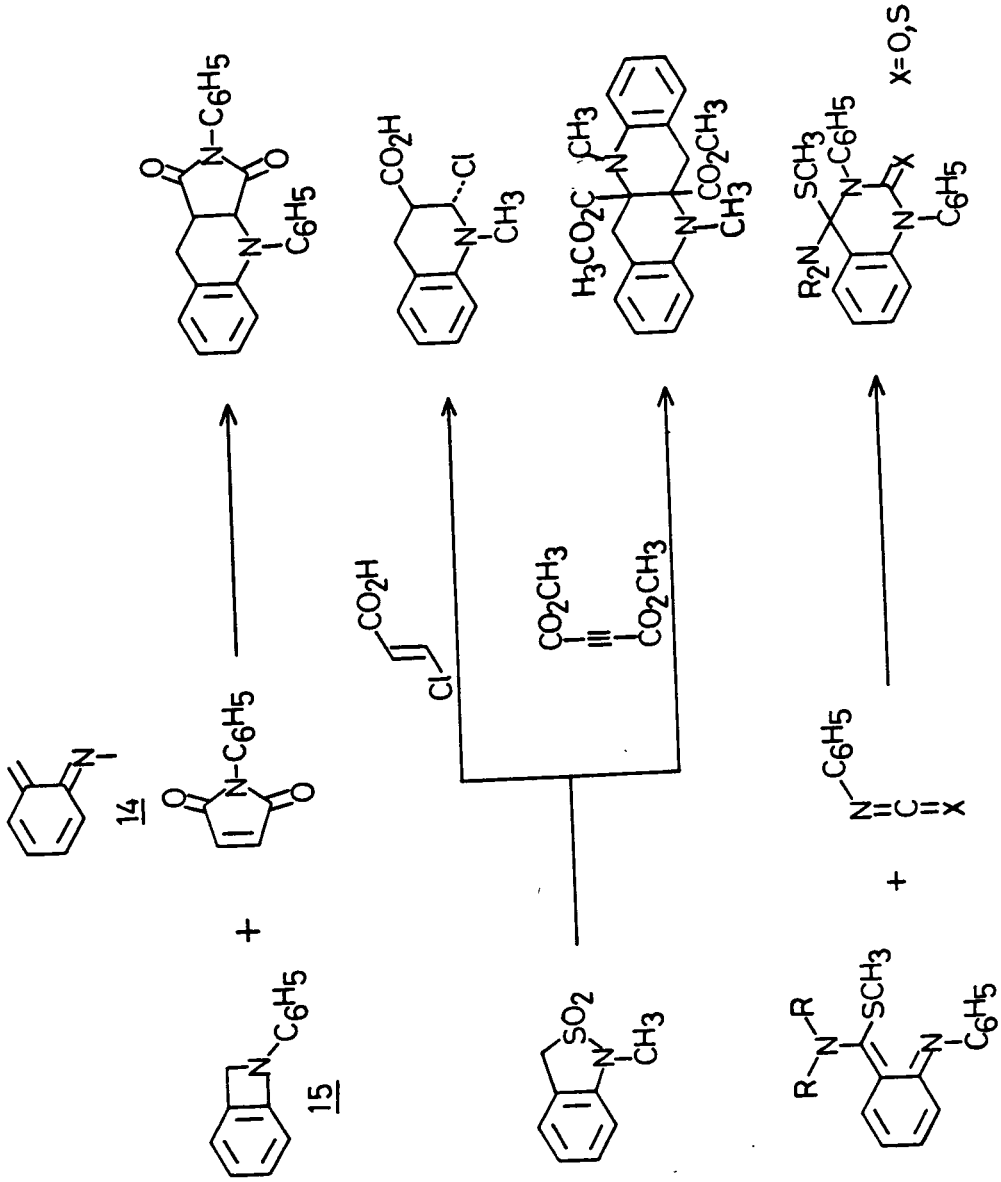

AcO
N
R
N
R
R
N
O

12 (9)


CH3
1. m-CPBA
2. H⊕
3. HIO4,CrO3
CH3
HO2C
4. SOCl2
5.
NH
OAc
CH3
N
AcO
O


H
CH3
N
O
+
H
CH3
N
O
H
CH3
N
O

(10)



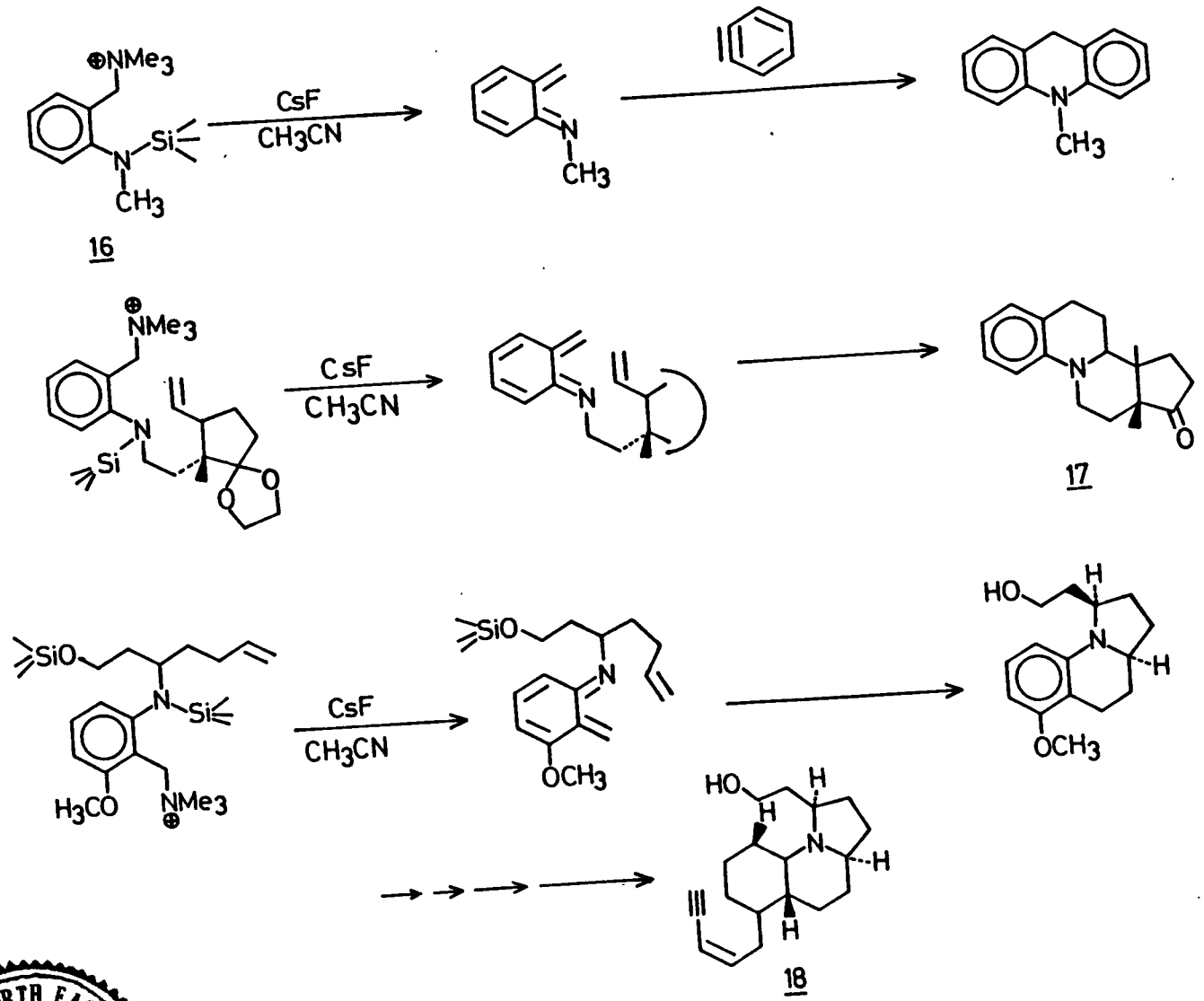
Scheme 3

induced elimination of trimethylsilylflouride and trimethylamine from [O-(trimethylsilyl)alkylamino]benzyl] trimethylammonium halides (16) generated the O-quinone methide-N-alkylimines[30]. This methodology has been applied for the total synthesis of 9-azo-1,3,5 (10)-triene-17-one (17)[30] and gephyrotoxin (18)[31] (scheme-4).

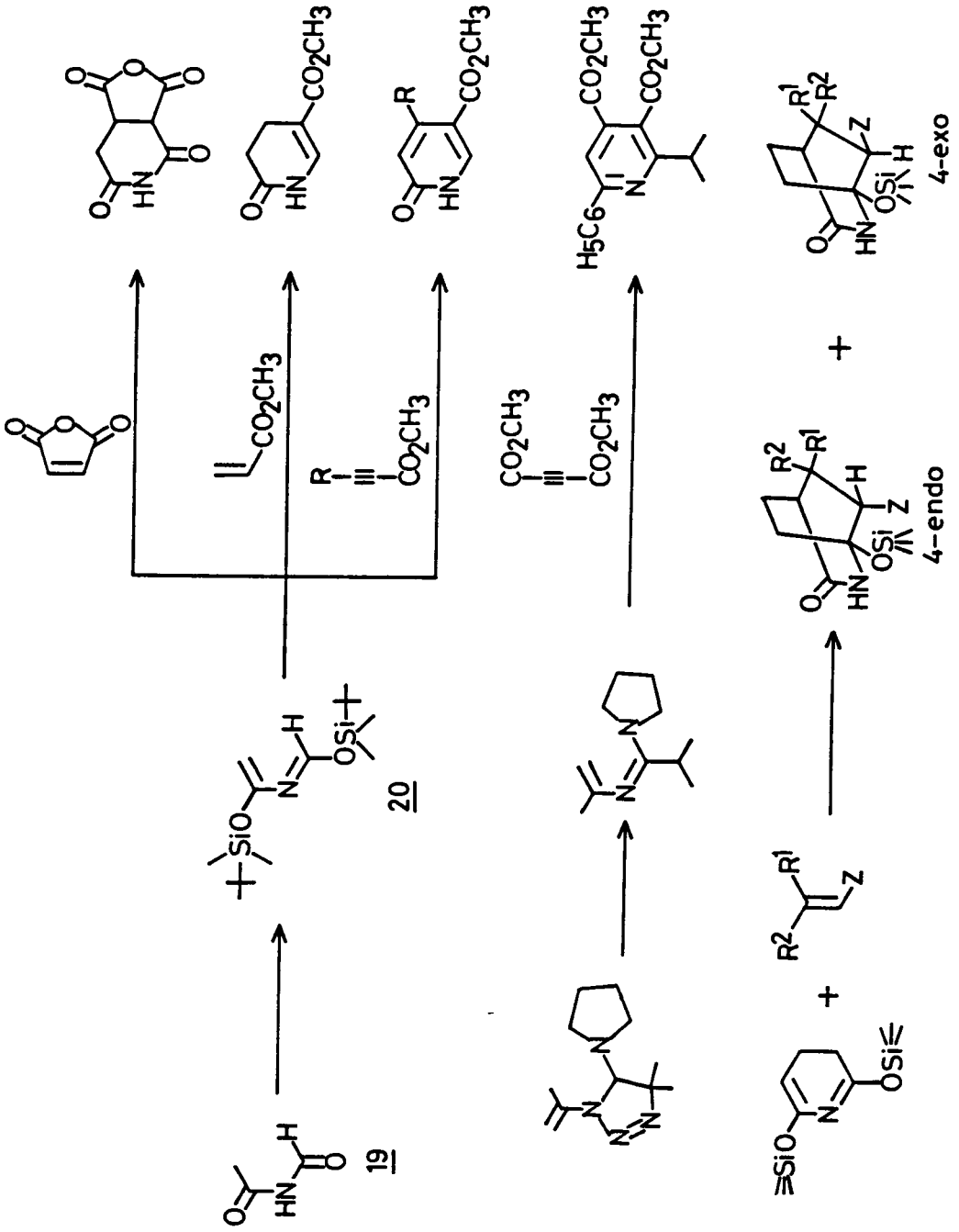
2-Aza-1,3-Butadienes

A number of reports dealing with (4+2) cycloaddition reactions of 2-aza-1,3-butadienes have been appeared in literature. In each instance the diene is usually substituted with strong electron-donating groups which enhance its reactivity towards representative electron-deficient dienophiles.

The apparent ease of preparation of the 1,3-bis (tert-butyldimethylsilyloxy)-2-aza-1,3-butadienes (20) from imides (19) and their participation in Diels-Alder reactions with a range of typical electron-deficient dienophiles contribute towards the synthetic potential of 2-aza-1,3-butadienes[34a]. The 2-aza-1,3-butadines 20, fulfil the necessary structural requirements to react successfully with electrophilic dienophiles. The presence of trimethylsilyloxy group at position-3 further enhances the reactivity of the π-system. Recently, Ghosez et al have described the disastereoselective synthesis of 2-



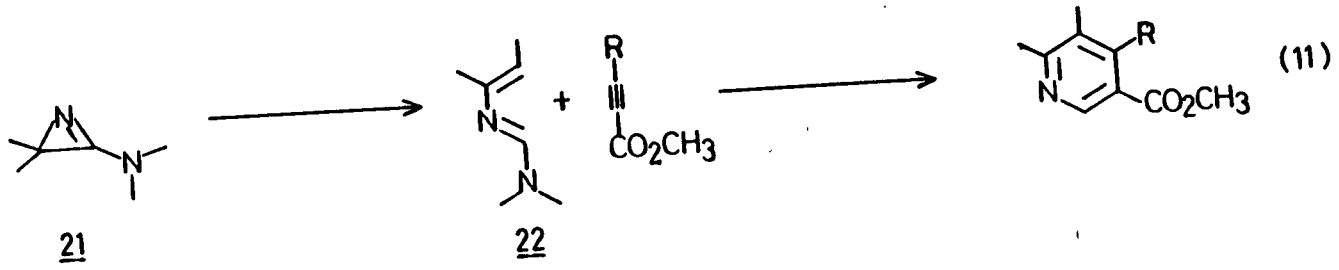
Scheme 4



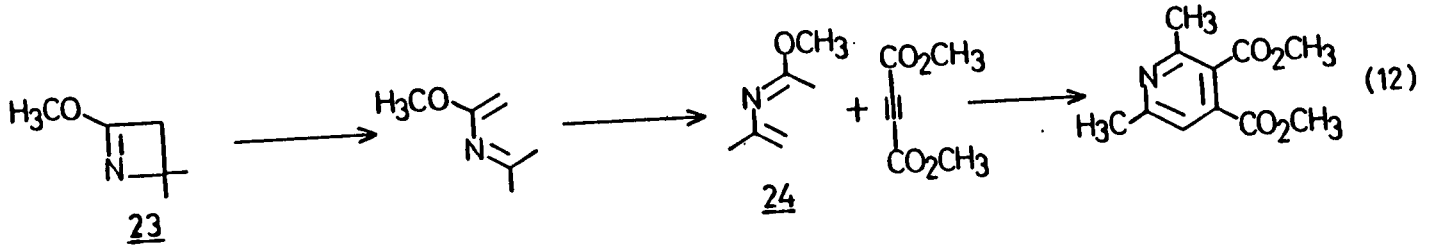
Scheme 5

azabicyclo[2.2.2]octan-2-ones by the Diels-Alder cycloaddition reactions of 1,3-bis(trimethylsilyloxy)-cyclohexa-2-aza-1,3-dienes with various substituted alkenes[34b] (scheme-5).

The flash vaccum pyrolysis (FVP) of 2-dimethylamino-3,3-dimethyl-1-azirine (21) results in its thermal isomerisation to 1-dimethylamino-3-methyl-2-aza-1,3-butadiene (22), which is useful for the synthesis of the pyridines or dihydropyridines [Eq-(11)][35]. A similar vaccum pyrrolysis of 2-methoxy-4,4-dimethyl-1-azetine (23) at 200°C for 8 hours, resulted in its complete conversion to unsaturated imino ether (24), which undergoes (4+2) cycloaddition reaction with dimethylacetytene dicarboxylate [Eq-12][36a]. Recently, Gilchrist et al have reported the Diels-Alder cycloaddition reaction of 3,4-dihydro-2H-pyran with benzylidene aniline [Eq-(13)][36b]. The reports concerning the cycloaddition reactions of simple, unsaturated imines are also available in the literature[37-40] (scheme-6). The unconjugated 2-aza-1,3-butadienes (25) readily isomerises to 2-aza-1,3-butadienes under basic condition and results into (4+2) cycloadducts with dimethylacetylene dicarboxylate[37]. It has also been reported that unsaturated imines yield (4+2) cycloadducts with 4-phenyl-1,2,4-triazoline-3,5-dione[38].

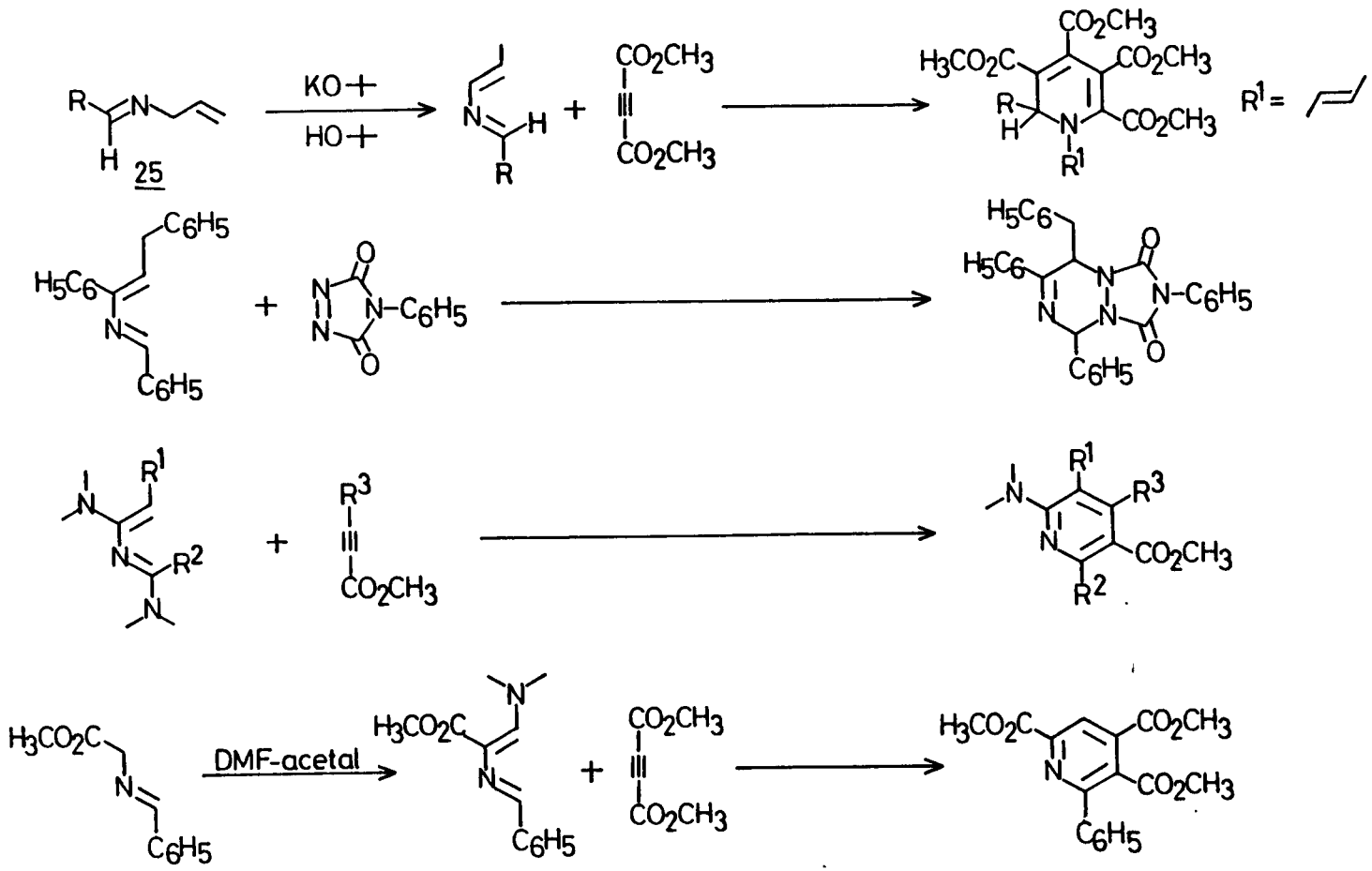


21 22 (11)



23 24 (12)

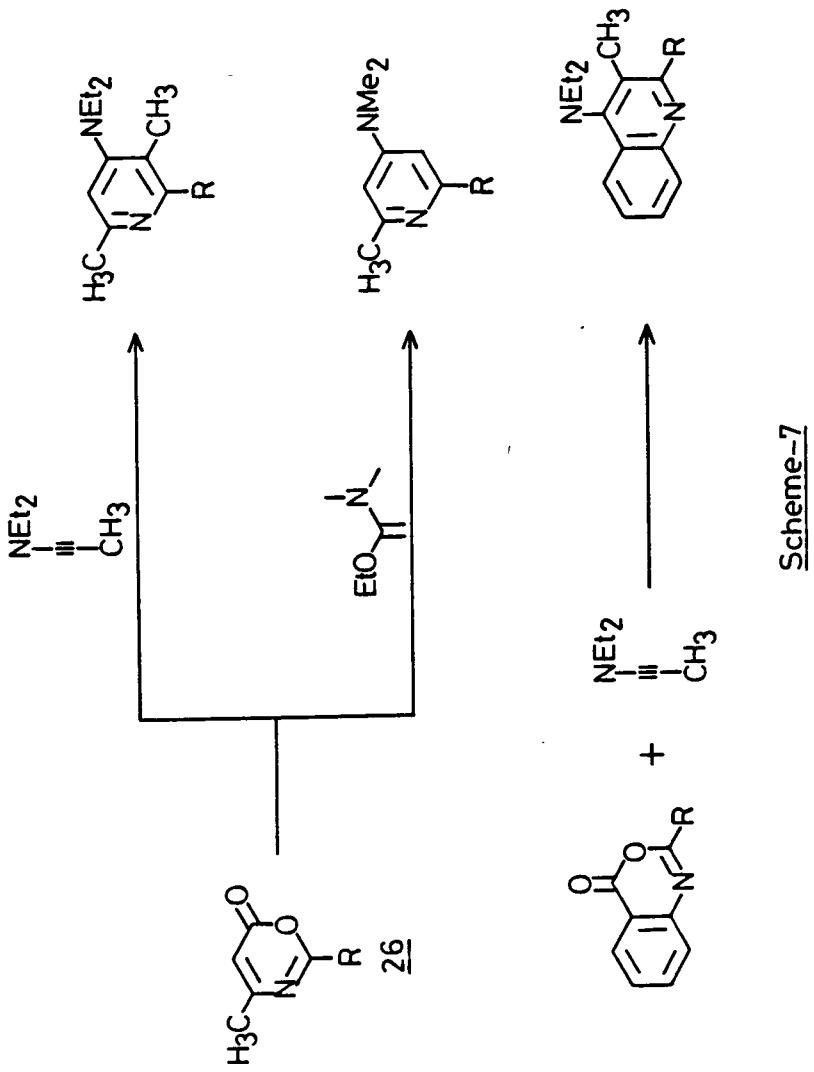
(13)



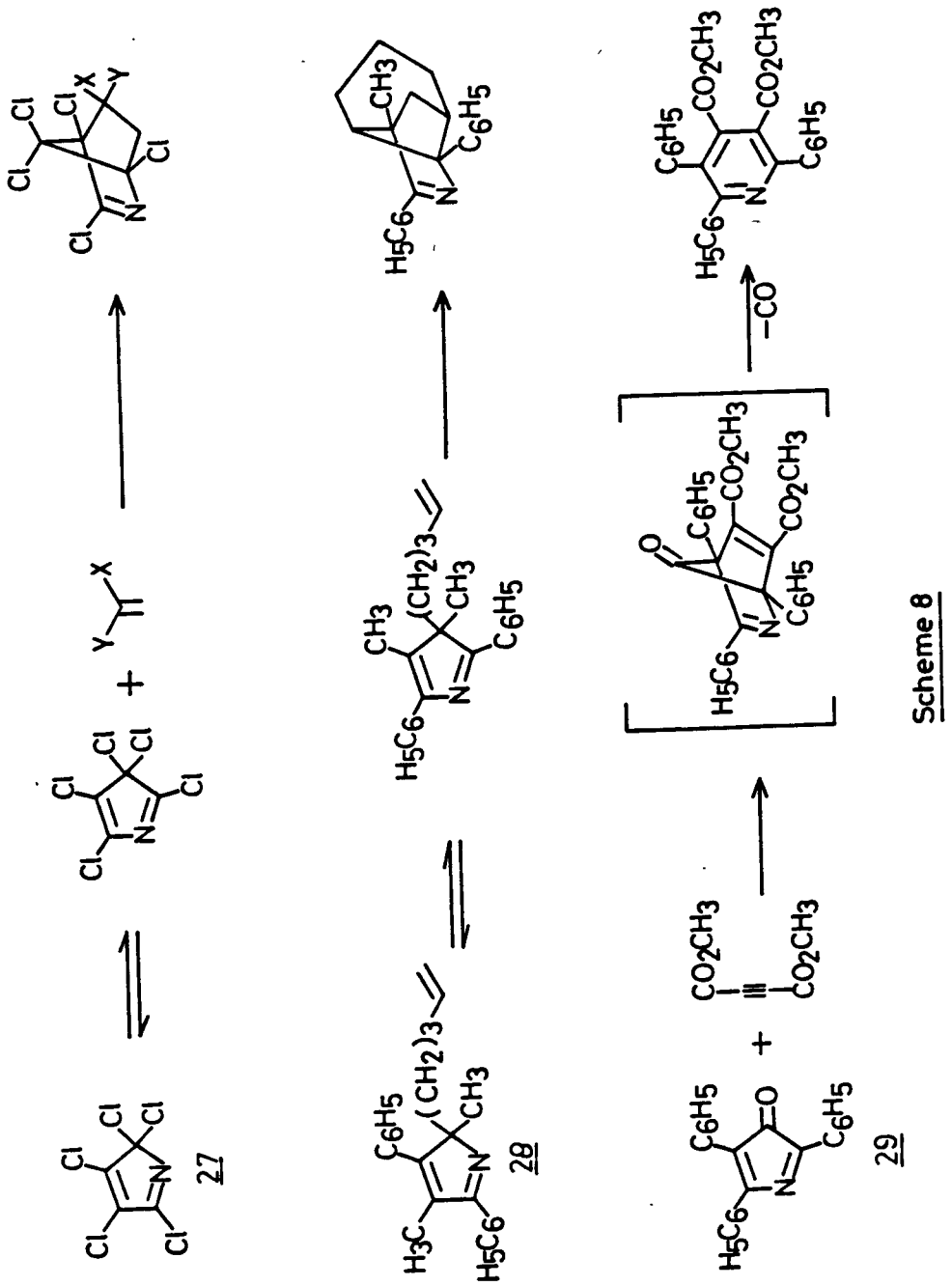
Scheme 6

Substituted 1,3-oxazin-6-one (26) were known to participate in Diels-Alder cycloaddition reactions with electron-rich reactive dienophiles[41-44] (scheme-7). The recent review[41] on cycloaddition reactions of substituted 1,3-oxazin-6-ones (26) gave detail information about the reactivity of 26 with ynamines, enamines, ketene-N,O-acetals, enol ethers, benzynes, strained olefins, reactive dienes, substituted acetylenes and some selected hetero-dienophiles including azirines.

2H-pyrroles, cyclic 1-azo-1,3-butadienes, including pentachloro-2H-pyrrole (27)[45,46] and the alkenyl-2H-pyrrole (28)[47] rearrange to the corresponding 3H-pyrrole (cyclic 2-aza-1,3-butadienes), prior to their participation in inter- or intra-molecular Diels-Alder cycloaddition reactions. The initial report of 27, participating directly in inverse electron demand Diels-Alder reaction as a cyclic 1-aza-1,3-butadiene has been shown to be incorrect[46]. The insitu generation of 2,4,5-triphenyl-3H-pyrrol-3-one (29) and subsequent Diels-Alder reaction of it with dimethylacetylene dicarboxylate represents an additional example of 3H-pyrroles participating as 2-aza-1,3-butadienes in (4+2) cycloaddition reactions[48] (scheme-8). Several examples of intra-molecular Diels-Alder reactions of unactivated 2-aza-1,3-butadienes have also been reported in the literature[49-51]. The entropic



Scheme-7

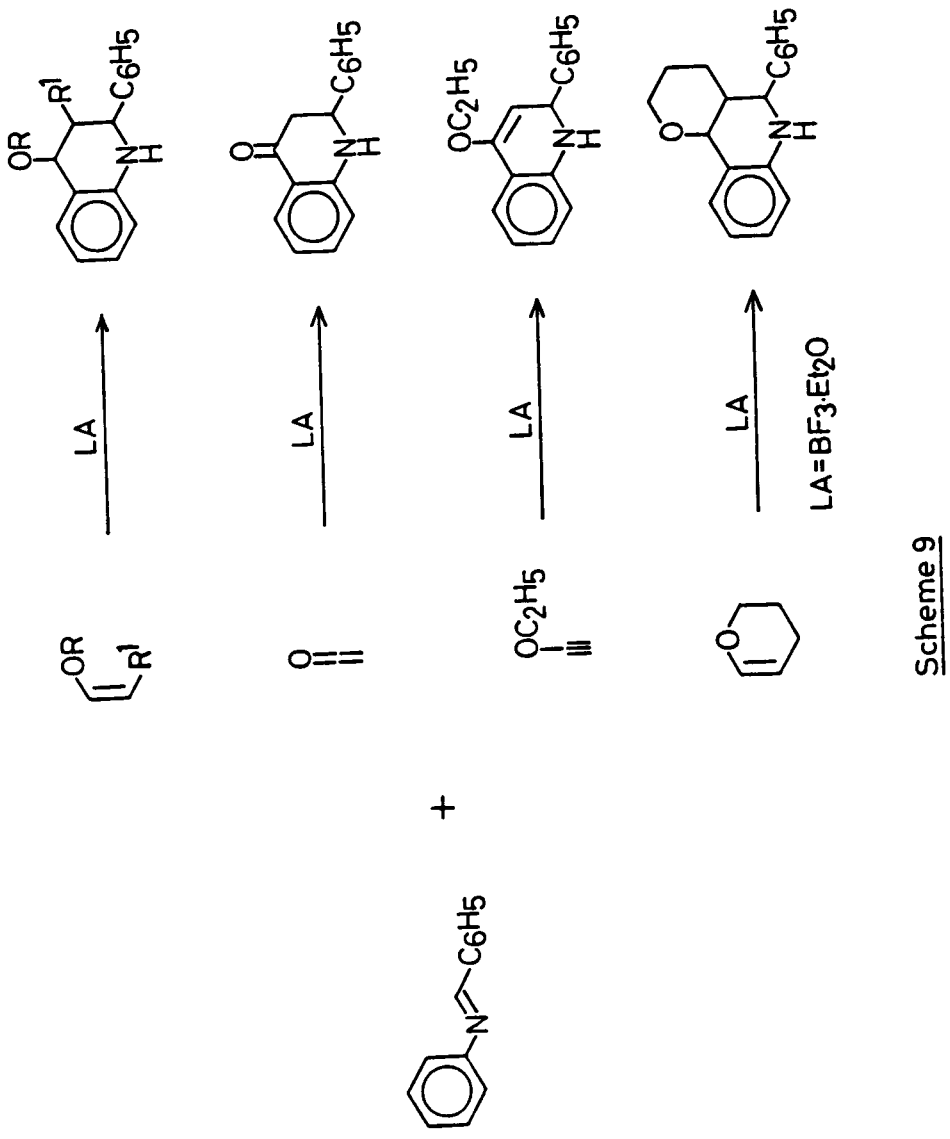


Scheme 8

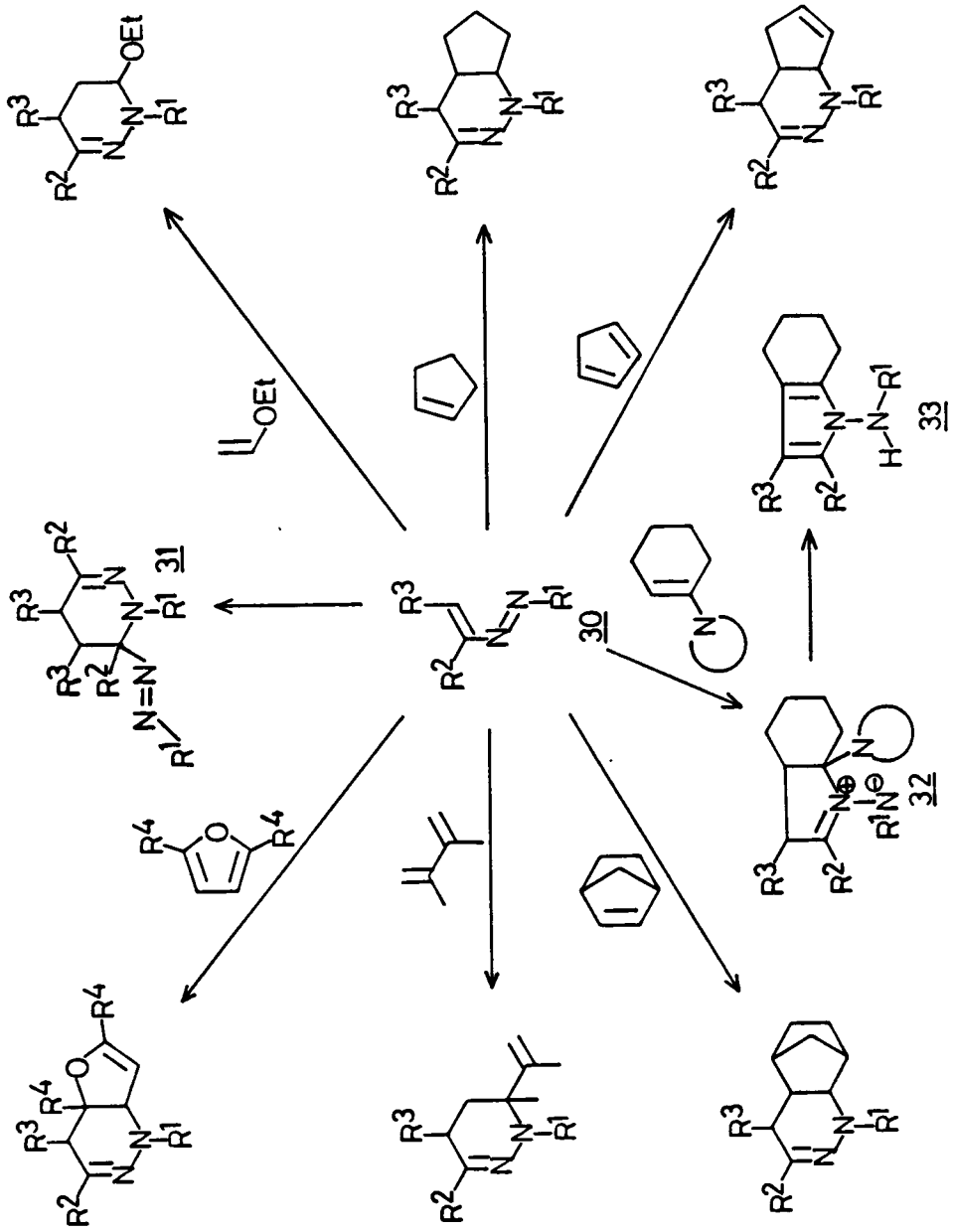
assistance provided by the intermolecular reactions is the driving force necessary to overcome the reluctant participation of the 2-aza-1,3-butadienes in Diels-Alder reactions. Simple 2-aza-1,3-butadienes which incorporate conjugatged imines, participate in lewis acid catalysed (4+2) cycloaddition reactions with a range of representative electronrich dienophiles[52] (scheme-9).

1,2-Diaza-1,3-Butadienes

Electron deficient azoalkenes, 1,2-diaza-1,3-butadienes, have been shown to participate as 4_π components in (4+2) cycloadditions with selected dienophiles. The azoalkene (30), which were generated in situ from appropriate hydrazone derivatives of α-bromo- or α-chloroacetophenone and sodium carbonate at 20°C, resulted in a cyclic dimer (31) in absence of suitable traping agent. Most of the cycloadditions of it with electron-rich dienophiles at room temperature resulted in good yields of cycloadducts[53,54] (scheme-10). However, the reactions of azoalkenes with enamines[55] yield (3+2) cycloadducts (32), which when heated above its melting point transform immidiately to N-aminopyrroles (33). The reactions of azoalkenes with vinylethers gave a mixture of (4+2) and (3+2) cycloadducts[56]. It was observed that (3+2) cycloaddition occurs only when the vinyl ether or enamine has



Scheme 9

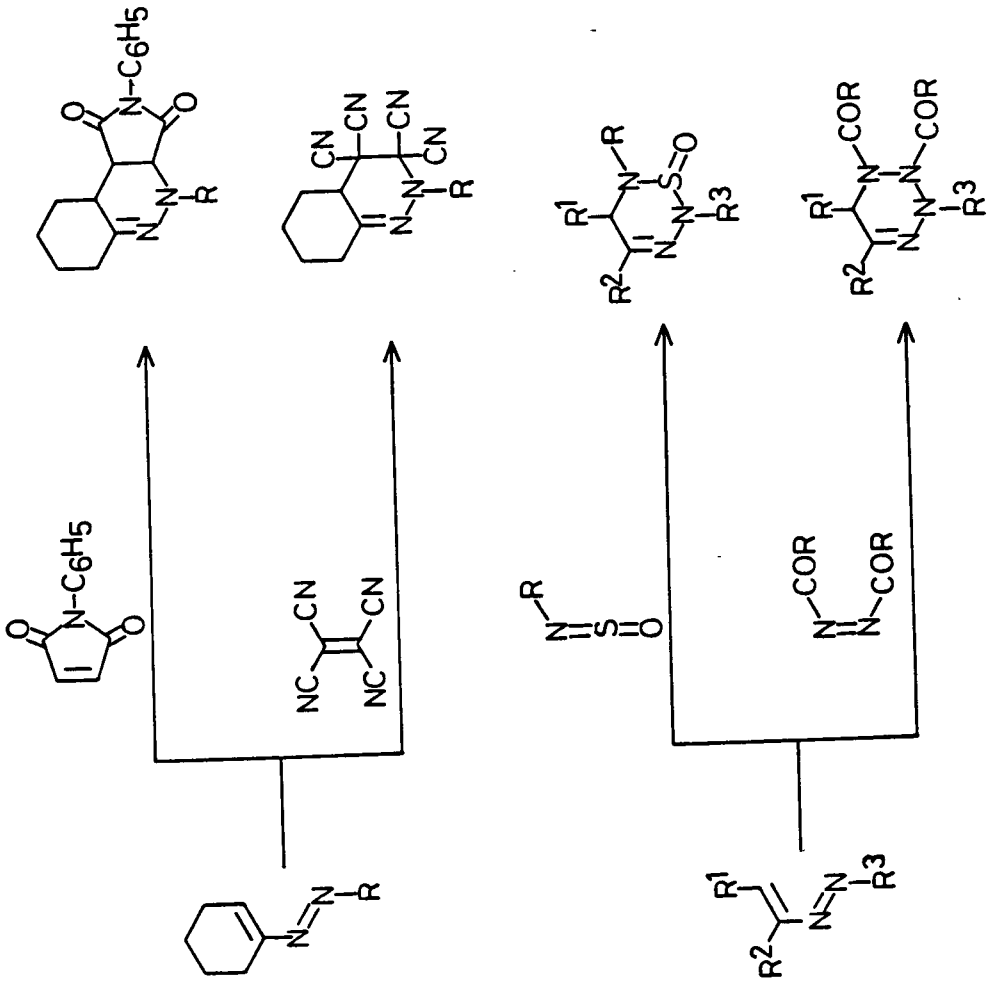


Scheme 10

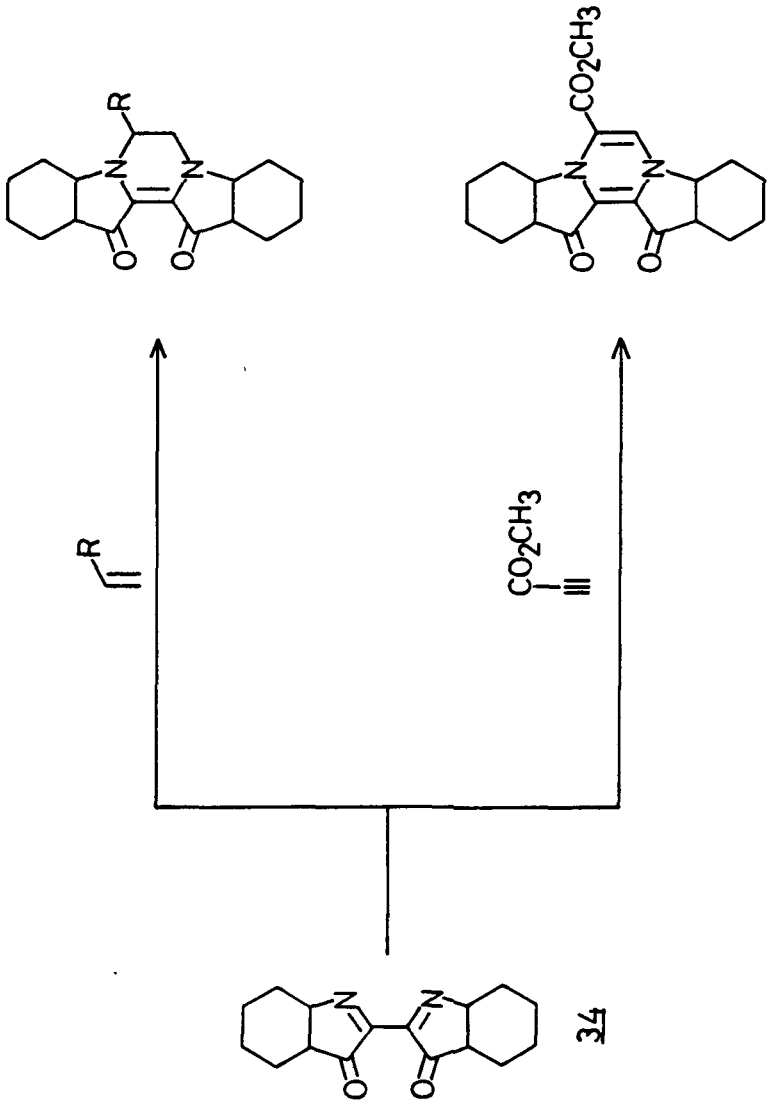
an additional alkyl group at carbon bearing hetero atom. The preference for the (3+2) cycloaddition reactions in case of nucleophilic olefins having an additional α-alkylsubstituent may be due to enhanced nucleophilicity of the olefin[56]. The (4+2) cycloadducts of these azoalkenes show high degree of endo-selectivity and there is no evidence, from the solvent effect on the rate, for the existence of a dipolar intermediate[56]. In complimentary series of observations, the simple azo- alkenes, 1,2-diaza-1,3-butadienes, were shown to participate in Diels-Alder reactions with typical electron- deficient dienophiles[57] and electrophilic hetero dienophiles including azodicarboxylate[58-61] (scheme-11).

1,4-Diaza-1,3-Butadienes

Reports of (4+2) cycloaddition reactions of 1,4-diaza-1,3-butadienes are very few. Earlier reports of such cycloadditions include dihydroindigo (34)[62], which gave (4+2) cycloadducts with styrene, acryonitrile, methylacrylate and methylpropiolate (scheme-12). The studies related to the dimerisation of substituted O-benzoquinone diimines[63] and their Diels-Alder reactions with diarylketenes[64] were available in the liteature. Similar reaction was also found to occur in case of diiminosuccnimide with electron-rich dienophiles[65]. Even though 1,4-diaryl-1,4-diaza-1,3-butadienes are known to undergo



Scheme 11



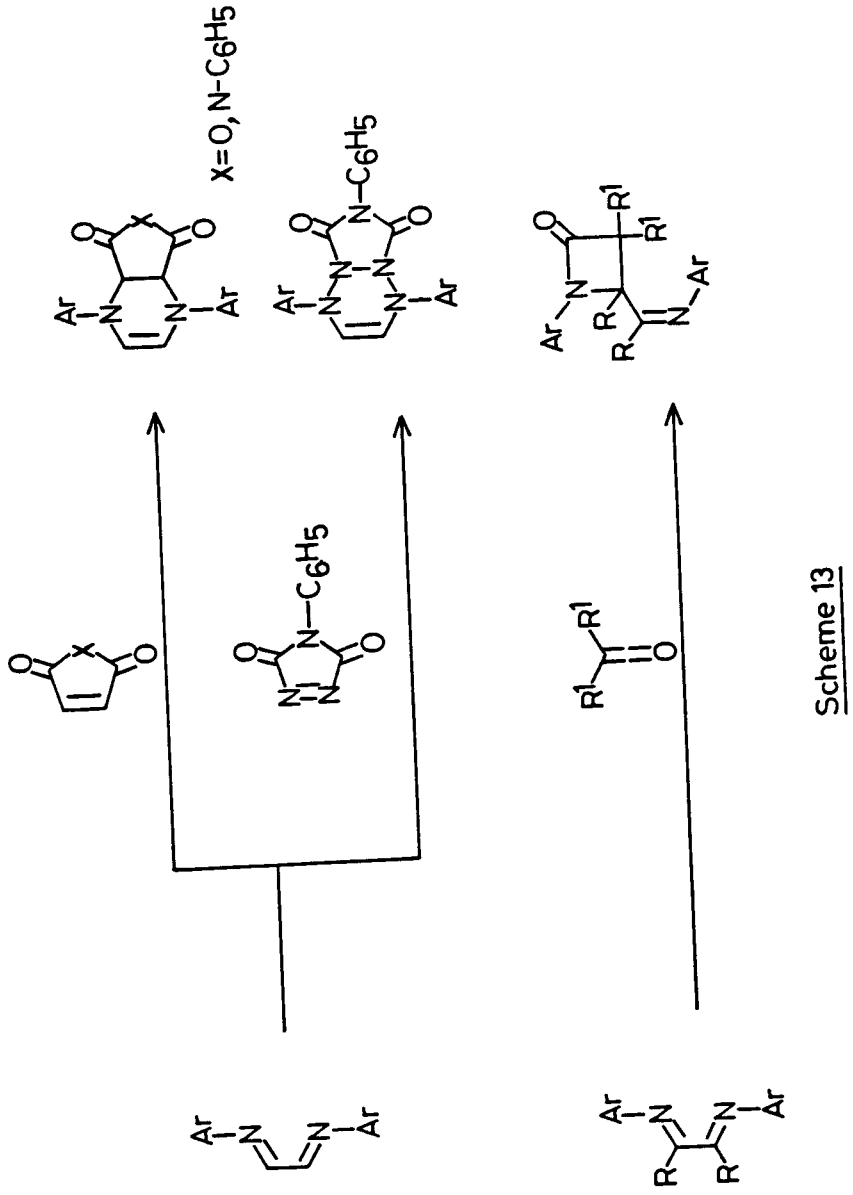
Scheme 12

(4+2) cycloaddition reactions with reactive dienophiles, but their reactions with diphenylketene follow (2+2) cycloaddition pathway resulting in azetidinones (scheme-13).

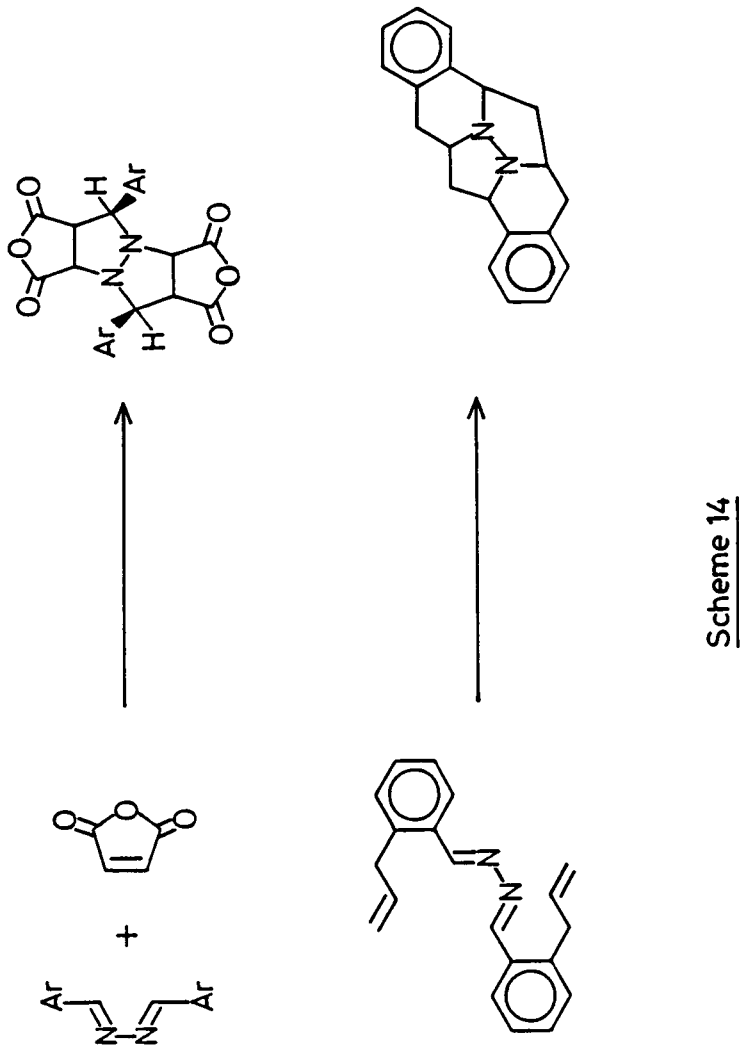
2,3-Diaza-1,3-Butadines

The 2,3-diaza-1,3-butadiene system rarely undergoes (4+2) cycloaddition with typical dienophiles and usually affords 2:1 adducts formed by a criss-cross (3+2) cycloaddition reactions[67] (scheme-14).

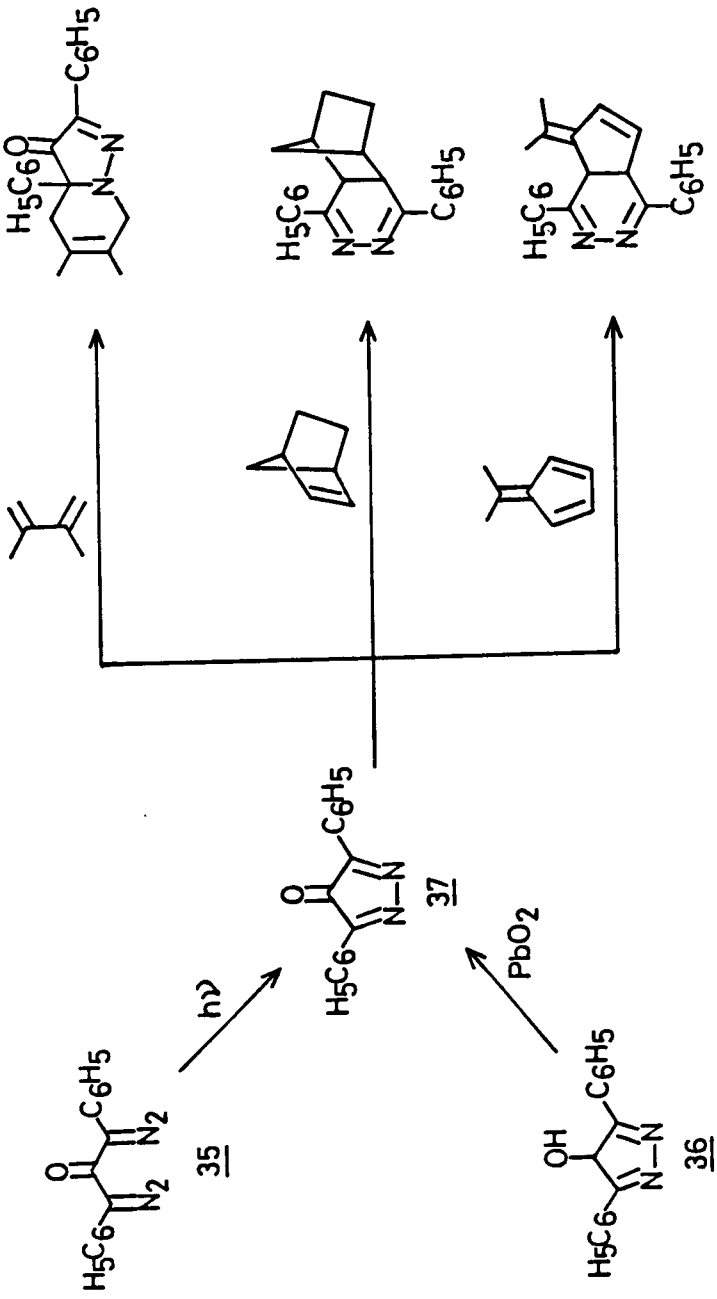
2,5-Diphenyl-3,4-diazacyclopentadienone (37), which can be generated in situ either by photolysis of 1,3-bis(diazo)-1,3-diphenyl-2-propanone (35)[68] or by oxidation of 1,3-diphenylpyrazol-4-ol (36) by lead dioxide[69] has been shown to participate both as diene[67,69,70] and dienophile[67,70,71] in Diels-Alder cycloaddition reactions (scheme-15). Also, 37 has been shown not to react with conventional dienophiles[69] e.g. maleic anhydride, dimethylacetylene dicarboxylate, dimethylfumarate, isobutylvinyl ether, cyclopentene and cyclohexene. 2,3-Diazacyclopentadienone also has been found to react with 1-phenyl- 1,3,4-triazolin-2,5-dione, resulting in (4+2) cycloadduct[72]. Steglich and co-workers[73] studied the cycloaddition reactions of 2,5-diphenyl-6-oxo-1,3,4-oxadiazin (38) with dimethylacetylene dicarboxylate, ynamines and benzynes, and observed that nitrogen is preferentially lost as



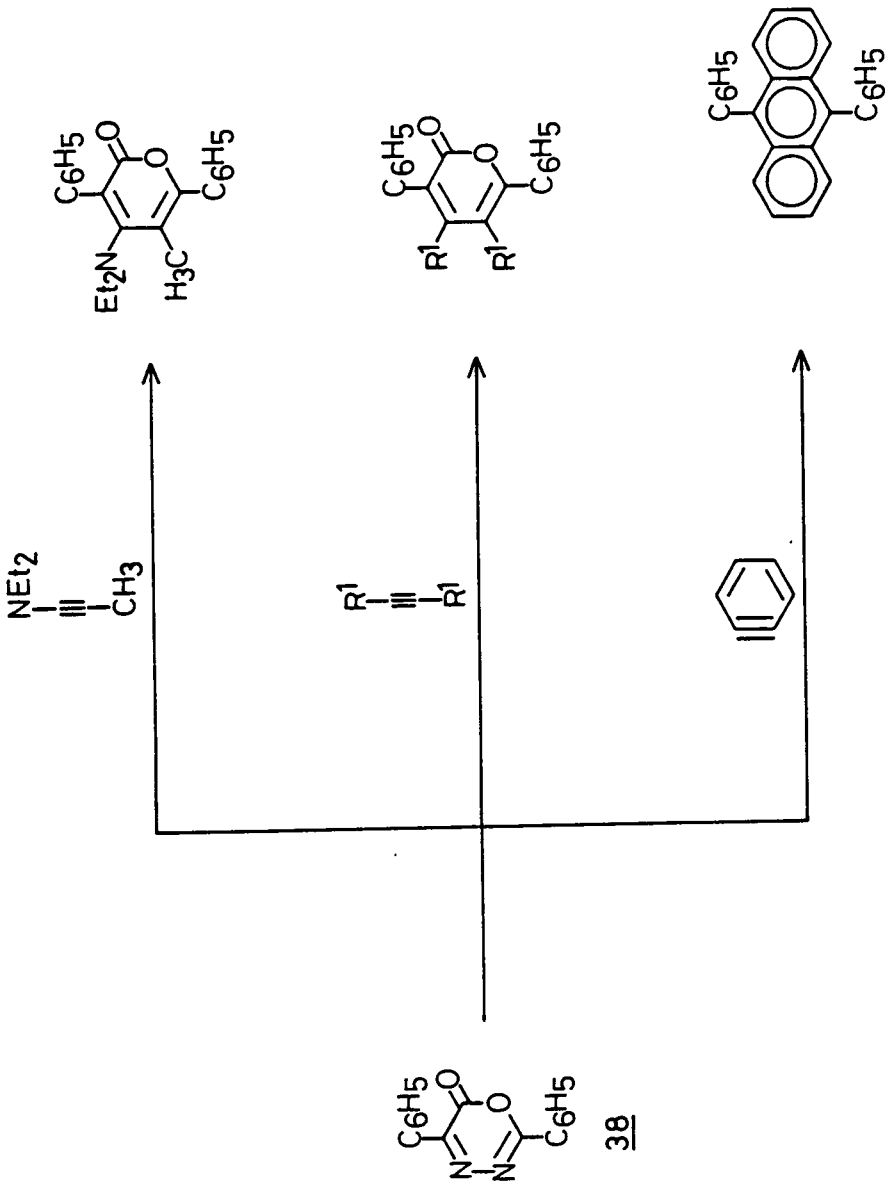
Scheme 13



Scheme 14



Scheme 15


NEt2
CH3
R1
R1
C6H5
C6H5
Et2N
H3C
C6H5
C6H5
R1
R1
C6H5
C6H5
C6H5
C6H5
N
N
38

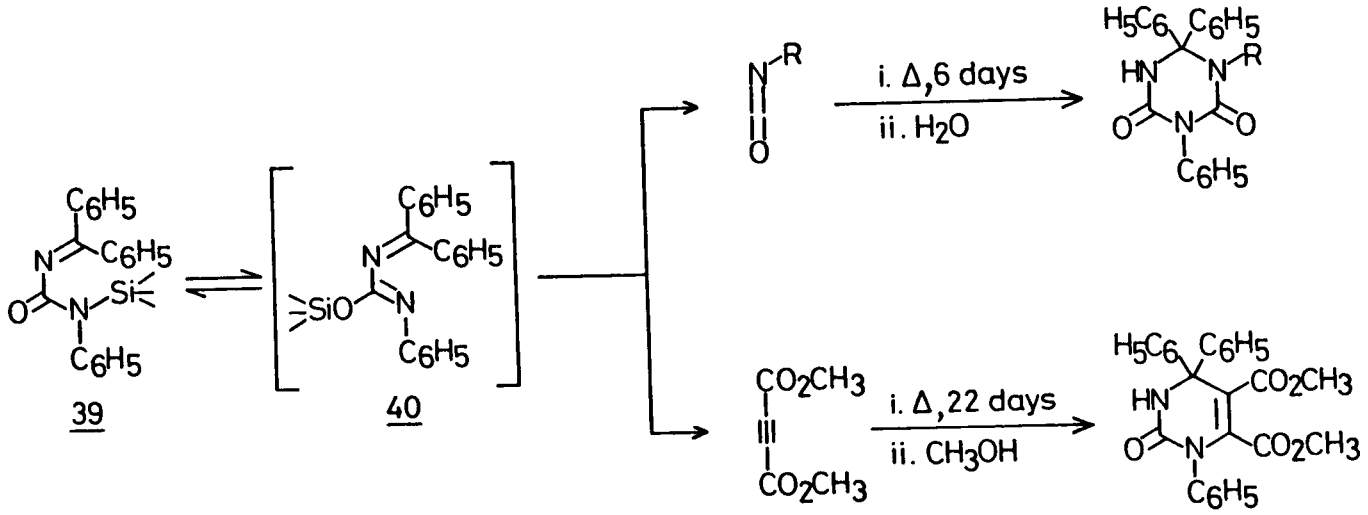
Scheme 16

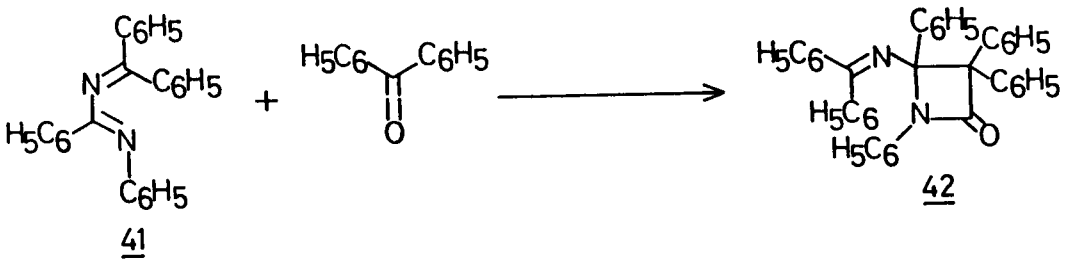
nitrogen molecule from the intermediate cycloadduct leading to the formation of the final products (scheme-16).

1,3-Diaza-1,3-Butadienes

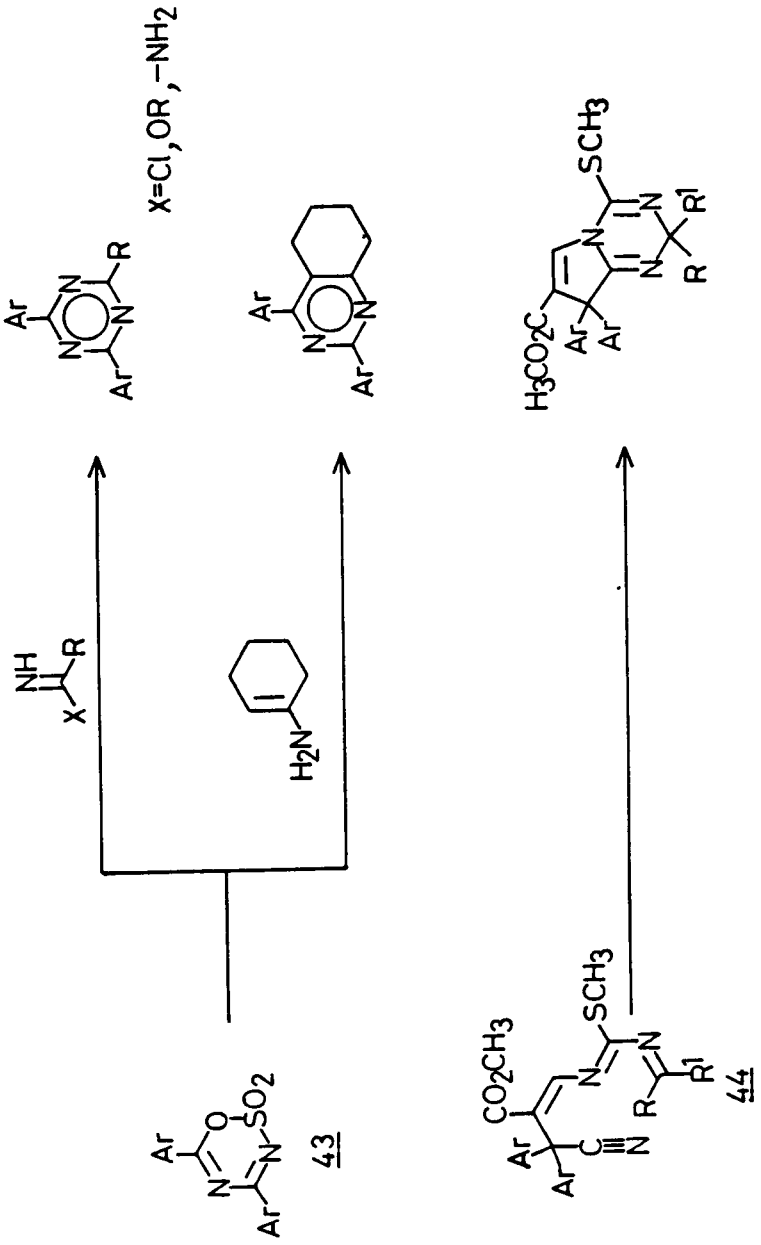
The reports concerning the participation of 1,3-diaza-1,3-butadienes in Diels-Alder reactions are very rare[11,14a]. The successive efforts described in the literature include the thermal isomerization of an unsaturated N-silylurea (39) to 2-trimethylsilyloxy-1,3-diaza-1,3-butadiene (40) and their subsequent Diels-Alder reaction. Their efficiency towards the cycloaddition reaction is doubtful because of long reaction time and other parameters[74]. Matsuda et al had also observed that a similar 1,3-diaza-1,3-butadiene, N-diphenylmethylene-N'-methylbenzamidine (1-methyl-2,4,4-triphenyl-1,3-diaza-1,3-butadiene) (41), failed to react with dimethylacetylene dicarboxylate and formed (2+2) cycloadducts (42) with diphenylketene (scheme-17)[74]. Weidinger et al have reported the (4+2) cycloaddition reactions of 4,6-diaryl-1,2,3,5-oxathiadiazine-2,2-dioxides (43) with nucleophilic hetero-dienophiles[85] and electron-rich olefins[76]. More et al have recently reported the in situ generation and subsequent intra-molecular Diels-Alder reactions of 2-thiomethyl-1,3-diaza-1,3-butadiene (44)[77] (Scheme-18).

Few reports of successful participation of hetero-





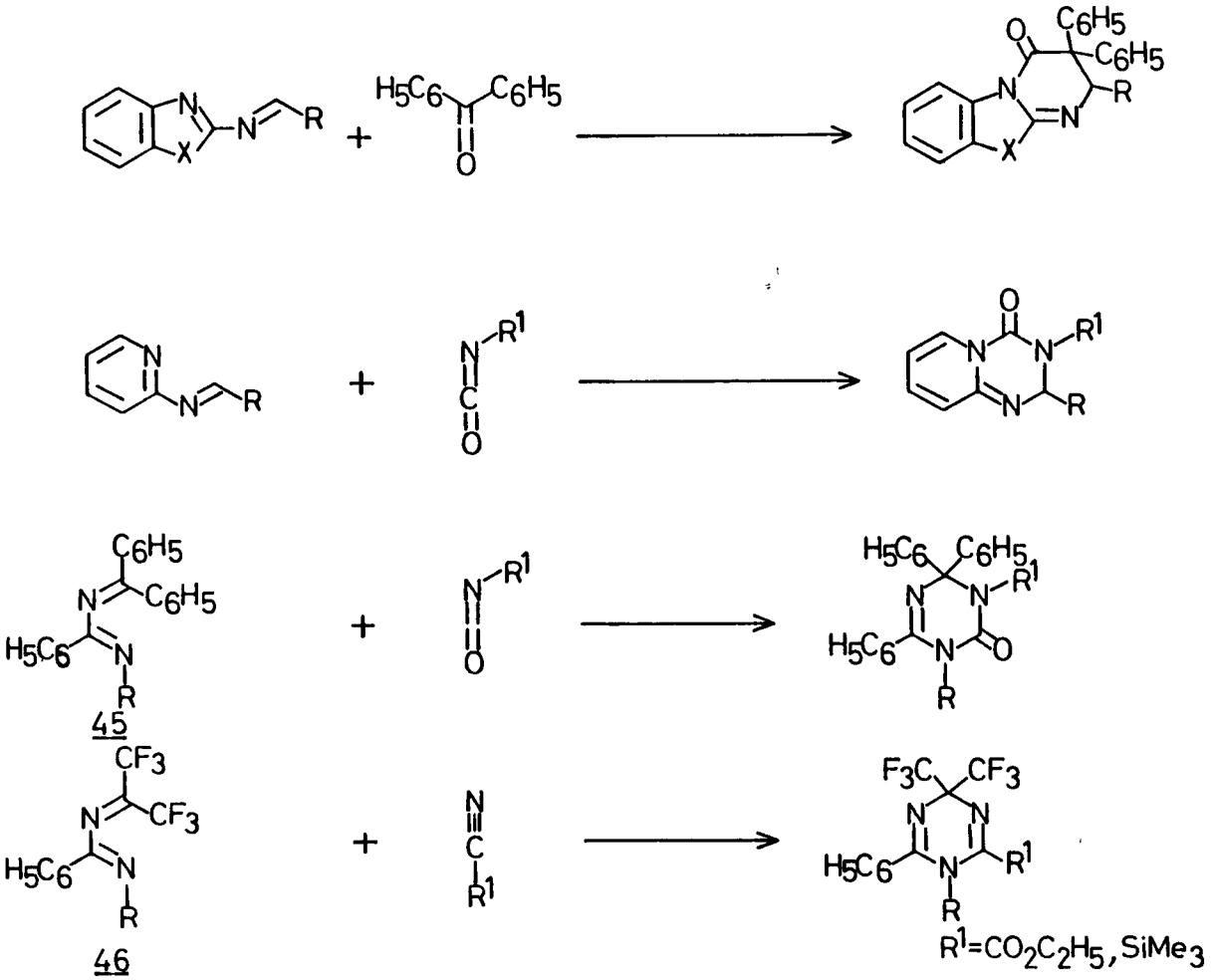
Scheme 17



Scheme 18

cyclic 1,3-diaza-1,3-butadienes as 4π components in Diels-Alder cycloaddition reactions with dienophiles are available in the literature[78-82] (Scheme-19). The only report regarding the (4+2) cycloaddition reaction of simple, yet isolable and stable 1,3-diaza-1,3-butadienes concern the reactions of 45 and 46 with isocynates[83] and substituted nitriles[84], respectively (Scheme-19).

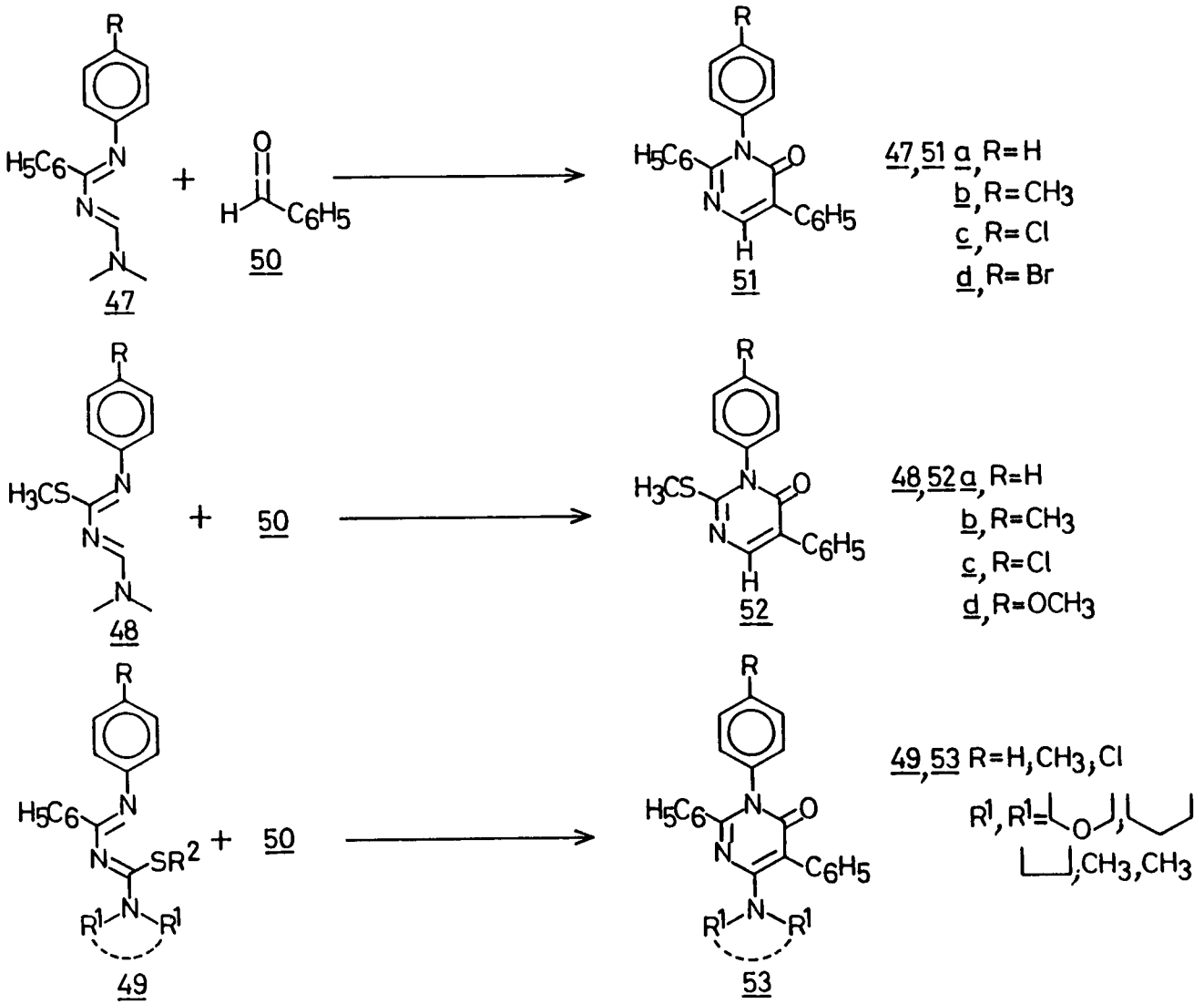
The literature survey clearly reveals that in contrast to 1,2- and 1,4-diaza-1,3-butadienes, much less attention has been paid to the Diels-Alder cycloaddition reactions of 1,3-diaza-1,3-butadienes. This may be attributed to (i) the lack of methods available for the preparation of stable 1,3-diaza-1,3-butadienes and (ii) their reluctance to participate in Diels-Alder reaction because of their inverse electron demand tendency for the unfavourable position of second nitrogen at position 3- of butadiene system. These, together with report of the failure of acyclic 1,3-diaza-1,3-butadiene as an effective 4π component in Diels-Alder cycloaddition reaction with Ketene, drew our attention to this synthetically important area in organic chemistry. This prompted us to explore simple methods for the preparation of altogether new, stable and reactive 1,3-diaza-1,3-butadienes (48, 49 and 61) having polarising function(s) at 4- and 2/4- positions and to investigate their cycloaddition reaction with ketenes


C6H5
C6H5
R
X
H5C6
C6H5
O
R1
45
CF3
CF3
46
F3C
CF3
R1=CO2C2H5, SiMe3

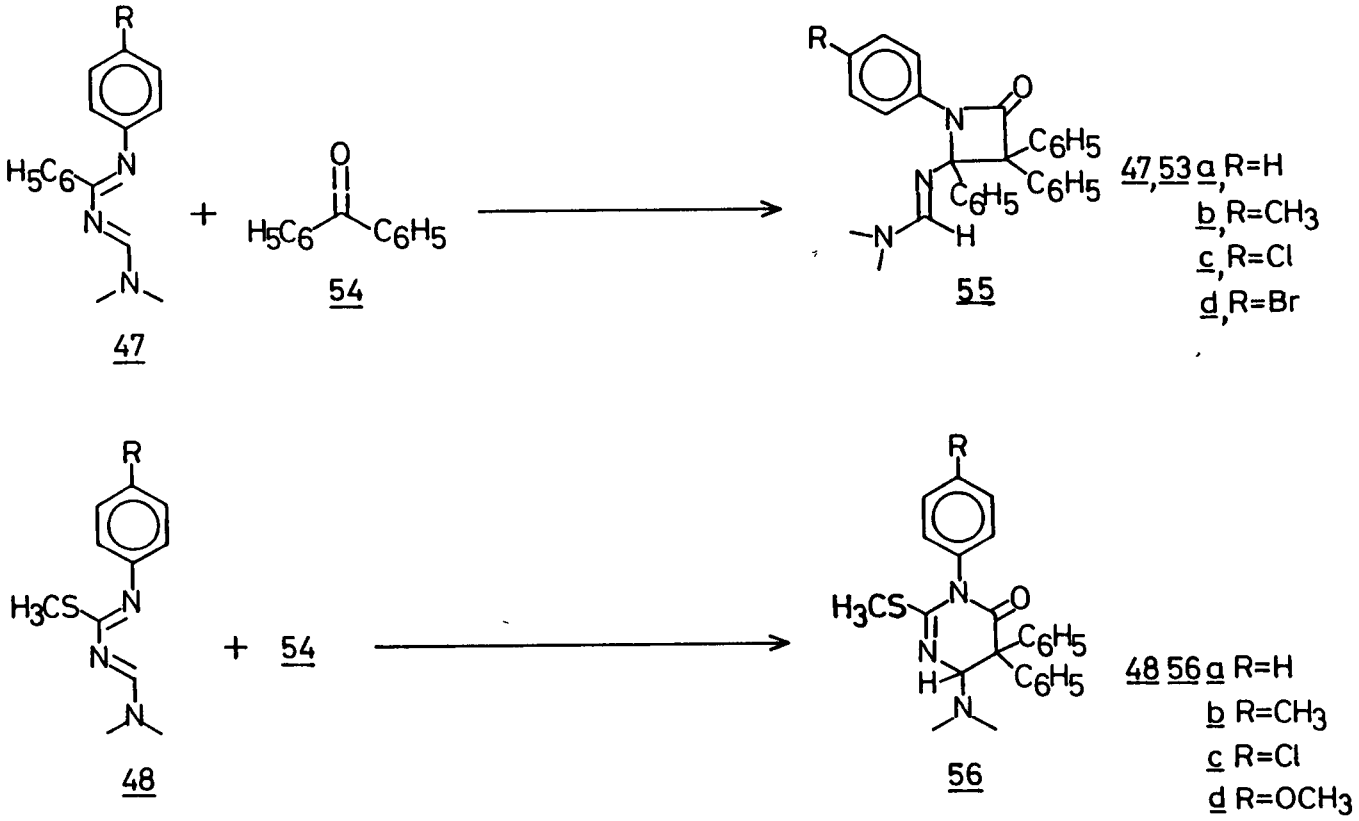
Scheme 19

and other heterodienophiles. We have also carried out the cycloaddition reactions of known 1,3-diaza-1,3-butadiene (47)[85], which remained totally unexploited for any type of cycloaddition reactions.

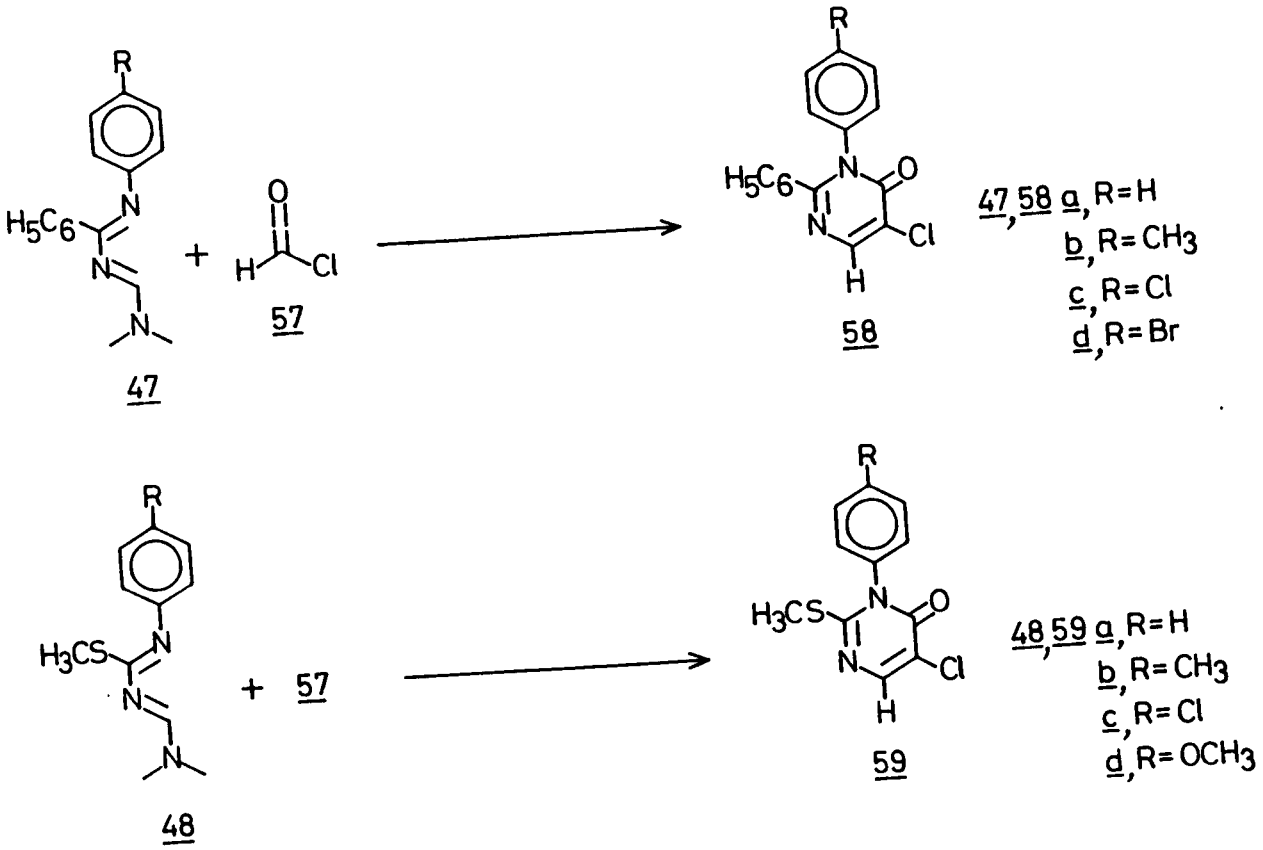
The reactions of 1,3-diaza-1,3-butadienes 47 and 48, with monophenyl ketene (50) resulted in 1,2,5-trisubstituted-1,6-dihydropyrimidin-6-ones (51 and 52). Similar reactions of 1,3-diaza-1,3-butadienes (49) with monophenyl ketene resulted in pyrimidin-6-ones (53) (Scheme-20). The reactions of 1,3-diaza-1,3-butadienes (47) with diphenyl ketene (54) resulted in (2+2) cycloadducts 55, in contrast to the reactions of 48 with 54, which gave (4+2) cycloadducts 56. However, no substantial cycloadducts could be obtained from the reactions of 49 with 54 (Scheme-21). Interesting results have been obtained from the reactions of these 1,3-diaza-1,3-butadienes with monochloroketene (57). The reactions of 1,3-diaza-1,3-butadienes 47 and 48 with monochloroketene yielded 1-aryl-5-chloro-2-phenyl-1,6-dihydropyrimidin-6-ones (58) and 1-aryl-5-Chloro-2- thiomethyl-1,6-dihydropyrimidin-6-ones (59), respectively by the preferential elimination of dimethylamine, rather than hydrogenchloride from the intermediate (4+2) cycloadducts (Scheme-22). Similar reactions of 49 with monochloroketene resulted pyrimidin-6-ones 60, which involved 1,2-RS shift from C-4 to C-5 in the intermediate


R
H5C6
N
N
N
47
+
O
H
C6H5
50
R
H5C6
N
O
N
C6H5
H
51
47, 51 a, R=H
b, R=CH3
c, R=Cl
d, R=Br
R
H3CS
N
N
N
48
+ 50
R
H3CS
N
O
N
C6H5
H
52
48, 52 a, R=H
b, R=CH3
c, R=Cl
d, R=OCH3
R
H5C6
N
N
SR2
R1
N
R1
49
+ 50
R
H5C6
N
O
N
C6H5
R1
N
R1
53
49, 53 R=H, CH3, Cl
R1, R1=O, CH3, CH3

Scheme 20


R
H_5C_6
N
N
N
47
+
O
H_5C_6
C_6H_5
54
R
O
N
C_6H_5
C_6H_5
C_6H_5
N
H
55
47,53 a, R=H
b, R=CH_3
c, R=Cl
d, R=Br
R
H_3CS
N
N
N
48
+ 54
R
N
O
H_3CS
N
H
C_6H_5
C_6H_5
N
56
48 56 a R=H
b R=CH_3
c R=Cl
d R=OCH_3

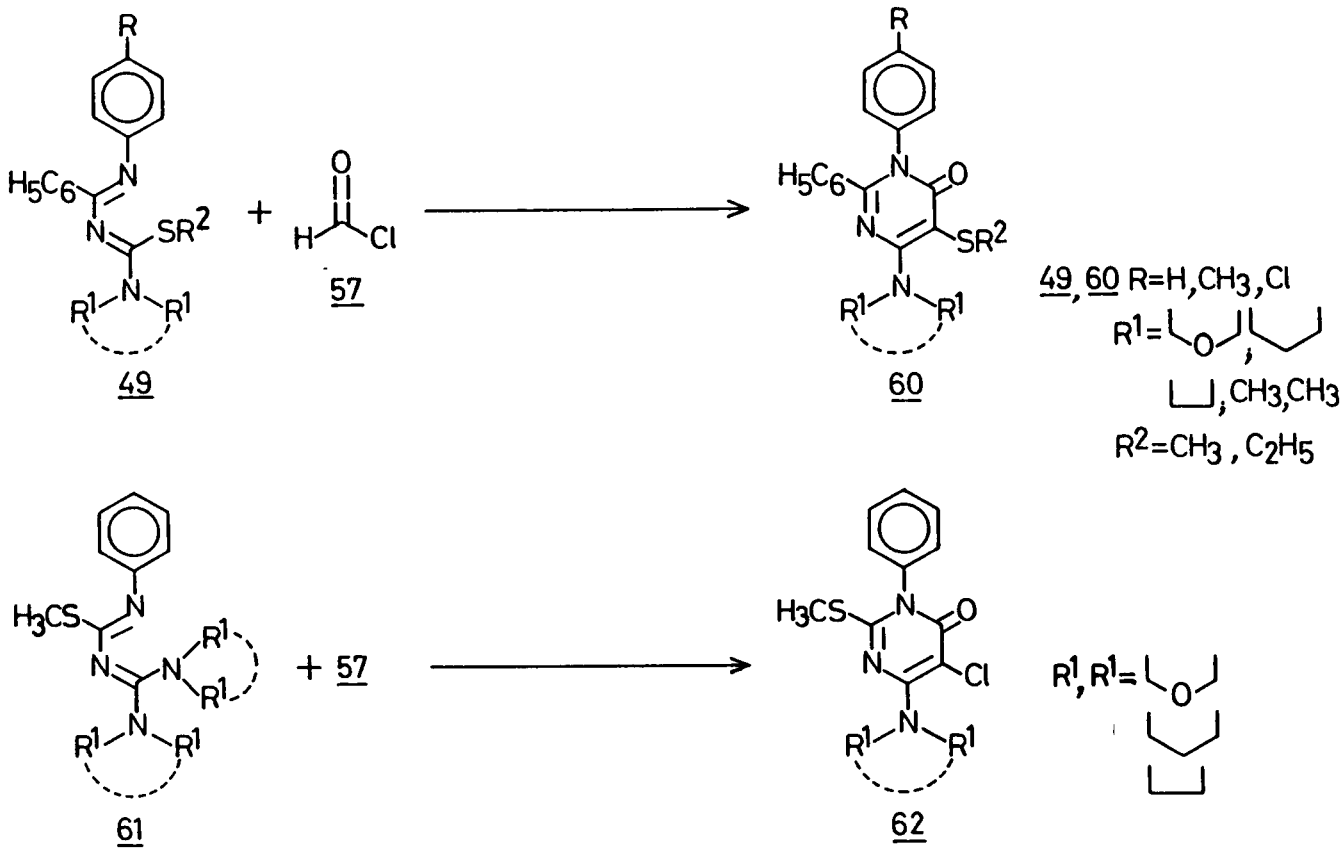
Scheme 21


R
H_5C_6
N
N
$N(CH_3)_2$
47
+
O
H
Cl
57
R
H_5C_6
N
O
N
Cl
H
58
47, 58 a, R=H
b, R=CH_3
c, R=Cl
d, R=Br
R
H_3CS
N
N
$N(CH_3)_2$
48
+ 57
R
H_3CS
N
O
N
Cl
H
59
48, 59 a, R=H
b, R=CH_3
c, R=Cl
d, R=OCH_3

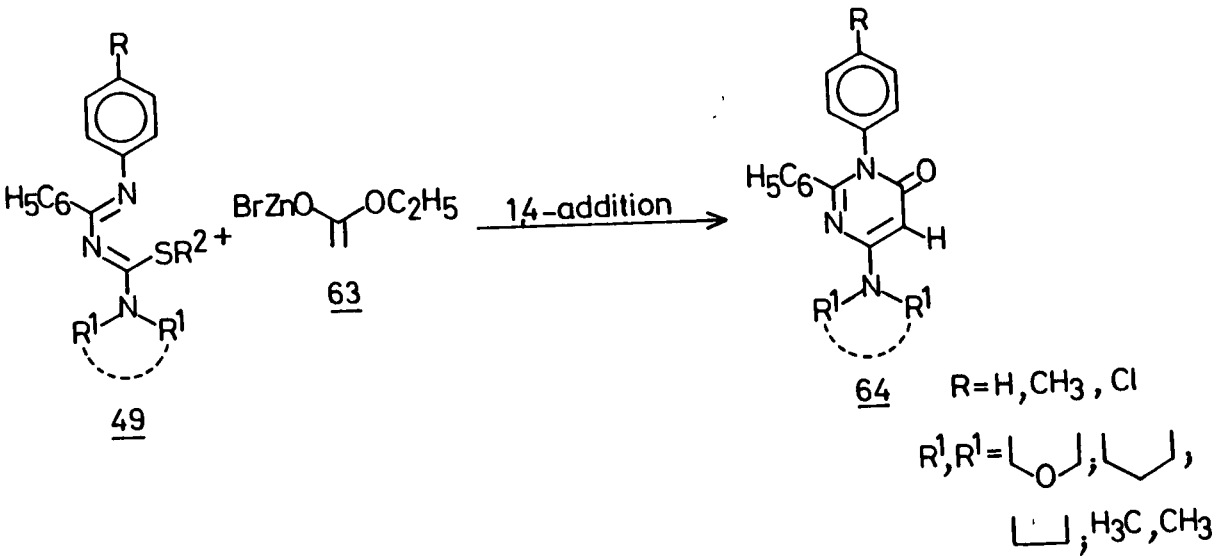
Scheme 22

(4+2) cycloadduct along with dehydrochlorination. However, similar migration was not observed in the reactions of 61 with monochloroketene and resulted in pyrimidin-6-ones (62) (Scheme-23). The reaction of 1,3-diaza-1,3-butadiene 49 with Reformatsky reagent (63), prepared from ethyl-bromoacetate afforded in 1-aryl-2-phenyl-4-sec. amino-1,6-dihydropyrimidin-6-ones (64) by the 1,4-conjugated addition of Reformatsky reagent to 1,3-diaza-1,3-butadienes (Scheme-24). The syntheses of different stable 1,3-diaza-1,3-butadienes and their reactions with ketenes and Reformatsky reagent are included in Chapter II and this constitutes the mainbody of the thesis. The products have been assigned structures on the basis of analytical data and spectral evidences and humble attempts have been made to discuss the mechanism of formation of various products.

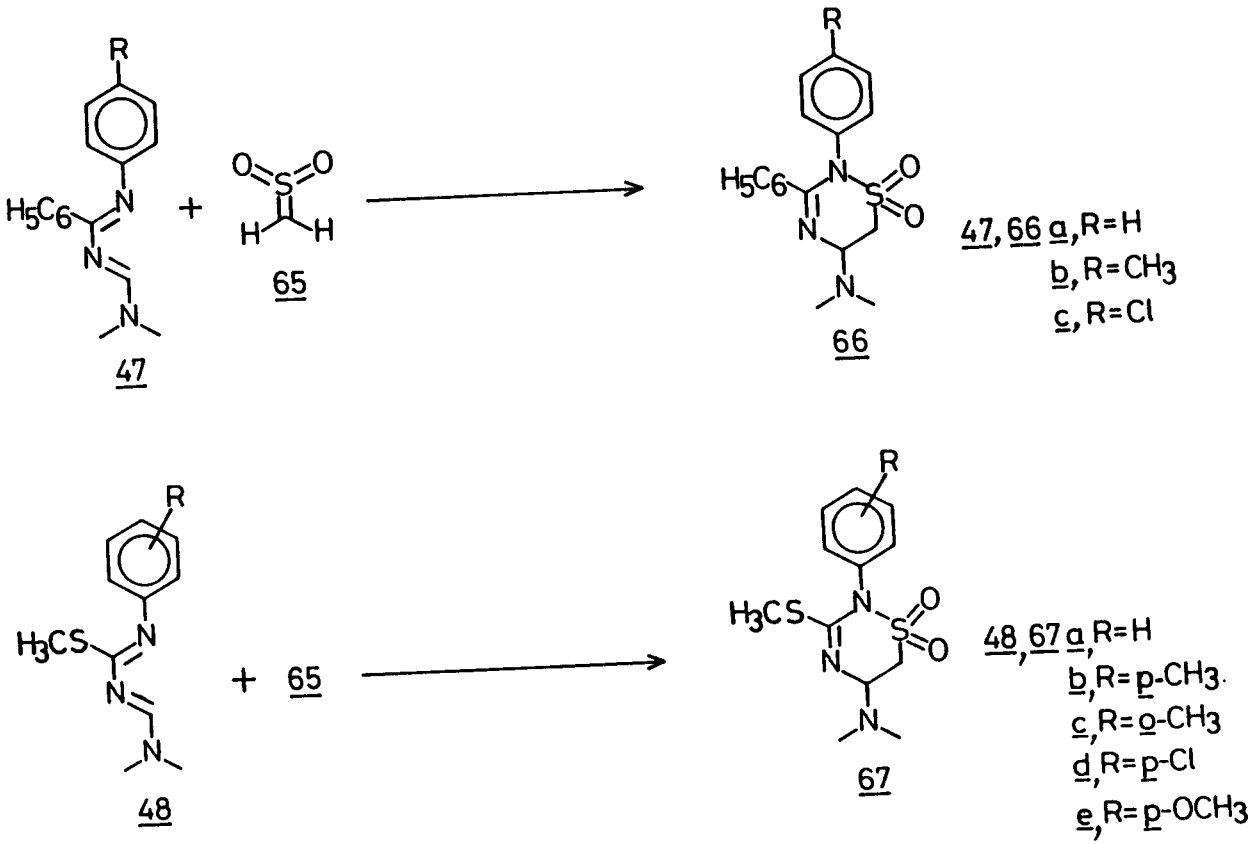
Though the benzoylsulphene have been reported to undergo cycloaddition reaction with 1-aza-1,3-butadiene[86], but surprisingly the simple sulphene (65), one of the most reactive heterodienophiles, has not been exploited much as 2π component in Diels-Alder reaction with heterodienes. Thus, it was considered worthwhile to investigate the reactivity of 1,3-diaza-1,3-butadienes 47 and 48 towards simple sulphene. These reactions resulted in hitherto unknown substituted 5,6-dihydro-2,4-thiadiazine-1,1-dioxide derivatives (66 and 67) arising from Diels-Alder


R
H5C6
N
SR2
R1
R1
49
O
H
Cl
57
60
49, 60 R=H, CH3, Cl
R1=
CH3, CH3
R2=CH3, C2H5
H3CS
61
+ 57
62
R1, R1=

Scheme 23


R
H5C6
N
N
SR2+
R1
N
R1
49
BrZnO
OC2H5
63
1,4-addition
R
H5C6
N
O
N
H
R1
N
R1
64
R=H, CH3, Cl
R1,R1=
O
H3C, CH3

Scheme 24

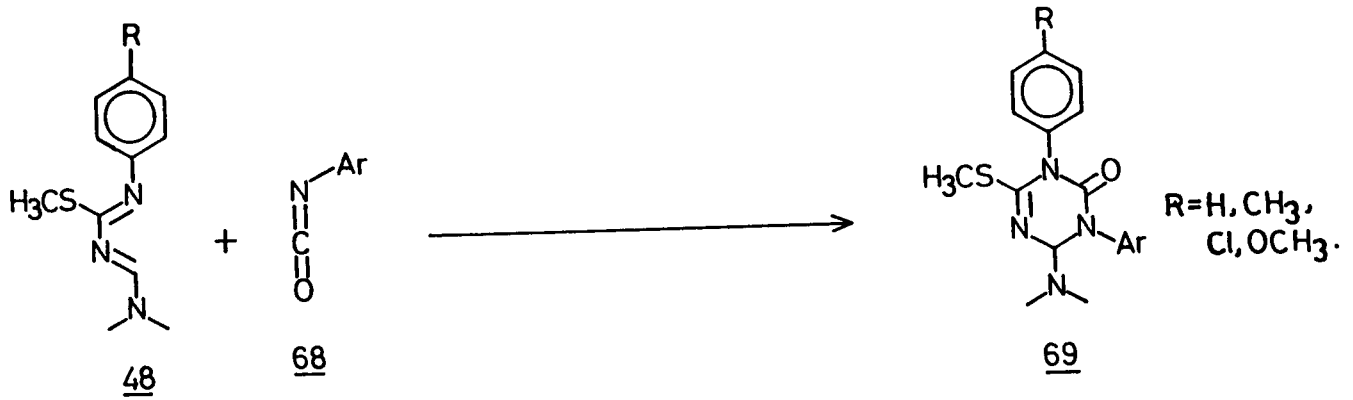

R
H_5C_6
N
N
N
47
+
O
S
O
H
H
65
R
H_5C_6
N
S
O
O
N
N
66
47, 66 a, R=H
b, R=CH_3
c, R=Cl
R
H_3CS
N
N
N
48
+ 65
R
H_3CS
N
S
O
O
N
N
67
48, 67 a, R=H
b, R=p-CH_3
c, R=o-CH_3
d, R=p-Cl
e, R=p-OCH_3

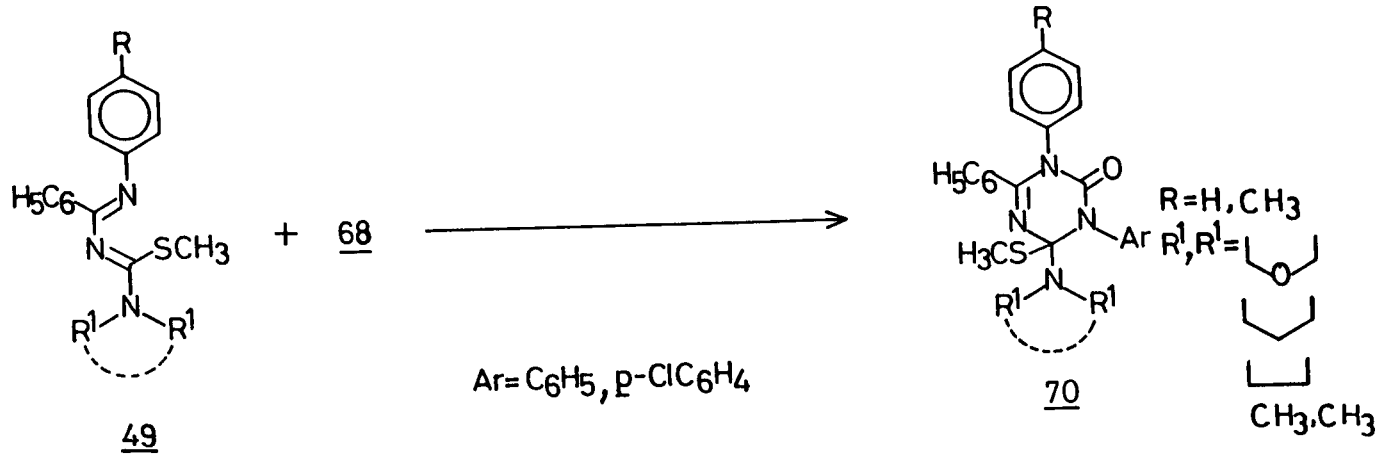
Scheme 25

cycloaddition reactions of 1,3-diaza-1,3-butadienes with sulphene (Scheme-25). The structural elucidation of the products were done on the basis of analytical data and spectral evidences, and are discussed in chapter-III.

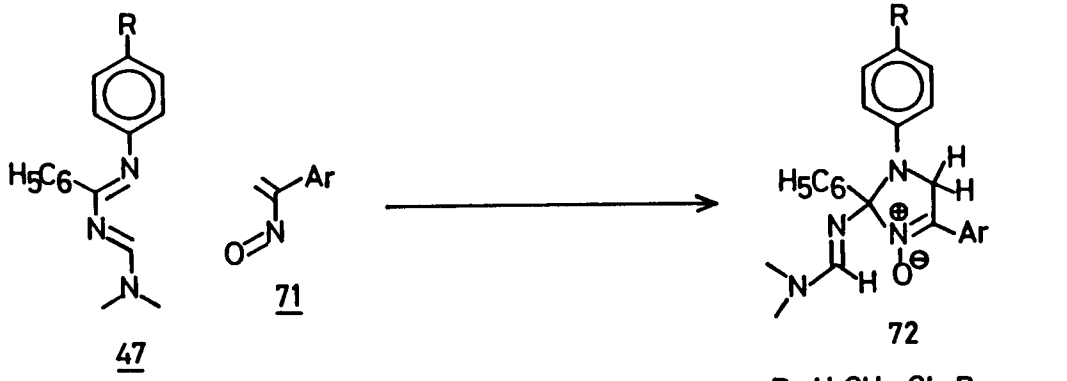
Almost quantative yields of substituted 3,4-dihydro-1,3,5-triazin-2(1H)-ones (69 and 70) were obtained as (4+2) cycloadducts of the reactions of 1,3-diaza-1,3-butadienes (48 and 49) with aryl isocyanates (68) (Scheme-26). The products were found to be unstable and decompose in solution. The details concerning the reaction conditions and analysis of the products are described in chapter IV.

In continuation of our studies concerning the reactivity of 1,3-diaza-1,3-butadienes, which proved to be efficient 4 π components in the Diels-Alder reactions, we considered it worthwhile to examine the behaviour of these towards other potential heterodienes. With this objective, we had carried out the reactions of these 1,3-diaza-1,3-butadienes (47) with nitrosoalkene (71) and isolated the cycloadducts, characterised as 1,4-diaryl-2-N'-(N,N-dimethylformamidino)-2-phenyl-Δ^3-imidazoline-3-oxides (72) (Scheme-27). The nitrones 72 were probably formed by an unusual (3+2) dipolar addition of α-nitroso-styrene in a 1,3-mode to 1,2-carbon-nitrogen double bond of 1,3-diaza-1,3-butadienes (47). The structural assign-


R
H3CS
N
Ar
O
R=H, CH3, Cl, OCH3.
48
68
69


R
H5C6
SCH3
R1
68
Ar= C6H5, p-ClC6H4
H3CS
Ar
R=H, CH3
R1, R1=
CH3, CH3
49
70

Scheme 26


R
H5C6
N
N
N
Ar
O
N
47
71
R
H5C6
N
H
H
N
N
Ar
H
O
N
72
R=H;CH3;Cl ;Br
Ar=C6H5;p-CH3C6H4

Scheme 27

ments and probable mechanism for the formation of these nitrones are described in the last chapter of the thesis.

REFERENCES

1. J. Hammer (Ed), **1,4-Cycloaddition Reactions,** Academic Press, New York, 1967.

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

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

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

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

6. (a). R. Gompper, **Angew. Chem. Int. Ed. Engl.,** 1969, **8,** 312.

   (b) R.R. Schmidt, **Angew. Chem. Int. Ed. Engl.,** 1973, **12,** 212.

7. G. Brieger and J.N. Bennet, **Chem. Rev.,** 1980, **80,** 63.

8.(a) J.L. Ripoll and A. Rouessac, **Tetrahedron,** 1978, **34,** 19.

   (b) A.R. Katritzky and N. Dennis, **Chem. Rev.,** 1989, 827.

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

10. K.N. Houk, **Acc. Chem. Res.,** 1975, **8,** 361.

11.(a) J.G. Martin and R.H. Hill, **Chem. Rev.,** 1961, **61,** 537.

(b)R. Huisgen, **Angew Chem. Int. Ed. Engl.**, 1963, **2**, 565.

(c)J. Sauer, **Angew. Chem. Int. Ed. Engl.**, 1966, **5**, 211.

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

13.(a)O.Tsuge, **Heterocycles**, 1979, **12**, 1067.

(b)T.L. Gilchrist, **Chem. Soc. Rev.**, 1983, **12**, 53.

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

(b)T. Kametani and S. Hibino, **Advances in Heterocyclic Chemistry**, Academic Press, New York, 1987, **42**, 246.

15. C.D. Nenitzescu, E. Cioranescu, and L. Birladeanu, **Commum. Acad. Rep. Populare Romine**, 1958, **8**, 775; **Chem. Abstr.**, 1958, 53, 18003.

16(a).Y. Tomimatsu, **J. Pharm. Soc. Japan**, 1957, **77**, 7.

(b)Y. Tomimatsu, **J. Pharm. Soc. Japan**, 1957, **77**, 186.

17. H.R.Synder, H. Cohen, and W.J. Tapp, **J. Am. Chem. Soc.**, 1939, **61**, 3530.

18(a).R. Gompper, **Angew. Chem. Int. Ed. Engl.**, 1969, **8**, 322.

(b)W.T. Brady and C.H. Shieh, **J. Org. Chem.**, 1983, 48, 2499.

19. A.O. Fitton, J.R. Frost, P.G. Houghton, and H. Suschizky, **J. Chem. Soc. Perkin Trans.I**, 1977, 1450.

20. M. Komamatsu, H. Ohgishi, Y. Ohshiro, and T. Agawa, **Tetrahedron Lett.**, 1976, 4589.

21. M. Komamatsu, H. Ohgishi, Y. Ohshiro, S. Takamatsu, and T. Agawa, **Angew. Chem. Int. Ed. Engl.**, 1982, **21**, 213.

22. B.S. Poncin, A.M.H. Frisque, and L. Ghosez, **Tetrahedron Lett.**, 1982, **23**, 3261.

23. Y.S. Chang, F.W. Fowler, and A.T. Lupo (Jr.), **J. Am. Chem. Soc.**, 1981, **103**, 2090.

24. Y.C. Hwang and F.W. Fowler, **J. Org. Chem.**, 1985, **50**, 2719.

25. R.L. Funk and K.P.C. Vollhardt, **Chem. Soc. Rev.**, 1985, **50**, 2719.

26. E.M. Burgeas and L.Mc Cullagh, **J. Am. Chem. Soc.**, 1966, **88**, 1580.

27. M. Lancaster and D.J.H. Smith, **J. Chem. Soc. Chem. Commun.**, 1980, 471.

28. M. Fisher and F. Wagner, **Chem. Ber.**, 1969, **102**, 3486.

29. Y.L. Mao and V. Bockelheide, **J. Org. Chem.**, 1980, **45**, 1547.

30. Y. Ito, S. Miyata, M. Nakatsuka and T. Saegusa, **J. Am. Chem. Soc.**, 1981, **103**, 5250.

31. Y. Ito, E. Nakajo, and T. Saegusa, **Tetrahedron Lett.**, 1983, **24**, 2881.

32. Y. Ito, E. Nakajo, and T. Saegusa, **Synth. Commun.**, 1986, **16**, 1073.

33. I. Hodgeths, S.J. Noyce, and R.C. Storr, **Tetrahedron Lett.**, 1984, **25**, 5435.

34(a).F.Sainte, B.S. Poncin, A.M.H. Frisque, and L. Ghosez, **J. Am. Chem. Soc.**, 1982, **104**, 1428.

(b)M. Rivera, H. Lamy-Schelkens, F. Sainte, K. Mbiya, and L. Ghosez, **Tetrahedron Lett.**, 1988, **29**, 4573.

35. A. Demoulin, H. Gorissen, A.M.H. Frisque, and L. Ghosez, **J. Am. Chem. Soc.**, 1975, **97**, 4409.

36(a).D.H.Aue and D.Thomas, **J. Org. Chem.**, 1975, **40**, 1349.

(b).T.L. Gilchrist and A.M. Standard, **Tetrahedron Lett.**, 1988, **29**, 3585.

37. K.G.Taylor, B. Venugopalan, and M.S. Clark(Jr.), **Tetrahedron Lett.**, 1978, **34**, 833.

38. D.H. Hunter and R.P. Steiner, **Can. J. Chem.**, 1975, **53**, 355.

39. R.Gompper and U. Heinemann, **Angew. Chem. Int. Ed. Engl.**, 1980, **19**, 217.

40. R. Gompper and U. Heinemann, **Angew. Chem. Int. Ed. Engl.**, 1981, **20**, 296.

41. W. Steiglich, R. Jescke, and E. Buschmann, **Gazz. Chim. Ital.**, 1986, **116**, 361.

42. W. Steiglich, E. Buschmann, and O. Hollitzer, **Angew. Chem. Int. Ed. Engl.**, 1974, **13**, 533.

43. W. Steiglich and E. Buschmann, **Angew. Chem. Int. Ed. Engl.**, 1974, **13**, 48.

44(a).G. Hofle, O. Hollitzer, and W. Steiglich, **Angew. Chem. Int. Ed. Engl.**, 1972, **11**, 720.

44(b).W. Steiglich and O. Hollitzer, **Angew. Chem. Int. Ed. Engl.**, 1973, **12**, 49.

45. M.E. Jung and J.J. Shapiro, **J. Am. Chem. Soc.**, 1980, **102**, 7862.

46. R.H. Daniels and J. Wong, **J. Org. Chem.**, 1980, **45** , 435.

47. A. Eddaif, A. Laurent, P.Misson, and N. Pellissier, **Tetrahedron Lett.**, 1984, **25**, 2779.

48. T. Eicher, F. Abdisakan, G. Franke, and J.L. Weber, **Tetrahedron Lett.**, 1975, **31**, 3919.

49. J. Hajicek and J. Trojanek, **Tetrahedron Lett.**, 1981, 1823.

50. I. Hassan and F.W. Fowler, **J. Am. Chem. Soc.**, 1978, **100**, 6696.

51. M. Nitta, A. Sekiguchi, and H. Koba, **Chem. Lett.** 1981, 933.

52. L.S. Povarov, **Izv. Akad. SSSR.**, 1963, 955, 2039; 1964, 179, 1693, 2221; 1965, 365; **Chem. Abstr.**, 1963, **59**, 7489; 1964, **60**, 5451, 9256; 1964, **61**, 16057; 1965, **62**, 7723, 14624.

53. R. Faragher and T.L. Gilchrist, **J. Chem. Soc. Chem. commun.**, 1976, 581.

54. R. Faragher and T.L. Gilchrist, **J. Chem. Soc. Perkin Trans.I**, 1979, 249.

55. S. Sommer, **Angew. Chem. Int. Ed. Engl.**, 1979, **18**, 695.

56. S.J. Clarke, D.E. Davies, and T.L. Gilchrist, **J. Chem. Soc. Perkin Trans.I**, 1983, 1803.

57. L. Caglioti, G. Rosini, P. Tundo, and A. Vigevani, **Tetrahedron Lett.**, 1970, **27**, 2349.

58. S. Sommer, **Angew. Chem. Int. Ed. Engl.**, 1979, **18**, 696.

59. S. Sommer, **Synthesis**, 1977, 305.

60. S. Sommer, **Angew Chem. Int. Ed. Engl.**, 1977, **16**, 59.

61. S. Sommer, **Angew. Chem. Int. Ed. Engl.**, 1976, 15, 432.

62(a).R. Pummer and H. Fiesselmann, **Liebigs. Ann. Chem.**, 1940, **544**, 206.

(b).R. Pummer and E. Stieglitz, **Chem. Ber.**, 1942, 75, 1072.

63. M.L. Tamayo, R.P. Ossorio, and M.S. Burata, **Ann. Chem. espan.**, 1975, **B50**, 765.

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

65. R. Begland, A. Cairneross, D.S. Donald, D.R. Hartter, W.A. Sheppard, and W.O. Webster, **J. Am. Chem. Soc.**, 1971, **93**, 4953.

66. M. Sakamoto, K. Miyazawa, Y. Ishihara, and Y. Tomimatsu, **Chem. Pharm. Bull. Tokyo**, 1974, **22**, 1419.

67. T.W. Iauregg, **Synthesis**, 1976, 349.

68. B.M. Trost and P.J. Whitmann, **J. Am. Chem. Soc.**, 1972, **94**, 8634; 1974, **96**, 7421, 7534.

69. P.F. Fagan, E.E. Niedert, M.J. Nye, M.J. O'Hare, and W.P. Tang, **Can. J. Chem.**, 1979, **57**, 904.

70. T. Sasaki, K. Kanematsu, and T. Kataoka, **J. Org. Chem.**, 1975, **40**, 201.

71. K. Harano, M. Yasuda, T. Ban, and K. Kamematsu, **J. Org. Chem.**, 1980, **45**, 4455.

72. A.B. Evnin and D.R. Arnold, **J. Am. Chem. Soc.**, 1968, **90**, 5330.

73. W. Steiglich, E. Buschmann, G. Gausen, and L. Wilschowitz, **Synthesis**, 1977, 252.

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

75. H. Wedinger and J. Krang, **Chem. Ber.**, 1963, **96**, 2070.

76. H. Wedinger and H.J. Sturm, **Liebigs Ann. Chem.**, 1968, **716**, 143.

77. G. Morel, E. Marchand, and A. Foucaund, **J. Org. Chem.**, 1985, **50**, 771.

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

79. R. Richter and H. Ulrich **Chem. Ber.**, 1970, **103**, 3525.

80. T. Morimoto and M. Sekeya, **Chem. Pharm. Bull. Tokyo**, 1977, **35**, 1607.

81. T. Kato and S. Matsuda, **Chem. Pharm. Bull. Tokyo**, 1974, **22**, 1542.

82. M. Sakamoto, M. Shibano, K. Miyazawa, M. Suzuki, and Y. Tomimatsu, **Chem. Pharm. Bull. Tokyo**, 1976, **24**, 2889.

83. I. Matsuda, K. Itoh and Y. Ishii, **J. Chem. Soc. Perkin Trans.I**, 1972, 1678.

84(a).K. Burger and S. Peninger, **Syntheses**, 1978, 524.

(b).K.Burger, E. Huber, T. Kahl H. Partscht, and M. Ganzer, **Synthesis**, 1988, 44.

85. M. Nishii, S. Tanimoto, M. Okano, and R. Oda, **Yuki Gosei Kagaku Kyokai Shi**, 1969, **27**, 754; **Chem. Abstr.**, 1969, 101438v.

86. O. Tsuge and S. Iwanami, **Bull. Chem. Soc. Japan**, 1971, **44**, 2750.

CHAPTER - II

CHAPTER-II

SYNTHESES OF 1,3-DIAZA-1,3-BUTADINES AND THEIR CYCLOADDITION REACTIONS WITH KETENES AND REFORMATSKY REAGENT

II.1 Syntheses of 1,3-Diaza-1,3-Butadienes

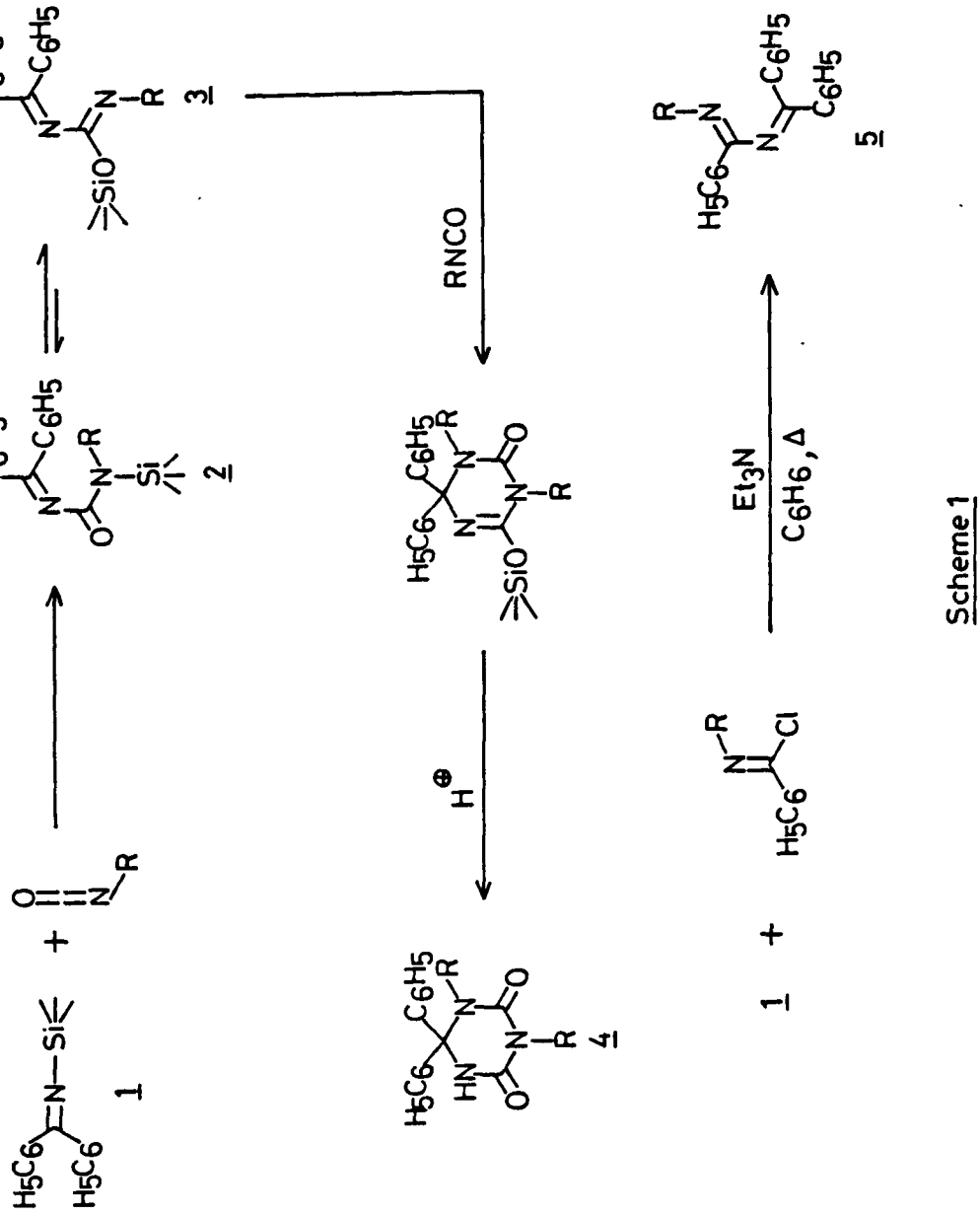
A very small group of 1,3-diaza-1,3-butadienes has been reported to undergo cycloaddition reactions[1,2]. The lack of extensive efforts with such system contrary to other diazabutadienes may probably be due to the difficulties encountered in the syntheses of stable 1,3-diaza-1,3-butadienes[2]. Of very few reports in this regard, a large proportion deals with the syntheses and cycloadditions of heterocyclic 1,3-diaza-1,3-butadienes[3-6].

The first successful synthesis and Diels-Alder

cycloaddition reaction of simple acylic 1,3-diaza-1,3-butadienes was reported by Matsuda et al[7]. They observed that the treatment of N-trimethylsilyl(diphenylmethylene)-amine(1) with two equivalents of isocaynates resulted in crystalline dihydrotriazinone(4). The formation of 4, a Diels-Alder adduct of 3 and isocaynate, indirectly established the intermediacy of 2-trimethylsilyl-1,3-diaza-1,3-butadiene(3), which is formed probably by thermal isomerisation of N-trimethylsilylurea(2) (Scheme-1). They also reported the syntheses of stable and isolable 1,3-diaza-1,3-butadienes, on treatment of 1 with imidoyl halides[7b]. The other report[8] involving the syntheses of stable 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes(8), by condensation of approapriate amidines (6) with N,N-dimethylformamidine dimethylacetal(7), however, remained unused in heterocyclic synthesis. Keeping this in view, as well as the growing significance of synthetic utility of heterodienes[1,2,9] the development of simple synthetic approaches to newer 1,3-diazabutadienes is thought to be of immense importance.

II.1.1 Results and Discussions

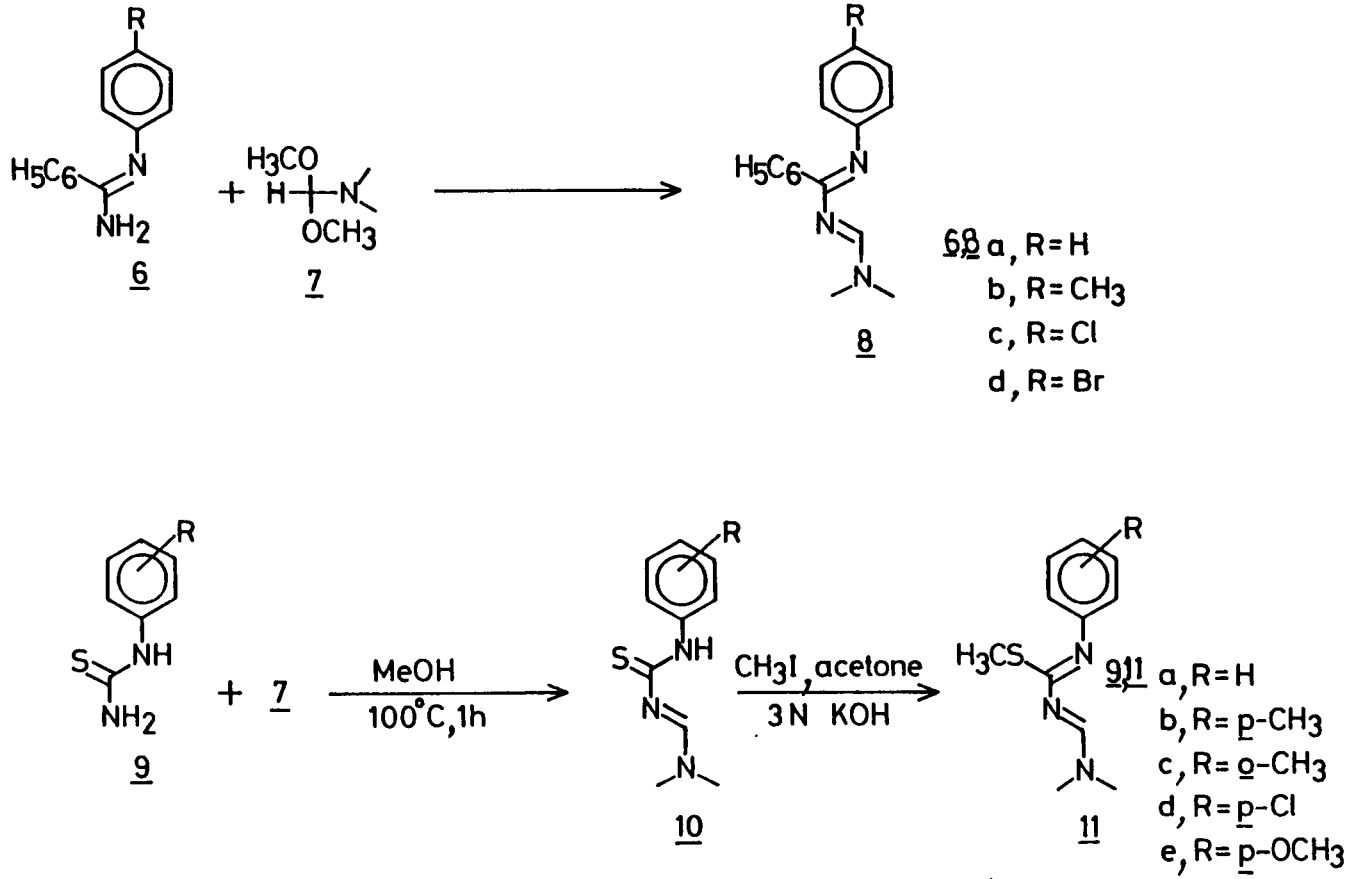
It was thought that 1,3-diaza-1,3-butadienes having electron donating functions at position(s)2- and/or 4- may prove to be more effective 4π component in Diels-Alder cycloaddition reactions. Thus, 1-aryl-4-dimethylamino-2-



Scheme 1

phenyl-1,3-diaza-1,3-butadienes (8), which were not used as 4 π component for any heterocyclic synthesis, and for which no spectral data were available, have been prepared by the reported method[8]. The diazabutadienes 8 have been characterised by analytical and spectral data. The diazabutadiene, 8b, for example was analysed for $C_{17}H_{19}N_3$ and its mass spectrum showed molecular ion peak at m/z 265. Its i.r. spectrum (KBr) showed a carbon-nitrogen double bond stretching at 1640 cm^{-1} and ^1H n.m.r. spectrum (CCl_4) exhibited sharp singlets at δ2.35(3H) and δ2.80(6H) due to p-methyl and $-N(CH_3)_2$ protons, respectively. The aromatic protons appeared as a multiplet at δ 7.16-7.56 and a singlet at δ7.90(1H) was assigned to the olefinic proton (Scheme 2).

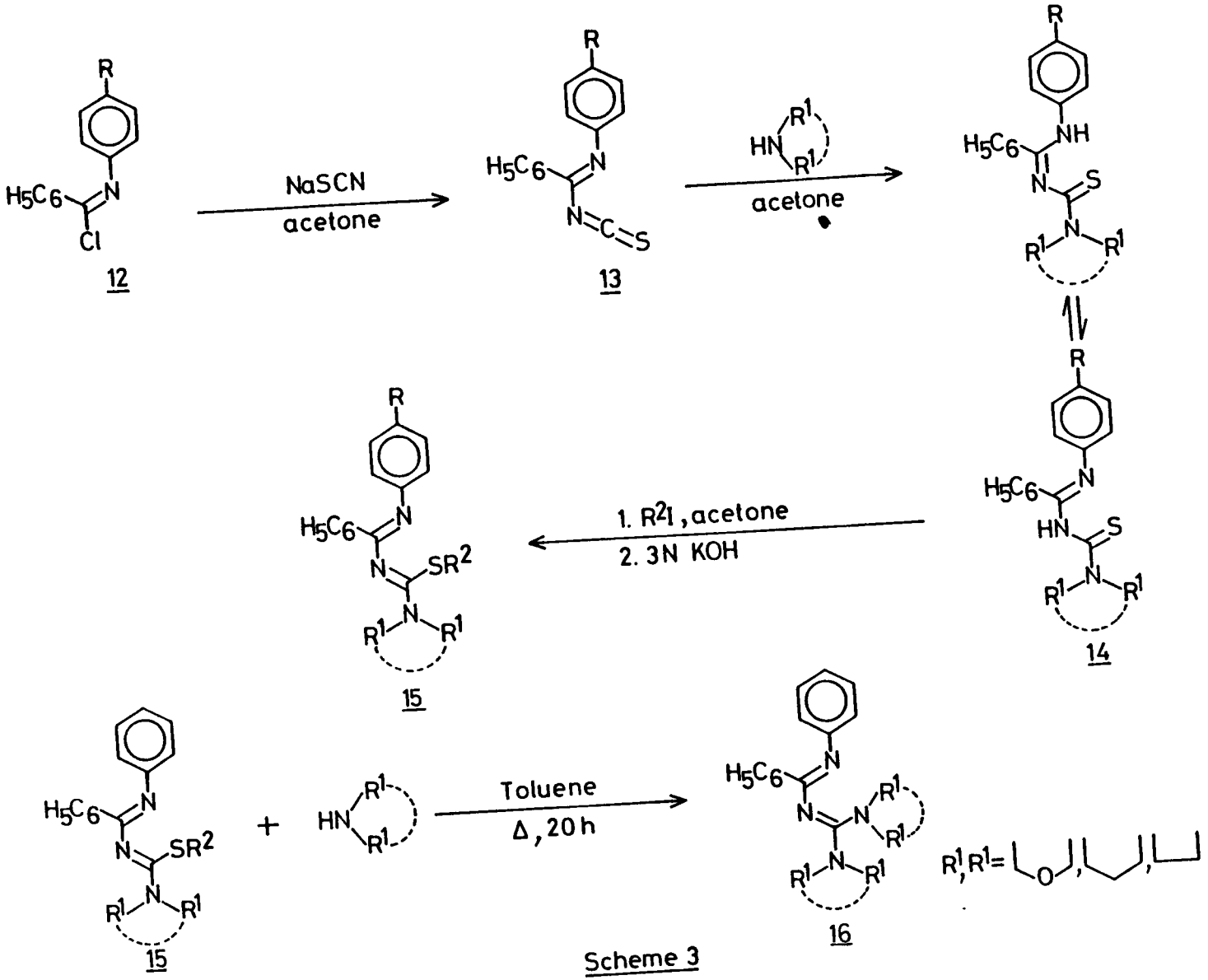
As the ease of cycloaddition reactions is dependent on the polarisability of the diene component, the introduction of another electron-donating group at position 2- of the 1,3-diaza-1,3-butadiene, is therefore expected to enhance such polarisability. This has been realised by the alkylation of N-arythiocarbamoyl formamidines (10), which could be obtained easily by refluxing N-aryl-thioureas (9) with dimethylformamidine dimethylacetal (7) in absolute methanol at 100°C. The alkylation of N-thiocarbamoyl formamidines (10) with methyl iodide in dry acetone resulted in the separation of corresponding hydroiodide salt, which on basification with 3N potassium


R
H5C6
N
NH2
6
H3CO
H
N
OCH3
7
8
6,8 a, R=H
b, R=CH3
c, R=Cl
d, R=Br
S
NH
9
MeOH
100°C,1h
10
CH3I, acetone
3N KOH
H3CS
9,11 a, R=H
b, R=p-CH3
c, R=o-CH3
d, R=p-Cl
e, R=p-OCH3
11

Scheme 2

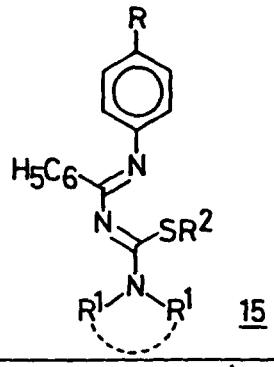
hydroxide solution afforded very good yields of previously unknown 1-aryl-4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadienes (11) (scheme2). Few of these 1,3-diazabutadienes (11) have been isolated as nice crystalline solids and other as viscous mass. All these 1,3-diazabutadienes have been found to be appreciably stable and pure enough to carry out further reactions. The identities of these have been established on the basis of analytical results and spectral evidences. Thus, the diazabutadienes, 11a (a pale viscous mass, 86% yield), for example, showed molecular ion peak at m/z 221 and its i.r. spectrum (nujol) exhibited carbon-nitrogen double bond stretching at 1640 cm^{-1}. Its ^{1}H n.m.r. spectrum (CCl_4) showed two singlets at δ2.30(3H) and δ 2.92(6H), and were assigned to $-SCH_3$ and $-N(CH_3)_2$ protons, respectively. The aromatic protons appeared as multiplet at δ 7.01-7.40(5H) while singlet at δ 8.08(1H) have been assigned to the olefinic proton. The chemical shift value for the olefinic proton (δ8.02) suggests probable cis-geometry for the 1,3-diaza-1,3-butadienes (11), as this compare very well with the literature value of δ8.30 for the olefinic proton in cis-geometry of related systems (cf trans δ_H : 7.10[10]). The yields of other members of 1,3- diaza-1,3-butadienes (11b-e) have been recorded in the range of 70-90% and were characterised by analytical and spectral data, and are listed in the experimental section.

In addition to such investigation we have also carried out the syntheses of 1,3-diaza-1,3-butadienes having two electron donating functions at 4-position. The alkylation of thioureas 14 with alkyl iodide and basification of hydroiodide salt so obtained, resulted in very good yields of hitherto unknown 1-aryl-2-phenyl-4-sec. amino (viz. dimethylamino/morpholino/piperidino/pyrrolidino)-4-thioalkyl (methyl/ethyl)-1,3-diaza-1,3-butadienes (15) (Table-I). The thioureas 14 are obtained by the reactions of secondary amines (dimethylamine, morpholine, piperidine, pyrrolidine) with N-aryliminoisothiocyanates (13), the latter being easily prepared by the reactions of sodium thiocyanate and N-arylbenzimidoylchloride (12) (Scheme-3). The 1,3-diaza-1,3-butadienes (15) (table-I) were characterised on the basis of analytical data and spectral evidences. The elemental analysis for 15a, for example, was in agreement with molecular formula $C_{19}H_{21}N_3O_S$ and its mass spectrum showed the molecular ion peak at m/z 339. A sharp band at 1600 cm^{-1} in its i.r. spctrum (KBr) was assigned to carbon-nitrogen double bond stretching frequency. Its ^1H n.m.r. spectrum (CCl_4) showed a singlet at δ2.10 (3H) due to $-SCH_3$ protons. The two triplets appeared at δ3.30-3.34 and δ 3.40-3.48 were assigned to the $-CH_2-N-CH_2-$ and $-CH_2-O-CH_2-$ of morpholine, respectively. The aromatic protons were observed as multiplets at δ 6.80-6.90 (2H,H_A), δ 6.94-7.26(6H,H_B) and δ 7.94-8.08 (2H,H_C). The appearance


R
H5C6
N
Cl
12
NaSCN
acetone
13
HN
R1
acetone
NH
S
14
1. R2I, acetone
2. 3N KOH
SR2
15
Toluene
Δ, 20h
16
R1,R1=
O

Scheme 3

TABLE I



15

15	R	R^1	R^1	R^2
a	H	$-(CH_2)_2-O-(CH_2)_2-$		CH_3
b	H	$-(CH_2)_2-CH_2-(CH_2)_2-$		CH_3
c	H	$-CH_2-(CH_2)_2-CH_2-$		CH_3
d	H	$-CH_3$	$-CH_3$	CH_3
e	H	$-(CH_2)_2-O-(CH_2)_2-$		C_2H_5
f	H	$-(CH_2)_2-CH_2-(CH_2)_2-$		C_2H_5
g	H	$-CH_2-(CH_2)_2-CH_2-$		C_2H_5
h	H	$-CH_3$	$-CH_3$	C_2H_5
i	CH_3	$-(CH_2)_2-O-(CH_2)_2-$		CH_3
j	CH_3	$-(CH_2)_2-CH_2-(CH_2)_2-$		CH_3
k	CH_3	$-CH_2-(CH_2)_2-CH_2-$		CH_3
l	CH_3	$-CH_3$	$-CH_3$	CH_3
m	Cl	$-(CH_2)_2-O-(CH_2)_2-$		CH_3
n	Cl	$-(CH_2)_2-CH_2-(CH_2)_2-$		CH_3
o	Cl	$-CH_2-(CH_2)_2-CH_2-$		CH_3
p	Cl	$-CH_3$	$-CH_3$	CH_3

of aromatic protons H_A (δ6.80-6.90) and H_C (δ7.94-8.08) lends credence to the higher polarisability of the new 1,3-diaza-1,3-butadines(15).

The treatment of 1,2-diphenyl-4-morpholino-4-thiomethyl-1,3-diaza-1,3-butadiene(15a) with morpholine, in refluxing toluene, resulted in heretofore unknown 4,4-bis(morpholino)-1,2-diphenyl-1,3-diaza-1,3-butadiene (16a). Under identical conditions 15b and 15c with on reaction with piperidine and pyrrolidine afforded 4,4-bis(piperidino)-1,2-diphenyl-1,3-diaza-1,3-butadiene (16b) and 4,4-bis(pyrrolidino)-1,2-diphenyl-1,3-diaza-1,3-butadiene (16c), respectively in good yields. The 1,3-diazabutadienes 16 were also characterised with the help of analytical results and spectral data. Thus, 16a, was analysed for $C_{22}H_{26}N_4O_2$ and its mass spectrum showed the molecular ion peak at m/z 378. The i.r. absorption band at 1630 cm^{-1} was assigned to carbon-nitrogen double bond stretching. Its ^1H n.m.r. ($CDCl_3$) showed two multiplets at δ2.84-3.02(8H) and δ3.43-3.60(8H) and were assigned to $-CH_2-N-CH_2-$ and $-CH_2-O-CH_2-$ protons of two morpholine units. The aromatic protons appeared as multiplets, at δ 6.91-7.05(2H,H_A), δ7.17-7.43(6H,H_B) and δ 7.87-8.02(2H,H_C) similar to the ones as observed in 15a. The microanalytical and spectral data for 16b and 16c are listed in the experimental section. To our knowledge this appears to be the first syste-

matic effort towards the synthesis of a large variety of 1,3-diaza-1,3-butadienes.

II.2.0 Cycloaddition Reactions of 1,3-Diaza-1,3-Butadienes with Ketenes.

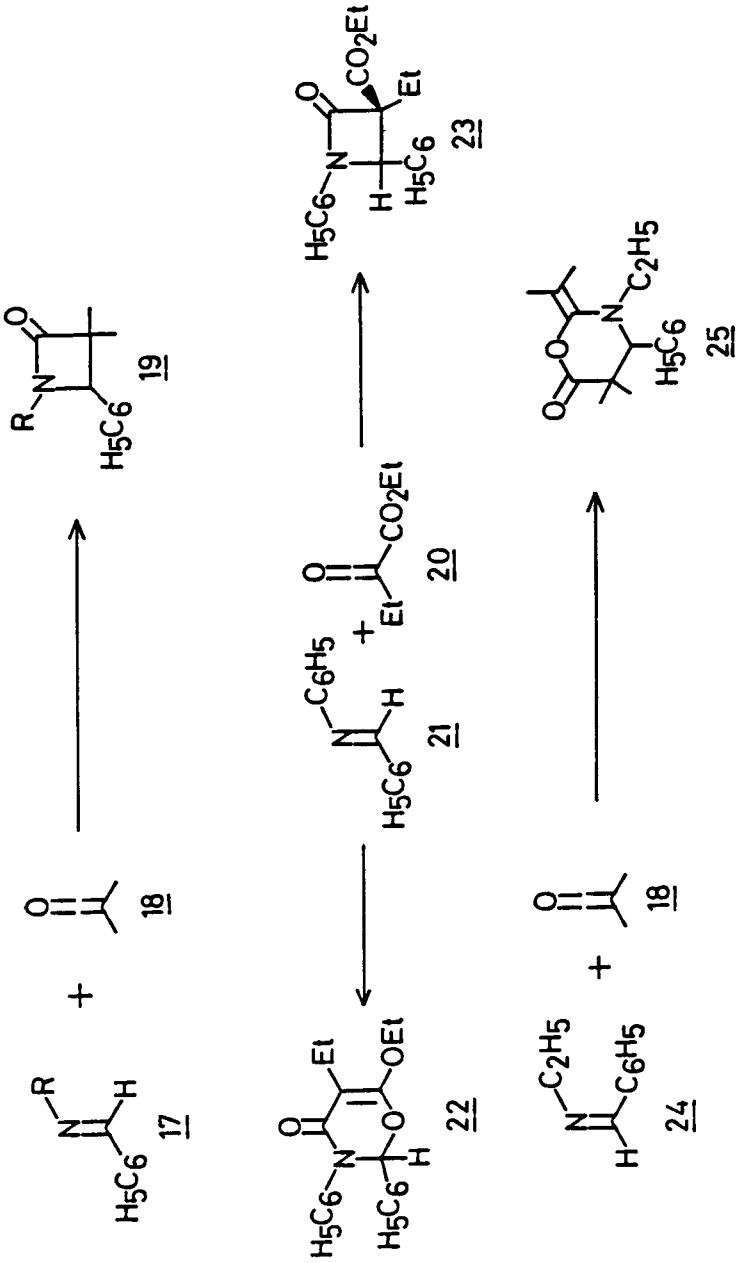
II.2.1 Introduction

The synthetic utility and interesting mechanistic features concerning the cycloaddition reactions of ketenes, have attracted a number of organic chemists who, over the years in last few decades had significantly contributed in this important area of organic chemistry. Staudinger synthesised a variety of substituted ketenes, and an attempt was made to correlate the general reaction pattern of them with other heterocumulenes[11]. Most of the reports deal with either unsubstituted or few relatively stable disubstituted ketenes; such as diphenylketene. The unstable monosubstituted ketene have received very little attention. Because of their instability, ketenes are often generated in situ from stable precursors in presence of suitable substrates. Base induced elimination of hydrogen chloride from an acid chloride, wolf rearrangement of an α-diazoketone, and zinc reduction of an α-chloroacid chloride are some of the more commonly used methods. Pyrolysis of esters[12], 1,5-sigmatropic rearrangement of conjugated dienals[13], ring opening of cyclobutanones[14], elimination from mixed anhydride[15], and a variety of pyrolytic fragmen-

tation processes[16] have been used with varying degrees of success. Ketenes readily dimerize, oligomerize and also react with nucleophiles. The success of inter- and intramolecular cycloaddition reactions of ketenes[17] is therefore critically dependent on the reactive rates of cycloaddition reactions.

The (2+2) cycloaddition reactions of ketenes constitute the single most important tool for the synthesis of four membered carbocylic and heterocyclic ring systems and examples involving -C≡C-, >C=C< , >C=N- , >C=S, -N=N-, -N=O, and P=N bonds were reported[11]. The participation of ketenes were not only limited to (2+2) cycloadditions but also several reaction were known where π bonds of ketene participate as dipolarophilic or dienophilic partners in 1,3-dipolar or (4+2) Diels-Alder cycloaddition reactions[11]. A brief account of cycloaddition reactions of ketenes across carbon-nitrogen double bond is presented here.

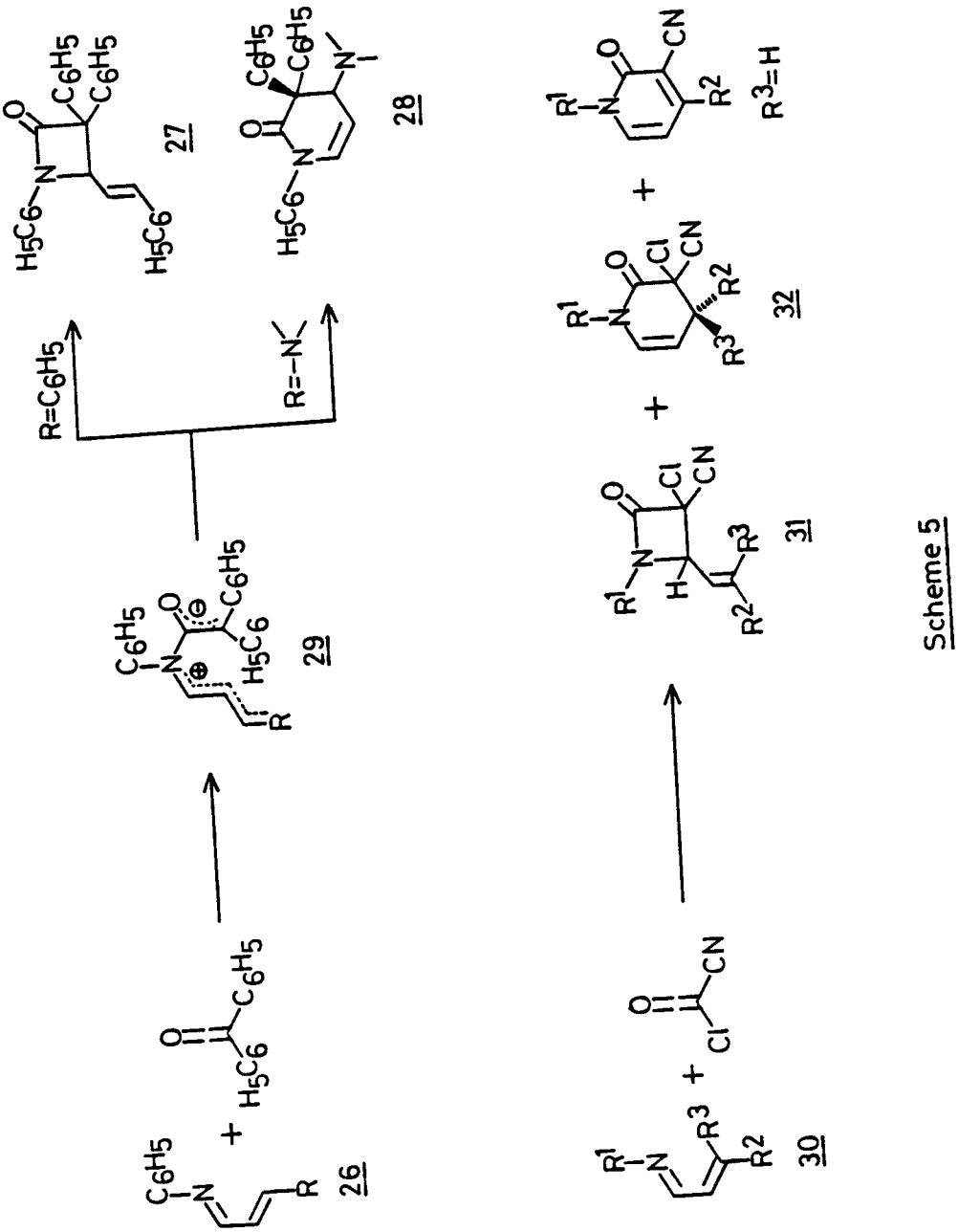
The addition of ketenes to isolated carbon-nitrogen double bond have been investigated by staundinger and co-workers, and depending upon the basicity (or perhaps better nucleophilicity) of nitrogen atom, 1:1 or 2:1 adducts were obtained. In most cases the less basic N-arylazomethines(17) afforded the 1,2-cycloadducts(19) with ketene (18)



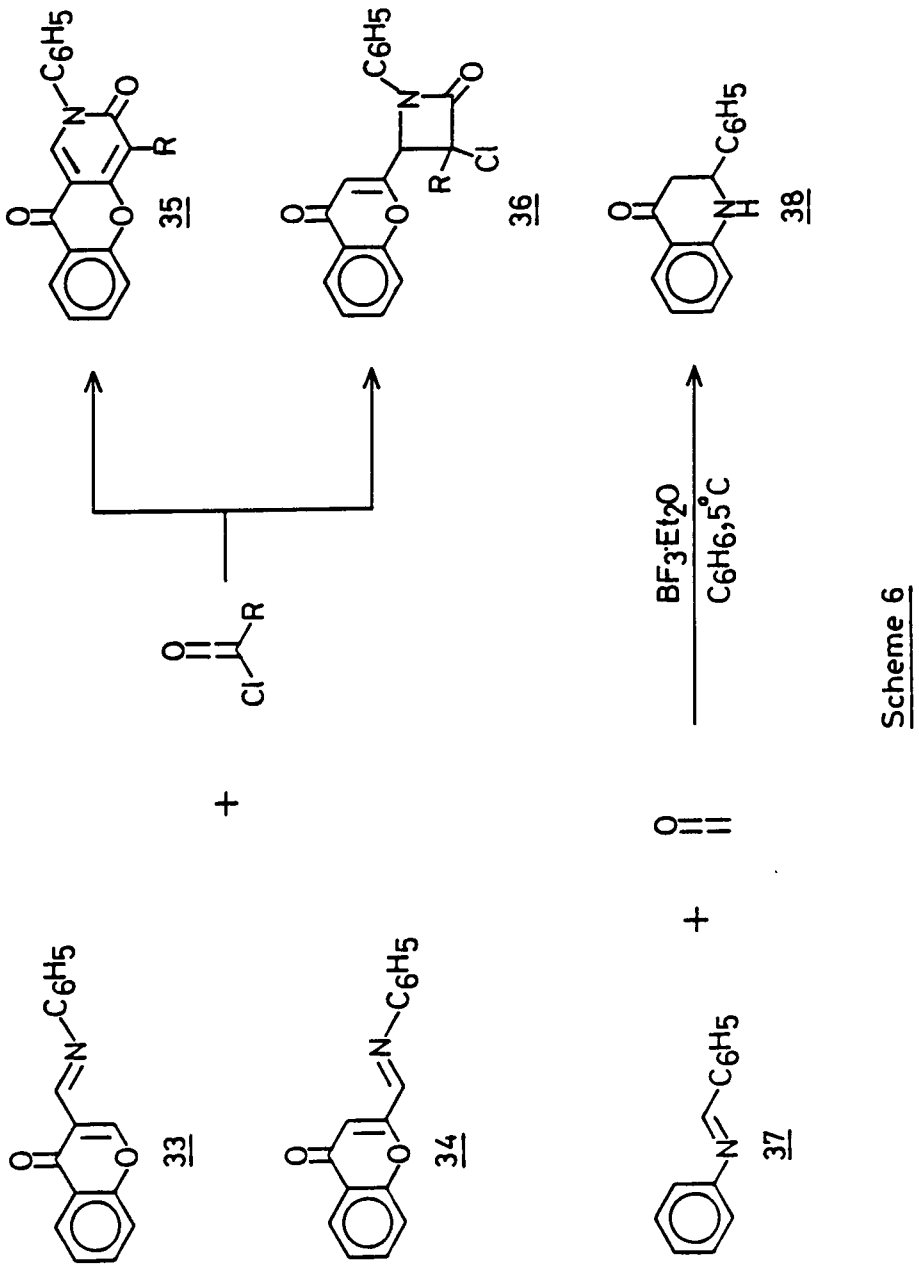
Scheme 4

forming β-lactams[18]. In the reaction of ethylcarbethoxy ketene (20) with benzlidenaniline (21), a labile 1:1 adduct (22) was formed at -10°C, which slowly decomposed to give starting materials at room temperature whereas, at elevated temperature 20 reacts with 21 to form the expected β-lactams(23)[18a]. In contrast to a aromatic azomethines, which react with ketenes to form β-lactam, aliphatic azomethine gives (2:1) adducts, most likely because of the higher basicity of the nitrogen atom[18-22]. Thus the reaction of C-phenyl-N-ethylazomethine (24) with dimethylketene gave a 2:1 adduct (25) (Scheme-4).

Azadienes have been reported[23] to undergo (2+2) and/or (4+2) cycloaddition with ketenes. Thus, 1-aza-1,3-butadiene (26) and diphenylketene, gave azetidinone(27) and dihydropyrimidone (28). The formation of 27 and 28 in these reactions has been explained through the intermediacy of a zwitterion (29). The reaction of chlorocyanoketene with similar 1-aza-1,3-butadiene (30), leading to (2+2) and (4+2) cycloadducts 31 and 32, reestablished the exisxtence of zwitterionic intermediate of type 29 (Scheme-5)[24]. Suschitzky et al[25] reported that the reactions of 3-(aryliminomethyl)chromones (33) and 2-(aryliminomethyl)chromones (34) with chloroketenes followed (4+2) and (2+2) cycloaddition pathway yielding pyridone 35 and β-lactam derivative 36, respectively (Scheme-6). A



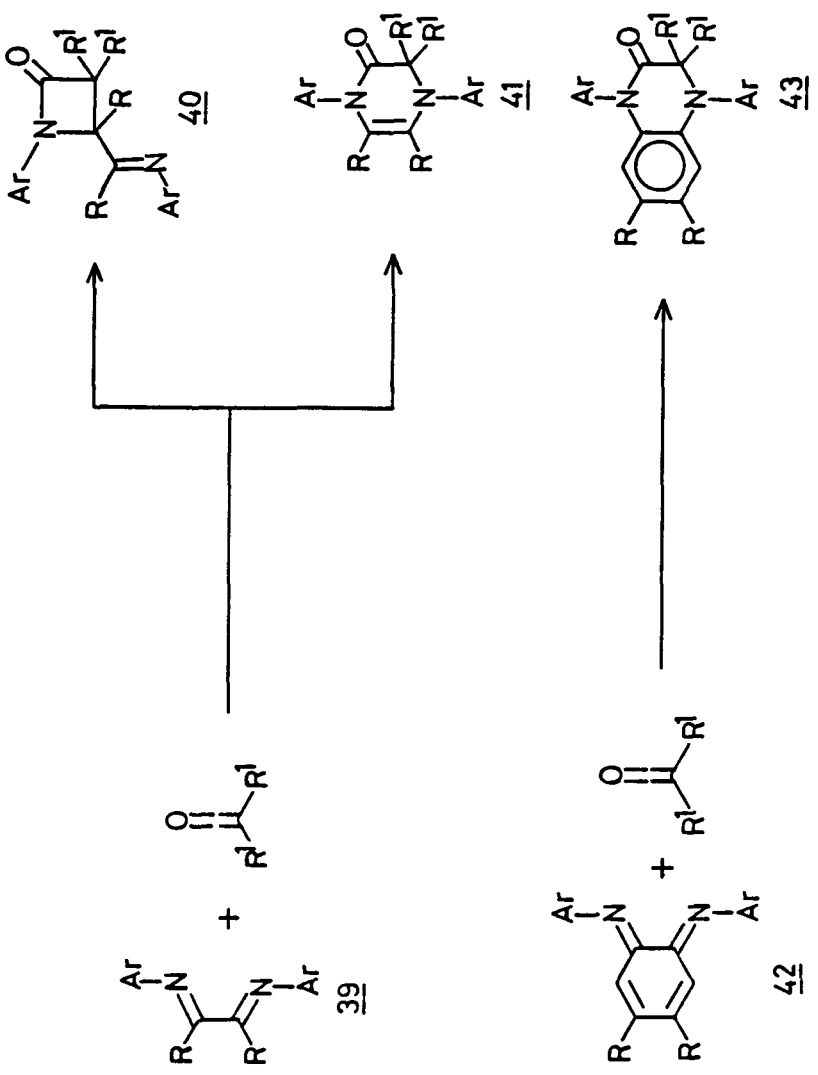
Scheme 5



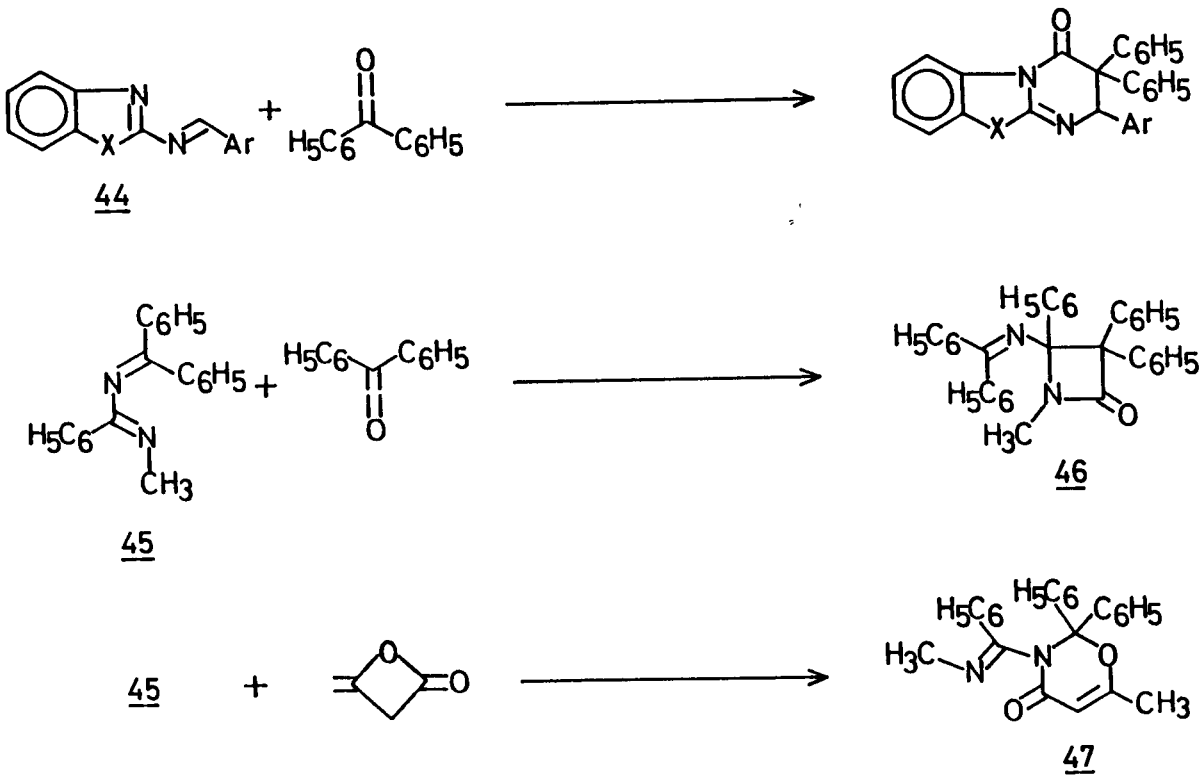
Scheme 6

few more similar reports[26-29] are also available in literature. The reports regarding the reactions of 2-aza-1,3-butadienes with ketenes are very rare[1,2]. For example, the lewis acid catalysed addition of anils (37) to ketene resulted in (4+2) cycloadduct (38)[30].

A few cycloaddition reactions of ketenes and 1,4-diaza-1,3-butadienes, have also been reported. For example, the reactions of diphenylketene or dimethylketene with α-diimines (39) yielded (2+2) cycloadduct (40), which were initially mistaken to be (4+2) cycloadducts 41[31-33]. However, substituted O-benzoquinonediimines (42) were shown to give (4+2) cycloadducts (43) with diphenylketene[34] (scheme-7). The heterocyclic 1,3-diaza-1,3-butadienes (44) is known to undergo facile (4+2) cycloaddition reactions with diketene and diphenylketene[4,35]. In contrast, the simple 1,3-diaza-1,3-butadiene (45) failed to give a formal cycloadduct with diketene, 46. Also, the reaction of 45 with diphenylketene did not give any (4+2) cycloadduct but underwent (2+2) cycloaddition leading to β-lactam 47[7] (scheme-8). It was thought that simple 1,3-diaza-1,3-butadienes having electron-donating functions at position 4- are perhaps best suited for (4+2) cycloaddition reactions with ketenes. In line with this, the investigations of reactions of simple acylic 1,3-diaza-1,3-butadienes (described in chapter II.1) with various ketenes were



Scheme 7



Scheme 8

considered to be of great interest.

II.2.2 Cycloaddition reactions with Monophenylketene.

The cycloaddition reactions of monophenylketene have not been much investigated and remained almost unexploited in organic synthesis. Monophenylketene, generation of which is simple and easy, could not evoke much interest among synthetic organic chemists possibly because of its instability[36]. In the present investigation we observed that cycloaddition could be realised by the slow generation of it in presence of reactive substrates. Thus, 1,3-diaza-1,3-butadienes (8, 11, 15 and 16) underwent (4+2) cycloaddition reactions with monophenylketene, which can be claimed to be the first known report of (4+2) cycloaddition of any ketene with acylic 1,3-diaza-1,3-butadienes. The result of the reactions of monophenylketene with 1,3-diaza-1,3-butadienes 8,11,15 and 16 are described as follows.

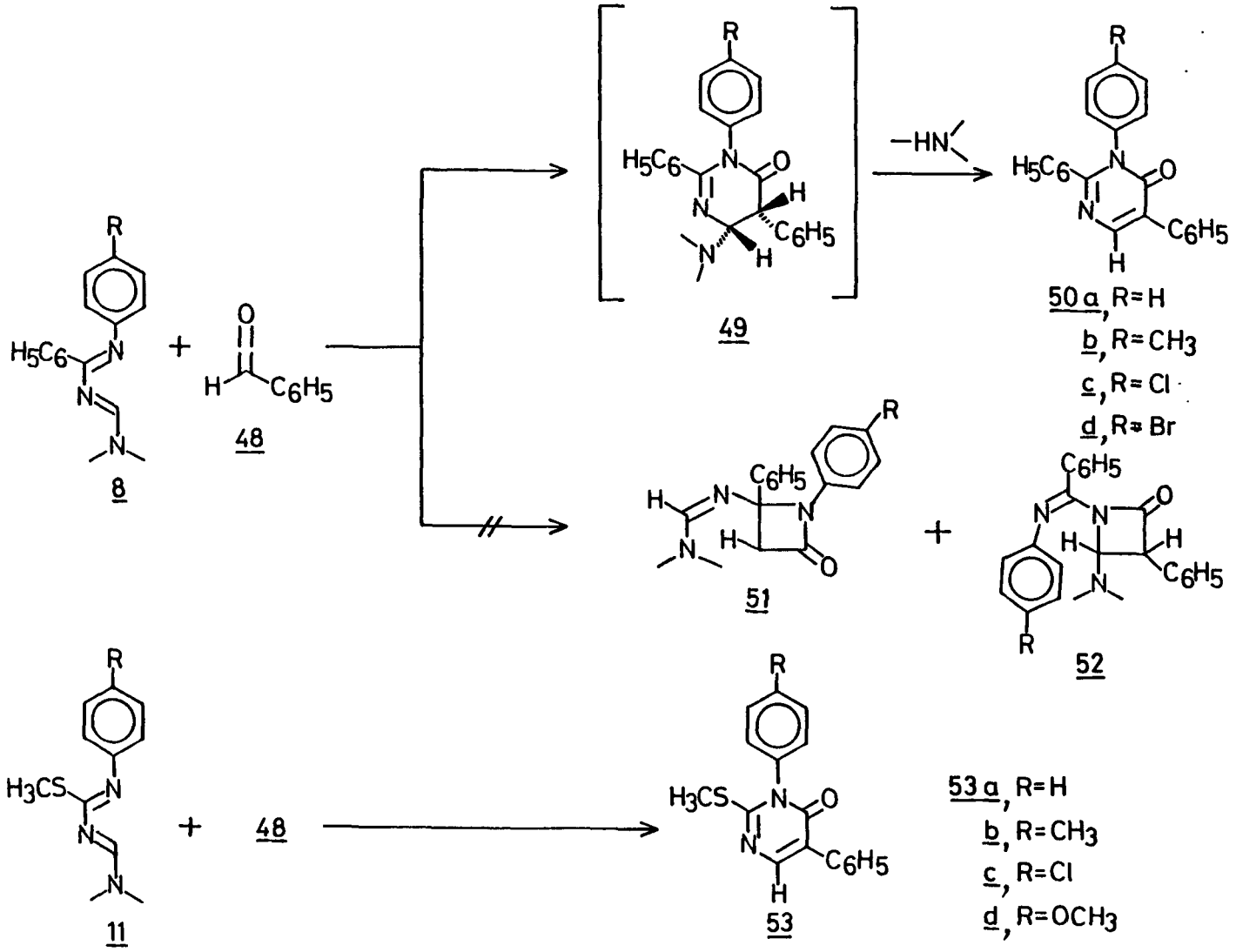
II.2.2a. Results and Discussions

The reactions of 1-aryl-4-dimethylamino-1,2-diphenyl-1,3-diaza-1,3-butadienes (8) with phenylacetylchloride, in benzene in presence of triethylamine, followed by careful workup of the reaction mixture resulted in very good yields of (4+2) cycloadducts (scheme-9). These cycloadducts have been characterised as 1-aryl-2,3-diphenyl-1,6-dihy-

dropyrimidin-6-ones(50) on the basis of analytical data and spectral evidences. The cycloadduct 50a, for example, was analysed for $C_{22}H_{16}N_2O$ and mass spectrum of it showed a molecular ion peak at m/z 324. Its i.r. spectrum (KBr) showed a strong absorption band at 1675cm^{-1}, characteristic of α,β-unsaturated carbonyl group. Further structural proof for 50a was obtained from its ^{1}H n.m.r. spectrum ($CDCl_3$), which showed a multiplet at δ 7.01-7.63(15H) for aromatic protons and a singlet at δ 8.10(1H) due to olefinic proton (-N=C-C).
|
H

The absence of any signal owing to dimethylamine protons ($-N(CH_3)_2$) in the ^{1}H n.m.r spectra of cycloadducts gave the first qualitative information regarding the formation of (4+2) cycloadducts. The formation of (2+2) cycloadduct 51 can thus be ruled out. Also the possibility of the formation of other (2+2) cycloadduct 52 was less likely because of the absence of dimethylamine group in the final product. This has been further substantiated with the help of i.r. data since the $\nu_{C=O}$ in case of 51 and 52 should have been around 1730cm^{-1}. The structures of 50b-d were evaluated similarly on the basis of their elemental and spectral data, which are given in the experimental section.

In order to investigate the effect of another


R
H5C6
N
O
H
C6H5
−HN
49
50 a, R=H
b, R=CH3
c, R=Cl
d, R=Br
8
48
51
52
H3CS
11
53
53 a, R=H
b, R=CH3
c, R=Cl
d, R=OCH3

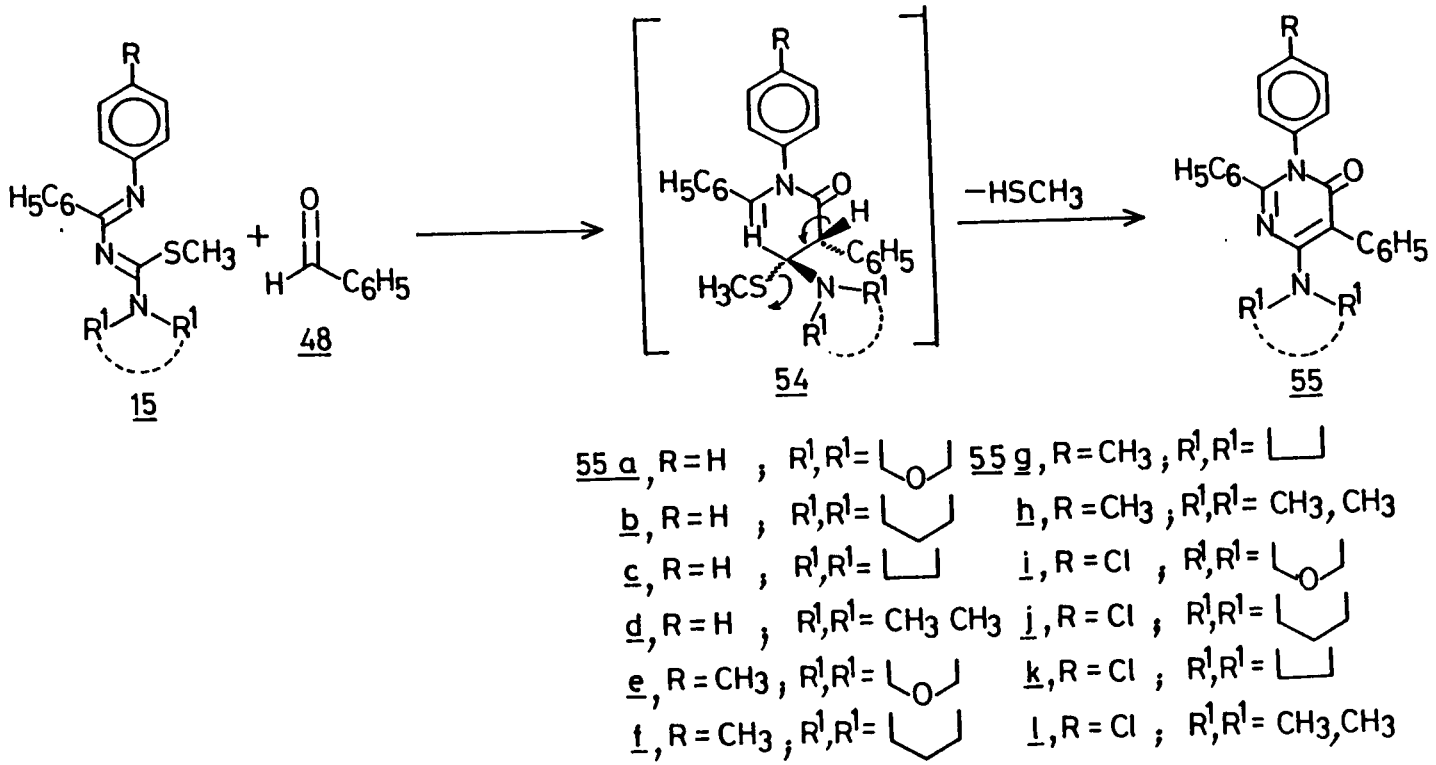
Scheme 9

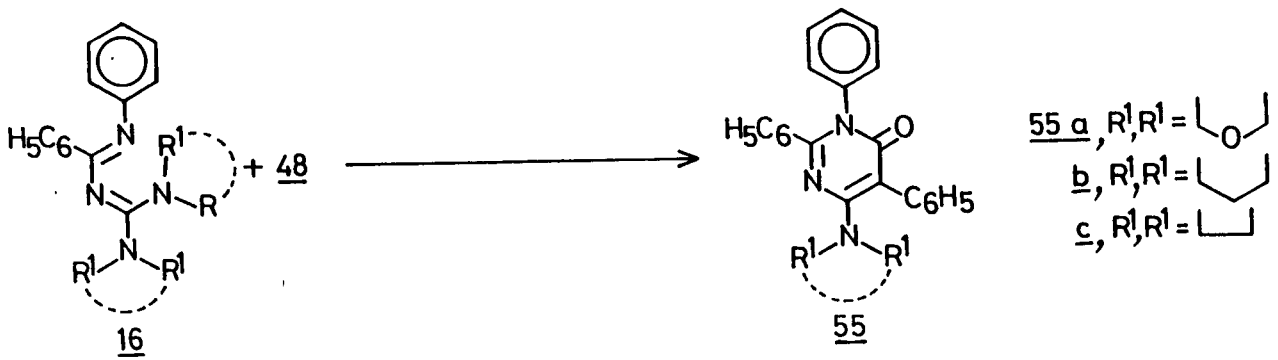
polarising function at position 2- of 1,3-diaza-1,3-butadiene on the reaction pathway, it was thought reasonable to examine the reactions of 1-aryl-4- dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadienes(11) with monophenylketene (48). Thus, the treatment of 48 with 11a resulted in very good yield of (4+2) cycloadduct, which was characterised as 1,5-diphenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one (53a) on the basis of analytical data and spectral evidences (Scheme-9). Its elemental analyses were in agreement with the molecular formula $C_{17}H_{14}N_2OS$ and molecular ion peak appeared at m/z 294 in its mass spectrum. The appearance of $\nu_{C=O}$ band at 1675cm^{-1} in i.r. spectrum (KBr) was also consistent with the presence of α,β-unsaturated carbonyl group in six-membered pyrimidine ring. The final structural proof was obtained from its ^{1}H n.m.r. spectrum ($CDCl_3$), which exhibited a singlet at δ2.40(3H), a multiplet δ7.20-7.70 (10H) and another singlet δ8.10(1H), assigned to $-SCH_3$ protons, aromatic protons, and olefinic proton, respectively. It may be mentioned here that the reactions of 1,3-diaza-1,3-butadienes (11) with monophenylketene are much more neat and yields of pyrimidones (53) were found to be much better compared to the reactions of 8 with 48.

In order to further generalise this reaction we have

examined the reactions of 1,3-diaza-1,3-butadienes (15) having two electron donating polarising functions at positions 4-, with monophenylketene (48). These reactions resulted in the formation of previously unknown 1-aryl-4-sec. amino-2.5-diphenyl-1,6-dihydropyrimidin-6-ones (55) via elimination of methylmercaptan from a initially formed cycloadduct (54) (Scheme-10).

The pyrimidin-6-ones (55) have been characterised on the basis of elemental and spectral data. The elemental analyses of 55a were in agreement with the molecular formula $C_{26}H_{23}N_3O_2$ and its mass spectrum showed the molecular ion peak at m/z 409. The i.r. spectrum (KBr) showed a band at 1660cm^{-1} due to α,β-unsaturated carbonyl group. Its ^{1}H n.m.r. spectrum ($CDCl_3$) exhibited two triplets at δ3.30-3.43(4H) and δ3.55-3.66 (4H), and were assigned to $-CH_2-N-CH_2-$ and $-CH_2-O-CH_2-$ of morpholine, respectively. The aromatic protons appeared as multiplet at δ 7.13-7.60 (15H). The elemental and spectral data for all other pyrimidin-6-ones prepared are listed in the experimental section. In continuation of our studies, we have carried out the reactions of 4,4-bis(sec. amino)-1,2-diphenyl-1,3-diaza-1,3-butadienes (16a-c) with monophenylketene, which also resulted in pyrimidin-6-ones (55a-c) by the elimination of one molecule of secondary amine from initially formed (4+2) cycloadducts as intermediate. The structure of pyri-

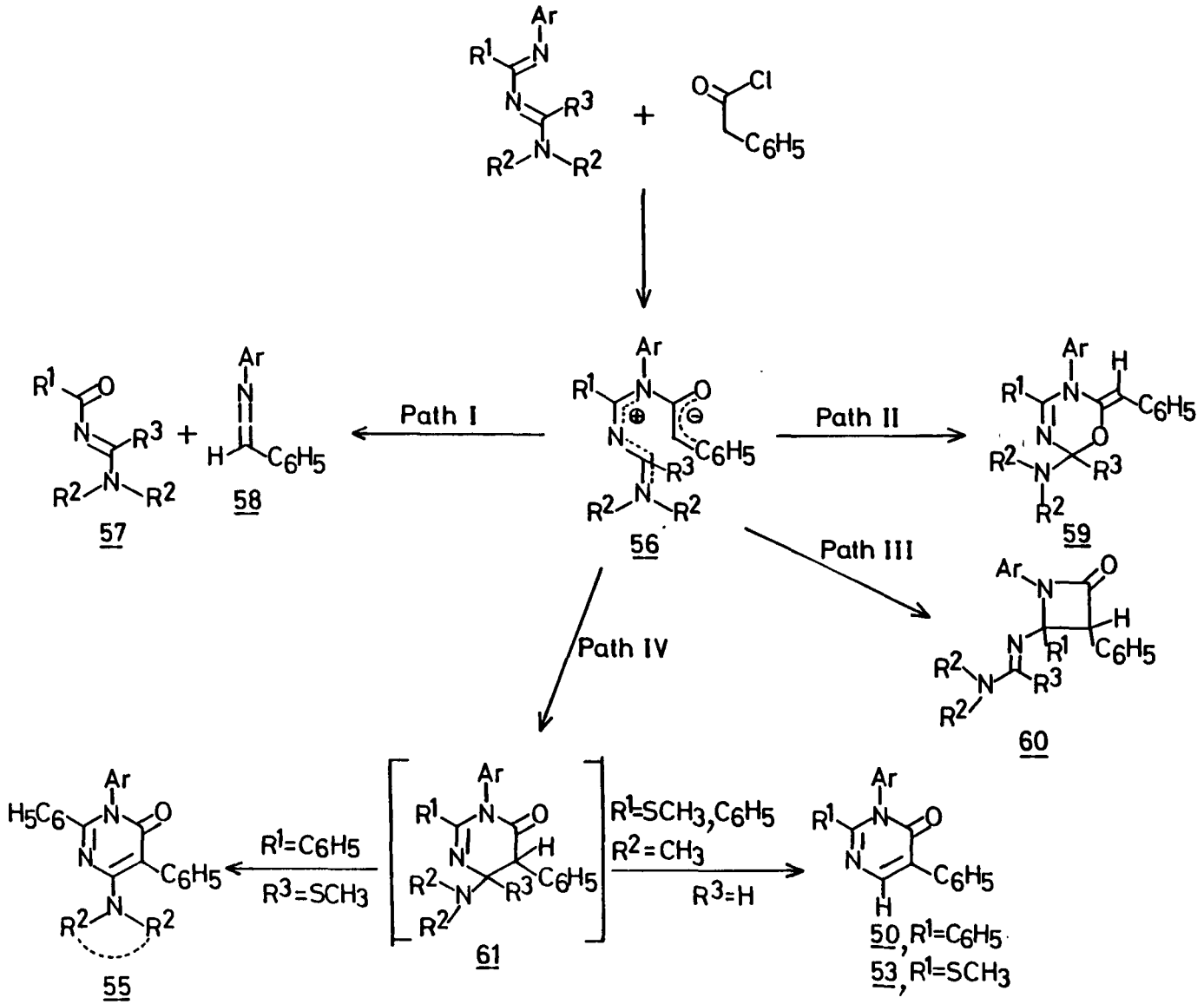

R
H5C6
N
SCH3
R1
R1
15
O
H
C6H5
48
54
−HSCH3
55
55 a, R=H ; R1,R1= O
b, R=H ; R1,R1=
c, R=H ; R1,R1=
d, R=H ; R1,R1= CH3 CH3
e, R=CH3 ; R1,R1= O
f, R=CH3 ; R1,R1=
55 g, R=CH3 ; R1,R1=
h, R=CH3 ; R1,R1= CH3, CH3
i, R=Cl ; R1,R1= O
j, R=Cl ; R1,R1=
k, R=Cl ; R1,R1=
l, R=Cl ; R1,R1= CH3,CH3


H5C6
N
R1
N
R
N
R1
R1
16
+ 48
55
55 a, R1,R1= O
b, R1,R1=
c, R1,R1=

Scheme 10

midin-6-ones formed in these cases were confirmed by their superimposable i.r., ^{1}H n.m.r. spectra and underpressed mixed melting point with 55a-c prepared by the reactions of 15a-c with 48.

The most probable mechanism for the formation of pyrimidin-6-ones 50, 53 and 55 is outlined in Scheme-11. In this mechanism, it is presumed that the initial nucleophilic attack takes place at position 1- of the 1,3-diaza-1, 3-butadiene, possibly because of greater stabilization of positive charge leading to zwitterionic intermediate 56, similar to the one proposed earlier[23]. This zwitterionic intermediate can undergo ring closure in a number of ways. The pathway I, which is less probable because of lower nucleophilicity of alkoxide anion would lead to products 57 and 58. Similarly, the pathway II, also involves attack by alkoxide anion, leading to the formation of oxazin derivatives 59 is less likely. The pathway III leads to β-lactam derivatives 60, a (2+2) cycloaddition product and pathway IV resulting in (4+2) cycloadduct, pyrimidin-6-ones (61). Of these, pathway IV is more likely since the resonance stabilized zwitterionic intermediate 56, would probably prefer formation of thermodynamically more stable six- membered pyrimidin-6-ones (61) since it does not involve serious hindrance to the approach of carbanion at position 4- of 1,3-diazabutadienes.


Path I
Path II
Path III
Path IV
R1=C6H5
R3=SCH3
R1=SCH3,C6H5
R2=CH3
R3=H
57
58
56
59
60
61
55
50, R1=C6H5
53, R1=SCH3

Scheme 11

The intermediate 61, could not be isolated and it undergoes (i) facile elimination of dimethylamine (in case of 8 and 11 leading to the formation of pyrimidin-6-ones 50 and 53, respectively), (ii) elimination of methyl mercaptan (in case of 15 leading to pyrimidin-6-ones 55), and (iii) elimination of secondary amines viz morpholine, piperidine and pyrrolidine (in case of 16 leading to 55).

A number of attemnpts, to isolate (2+2) cycloadducts i.e. β-lactam derivatives 60, which have possibly formed by quaternization of N-1 of 1,3-diaza-1,3-butadienes by phenylacetylchloride and subsequent basification with triethylamine, proved to be unsuccessful. Also, all attempts to isolate intermediate 61 failed and treatment of azadienes even with 1.1 equivalent of phenylacetylchloride and 1.1 equivalent of base resulted in the isolation of dihydropyrimidones. The monitoring of the reaction mixture (TLC) showed the spots of starting material and product. It is perhaps because of the slow formation of intermediate 61 and fast elimination of secondary amine or methyl mercaptan from this intermediate.

ii.2.3 Cycloaddition reactions with Monochloroketene

Earlier, in this chapter, it has been shown that monophenylketene (48), derived from phenylacetylchloride

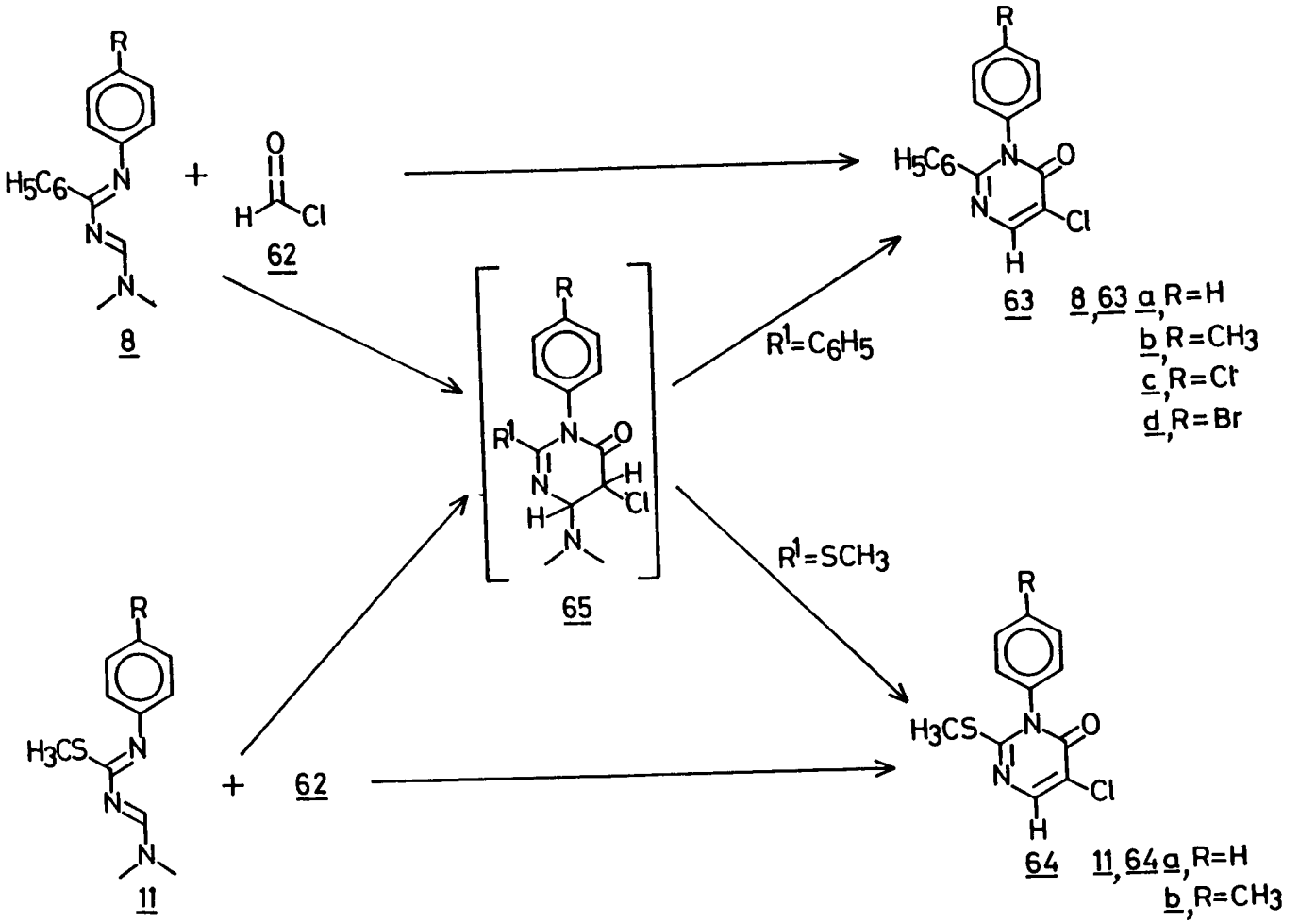
undergoes Diels-Alder cycloaddition reactions with 1,3-diaza-1,3-butadienes. In order to establish that 1,3-diaza-1,3-butadienes (8, 11, 15 and 16) participate as 4π components in cycloaddition reactions with a variety of ketenes, we have investigated reactions of 8, 11, 15 and 16 with monochloroketene. The use of monochloroketene in the cycloaddition reactions with heterodienes has been rare, possibly because of its fast polymerization. This in the present case was, however, overcome by slow addition of 2 equivalents of chloroacetylchloride to the dry methylene chloride solution of 1,3-diaza-1,3-butadienes in presence of triethylamine.

II.2.3a Results and Discussions

Thus, very slow addition of (ca 1 h) of methylene chloride solution of chloroacetylchloride (4 mmole) to the methylene chloride solution of 4-dimethylamino-1,2-diphenyl-1,3-diaza-1,3-butadiene(8a) (2 mmole) and triethylamine (6 mmole) followed by careful workup of the reaction mixture resulted in very good yield (97%) of a previously unknown crystalline product. It has been characterised as 5-chloro-1,2-diphenyl-1,6-dihydropyrimidin-6-one (63a) on the basis of analytical data and spectral evidences. Thus, it was analysed for $C_{16}H_{11}ClN_2O$ and mass spectrum of it showed the molecular ion peak at m/z 282. Its i.r. spectrum (KBr) exhibited a strong absorption band at 1670cm^{-1}

owing to α,β-unsaturated carbonyl group and was comparable to the carbonyl absorption of pyrimidin-6- ones 50 and 53. Its ^{1}H n.m.r. spectrum showed multiplets at δ7.23-7.60 (8H), δ7.83-7.93(2H) and a lone singlet at δ8.13(1H), while the multiplets were assigned to aromatic protons and the singlet was due to olefenic proton (-N=C-C), respectively. Similar reactions of 1,3-diaza-1,3-butadienes (8b-d) with monochloroketene (62) resulted in pyrimidin-6- ones (63b-d). The analytical and spectral data for 63b-d are incorporated in the experimental section (Scheme 12).

It has been observed that in case of reactions of 1,3-diaza-1,3-butadienes 11 with monochloroketene 62, the presence of another polarising function at position 2- of 11 did not effect the course of the reaction. Thus, the reactions of 1,3-diaza-1,3-butadienes (11) with monochloroketene (62) resulted in almost quantative yields of hitherto unknown 5-chloro-1-aryl-2-thiomethyl-1,6-dihydropyrimidin-6-ones (64). The structure of 64 have been elucidated on basis of elemental analysis and diagnostic spectroscopic features. Thus, 64a, for instance, was analysed for $C_{11}H_9ClN_2O_S$ and showed molecular ion peak at m/z 252. Its i.r. spectrum (KBr) showed a sharp absorption band at 1680cm^{-1}, which is characteristic for α,β-unsaturated carbonyl stretching frequency. Its final structural proof was obtained from its ^{1}H n.m.r. spectrum


R
H5C6
N
N
N
8
+
O
H
Cl
62
R
H5C6
N
N
O
Cl
H
63
8, 63 a, R=H
b, R=CH3
c, R=Cl
d, R=Br
R
R1
N
O
H
N
H
Cl
N
65
R1=C6H5
R1=SCH3
R
H3CS
N
N
N
11
+
62
R
H3CS
N
N
O
Cl
H
64
11, 64 a, R=H
b, R=CH3
c, R=Cl
d, R=OCH3

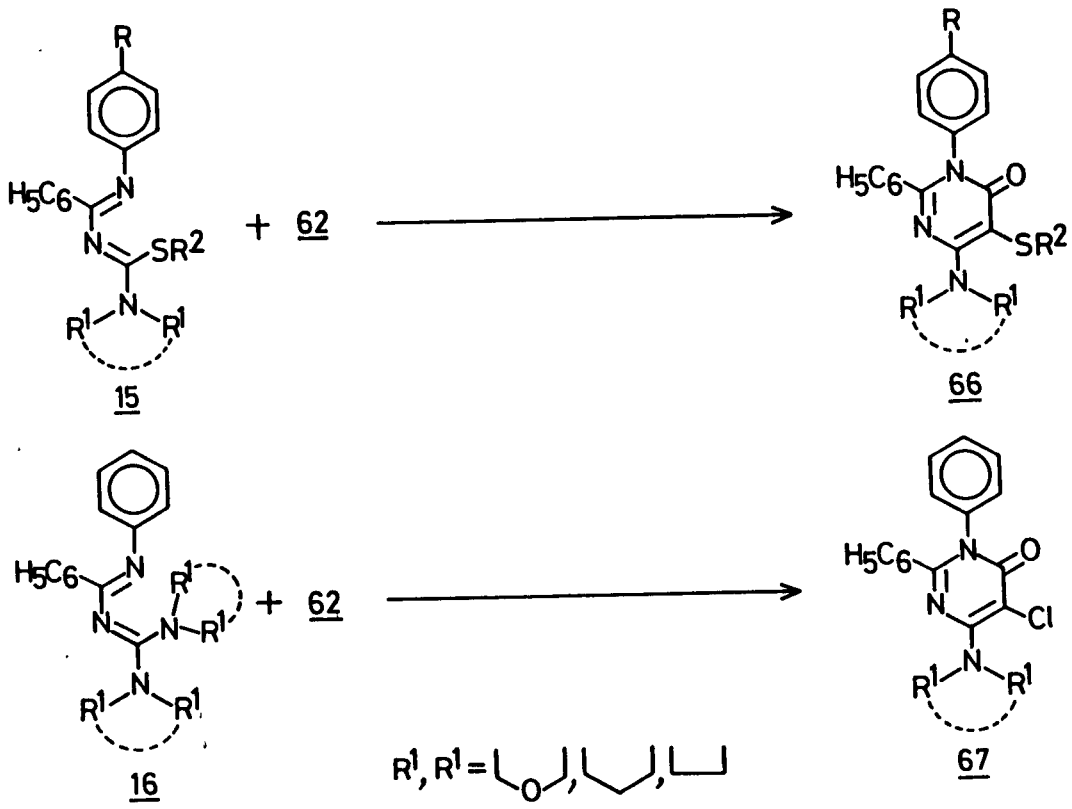
Scheme 12

($CDCl_3$), which showed two singlets at δ 2.40(3H) and δ8.10 (1H), and were assigned to $-SCH_3$ protons and olefinic proton (N=C(H)-C), respectively. The aromatic protons were observed as multiplets at δ 7.20-7.36(3H) and δ7.50-7.60(2H). The elemental and spectral data for other pyrimidin-6-ones (64b-d) are given in the experimental section. The mechanism for the formation of products 63 and 64 is seemed to be similar to the one described for the reactions of 1,3-diaza-1,3- butadienes(8) and monophenylketene(48) (Scheme-11) and probably involves in the formation of (4+2) cycloadducts 65 as intermediate (Scheme-12).

The intermediate 65, which may undergo either elimination of one molecule of dimethylamine or hydrogen chloride, but preferential elimination of dimethylamine molecule was observed leading to the formation of 63 and 64. It is difficult to discuss about the precise stereochemistry at position 4- and 5- of the intermediate 65, but orientation of dimethylamine and chlorine may probably be trans to avoid the steric interaction and this may be assisted by the delocalised enolate anion which can be formed in presence of excess triethylamine as base.

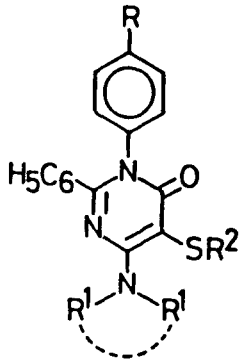
Interestingly the reactions of 1,3-diaza-1,3-butadienes (15) with monochloroketene (62) under similar reac-

tion conditions resulted in the products which indicated the loss of hydrogen chloride from the same carbon atom (C-5) and transposition of $-SCH_3$ from position 4- to position 5- of initially formed (4+2) cycloadducts (Scheme-13). The structure of 66 has been assigned on the basis of analytical and spectral results. The elemental analysis of the product, for example, was consistent with its molecular formula, $C_{21}H_{21}N_3O_2S$ and mass spectrum of it showed its molecular ion peak at m/z 379. Its i.r. spectrum showed a strong absorption band at $1670cm^{-1}$ assignable to α,β-unsaturated carbonyl group. The ^1H n.m.r. spectrum ($CDCl_3$) of it showed a singlet at δ2.36(3H) due to $-SCH_3$. The two multiplets appeared at δ2.86-2.93(8H) and δ7.10-7.33 (10H) were assigned to morpholine and aromatic protons. This reaction has been extended to the syntheses of various 1-aryl-4-sec. amino-5-thioalkyl-1,6-dihydropyrimidin-6-one derivatives. (66a-p) (Table-II). The elemental and spectral data of these are given in the experimental section. It is further interesting to observe that the reactions of 4,4-bis(sec. amino)-1,2-diphenyl-1,3-diaza-1,3-butadienes (16) with monochloroketene (62) under similar reaction conditions resulted in products (67), which did not show loss of hydrogen chloride and instead showed the loss of secondary amine (Scheme-13). Further, the products did not exhibit any rearrangement or migration of sec.



Scheme 13

TABLE-II

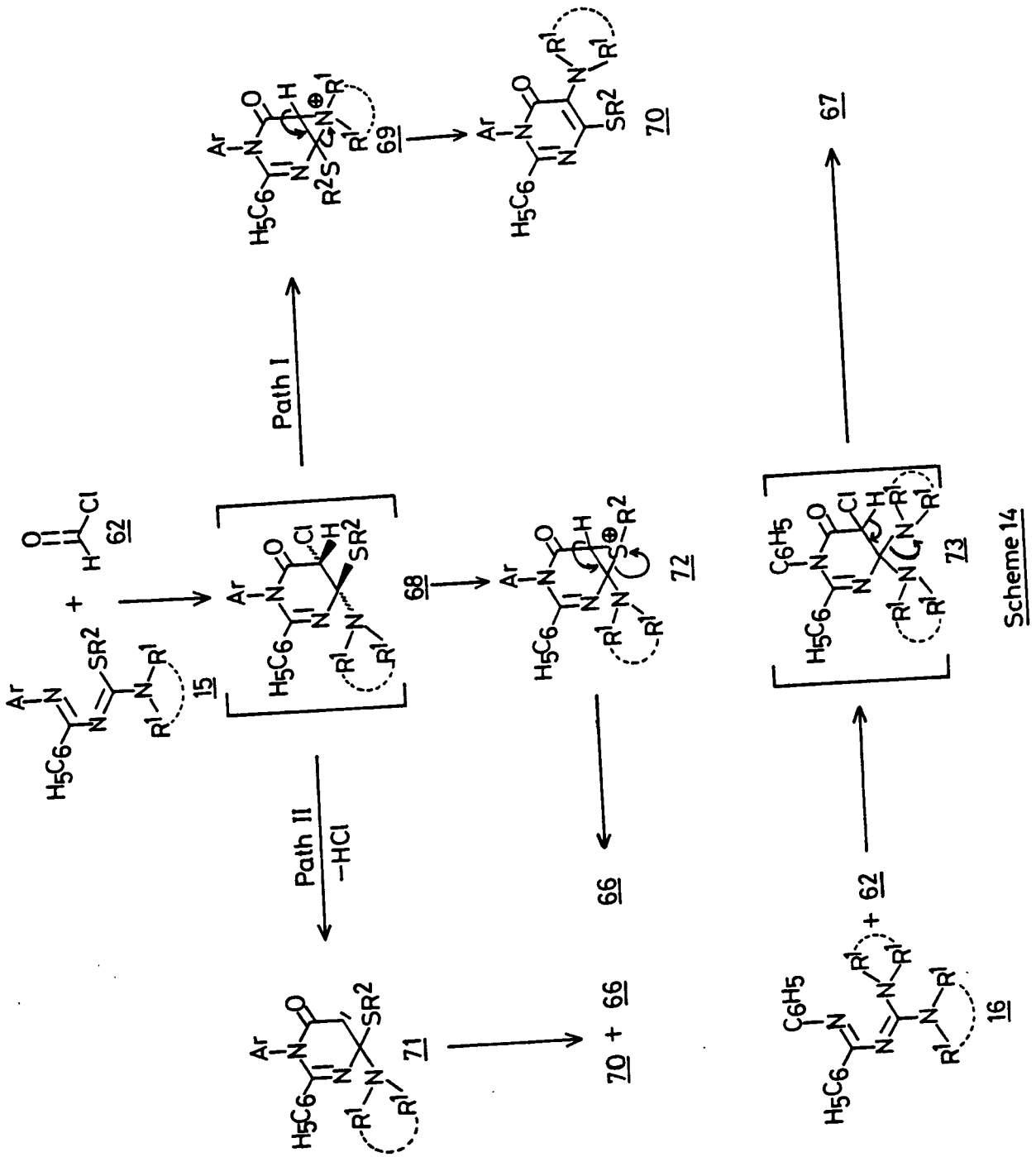


66

66	R	R^1 R^1	R^2
a	H	$-(CH_2)_2-O-(CH_2)_2-$	CH_3
b	H	$-(CH_2)_2-CH_2-(CH_2)_2-$	CH_3
c	H	$-CH_2-(CH_2)_2-CH_2-$	CH_3
d	H	$-CH_3$ $-CH_3$	CH_3
e	H	$-(CH_2)_2-O-(CH_2)_2-$	C_2H_5
f	H	$-(CH_2)_2-CH_2-(CH_2)_2-$	C_2H_5
g	H	$-CH_2-(CH_2)_2-CH_2-$	C_2H_5
h	H	$-CH_3$ $-CH_3$	C_2H_5
i	CH_3	$-(CH_2)_2-O-(CH_2)_2-$	CH_3
j	CH_3	$-(CH_2)_2-CH_2-(CH_2)_2$	CH_3
k	CH_3	$-CH_2-(CH_2)-CH_2-$	CH_3
l	CH_3	$-CH_3$ $-CH_3$	CH_3
m	Cl	$-(CH_2)_2-O-(CH_2)_2-$	CH_3
n	Cl	$-(CH_2)_2-CH_2-(CH_2)_2-$	CH_3
o	Cl	$-CH_2-(CH_2)_2-CH_2-$	CH_3
p	Cl	$-CH_3$ $-CH_3$	CH_3

amino functions. Thus 67a, for example, was analysed for $C_{20}H_{18}ClN_3O_2$ and its mass spectrum showed the molecular ion peak at m/z 367. Its i.r. (KBr) showed the characteristic peak for α,β-unsaturated carbonyl group at 1680cm^{-1}. The ^{1}H n.m.r. showed two multiplets at δ3.66-3.94(8H) and δ7.15-7.50 (10H), assignable to morpholine and aromatic protons, respectively. The analytical and spectral data 67b and 67c are described in the experimental section.

The mechanistic pathways leading to the formation of rearranged pyrimidin-6-ones (66), are outlined in scheme-14. The 1,3-diaza-1,3-butadienes (15) undergoes (4+2) cycloaddition with monochloroketene (62). formed an intermediate (68) (cf. scheme-11). This intermediate can follow three different reaction pathways. The pathway I, involves an attack by a secondary amino nitrogen attached to 4-position of intermediate 69 at neighbouring carbon (C-5) bearing a leaving group viz. chlorine, leads to aziridinium ion intermediate, 69. This intermediate 69 may lose a proton accompanied by migration of secondary amine to C-5 forming 1-aryl-2-phenyl-5-sec. amino-4-thioalkyl-1,6-dihydropyrimidin-6-ones (70). The pyrimidin-6-one (70) is isomeric with pyrimidin-6-ones (66) and only on the basis of elemental analyses, i.r., ^{1}H n.m.r. and mass spectra it is difficult to distinguish between 66 and 70. The formation of 70 was found to be less likely and may be



Scheme 14

ruled out on the basis of following arguments; (i)the intermediate 68, should preferentially lead to intermediate 72 rather than 68, because of higher nucleophilicity of sulphur, (ii) the reactions of 1,3-diaza-1,3-butadienes 16 and 62, which presumably proceed through intermediate 73, exclusively lead to the formation of 67, possibly via elimination of secondary amines from 73 and in fact no product arising from the migration of secondary amine function was isolated. Tne pathway II assumes that intermediate 68, in presence of excess triethylamine as base, may lead to a carbene intermediate 71. But here again, the formation of such an intermediate may be ruled out since (i) this intermediate should result in a mixture consisting of 66 as major and 70 as minor products and (ii) if carbene is formed in these reactions then the rearranged products should also be observed in cases of the reactions of 8 with 62, 11 with 62, and 16 with 62. The reaction pathway III, which is most likely where the intermediate 68 is transformed into an episulphonium intermediate 72 by the nucleophilic attack of sulphur at C-5 bearing chlorine as leaving group. The intermediate 72, then rearranges by the loss of a proton accompanied by the migration of S-alkyl, to product 66. This lead us to conclude that the chlorine at position 5- of 68 is possibly trans to bulkier S-alkyl function at position 4- of 68. It is noteworthy to mention in this context, such rearrangement involving episulphonium ion

intermediate has earlier being reported[37], where a cyclic carbocation has been involved.

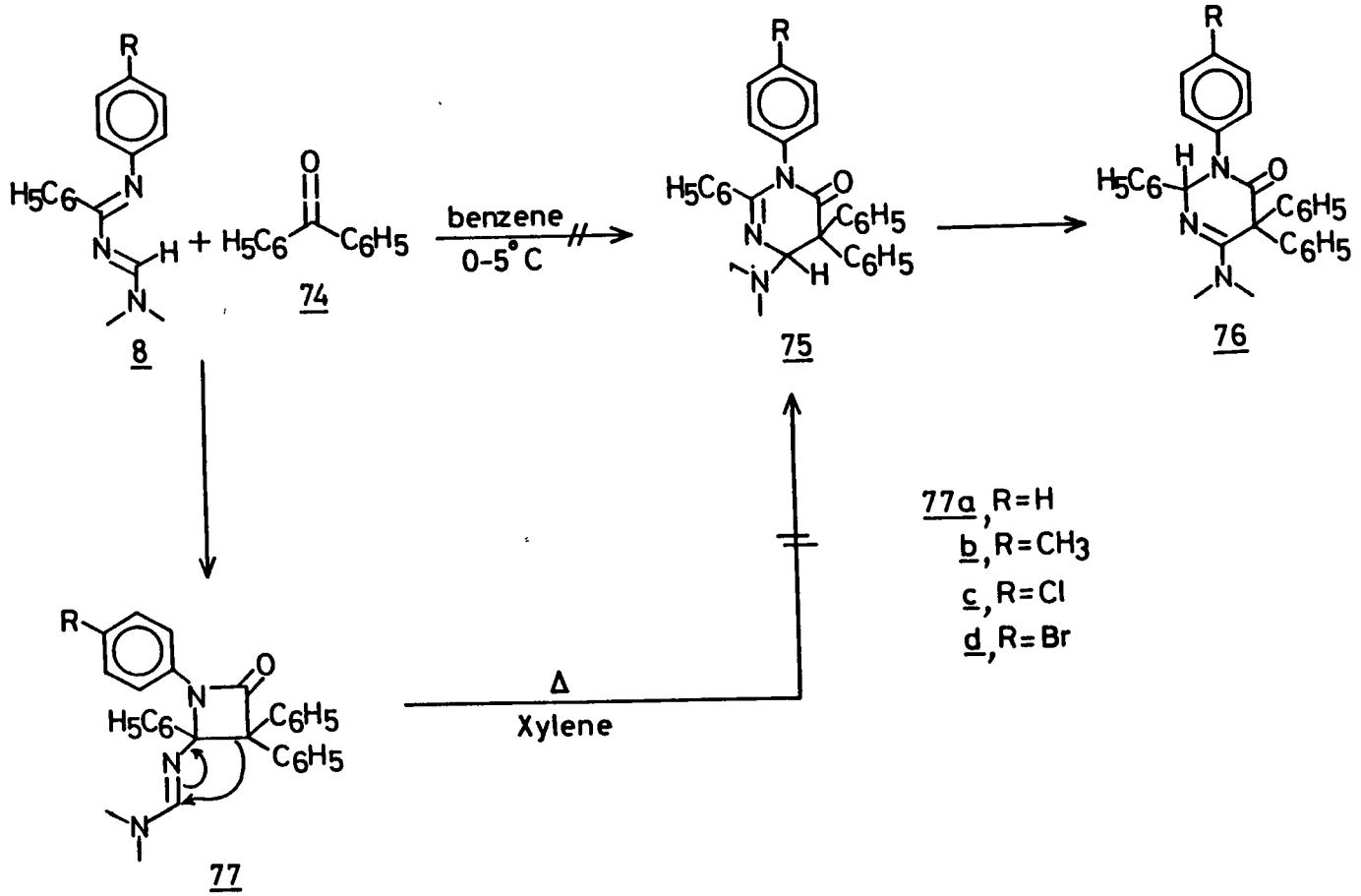
II.2.4 Cycloaddition Reactions with Diphenylketene

Diphenylketene, in contrast to other ketenes, is exclusively used as an effective 2π component in (2+2) and (4+2) cycloaddition reactions. This may probably be due to easier synthetic accessibility, isolation in free monomeric state and higher stability as compared to other ketenes. Diphenylketene has also been shown[2] to participate as 2 π component in hetero Diels-Alder cycloaddition reactions with most mono- and diazabutadienes. The 1,3-diaza-1,3-butadienes, as substructure of heterocyclic system have been reported[31-34] to yield (4+2) cycloadducts with diphenylketene, whereas, the simple 1,3-diaza-1,3-butadienes gave (2+2) cycloadduct with diphenylketene[7]. Earlier, in section II.2.1 and II.2.2 of this chapter it has been shown that simple 1,3-diaza-1,3-butadienes (8, 11, 15 and 16) undergo successful Diels-Alder cycloaddition reactions with monophenylketene(48) and monochloroketene (62) resulting in very good yields of previously unknown pyrimidin-6-one derivates. In continuation of our investigation on the reactions of 1,3-diaza-1,3-butadienes with ketenes, we considered it worthwhile to investigate the reactions of these 1,3-diaza-1,3-butadienes with diphenylketene, especially

with a view to understand the steric effect of two phenyl groups in diphenylketene, on the course of reaction. The results concerning these investigations are discussed below.

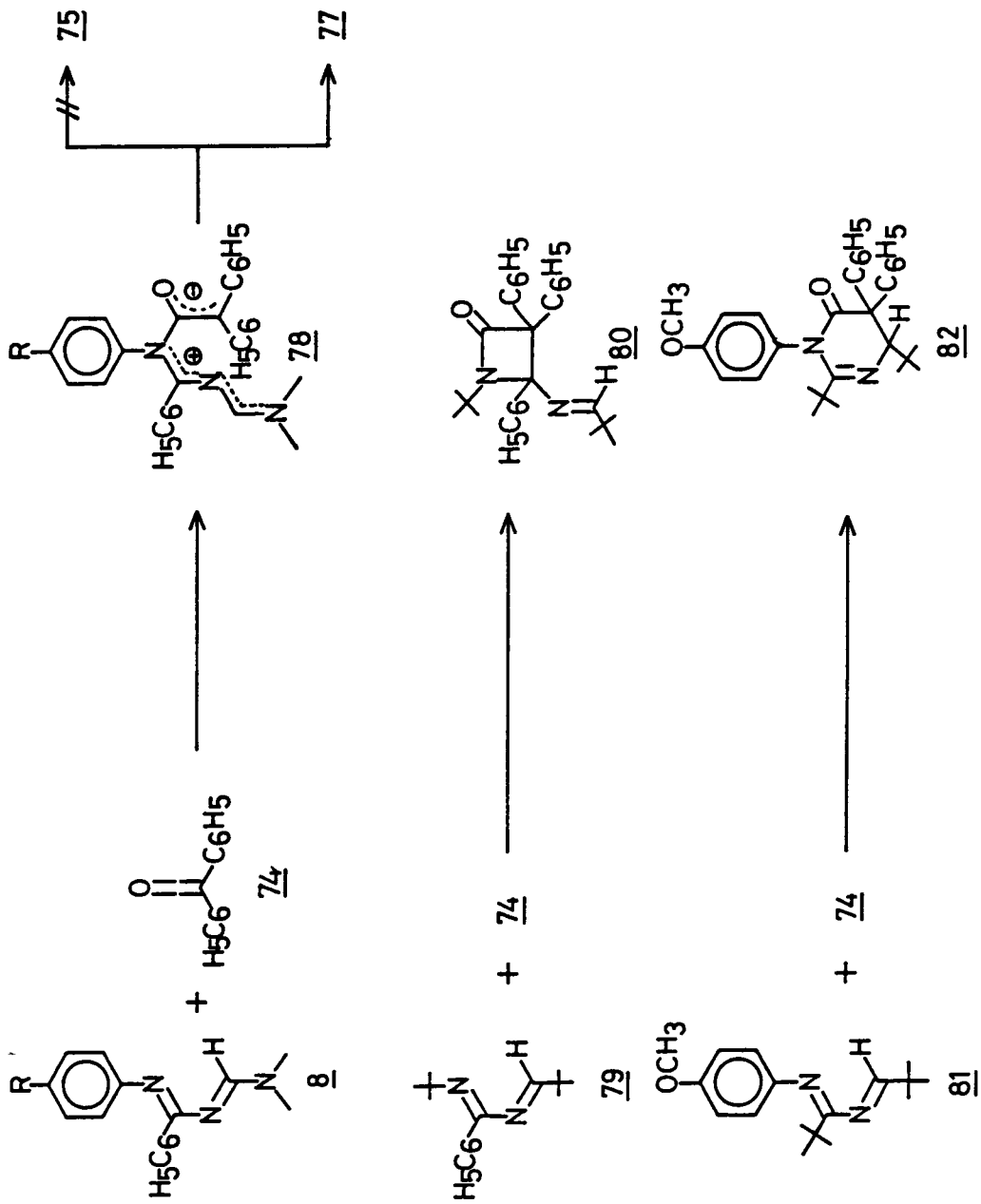
II.2.4a RESULTS AND DISCUSSIONS

The treatment of 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes(8) with diphenylketene (74), generated from diphenylacetylchloride and triethylamine in situ, in well cooled dry benzene followed by careful work up of the reaction mixture, gave white crystalline compounds in very good yields. The products, which were initially thought to be 1-aryl-4-dimethylamino-2,5,5-triphenyl-1,2,5,6-tetrahydropyrimidin-6-ones(76), arising via isomerisation of (4+2) cycloadducts (75) (Scheme-15)[38], have finally been characterised as 1-aryl-4(N,N-dimethylformamidino)-3,3,4- triphenylazetidin-2-ones (77)[39] on the basis of analytical data and spectral evidences. Thus, compound 77a, for example, was analysed for $C_{23}H_{27}N_3O$ and its mass spectrum showed molecular ion peak at m/z 445. Its i.r. spectrum (KBr) showed carbonyl absorption at 1730cm^{-1}. The ^{1}H n.m.r. spectrum ($CDCl_3$) of it showed a singlet at δ 2.70(6H) due to $-N(CH_3)_2$ protons and a multiplet at δ7.16-7.54(20H) due to aromatic protons of four phenyl groups. The singlet at δ6.83 was initially assigned to the methine proton of 76[38] formed by the isomerisation of methine proton from position 4- of 75 to position 2- of 76, was later on correctly


R
H5C6
N
H
N
8
+ H5C6
O
C6H5
74
benzene
0-5° C
75
C6H5
C6H5
76
77
Δ
Xylene
77a, R=H
b, R=CH3
c, R=Cl
d, R=Br

Scheme 15

assigned to the olefinic proton of 77. The β-lactam structure was further supported by ^{13}C n.m.r. spectrum[39], which showed imino carbon as doublet at δ152.2. The singlets at δ79.6, δ86.0 and δ168.00 were assigned to C-3, C-4 and carbonyl carbon, respectively. Clearly the formation of (2+2) cycloadduct 77 in which three phenyl groups are vicinal is preferred to (4+2) cycloadduct 75/76 where two phenyl groups are vicinal to dimethylamino function. The most probable mechanism leading to the formation of β-lactam derivatives 77 in these reactions, is outlined in Scheme-16. As, in case of monophenylketene and monochloroketene, it is assumed that the reaction of 1,3-diaza-1,3-butadienes (8) with diphenylketene (74) leads initially to a zwitterionic intermediate 78. This intermediate prefers formation of β-lactam derivative 77 and the probable reason for this could be higher steric hindrance to the approach of two phenyl groups to the dimethylamino function (leading to 75/76) as compared to the approach of two phenyl group to C-2 (leading to 77). Luthardt and Wurthwein[39] extended the steric arguments to the formation of 80 in case of reaction of 1,3-diaza-1,3-butadienes (79) with diphenylketene (74) and formation of 82 in case of reaction of 1,3-diaza-1,3-butadiene 81 with 74. On the basis of their theoretical calculations, it is found that; (i) the best conformer for 1,3-diaza-1,3-butadienes is S-trans form, (ii) the barriers for the rotation around the carbon-nitro-



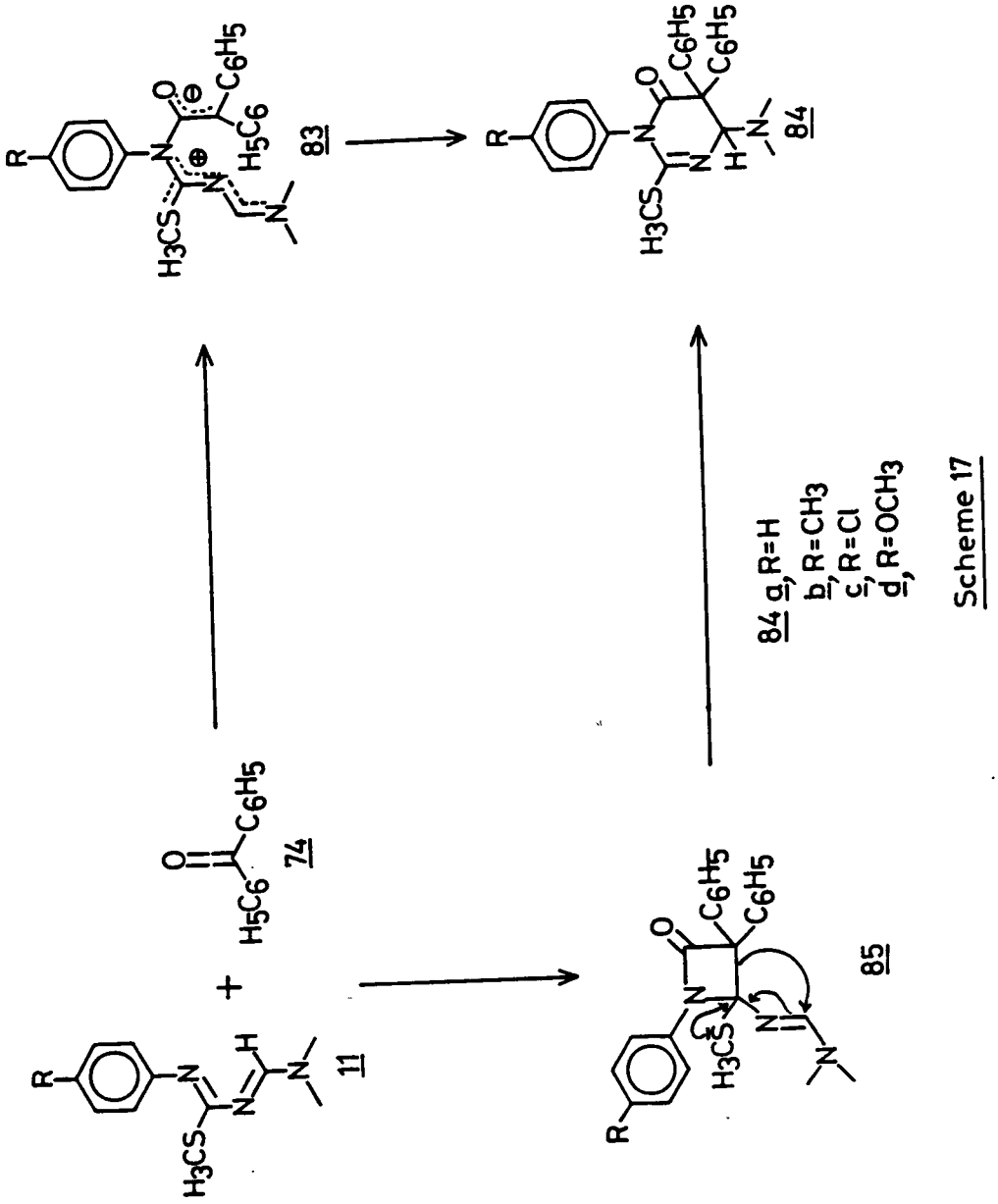
Scheme 16

gen bond for series ($^{Z}C=N$ units and $^{E}C=N$ units) are small (4-6 K cal/mole), sterically and electrochemically favourable arrangements for (2+2) and (4+2) cycloaddition reactions can be expected, (iii) the formation of β-lactam derivatives is a kinetically controlled process, as this β-lactam is predicted to be ca. 32 K cal/mole higher in energy as compared to the corresponding 4,5-dihydropyrimidin-6-one system. *Heats of reaction for the formation of four-membered* ring ca. -34 K cal/mole and for six-membered ring of -66 K cal/mole were predicted (both reactions are being fairly exothermic process); (iv) because of substantial differences in electronegativity of the reacting atoms a non-synchronous concerted or even stepwise mechanism was proposed[40], and (v) the (2+2) cycloaddition of 1,3-diaza- 1,3-butadienes across 3,4- C=N double bond with ketenes would lead to a regioisomer of 77, such N-substituted β-lactam (according to AM1[41]) is a ca. 6 K cal/mole higher in energy than the observed isomer.

We thought that if the formation of β-lactam is kinetically controlled, it would be possible to convert it (by heating) to thermodynamically more stable six-membered ring 75 (Scheme-15), but 77 was recovered unchanged even by refluxing it in xylene/chlorobenzene more than 12 hours. It appears that steric factors dominate the formation of 77 and perhaps don't allow its conversion to 75.

Further, if the barrier to rotation around carbon-nitrogen is very small it can perhaps be easily overcome by introducing another polarising function in 1,3-diaza-1,3-butadiene which in turn can further stabilise the initially formed zwitterionic intermediate. Hence, in order to observe the influence of another polarising function in 1,3-diaza-1-3-butadiene on the reaction pathway followed, we have carried out the reactions of 1-aryl-4-dimethylamino-2-thiomethyl-, 1-3-diaza-1,3-butadienes(11) with diphenylketene (74). Interestingly, these reactions resulted in very good yields of (4+2) cycloadducts 84, which have been characterized as, previously unknown, 1-aryl-4-dimethylamino-5,5-diphenyl-2 -thiomethyl-1,4,5,6-tetrahydropyrimidin-6-ones on the basis of analytical data and spectral evidences. Thus, 84a for example, was analysed for $C_{25}H_{25}N_3OS$ and its mass spectrum showed the molecular ion peak at m/z 415. Its i.r. spectrum (KBr) showed a strong peak around 1700cm^{-1} due to carbonyl absorption and is comparable to the literature value for such systems[39]. Its ^{1}H n.m.r. spectrum ($CDCl_3$) exhibited singlets at δ2.50(3H), δ 3.50(6H) and δ5.20(1H), and were assigned to $-SCH_3$, $-N(CH_3)_2$ protons and methine proton, respectively. The aromatic protons appeared as a multiplet at δ7.06-7.60(15H). The structures of 84b-d are included in the experimental section.

The probable mechanism leading to the formation



84 a, R=H
b, R=CH3
c, R=Cl
d, R=OCH3

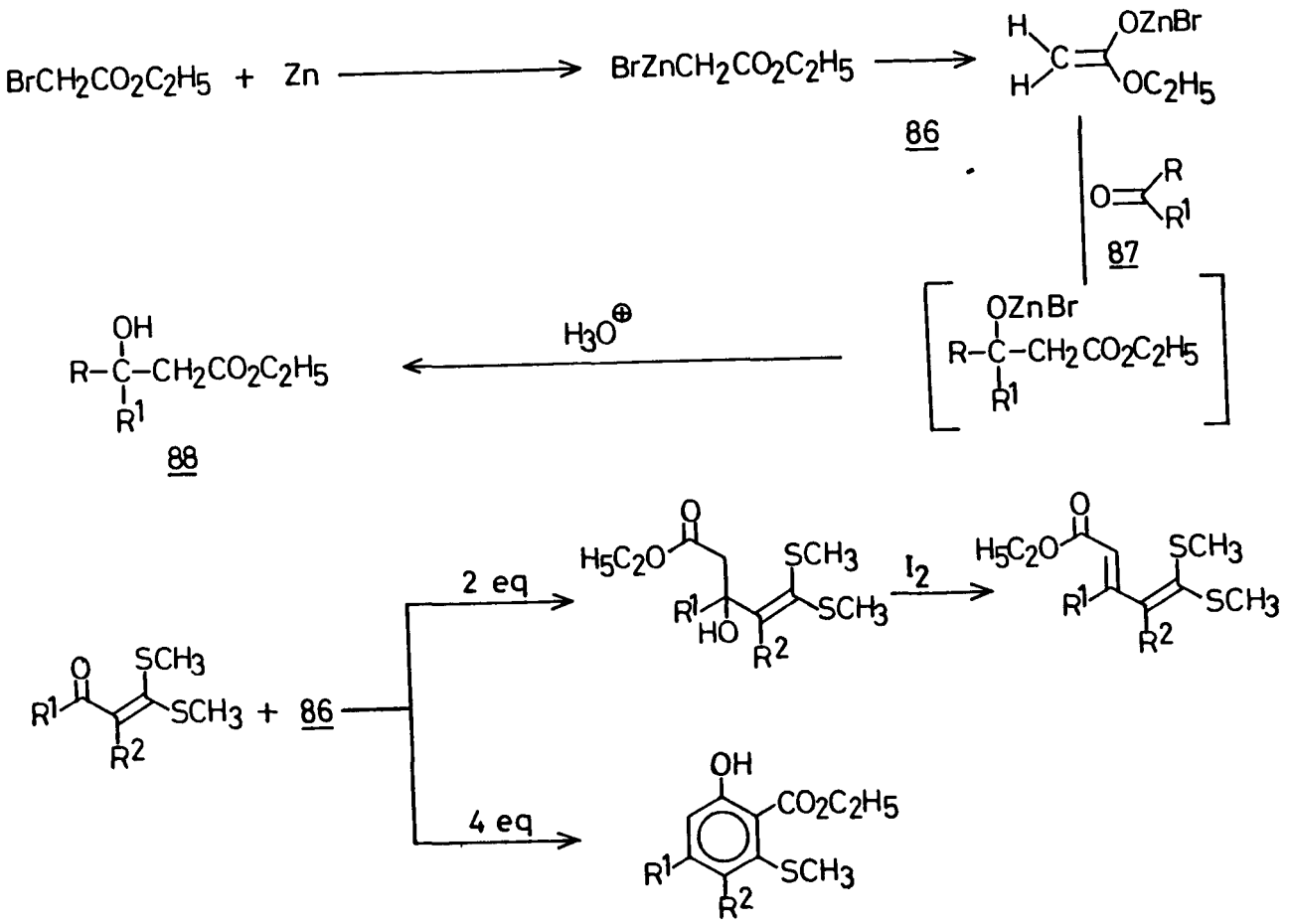
Scheme 17

of tetrahydropyrimidin-6-one(84) is outlined in scheme-17. In this case, the highly stabilised zwitterionic intermediate would prefer formation of thermodynamically more stable pyrimidin-6-one(84). The preferred formation of 84 over 85 can also be explained on steric grounds, since the approach of carbon bearing two phenyl groups to the carbon bearing thioalkyl group involves larger steric interaction compared to the terminal carbon bearing dimethylamino function (compare size of sulphur and nitrogen). The formation of 84 may also involve initial formation of β-lactam 85, which due to the presence of the polarising $-SCH_3$ function at position 4- of β-lactam perhaps rapidly rearrnages to 84(Scheme-17). At this stage, this mechanism for the formation of 84 can not be ruled out. However, we failed in all our attempts (even carrying out reaction of 11 and 74 in a n.m.r. tube) to detect and isolate the intermediate 85, in these reactions. The exact mechanism followed in these reactions is being further investigated by carrying out reactions of 1,3-diaza-1,3-butadienes having different polarising functions at positions 2- and 4-, with diphenylketene. It may also be mentioned here that all attempts to realise the reactions of diphenylketene with 1,3-diaza-1,3-butadienes (15) invariably resulted either in starting materials or untraceable mixture of products. Efforts are still on to standerdise the proper reaction conditions for realising these reactions.

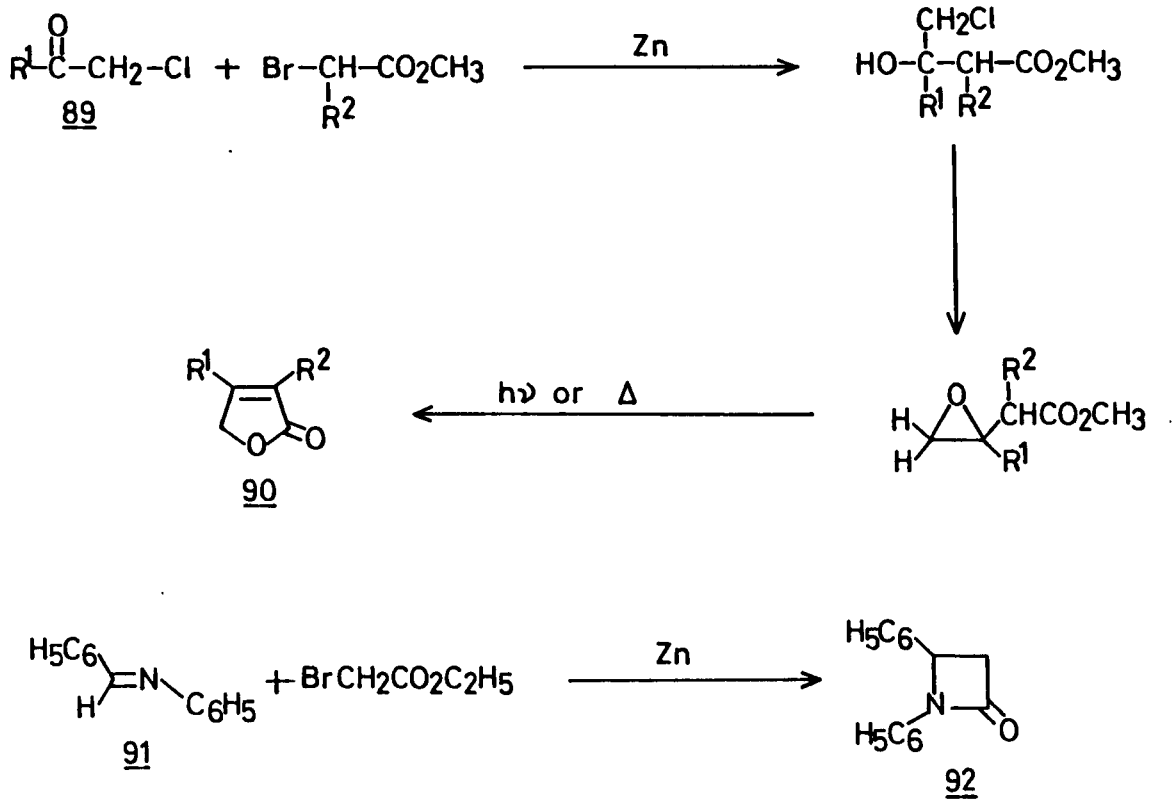
II.3 REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES(15) WITH REFORMATSKY REAGENT.

Reformatsky reaction is one of the oldest and best known condensation reaction[42], in which a halozinc enolate (86) (formed by the reduction of haloester with zinc metal) undergoes addition to an aldehyde or a ketone (87), followed by hydrolysis of the reaction mixture, provided an excellent route to β-hydroxy ester(88). The Reformatsky reagent (86) generally, undergoes 1,2-addition to aldehydes and keteones[42-46]. The β-hydroxyester formed after hydrolysis may undergo further transformations through dehydration, retrograde aldol condensation or cyclisation[42,47-51] (Scheme-18). The zinc enolate, which serves as an intermediate in Reformatsky reaction, is also known to add to α-chloroketones (89) yielding β-hydroxyester which have been made use of in γ-lactone(90) synthesis[52]. The reports concerning the 1,2-addition of Reformatsky reagent to the carbon-nitrogen hetero multiple bonds, viz. nitriles[53,54] and imines[55-57] are very rare (Scheme-19).

A few isolated examples of 1,4-addition of Reformatsky reagent have been reported and the reagent derived only from α-bromopropionate and α-bromobutyrate/isobutyrate were found to undergo partial or exclusive 1,4-addition[58-60] (scheme-20). Only very recently there has been a report of 1,4-addition zinc enolate, derived from ethylbromoacetate,

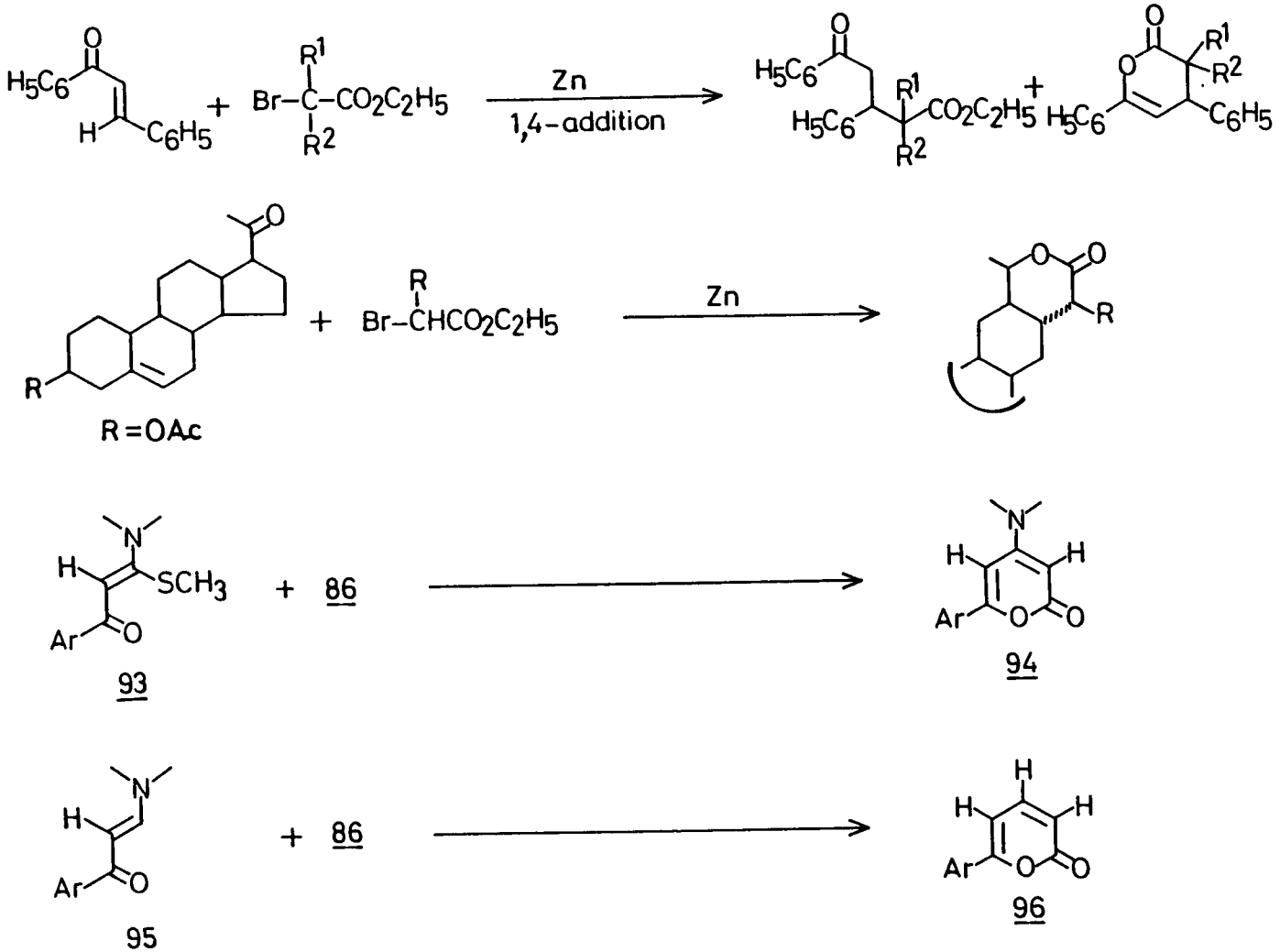


Scheme 18



89 90 91 92

Scheme 19

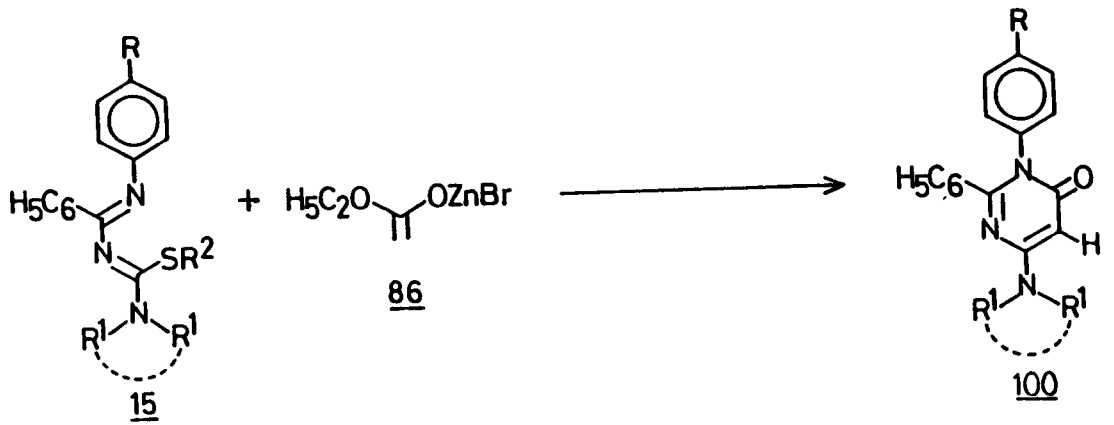


Scheme 20

to α-oxo-ketene-S,N-acetals (93) and enaminone (95) resulting in very good yields of pyran-2-ones 94 and 96, respectively[61] (Scheme-20). Although, there are few reports concerning the 1,2-addition of Reformatsky reagent to carbon-nitrogen double bond but there is no such report concerning the 1,4-addition of it to various mono- and diaza-1,3-butadienes. In continuation of our interest in the chemistry of 1,3-diaza-1,3-butadienes, we have initiated some investigation in this direction. The results of these studies are described below.

II.3.1 RESULTS AND DISCUSSION

The treatment of 1,3-diaza-1,3-butadienes (15) with zinc enolate of ethylbromacetate in ether, subsequent refluxing of reaction mixture in dry toluene for 20-30h followed by careful work up of the reaction mixture afforded very good yields (70-92%) of white crystalline products. These products have been characterised as 1,2-diphenyl-4-sec. amino(morpholino/piperidino/pyrrolidino/dimethylamino)-1,6-dihydropyrimidin-6-ones (100) on the basis of elemental analyses and spectral evidences (Scheme-21). Thus, 100a, for example, was analysed for $C_{20}H_{19}N_3O_2$ and its mass spectrum showed the molecular ion peak at m/z 333. Its i.r. spectrum ($CDCl_3$) exhibited a strong absorption peak at 1680cm^{-1} assignable to α,β-unsaturated carbonyl group. This is characteristic for 1,6-dihydropyrimidin-6-ones as described earlier in



15, 100 a, R = H; R^1, R^1 = O

b, R = H; R^1, R^1 = $(CH_2)_4$

c, R = H; R^1, R^1 = $(CH_2)_5$

d, R = H; R^1, R^1 = CH_3, CH_3

e, R = CH_3; R^1, R^1 = O

f, R = CH_3; R^1, R^1 = $(CH_2)_4$

g, R = CH_3; R^1, R^1 = $(CH_2)_5$

h, R = CH_3; R^1, R^1 = CH_3, CH_3

i, R = Cl; R^1, R^1 = $(CH_2)_4$

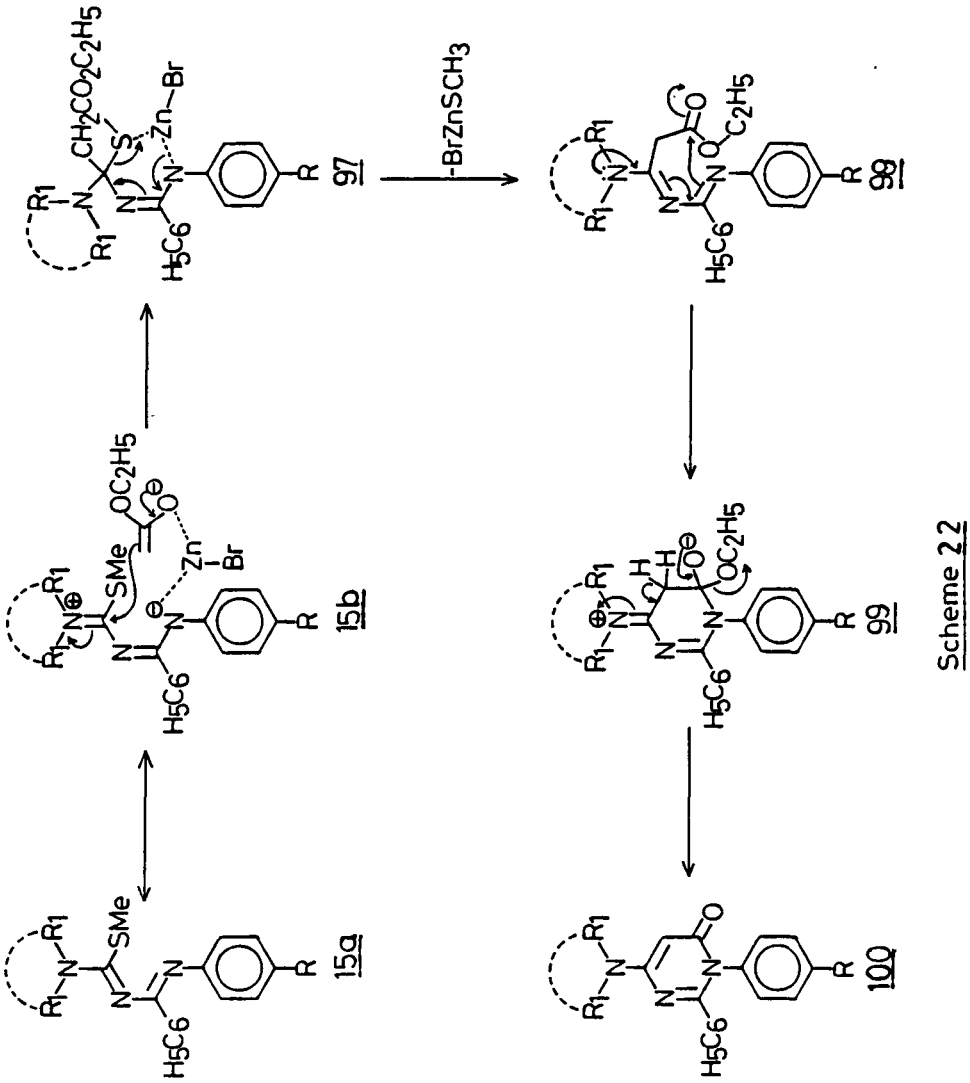
j, R = Cl; R^1, R^1 = $(CH_2)_5$

k, R = Cl; R^1, R^1 = CH_3, CH_3

Scheme 21

this chapter. The ^1H n.m.r. spectrum ($CDCl_3$) of it, displayed two triplets at δ3.50-3.63(4H) and δ3.72-3.85(4H) and were assigned to $-CH_2-N-CH_2-$ and $-CH_2-O-CH_2-$ protons of morpholine. The singlet at δ5.53(1H) was due to the olefinic proton and is in conformity with the literature value[61] of such proton which is shielded by a secondary amino function and deshielded by a carbonyl group. The aromatic proton appeared as multiplet at δ7.00-7.36(10H). The analytical analysis and spectral data for other pyrimidones (100b-k) are in conformity with the assigned structure, and are described in the experimental section. The reactions of 1,3-diaza-1,3-butadienes (8 and 11) with Reformatsky reagent under similar reaction conditions resulted in an untraceable mixtue of products from which no pure product could be isolated. However, further investigations into the reactions of various zinc enolates with different 1,3-diaza-1,3-butadienes are in progress.

The probable mechanism for the formation of pyrimidones (100) in these reactions is shown in scheme-22. In this mechanism it is presumed that the polarised 1,3-diaza-1,3-butadienes(15) undergo 1,4-addition by zinc enolate (86) resulting in an intermediate (97), wherein zinc is co-ordinated to N-1 and sulphur of alkylthio function. The intermediate 97 then undergoes elimination of methylthio zinc bromide leading to the formation of another intermediate



Scheme 22

98. The intermediate 98 then undergoes secondary amino assisted ring closure, involving attack by N-1 at the carbonyl carbon of carbethoxy function, resulting in another intermediate 99, which finally undergoes very facile loss of a proton to yield pyrimidin-6-ones (100) as products. It is pertinent to mention here that these pyrimidones (100) are expected product of (4+2) cycloaddition reactions of 1,3-diaza-1,3-butadienes 15 and unsubstituted ketene. However, because of the difficulties encountered in its isolation in the pure monomeric form (by cracking diketene at higher temperature) and the reported participation of diketene itself in cycloaddition[7,35], the synthesis of 100 by this method should perhaps be considered to be of great synthetic significance. This is the reason for which the Reformatsky reaction on 1,3-diaza-1,3-butadienes is included together with the Diels-Alder cycloaddition reaction of 1,3-diaza-1,3-butadienes with ketenes in this chapter.

II.4 EXPERIMENTAL

Melting points were determined on a Toshniwal melting point apparatus and are uncorrected. ^1H n.m.r. spectra were recorded on a varian EM390 90MHz spectrometer and chemical shift values are expressed in δ(ppm) downfield from $(CH_3)_4Si$ as internal standard. I.r and Mass spectra were recorded on a Perkin-Elmer 297 spectrophotometer and Jeol-D 300 mass spectrometer respectively. Carbon, Hydrogen and

and Nitrogen analysis were done at RSIC, Central Drug Research Institute, Lucknow, India.

Starting Materials:

N-Arylbenzamidines[62] N-arylthioureas[63],N,N-dimeltyl-formamide dimethylacetal[64], N-arylthiocarbamoyl formamidines[66], N-arylimidoyl chlorides[66], 4-[(α-arylamino)benzylidene thiocarbamoyl)]sec.amine[67], diphenyl acetyl chloride[68], and diphenylketene[69] were prepared by the reported procedures. The commercial samples of phenylacetylchloride, chloroacetylchloride and ethylbromoacetate were freshly distilled before use. Absolute dry triethylamine and extra pure AP-325 mesh zinc were used for generation of ketene and Reformatsky reagent, respectively. 1-Aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes 80-d were prepared by known procedure[8] and their analytical results and spectral data given below.

4-Dimethylamino-1,2-diphenyl-1,3-diaza-1,3-butadiene; (8a): pale yellow solid(pet.ether); yield, 93%; m.p. 91-2°C (90-90.5)[8]. (Found: C,77.93; H,6.79; N,16.76. $C_{16}H_{17}N_3$ requires C,76.49; H,6.77; N,16.73). ν_{max}(KBr): 1640cm^{-1}(C=N). δ_H ($CDCl_3$): 2.85(s,6H,-N(CH_3)$_2$); 7.15-7.40(m,10H,arom) and 7.90(s,1H,olefinic).M^+251.

4-Dimethylamino-2-phenyl-1-p-tolyl-1,3-diaza-1,3-butadiene; (8b): Pale yellow solid (pet.ether); yield 82%. m.p. 85-6°C.

(Found: C,78.10; H,7.24; N,15.82. $C_{17}H_{19}N_3$ requires C,76.98; H,7.17; N,15.85). ν_{max}(KBr): 1640cm^{-1}(C=N). δ_H($CDCl_3$): 2.35(s,3H, $-CH_3$); 2.80(s,6H,$-N(CH_3)_2$; 7.12-7.45(m,9H,arom) and 7.90 (s,1H,olefinic). M^+265.

1-p-Chlorophenyl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadiene;(8c): Yellow solid (benzene/pet.ether); yield, 52%; m.p.90-91(86-90)[8]. (Found: C,67.93; H,5.64; N,14.75. $C_{16}H_{16}ClN_3$ requires C,67.25; H,5.60; N, 14.71). ν_{max}(KBr): 1640cm^{-1}(C=N). δ_H($CDCl_3$):2.80(s,6H,$-N(CH_3)_2$; 6.80-7.33(m,9H, arom) and 7.80(s,1H,olefinic).M^+285.

1-p-Bromophenyl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadiene;(8d): Pale yellow solid (benzene/pet.ether); yield, 48%; m.p.-97-8°C.(Found:C.59.47; H,4.97; N,13.06. $C_{16}H_{16}BrN_3$ requires C,58.18; H,4.85; N,12.93). ν_{max}(KBr): 1640cm^{-1} (C=N). δ_H($CDCl_3$): 2.90(s,6H,$-N(CH_3)_2$; 7.17-7.42(m,9H,arom) and 7.85(s,1H,olefinic).M^+330.

Syntheses of 1-aryl-4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadienes(11a-e): General Procedure: A solution of N-arylthiocarbamoylformamidines(10), (0.01 mole) and methyl iodide (0.22 mole) in dry acetone (250ml) was stirred at room temperature for 10h. The seperated hydroiodide salt of 1,3-diazabutadienes were filtered and basified with

3N potassium hydroxide solution. The reaction mixture was extracted with benzene (3x100ml) and the combined benzene extracts were washed with water and dried over anhydrous magnesium sulphate. The removal of solvent under reduced pressure resulted in 1-aryl-4-dimethylamino-2-thiomethyl-1, 3-diaza-1,3-butadienes, which were sufficiently pure enough to carryout further reactions and stable enough to be stored for several months without decomposition. (Micro analysis of only solid compounds were obtained).

4-Dimethylamino-1-phenyl-2-thiomethyl-1,3-diaza-1,3-butadiene;(11a): pale yellow viscous liquid; yield, 86%. ν_{max} (nujol): 1640cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.30(s,3H,-SCH_3); 2.92(s,6H, -$N(CH_3)_2$); 7.01-7.40(m,5H,arom) and 8.08(s,1H,olefinic). M^+221.

4-Dimethylamino-2-thiomethyl-1-p-tolyl-1,3-diaza-1,3-butadiene;(11b): White solid (pet.ether); yield, 90%; m.p. 78-80°C. (Found: C,61.04; H,7.20; N,17.87. $C_{12}H_{17}N_3S$ requires C,61,27; H,7.23; N,17.87). ν_{max}(KBr):1640cm^{-1}(C=N). δ_H (CCl_4): 2.20(s,3H,-CH_3); 2.28(s,3H,-SCH_3); 2.92(s,6H, -$N(CH_3)_2$); 7.03-7.43(m,4H,arom) and 8.10(s,1H,olefinic).M^+235

4-Dimethylamino-2-thiomethyl-1-o-tolyl-1,3-diaza-1,3-butadiene;(11c): pale yellow viscous liquid; yield, 70%. ν_{max}

(nujol): 1640cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.06(s,3H,-CH_3), 2.28(s, 3H, -SCH_3); 2.92(s,6H,-$N(CH_3)_2$); 6.92-7.26(m,4H,arom) and 8.10 (s,1H,olefinic).M^+235.

1-p-Chlorophenyl-4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadiene;(11d): white solid (pet.ether); yield, 82%; m.p. 54-5°C. (Found: C,52.03; H,5.49, N,16.45. $C_{11}H_{14}ClN_3S$ requires C,51.66; H,5.48; N, 16.43). ν_{max}(KBr): 1630cm^{-1} (C=N). δ_H (CCl_4):2.31(s,3H,-SCH_3); 2.92(s,6H,-$N(CH_3)_2$); 7.02-7.38(m,4H, arom) and 8.10(s,1H,olefinic).M^+255.

4-Dimethylamino-1-p-methoxyphenyl-2-thiomethyl-1,3-diaza-1,3-butadiene;(11e): pale yellow viscous liquid, Yield, 86%. ν_{max} (nujol): 1640cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.28(s,3H,-SCH_3); 3.10(s, 6H, -$N(CH_3)_2$); 3.62(s,3H,-OCH_3); 7.06-7.42(m,4H,arom) and 8.10 (s,1H,olefinic).M^+251.

Syntheses of 1-aryl-4-sec.amino-4-thiomethyl-2-phenyl-1,3-diaza-1,3-butadienes,(15): General Procedure:

A solution of 4-[α-aryl)benzylidenethiocarbamoyl]sec. amine (0.1 mole) and methyl iodide (0.22 mole) in dry acetone (250ml) was stirred at room temperature for 10h. The separated hydroiodide salt of 1,3-diazabutadiene was filtered and basified with 3N potassium hydroxide solution. The reaction mixture was then extracted with chloroform

(3x100) and the combined chloroform extracts were washed with water (3x50ml) and finally dried over anhydrous sodium sulphate. The removal of chloroform under reduced pressure afforded 1-aryl-4-sec.amino-2-phenyl- 4-thiomethyl-1,3-diaza-1,3-butadienes(15), which were sufficiently pure to carryout further reactions.

1,2-Diphenyl-4-morpholino-4-thiomethyl-1,3-diaza-1,3-butadiene;(15a): pale yellow solid (benzene/pet. ether); yield, 98%; m.p. 108°C. (Found:C,68.15; H,6.24; N,12.47. $C_{19}H_{21}N_3OS$ requires C,67.25; H,6.19; N,12.39). ν_{max}(KBr): 1600cm^{-1} (C=N). $\delta_H(CDCl_3)$: 2.10(s,3H,-SCH_3); 3.30-3.34(t,4H,-CH_2-N-CH_2-); 3.40-3.48(t,4H,-CH_2-O-CH_2-); 6.80-6.90(m,2H,arom); 6.94-7.26(m,6H,arom) and 7.94-8.08(m,2H,arom).M^+339.

1,2-Diphenyl-4-piperidino-4-thiomethyl-1,3-diaza-1,3-butadiene;(15b): Yellow solid(benzene/pet.ether); yield, 95%; m.p.44-6°C. (Found: C,70.82; H,6.86; N,12.46. $C_{20}H_{23}N_3S$ requires C,71.22; H,6.82; N,12.46). ν_{max}(KBr): 1590cm^{-1}(C=N). $\delta_H(CDCl_3)$: 1.10-1.43(m,6H,-CH_2-CH_2-CH_2-); 2.12(s,3H,-SCH_3); 2.97-3.16(m,4H,-CH_2-N-CH_2-); 6.86-8.78(m,2H,arom); 6.97-7.23 (m,6H,arom) and 7.81-7.95(m,2H,arom).M^+337.

1,2-Diphenyl-4-pyrrolidino-4-thiomethyl-1,3-diaza-1,3-butadiene;(15c): white solid(benzene/Pet.ether); yield, 97%; m.p.106°C. (Found: C,71.62; H,6.53; N,13.00. $C_{19}H_{21}N_3S$

requires C,70.59; H,6.50; N,12.46). ν_{max}(KBr): 1590cm^{-1}(C=N). δ_H($CDCl_3$):1.60-1.74(m,4H,-CH_2-CH_2-); 2.25(s,3H,-SCH_3), 2.97-3.14(m,4H,-CH_2-N-CH_2-); 6.70-6.88(m,2H,arom); 7.00-7.30 (m,6H,arom) and 7.94-8.07(m,2H,arom).M^+323.

4-Dimethylamino-1,2-diphenyl-4-thiomethyl-1,3-diaza-1,3-butadiene;(15d): grey white solid(benzene/Pet.ether, crystallises very slowly); yield, 96%; m.p. 78-80°C. (Found: C,69.91; H,6.44; N,14.09. $C_{17}H_{19}N_3S$ requires C,68.69; H,6.40; N,14.14). ν_{max}(KBr):1600cm^{-1}(C=N). δ_H($CDCl_3$): 2.01(s,3H,-SCH_3); 2.68(s,6H,-$N(CH_3)_2$); 6.63-6.88(m,2H,arom); 7.00-7.30(m,6H, arom) and 7.95-8.10(m,2H,arom).M^+297.

1,2-Diphenyl-4-morpholino-4-thioethyl-1,3-diaza-1,3-butadiene;(15e): pale yellow solid (benzene/pet.ether), yield, 94%; m.p.88°C. (Found: C,68.31;H,6.57; N,11.92. $C_{20}H_{23}N_3OS$ requires C,67.99; H,6.52; N,11.90). ν_{max}(KBr): 1600cm^{-1} (C=N).δ_H(CCl_4): 0.98-1.07(t,3H,-CH_3, J=8.00Hz; 2.48-2.73(q, 2H,-SCH_2-, J=10.00Hz); 3.23-3.34(t,4H,-CH_2-N-CH_2-); 3.38-3.48 (t,4H,-CH_2-O-CH_2-); 6.80-6.93(m,2H,arom); 7.04-7.34(m,6H, arom) and 7.87-8.03(m,2H,arom).M^+353.

1,2-Diphenyl-4-piperidino-4-thioethyl-1,3-diaza-1,3-butadiene;(15f): viscous orange coloured liquid; yield, 94%. ν_{max}(KBr): 1580cm^{-1}(C=N). δ_H(CCl_4): 0.94-1.12(t,3H,-CH_3, J=8.00Hz); 1.27-1.53(m,6H,-CH_2-CH_2-CH_2-); 2.45-2.71(q,2H,-SCH_2-,

J=10.00Hz); 3.17-3.33(m,4H,$-CH_2-N-CH_2-$); 6.76-6.91(m,2H, arom), 7.10-7.40(m,6H,arom) and 7.90-8.03(m,2H,arom).M^+351.

1,2-Diphenyl-4-pyrrolidino-4-thioethyl-1,3-diaza-1,3-butadiene;(15g): light orange coloured liquid; yield, 94%. ν_{max} (KBr): 1590cm^{-1}(C=N). $\delta_H(CCl_4)$: 1.15-1.31(t,3H,$-CH_3$, J= 8.00H); 1.56-1.73(m,4H,$-CH_2-CH_2-$); 2.73-3.00(q,2H,$-SCH_2-$, J=10.00H); 3.03-3.30(m,4H,$-CH_2-N-CH_2-$); 6.73-6.88(m,2H, arom); 7.06-7.33 (m,6H,arom) and 8.00-8.13(m,2H,arom).M^+337.

1,2-Diphenyl-4-dimethylamino-4-thioethyl-1,3-diaza-1,3-butadiene;(15h): pale yellow viscous liquid; yield, 97%. ν_{max} (KBr): 1600cm^{-1}(C=N). $\delta_H(CCl_4)$:1.03-1.22(t,3H,$-CH_3$, J= 8.00Hz); 2.63-2.82(q,2H,$-SCH_2-$, J=10.00Hz), 2.78(s,6H,$-N(CH_3)_2$; 6.78-6.88(m,2H,arom), 7.08-7.34(m,6H,arom) and 9.79-8.06(m, 2H, arom).M^+311.

4-Morpholino-2-phenyl-4-thiomethyl-1-p-tolyl-1,3-diaza-1,3-butadiene;(15i): pale yellow solid(benzene/Pet.ether); yield, 98%; m.p.105-6°C. (Found: C,69.16; H,6.55; N,12.25. $C_{20}H_{23}N_3OS$ requires C,67.99; H,6.52, N,11.90). ν_{max}(KBr): 1580cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.02(s,3H,$-CH_3$); 2.31(s,3H,$-SCH_3$); 3.28-3.42(t,4H, $-CH_2-N-CH_2-$); 3.47-3.66(t,4H,$-CH_2-O-CH_2-$); 6.78-6.97(m,2H, arom); 7.26-7.38(m,5H,arom) and 7.85-8.03(m, 2H,arom).M^+353.

4-Piperidino-2-phenyl-4-thiomethyl-1-p-tolyl-1,3-diaza-1,3-

butadiene; (15j): orange coloured viscous liquid; yield,97%. δ_{max} (KBr): 1590cm^{-1}(C=N). $\delta_H(CCl_4)$: 1.43-1.68(m,6H,-CH_2-CH_2-CH_2); 2.15(s,3H,-CH_3); 2.33(s,3H,-SCH_3); 3.35-3.50(m,4H, -CH_2-N- CH_2-); 6.69-7.01(m,2H,arom); 7.30-7.48(m,5H,arom) and 7.98-8.10 (m,2H,arom).M^+351.

4-Pyrrolidino-2-phenyl-4-thiomethyl-1-p-tolyl-1,3-diaza-1,3-butadiene;(15k): pale yellow solid(benzene/pet.ether); yield, 97%; m.p.72-4°C. (Found: C,70.83; H,6.80; N,12.46, $C_{20}H_{23}N_3S$ requires C,71.22; H,6.82; N,12.46). ν_{max}(KBr): 1590cm^{-1} (C=N). $\delta_H(CCl_4)$: 1.52-1.70(m,4H,-CH_2-CH_2-); 2.26 (s,6H,-CH_3 and -SCH_3); 2.92-3.12(m,4H,-CH_2-N-CH_2-); 6.63 -7.00 (m,2H,arom); 7.20-7.34(m,5H,arom) and 7.97-8.13(m,2H, arom). M^+337.

4-Dimethylamino-2-phenyl-4-thiomethyl-1-p-tolyl-1,3-diaza-1,3-butadiene;(15l): pale yellow viscous liquid; yield, 94%, ν_{max}(KBr): 1590cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.13(s,3H,-CH_3); 2.25 (s,3H,-SCH_3); 2.75(s,6H,N(CH_3)$_2$); 6.68-7.02(m,2H,arom); 7.20-7.33(m,5H,arom) and 7.90-8.03(m,2H,arom).M^+311.

1-p-Chlorophenyl-4-morpholino-2-phenyl-4-thiomethyl-1,3-diaza-1,3-butadiene; (15m): pale yellow solid(benzene/Pet. ether); yield, 94%; m.p.136-8°C. (Found: C,62.00; H,5.41; N,11.24. $C_{19}H_{20}ClN_3OS$ requires C,61.04; H,5.35; N,11.32). ν_{max}(KBr):1600cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.12(s,3H,-SCH_3); 3.34-3.55

(t,4H,-CH_2-N-CH_2-); 3.50-3.64(t,4H,-CH_2-O-CH_2-); 6.83-6.98 (m,2H,arom); 7.13-7.47(m,5H,arom) and 7.94-8.06(m,2H,arom). M^+373.

1-p-Chlorophenyl-4-piperidino-2-phenyl-4-thiomethyl-1,3-diaza- 1,3-butadiene; (15n): pale yellow solid (benzene/pet. ether); yield, 92%; m.p. 66-7°C. (Found: C,65.32; H,6.03; N,11.36. $C_{20}H_{22}ClN_3S$ requires C,64.60; H,5.92; N,11.31). ν_{max} (KBr): 1580cm^{-1}. $\delta_H(CCl_4)$: 1.32-2.53(m,6H,-CH_2-CH_2-CH_2-); 2.08(s,3H, -SCH_3); 3.25-3.46(m,4H,-CH_2-N-CH_2-); 6.78-6.81(m, 2H,arom); 7.07-7.34(m,5H,arom) and 7.87-8.00(m,2H,arom).M^+371.

1-p-Chlorophenyl-4-pyrrolidino-2-phenyl-4-thiomethyl-1,3-diaza-1,3-butadiene; (15o): pale yellow solid (benzene/pet. ether); yield, 93%; m.p. 96°C. (Found: C,64.56; H,5.63; N,11.76. $C_{19}H_{20}ClN_3S$ requires C,63.78; H,5.59; N,11.75). ν_{max}(KBr): 1590cm^{-1}(C=N). $\delta_H(CCl_4)$: 1.68-1.92(m,4H,-CH_2-CH_2-); 2.30(s, 3H, -SCH_3); 3.07-3.26(m,4H,-CH_2-N-CH_2-); 6.82-6.95(m,2H, arom); 7.15-7.43(m,5H,arom) and 8.02-8.15(m,2H,arom).M^+.357.

1-p-Chlorophenyl-4-dimethylamino-2-phenyl-4-thiomethyl-1,3-diaza-1,3-butadiene;(15p): yellow solid (benzene/pet. ether); yield, 94%; m.p.98-100°C. (Found: C,62.00; H,5.48; N,12.71. $C_{17}H_{18}ClN_3S$ requires C,61.54; H,5.45; N,12.67). ν_{max}(KBr): 1590cm^{-1}(C=N). $\delta_H(CCl_4)$: 2.16(s,3H,-SCH_3); 2.95(s,6H,-$N(CH_3)_2$); 6.85-6.95 (m,2H,arom); 7.13-7.32(m,5H,arom) and 7.87-8.02(m,

2H,arom).M^+331.

Syntheses of 1,2-Diphenyl-4,4-bis(sec. amino)-1,3-diaza-1,3-butadienes, (16a-c): General Procedure: A solution of 1,2-Diphenyl-4-sec.amino-4-thiomethyl-1,3-diaza-1,3-butadienes 15a-c (0.01 mole) and secondary amine (morpholine, piperidine and pyrrolidine) (0.02 mole) in 50ml of dry toluene was refluxed for a period of 20-30h. The reaction mixture was then stripped of the solvent under reduced pressure and the solid so obtained was recrystallised from benzene.

1,2-Diphenyl-4,4-bis(morpholino)-1,3-diaza-1,3-butadine; (16a): pale yellow solid; yield, 92%; m.p. 195°C. (Found: C,70.53; H,6.92; N,14.84. $C_{22}H_{26}N_4O_2$ requires C,69.84; H,6.88; N,14.81). ν_{max}(KBr): 1630cm^{-1}(C=N). $\delta_H(CDCl_3)$: 2.84-3.02(m, 8H,-CH_2-N-CH_2-); 2.43-3.60(m,8H,-CH_2-O-CH_2-); 6.91-7.05(m,2H, arom); 7.17-7.43(m,6H,arom) and 7.87-8.02(m,2H,arom).M^+378.

1,2-Diphenyl-4,4-bis(piperidino)-1,3-diaza-1,3-butadiene; (16b): Yellow solid; yield, 89%; m.p. 134-5°C. (Found: C,78.05; H,8.04; N,15.00. $C_{24}H_{30}N_4$ requires C,77.00; H,8.02; N,14.97). ν_{max}(KBr): 1630cm^{-1} (C=N). $\delta_H(CDCl_3)$: 1.32-1.53(m,12H,-CH_2-CH_2-CH_2-); 2.70-2.93(m,8H,-CH_2-N-CH_2-); 6.91-2.93(m,2H,arom); 7.37-7.45(m,6H,arom) and 8.05-8.23(m,2H,arom).M^+374.

1,2-Diphenyl-4,4-bis(pyrrolidino)-1,3-diaza-1,3-butadiene; (16c): yellow solid; yield, 90%; m.p. 144-6°C. (Found: C,77.19; H,7.54; N,16.21. $C_{22}H_{26}N_4$ requires C,76.30; H,7.51; N,16.18).

ν_{max}(KBr): 1630cm^{-1}(C=N). δ_H($CDCl_3$): 1.56-1.73(m,8H,-CH_2-CH_2-); 2.78-3.10(m,8H,-CH_2-N-CH_2-); 6.73-7.03(m,2H,arom): 7.30-7.40 (m,6H,arom) and 8.06-8.20(m,2H,arom).M^+346.

Reactions of 1,3-diaza-1,3-butadienes (8,11 and 15) with monophenylketene; General Procedure: A solution of phenylacetylchloride (2.4 mmole) in dry thiophene free benzene (10ml) was added dropwise to an ice-cooled (5-10°C) well stirred benzene solution (20 ml) of 1,3-diaza-1,3-butadiene (2.0 m mole) and triethylamine (4 m mole). After the complete addition of acid chloride (ca.1h), the reaction mixture was stirred for a further period of 30 min at the same temperature. It was then washed with cold water (4x50ml), saturated sodium hydrogen carbonate (2x25ml), again with water (2x25ml) and finally dried over anhydrous sodium sulphate. The crude product so obtained after the removal of solvent under reduced pressure was further purified by passing through a silicagel column (1:4::ethylacetate: pet.ether) and were recrystallised from a maxture of benzene and pet.ether.

1,2,5-Triphenyl-1,6-dihydropyrimidin-6-one;(50a): white solid; yield, 96%; m.p. 166-7°C. (Found: C,82.00; H,4.90; N,8.62. $C_{22}H_{16}N_2O$ requires C,81.48; H,4.93; N,8.64). ν_{max}(KBr): 1675 cm^{-1} (C=O). δ_H($CDCl_3$): 7.01-7.63(m,15H,arom) and 8.10(s,1H, olefinic).M^+324.

2,5-Diphenyl-1-p-tolyl-1,6-dihydropyrimidin-6-one; (50b): white solid; yield, 92%; m.p.196-7°C. (Found: C,81-60; H,5.40; N,8.30. $C_{23}H_{18}N_2O$ requires C,81.65; H,5.32; N,8.28). ν_{max} (KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.35(s,3H,-CH_3); 6.96-7.68(m, 14H, arom) and 8.10(s,1H,olefinic).M^+338.

1-p-chlorophenyl-2,5-diphenyl-1,6-dihydropyrimidin-6-one; (50c): white solid; yield, 86%; m.p. 163-4°C. (Found: C,74.00; H,4.20; N,7.85. $C_{22}H_{15}ClN_2O$ requires C,73.64; H,4.18; N,7.81). ν_{max}(KBr): 1680cm^{-1}(C=O). $\delta_H(CDCl_3)$: 7.02-7.70(m,14H,arom) and 8.03(s,1H,olefinic).M^+358.

1-p-Bromophenyl-2,5-diphenyl-1,6-dihydropyrimidin-6-one; (50d): white solid; yield, 84%; m.p. 222-3°C (Found: C,66.03; H,3.81; N,6.93. $C_{22}H_{15}BrN_2O$ requires C,65.50; H,3.72; N,6.94). ν_{max}(KBr): 1680cm^{-1}(C=O). $\delta_H(CDCl_3)$: 7.00-7.68(m,14H,arom) and 8.03(s,1H,olefinic).M^+403.

1,5-Diphenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one; (53a): white solid; yield, 99%; m.p. 112°C. (Found: C,69.78; H,4.75; N,9.50. $C_{17}H_{14}N_2OS$ requires C,69.38; H,4.76; N,9.52). ν_{max} (KBr): 1675cm^{-1}(C=O). $\delta_H(CDCl_3)$ 2.40(s,3H,-SCH_3), 7.20-7.70 (m,10H,arom) and 8.01(s,1H,olefinic).M^+294.

5-Phenyl-2-thiomethyl-1-p-tolyl-1,6-dihydropyrimidin-6-one; (53b): white solid; yield, 98%; m.p. 112°C (Found: C,74.21;

H,5.24; N,9.02; $C_{17}H_{14}N_2OS$ requires C,70.12; H,5.19; N,9.02). ν_{max}(KBr): 1680cm^{-1} (C=O). δ_H($CDCl_3$): 2.40(s,6H,-CH_3 and -SCH_3); 7.06-7.70(m,9H,arom) and 7.98(s,1H,olefinic).M^+308.

1-p-Chlorophenyl-5-phenyl-2-thiomethyl-1,6-dihydropyrimidin-6 - one;(53c): white solid; yield, 96%; m.p.194°C. (Found: C,62.98; H,3.97; N,8.57. $C_{17}H_{13}ClN_2OS$ requires C,62.10; H,3.95; N,8.52). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 2.42(s,3H,-SCH_3); 7.16-7.63(m,9H,arom) and 8.03(s,1H,olefinic).M^+328.

1-p-Methoxyphenyl-5-phenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one; (53d): white solid; yield, 90%; m.p. 207°C. (Found: C,66.60, H,4.92; N,8.64. $C_{18}H_{16}N_2O_2S$ requires C,66.66; H,4.93; N,8.64).ν_{max}(KBR): 2.43(s,3H,-SCH_3); 3.83(s,3H,-OCH_3); 6.96-7.50(m,9H,arom) and 8.06(s,1H,olefinic).M^+324.

4-Morpholino-1,2,5-triphenyl-1,6-dihydropyrimidin-6-one; (55a): white solid; yield, 96%; m.p. 199-200°C. (Found: C,76.60; H,5.68; N,10.26. $C_{26}H_{23}N_3O_2$ requires C,76.28; H,5.62; N,10.27). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 3.30-3.43(t, 4H,-CH_2-N-CH_2-); 3.50-3.66(t,4H,-CH_2-O-CH_2-) and 7.13.7.60(m, 15H,arom).M^+409.

4-Piperidino-1,2,5-triphenyl-1,6-dihydropyrimidin-6-one; (55b): white solid; yield, 96%; m.p. 191°C. (Found: C,79.00; H,6.00; N,10.52. $C_{27}H_{25}N_3O$ requires C,79.61; H,6.14; N,10.32). ν_{max}(KBr): 1670cm^{-1} (C=O). δ_H($CDCl_3$): 1.33-1.56(m.,6H,

$-CH_2-CH_2-CH_2-$); 3.20-3.43(m,4H,$-CH_2-N-CH_2-$) and 7.13-7.53(m,15H, arom).M^+407.

4-Pyrrolidino-1,2,5-triphenyl-1,6-dihydropyrimidin-6-one; (55c): white solid; yield, 95%; m.p. 211°C. (Found: C,80.04; H,5.88; N,10.72. $C_{26}H_{23}N_3O$ requires C,79.39; H,5.85; N,10.69). ν_{max}(KBr): 1670cm^{-1}(C=O).$\delta_H(CDCl_3)$: 1.60-1.80(m,4H,$-CH_2-CH_2$); 3.16-3.30(m,4H,$-CH_2-N-CH_2-$) and 7.13-7.43(m,15H,arom).M^+393.

4-Dimethylamino-1,2,5-triphenyl-1,6-dihydropyrimidin-6-one; (55d): white solid; yield,97%; m.p. 174-5°C. (Found: C,79.51; H.5.83; N,11.46. $C_{24}H_{21}N_3O$ requires, C,78.47; H,5.72; N,11.44). ν_{max}(KBr): 1660cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.85(s,6H,$-N(CH_3)_2$) and 7.10-7.50(m,15H,arom).M^+367.

2,5-Diphenyl-4-morpholino-1-p-tolyl-1,6-dihydropyrimidin-6-one; (55e): pale yellow solid; yield, 94%; m.p. 214-5°C. (Found: 77.15; H,5.94; N,9.97. $C_{27}H_{25}N_3O_2$ requires C,76.60; H,5.91; N,9.93). ν_{max}(KBr): 1660cm^{-1}(C=O). $\delta_H(CDCl_3)$. 2.25(s, 3H,$-CH_3$); 3.25-3.40(t,4H,$-CH_2-N-CH_2-$); 3.50-3.63(t,4H,$-CH_2-O-CH_2-$), 6.90-7.06(m,4H,arom) and 7.16-7.60(m,10H,arom).M^+423.

2,5-Diphenyl-4-piperidino-1-p-tolyl-1,6-dihydropyrimidin-6-one;(55f): white solid; yield, 97%; m.p. 212-3°C. (Found: C,79.46; H,6.23; N,9.92. $C_{28}H_{27}N_3O$ requires C,79.81; H,6.41; N,9.98). ν_{max}(KBr): 1660cm^{-1} (C=O).$\delta_H(CDCl_3)$: 1.40-1.60(m,6H,

$-CH_2-CH_2-CH_2-$); 6.90-7.08(m,4H,arom) and 7.16-7.60(m,10H,arom). M^+421.

2,5-Diphenyl-4-pyrrolidino-1-p-tolyl-1,6-dihydropyrimidin-6-one; (55g): white solid, yield, 90%; m.p. 208-10°C. (Found: C,80.32; H,6.23; N,10.16. $C_{27}H_{25}N_3O$ requires C,79.61; H,6.14; N,10.32). ν_{max}(KBr): 1660cm^{-1}(C=O). $\delta_H(CDCl_3)$: 1.30-1.46(m,4H, $-CH_2-CH_2-$); 2.03(s,3H,$-CH_3$); 2.83-3.03 (m,4H,$-CH_2-N-CH_2-$); 6.83-6.90(m,4H,arom) and 6.96-7.30(m,10H,arom).M^+407.

4-Dimethylamino-2,5-diphenyl-1-p-tolyl-1,6-dihydropyrimidin-6- one;(55h): White solid; yield, 96%; m.p. 228°C. (Found: C,79.61; H,6.07; N,11.06. $C_{25}H_{23}N_3O$ requires C,78.74; H,6.04; N,11.02). ν_{max}(KBr): 1660cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.23(s,3H,$-CH_3$); 2.85(s, 6H,$-N(CH_3)_2$); 6.90-7.06(m,4H,arom) and 7.16-7.50(m, 10H, arom). M^+381.

1-p-Chlorophenyl-2,5-diphenyl-4-morpholino-1,6-dihydropyrimidin-6-one;(55i): white solid; yield, 94%; m.p. 234°C. (Found: C,70.00; H,4.96; N,9.39. $C_{26}H_{22}ClN_3O_2$ requires C,70.35; H,4.96; N,9.47). ν_{max}(KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$: 3.23-3.96(t,4H, $-CH_2-N-CH_2-$); 3.46-3.60(t,4H,$-CH_2-O-CH_2-$) and 6.96-7.50(m, 14H, arom).M^+443.

1-p-Chlorophenyl-1,5-diphenyl-4-piperidino-1,6-dihydropyrimidin-6-one;(55j): white solid; yield, 90%; m.p. 195°C. (Found:

C,74.01; H,5.51; N,9.54. $C_{27}H_{24}ClN_3O$ requires C,73.39; H,5.44; N,9.51). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$):1.36-1.56(m,6H,-CH_2--CH_2-CH_2-); 3.20-3.40(m,4H,-CH_2-N-CH_2-) and 7.00-7.53(m,14H, arom).M^+441.

1-p-Chlorophenyl-1,5-diphenyl-4-pyrrolidino-1,6-dihydropyrimidin-6-one;(55k): white solid; yield, 90%; m.p. 218-20°C. (Found: C,72.68; H,5.07; N,9.87. $C_{26}H_{22}ClN_3O$ requires C,72.98; H,5.15; N,9.82). ν_{max}(KBr): 1660m^{-1}(C=O). δ_H($CDCl_3$): 1.63-1.83(m,4H, -CH_2-CH_2-); 3.13-3.43(m,4H,-CH_2-N-CH_2) and 7.00-7.50(m,14H, arom). M^+427.

1-p-Chlorophenyl-4-dimethylamino-2,5-diphenyl-1,6-dihydropyrimidin-6-one;(55l): white solid; yield, 96%; m.p. 225°C. (Found: C,71.43; H,4.93; N,10.39. $C_{24}H_{20}ClN_3O$ requires C,71.73; H,4.98; N,10.46). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 2.86(s,6H,--$N(CH_3)_2$) and 7.06-7.50(m,14H,arom).M^+401.

Reactions of 1,3-diaza-1,3-butadienes (8, 11, 15 and 16) with monochloroketene (62); General Procedure: A solution of chloroacetylchloride (4 mmole) in dry dichloromethane (10ml) was added dropwise to an ice-cooled (0-5°C), well stirred dichloromethane solution (20ml) of 1,3-diaza-1,3-butadiene (2 mmole) and triethylamine (6 mmole). After complete addition of the acid chloride(Ca.1h), the reaction mixture

was stirred for a further period of 30 min at the same temperature. It was then washed with cold water (4x50ml), saturated sodium hydrogen carbonate solution (2x25ml), again with water (2x25ml) and finally dried over anhydrous magnesium sulphate. The crude product so obtained after removal of solvent under reduced pressure was purified by passing through a silicagel column (1:9::ethylacetate: hexane). These compounds were further purified by recrystallisation from a mixture of benzene and petrolium ether.

5-Chloro-1,2-diphenyl-1,6-dihydropyrimidin-6-one; (63a): white solid; yield, 97%; m.p. 227°C. (Found: C,68.90; H,3.90; N,9.33. $C_{16}H_{11}ClN_2O$ requires C, 67.96; H,3,89; N,9.91). ν_{max} (KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$: 7.23-7.60(m,8H,arom); 7.83-7.93(m,10H,arom) and 8.13(s,1H,olefinic).M^+282.

5-Chloro-2-phenyl-1-p-tolyl-1,6-dihydropyrimidin-6-one;(63b): white solid; yield, 97%; m.p.156-7°C. (Found: C,69.82; H,4.43; N,9.40. $C_{17}H_{13}ClN_2O$ requires C,68.80; H,4.38; N,9.44). ν_{max} (KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.43(s,3H,-CH_3); 7.20-7.53 (m,7H,arom); 7.80-7.93(m,2H,arom) and 8.18(s,1H,olefinic). M^+296.

5-Chloro-1-p-Chlorophenyl-2-phenyl-1,6-dihydropyrimidin-6-one; (63c): grey white solid; yield, 96%, m.p. 125°C. (Found:C,61.40; H,3.17; N,8.83. $C_{16}H_{10}Cl_2N_2O$ requires C,60.56; H,3.15; N,8.83). ν_{max}(KBr): 1680cm^{-1}(C=O). $\delta_H(CDCl_3)$:7.26-7.53(m,7H,arom);

7.70-7.90(m,2H,arom) and 8.10(s,1H,olefinic).M^+317.

1-p-Bromophenyl-5-Chloro-2-phenyl-1,6-dihydropyrimidin-6-one; (63d): White solid; yield, 96%; m.p. 125°C. (Found:C,53.52; H,2.70; N,7.76. $C_{16}H_{10}BrClN_2O$ requires C,53.18; H,2.77; N,7.74). ν_{max}(KBr): 1670cm^{-1} (C=O).$\delta_H(CDCl_3)$: 7.20-7.53(m,7H,arom); 7.70-7.90(m,2H,arom) and 8.12(s,1H,olefinic).M^+361.

5-Chloro-1-phenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one; (64a): white solid; yield, 98%; m.p.147-8°C. (Found:C,53.37; H,3.54; N,11.00. $C_{11}H_9ClN_2OS$ requires C,52.27; H,3.56; N,11.08). ν_{max}(KBr): 1680cm^{-1}(C=O).$\delta_H(CDCl_3)$:2.43(s,3H,-SCH_3), 7.20-7.36 (m,3H,arom); 7.50-7.60(m,2H,arom) and 8.03(s,1H,olefinic).M^+252.

5-Chloro-2-thiomethyl-1-p-tolyl-1,6-dihydropyrimidin-6-one; (64b): white solid; yield, 98%; m.p. 174-5°C. (Found: C,54.63; H,4.06; N,10.56. $C_{12}H_{11}ClN_2OS$ requires C,54.03; H,4.13; N,10.56). ν_{max}(KBr):1685cm^{-1}(C=O).$\delta_H(CDCl_3)$: 2.40(s,3H,-CH_3), 2.45(s,3H, -SCH_3); 7.08-7.18(m,2H,arom); 7.26-7.43(m,2H,arom) and 8.03 (s,1H,olefinic).M^+266.,

5-Chloro-1-p-Chlorophenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one; (64c): white solid; yield, 97%; m.p. 187°C. (Found: C,46.66; H,2.78; N,9.76. $C_{11}H_8Cl_2N_2OS$ requires C,45.99; H,2.79; N,9.75).ν_{max}(KBr): 1680cm^{-1}(C=O).$\delta_H(CDCl_3)$:2.33(s,3H,-SCH_3); 7.03-7.16(m,2H,arom); 7.33-7.50(m,2H,arom) and 7.93(s,1H, olefinic).M^+287.

5-Chloro-1-p-methoxyphenyl-2-thiomethyl-1,6-dihydropyrimidin-6-one;(64d): white solid; yield, 96%; m.p. 164-5°C. (Found: C,50.95; H,3.85; N,9.95. $C_{12}H_{11}ClN_2OS$ requires C,50.97; H,3.89; N,9.91). ν_{max}(KBr): 1680 cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.40(s,3H,$-SCH_3$); 3.86(s,3H,$-OCH_3$); 6.96-7.08(m,2H,arom); 7.13-7.30(m,2H,arom) and 8.01(s,1H,olefinic).M^+282.

1,2-Diphenyl-4-morpholino-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66a): white solid; yield, 96%; m.p.176°C. (Found:C,66.12; H,5.52; N,11.02. $C_{21}H_{21}N_3O_2S$ requires C,66.49; H,5.54; N,11.08). ν_{max}(KBr):1670cm^{-1}(C=O). $\delta_H(CDCl_3)$:2.36(s,3H,$-SCH_3$); 3.86-3.92 (m,8H,morpholine) and 7.10-7.33(m,10H,arom).M^+379.

1,2-Diphenyl-4-piperidino-50thiomethyl-1,6-diohydropyrimidin-6-one; (66b): white solid; yield, 92%; m.p. 126-7°C. (Found: C,69.60; N,6.03; N,11.00. $C_{22}H_{23}N_3OS$ requires C,70.03; H,6.10; N,11.14).ν_{max}(KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$: 1.63-1.80(m,6H, $-CH_2-CH_2-CH_2-$); 2.33(s,3H,$-SCH_3$); 3.66-3.86(m,4H,$-CH_2-N-CH_2-$) and 7.10-7.36(m,10H,arom).M^+377.

1,2-Diphenyl-4-pyrrolidino-5-thiomethyl-1,6-dihydropyrimidin-6-one; (66c): grey white solid; yield, 95%; m.p. 152°C. (Found: C,68.93; H,5.84; N,11.40. $C_{21}H_{21}N_3OS$ requires C,69.47; H,5.79; N,11.57). ν_{max}(KBr): 1670cm^{-1}(C=O). $\delta_H(CDCl_3)$:1.80-2.03(m,4H, $-CH_2-CH_2-$); 2.33(s,1H,$-SCH_3$); 3.80-4.02(m,4H,$-CH_2-N-CH_2-$)

and 7.10-7.30(m,10H,arom).M^+363.

4-Dimethylamino-1,2-diphenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one; (66d): white solid; yield, 96%; m.p. 128-30°C. (Found:C,67.50; H,5.68; N,12.40. $C_{19}H_{19}N_3OS$ requires C,67.66; H,5.64; N,12.46). ν_{max}(KBr): 1670cm^{-1} (C=O). δ_H($CDCl_3$): 2.28 (s,3H,-SCH_3); 3.26(s,6H,-$N(CH_3)_2$) and 7.13-7.33(m,10H,arom). M^+337.

1,2-Diphenyl-4-morpholino-5-thioethyl-1,6-dihydropyrimidin-6-one; (66e): white solid; yield, 93%; m.p. 183°C. (Found: C,68.03; H,5.90; N,10.68. $C_{22}H_{23}N_3O_2S$ requires C,67.18; H,5.85; N,10.69). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 1.19-1.30(t,3H, -CH_3, J=8.00Hz); 2.73-3.00(q,2H,-SCH_2-,J=6.00Hz); 3.70-3.86(m, 8H, morpholine) and 7.06-7.28(m,10H,arom).M^+393.

1,2-Diphenyl-4-piperidino-5-thioethyl-1,6-dihydropyrimidin-6-one;(66f): white solid; yield, 93%; m.p. 137-8°C. (Found: C,70.40; H,6.44; N,10.70. $C_{23}H_{25}N_3OS$ requires C,70.59; H,6.39; N,10.74).ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 1.16-1.33(t,3H, -CH_3,J=8.00Hz); 1.66-1.80(m,6H,-CH_2-CH_2-CH_2-); 2.80-3.095(q, 2H, -SCH_2-,J=6.00Hz); 3.73-3.90(m,4H,-CH_2-N-CH_2-) and 7.06-7.33 (m,10H, arom).M^+391.

1,2-Diphenyl-4-pyrrolidino-5-thioethyl-1,6-dihydropyrimidin-

6-one;(66g): Pale yellow solid; yield, 90%; m.p. 164°C. (Found: C,70.30; H,6.17; N,10.97. $C_{22}H_{23}N_3OS$ requires C,70.03; H,6.10; N,11.14). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 1.16-1.33(t,3H, $-CH_3$,J=8.00Hz); 1.83-2.00(m,4H,$-CH_2-CH_2-$); 2.68-2.93(q,2H,$-SCH_2-$, J=6.00Hz); 3.83-4.00(m,4H,$-CH_2-N-CH_2-$) and 7.06-7.36(m,10H, arom). M^+377.

4-Dimethylamino-1,2-diphenyl-5-thioethyl-1,6-dihydropyrimidin-6-one;(66h): white solid; yield, 91%; m.p. 107-8°C. (Found: C,68.01; H,6.01; N,11.93. $C_{20}H_{21}N_3OS$ requires C,68.38; H,5.98; N,11.97). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$):1.13-1.30(t,3H, $-CH_3$,J=8.00Hz); 2.70-2.93(q,2H,$-SCH_2-$,J=6.00Hz); 3.30(s,6H, $-N(CH_3)_2$) and 7.06-7.36(m,10H,arom).M^+351.

4-Morpholino-2-phenyl-5-thiomethyl-1-p-tolyl-1,6-dihydropyrimidin-6-one;(66i): pale yellow solid; yield, 97%; m.p. 168-70°C. (Found:C,67.70; H,5.84; N,10.72. $C_{22}H_{23}N_3O_2S$ requires C,69.18, H,5.85; N,10.69). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 2.22(s,3H,$-CH_3$); 2.35(s,3H,$-SCH_3$); 3.73-3.88(m,8H,morpholine);7.00-7.10(m,4H,arom) and 7.20-7.40(m,5H,arom).M^+393.

4-Piperidino-2-phenyl-5-thiomethyl-1-p-tolyl-1,6-dihydropyrimidin-6-one;(66j): pale yellow solid; yield, 94%; m.p. 174-5°C. (Found: C,70.51; H,6.40; N,10.82. $C_{23}H_{25}N_3OS$ requires C,70.59; H,6.39; N,10.74). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 1.66-1.82

(m,6H,-CH_2-CH_2-CH_2-); 2.28(s,3H,-CH_3); 2.33(s,3H,-SCH_3); 3.70-3.90(m,4H,-CH_2-N-CH_2-); 7.00-7.10(m,4H,arom) and 7.23-7.33 (m,5H,arom).M^+391.

4-Pyrrolidino-2-phenyl-5-thiomethyl-1-p-tolyl-1,6-dihydropyrimidin-6-one;(66k): white solid; yield, 94%; m.p. 164°C. (Found:C,69.70; H,6.08; N,11.20. $C_{22}H_{23}N_3OS$ requires C,70.03; H,6.10, N,11.14).ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$):1.83-2.03 (m,4H,-CH_2 CH_2-); 2.33(s,6H,-CH_3 and -SCH_3); 3.80-3.98(m,4H, -CH_2-N-CH_2-); 7.00-7.08(m,4H,arom) and 7.13-7.33(m,5H,arom). M^+377.

4-Dimethylamino-2-phenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66l): pale yellow solid; yield, 95%; m.p. 129-30°C. (Found:C,68.58; H,5.78; N,11.99. $C_{20}H_{21}N_3OS$ requires C,66.38; H,5.98; N,11.97).ν_{max}(KBr): 1660cm^{-1}(C=O).δ_H($CDCl_3$): 2.30(s,3H, -CH_3); 2.33(s,3H,-SCH_3); 3.30(s,6H,-$N(CH_3)_2$); 6.97-7.06(m, 4H,arom) and 7.16-7.26(m,5H,arom).M^+351.

1-p-Chlorophenyl-4-morpholino-2-phenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66m): white solid yield, 90%; m.p. 233°C. (Found:C,60.50; H,4.87; N,10.21. $C_{21}H_{20}ClN_3O_2S$ requires C,60.94; H,4.84; N,10.16).ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 2.26(s,3H, -SCH_3); 3.68-3.90(m,8H,morpholine) and 7.00-7.36(m,9H,arom). M^+413.

1-p-Chlorophenyl-4-piperidino-2-phenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66n): pale yellow solid; yield, 92%; m.p. 195°C. (Found: C,63.34; H,5.26; N,10.22. $C_{22}H_{22}ClN_3OS$ requires C,64.16; H,5.35; N,10.21). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 1.60-1.76(m,6H,-CH_2-CH_2-CH_2-); 2.32(s,3H,-SCH_3); 3.70-3.86(m,4H,-CH_2-N-CH_2-) and 7.00-7.36(m,9H,arom).M^+411.

1-p-Chlorophenyl-4-pyrrolidino-2-phenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66o): white solid; yield, 93%; m.p. 169-71°C. (Found:C,64.40; H,5.06; N,11.51. $C_{21}H_{20}ClN_3OS$ requires C,63.40; H,5.03; N,11.57). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$):1.83-2.00(m,4H,-CH_2-CH_2-); 2.30(s,3H,-SCH_3); 3.80-4.00 (m,4H,-CH_2-N-CH_2-) and 7.00-7.33(m,9H,arom).M^+397.

1-p-chlorophenyl-4-dimethylamino-2-phenyl-5-thiomethyl-1,6-dihydropyrimidin-6-one;(66p): white solid; yield, 90%; m.p. 127°C. (Found: C,60.90; H,4.78; N,11.34. $C_{19}H_{18}ClN_3OS$ requires C,61.37; H,4.85; N,11.31). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 2.32(s,3H,-SCH_3); 3.33(s,6H,-$N(CH_3)_2$) and 7.00-7.33(m,9H,arom). M^+371.

5-Chloro-1,2-diphenyl-4-morpholino-1,6-dihydropyrimidin-6-one;(67a): white solid; yield, 93%; m.p. 222-3°C. (Found: C,66.02; H,4.84; N,11.48. $C_{20}H_{18}ClN_3O_2$ requires C,65.31; H,4.90; N,11.43). ν_{max}(KBr): 1680cm^{-1}(C=O). δ_H($CDCl_3$): 3.66-3.94

(m,8H,morpholine) and 7.15-7.50(m,10H,arom).M^+367.

5-Chloro-1,2-diphenyl-4-piperidino-1,6-dihydropyrimidin-6-one;(67b): grey white solid; yield, 93%, m.p. 200-201°C. (Found:C,68.02; H,5.46; N,11.54. $C_{21}H_{20}ClN_3O$ requires C,68.95; H,5.47; N,11.49).ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 1.60-1.76 (m,6H,$-CH_2-CH_2-CH_2$); 3.65-3.82(m,4H,$-CH_2-N-CH_2-$) and 6.98-7.35 (m,10H,arom).M^+365.

5-Chloro-1,2-diphenyl-4-pyrrolidino-1,6-dihydropyrimidin-6-one;(67c): white solid; yield, 86%, m.p. 210-12°C. (Found: C,69.03; H,5.06; N,12.03. $C_{20}H_{18}ClN_3O$ requires C,68.28; H,5.12; N,11.95).ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$):1.83-2.03(m,4H, $-CH_2-CH_2-$); 3.80-4.00(m,4H,$-CH_2-N-CH_2-$) and 6.93-7.42(m,10H, arom).M^+351.

Reactions of 1,3-diaza-1,3-butadienes (8 and 11) with diphenylketene(74); General Procedure: A solution of diphenylacetylchloride (3 mmole) in dry benzene (10ml) was added to a well stirred ice-cooled (5-10°C) benzene solution (20ml) of 1,3-diaza-1,3-butadiene (2 mmole) and triethylamine (4 mmole). After the complete addition of acid chloride (Ca.1h) the reaction mixture was further stirred for a period of 30 min at the same temperature. The reaction mixture was then washed with cold water (4x50ml), saturated sodium hydrogen carbonate

(2x25ml) saturated brine solution (2x25ml), cold water (2x25ml) and finally dried over anhydrous magnesium sulphate. The removal of solvent under reduced pressure gave the crude products, which were purified by passing through a silica gel column (1:4::ethylacetate:pet.ether), and were recrystallised from appropriate solvents.

4-(N,N-Dimethylformamidino)-1,3,3,4-tetraphenylazetidin-2-one;(77a): white solid (benzene/pet.ether); yield, 91%; m.p.164-5°C. (Found: C,80.95; H,6.05; N,9.40, $C_{30}H_{27}N_3O$ requires C.80.89; H,6.06; N,9.43). ν_{max}(KBr):1730cm^{-1}(C=O). δ_H ($CDCl_3$):2.70(s,6H,-N(CH_3)$_2$); 6.83(s,1H,olefinic) and 7.16-7.54(m,20H,arom). M^+445.

4-(N,N-Dimethylformamidino)-1-p-tolyl-3,3,4-triphenylazetidin-2-one;(77b): white solid (benzene/pet.ether); yield, 95%; m.p.148.(Found: C,82.00; H,6.33; N,9.10. $C_{31}H_{29}N_3O$ requires C,81.04; H,6.31; N,9.15). ν_{max}(KBr): 1730cm^{-1}(C=O). δ_H($CDCl_3$):2.20(s,3H,-CH_3); 2.75(s,6H,-N(CH_3)$_2$); 6.90(s,1H, olefinic) and 7.23-7.56(m,19H,arom). M^+459.

1-p-Chlorophenyl-4-(N,N-dimethylformamidino)-3,3,4-triphenylazetidin-2-one;(77c): white solid (benzene); yield, 95%; m.p.180-81°C. (Found: C,76.02; H,5.42; N,8.75. $C_{30}H_{26}ClN_3O$ requires C,75.07; H,5.42; N,8.75). ν_{max}(KBr):1730cm^{-1}(C=O).

$\delta_H(CDCl_3)$: 2.70(s,6H,$-N(CH_3)_2$); 6.86(s,1H,olefinic) and 7.15-7.55(m,19H,arom).M^+479.

1-p-Bromophenyl-4-(N,N-dimethylformamidino)-3,3,4-triphenyl azetidin-2-one;(77d): White solid(benzene); yield, 96%; m.p. 174-6°C. (Found: C,68.80; H,4.99; N,8.04. $C_{30}H_{26}BrN_3O$ requires C,68.70; H,4.96; N,8.01).ν_{max}(KBr): 1730cm^{-1}(C=O). $\delta_H(CDCl_30$. 2.68(s,6H,$-N(CH_3)_2$); 6.83(s,1H,olefinic) and 7.20-7.63 (m,19H,arom).M^+524.

4-Dimethylamino-2-thiomethyl-1,5,5-triphenyl-1,4,5,6-tetrahydropyrimidin-6-one;(84a): white solid (benzene/pet.ether); yield, 94%; m.p.122°C. (Found:C,73.10; H,6.05; N,10.10. $C_{23}H_{25}N_3OS$ requires C,72.28; H,6.02; N,10.12).ν_{max}(KBr): 1700cm^{-1}(C=O).$\delta_H(CDCl_3)$: 2.26(s,3H,$-SCH_3$); 2.34(s,6H, $-N(CH_3)2$); 5.16(s,1H,methine) and 7.06-7.60(m,15H,arom).M^+ 415.

4-Dimethylamino-5,5-diphenyl-2-thiomethyl-1-p-tolyl-1,4,5,6-tetrahydropyrimidin-6-one;(84b): white solid (benzene/pet. ether); yield, 90%; m.p. 194-6°C. (Found: C,72.80; H,6.05; N,9.81. $C_{26}H_{27}N_3OS$ requires, C,72.72; H,6.29; N,9.79).ν_{max} (KBr): 1700cm^{-1}(C=O).$\delta_H(CDCl_3)$: 2.26(s,3H,$-SCH_3$); 2.36(s,6H, $-N(CH_3)_2$); 5.16(s1H,methine), and 7.06-7.54(m,14H,arom).M^+429.

1-p-Chlorophenyl-4-dimethylamino-5,5-diphenyl-2-thiomethyl-

1,4,5,6-tetrahydropyrimidin-6-one;(84c): white solid (benzene/pet.ether); yield, 93%; m.p.148°C. (Found: C,67.70; H,5.36; N,9.39.$C_{25}H_{24}ClN_3OS$ requires C,66.74; H,5.33; N,9.34). ν_{max}(KBr): 1700cm^{-1}(C=O). δ_H($CDCl_3$): 2.28(s,3H,-SCH_3); 2.32 (s,6H,-$N(CH_3)_2$); 5.16(s,1H,methine) and 7.00-7.50(m,14H, arom).M^+449.

4-Dimethylamino-5,5-diphenyl-1-p-methoxyphenyl-2-thiomethyl-1,4,5,6-tetrahydropyrimidin-6-one;(84d): white solid (benzenepet.ether); yield, 94%; m.p. 134-5°C. (Found: C,71.20; H,6.04; N,9.45. $C_{26}H_{27}N_3O_2S$ requires C,70.11; H,6.00; N,9.43). ν_{max}(KBr): 1700cm^{-1}(C=O). δ_H($CDCl_3$): 2.26(s,3H,-SCH_3); 3.03 (s,6H,-$N(CH_3)_2$); 3.73(s,3H,-OCH_3); 5.16(s,1H,methine); 6.76-6.96(m,2H,arom) and 7.16-7.60(m,12H,arom).M^+445.

Reactions of 1,3-diaza-1,3-butadienes(15)with Reformatsky reagent(86); General procedure: To a suspension of zinc (0.7g, 12 mmole, preheated at 110°C for 1h) and a few crystals of iodine in dry ether (20ml), bromoethylacetate (1.0g, 6 mmole) in dry ether (10ml) is added dropwise (10min) with stirring and the reaction mixture refluxed for 30 min. A solution of 1,3-diaza-1,3-butadiene (3 mmole) in dry toluene (25ml) then added dropwise (30min) and the reaction mixture refluxed for a further period of 20 to 30h. It was then poured over ice-cold 10% sulphuric acid (100ml), organic layer was seperated, washed with water (1x50ml),

satuated sodium hydrogen carbonate (2x25ml), again with water (2x25ml) and finally dried over anhydrous magnesium sulphate. The solvent was removed under reduced pressure. The crude product so obtained was then recrystallised from a mixture of benzene and petrolium ether.

1,2-Diphenyl-4-morpholino-1,6-dihydropyrimidin-6-one; (100a): White solid; yield, 92%; m.p. 198-99°C. (Found: C,72.86; H,5.76; N,12.58. $C_{20}H_{19}N_3O_2$ requires C,72.07; H,5.71; N,12.61). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 3.50-3.63(t,4H,-CH_2-N-CH_2-); 3.72-3.85(t,4H,-CH_2-O-CH_2-); 5.53(s,1H,olefinic) and 7.00-7.36(m,10H,arom).M^+333.

1,2-Diphenyl-4-piperidino-1,6-dihydropyrimidin-6-one;(100b): white solid; yield, 90%; m.p. 162°C. (Found: C,76.00; H,6.41; N,12.69. $C_{21}H_{21}N_3O$ requires C,76.13; H,6.34; N,12.69).ν_{max} (KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 1.50-1.73(m,6H,-CH_2-CH_2-CH_2-) 3.46-3.66(m,4H,-CH_2-N-CH_2-); 5.55(s,1H,olefinic) and 7.00- 7.40(m,10H,arom).M^+331.

1,2-Diphenyl-4-pyrrolidino-1,6-dihydropyrimidin-6-one; (100c): white solid; yield, 86%; m.p. 178-9°C. (Found: C,75.82; H,6.06; N,13.30. $C_{20}H_{19}N_3O$ requires C,75.71; H,5.99; N,13.25). ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 1.83-2.08(m, 4H,-CH_2-CH_2-); 3.32-3.63(m,4H,-CH_2-N-CH_2-); 5.35(s,1H,olefinic) and 7.03-7.40(m,10H,arom).M^+317.

4-Dimethylamino-1,2-diphenyl-1,6-dihydropyrimidin-6-one; (**100d**): white solid; yield, 86; m.p. 173-4°C. (Found: C,75.04; H,5.83; N,14.34. $C_{18}H_{17}N_3O$ requires C,74.23; H,5.84; N,14.34). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 3.18(s,6H,-N(CH_3)$_2$); 5.45(s,1H,olefinic) and 7.03-7.23(m,10H,arom).M^+291.

4-Morpholino-2-phenyl-1-p-tolyl-1,6-dihydropyrimidin-6-one; (**100e**): white solid; yield, 86%; m.p. 225°C. (Found: C,73.04; H,6.07; N,12.07. $C_{21}H_{21}N_3O_2$ requires C,72.62; H,6.05; N,12.10). ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 2.26(s,6H,-CH_3); 3.50-3.63(t,4H,-CH_2-N-CH_2-); 3.71-3.87(t,4H,-CH_2-O-CH_2-); 5.55 (s,1H,olefinic) and 7.00-7.30(m,9H,arom).M^+437.

2-Phenyl-4-piperidino-1-p-tolyl-1,6-dihydropyrimidin-6-one; (**100f**): white solid; yield; 84%; m.p. 232°C. (Found: C,76.87; H,6.74; N,12.13. $C_{22}H_{23}N_3O$ requires C,76.52; H,6.67; N,12.17). ν_{max}(KBr): 1670cm^{-1}(C=O). δ_H($CDCl_3$): 1.55-1.76(m,6H,-CH_2-CH_2-CH_2-); 2.26(s,3H,-CH_3); 3.46-3.67(m,4H,-CH_2-N-CH_2-); 5.55(s, 1H, olefinic) and 7.00-7.33(m,9H,arom).M^+345.

2-Phenyl-4-pyrrolidino-1-p-tolyl-1,6-dihydropyrimidin-6-one; (**100g**): grey white solid; yield, 83%; m.p. 186°C. (Found: C,77.00; H,6.49; N,12.71. $C_{21}H_{21}N_3O$ requires C,76.13; H,6.34; N,12.69). ν_{max}(KBr): 1670cm^{-1}(C=O).δ_H($CDCl_3$): 1.80-2.06(m, 4H, -CH_2-CH_2-); 2.35(s,3H,-CH_3); 3.26-3.60(m,4H,-CH_2-N-CH_2-);

5.50(s,1H,olefinic) and 7.00-7.40(m,9H,arom).M^+331.

4-Dimethylamino-2-phenyl-1-p-tolyl-1,6-dihydropyrimidin-6-one; (100h): pale yellow solid; yield, 83%; m.p. 193-4°C. (Found: C,75.28; H,6.27; N,13.75. $C_{19}H_{19}N_3O$ requires C,74.75; H,6.28; N,13.77).ν_{max}(KBr): 1660cm^{-1}(C=O). $\delta_H(CDCl_3)$: 2.23(s,3H,$-CH_3$); 3.08(s,6H,$-N(CH_3)_2$); 5.43(s,1H,olefinic) and 6.93-7.23(m,9H, arom).M^+305.

1-p-Chlorophenyl-4-piperidino-1,6-dihydropyrimidin-6-one; (100i): white solid; yield, 85%; m.p. 235°C. (Found: C,69.00; H,5.58; N,11.53.$C_{21}H_{20}ClN_3O$ requires C,68.95; H,5.47; N,11.49). ν_{max}(KBr): 1660cm^{-1}(C=O).$\delta_H(CDCl_3)$: 1.53-1.76(m,6H,$-CH_2-CH_2-CH_2-$); 3.50-3.70(m,4H,$-CH_2-N-CH_2-$); 5.55(s,1H,olefinic) and 7.00-7.33(m,9H,aromatic).M^+365.

1-p-Chlorophenyl-4-pyrrolidino-2-phenyl-1,6-dihydropyrimidin-6-one;(100j): white solid; yield, 70%; m.p. 220°C. (Found: C,69.04; H,5.21; N,11.97. $C_{20}H_{18}ClN_3O$ requires C,68.28; H,5.12; N,11.95).ν_{max}(KBr): 1660cm^{-1}(C=O).$\delta_H(CDCl_3)$: 1.90-2.20(m,4H,$-CH_2-CH_2-$); 3.33-3.63(m,4H,$-CH_2-N-CH_2-$); 5.28(s,1H,olefinic) and 6.98-7.30(m,9H,arom).M^+331.

1-p-Chlorophenyl-4-dimethylamino-2-phenyl-1,6-dihydropyrimidin-6-one;(100k): white solid; yield, 80%; m.p. 194°C.

(Found: 66.68; H,5.97; N,12.97; $C_{18}H_{16}ClN_3O$ requires C,66.36; H,4.92; N,12.90). ν_{max}(KBr): 1660cm^{-1}(C=O). δ_H($CDCl_3$): 3.12 (s,6H,-N(CH_3)$_2$); 5.38(s,1H,olefinic) and 7.00-7.33(m,9H, arom). M^+325.

REFERENCES

1. D.L. Boger, Tetrahedron, 1983, 39, 2869.

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

3.(a) H. Weidinger and J. Kranz, Chem. Ber., 1963, 96, 2070.

(b) H. Weidinger and J. Sturm, Liebigs Ann. Chem., 1968, 716, 143.

4.(a) M. Sakamoto, K. Miyazawa, and Y. Tomimatsu, Chem. Pharm. Bull. Tokyo, 1976, 24, 2532.

(b) M. Sakamoto, M. Shibano, K. Miyazawa, M. Suzuki, and Y. Tomimatsu, Chem. Pharm. Bull. Tokyo, 1976, 24, 2889.

5. R. Richter and H. Ulrich, Chem. Ber., 1970, 103, 3525.

6.(a) T. Kato and S. Masuda, Chem. Pharm. Bull. Tokyo, 1974, 22, 2251.

(b) T. Kato and S. Masuda, Chem. Pharm. Bull. Tokyo, 1975, 23, 2251.

(c) N. Katagiri, R. Niwa, and T. Kato, Chem. Pharm. Bull. Tokyo, 1983, 31, 2899.

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

8. M. Nishi, S. Tanimoto, M. Okano, and R. Oda, **Yuki Gosei Kagaku Kyokai Shi**, 1969, **27**, 754; **Chem. Abstr.**, 1969, **71**, 101438v.

9. T. Kametani and S. Hibino, **Advances in Heterocyclic Chemistry**, Academic Press, 1987, **42**, 246.

10. B. Adetare, J.P. Guemas, and H. Quinou, **Bull. Soc. Chim. France**, 1987, 517.

11. H. Ulrich, **Cycloaddition Reactions of Heterocumulenes**, Academic Press, New York, 1967, p.38.

12. F. Arya, J. Bouquant, and J. Chuche, **Tetrahedron Lett.**, 1986, **27**, 1913.

13. A. Smith, J.G.J. Kok, and H.W. Geluk, **J. Chem. Soc. Chem. Commun.**, 1975, 513.

14. S.Y. Lee, Y.S. Kulkarni, B.W. Burbaum, M.I. Johnston, and B.B. Snidder, **J. Org. Chem.**, 1988, **53**, 1848.

15. W.T. Brady, A.P. Marchand, Y.F. Giang, and A.H. Wu, **Synthesis**, 1987, 395.

16. O.L. Chapmann and J.D. Lassilen, **J. Am. Chem. Soc.**, 1968, **90**, 2449.

17. B.B. Snidder, **Chem. Rev.**, 1988, **88**, 793.

18(a) H. Staudinger, **Chem. Ber.**, 1917, **50**, 1035.

(b) H. Staudinger and H.W. Klever, **Chem. Ber.**, 1907, **40**, 1149.

(c)H. Staudinger, **Ann.**, 1907, **356**, 51.

19. T.Kato, T. Kitagawa, and Y. Yamamato, **Yakugaku Zasshe**, 1963, **83**, 267; **Chem. Abstr.**, 1963, **59**, 6371.

20. R.D. Kimbrough, (Jr); **J. Org. Chem.**, 1964, **29**, 1242.

21. O. Wollenberg, **Chem. Ber.**, 1934, **67**, 1675.

22. S.A. Procter and G.A. Taylor, **J. Chem. Soc. Chem. Commun.**, 1965, 569.

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

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

25. A.O. Fitton, J.R. Frost, P.G. Houton, and H. Suschitzky, **J. Chem. Soc. Perkin Trans.I**, 1977, 1450.

26. T. Kato, T. Chiba and S. Tanaka, **Chem. Pharm. Bull. Tokyo**, 1974, **22**, 744.

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

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

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

30. L.S. Povarov, **Chem. Abstr.**, 1963, **59**, 7489; 1964, **60**, 5451; 1964, **61**, 16057, 1965; **62**, 7723; 14624.

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

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

33. M. Sakamoto, K. Miyazawa, Y. Ishihara, and Y. Tomimatsu, **Chem. Pharm. Bull. Tokyo**, 1974, **22**, 1419.

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

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

36. D.G. Farnum, J.R. Johnson, R.F. Hess, T.B. Marshall, and B. Wester, **J. Am. Chem. Soc.**, 1965, **87**, 5191.

37. C.V. Asokan, H. Ila, and H. Junjappa, **Tetrahedron Lett.**, 1985, 1087.

38. S.N. Mazumdar, I. Ibnusaud, and M.P. Mahajan, **Tetrahedron Lett.**, 1986, 5875.

39. P. Luthardt and E. Wurthwein, **Tetrahedron Lett.**, 1988, **29**, 921.

40. M.A. Pricas, F. Serratosa and E. Valenti, **J. Chem. Soc. Perkin Trans. II**, 1987, 151.

41. M.J.S. Dewar, E.G. Zoebisch, E.F. Healy, and J.J.P. stewart, **J. Am. Chem. Soc.**, 1985, **107**, 3902.

42. R.L. Shriner, **Organic Reactions**, 1942, **1**, 1.

43. N.W. Rathe, **Organic Reactions**, 1975, **22**, 423.

44. J. Dekker, J. Boersma, and C.J.M. Vander Kark, **J. Chem. Soc. Chem. Commun.**, 1988, 533.

45. T. Harada and T. Mukaiyamma, **Chemistry Lett.**, 1982, 161.

46. F. Orsini, F. Pelizzoni, and G. Ricca, **Tetrahedron Lett.**, 1982, **29**, 3945.

47. P.A. Cornforth, A.E. Opara, and G. Read, **J. Chem. Soc.**, 1969, **C**, 2799.

48. J.W. Frankenfeld and J.J. Werner, **J. Org. Chem.**, 1968, **34**, 3689.

49. E.H. Charlesworth and P. Charlson, **Can. J. Chem.**, 1968, **46**, 1843.

50. A. Dutta, S. Apparao, H. Ila, and H. Junjappa, **Tetrahedron Lett.**, 1985, 169.

51. A. Dutta, H. Ila and H. Junjappa, **Tetrahedron Lett.**, 1988, 497.

52. W.W. Epstein and A.C. Sonntag, **Tetrahedron Lett.**, 1966, 791.

53. H.B. Kagan and Y.H. Suen, **Bull. Chem. Soc. Chim. France**, 1966, 1819.

54. E. Muller in Houben-Weyl, **Methoden der Organische Chemie**, Georg Thieme Verlag, Stuttgart, Vol.XIII/2a, 1973, p.796.

55. P.A. Bar, P. Marcinal, and A.M. Lefebvre, **Bull. Soc. Chim. France**, 1972, 2484.

56. P.F. Dardoize, J.L. Moreau, and M. Gaudemar, **Bull. Soc. Chim. France**, 1972, 3841; 1973, 1668.

57. P.F. Dardoize and M. Gaudemar, **Bull. Soc. Chim. France,** 1974, 939.

58. J.C. Dubois, J.P. Guette, and H.B. Kagan, **Bull. Soc. Chem. France,** 1969. 3008.

59. E. Mullerin Houben-Weyl, **Methoden der Organische Chemie,** Georg Thieme Verlag, Stuttgart, Vol.XIII/2a, 1973, p.826-827.

60. C. Gandolfi, G. Doria, M. Amendol, and E. Dradi, **Tetrahedron Lett.,** 1970, 3923.

61. A. Dutta, H. Ila, and H. Junjappa, **Synthesis,** 1988, 248.

62. S. Chaudhury, A. Debroy, and M.P. Mahajan, **Can. J. Chem.,** 1982, 60, 1122.

63. **Organic Synthesis Coll. Vol.III,** 1955, p-735.

64. Z. Arnold and M. Kornilov, **Collection, Czech. Chem. Commun.,** 1964, **29,** 645; **Chem. Abstr.** 1964, **60,** 7909a.

65. Y. Lin, S.A. Lang(Jr), and S.R. Petty, **J. Org. Chem.,** 1980, **45,** 2885.

66. R. Huisgen, J. Sauer, and M. Seidel, **Chem. Ber.,** 1960, **93,** 2885.

67. J.C. Brindley, J.M. Caldwell, G.D. Meakins, S.J. Plackett, and S.J. Price, **J. Chem. Soc. Perkin Trans.I,** 1987, 1153.

68. C.L. Stevenes and J.C. French, **J. Am. Chem. Soc.,** 1953, **75**, 657.

69. I. Smith and H.H. Hoehn, **Organic Synthesis Coll. Vol.III**, 1955, p.356.

CHAPTER - III

CHAPTER-III

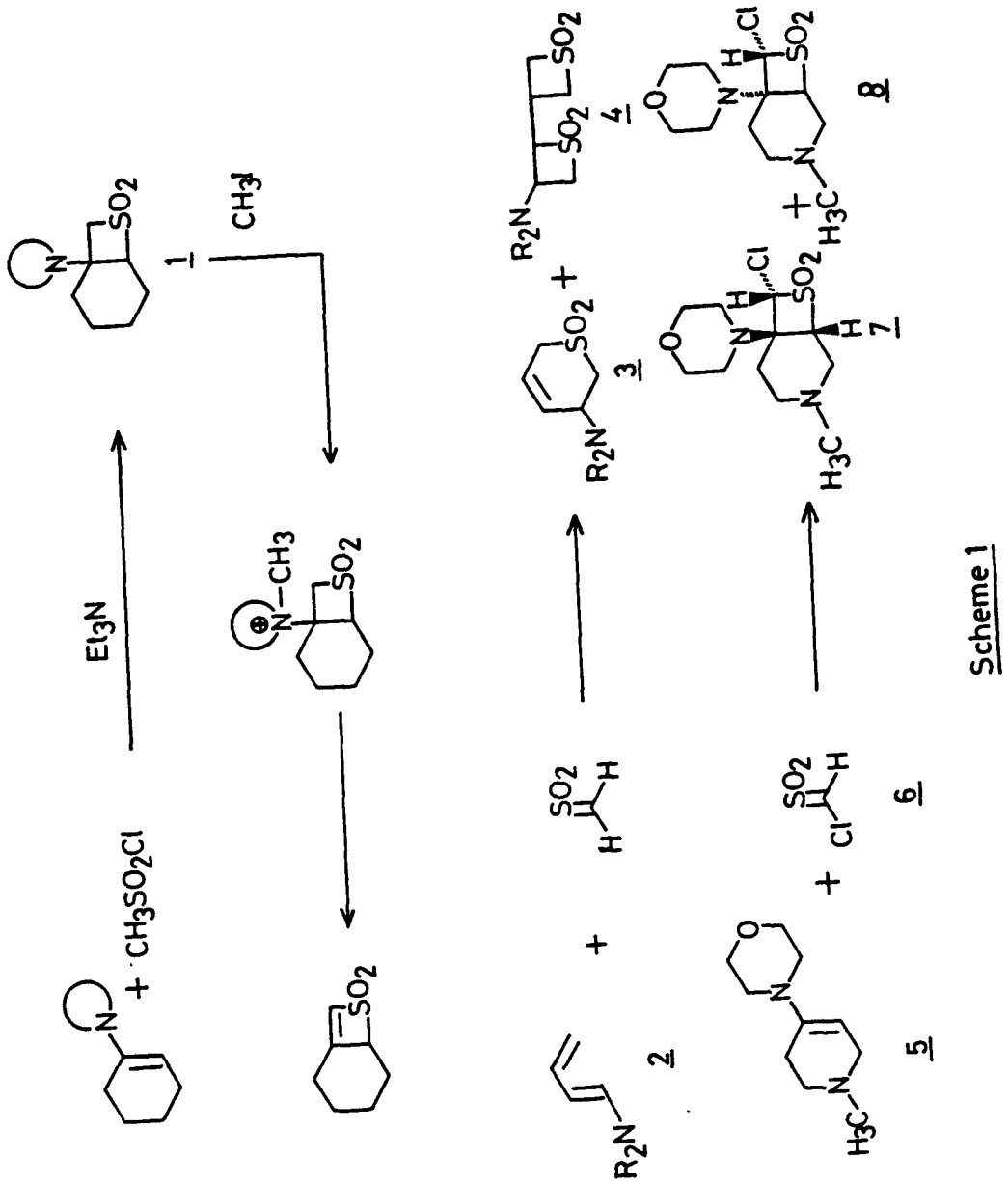
CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH SULPHENE

III.1 INTRODUCTION

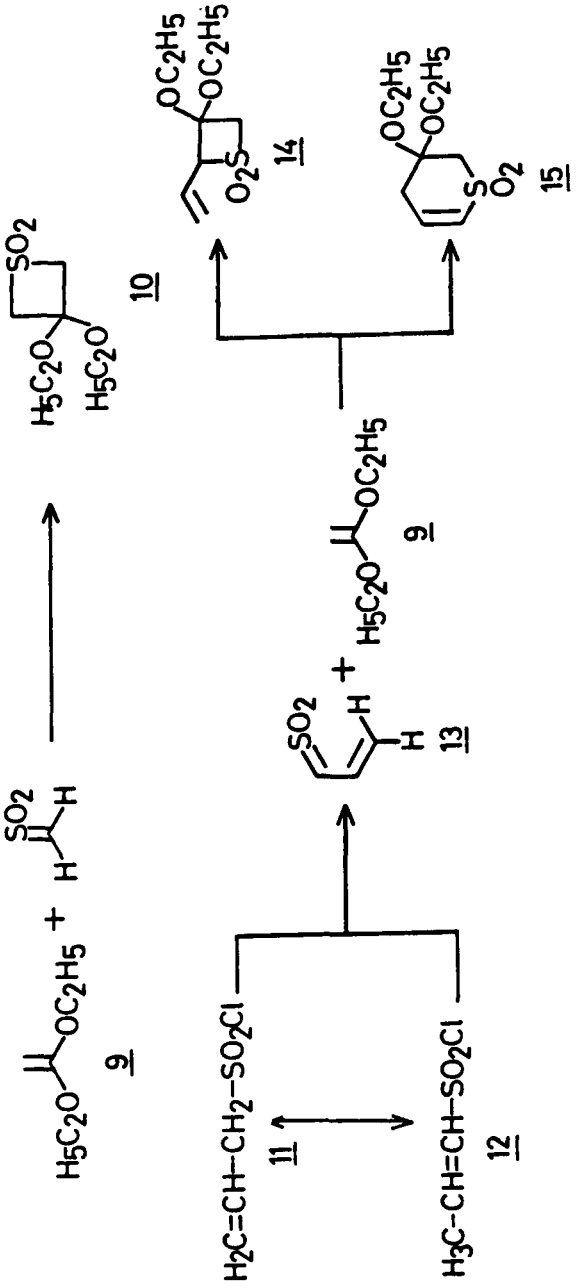
Considering the general reactivity scale of hetero-cumulenes, the sulphene has been found to be the most reactive of all heterocumulenes (viz. sulphene, carbonsuboxide, ketenes, isocyanates, carbodiimides etc.). The generation of sulphene can be realised by either reacting suitable alkane/alkene sulphonylchloride with triethylamine[1] in an inert solvent viz. diethyl ether, benzene, dioxane, chloroform etc. or by reacting diazoalkane with sulphur-dioxide[2]. Although the sulphenes have not been isolated, but their intermediacy has been well established[3,4]. The report concerning the preparation of crystalline sulphene[5]

with mesylchloride resulted in 5-dialkylamino-1-thiacyclohex-3-ene-1,1-dioxide(3) and 3-dialkylamino-2,3-bis(thietene)-1,1,1',1'-tetroxide[16](4) (Scheme-1). Chlorosulphene, generated similarly from chloromethylsulphonylchloride, has also been shown to undergo (2+2) cycloaddition reactions with a variety of morpholine enamines[17]. Generally only one of the two possible isomers have been isolated, except incase of the reaction of 4-morpholino-1,2, 5,6-tetrahydropyridine(5) and chlorosulphene(6) where both possible isomers 1 and 8 have been isolated (scheme-1).

True and co-workers[18] reported the facile 1,2-cycloaddition of sulphene to ketene diethylacetal (9) resulting in good yields of thietene-1,1-dioxide(10) (scheme-2). The reaction was extended to a variety of sulphenes, except in cases of allyl-(11) and propanesulphonylchloride (12) where the generated sulphene (13) gave both 1,2-cycloadduct (14) and 1,4-cycloadduct (15). The preference for 1,2-addition over 1,4-addition was indicated by an approximate ratio of 7:1 in favour of 15 (scheme-2). Alkanesulphonyl chlorides having α-hydrogen such as ethane, n-butane, cyclopentane, iso-propane and phenylethanesulphonylchloride failed to undergo cycloaddition reactions with ketene diethylacetal[18]. Reaction of methanesulphonylchloride with two equivalents of ketene diethylacetal, in the absence of triethylamine, afforded (2+2+2) cycloadduct 3,5-diethoxy-



Scheme 1

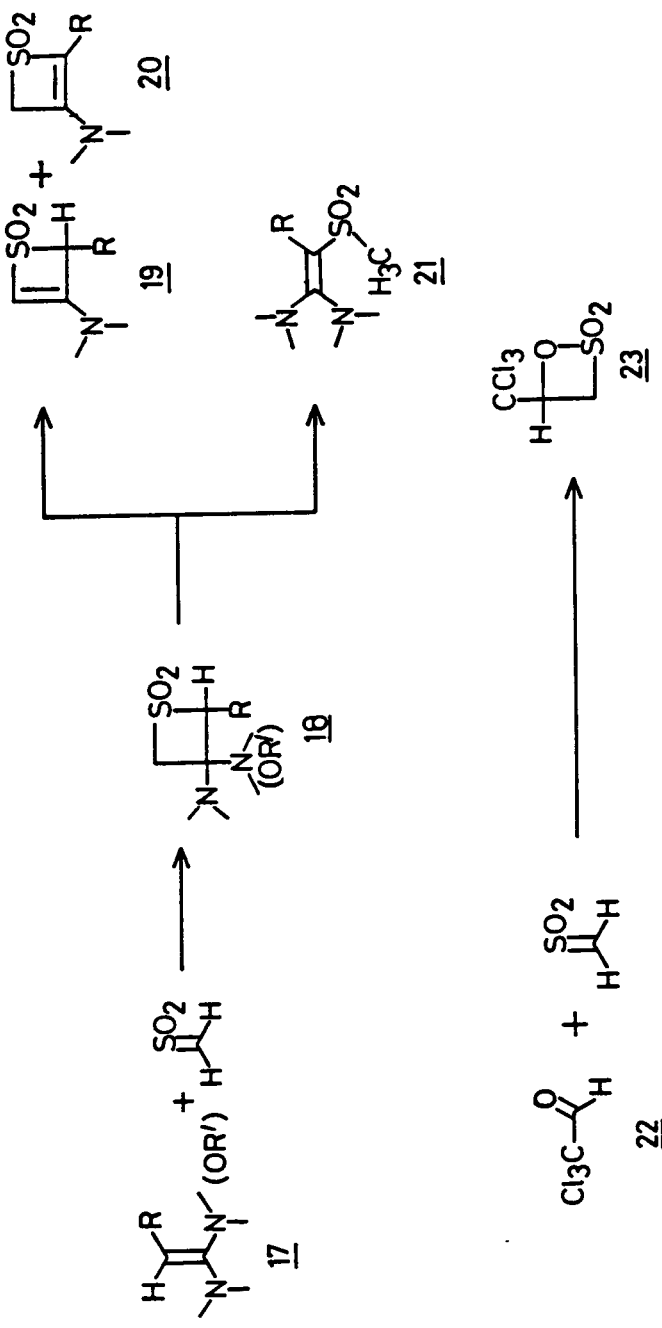


Scheme 2

2,4-thiacyclohexadiene-1,1-dioxide(16) (scheme-2).

Ketene-O,N-acetals and ketene aminals (N,N-acetals) (17) reacted with sulphene to afford either (2+2) cycloadduct (19 and 20) or linear (21) adducts[19-22]. The initial cycloadduct (18), by elimination of an alcohol or amine molecule resulted in the formation of isomeric 3-dialkylamino-thiete-1,1-dioxide 19 and 20 and by ring distribution was often found to be solvent dependant, for example, in chloroform, reactions afforded linear adducts 21 and in tetrahydrofuran/diethylether cyclic adducts were obtained preferentially[19-22]. The polarised carbonyl compounds such as chloral (22) reacts with sulphene to afford δ-sultone (23)[23] (scheme-3).

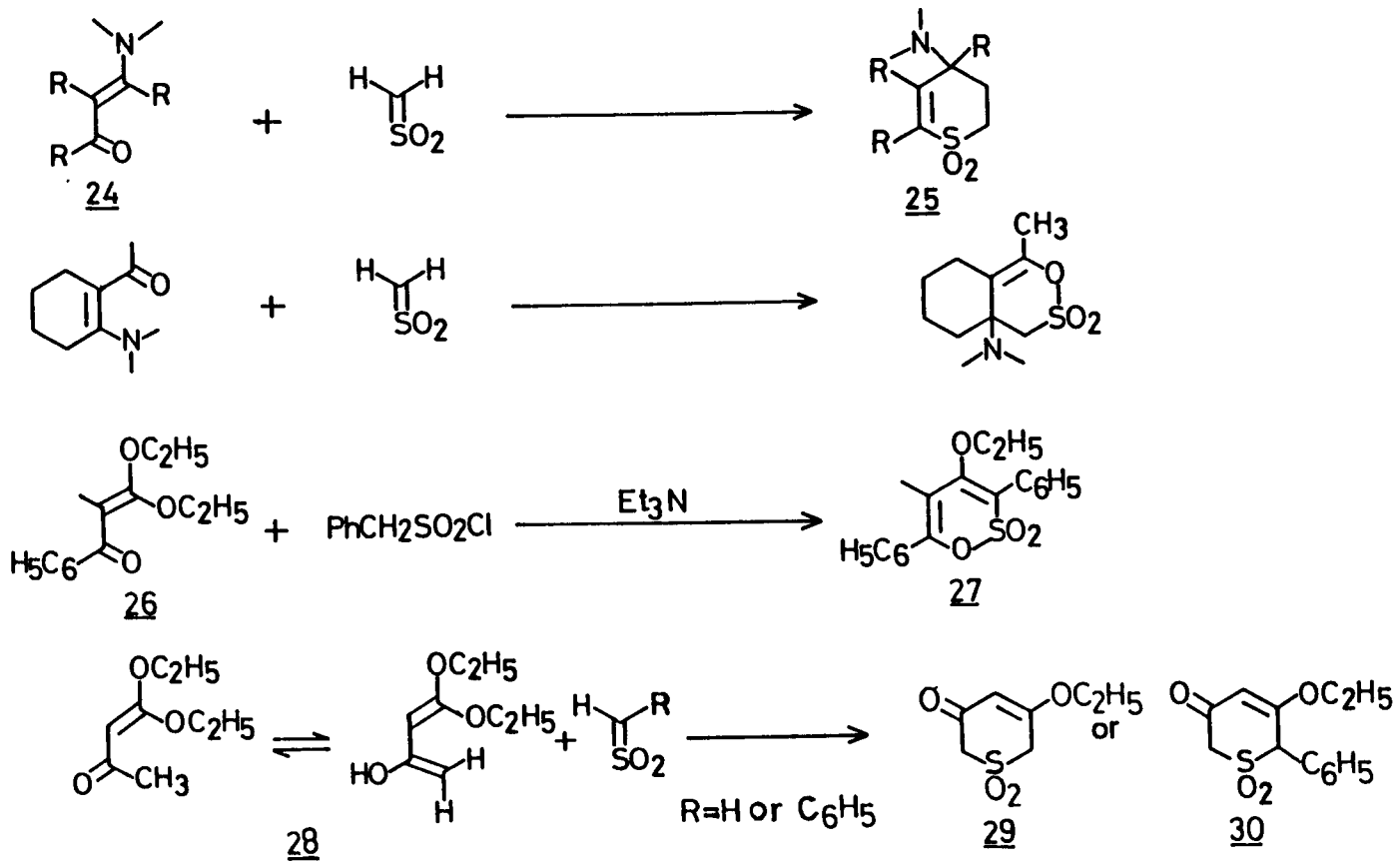
In addition to the well documented 1,2-cycloaddition mode, the sulphenes are known to undergo Diels-Alder cycloaddition reactions with conjugated systems. The vinylgous carboxamide (24) reacted with sulphene to give the cyclic sulphones (25) and was the first example of sulphene behaving as a "dienophile" in a (4+2) cycloaddition reaction[24]. Treatment of phenylmethanesulphonylchloride with benzoylketene diethylacetal (26) and triethylamine in ether gave rise to an unsaturated δ-sultone (27)[25]. However, acetylketenediethylacetal(28) was shown to behave quite differently i.e. it formed cyclic ketosulphones[25] (29) and (30) with methanesulphonylchloride and phenyl methanesulphonylchlo-



Scheme 3

was later on disproved by J.F. King.[6] As only a limited number of sulphenes have been generated in situ, it could be visualised that these are stable species which allow their reactions under suitable conditions, certain aldo[7]- and ketosulphenes[8], for example, have been reported to be stable upto their melting points. While sulphenes have not been isolated, their cycloaddition reactions to a large variety of reactive olefins have been reported and are briefly summarised below.

The cycloaddition reactions of enamines with sulphene have been extensively investigated. The reaction was simultaneously discovered by Stork and Borowitz[9], and by Opitz and Adolph[10], who obtained aminothietene sulphenes (1) from sulphene and enamine (Scheme-1). Borowitz clearly demonstrated that, a reactive intermediate, sulphene is indeed involved in this reaction[9]. The general nature of enamine-sulphene cycloaddition has been demonstrated by the use of various linear and cyclic enamines in these reactions[11-15]. Primary sulphonylchlorides have been found to react better than secondary sulphonylchlorides[12], however, the cycloadducts of secondary sulphonylchlorides and enamines were obtained in excellant yields at -40°C using acetonitrile as inert solvent[13]. Dialkylaminobutadienes have been shown to react with mesylchloride affording 1,2- and 1,4-cycloadducts. Thus, the reactions of 1-dialkylamino-1,3-butadiene(2)



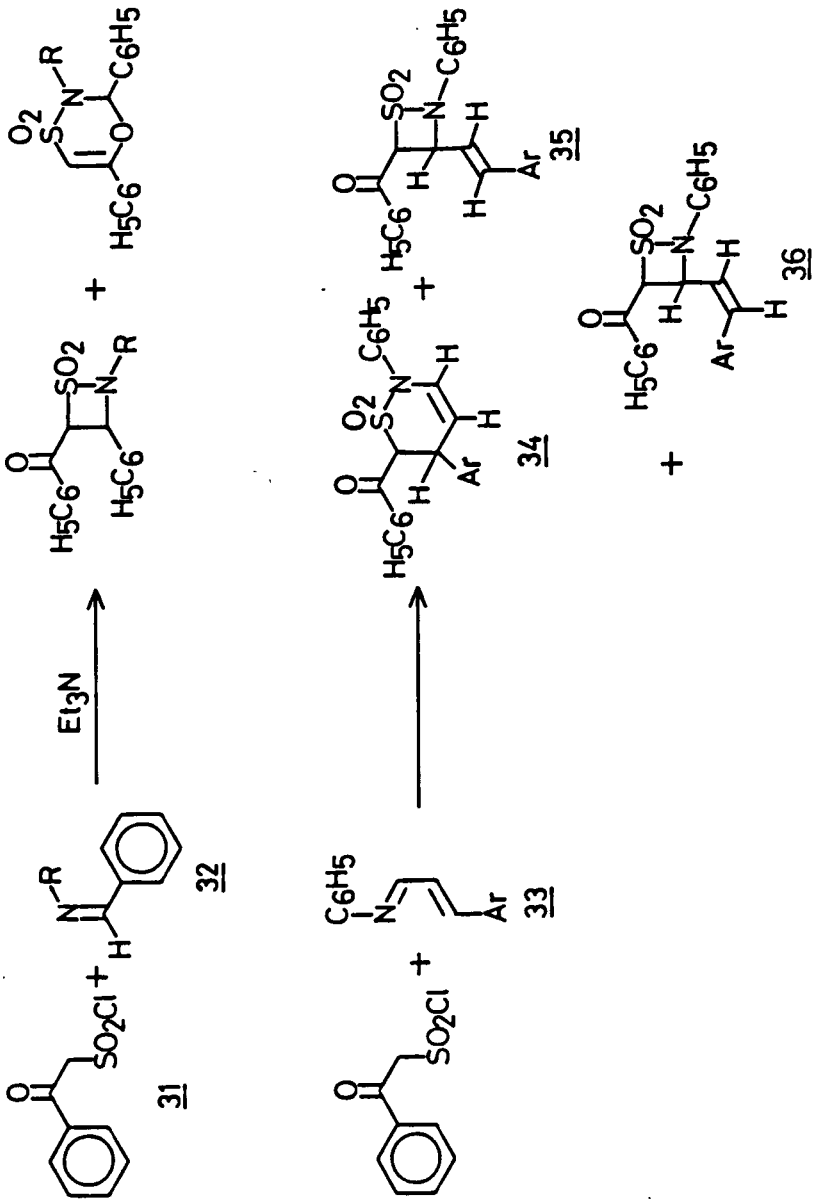
Scheme 4

ride, respectively (scheme-4).

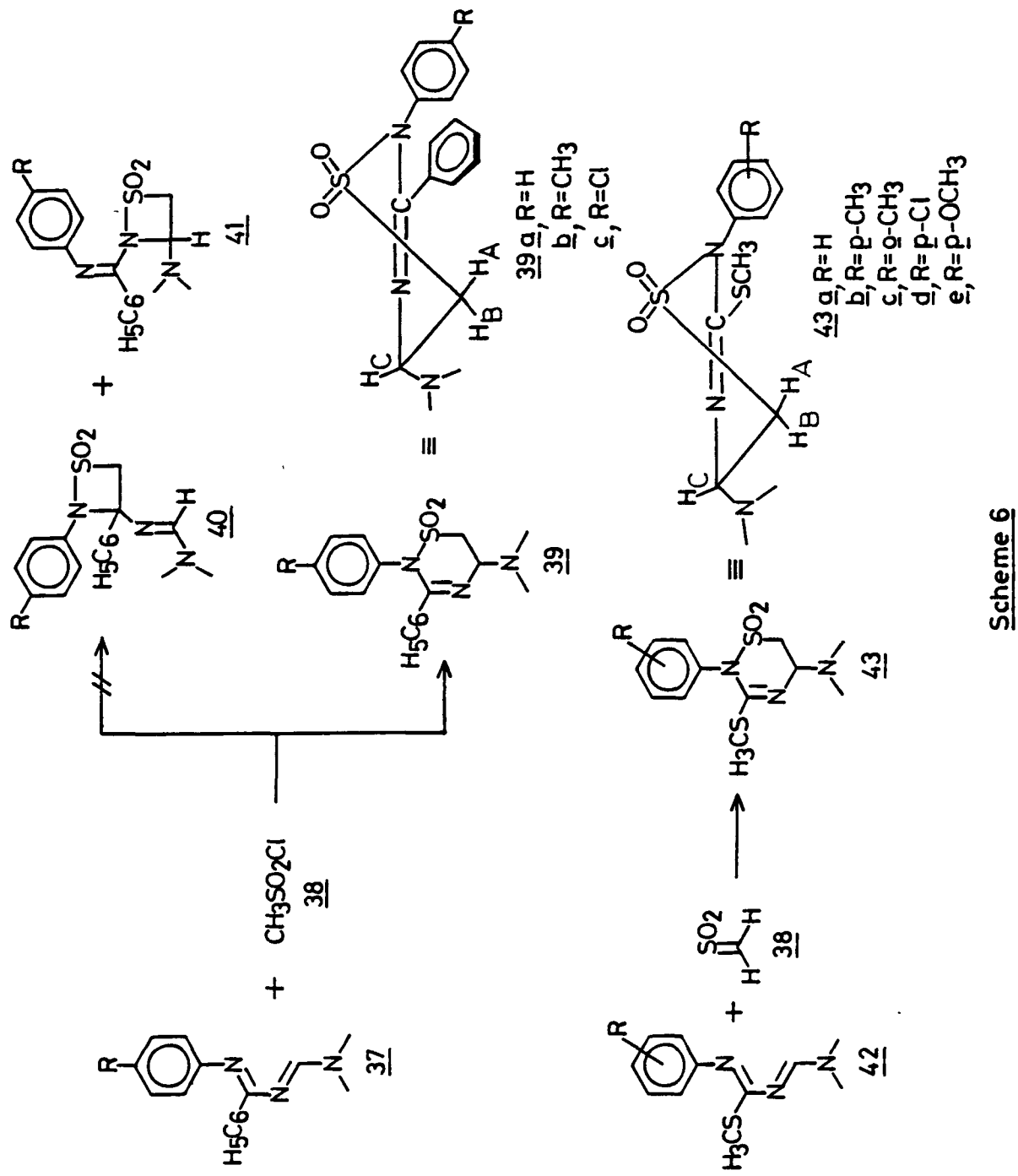
It has been reported that highly reactive heterodienophile, simple sulphene, do not add to C=N double bond[26]. On the other hand benzoylsulphene (31) is reported to react with anils(32) and depending on the nature of substituents on anils (4+2) and / (2+2) cycloadducts were isolated[27,28]. This reaction was extended further to α,β-unsaturated anils (33) which resulted in (2+2) cycloadducts 35 and 36, and (4+2) cycloadduct 34 (scheme-5). We have investigated, here, the reactions of 1,3-diaza-1,3-butadienes with simple sulphene especially with a view to examine the cycloaddition pathway followed and nature of products formed in these cases.

III.2 RESULTS AND DISCUSSIONS

Thus, the treatment of 4-dimethylamino-1,2-diphenyl-1,3-diaza-1,3-butadiene(37a) with methanesulphonylchloride (38), in presence of triethylamine, in dry benzene (5-10°C) by careful work up of the reaction mixture resulted in good yield (64%) of a crystalline product (39a). The elemental analysis and molecular weight (m/z 329, mass spectrometry) of the product is consistent with 1:1 adduct of sulphene and 37a. On this basis, the product could be assigned any one of the three possible structures 39, 40 or 41 (scheme-6). The structure 41, a (2+2) adduct formed



Scheme 5



Scheme 6

by the addition of sulphene to 3,4-C=N double bond of 1,3 -diaza-butadiene, may be ruled out since in all reported cases of cycloaddition of 1,3-diaza-1,3-butadienes the initial nucleophilic attack involves N-1 of 1,3-diaza-1,3-butadienes[29-31]. The structure 10, another (2+2) cycloadduct formed by 1,2- addition of carbon-nitrogen double bond of 1,3-diaza-1,3- butadiene to sulphene was ruled out on the basis of ^{1}H n.m.r. spectral data. Thus, the structure of the compound 39a was assigned as 5-dimethylamino-2,3 -diphenyl-5,6-dihydro- 1,2,4-thiadiazine-1,1-dioxide, a (4+2) cycloadduct of 37a and 38, exclusively on the basis of ^{1}H n.m.r. data.

The i.r. spectrum of the cycloadduct showed the characteristic absorption frequencies at 1620cm^{-1} (νC=N), 1300 and 1140cm^{-1} (νSO$_2$). The ^{1}H n.m.r spectrum ($CDCl_3$) showed a singlet at δ2.50(6H), two quartets at δ3.03-3.23 (1H) and δ3.26-3.46(1H), a doublet of doublet at δ 4.86-5.06(1H), and multiplets at δ7.00-7.30(8H) and δ7.46-7.60(2H). The singlet at δ2.50(6H) was assigned to $-N(CH_3)_2$ protons, the quartets, which were expected because protons H_A and H_B were split by each other as well as by H_C, around δ 3.03 -3.23 (J_{AB}=12.00Hz, J_{AC}=10.00Hz) and δ 3.26-3.476 (J_{AB}= 12.00Hz, J_{BC}=4.00Hz) were assigned to non-equivalent protons H_A an H_B, respectively. The doublet of doublet, expected

because of the splitting of H_C by both H_A and H_B at δ4.86-5.06 (J_{AC}=10.00Hz, J_{BC}=4.00Hz) could be assigned to methine proton H_C and the aromatic proton appeared as a multiplets at δ7.00-7.30(8H) and δ 7.46-7.60 (2H). These spectral assignments were in conformity with the literature data on similar systems[28]. In the ^1H n.m.r. spectrum, the presence of two quartets and one doublet of doublet, and the absence of a olefinic proton clearly ruled out the structure 40, for the product which has been characterised as 5-dimethylamino-2,3-diphenyl-5,6-dihydro-1,2,4- thiadiazine-1,1-dioxide(39a). The reaction has been generalised by carrying out the reactions of other substituted 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadines with simple sulphene. All these reactions were found to follow (4+2) cycloaddition pathway resulting thereby in very good yields (60-80%) of hitherto unknown 2-aryl-5- dimethylamino-3-phenyl-5,6-dihydro-1,2,4-thiadiazin -1,1- dioxide(39b-c). The analytical and spectral data for products listed in the experimental section are in full conformity with the assigned structures.

Further to our studies it was thought worthwhile to examine the reactions of 1,3-diaza-1,3-butadines having another polarising function at the second position especially with a view to understand the nature of the cycloaddition pathway followed in these cases. Thus, the reaction of

4-dimethylamino-1-phenyl-2-thiomethyl-1,3-diaza-1,3-butadiene (42a) with sulphene in dry benzene at 5-10°C gave very good yield (80%) of a white crystalline compound. The elemental analysis and molecular weight (m/z,299, mass spectrometry) indicated the molecular formula $C_{12}H_{17}N_3O_2S_2$ for the product, which has been characterised as previously unknown 5-dimethylamino-2-phenyl-3-thiomethyl-5,6-dihydro-1,2,4-thiadiazine-1,1-dioxide (43a) on the basis of spectral evidences.

The i.r. spectrum of 43a showed absorption bands at 1650cm^{-1} (νC=N), 1320 and 1140cm^{-1} (νSO_2). Its ^{1}H n.m.r. spectrum in $CDCl_3$ exhibited a singlet at δ 2.20(3H) for $-SCH_3$, another singlet at δ2.38(6H) due to $-N(CH_3)_2$ protons, two distinct quartets at δ3.03-3.26(H_A, J_{AB}=12.00Hz; J_{AC}= 10.00Hz) and δ 3.40-3.56(H_B,J_{AB}=12.00Hz; J_{BC}=4.00Hz) due to two non- equivalent-CH_2-protons, a doublet of doublet at δ4.73-4.96 (H_C, J_{AC}=10.00Hz, J_{BC}=4.00Hz) due to methine proton H_C and a multiplet around δ7.30-7.50(5H) for aromatic protons. The above spectral information clearly ruled out any (2+2) cycloadduct and confirmed the product to be (4+2) cycloadduct 43. This reaction was also extended to various substituents 1-aryl-4-dimethylamino-2-thiomethyl,1,3-diaza -1,3- butadienes (42b-e) leading to very good yields (82-94%) of 2-aryl-5-dimethyl amino-3-thiomethyl-5,6-dihydro-1,2,4-thiadiazin -1,1-dioxide (43b-e). All these products have

been characterised on the basis of analytical and spectral data described in experimental section. It may be mentioned here that the reaction of 1,3-diazabutadienes (42) with sulphene, as compared to the reactions of 37, have been found to be much more neat and result in better yields of products. The products 39 and 43 did not undergo elimination of dimethylamine even in refluxing benzene in presence of triethylamine. The reactions of 1,3-diazabutadienes 37 and 42 with sulphene constitute the first few example of addition of simple sulphene to carbon-nitrogen double bond. Also, it may be noted that these reactions resulted selectively in (4+2) cycloadducts in good yields.

III.3 EXPERIMENTAL

General conditions are same as described in Chapter II.

Starting materials

1-Aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes (37a-c) and 1-aryl-4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadienes (42a-e) were prepared as described in the earlier chapter. Methanesulphonylchloride was freshly distilled before use. Triethylamine and thiophene free benzene were dried over sodium wire.

Reactions of 1,3-diaza-1,3-butadienes (37 and 42) with sulphene (38); General Procedure: A solution of methane

sulphonyl chloride (2.4 mmole) in dry benzene (10 ml) was added to an ice cooled (5-10°C) stirred benzene solution (20 ml) of 1,3-diaza-1,3-butadiene (2 mmole) and triethylamine (4 mmole). After the addition of methanesulphonyl chloride (1 h) was complete. The reaction mixture was stirred for a further period of 30 min at the same temperature. It was then washed with cold water, saturated sodium hydrogen carbonate followed again by water, and finally dried over anhydrous magnesium sulphate. The crude product so obtained after removal of solvent under reduced pressure, was recrystallised from a mixture(1:1) of benzene and hexane. The analytical and spectral data of the compounds are given below.

5-Dimethylamino-2,3-diphenyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide; (39a): white solid; yield, 64%, m.p. 121-2°C. (Found: C,62.47; H,5.31; N,12.75. $C_{17}H_{19}N_3O_2S$ requires C,62.00; H,5.77; N,12.76). ν_{max}(KBr): 1620cm^{-1}(C=N), 1300 and 1140cm^{-1}(SO_2). δ_H($CDCl_3$): 2.53(s,6H,-N(CH_3)$_2$); 3.05-3.25 (q,1H,H_A,J_{AC}=10.00Hz and J_{AB}=12.00Hz), 3.26-3.46(q,1H,H_B,J_{AB} = 12.00Hz and J_{BC}=4.00Hz); 4.86-5.06(dd,1H,H_C,J_{AC}=10.00 Hz. and J_{BC}=4.00Hz), 7.00-7.30(m,8H,H_D,arom) and 7.46-7.63 (m,2H, H_E,arom). M^+329.

5-Dimethylamino-3-phenyl-2-p-tolyl-5,6-dihydro-1,2,4-thia-

diazin-1,1-dioxide; (39b): white solid; yield, 80%, m.p. 161-2°C. (Found: C,63.24; H,6.14; N,12.39.$C_{18}H_{21}N_3O_2S$ requires C,62.97; H,6.12; N,12.24).ν_{max}(KBr): 1620cm^{-1}(C=N), 1300 and 1140cm^{-1}(SO_2).δ_H($CDCl_3$):2.20(s,3H,$-CH_3$); 2.50(s,6H, $-N(CH_3)_2$); 3.10-3.23(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=9.00Hz); 3.33-3.53(q,1H,H_B,J_{AB}=12.00Hz and J_{BC}=4.00Hz); 4.83-5.03 (dd,1H,H_C,J_{AC}=9.00Hz and J_{BC}=4.00Hz); 6.93-7.26(m,7H,H_D, arom) and 7.46-7.53(m,2H,H_E,arom).M^+343.

2-p-Chlorophenyl-5-dimethylamino-3-phenyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide;(39c):white solid; yield, 60%; m.p. 115-6°C. (Found: C,56.37; H,4.98; N,11.60.$C_{17}H_{18}ClN_3O_2S$ requires C,56.12; H,4.95; N,11.55).ν_{max}(KBr): 1630cm^{-1}(C=N), 1300 and 1130cm^{-1}(SO_2).δ_H($CDCl_3$): 2.50(s,6H,$-N(CH_3)_2$); 3.16-3.36(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=9.00Hz) 3.40-3.58(q,1H, H_B,J_{AB}=12.00Hz and J_{BC}=4.00Hz), 4.85-5.05(dd,1H,H_C,J_{AC}= 9.00Hz and J_{BC}=4.00Hz), 7.00-7.30(m,7H,H_D,arom) and 7.43-7.63(m,2H,H_E,arom).M^+363.

5-Dimethylamino-2-phenyl-3-thiomethyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide; (43a): white solid; yield, 80%, m.p. 111-2°C. (Found: C,49.12; H,5.69; N,14.14.$C_{12}H_{17}N_3O_2S_2$ requires C,48.16; H,5.68; N,14.04).ν_{max}(KBr): 1600cm^{-1}(C=N), 1320 and 1140cm^{-1}(SO_2).δ_H($CDCl_3$):2.20(s,3H,$-SCH_3$); 2.38(s,6H, $-N(CH_3)_2$); 3.03-3.26(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=10.00Hz); 3.40-3.56(q,1H,H_B,J_{AB}=12.00 Hz and J_{BC}=4.00Hz); 4.73-4.96

(dd,1H,H_C,J_{AC}=10.00Hz and J_{BC}=4.00Hz) and 7.30-7.50(m,5H, arom).M^+299.

5-Dimethylamino-3-thiomethyl-2-p-tolyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide;(43b): white solid; yield, 94%; m.p. 161-3°C. (Found: C,49.96; H,6.68; N,13.51. $C_{13}H_{19}N_3O_2S_2$ requires C,49.84; H,6.07; N,13.41).ν_{max}(KBr): 1600cm^{-1}(C=N), 1320 and 1120cm^{-1}(SO_2).δ_H($CDCl_3$):2.20(s,6H,-SCH_3 and -CH_3); 2.36(s,6H,-$N(CH_3)_2$); 3.06-3.23(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=10.00Hz); 3.38-3.50(q,1H,H_B,J_{AB}=12.00Hz and J_{BC}=4.00Hz); 4.73-4.90(dd,1H,H_C,J_{AC}=10.00Hz and J_{BC}=4.00Hz) and 7.20-7.34 (m,4H,arom).M^+313.

5-Dimethylamino-3-thiomethyl-2-o-tolyl-5,6-dihydro-1,2,4-thiadiazine-1,1-dioxide;(43c): white solid; yield, 86%; m.p. 86-8°C.(Found:C,50,06; H,6.09; N,13.53.$C_{13}H_{19}N_3O_2S_2$ requires C,49.84; H,6.07; N,13.41).ν_{max}(KBr): 1620cm^{-1}(C=N), 1330 and 1130cm^{-1}(SO_2). δ_H($CDCl_3$):2.20(s,6H,-SCH_3 and CH_3); 2.40(s,6H,-$N(CH_3)_2$); 3.06-3.23(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=10.00Hz); 3.38-3.50(q,1H,H_B,J_{AB}=10.00Hz and J_{BC}=4.00Hz); 4.76-4.96(dd,1H,H_C,J_{AC}=10.00Hz and J_{BC}=4.00Hz) and 7.20-7.35 (m,4H,arom).M^+313.

2-p-Chlorophenyl-5-dimethylamino-3-thiomethyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide;(43d): white solid; yield, 90%: m.p. 109-10°C. (Found:C,44.00; H,4.83; N,12.42.

$C_{12}H_{16}ClN_3O_2S_2$ requires C,43.17; H,4.79; N,12.59). ν_{max}(KBr): 1620cm^{-1}(C=N), 1340 and 1140cm^{-1}(SO_2). δ_H($CDCl_3$):2.23(s, 3H,-SCH_3); 2.40(s,6H,-$N(CH_3)_2$); 3.16-3.40(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=9.00Hz), 3.46-3.66(q,1H,H_B,J_{AB}=12.00Hz and J_{BC}= 4.00Hz); 3.75-3.95(dd,1H,H_C,J_{AC}=9.00Hz and J_{BC}=4.00Hz) and 7.20-7.50(m,4H,arom).

4-Dimethylamino-2-p-methoxyphenyl-3-thiomethyl-5,6-dihydro-1,2,4-thiadiazin-1,1-dioxide;(43e): white solid; yield, 82%; m.p. 84-6°C. (Found:C,48.47; H,5.79; N,12.76.$C_{13}H_{19}N_3O_3S_2$ requires C,47.41; H,5.77; N,12.76). ν_{max}(KBr):1600cm^{-1}(C=N), 1340 and 1140cm^{-1}(SO_2). δ_H($CDCl_3$): 2.26(s,3H,-SCH_3); 2.43(s,6H, -$N(CH_3)_2$); 3.20-3.43(q,1H,H_A,J_{AB}=12.00Hz and J_{AC}=9.00Hz); 3.46-3.66(q,1H,H_B,J_{AB}=12.00Hz and J_{BC}=4.00Hz); 3.80(s,3H, -OCH_3); 4.80-4.96(dd,1H,H_C,J_{AC}=9.00Hz and J_{BC}=4.00Hz); 6.86-6.96(m,2H,arom) and 7.20-7.33(m,2H,arom). M^+329.

REFERENCES

1. G. Hesse and S. Majumdar, **Chem. Ber.**, 1960, **93**, 1129.

2. L.V. Vargha and E. Kovas, **Chem. Ber.**, 1942, **75**, 794.

3. J.F. King and T. Durst, **J. Am. Chem. Soc.**, 1964, **86**, 287; 1965, **87**. 6684.

4. W.E. Truce, J. Campbell, and J.R. Norell, **J. Am. Chem. Soc.**, 1964, **86**, 288.

5. A. Locher and H.E. Fiertz, **Helv. Chim. Acta.**, 1927, **10**, 642.

6. J.F. King, P. de Mayo, E. Morkved, A.B.M.A. Sattar, and A. Stoessel, **Can. J. Chem.**, 1963, **41**, 100.

7. J. Strating, L. Thijs, and B. Zwanenburg, **Rec. Trav. Chim.**, 1964, **83**, 631.

8. J. Strating, L. Thijs ,and B. Zwanenburg, **Tetrahedron Lett.**, 1965, 3977.

9. G.Stork and I.J. Borowitz, **J. Am. Chem. Soc.**, 1962, **64**, 313.

10. G. Opitz and H. Adolph, **Angew. Chem.**, 1962, **74**, 77.

11. I.J. Borowitz, **J. Am. Chem. Soc.**, 1964, **86**, 1146.

12. G. Opitz, H. Schemp, and H. Adolph, **Ann.**, 1965, **684**, 92.

13. G. Opitz and K. Reith, **Tetrahedron Lett.**, 1965, 3977.

14. L.A. Paquette, **J. Org. Chem.**, 1964, **29**, 2851.

15. G. Stork and I.J. Borowitz, **J. Am. Chem. Soc.**, 1962, **84**, 313.

16. G. Opitz and F. Schwensberg, **Angew. Chem. Int. Ed. Engl.**, 1965, **4**, 786.

17. L.A. Paquette, **J. Org. Chem.**, 1964, **29**, 2854.

18. W.E. Truce, J.J. Breitter, D.J. Abraham, and J.R. Novell, **J. Am. Chem. Soc.**, 1962, **84**, 3030.

19. R.H. Hasck, P.G. Gott, R.H. Meen, and J.C. Martin, **J. Org. Chem.**, 1963, **28**, 2496.

20. R.H. Hasek, R.H. Meen, and J.C. Martin, **J. Org. Chem.**, 1965, **30**, 1495.

21. G. Opitz and H. Schemp, **Ann.**, 1965, **684**, 103.

22. W.E. Truce and P.N. Son, **J. Org. Chem.**, 1965, **30**, 71.

23. D. Bromann and R. Wegler, **Chem. Ber.**, 1960, **99**, 1245.

24. G. Optiz and E. Tempel, **Angew. Chem.**, 1964, **76**, 922.

25. W.E. Truce, D.J. Abraham, and P.N. Son, **J. Org. Chem.**, 1967, **32**, 990.

26. H. Ulrich, **Cycloaddition reactions of Heterocumulenes**, Academic Press, New York-London, 1967, p.286.

27. O. Tsuge and S. Iwanami, **Bull. Chem. Soc. Japan**, 1970, **43**, 3543.

28. O. Tsuge and S. Iwanami, **Bull. Chem. Soc. Japan**, 1971, **44**, 2750.

29. I. Matsuda, K. Itoh,and Y. Ishii, **J. Chem. Soc. Perkin Trans.I**, 1972, 1678.

30. S.N. Mazumdar, I. Ibnusaud,and M.P. Mahajan, **Tetrahedron Lett.**, 1986, **27**, 5875.

31. P. Luthhardt and E.U. Wurthwein, **Tetrahedron Lett.**, 1988, **29**, 921.

CHAPTER - IV

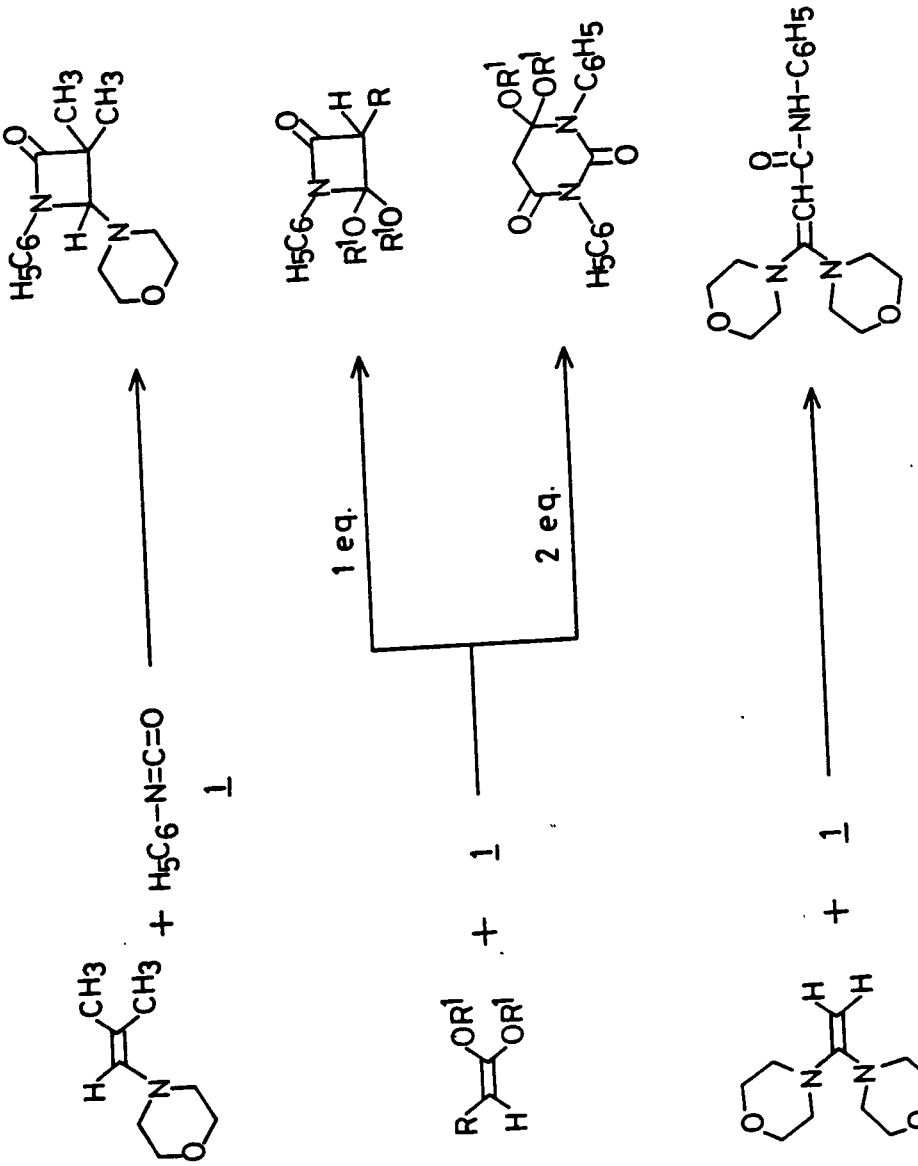
CHAPTER-IV

CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH ISOCYANATES

IV.1 INTRODUCTION

The chemistry of isocyanates dates back to over hundred years. Staudinger was the first to investigate and realise the importance of reactive cumulative bond system in isocyanates, especially with regard to cycloaddition reactions. The high applicability of the isocyanates among heterocumulenes may be attributed to (i) its facile synthesis and (ii) its stability in the anhydrous reaction medium[1].

Simple olefins rarely add to isocyanates(1), however, nucleophilic olefins such as enamines[2], ketene acetals[3,4], ketene aminals[5] etc. do form addition products with aryl

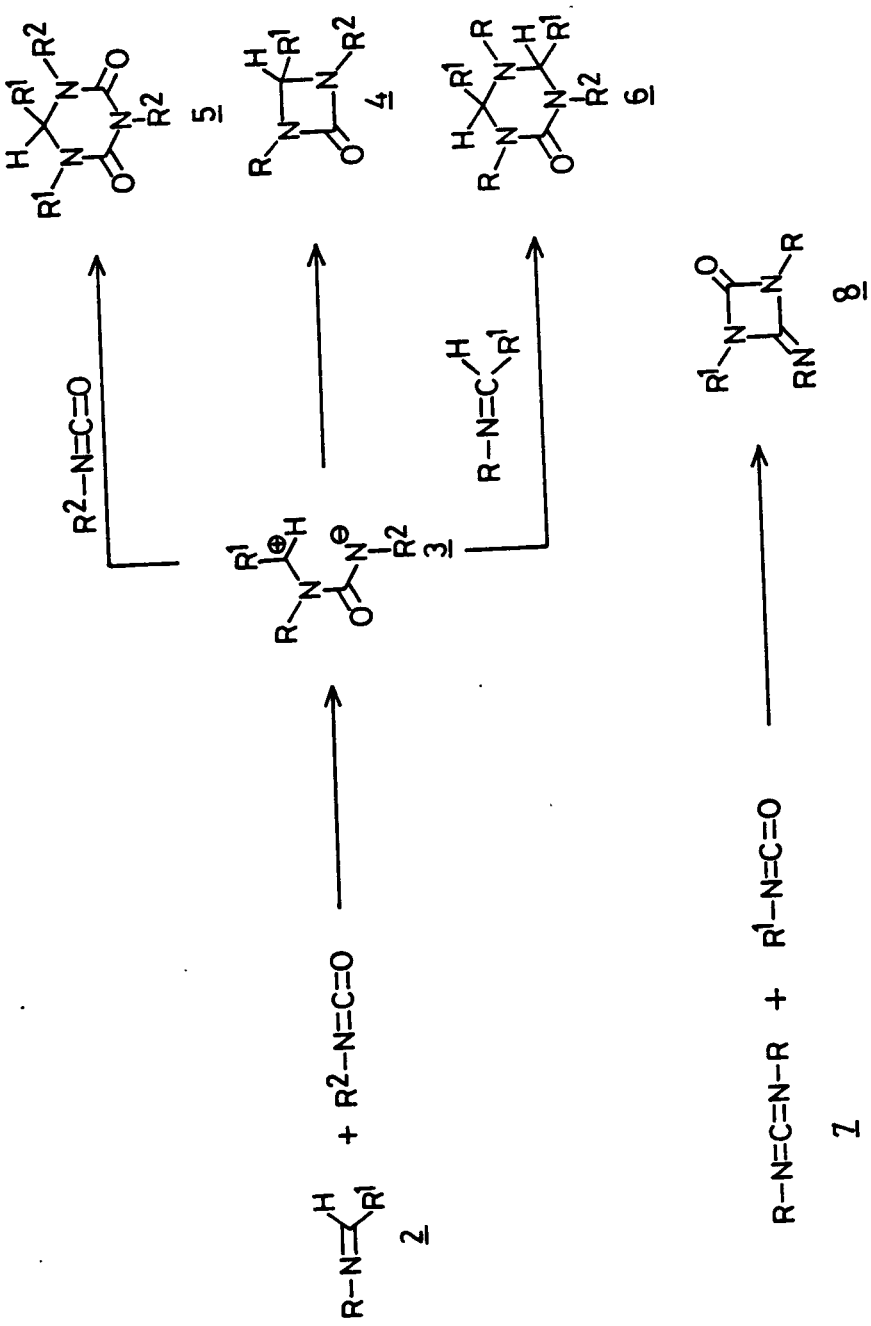


Scheme 1

and less readily with alkyl isocyanates (scheme-1).

Reports concerning the (2+2) cycloaddition reactions of isocyanates across carbon-nitrogen double bond are fewer as compared to that of other heterocumulenes e.g. ketenes, sulphene etc (Chapter II and chapter III of this thesis). The reactions of isocyanates(1) with azomethines(2) have been shown to result in different cycloadducts depending upon the reaction conditions and substitution on azemethine (scheme-2). It was observed that monosubstituted azomethine (2) afforded (2:1) cycloadducts(5)[6,7], while N-alkyl-C-aryl azomethines at elevated temperatures resulted in (1:2) cycloadducts(6)[8,9]. On the other hand, low temperature reactions of isocyanates with azomethines afforded simple (2+2) cycloadducts(4)[10]. The formation of cycloadducts 4, 5 and 6 in these cases could be rationalised on the basis of initial formation of 1:1 ionic intermediate 3. Similarly the products formed in case of reactions of aryl isocyanates with formamidines[11,12] have been shown to depend on the reaction conditions maintained. However, the reactions, of carbodiiomides(7) with isocyanates led invariably to (2+2) cycloadducts[13], 1,3-diazetidine-2,4-dione-4-imine derivatives(8). The products in these cases were shown to be independent of reaction conditions and effects of substituents.

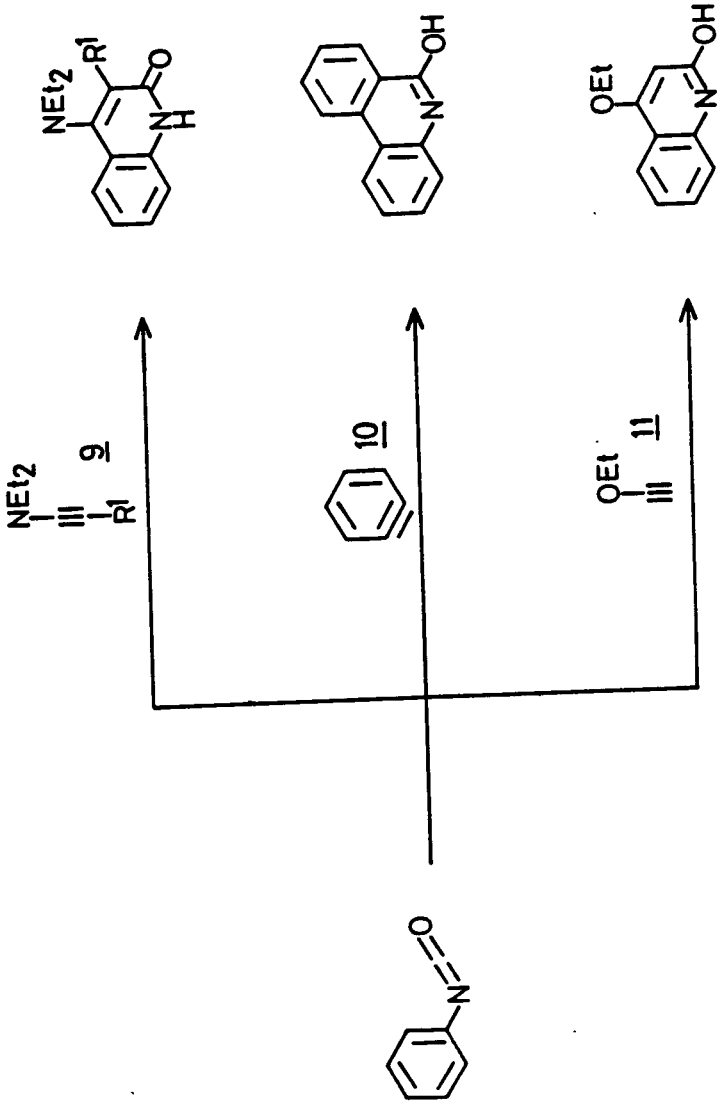
Aryl isocyanates have been reported to give (4+2)



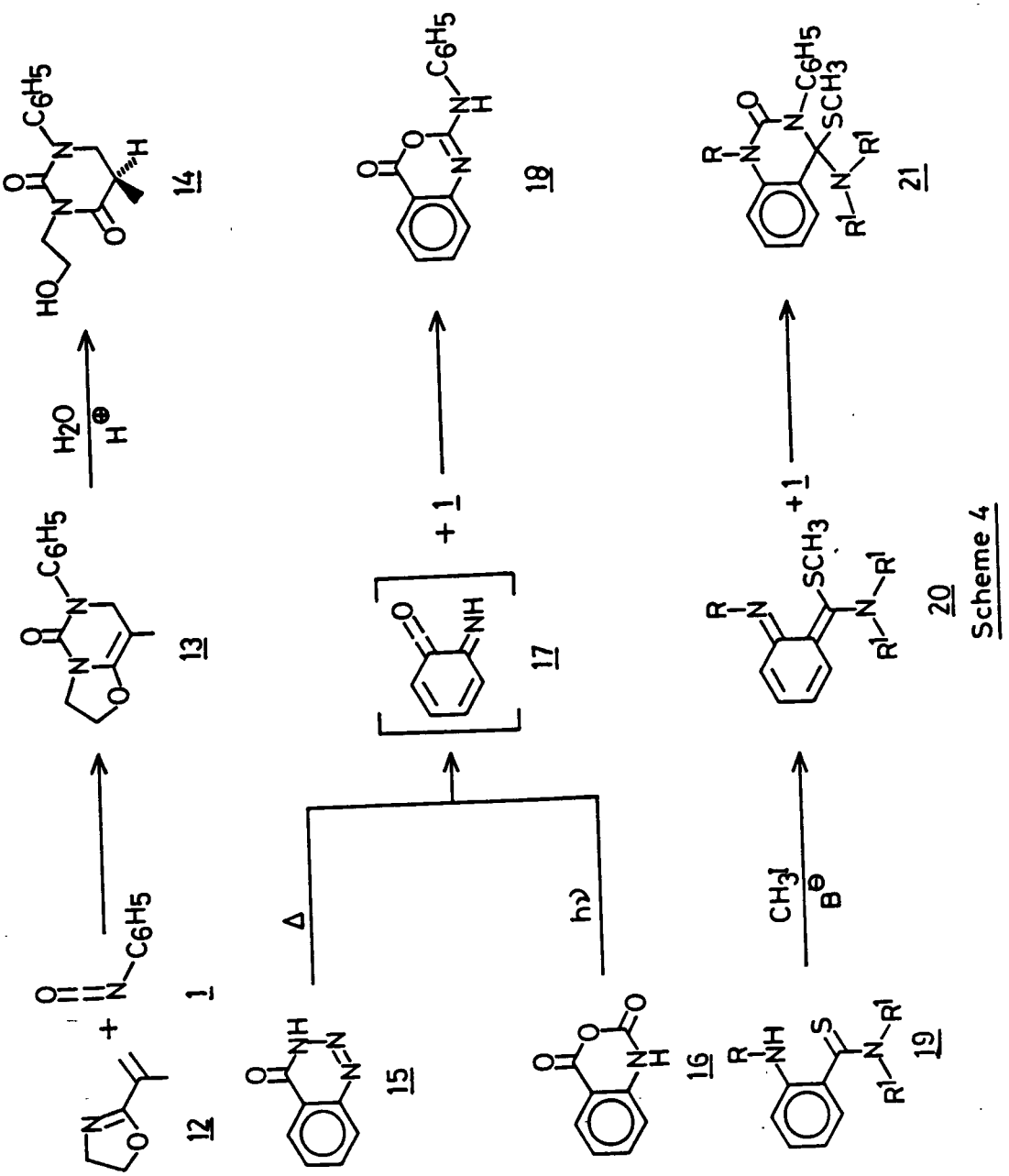
Scheme 2

cycloadducts with ynamines(9)[14], benzynes(10)[15], and ethoxy acetylene(11)[16] (scheme-3). The course of the reaction of ynamines with arylisocyanate is strongly dependent on the reaction conditions. Nature of the cycloaddition reaction was found to be solvent (polar or non-polar) dependent Isocyanates having vinyl[17], carbonyl, thiocarbonyl and imidoyl group[18] adjacent to the cumulative double bond have been reported to react as diene as well as dienophile in Diels-Alder reactions.

There are a few reports concerning the isocyanates taking part as an effective 2π component in hetero Diels-Alder cycloaddition reaction with monoaza-and diaza-1,3-butadienes[19,20]. The reaction of 2-isopropenyl-Δ^2-oxozoline(12) with phenylisocyanate(1) led to an unstable (4+2) cycloadduct (13)[21], which tends to polymerise. The unstable cycloadduct 13 was shown to undergo facile hydrolysis with aqueous acid, resulting in product 14. The thermolysis of benzo-1,2,3-triazin-4-one(15) and photolysis of carbamate 16 led to the generation of o-quinone methide ketene(17), which in the presence of phenyl isocyanate afforded good yield of (4+2) cycloadduct, 2-anilino-benz-3,4-oxazin-4-one(18)[22]. The stable o-quinone methide imine(20), derived by the alkylation of N,N-disubstituted thioanthranilides(19) gave similar (4+2) cycloadduct(21) with phenyl isocyanate[23](scheme-4).



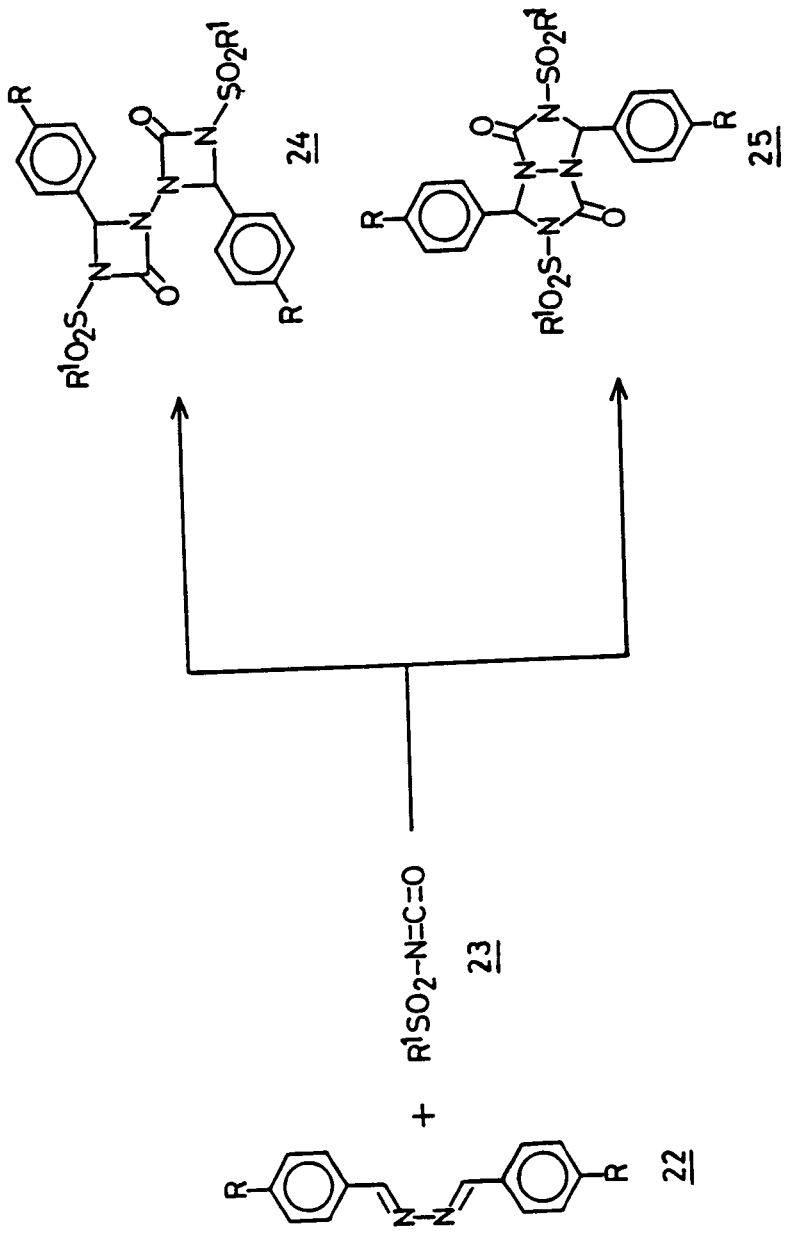
Scheme 3



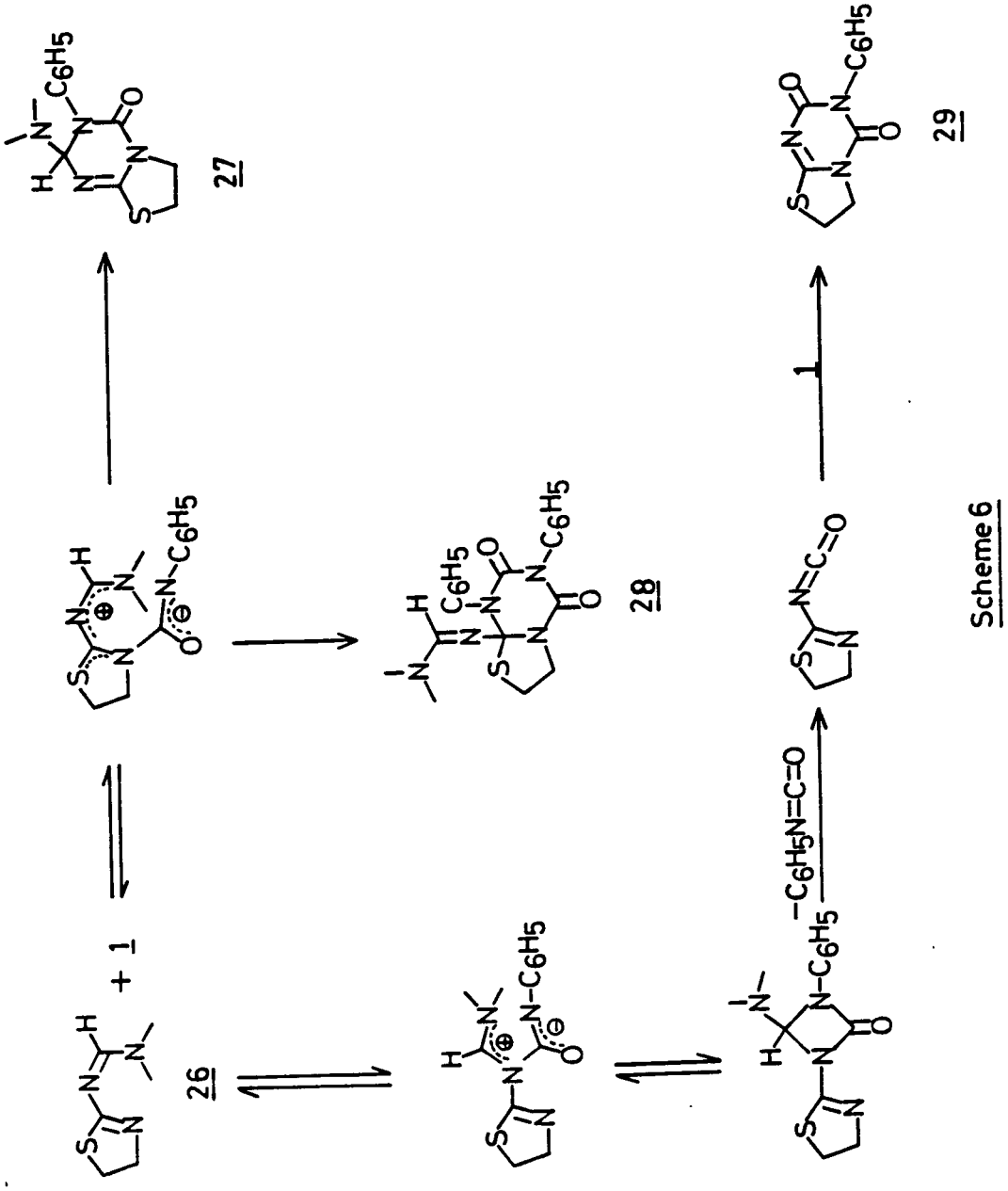
Scheme 4

There is no report in the literature concerning such cycloadditions of 2-aza-,1,2-diaza- and 1,4-diaza-1,3-butadienes with isocyanates[19,20]. This may probably be due to the non-nucleophilic nature of these heterodienes because of the unfavourable position of nitrogen. However, 2,3-diaza-1,3-butadienes(22), prepared by the condensation of substituted benzaldehydes with hydrazine, were found to undergo criss-cross addition with arylsulphonyl isocyanate(23) to yield tetrahydro-s-triazolo-[1,2-a] -s-triazole[24] (Scheme-5).

There are few reports concerning the cycloaddition reactions of isocyanates with 1,3-diaza-1,3-butadienes, which are the substructures of heterocyclic imines. Ulrich et al[25] had reported that the treatment of N,N-dimethyl-N'-[Δ^2-thiazolinyl-(2)]-formamidines(26) with equivalent amount of aryl isocyanates resulted in exothermal reactions and gave very good yields of (4+2) cycloadducts(27). These cycloadducts, on allowing to stand for longer periods, reported to decompose to yellow-brownish semisolids. They also observed that the reactions of 26 with excess of 1 in benzene at 80°C resulted (2+2+2) cycloadducts 28. It was also observed that heating 26 with excess of isocyanates at 240-250°C yielded 3-aryl-3,4,6,7- thiazolo[3,2-a]-s-triazin-2,4-dione(29). The formation of 27, 28 and 29 in



Scheme 5

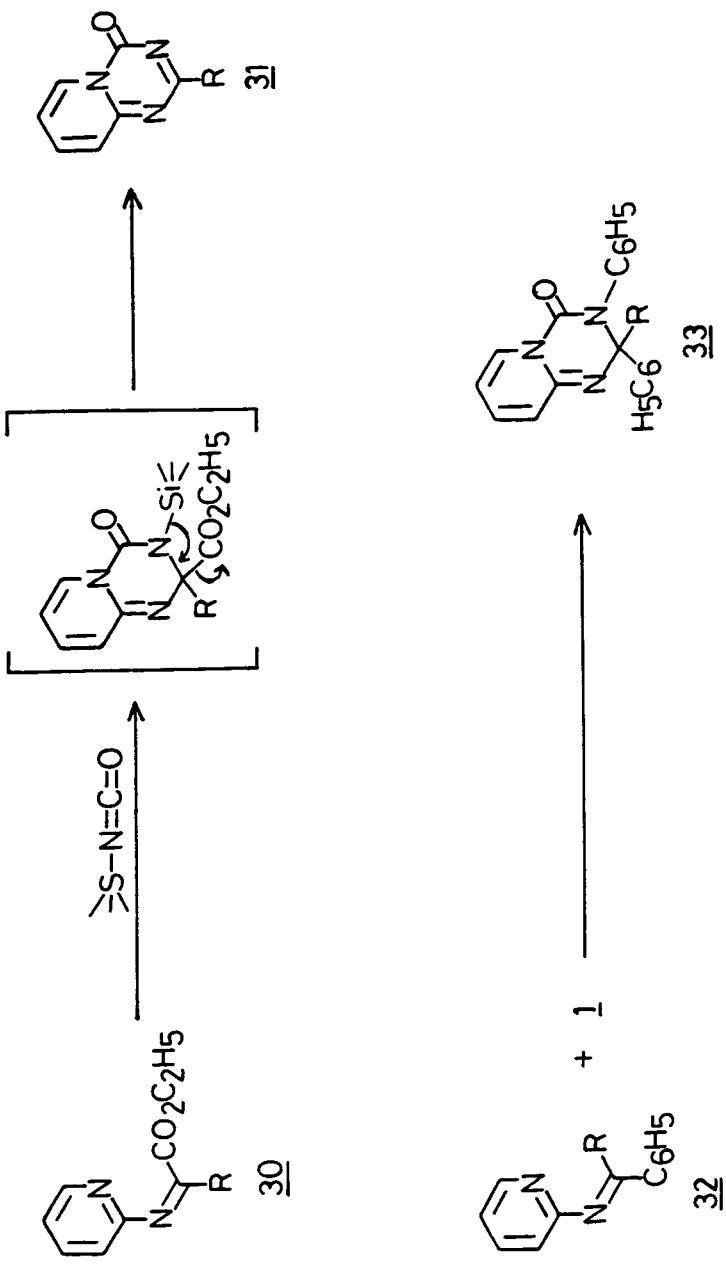


Scheme 6

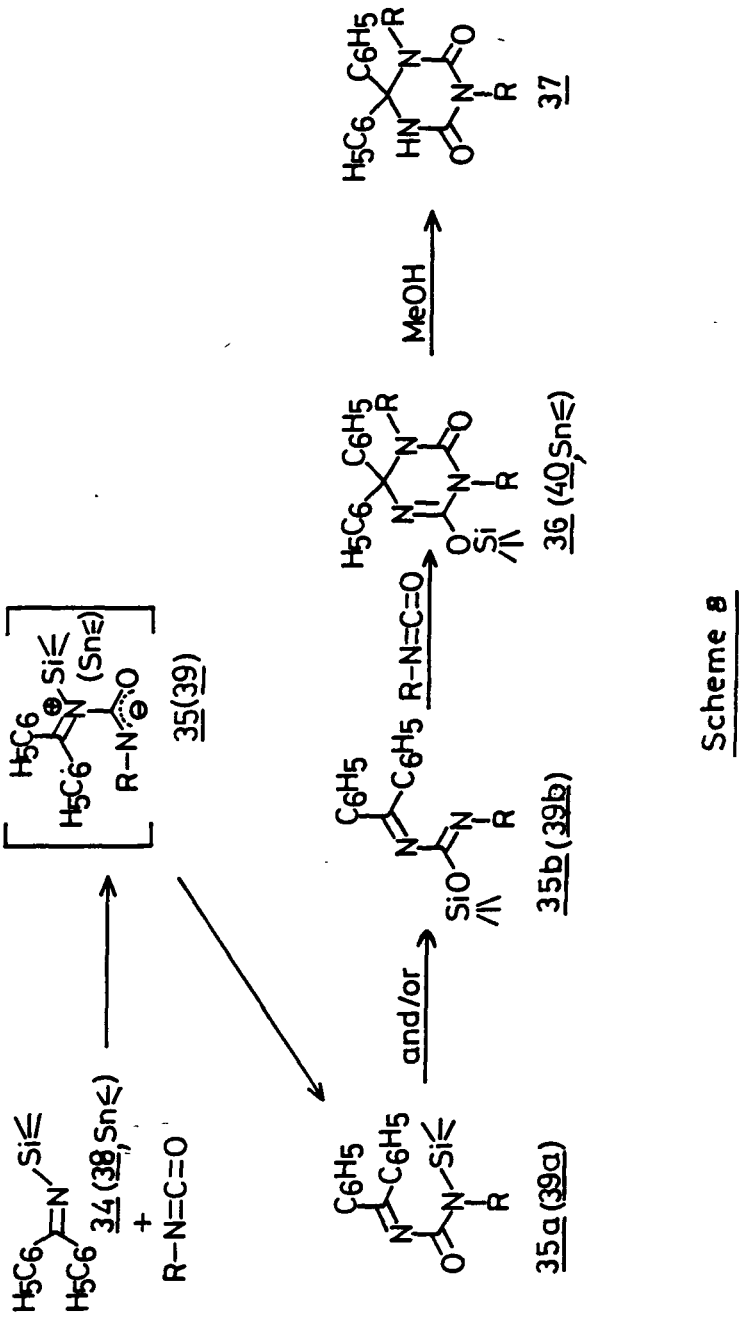
reactions is shown in scheme-6.

The treatment of ethyl-N-(2-pyridyl)imidates(30) with trimethylsilylisocyanate at room temperature was shown to result in very good yields of 4H-pyrido[1,2-a]-s- triazin-4-ones(31)[26]. Similar reaction of 2-benzylidene aminopyridine(32) with trimethylsilylisocyanate did not afford any product corresponding to pyrido-triazine derivative, such as 31. However, the reaction of 32 with phenylisocyanate gave rise to good yields of 2,3-diphenyl-4H- pyrido[1,2-a]-s-2,3-dihydrotriazin-4-one (33) (Scheme-7). Similar reactions of 30 with phenylisocyanate afforded crystalline (4+2) cycloadducts in good yields.

A few acyclic 1,3-diaza-1,3-butadienes, generated in situ, have also been shown to undergo (4+2) cycloaddition reactions with arylisocyanates. Thus, 3,4-dihydro-3-alkyl (aryl)-1,4,4-triphenyl-6-trimethylsilyloxy-1,3,5-triazin-2(H)-ones(36) were obtained by the reactions of N-trimethylsiyl-(diphenylmethylene)amine(34) with two equivalents of isocyanates[27,28]. The reaction was shown to proceed in a stepwise manner i.e. with the formation of a 1:1 insertion product 35 followed by its reaction with another molecule of isocyanate. The insertion product 35 was considered to be in thermodynamic equilibrium between urea (35a) and the imidate(35b) (scheme-8). Similar observations were made by



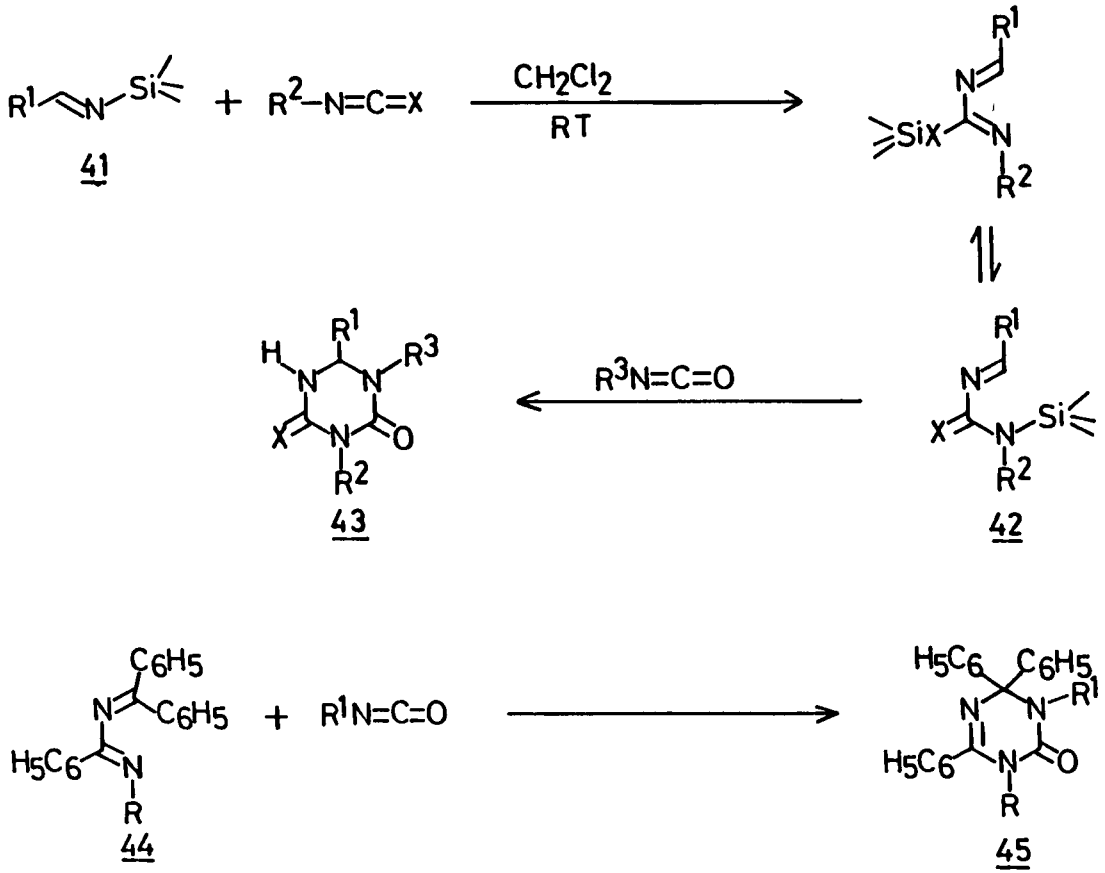
Scheme 7



Scheme 8

the same group, Matsuda et al[29], concerning the reactions of organostannyl(alkylidene)amine(38) with isocyanate (scheme -8). The treatment of 38 with one equivalent of phenylisocrynate gave the corresponding insertion product 39, which on subsequent addition of another molecule of isocyanate resulted in polar (4+2) cycloadduct 40. The destannylation of 39 with ethanethiol gave hexahydro-1,3-dialkyl-1,3,5-triazin-2,5-dione(37), identical with the one obtained by hydrolysis of 36. Similarly, Barluega et al[30] have recently reported that 2-trimethylsilyloxy- and 2-trimethyl-silyl-thio- 1,3-diaza-1,3-butadienes(42), formed on reaction of N-trimethylsilylimines (41) with isocyanates, react with another molecule of isocyanates to give high yields of substituted 5,6-dihydro-1,3,5-triazin-2,4(1H,3H)-dione (43) (scheme-9). It has also been reported that the reactions of 1-alkyl (aryl)-2,4,4-triphenyl-1,3-diaza-1,3-butadienes(44) with isocyanates resulting (4+2) cycloadducts(45).

We assumed that the cycloaddition reactions of isocyanates with 1,3-diaza-1,3-butadienes, having polarising functions at positions at 2- and 4-, and 4- and 4- may be much more facilitated. Hence, we have investigated the reactions of 1,3-diaza-1,3-butadienes 46 and 52 with isocyanates.

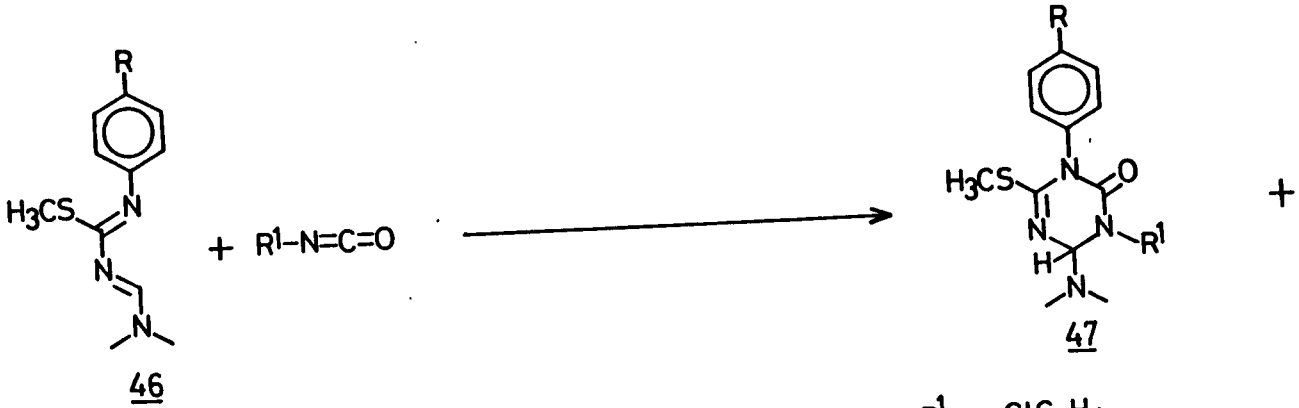


41 43 42 44 45

Scheme 9

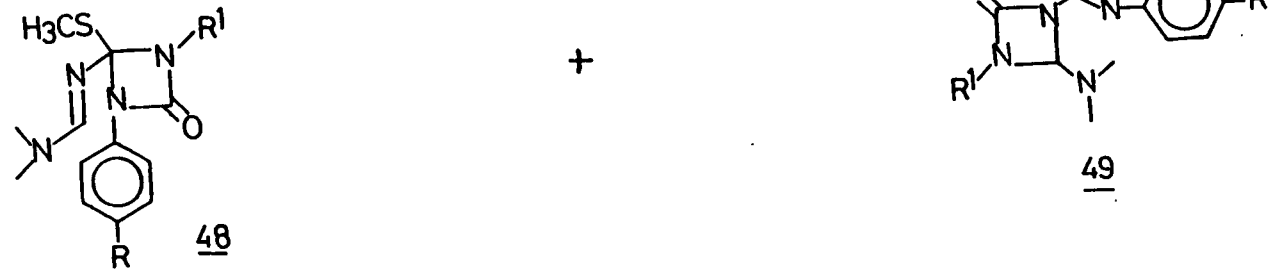
IV.2 RESULTS AND DISCUSSION

The treatment of 1-aryl-4-dimethylamino-2-thiomethyl-1,3-diaza-1,3-butadines(46) with phenylisocyanate in minimum amount of dry benzene (1ml) resulted in very good yields of previously unknown 1-aryl-3,4-dihydro-4-dimethylamino-3-phenyl-6-thiomethyl-1,3,5-triazin-2(1H)-ones(47) (scheme-10). The reactions are exothermic and the completion of reactions take few minutes (10min), leading to the separation of 47 as white crystalline solids. The structure of 47 has been assigned to the products on the basis of spectral data. Elemental analysis for these products could not be obtained since these tend to decompose on attempted recrystallisation. Their mass spectra showed the absence of molecular ion peaks and exhibited peaks due to retero Diels-Alder fragments. The i.r. spectrum (KBr) of 47a, for example, exhibited two strong absorption bands at 1690 and 1620cm^{-1} assigned to $\nu_{C=O}$ and $\nu_{C=N}$, respectively. These assignments are comparable with the literature values for similar substituted 3,4-dihydro-1,3,5-triazin-2(1H)-ones. Its ^1H n.m.r. spectrum ($CDCl_3$) showed three singlets at δ2.21(3H), δ 2.54(6H), and δ5.88(1H) assigned to $-SCH_3$, $-N(CH_3)_2$ protons and methine proton, respectively. The aromatic protons appeared as a multiplet at δ 7.00-7.60(10H). The formation of (2+2) cycloadducts e.g. 48 and 49 are ruled out, since in cases of 48 and 49 the i.r. spectrum



46

47 a, R = H ; $R^1 = C_6H_5$. e, R = H ; $R^1 = p\text{-}ClC_6H_4$.
b, $R = CH_3$; $R^1 = C_6H_5$. f, $R = CH_3$; $R^1 = p\text{-}ClC_6H_4$.
c, R = Cl ; $R^1 = C_6H_5$. g, R = Cl ; $R^1 = p\text{-}ClC_6H_4$.
d, $R = OCH_3$; $R^1 = C_6H_5$. h, $R = OCH_3$; $R^1 = p\text{-}ClC_6H_4$.



48 49

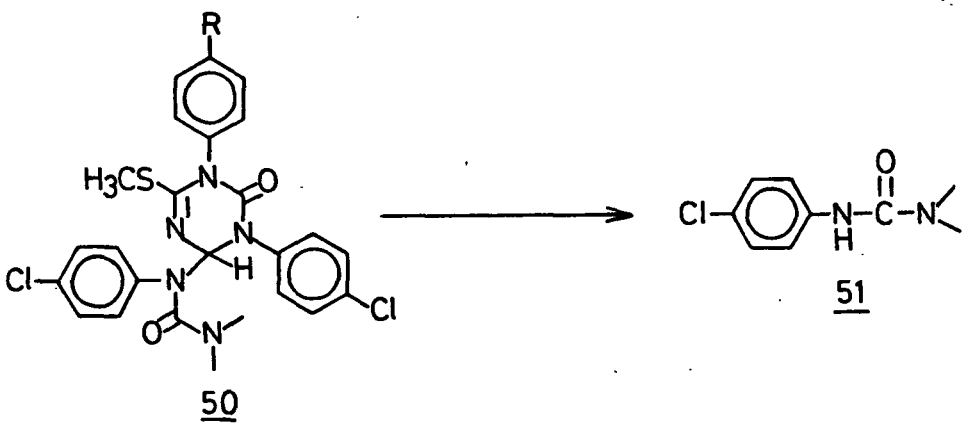
Scheme 10

should have shown the $\nu_{C=O}$ at 1720cm^{-1}. The presence of a proton around δ5.88 on the ^{1}H n.m.r. spectrum matches well with the literature chemical shift value for such a proton[11,12,25] and confirm structure 47 for the products.

Similar reaction of 46a with p-chlorophenylisocyanate gave 3-p-chlorophenyl-3,4-dihydro-4-dimethylamino-1-phenyl-6-thiomethyl-1,3,5-triazin-2(1H)-one(47e). Its i.r. spectrum (KBr) showed absorption peaks at 1685 and 1625cm^{-1} due to $\nu_{C=O}$ and $\nu_{C=N}$ respectively. The singlets at δ2.35(3H) and δ2.87(6H) in ^{1}H n.m.r. spectrum($CDCl_3$) were attributed to $-SCH_3$ and $-N(CH_3)_2$ protons, respectively. The methine proton appeared as a multiplet at δ 6.90-7.40(9H).

The cycloadducts 47 were found to undergo slow decomposition to yellow-brownish viscous mass on standing at room temperature. Ulrich et al had also reported this kind of decomposition in case of closely related triazinone derivatives(27)[25]. The products 47a-d decompose faster than to 47e-h decomposition products of 47a-d could not be isolated. The products 47e-h on refluxing in dry benzene for 4 hrs, resulted in the isolation of same compound. The ^{1}H n.m.r. spectrum ($CDCl_3$) of these compounds showed a singlet at δ2.80(6H), a multiplet at δ 7.10-7.33(4H) and a broad singlet, exchangable with D_2O, at δ6.20-6.42(1H)

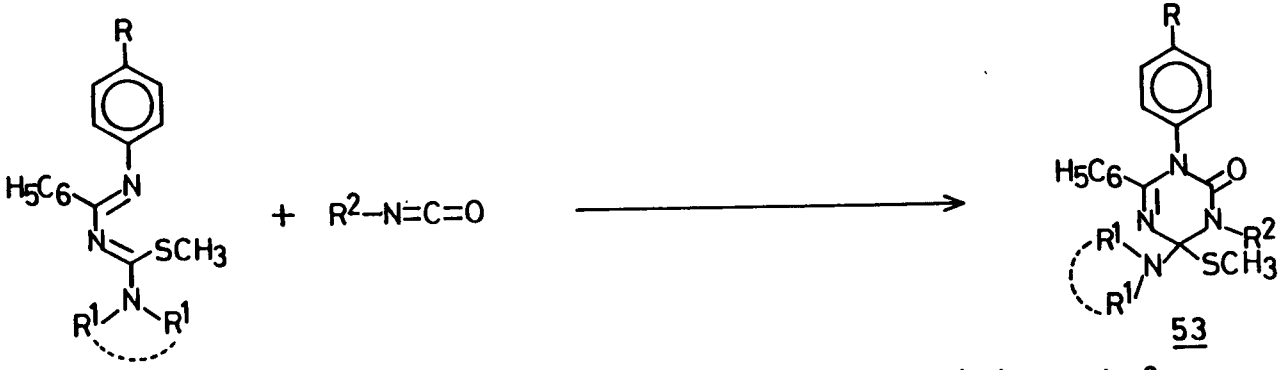
and were assigned to $-N(CH_3)_2$, aromatic protons and -NH-proton, respectively. Its i.r. spectrum (KBr) showed absorption bands at 3300 and 1640cm^{-1} assignable to ν_{NH} and $\nu_{C=O}$, respectively. On the basis of these spectral data, the compound could be tentatively characterised as 1-p-chlorophenyl-3,3-dimethylurea(51). Further proof for its structure was obtained from its mass spectrum, which showed the molecular ion peak at m/z 198(17%). The melting point of this compound (168-9°C) is also comparable to its reported melting point (170-71°C)[32]. The probable mechanism for the formation of related urea may be similar to the one proposed by Dyer et al[11]. In this mechanism it is assumed that the p-chlorophenyl isocyanate, formed by the retero Diels-Alder fragmentation of 47e-h, react with 47e-h to yield an intermediate 50 which leads to the formation urea 51.



In continuation of these studies, we have also investigated the reaction of 1-aryl-2-phenyl-4-secamino-4-

thiomethyl-1,3-diaza-1,3-butadienes(52) with arylisocyanates. Thus, the treatment of 1,2-diphenyl-4-morpholino-4-thiomethyl-1,3- diaza-1,3-butadiene(52a) with phenylisocyanate(1) resulting in an exothermic reaction, which completes in 10-15 minutes giving rise to 3,4-dihydro-4-morpholino-4-thiomethyl-1,3,6- triphenyl-1,3,5-triazin-2(1H)-one(53a) in 92% yield. The compound was purified by repeated washing and reprecepitating with a mixture of (1:1) dry diethylether and petrolium ether. The elemental analysis of these products could not be carried out as repeated crystallisations resulted in decomposition of the compounds. However, some of the compounds could be obtained in sufficiently pure form by fast crystallisation for mass spectra (Scheme 11).

As observed earlier in the mass spectrum of 47a, for example 53a, did not show molecular ion peak, however it exhibited the base peak at m/z 119 corresponding to the phenylisocyanate fragment. Its i.r. spectrum (KBr) showed two strong absorption bands at 1695cm^{-1} and 1635cm^{-1} assigned to $\nu_{C=O}$ and $\nu_{C=N}$, respectively. The ^{1}H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 2.30(3H) for $-SCH_3$ protons. The two triplets at δ 3.13-3.80(4H) and δ3.36-3.50 (4H), were assigned to $-CH_2-N-CH_2-$ and $-CH_2O-CH_2-$ protons of morpholine, respectively. The aromatic protons appeared as a multiplet at δ7.00-7.60(15H). Similar reaction of



52 53

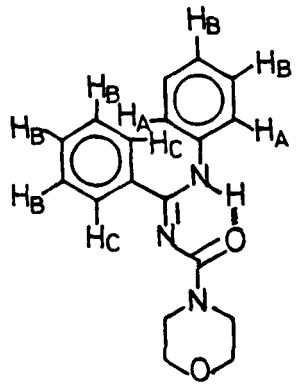
53 a, R=H ; R^1,R^1=O(CH2)2; $R^2=C_6H_5$. 53 h, R=H ; R^1,R^1=O(CH2)2; R^2= p-ClC_6H_4.
b, R=H ; R^1,R^1=(CH2)3; $R^2=C_6H_5$. i, R=H ; R^1,R^1=(CH2)3; R^2= p-ClC_6H_4.
c, R=H ; R^1,R^1=(CH2)2 ; $R^2=C_6H_5$. j, R=H ; R^1,R^1=(CH2)2 ; R^2= p-ClC_6H_4.
d, R=H ; R^1,R^1=CH_3 CH_3; $R^2=C_6H_5$. k, R=H ; R^1,R^1=CH_3 CH_3; R^2= p-ClC_6H_4.
e, R=CH_3; R^1,R^1=O(CH2)2; $R^2=C_6H_5$. l, R=CH_3; R^1,R^1=O(CH2)2; R^2= p-ClC_6H_4.
f, R=CH_3; R^1,R^1=(CH2)3; $R^2=C_6H_5$. m, R=CH_3; R^1,R^1=(CH2)3; R^2= p-ClC_6H_4.
g, R=CH_3; R^1,R^1=(CH2)2; $R^2=C_6H_5$. n, R=CH_3; R^1,R^1=(CH2)2; R^2= p-ClC_6H_4.

Scheme 11

52a with p-chlorophenylisocyanate resulted in 3-p-chlorophenyl-3,4-dihydro-1,6-diphenyl-4-morpholino-4-thiomethyl-1,3,5-triazin-2(1H)-one(53e). Its i.r. spectrum (KBr) showed absorption bands at 1695cm^{-1} and 1625cm^{-1}, and were assigned to $\nu_{C=O}$ and $\nu_{C=N}$, respectively. Its ^{1}H n.m.r ($CDCl_3$) showed a singlet at δ2.06(3H) due to $-SCH_3$ protons. The triplets at δ3.13-3.30(4H) and δ3.36-3.50(4H) were assigned to $-CH_2-N-CH_2-$ and $-CH_2O-CH_2-$ protons of morpholine, respectively. The aromatic protons appeared as a multiplet at δ7.00-7.60(14H).

The decompositions of triazinones(53) were found to be slower as compared to the decompositions of 47 and therefore a few of the triazinones, 53 could be purified by crystallisation. The triazinones 53, on prolonged refluxing in benzene (about 12h) led to their complete decomposition. Only a few of the decomposed samples could be isolated in pure form. Thus, 52a on refluxing with benzene for 12 hours, gave a white crystalline product, m.p. 153-4°C. Its mass spectrum showed the molecular ion peak at m/z 309(21%). Its i.r. spectrum (KBr) showed sharp absorption peaks at 3250, 1605 and 1580cm^{-1}, and were assigned to ν_{NH}, $\nu_{C=O}$ and $\nu_{C=N}$, respectively. Its ^{1}H n.m.r. ($CDCl_3$) exhibited a multiplet at δ3.58-3.80(8H) and was assigned to the morpholine protons. The multiplets appeared at δ7.10-7.28(2H,H_A), δ7.33-7.60(6H,H_B) and δ8.26-8.40(2H,H_C), and were assigned

to aromatic protons. A broad signlet at δ11.86-12.06, exchangable



54

with D_2O, was assigned to the -NH- proton. On the basis of these spectral data, the decomposed compound has been tentatively characterised as N-phenyl-N'-(morpholino carbamoyl) benzamidine. The detail study concerning the reactions of these 1,3-diaza-1,3-butadienes with arylisocyanates under various reaction conditions, are now underway.

EXPERIMENTAL

General conditions are same as described in Chapter II.

Starting Material

The phenyl isocyanate and p-chlorophenyl isocyanates were prepared by the reported procedure[33].

Reactions of 1,3-diaza-1,3-butadienes (46 and 52) with arylisocyanates; General Procedure: 1,3-Diaza-1,3-butadines (2 mmoles) and arylisocyanate (2.5 mmole) were stirred

in 1 ml of dry benzene for 10-20 minutes. The reaction is exothermic and resulted in the dissolution of the starting material. After few minutes (10 min) of stirring of the reaction mixture, the products started separating out, but stirring was continued for a further period of 20 minutes after addition of 5 ml of dry ether. The white compounds so obtained after filtration were purified by repeated washing with dry ether or reprecitating with petrolium ether.

The elemental analysis of the products could not be obtained as these tend to decompose on attempted recrystallisations. These compounds also did not show molecular ion peaks in the mass spectra.

3,4-Dihydro-4-dimethylamino-1,3-diphenyl-6-thiomethyl-1,3,5-triazin-2(1H)-one;(47a): white solid, 96%; m.p. 92-4°C. ν_{max} (KBr): 1690cm^{-1}(C=O) and 1620cm^{-1}(C=N). δ_H($CDCl_3$): 2.21(s,3H, -SCH_3); 2.54(s,6H,-$N(CH_3)_2$); 5.88(s,1H,methine) and 7.03-7.60(m,10H,arom).

3,4-Dihydro-4-dimethylamino-3-phenyl-6-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(47b): white solid, yield, 93%; m.p. 74-6°C. ν_{max}(KBr): 1690cm^{-1}(C=O) and 1625cm^{-1}(C=N). δ_H($CDCl_3$): 2.24(s,3H,-CH_3); 2.33(s,3H,-SCH_3); 2.87(s,6H,-$N(CH_3)$);

5.74(s,1H,methine) and 7.00-7.46(m,9H,arom).

1-p-Chlorophenyl-3,4-dihydro-4-dimethylamino-1-phenyl-6-thiomethyl-1,3,5-triazin-2(1H)-one;(47c): white solid yield, 90%; m.p.87°C. ν_{max}(KBr): 1690cm^{-1}(C=O) and 1640cm^{-1}(C=N). $\delta_H(CDCl_3)$: 2.43(s,3H,-SCH_3); 3.08(s,6H,-$N(CH_3)_2$); 5.75(s,1H methine) and 6.90-7.40(m,9H,arom).

3,4-Dihydro-4-dimethylamino-1-p-methoxyphenyl-3-phenyl-6-thiomethyl-1,3,5-triazin-2(1H)-one;(47d): white solid, yield, 98%; m.p.88-90°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1625cm^{-1} (C=N). $\delta_H(CDCl_3)$:2.35(s,3H,-SCH_3); 2.87(s,6H,-$N(CH_3)_2$); 3.70(s,3H,-OCH_3); 5.65(s,1H,methine) and 7.00-7.43(m,9H, arom).

3-p-Chlorophenyl-3,4-dihydro-4-dimethylamino-1-phenyl-6-thiomethyl-1,3,5-triazin-2(1H)-one;(47e): white solid, yield, 94%; m.p.112°C. ν_{max}(KBr): 1685cm^{-1}(C=O) and 1625cm^{-1} (C=N). $\delta_H(CDCl_3)$ 2.35(s,3H,-SCH_3); 2.87(s,6H,-$N(CH_3)_2$); 5.69(s,1H,methine) and 7.00-7.40(m,2H,arom).

3-p-Chlorophenyl-3,4-dihydro-4-dimethylamino-6-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(47f): white solid, yield, 89%; m.p.89-90°C. ν_{max}(KBr): 1685cm^{-1}(C=O) and 1625cm^{-1}(C=N). $\delta_H(CDCl_3)$:2.28(s,3H,-CH_3); 2.36(s,3H,-SCH_3); 2.88(s,6H,

$-N(CH_3)_2$); 5.65(s,1H,methine) and 7.02-7.40(m,8H,arom).

1,3-Bis(p-Chlorophenyl)-3,4-dihydro-4-dimethylamino-6-thiomethyl-1,3,5-triazin-2(1H)-one;(47g): white solid, yield, 86%; m.p.98°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1625cm^{-1} (C=N). $\delta_H(CDCl_3)$: 2.28(s,3H,$-SCH_3$); 3.01(s,6H,$-N(CH_3)_2$); 5.67(s,1H,methine) and 6.88-7.40(m,8H,arom).

3-p-Chlorophenyl-3,4-dihydro-4-dimethylamino-1-p-methoxyphenyl-6-thiomethyl-1,3-5-triazin-2(1H)-one;(47h): white solid, yield, 86%; m.p. 86°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1625cm^{-1}(C=N). $\delta_H(CDCl_3)$:2.27(s,3H,$-SCH_3$); 2.90(s,3H,$-N(CH_3)_2$); 3.72(m,3H,$-OCH_3$); 5.65(s,1H,methine) and 6.80-7.33(m,8H,arom).

3,4-Dihydro-4-morpholino-4-thiophenyl-1,3,6-triphenyl-1,3,5-triazin-2(1H)-one;(53a): white solid, yield, 94%; m.p.112-4°C. ν_{max}(KBr): 1695cm^{-1}(c=O) and 1635cm^{-1}(C=N). $\delta_H(CDCl_3)$:2.05 (s,3H,$-SCH_3$); 3.13-3.30(t,4H,$-CH_2-N-CH_2-$); 3.36-3.50(t,4H, $-CH_2-O-CH_2-$) and 7.00-7.60(m,15H,arom).

3,4-Dihydro-4-piperidino-4-thiomethyl-1,3,6-triphenyl-1,3,5-triazin-2(1H)-one;(53b): white solid, yield, 94%; m.p. 138-40°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1635cm^{-1}(C=N). δ_H ($CDCl_3$): 1.10-1.53(m,6H,$-CH_2-CH_2-CH_2-$), 2.08(s,3H,$-SCH_3$); 3.03-3.21(m,4H,$-CH_2-N-CH_2-$) and 6.96-7.56(m,15H,arom).

3,4-Dihydro-4-pyrrolidino-4-thiomethyl-1,3,6-triphenyl-1,3,5-triazin-2(1H)-one;(53c): white solid, yield, 89%; m.p. 153-5°C. ν_{max}(KBr): 1700cm^{-1}(C=O) and 1620cm^{-1}(C=N). δ_H($CDCl_3$): 1.60-1.96(m,4H,-CH_2-CH_2-); 2.37(s,3H,-SCH_3); 3.26-3.53(m, 4H,-CH_2-N-CH_2-) and 7.00-7.63(m,15H,arom).

3,4-Dihydro-4-dimethylamino-4-thiomethyl-1,3,6-triphenyl-1,3,5-triazin-2(1H)-one;(53d): white solid, yield, 93%; m.p. 122-4°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1625cm^{-1}(C=N). δ_H($CDCl_3$): 2.37(s,3H,SCH_3); 2.98(s,6H,-$N(CH_3)_2$) and 7.00-7.60(m,15H,arom).

3-p-Chlorophenyl-3,4-dihydro-1,6-diphenyl-4-morpholino-4-thiomethyl-1,3,5-triazin-2(1H)-one;(53e): white solid, yield, 89%; m.p. 130°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1625cm^{-1} (C=N). δ_H($CDCl_3$): 2.06(s,3H,-SCH_3); 3.13-3.30(t,4H,-CH_2-N-CH_2-); 3.36-3.50(t,4H,-CH_2-O-CH_2-) and 7.00-7.60(m,14H,arom).

3-p-Chlorophenyl-3,4-dihydro-1,6-diphenyl-4-piperidino-4-thiomethyl-1,3,5-triazin-2(1H)-one;(53f): white solid, yield; 89%; m.p. 110°C. ν_{max}(KBr): 1695cm^{-1}(C=O) and 1630cm^{-1} (C=N). δ_H($CDCl_3$): 1.13-1.50(m,6H,-CH_2-CH_2-CH_2-); 2.10(s,3H, -SCH_3); 3.13-3.30(m,4H,-CH_2-N-CH_2-) and 6.90-7.00(m,14H,arom).

3-p-Chlorophenyl-3,4-dihydro-1,6-diphenyl-4-pyrrolidino-4-thiomethyl-1,3,5-triazin-2(1H)-one;(53g): white solid, yield, 86%; m.p.156°C. ν_{max}(KBr): 1700cm^{-1}(C=O) and 1640cm^{-1}

(C=N). $\delta_H(CDCl_3)$: 1.58-1.96(m,4H,$-CH_2-CH_2-$); 2.30(s,3H,$-SCH_3$); 2.96-3.30(m,4H,$-CH_2-N-CH_2-$) and 7.00-7.60(m,14H,arom).

3-p-Chlorophenyl-3,4-dihydro-4-dimethylamino-1,6-diphenyl-4-thiomethyl-1,3,5-triazin-2(1H)-one;(53h): white solid, yield, 90%; m.p.109°C. ν_{max}(KBr): 1700cm^{-1}(C=O) and 1625cm^{-1} (C=N). $\delta_H(CDCl_3)$: 2.40(s,3H,$-SCH_3$); 3.03(s,6H,$-N(CH_3)_2$) and 6.96-7.45(m,14H,arom).

3,4-Dihydro-3,6-diphenyl-4-morpholino-4-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53i): white solid, yield, 96%; m.p. 121-22°C. ν_{max}(KBr): 1700cm^{-1}(C=O) and 1635cm^{-1} (C=N). $\delta_H(CDCl_3)$: 2.06(s,3H,$-CH_3$); 2.23(s,3H,$-SCH_3$); 3.06-3.23 (t,4H,$-CH_2-N-CH_2-$); 3.33-3.50(t,4H,$-CH_2-O-CH_2-$) and 7.00-7.60 (m,14H,arom).

3,4-Dihydro-3,6-diphenyl-4-piperidino-4-thio- methyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53j): white solid, yield, 92%; m.p. 192-4°C. ν_{max}(KBr): 1700cm^{-1}(C=O) and 1640cm^{-1} (C=N). $\delta_H(CDCl_3)$: 1.13-1.50(m,6H,$-CH_2-CH_2-CH_2-$); 2.04(s,3H, $-CH_3$); 2.18(s,3H,$-SCH_3$); 3.10-3.30(m,4H,$-CH_2-N-CH_2-$) and 7.00-7.60(m,14H,arom).

3,4-Dihydro-3,6-diphenyl-4-pyrrolidino-4-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53k): white solid, yield, 94%; m.p. 254°C. $\nu_{max}(CDCl_3)$: 1700cm^{-1}(C=O) and 1625cm^{-1}(C=N).

$\delta_H(CDCl_3)$:1.53-1.96(m,4H,$-CH_2-CH_2-CH_2-$); 2.06(s,3H,$-CH_3$) 2.24(s,3H,$-SCH_3$); 3.00-3.33(m,4H,$-CH_2-N-CH_2-$) and 7.00-7.56 (m,14H,arom).

3-p-Chlorophenyl-3,4-dihydro-6-phenyl-4-morpholino-4-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53l): white solid, yield, 92%; m.p.l 136°C.ν_{max}(KBr): 1700cm^{-1}(C=O) and 1630cm^{-1} (C=N).$\delta_H(CDCl_3)$:1.94(s,3H,$-CH_3$); 2.12(s,3H,$-SCH_3$); 3.10-3.23 (t,4H,$-CH_2-N-CH_2-$); 3.40-3.53(m,4H,$-CH_2-O-CH_2-$) and 6.80-7.40(m,13H,arom).

3-p-Chlorophenyl-3,4-dihydro-6-phenyl-4-piperidino-4-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53m): white solid, yield, 86%; m.p. 181-3°C.ν_{max}(KBr): 1700cm^{-1}(C=O) and 1640cm^{-1} (C=N).$\delta_H(CDCl_3)$: 1.15-1.50(m,6H,$-CH_2-CH_2-CH_2-$); 2.02(s,3H, $-CH_3$); 2.22(s,3H,$-SCH_3$); 3.00-3.46(m,4H,$-CH_2-N-CH_2-$) and 6.80-7.40(m,13H,arom).

3-p-Chlorophenyl-3,4-dihydro-6-phenyl-4-pyrrolidino-4-thiomethyl-1-p-tolyl-1,3,5-triazin-2(1H)-one;(53n): white solid, yield, 82%; m.p. 262°C.ν_{max}(KBr): 1700cm^{-1}(C=O) and 1630cm^{-1}(C=N).$\delta_H(CDCl_3)$:1.56-1.93(m,4H,$-CH_2-CH_2-$); 2.08(s,3H,$-CH_3$); 2.20(s,6H,$-SCH_3$); 3.00-3.36(m,4H,$-CH_2-N-CH_2-$)and 6.86-7.43(m,13H,arom).

REFERENCES

1. H. Ulrich, **Cycloaddition Reactions of Heterocumulenes**, Academic Press, New York, 1967, p.120.

2. M. Perrelmann and S.A. Mizsak, **J. Am. Chem. Soc.**, 1962, **84**, 4988.

3. R. Scarpati, G. Del Re, and T. Naone, **Rend. Accad. Sci, Fis Mat.**, 1959, 26, 26; **Chem. Abstr.**, 1961, 55, 11423.

4. R. Scarpati and R.A. Nicolaus, **Rend. Accad. Sci. Fis. Mat.**, 1962, **29**, 2932.

5. D.H. Clemens, A.J. Bells, and J.L. O'Brien, **J. Org. Chem.**, 1964, **29**, 2932.

6. W.J. Hale and N.A. Lange, **J. Am. Chem. Soc.**, 1902, **95**, 379.

7. N.A. Lange, **J. Am. Chem. Soc.**, 1926, **48**, 2440.

8. A.G. Davies and G.J.D. Peddle, **J. Chem. Soc. Chem. Commun.**, 1965, 96.

9. J. Goerdler and H. Schenk, **Chem. Ber.**, 1965, 98, 2954.

10. A. Sanier and F.G. Shephardt, **J. Chem. Soc.**, 1909, **41**, 379.

11. E. Dyer, T.E. Majewski, and J.D. Travis, **J. Org. Chem.**, 1968, 33, 3931.

12. H. Ulrich, B. Tucker, F.A. Stuber, and A.A.R. Sayeigh, **J. Org. Chem.**, 1968, 33, 3928.

13. R. Hofmann, E. Schmidt, A. Richle, and F. Moosmuller, **Chem. Abstr.**, 1959, 53, 19892.

14. M.E. Kuehne and P.J. Sheeran, **J. Org. Chem.**, 1966, **33**, 4406.

15. J.C. Sheehan and G.D. Daves, **J. Org. Chem.**, 1965, **30**, 3247.

16. J. Nieuwenhuis and J.F. Arenes, **Rec. Trav. Chim. Pays-Bas.**, 1957, **76**, 999.

17(a) R. Fuks, **Tetrahedron**, 1970, **26**, 2161.

(b) A. Dondoni, L. Kniezo, and A. Medici, **J. Org. Chem.**, 1982, **47**, 3995.

18. B.A. Abbuzov and N.N. Zobova, **Synthesis**, 1974, 461, and references cited therein.

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

20. D.L. Boger and S.M. Weinreb, **Hetero Diels-Alder Methodology in Organic Synthesis**, Academic Press, New York, 1967, p.239.

21. W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier, and H. Hellman, **Angaw, Chem. Int. Ed. Engl.**, 1966, **7**, 93.

22. H. Herlinger, **Angew. Chem.**, 1964, **76**, 437.

23. R. Gompper and H.D. Lehmann, **Angew. Chem.**, 1968, **80**, 38.

24. W. Bartman, **Chem. Ber.**, 1967, **100**, 2938.

25. R. Richter and H. Ulrich, **Chem. Ber.**, 1970, **103**, 3525.

26. T. Kato and S. Masuda, **Chem. Pharm. Bull. Tokyo,** 1975, **23**, 2251.

27. I. Matsuda, K. Itoh, and Y. Ishii, **J. Chem. Soc. Perkin Trans.I,** 1976, 1523.

28. I. Maksuda, S. Yamamoto, and Y. Ishii, **J. Chem. Soc. Perkin Trans.I,** 1976, 1523.

29. H. Suzuki, I. Itoh, I. Matsuda, and Y. Ishii, **Bull. Chem. Soc. Japan,** 1974, **47**, 3131.

30. J. Barluenga, M. Tomas, A. Ballesteros, and L.A. Lopez, **Synthesis,** 1989, 228.

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

32. N.N. Mel'nikov, K.D.S. Shilovskaya, and E.I. Levedeva, **Zh. Obsch. Khim,** 1962, **32**, 3957; **Chem. Abstr.,** 1963, **58**, p11245.

33. G. Schroeter, **Chem. Ber.,** 1909, **42**, 3356.

CHAPTER - V

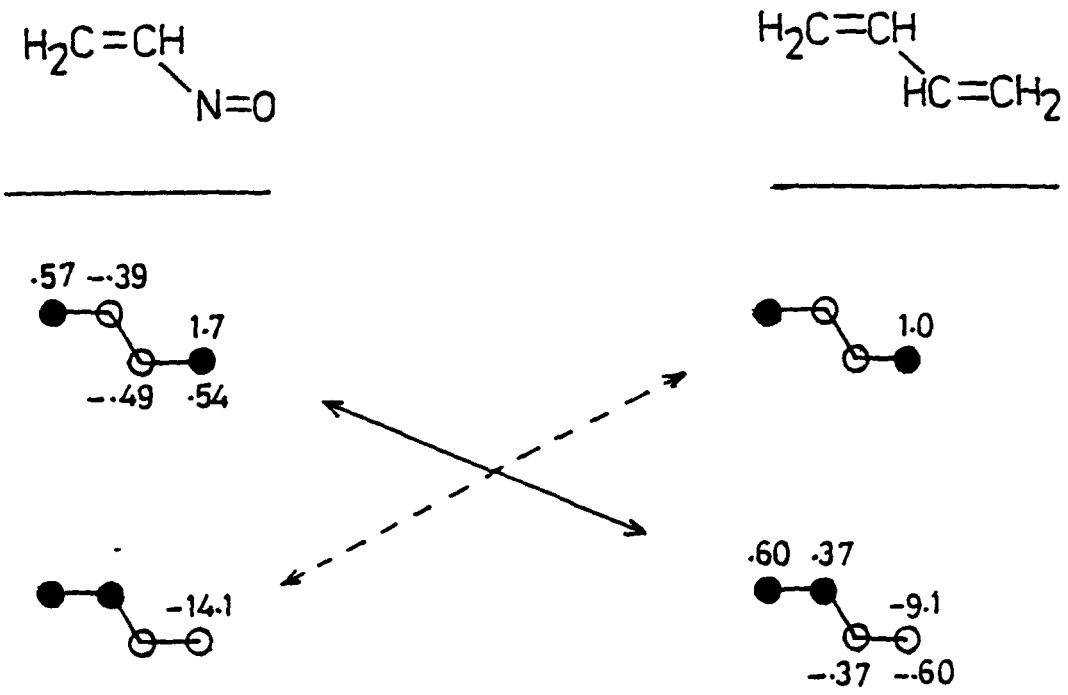
CHAPTER-V

CYCLOADDITION REACTIONS OF 1,3-DIAZA-1,3-BUTADIENES WITH NITRSOALKENES

V.I INTRODUCTION

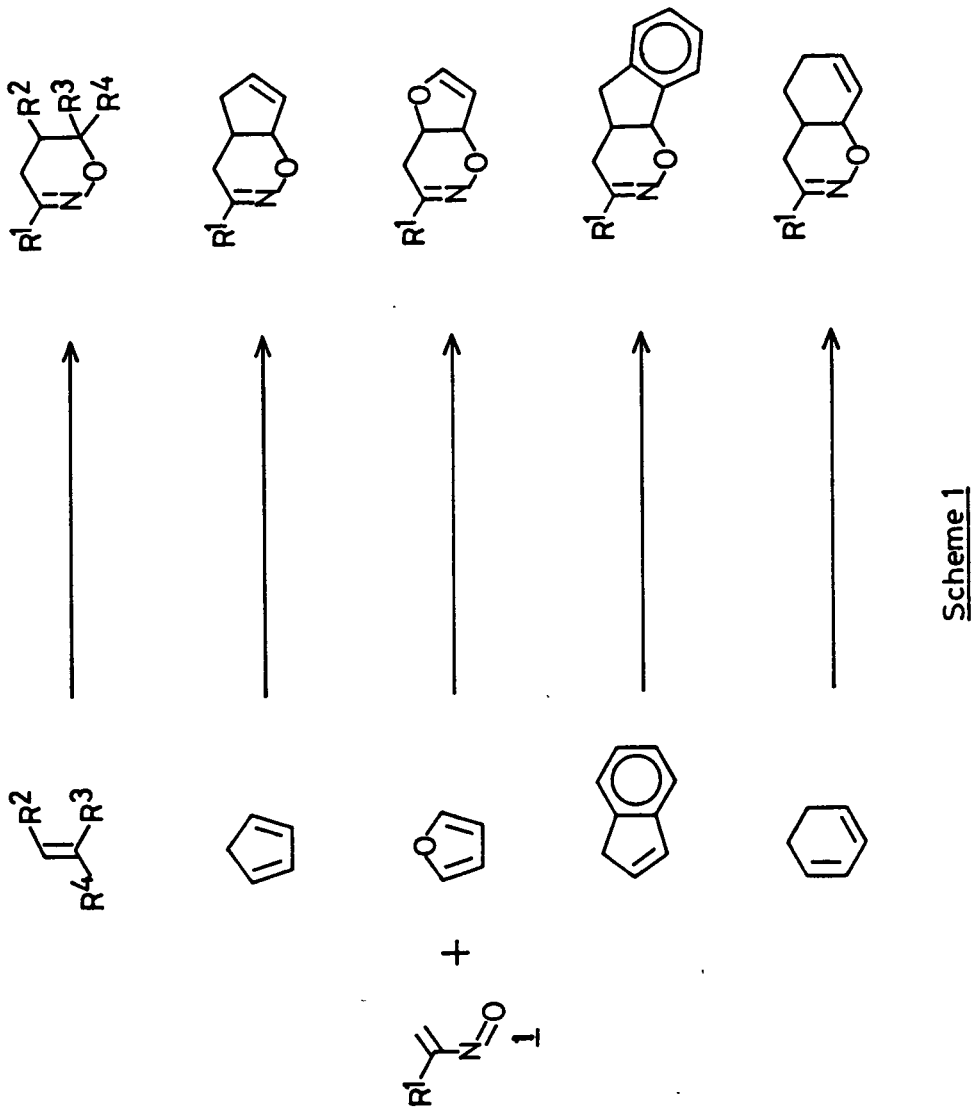
Diels-Alder cycloaddition reactions in which a nitroso group (-N=O) participates as 2π component have been known for several years[1]. The synthetic scope of such cycloaddition reactions has been extended by use, either as diene or dienophile, of nitrosocarbonyl compounds[2,3], nitrosoimines[4,5] and nitrosyl cyanide[6,7]. The nitrosoalkenes(1) usually generated in situ and isolable only if subsituated by bulky alkyl[8] or aryl[9] groups, form another group of extremely reactive synthetic intermediates and have been successfully

trapped as 4π or 2π component in a variety of Diels-Alder cycloaddition reactions[10,11].



Frontier Orbital Energies (ev) and co-efficients for nitroso-ethylene and butadiene.

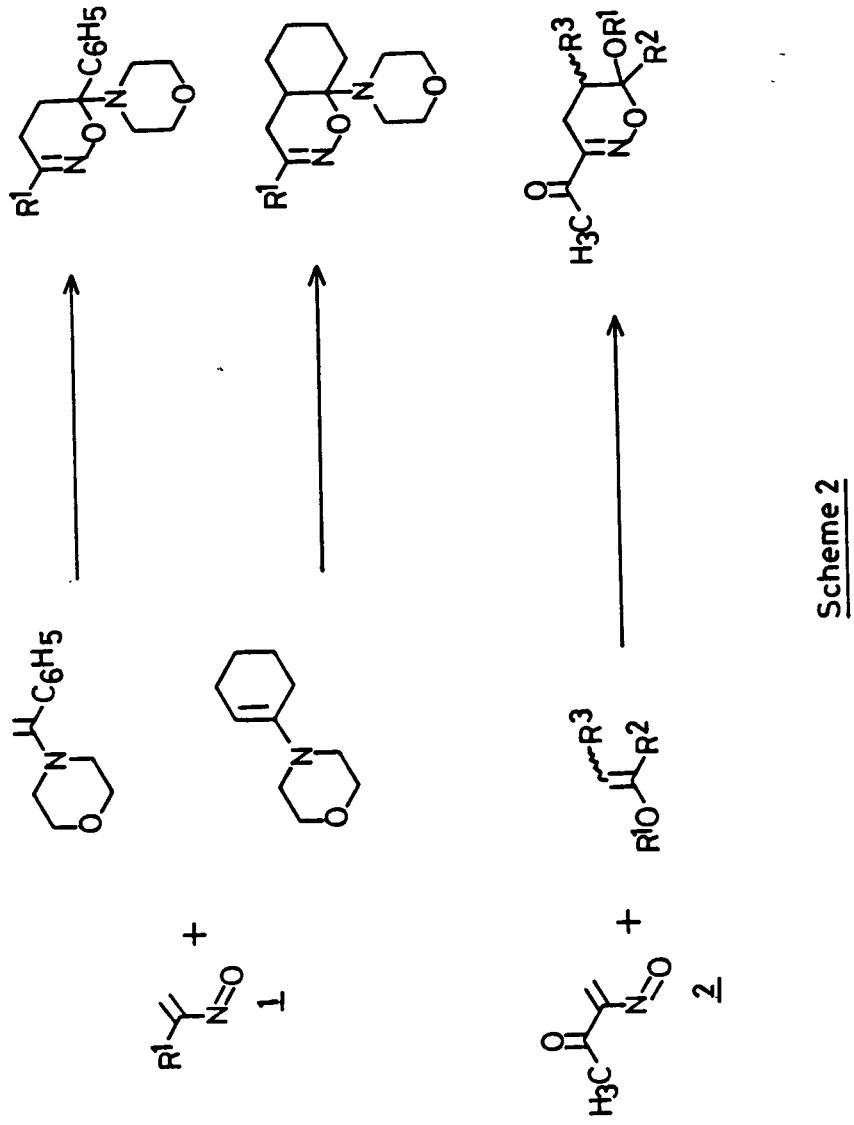
The CNDO/2 calculations of nitrosoalkenes and their comparison with that of butadiene, revealed that major interaction exists between HOMO of butadiene and LUMO of nitroso ethylene, implying that the former acts as a donor and later as an acceptor[10]. The critical examination of orbital ener-



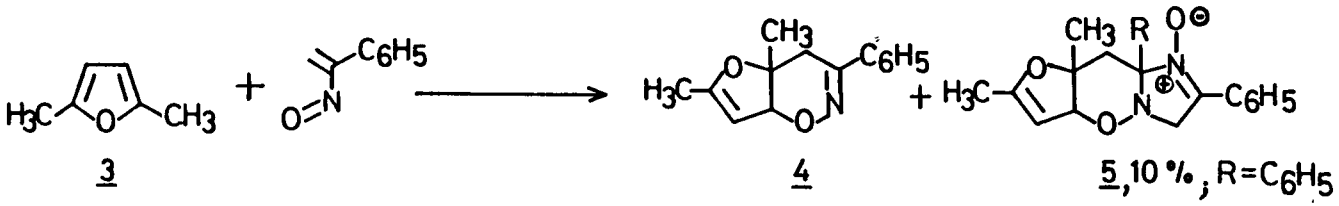
Scheme 1

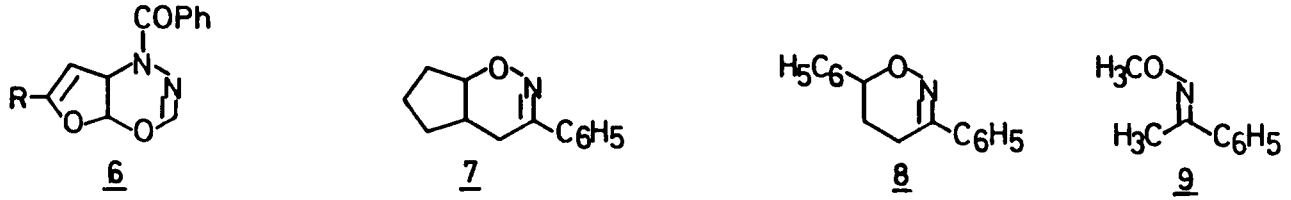
gies further revealed that the nitrosoethylene behaves as an ideal 4π system[13]. This was subsequently experimentally verified by carrying out the reactions of nitrosoalkenes with carbon-carbon double bonds of alkenes and dienes[16] (scheme-1). In the reactions of nitrosoalkenes with all carbon dienes, nitroasoalkenes were shown to act as a 4π component to the more nucleophilic double bond of the dienes[14]. The addition of nitrosoalkenes to electron rich dienophiles e.g. enemines[15,16], enol ethers[17] etc. was found to occur in a stepwise manner through a zwitterionic intermediate (scheme-2). On the other hand, it has been observed that the nitrosoalkenes add to simple alkenes in a concerted manner.

The reports concerning the cycloadditions of nitrosoalkenes with carbon-nitrogen double bond are very rare. Mackay et al[18,19] reported that the reactions of 2,5-dimethylfuran(3) with two equivalents of α-nitrosostyrene resulted in (1:1) adduct 4 as the major product and 10% of a bis-adduct 5 (scheme-3). The nitrones 5 are the result of the formal (3+2) dipolar addition of nitrosoethylene in a 1,3-mode to the oxazine 4, which has been proved by the isolation of 5 in 35% yield by the reaction of 4 with α-nitrosostyrene. Mackay et al[18] had also observed that nitrosoalkenes do not react with carbon-nitrogen double bond of 6, 7, 8



Scheme 2


H3C
CH3
O
3
C6H5
O=N
CH3
C6H5
H3C
O
N
4
CH3
R
O⊙
N⊕
5, 10 %; R=C6H5

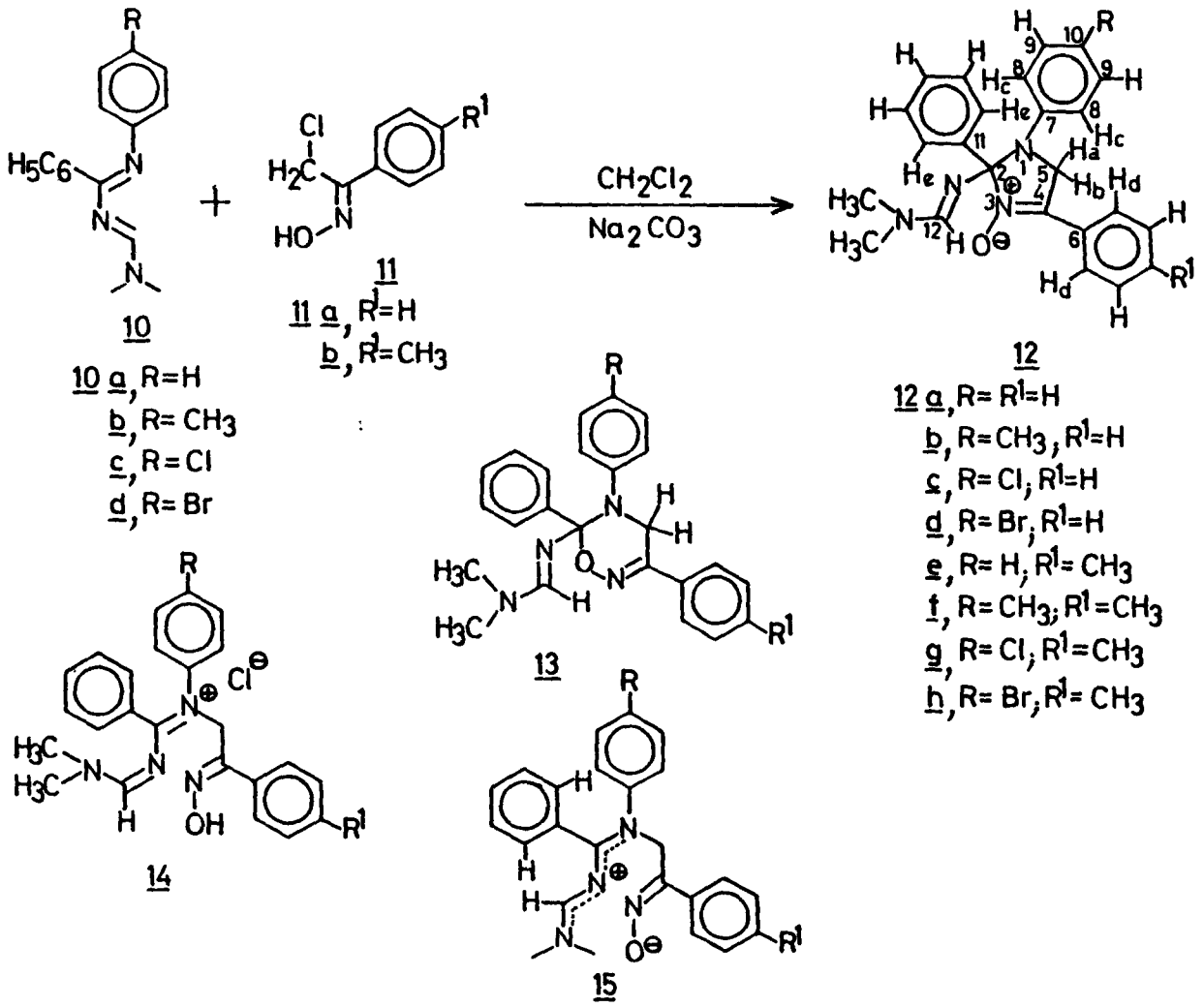

COPh
N
R
O
6
O
N
C6H5
7
H5C6
8
H3CO
H3C
9

Scheme 3

and 9. From the failure of these, taken in order, it was concluded that primary requirement for such a reaction is the oxazin's oxygen and secondary one is an alkene function allylic to this oxygen in a rigid bycyclic systems. Taking these observations into consideration it was though worthwhile to investigate the reactions of 1,3-diaza-1,3-butadienes with nitrosoalkene especially with a view to examine the nature of cycloaddition pathway followed and products formed in these cases.

V.2 RESULTS AND DISCUSSIONS

Treatment of 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes (10a-d) with α-nitrosoalkenes, generated in situ from α-halooximes of acetophenones (11a,b) and sodium carbonate resulted in very good yields of (76-90%) of products 12 (scheme-4). Of the various possible regioisomeric cycloadducts, only the heterocycles 12 have been isolated. This may be expected in view of the higher nucleophilicity of N-1 of 1,3-diaza-1,3-butadienes (10). The products 12 have been characterised as previously unknown 1,4-diaryl-2-N'-(N, N-dimethylformamidino)-2-phenyl-Δ^3-imidazoline-3-oxides on the basis of analytical data and spectral evidences. The product 12a, for example, was analysed for $C_{24}H_{24}N_4O$. Its i.r. spectrum (KBr) showed strong absorption peaks at 1630cm^{-1} and 1590cm^{-1} due to C=N of imine and nitrone, respec-



10

10 a, R=H
b, R= CH3
c, R=Cl
d, R= Br

11

11 a, R1=H
b, R1=CH3

12

12 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= CH3; R1=CH3
g, R= Cl; R1=CH3
h, R= Br; R1= CH3

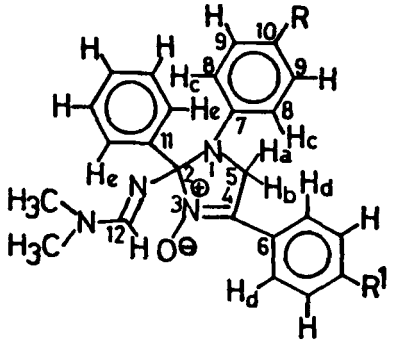
13

14

15

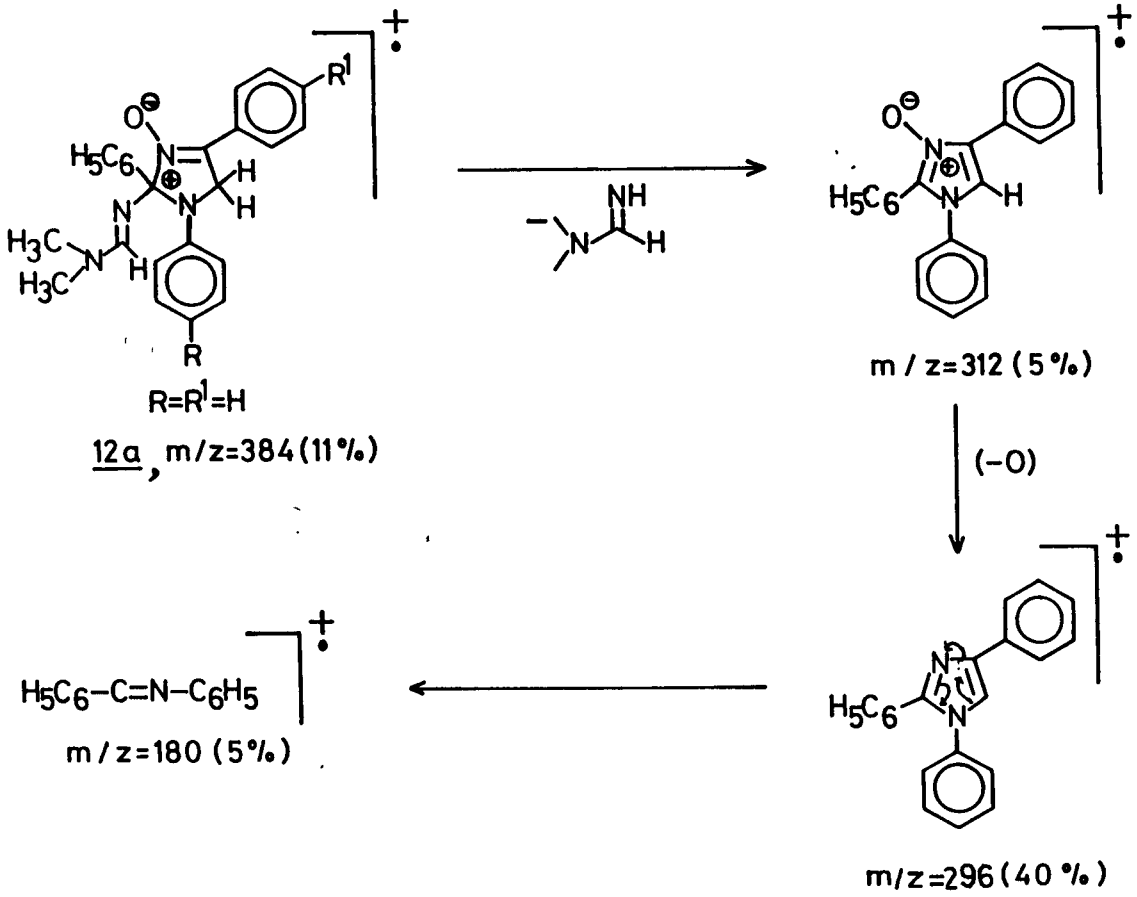
Scheme 4

tively. Its mass spectrum exhibited molecular ion peak at m/z 384(11%). The other major fragments appear at m/z 312(5%) (M^+-72),296(40%)(M^+-88) and 180(5%)(M^+-204). The formation of these fragments in mass spectrum of 12a are explained in scheme-5. The appearance of strong peaks due to loss of N,N-dimethylformamidine (m/z 312) and oxygen (m/z-296) strongly supports the nitrone structure 12 over closely related oxadiazine structure 13. Further, the peak at m/z 296, due to loss of oxygen is diagnostic of nitrones[18,20]. Further support of nitrone structure for 12a is obtained from ^{1}H n.m.r and ^{13}C n.m.r. spectra. Its ^{1}H n.m.r. spectrum exhibited a broad doublet at δ2.81-2.93(6H) for two assymetric methyl groups of $-N(CH_3)_2$ and an unresolved ABq at δ4.93-4.97 (2H) for $-CH_2-$ protons. These methylene protons appeared as clear ABq with Jab=14.40Hz in 200 M.Hz ^{1}H n.m.r. spectra. The aromatic protons appeared at δ6.72-6.80(m,2H,H_c), δ7.60 -7.74(m,2H,may be H_e), δ8.30-8.43(d,2H,H_d) and δ7.01-7.43

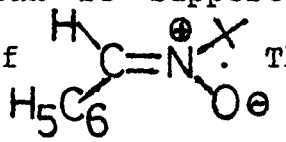


12 a, R= R¹=H

(m,9H,arom). A distinct singlet, except in 12d, in which, it merged with aromatic protons, at δ7.48(1H) was assigned to the formamidino-proton and is comparable with the literature



Scheme 5

value[21,22]. The assignments of doublet at δ8.30-8.43 for two H_d protons is also comparable to the literature value for similar protons in case of nitrones[23]. Its off resonance decoupled ^{13}C n.m.r. spectrum showed peaks at δ 49.2 and δ51.0 ($-N(CH_3)_2$), δ 66.8 (C-5), δ 100.9(C-2), δ 113.07(C-8/8'), δ118.14(C-10), δ 140.5, δ 141.2 and δ141.5(C-7/4/9). The other aromatic carbons appear at δ126.8, δ127.9, δ128.2, δ128.7, δ128.8, δ130.5 and δ133.2. Finally the peak at δ160.72 attached to a hydrogen was assigned to formamidino carbon and this value compares well with the literature value[22]. The assignment of nitrone carbon (C-4) at around δ140.0 can be supported by the reported value of δ129.6 in case of  The replacement of the hydrogen with a methylene of the aforesaid nitrone can thus lead to the carbon value around δ140.0, as observed. The oxadiazine structure can again be ruled out since in this case C-3 carbon is expected around δ156.0[24].

The nitrones 12 are probably the result of the formal (3+2) dipolar addition of free α-nitrosostyrene in a 1,3-mode to 1,2-carbon-nitrogen double bond of 1,3-diaza-1,3-butadienes (10). The formation of nitrones (12) may also be explained by initial formation of resonance stabilised intermediate 14, via displacement of halide by N-1 of 10 from α-chloro-acetophenoneoxime. The intermediate 14 on deprotonation

yield the products 12. Analogies to such two steps cyclization of α-chloroximes including one to N-oxides were known[18], but in all such cases recognizably strong nucleophile is involved. It is unlikely that oximino function could behave in this way. On the other hand there is very strong indication for the free α-nitrososstyrene in these reactions since in the early stages of the reaction a faint but persistent bluish green colour is visible in the stirred suspension and the reaction does not occur at all in the absence of sodium carbonate. The presence of a two proton multiplet at δ7.70 in all derivatives of 12 could not be clearly explained. It may either be due to deshielding of protons H_C of C-2 phenyl or due to the partial opening up of 12 in solution resulting in stabilised zwitterionic species 15.

In order to explain all these aspects, the detailed study concerning the cycloaddition of α-nitrososstyrene with various carbon-nitrogen double bonded substrates is underway.

V.3 EXPERIMENTAL

General conditions are same as described in Chapter II The ^{13}C n.m.r. spectra of compounds 12a, 12b and 12h and 200MHz ^{1}H n.m.r. spectra of compound 12h were obtained from Department of chemistry Glasgow University, Glasgow, U.K.

Starting Materials:

All 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadienes were prepared as described in the experimental section of chapter II. α-Chlorooxime of acetophenone and p-methylacetophenone were prepared by the reported procedure[25]. Anhydrous sodium carbonate used, was preheated at 130°C in hotair oven for 3h.

Reactions of 1,3-Diaza-1,3-butadienes (10a-d) with α-nitrosostyrene; General Procedure: A solution of 1-aryl-4-dimethylamino-2-phenyl-1,3-diaza-1,3-butadiene (4 mmole) and α-chlorooxime (4.2 mmole) in dry dichloromethane (50ml) was stirred at room temperature in presence of anhydrous sodium carbonate (6 mmole) for 48-50 hours. The seperated salt after reaction and excess of sodium carbonate were removed by filtration and the residue was washed with small portions of dichloromethane. The combined filtrate was concentrated under reduced pressure which was then titurated with hexane to precipitate the crude product. The crude products were purified by crystallization from appropriate solvent(s).

2-N'-(N,N-Dimethylformamidino)-1,2,4-triphenyl-Δ^3-imidazoline-3-oxide;(12a): white solid (benzene/pet.ether); yield 80%, m.p. 131-2°C. (Found: C,76.52; H,6.31; N,14.60.$C_{24}H_{24}N_4O$ requires C,75.00; H,6.25; N,14.58).ν_{max}(KBr): 1590 and 1630cm^{-} (C=N).$\delta_H(CDCl_3)$:2.81-2.93(bd,6H,-N$(CH_3)_2$); 4.93-4.97 (unresolved

AB_q,2H,$-CH_2-$); 6.72-6.80(m,2H,H_c,arom), 7.01-7.43 (m,9H,arom); 7.48(s,1H,N=C-H);7.60-7.74(m,2H,H_e,arom) and 8.30-8.43(d,2H, H_d,J=8.00Hz, arom). $\delta_c(CDCl_3)$: 49.2, 51.00 ($-N(CH_3)_2$); 66.8 (C-5);100.9(C-2); 113.07(C-8/8'); 118.14(C-10); 140.5, 141.2, 141.5(C-7/8/9); 133.2(C-6); 126.8, 127.9; 128.2, 128.7, 128.8, 130.5(aromatic carbons) and 160.72(C-12). M^+384.

2-N'-(N,N-dimethylformamidino)-2,4-diphenyl-1-p-tolyl-Δ^3-imidazoline-3-oxide; (12b): white solid(benzene); yield, 86%; m.p.151°C (Found: C,76.50; H,6.57; N,14.00, $C_{25}H_{26}N_4O$ requires C,75.38; H,6.53; N,14.07).ν_{max}(KBr): 1690 and 1630cm^{-1} (C=N). $\delta_H(CDCl_3)$:2.42(s,3H,$-CH_3$); 2.86-2.97(bd,6H,$-N(CH_3)_2$); 4.85-4.93(unresolved AB_q,2H,$-CH_2-$); 6.66-6.80(AA'BB',2H,H_c,arom); 7.03-7.36(m,8H,arom); 7.51(s,1H,N=C-H); 7.56-7.88(m,2H,H_e, arom) and 8.23-8.33(d,2H,H_d, J=8.00Hz, arom).$\delta_C(CDCl_3)$: 20.19(CH_3); 34.4 and 40.3($-N(CH_3)_2$); 50.5(C-5); 104.17(C-2), 113.8(C-7); 127.0, 127.4(C-8/10); 131.7(C-9); 139.9, 140.12 (C-4/6); 126.7, 128.0, 128.2, 128.5, 128.69, 129.2, 130.4 (aromatic carbons) and 154.88(C-12).M^+ 398.

1-p-Chlorophenyl-2-N'-(N,N-dimethylformamidino)-2,4-diphenyl-Δ^3-imidazoline-3-oxide; (12c): white solid(chloroform/pet.ether); yield, 76%; m.p. 188-9°C. (Found:C,70.07; H,5.53; N,13.42. $C_{24}H_{23}ClN_4O$ requires C,68.82; H,5.50; N,13.38).ν_{max}(KBr):

1600 and 1630cm^{-1}(C=N).δ_H($CDCl_3$):2.85-2.92(bd,6H,-N(CH_3)$_2$); 4.92-4.95(unresolved AB_q,2H,-CH_2-); 6.66-6.76(AA'BB',2H,H_c, arom); 7.03-7.36(m,8H,arom); 7.54(s,1H,N=C-H); 7.57-7.70 (m,2H, H_e,arom) and 8.33-8.43(d,2H,H_d, J=8.00Hz, arom).M^+418.

1-p-Bromophenyl-2-N'-(N,N-dimethylforamidino)-2,4-diphenyl-Δ^3-imidazoline-3-oxide;(12d): white solid(chloroform) pet.ether); yield,78%; m.p.193-4°C. (Found:C,61.37; H,4.91; N,12.14. $C_{24}H_{23}BrN_4O$ requries C,62.20; H,4.97; N,12.10).ν_{max}(KBr): 1600 and 1630cm^{-1}(C=N).δ_H($CDCl_3$):2.85-3.00(bd,6H,-N(CH_3)$_2$); 4.92-4.95(unresolved AB_q,2H,-CH_2-); 6.63-6.73(AA'BB',2H,H_c, arom); 7.20-7.56(m,9H,arom and N=C-H); 7.58-7.70(m,2H,H_e,arom) and 8.30-8.43(d,2H,H_d,J=8.00Hz, arom).M^+463.

2-N'-(N,N-dimethylformamidino)-1,2-diphenyl-4-p-tolyl-Δ^3-imidazoline-3-oxide; (12e): white solid(benzene); yield, 85%, m.p.149-50°C.(Found: C,77.10; H,6.56; N,14.10.$C_{25}H_{26}N_4O$ requires C,75.38; H,6.53; N,14.07).ν_{max}(KBr): 1590 and 1630cm^{-1} (C=N).δ_H($CDCl_3$): 2.38(s,3H,-CH_3); 2.80-3.00(bd,6H,-N(CH_3)$_2$); 4.93-5.00(unresolved AB_q,2H,-CH_2-); 6.63-6.76(m,2H,H_c,arom); 7.03-7.40(m,8H,arom); 7.50(s,1H,N=C-H); 7.63-7.80(m,2H,H_e, arom) and 8.26-8.35(d,2H,H_d,J=8.00Hz,arom).M^+398.

1,4-Bis(p-tolyl)-2-N'-(N,N-dimethylformamidino)-2-phenyl-Δ^3-imidazoline-3-oxide;(12f): white solid(benzene); yield, 90%; m.p. 135°C.(Found: C,76.12; H,6.28; N,13.57.$C_{26}H_{28}N_4O$

requires C,75.73; H,6.80; N,13.59).ν_{max}(KBr): 1600 and 1630 cm^{-1}(C=N).$\delta_H(CDCl_3)$: 2.16(s,3H,$-CH_3$); 2.36(s,3H,$-CH_3$); 2.80 -2.98 (bd,6H,$-N(CH_3)_2$); 4.90-4.94(unresolved AB_q,2H,$-CH_2-$); 6.63- 7.00(AA'BB',2H,H_c,arom); 7.20-7.33(m,8H,arom); 7.50(s, 1H,N=C-H); 7.62-7.76(m,2H,H_e,arom) and 8.20-8.33(d,2H,H_d, J=8.00Hz, arom).M^+412.

1-p-Chlorophenyl-2-N'-(N,N-dimylformamidino)-2-phenyl-4-p-tolyl-Δ^3-imidazoline-3-oxide;(12g): white solid; (Chloroform/ pet.ether); yield, 76%; m.p. 193°C. (Found: C,70.46; H,5.78; N,12.84.$C_{25}H_{25}ClN_4O$ requires C,69.36; H,5.78; N,12.95).ν_{max} (KBr): 1600 and 1630cm^{-1}(C=N).$\delta_H(CDCl_3)$:2.38(s,3H,$-CH_3$); 2.83-2.93(bd,6H,$-N(CH_3)_2$); 4.90-4.93(unresolved AB_q,2H,$-CH_2-$); 6.63-6.74(AA'BB',2H,H_c,arom); 7.14-7.36(m,7H,arom); 7.50(s,1H, N=C-H); 7.60-7.73(m,2H,H_e,arom) and 8.23-8.35(d,2H,H_d,J= 8.00Hz).M^+432.

1-p-Bromophenyl-2-N'-(N,N-dimethylformamidino)-2-phenyl-4-p-tolyl-Δ^3-imidazoline-3-oxide;(12h): white solid (Chloroform/ pet.ether); yield, 90%; m.p.198°C. (Found:c,64.04; H,5.27; N,11.76.$C_{25}H_{25}BrN_4O$ requires C,62.89; H,5.24; N,11.74).ν_{max} (KBr): 1600 and 1630cm^{-1}(C=N).$\delta_H(CDCl_3)$:2.40(s,3H,$-CH_3$); 2.86-2.96(bd,6H,$-N(CH_3)_2$); 4.90-4.93(unresolved AB_q,2H,$-CH_2-$); 6.63-6.73(AA'BB',2H,H_c,arom); 7.12-7.36(m,7H,arom); 7.53 (s,1H,N=C-H); 7.56-7.70(m,2H,H_e,arom) and 8.23-8.34(d,2H,H_d,

J=8.00Hz,arom). 200MHz ^{1}H n.m.r. spectrum; $\delta_H(CDCl_3)$: 2.42 (s,3H,$-CH_3$); 2.87(s,3H,-N-CH_3), 3.04(s,3H,-N-CH_3); 4.94(AB_q, 2H,$-CH_2-$, J_{AB}=14.4Hz); 6.72(AA'BB',2H,H_c, J=9.1Hz,arom); 7.20-7.40(m,7H,arom),7.54(s,1H,N=C-H); 7.65-7.73(m,2H,H_e, arom)1 and 8.30-8.34(d,2H,H_d,J=8.3Hz arom).$\delta_C(CDCl_3)$: 21.54 ($\underline{C}H_3$); 34.32(-N-$\underline{C}H_3$);40.30(-N-$\underline{C}H_3$); 50.39(C-5), 103.78(C-2); 110.19 (C-10), 115.57(C-8,8'), 139.47,141.09,141.46(C-2,4,7); 124.36, 126.77,128.00,128.08,128.85,129.23,131.28,131.88 (aromatic carbons) and 154.67(C-12).M^+477.

REFERENCES

1. J. Hammer and M. Ahmed, **1,4-Cycloaddition Reactions**, Ed. J.Hammer, Academic Press, New York, 1967, p.419
2. G.W. Kirby and J.G. Sweeny, **J. Chem. Soc. Chem. Commun.**, 1973, 704.
3. G.W. Kirby and J.W.M. Mackinon, **J. Chem. Soc. Chem. Commun.**, 1977, 23.
4. T.L. Gilchrist, M.E. Peek, and C.W. Rees, **J. Chem. Soc. Chem. Commun.**, 1975, 913, 914.
5. T.L. Gilchrist, C.J. Harries, F.D. King, M.E. Peek, and C.W. Rees, **J. Chem. Soc. Perkin Trans. I**, 1976, 2161.
6. P. Horswood and G.W. Kirby, **J. Chem. Soc. Chem. Commun.**, 1971, 1139.
7. G.W. Kirby, **Chem. Soc. Rev.**, 1977, **1**, 6.
8. K. Weisser and A. Berndt, **Angew. Chem. Int. Ed. Engl.**, 1975, **14**, 70.
9. W. Hobold, U. Prietz, and W. Pritzkow, **J. Prakt. Chem.**, 1969, **311**, 260.
10. R. Faragher and T.L. Gilchrist, **J. Chem. Soc. Perkin Trans. I**, 1979, 249.
11. T.L. Gilchrist, **Chem. Soc. Rev.**, 1983, **12**, 53.
12. E.J.T. Chrystal, T.L. Gilchrist, and W. Stretch, **J. Chem. Res(S).**, 1987, 180; **J. Chem. Res(M).**, 1987, 1563.
13. D.Y.Curtin and E.W. Tristram, **J. Am. Chem. Soc.**, 1950, **72**, 5238.

14. R. Faragher and T.L. Gilchrist, **J. Chem. Soc. Chem. Commun.**, 1976, 581.

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

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

17. R. Faragher and T.L. Gilchrist, **J. Chem. Soc. Perkin Trans.I**, 1979 258

18. D. Mackay and K.N. Walson, **J. Chem. Soc. Chem. Commun.**, 1982, 775.

19. D. Mackay and K.N. Walson, **J. Chem. Soc. Chem. Commun.**, 1982, 777.

20(a) T.A. Bryce and J.R.Maxwell, **J. Chem. Soc. Chem. Commun.**, 1965, 206.

(b) R.G. Kostyanovskii, A.P. Pleshkova, V.N. Voznesenskii A.I. Mischenko, A.V. Prosyanik, and V.I. Markow, **Izv. Akad. Nauk SSSR, Ser. Khim. (Engl. Transl.)**, 1980, 240.

21. J.P. Marsh and L. Goodmann, **Tetrahedron Lett.**, 1968, 5225.

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

23. Nitric Oxides, Nitrones and Nitronates in Organic Synthesis,**Novel Strategis in Synthesis**, Ed., K.B.G. Torsell, VCH Publishers, 1988, p-78.

24. R. Zimmer and H.U. Reißig, **Angew. Chem. Int. Ed. Engl.**, 1988, **27**, 1518.

25. H. Korten and R. Scholl, **Chem. Ber.**, 1901, **34**, 1901.