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

ABSTRACT

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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 4 π 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.

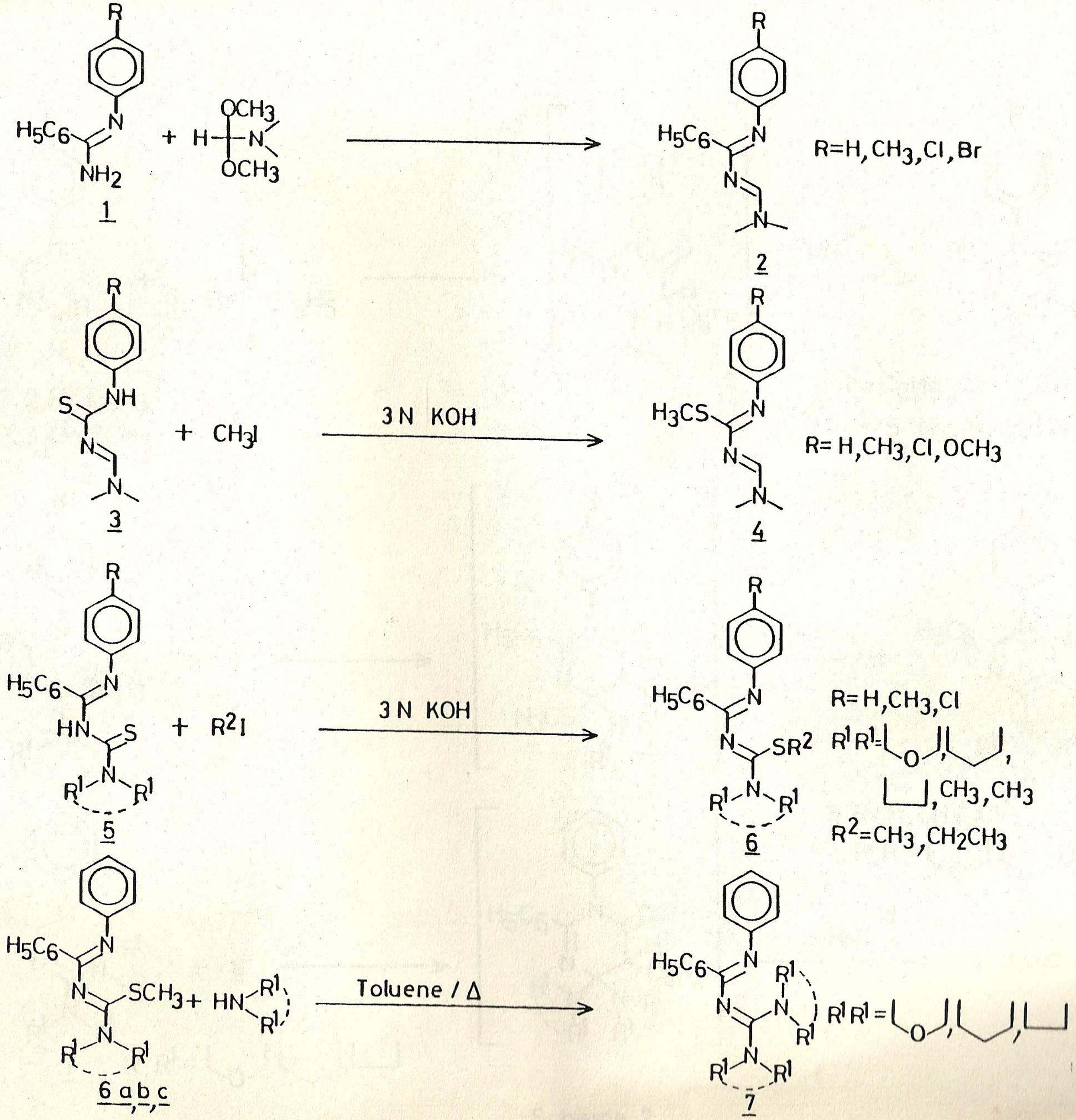
The thesis is divided into five chapters. The first chapter deals with an uptodate literature survey concerning Diels-Alder cycloaddition reactions of various mono- and diazabutadienes.

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-

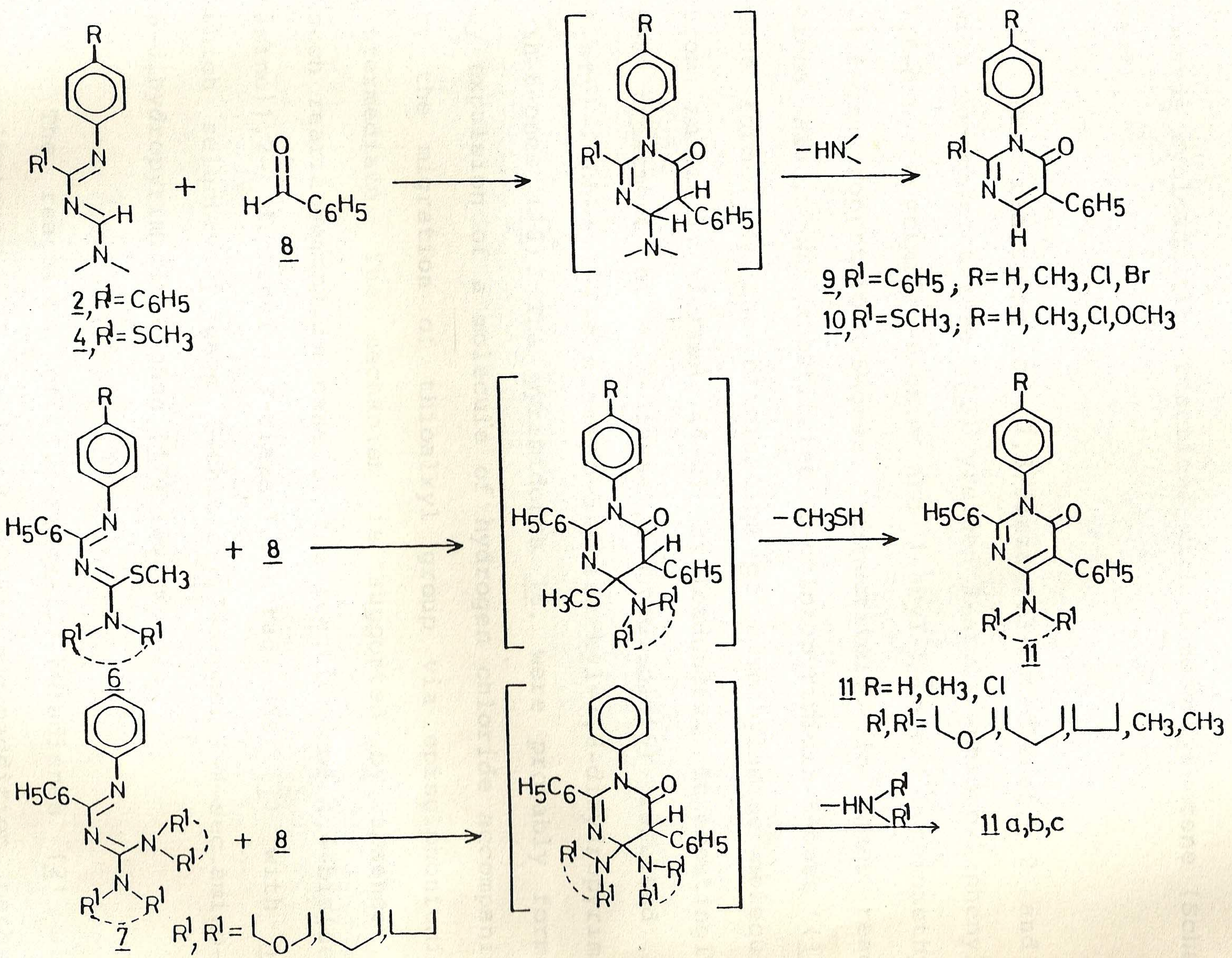
2-phenyl-1,3-diaza-1,3-butadienes(2).

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


1
3N KOH
3
+ CH3I
2
R=H, CH3, Cl, Br
4
R= H, CH3, Cl, OCH3
5
+ R2I
3N KOH
6
R= H, CH3, Cl
R1R1 = , , , CH3, CH3
R2=CH3, CH2CH3
6 a, b, c
Toluene / Δ
7
R1R1 = , ,

Scheme 1

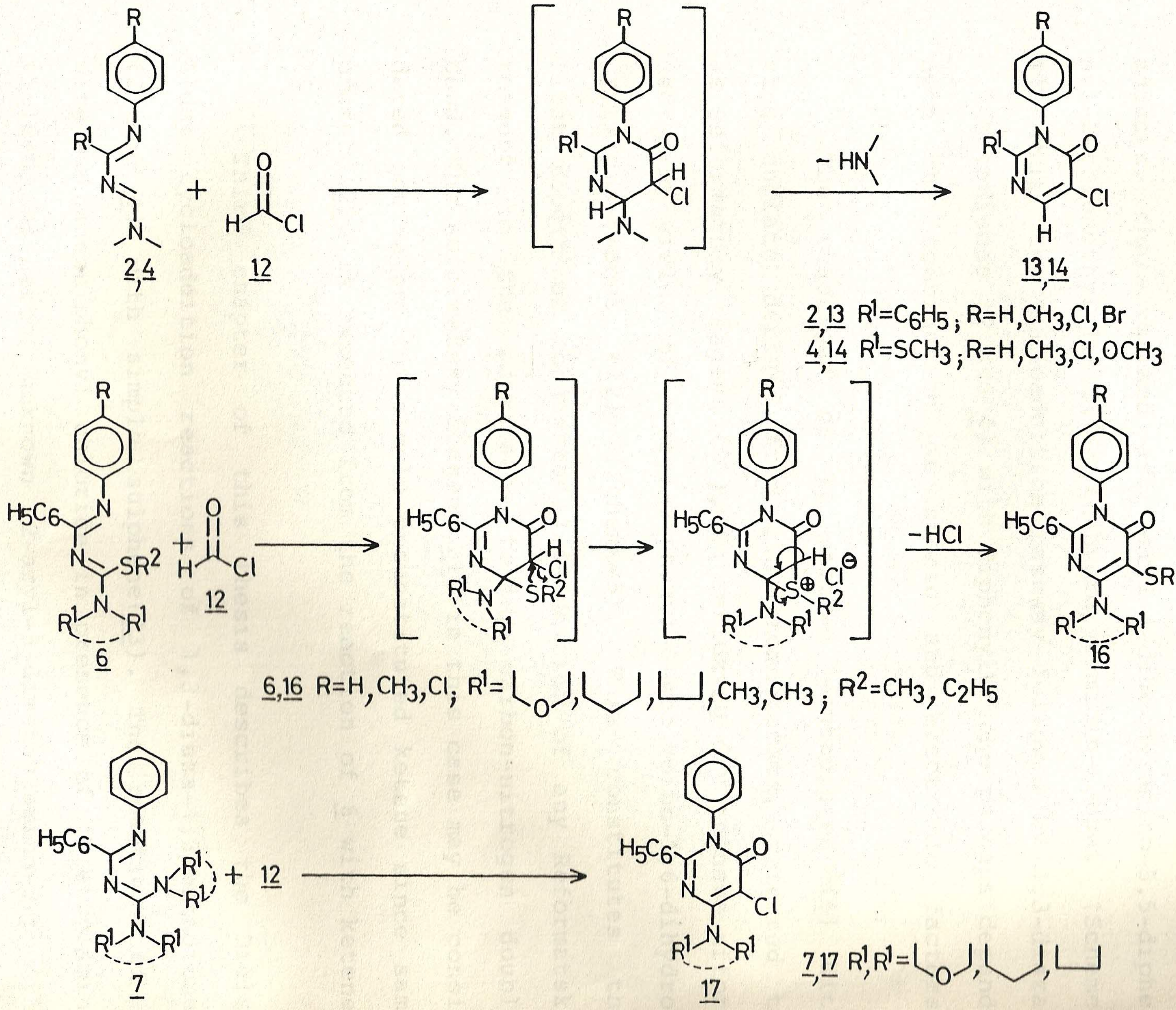

R
R1
N
N
H
N
2, R1= C6H5
4, R1= SCH3
+
H
O
C6H5
8
N
O
H
C6H5
H
N
-HN<
O
C6H5
H
9, R1=C6H5 ; R= H, CH3, Cl, Br
10, R1=SCH3; R= H, CH3, Cl, OCH3
H5C6
SCH3
6
+ 8
H3CS
N-R1
-CH3SH
11
11 R= H, CH3, Cl
R1, R1= ⌊O⌋, ⌊⌋, ⌊⌋, CH3, CH3
7
R1, R1= ⌊O⌋, ⌊⌋, ⌊⌋
-HN(R1)R1
11 a,b,c

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

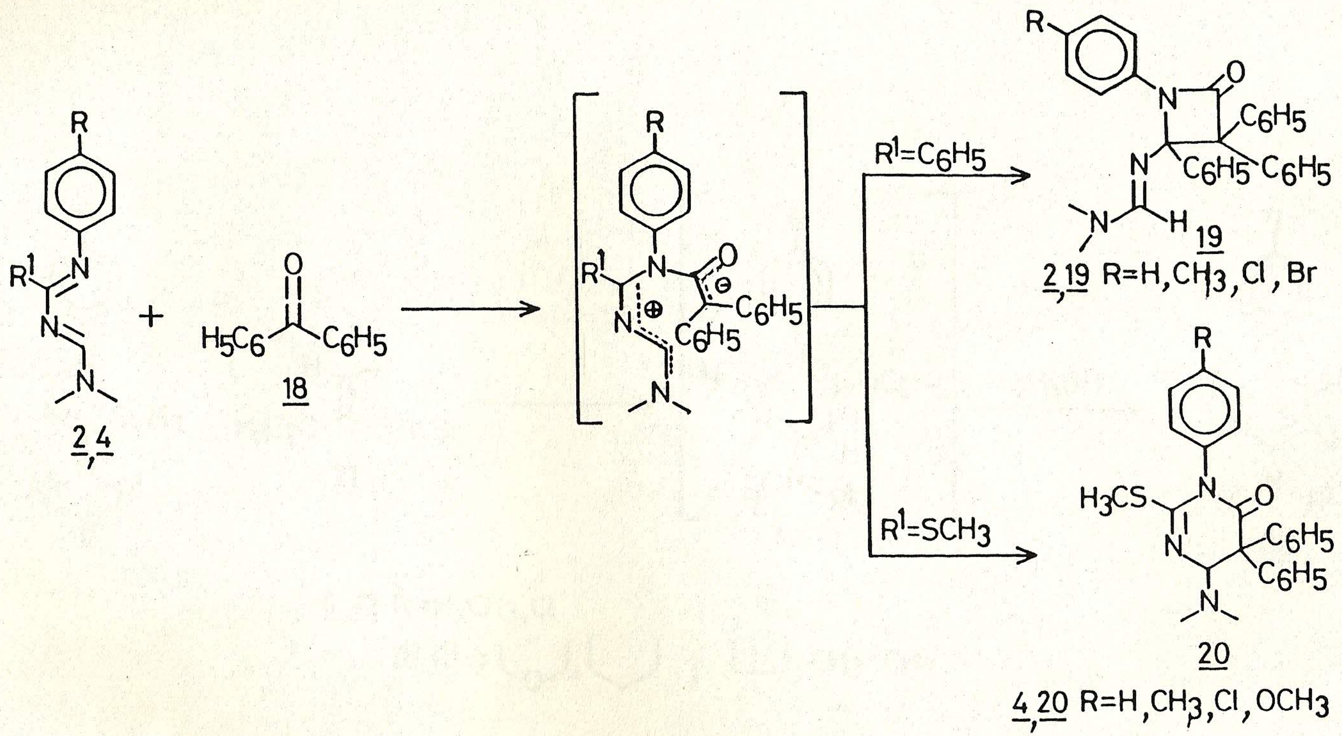

2,4
12
13,14
- HN
2,13 R1=C6H5; R=H,CH3,Cl,Br
4,14 R1=SCH3; R=H,CH3,Cl,OCH3
6
12
-HCl
16
6,16 R=H,CH3,Cl; R1= , , ,CH3,CH3; R2=CH3, C2H5
7
12
17
7,17 R1,R1= , ,

Scheme 3

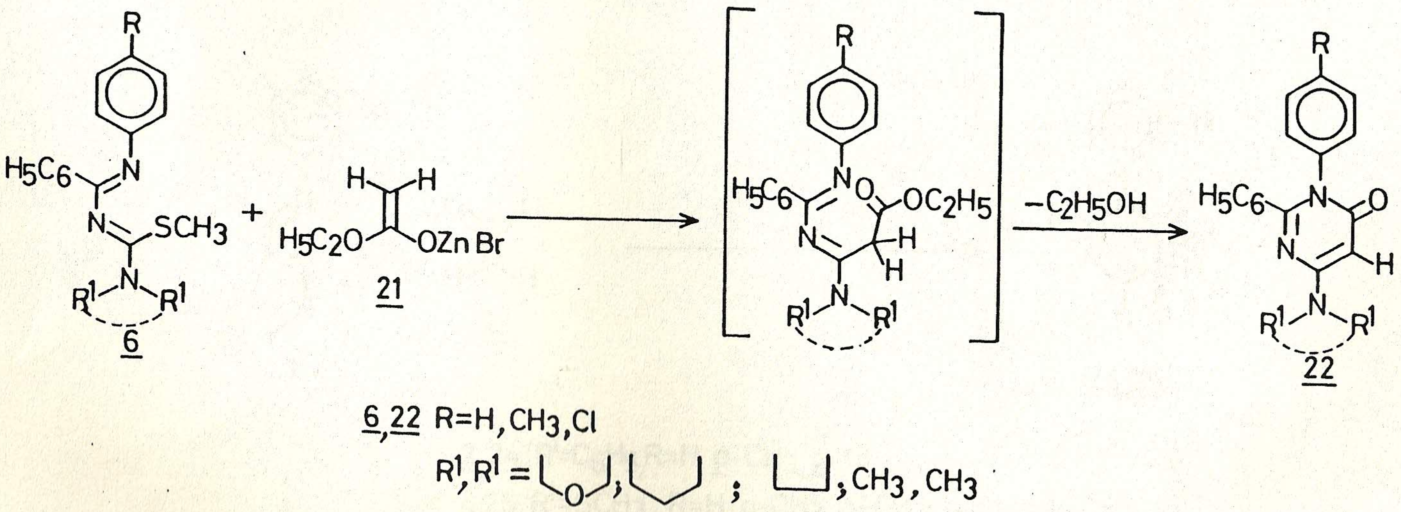
to the steric reasons. However, similar reactions of diphenylketene with 4, gave excellent yields of (4+2) cycloadducts, characterised as 1-aryl-4-dimethylamino-5,5-diphenyl-2-thiomethyl-1,4,5,6-tetrahydropyrimidin-6-ones (Scheme-4). Thus, the cycloaddition pathway followed by 1,3-diaza-1,3-butadienes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

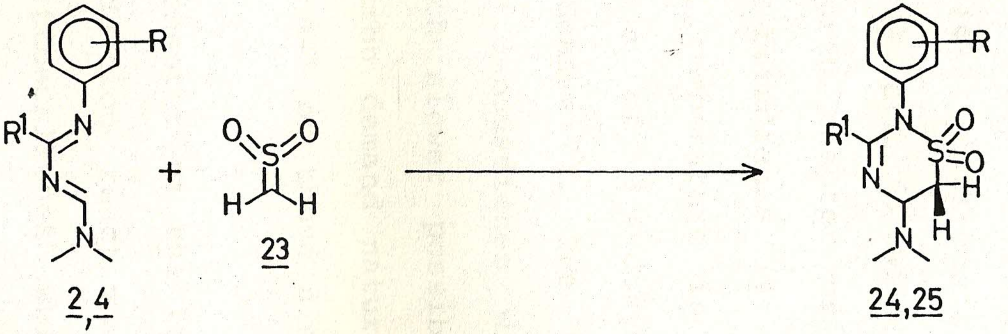
Third chapter of this thesis describes the Diels-Alder cycloaddition reactions of 1,3-diaza-1,3-butadienes (2 and 4) with simple sulphene(23). The reactions of 2 with methanesulphonyl chloride in presence of triethylamine yielded hitherto unknown 2-aryl-5-dimethylamino-3-phenyl-1,2,4-thiadiazin-1,1-dioxide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



Scheme 4



Scheme 5



$\underline{2},\underline{24}$ $R^1=C_6H_5$; R=H, p-CH_3, p-Cl

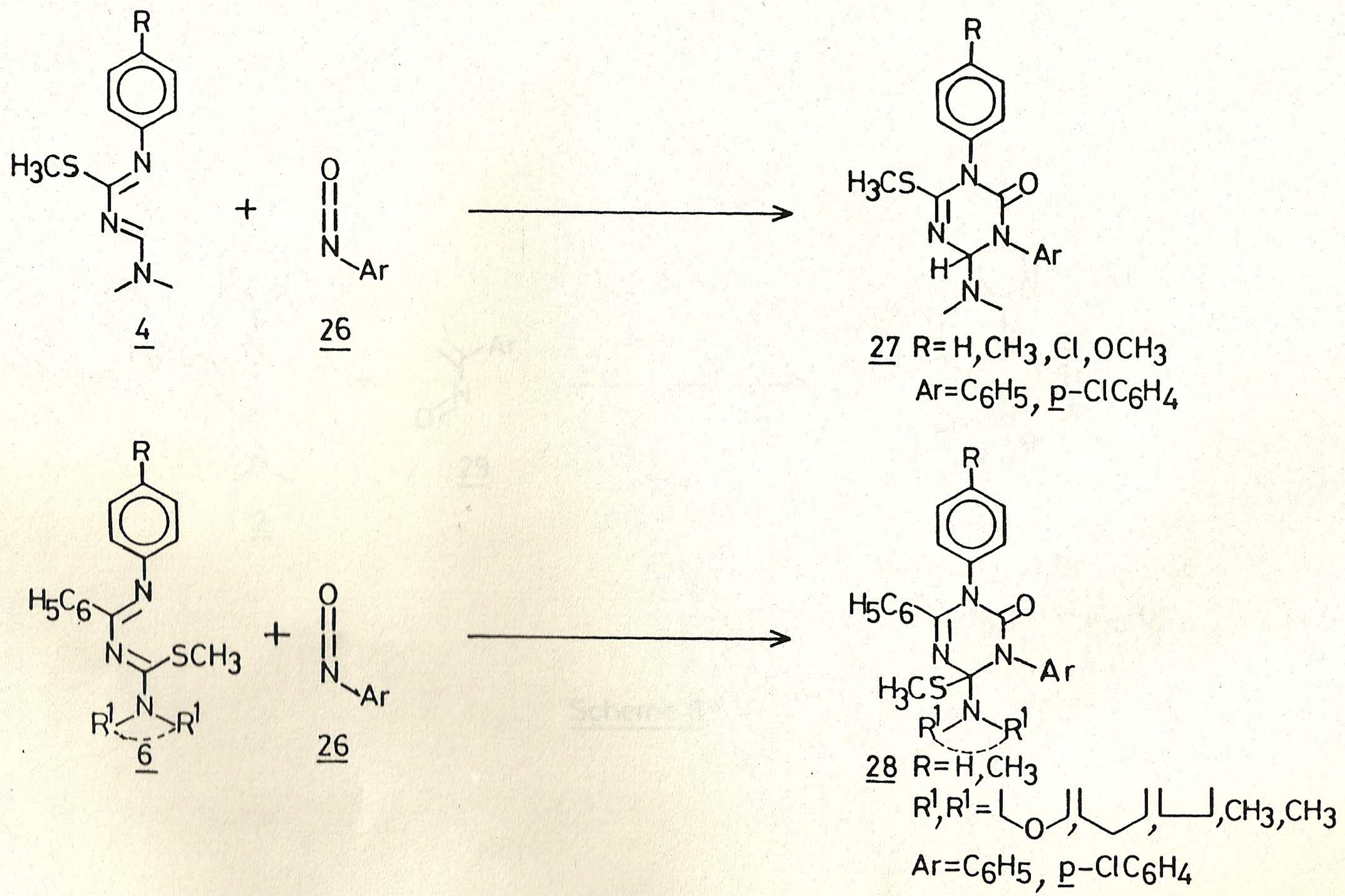
$\underline{4},\underline{25}$ $R^1=SCH_3$; R=H, p-CH_3, o-CH_3, p-Cl, p-OCH_3

Scheme 6

tions of 4 with sulphene resulted in 2-aryl-5-dimetnylamino-3-thiomethyl-1,2,4-thiadiazin-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 inverse electron demand nature of 1,3-diaza-1,3-butadienes which makes N-1 of those dienes less nucleophilic[11-13].

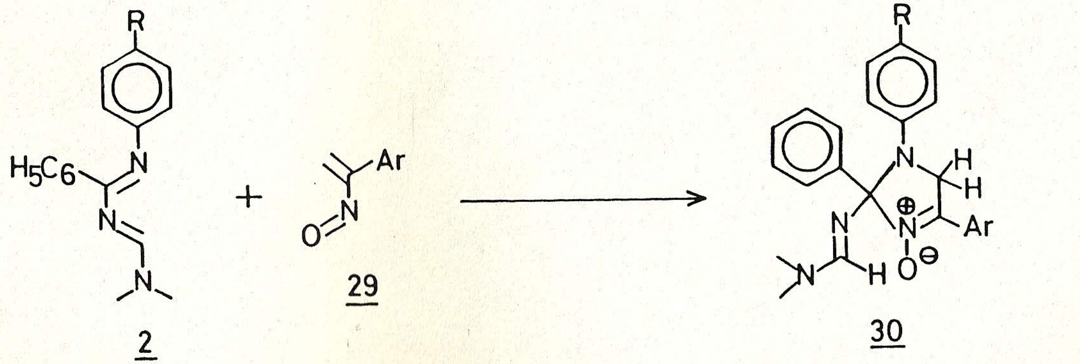
The last chapter of the thesis deals with the regioselctive cycloaddition reactions of 1,3-diaza-1,3-butadienes(2) with nitrosoalkenes which interestingly resulted in 1,4-diaryl-2-N'-(N,N-dimethylformamidino)-2-phenyl-Δ^3-imidazoline-3-oxide (30) (Scheme-8). The nitrones (30) are probably formed by an 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).



27 R= H,CH_3,Cl,OCH_3
Ar=C_6H_5, p-ClC_6H_4

28 R=H,CH_3
R^1,R^1= , , ,CH_3,CH_3
Ar=C_6H_5, p-ClC_6H_4

Scheme 7



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.

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