NOVEL HETEROCYCLIC SYNTHESIS INVOLVING STUDIES RELATED TO 1,3-DIAZABUTADIENES-KETENES CYCLOADDITIONS

ABSTRACT

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CHAPTER-I

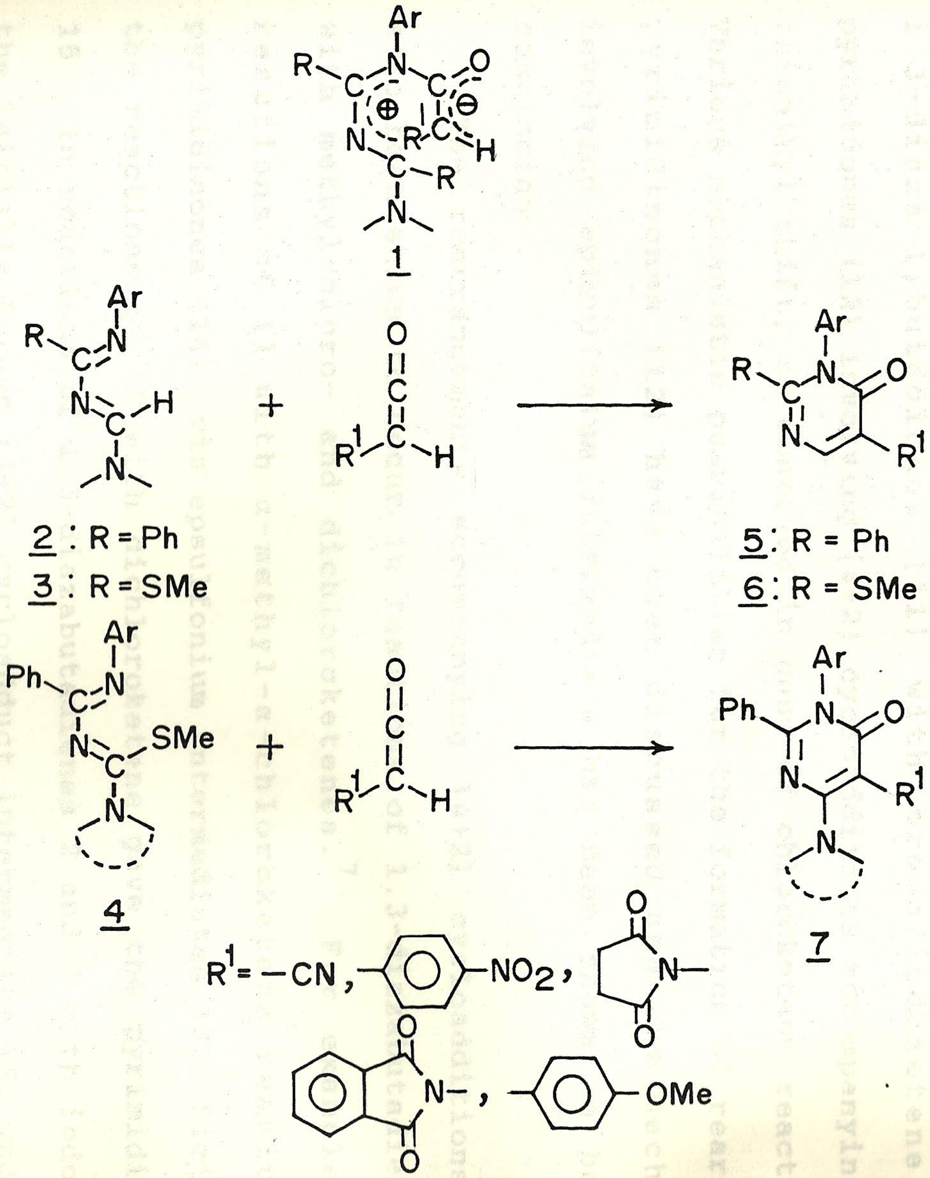
Ketene Chemistry is dominated by [2+2] cycloadditions, which over the years has proved to be an important well documented route to the synthesis of four membered carbocyclic and heterocyclic systems.[1-4] There are numerous reports concerning [2+2] cycloadditions of alkenes with ketenes to yield various cyclobutanone derivatives and of imine-hetene cycloadditions leading to a variety of substituted β-lactam derivatives.[5] A brief review of the cycloadditions of ketenes to alkenes and imines, including monoaza and diazabutadienes, is presented in the first chapter of this thesis.

CHAPTER-II

It has recently been observed that the reactions of polarized 1,3-diaza-1,3-butadienes with monophenyl and monochloroketenes followed [4+2] cycloaddition mode, leading to pyrimidinones as products.[6] The formation of [4+2] cycloadducts in these cases was thought probably due to the higher stability of zwitterionic intermediate (**1**). In order to examine the influence of the stability of zwitterionic intermediate on the mode of cycloaddition, we have examined in this chapter the reactions with ketenes which can either stabilise the anionic component of such a zwitterion. Thus the reactions of 1,3-diaza-1,3-butadienes (**2-4**) with cyano-, p-nitrophenyl-, succinimido, phthalimido- and phenoxyketenes were investigated and all these reactions were also found to follow [4+2] cycloaddition mode leading to 3-aryl-pyrimidin-4(3*H*)-one derivatives **5**,**6**,**7** (Scheme-1). The products were assigned these structures on the basis of analytical and spectral data. From the results above, it may be concluded that the stability of zwitterion/anionic component of zwitterion and to some extent steric factors may not be playing predominant or exclusive role in the observed mode of cycloaddition.

CHAPTER-III

The Chapter III of the thesis describes the reactions of various 1,3-diazabutadienes with bromo-, Iodo-, chloromethyl- and

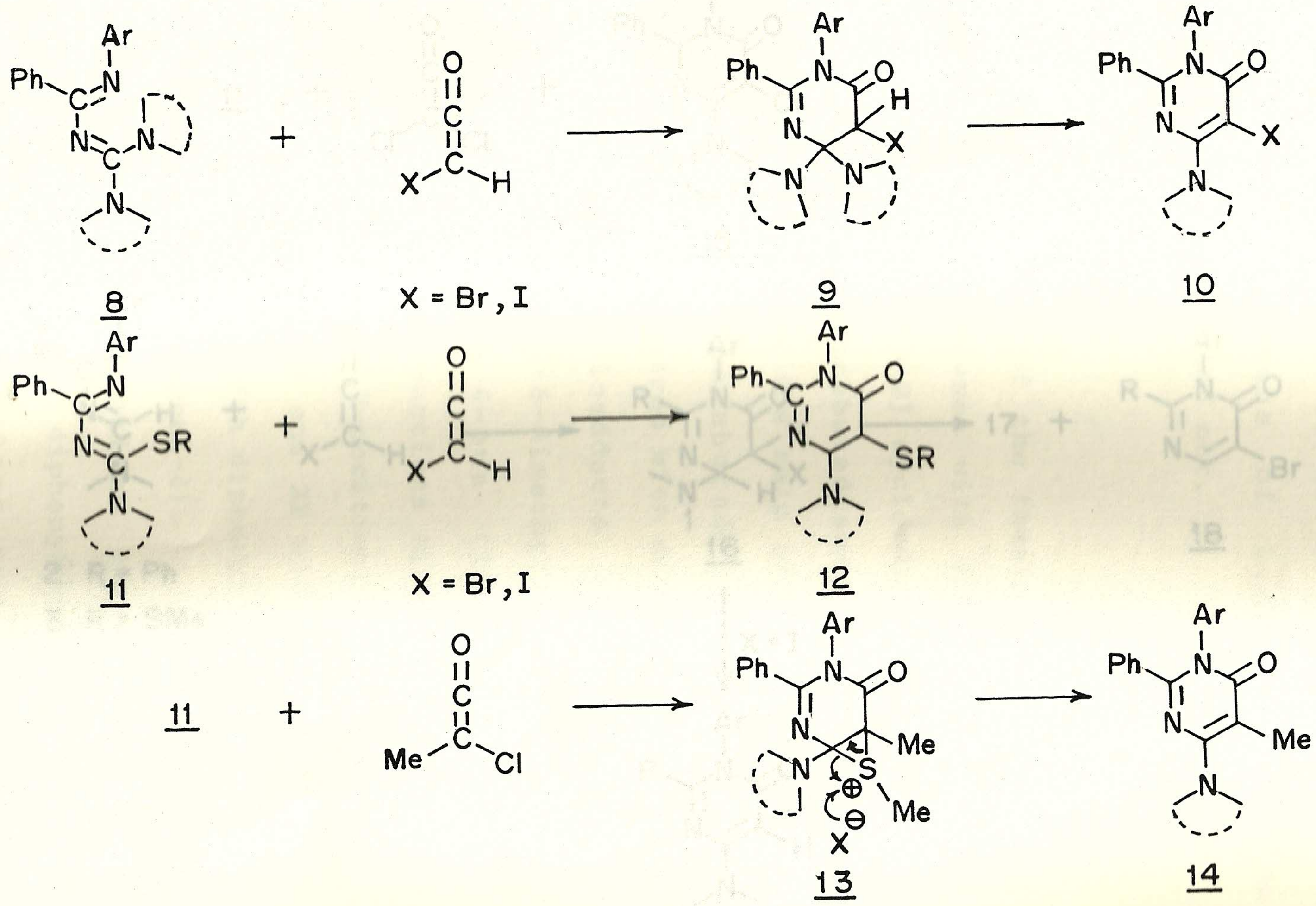

Ar
R
N
C
O
⊕
⊖
N
R
C
H
R
N
1
2 : R = Ph
3 : R = SMe
+
R1
H
5: R = Ph
6: R = SMe
Ph
SMe
4
7
R1 = —CN,
NO2,
N—
OMe

Scheme-1

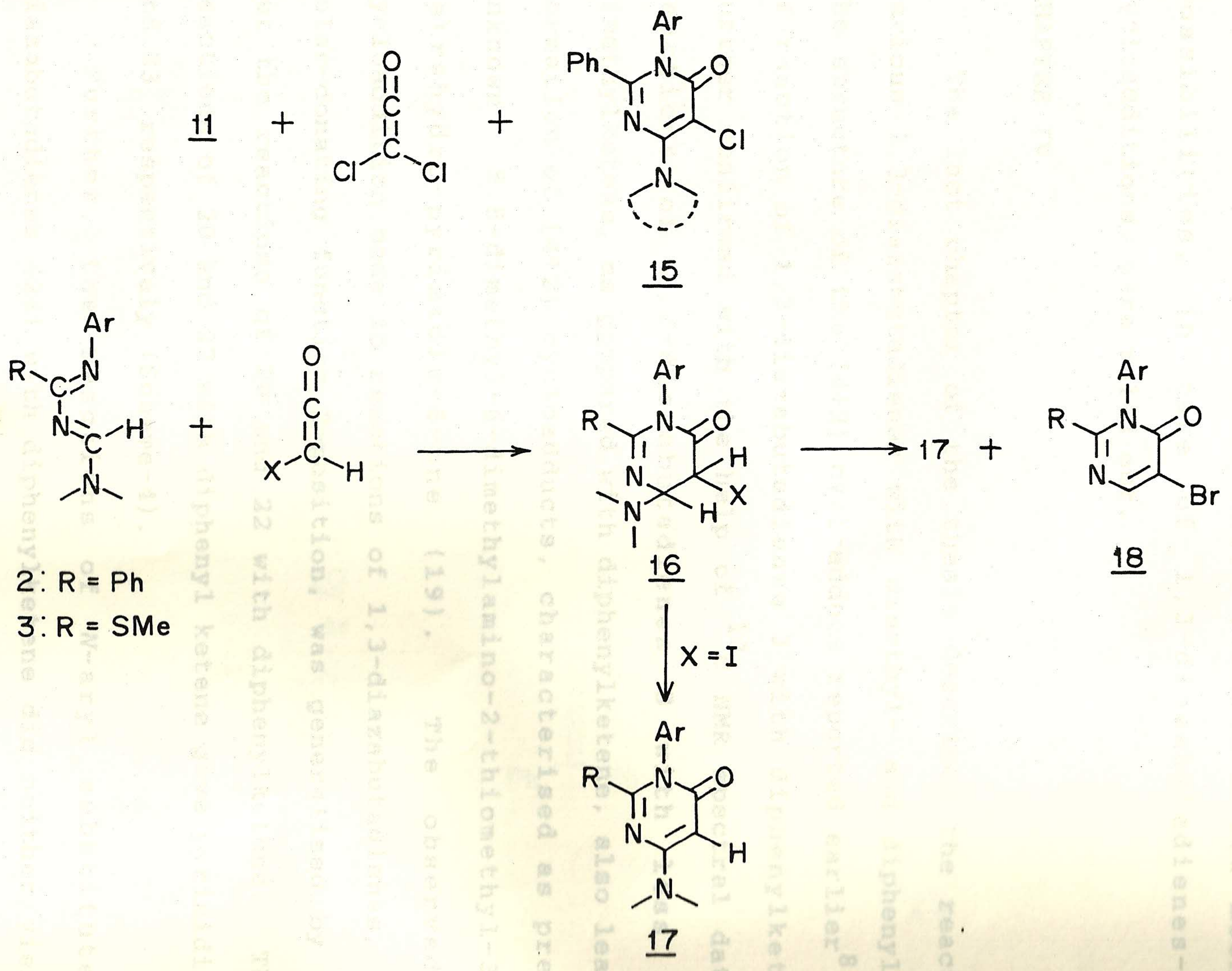
dichloroketene. The reactions of 1-aryl-2-phenyl-4-bis (sec. amino)-1,3-diaza-1,3-butadienes (8) with monobromo- and monoiodoketenes, resulted in good yields of 3-aryl-6-sec. amino-5-bromo/iodo-2-phenyl-pyrimidin-4(3*H*)-one (10), presumably formed *via* the elimination of sec. amines from the initially formed [4+2] cycloadducts 9, as intermediates (Scheme-2).

The reactions of 1-aryl-2-phenyl-4-thioalkyl-4-sec. amino-1,3-diaza-1,butadienes (11) with bromo/iodoketene gave pyrimidones (12) involving [4+2] cycloadditions accompanying 1,2-thioalkyl shift, as observed in case of chloroketene reactions.[7] Various mechanistic possibilities for the formation of rearranged pyrimidinones (12) have been discussed and the mechanism involving episulfonium intermediate has been shown to be most convincing.

The rearrangements accompanying [4+2] cycloadditions have also been shown to occur in reactions of 1,3-diazabutadienes 11 with methylchloro- and dichloroketenes.[7] For example, the reactions of 11 with α-methyl-α-chloroketene resulted in pyrimidinones (14), via epsulfonium intermediates 13. Similarly, the reactions of 11 with dichloroketene gave the pyrimidinones. 15 In reactions of 1,3-diazabutadienes 2 and 3 with iodoketene the initially formed [4+2] cycloadduct intermediate 16, underwent exclusive elimination of hydroiodic acid, in contrast to elimination of dimethylamine in case of chloroketene, to yield pyrimidinones 17 (Scheme-3). In case of bromoketene



Scheme-2



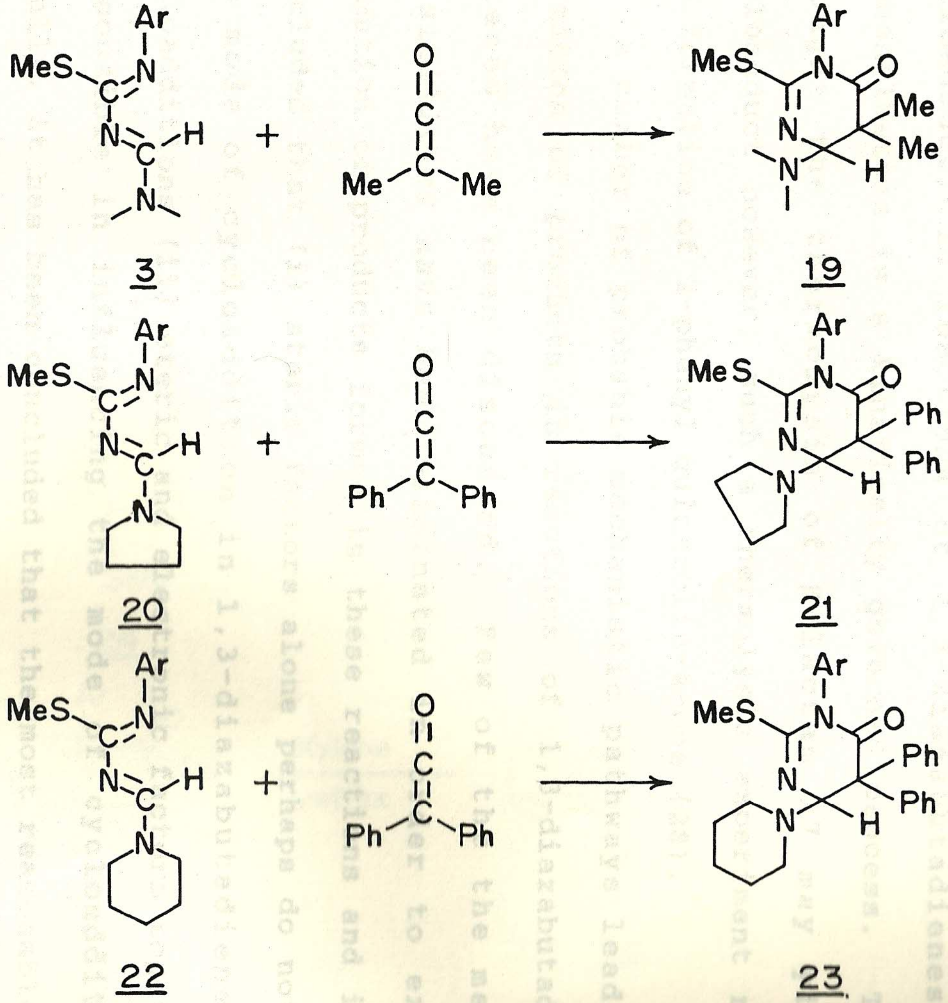
Scheme-3

cycloadditions the intermediate 16 underwent loss, both of dimethylamine and hydrobromic acid to yield pyrimidinones 17 & 18 almost in 1:1 ratio as indicated by the ^{1}H NMR spectrum of the mixture. On the basis of above results a few mechanistic possibilities, in case of 1,3-diazabutadienes-ketenes cycloadditions, were ruled out.

CHAPTER IV

The last chapter of the thesis describes the reactions of various 1,3-diazabutadienes with dimethyl- and diphenylketenes. The structure of the [4+2] cycloadduct reported earlier[8] in case of reaction of 1,3-diazabutadienes 3 with diphenylketene was further confirmed with the help of ^{13}C NMR spectral data. The reactions of 1,3-diazabutadienes 3 with less bulkier dimethylketene, as compared with diphenylketene, also lead to the formation of [4+2] cycloadducts, characterised as previously unknown 5,5-dimethyl-6-dimethylamino-2-thiomethyl-3,4,5,6-tetrahydro-pyrimidin-6-one (19). The observed [4+2] cycloaddition mode in reactions of 1,3-diazabutadienes, having a polar-donating function 2-position, was generalised by carrying out the reactions of 20 and 22 with diphenylketene. Thus, the reactions of 20 and 22 with diphenyl ketene gave pyrimidinones 21 and 23, respectively (Scheme-4).

Further, the reactions of *N*-aryl substituted 1,3-diazabutadienes (24) with diphenylketene did neither yield [2+2] cycloadducts the β-lactams nor [4+2] cycloadducts the

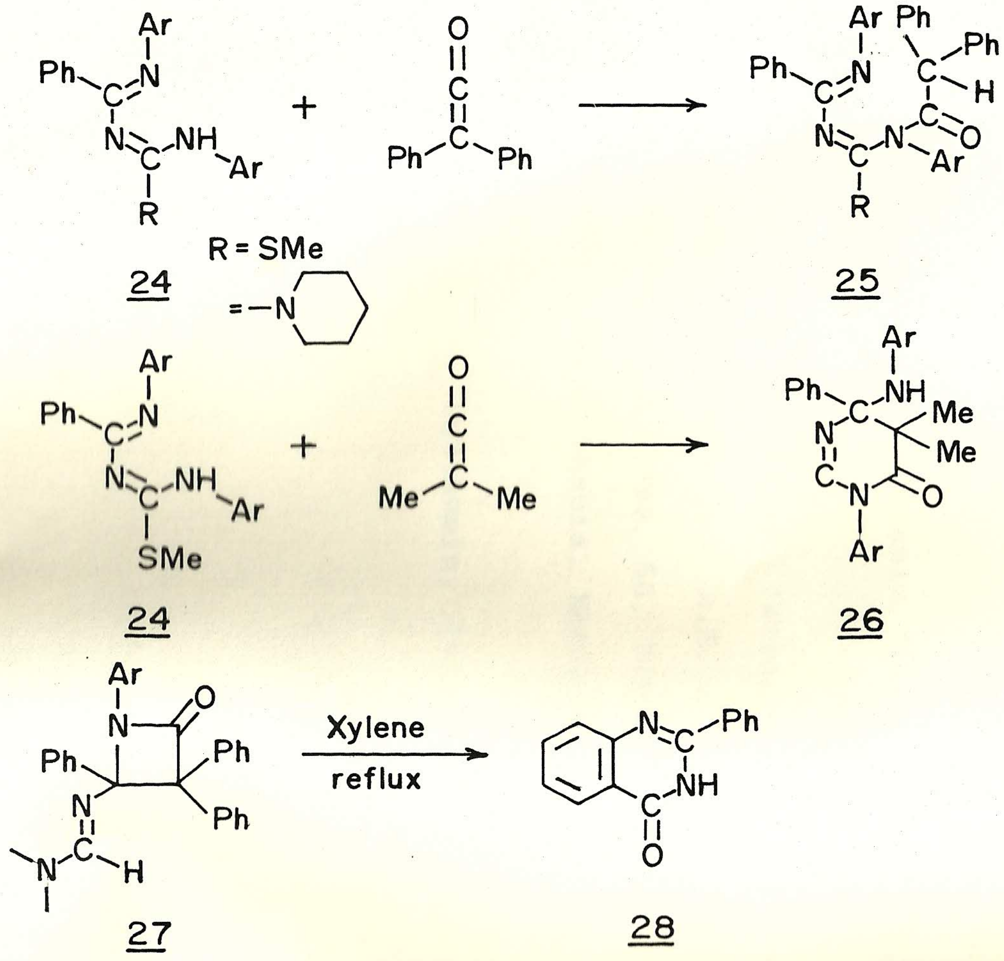


Scheme-4

pyrimidinones, instead resulted in the formation of N-aryl-N-aryl-amino substituted 1,3-diaza-1,3-butadienes 25 (Scheme-5). However, the reaction of N-diazabutadiene 24 with less bulkier dimethylketene resulted in the formation of [4+2] cycloadduct the pyrimidinone 26.

It has been reported[9] that the formation of β-lactam, [2+2] cycloadduct, in reactions of 1,3-diazabutadienes (2) with diphenylketene is a kinetically governed process. Thus it was thought the thermolysis of β-lactam 27 may yield [4+2] cycloadduct however, such a thermolysis experiment resulted in the formation of 2-phenyl quinazolin-4-one (28).

A number of probable mechanistic pathways leading to the formation of products in reactions of 1,3-diazabutadienes with ketenes have been discussed. Few of the the mechanistic possibilities have been eliminated in order to explain the formation of products formed in these reactions and it could be concluded that (i) steric factors alone perhaps do not influence the mode of cycloaddition in 1,3-diazabutadienes-ketenes cycloadditions (ii) steric and electronic factors together may be responsible in influencing the mode of cycloaddition (iii) Finally, it has been concluded that the most reasonable mechanism which can explain the formation of various products assumes that kinetic control leads to the ring closure of zwitterionic intermediate to initially give β-lactam. Further, the formation of β-lactam is reversible due to the presence of polar donating



Scheme-5

formamidine and/or thiomethyl functions and the reversal to zwitterion allows for the formation of [4+2] adducts and this argument has been reasonably used to rationalise the products formed in reactions of various 1,3-diazabutadienes-ketenes cycloadditions.

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