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

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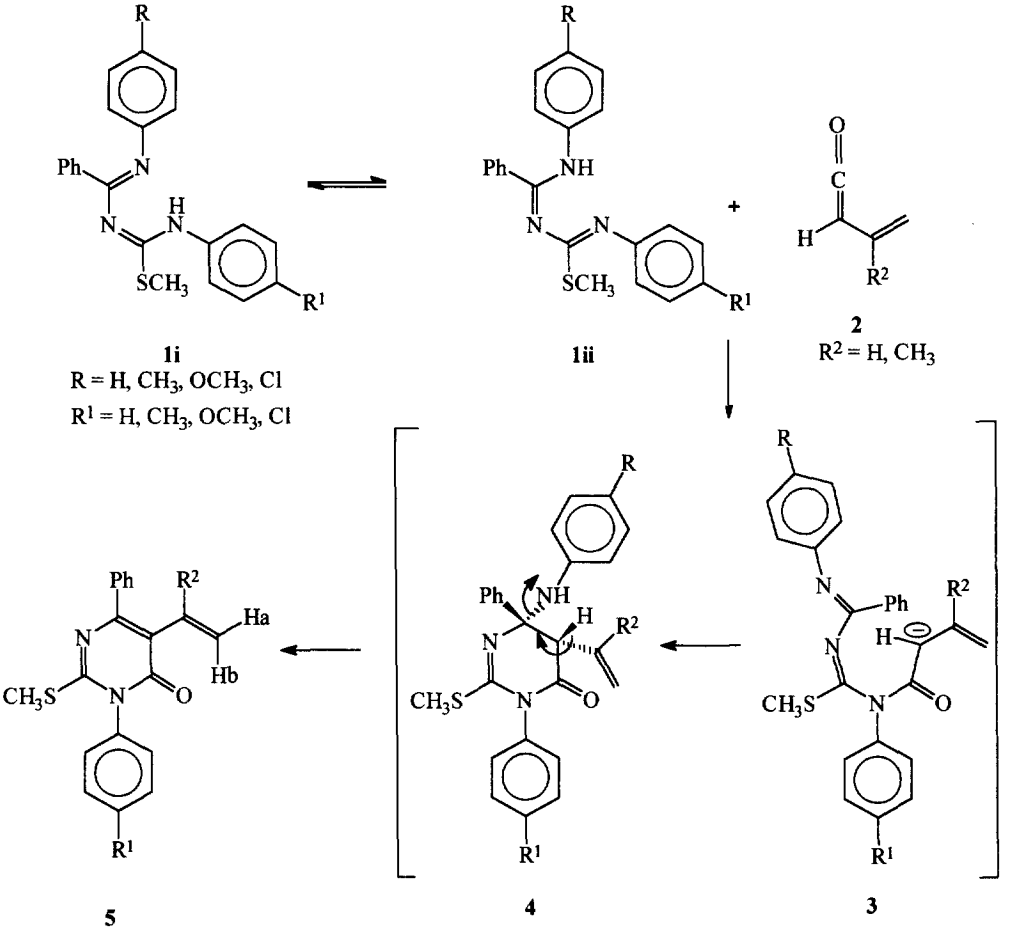
Abstract: A novel synthetic method for 3-aryl-6-phenyl-2-methylthio/secondaryamino substituted-4(3*H*)-pyrimidinones **5** and **9** by the reactions of *N*-arylamino substituted 1,3-diaza-1,3-butadienes **1** and **6** with phenyl-, vinyl- and isopropenylketenes is explored. Semi emperical AM1 calculations on **1** and **6** are performed to explain the mechanism of their reaction with ketenes. Transformations of **5** and **9** leading to fused pyrimidinones **10** are also reported. © 1997 Elsevier Science Ltd.

In recent years, the dienes containing nitrogen atoms are attracting the increasing attention because of their importance in natural product synthesis.[2-5] The advent of various diazabutadienes as potential 4π component has further extended their versatility by allowing an easy access to various functionalised six membered heterocyclic systems. Considerable attention is also being paid to the development of suitable synthetic methodologies for efficient synthesis of appropriately substituted diazabutadienes including 1,3-diaza-1,3-butadienes. We reported simple methods for the preparation of various acyclic 1,3-diaza-1,3-butadienes[1,9] and during the course of studies on the chemistry of ketenes, were utilised successfully in [4+2] cycloaddition reactions with phenyl-, chloro-, bromo-, iodo-, chloromethyl-, dichloro-, vinyl-, isopropenyl- and various other ketenes[10,11] yielding a variety of pyrimidinones. Also, vinylketenes were known to participate as 2π component in [2+2] cycloaddition reactions[12-14] and as 4π component in [4+2] cycloaddition reactions. We have recently reported their participation as 2π component in [4+2] cycloaddition reactions with polarised acyclic 1,3-diaza-1,3-butadienes.[15] Further, the incorporation of an unsaturated side chain (1-propenyl) at C-5 of uridine has recently been reported to increase binding to both single strand RNA and double strand DNA[16]. In continuation of our studies concerning regioselective reactions of *N*-arylamino substituted 1,3-diaza-1,3-butadienes with ketenes and in view of the reported biological significance of vinyl

substituted pyrimidinones, we have further examined the reactions of these diazabutadienes with phenyl-, vinyl- and isopropenylketenes.

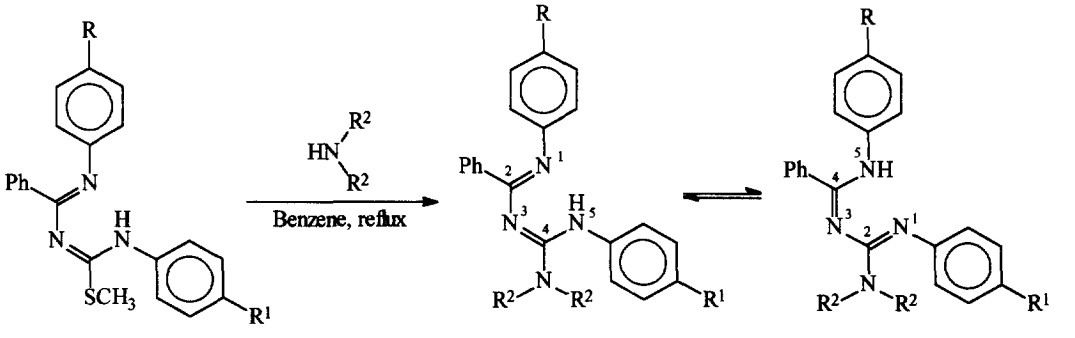
Thus, the treatment of 1-aryl-4-(*N*-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **1** with isopropenyl/vinylketenes **2**, generated *in situ* from 3,3-dimethylacryloyl chloride/crotonyl chloride in presence of triethylamine, in dry methylene chloride at room temperature, afforded good yields (70-75%) of



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

Scheme 1

previously unknown 3-aryl-2-methylthio-6-phenyl-5-isopropenyl/vinyl-4(3*H*)-pyrimidinones **5** (Scheme 1). The products were characterised on the basis of analytical results and spectral evidences. Thus, compound **5a**, for example analysed for $C_{20}H_{18}N_2OS$ showed in its mass spectrum a molecular ion peak at *m/z* 334. Its IR spectrum (KBr) showed a strong absorption at 1668 cm^{-1} assigned to α,β-unsaturated carbonyl group. Its ^1H NMR (300 MHz) spectrum exhibited the presence of two singlets at ca. δ 2.00 (3H) and 2.46 (3H) assigned to methyl and methylthio groups and also two broad singlets centred at ca. δ 4.87 (1H) and 5.17 (1H) assignable to H_a and H_b, respectively. It also exhibited the absence of protons due to *N*-arylamino function next to the carbon bearing the phenyl group. The compound **5e** in its mass spectrum showed a molecular ion peak at *m/z* 320 and its IR spectrum (KBr) showed a strong absorption peak at 1667 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^1H NMR spectrum, in addition to other protons exhibited the presence of three doublet of doublets at ca. δ 5.37, 6.17 and 6.59. The probable mechanism for the formation of pyrimidinone derivatives **5** is similar to the one discussed in our earlier communication.[1] It may be concluded that the formation of pyrimidinones **5**, in these reactions, involves initial nucleophilic attack by the non-bonding electrons of the amino nitrogen of 1-aryl-4-(*N*-arylamino)-4-methylthio-2-phenyl-1,3-diaza-1,3-butadienes **1** at the ketene carbonyl, leading to an intermediate **3**, which on ring closure and subsequent elimination of aromatic amines from intermediate **4** results in pyrimidinones **5** (Scheme 1).



1 **6i** **6ii**

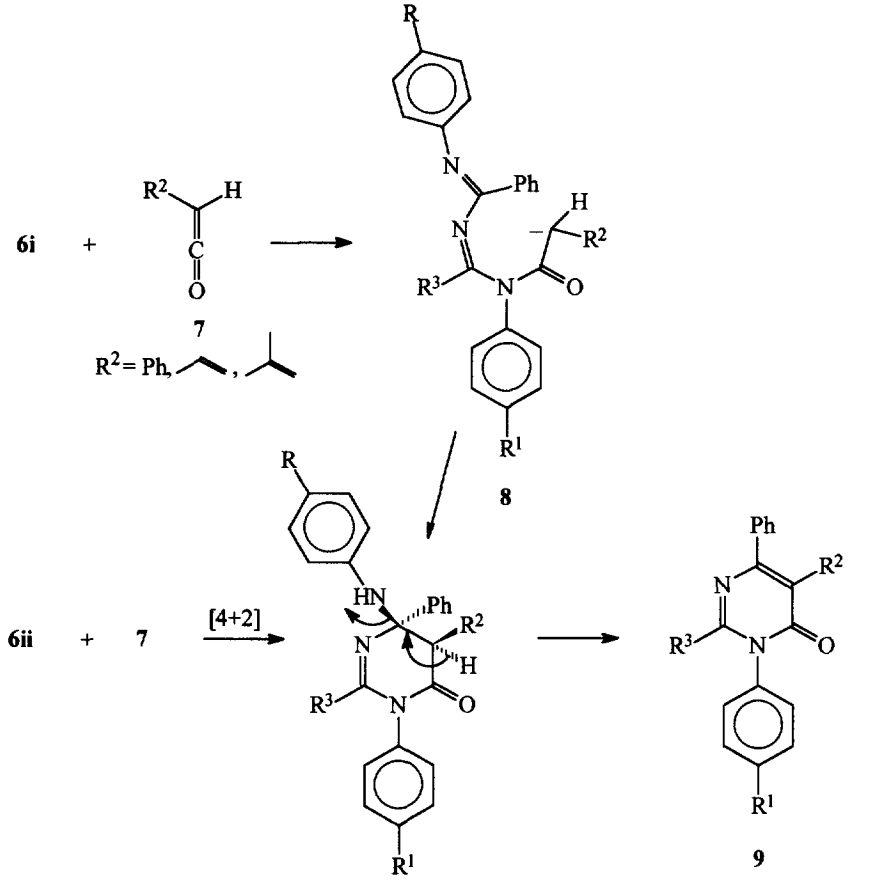
6. a. R = H; $R^1 = CH_3$; R^2,R^2 = ⌐¬ **6 b.** R = CH_3; $R^1 = CH_3$; R^2, R^2 = ⌐¬

6 c. R = CH_3; $R^1 = CH_3$; R^2, R^2 = ⌐⌐

Scheme 2

In continuation of our investigations, it was thought worthwhile to examine cycloaddition reactions of 1,3-diaza-1,3-butadienes **6** bearing *N*-arylamino and secondary amino substituents. The interest in such investigations was stimulated primarily because of the possible dominance of tautomer **6ii**, due to better

polarizing ability of secondary amino functions, which in comparison to earlier observations[1] may yield products arising from reversed regioselectivity. The required 1,3-diaza-1,3-butadienes **6** were obtained by the replacement of methylthio function of **1** with secondary amine in refluxing benzene (Scheme 2) and the treatment of 1,3-diaza-1,3-butadienes **6** with phenyl-, vinyl- and isopropenylketenes resulted in good



9. a. $R^1 = H$; $R^2 = Ph$; $R^3 =$ 

b. $R^1 = CH_3$; $R^2 = Ph$; $R^3 =$ 

c. $R^1 = H$; $R^2 =$  ; $R^3 =$ 

d. $R^1 = CH_3$; $R^2 =$  ; $R^3 =$ 

e. $R^1 = CH_3$; $R^2 =$  ; $R^3 =$ 

f. $R^1 = CH_3$; $R^2 =$  ; $R^3 =$ 

Scheme 3

yields of previously unknown 3-aryl-2-dialkylamino-6-phenyl-5-substituted-4(3*H*)-pyrimidinones. The structure **9** was assigned to these pyrimidinones on the basis of analytical and spectral evidence. The ^{1}H NMR spectra of **9** showed the absence of *N*-arylamino groups attached to the carbon bearing phenyl and the presence of secondary amino protons and *N*-arylamino protons attached to the carbon bearing the secondary amino function. The formation of pyrimidinones **9** might be following either the [4+2] cycloadditions of tautomer **6ii** with ketenes or the initial nucleophilic attack by *N*-arylamino function of tautomer **6i** on the ketene carbonyl leading to an intermediate **8** which on sequential cyclization and elimination of aromatic amine gave **9** (Scheme 3).

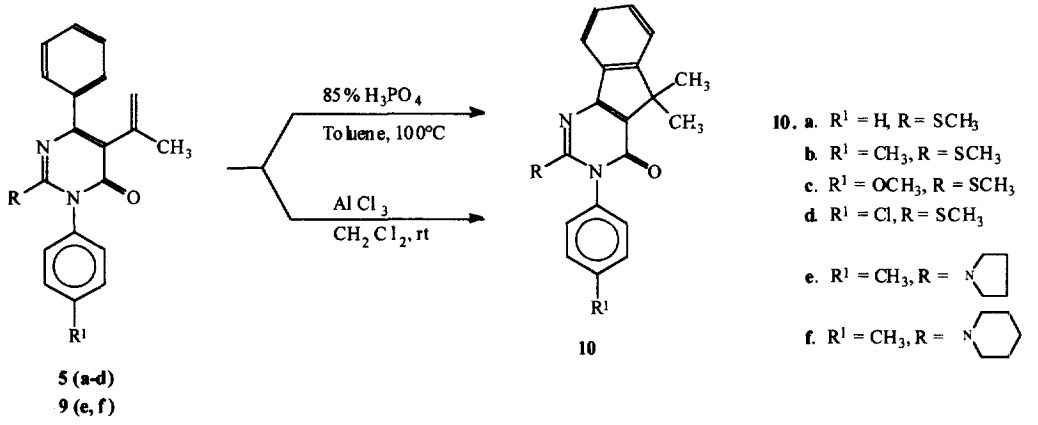
In order to have further insight into the mechanistic paths followed in these reactions we have performed AM1 calculations[17] on **1** and **6**. Complete optimization of **1i, 1ii, 6i** and **6ii** has shown that the N-C-N-C-N framework prefers to be planar. Earlier theoretical (*ab initio*) studies on 1,3-diazabutadienes[18,19] showed that the s-*trans* arrangement corresponds to stable molecule and the s-*cis* arrangement does not correspond to minimum on the potential energy surface. However, in substituted 1,3-diazabutadienes like 1 and **6**, the substituents (NHR) provide hydrogen atom for the formation of intramolecular hydrogen bond and stabilize the s-*cis* isomers. AM1 calculations showed that the s-*cis* isomers are at least 6-7 kcal/mol more stable than the s-*trans* isomers. The N-H ... N hydrogen bond lengths are in the range of 2.1 to 2.2 Å. This distance corresponds to strong intermolecular hydrogen bonding interaction. For example, the H_2O ... H-OH hydrogen bond distance is 2.14 Å according to AM1 calculations. The amino group is planar in **1** and **6**, as evidenced by the sum of angles around amino N (~ 360°).

Tautomer **1i** is more stable than **1ii** by about 0.81 kcal/mol. Though the difference is very small, it may be concluded that in solution, **1i** exists predominantly. In **1i** the amino nitrogen is more charged and in **1ii** the imino nitrogen is more charged. This, coupled with the observed formation of pyrimidinones **5**, led to the conclusion that the reactions of **1** with ketenes proceed predominantly by the nucleophilic attack of *N*-arylamino function of the tautomer **1i** on the ketene carbonyl.[1] The energy difference between **6i** and **6ii** is 0.02 kcal/mol in favour of **6ii**. This indicates that the dominance of tautomer **ii** increases with the secondary amine substituent, which is in accordance with expectations from the polarizing ability considerations. Charge densities and HOMO coefficients of **6** obtained using AM1 method are given in table 1. In both the tautomers of **6**, imino nitrogen is found to be more charged. Similarly, in the HOMO coefficients of **6i** and **6ii**, the p-orbital coefficients on the imino nitrogens are more predominant. This shows that the imino nitrogen is more active in both **6i** and **6ii**, in contrast to the observations made in **1i** and **1ii**. Thus, based on experimental observations, higher charge densities at imino nitrogen and relative higher stability of **6ii** in solution, it could be concluded that pyrimidinones **9** are formed *via* [4+2] cycloaddition reactions of **6ii** with various ketenes.

Table 1: Charge Densities and HOMO Coefficients of **6** using AM1 method

Atoms	Charges		HOMO Coefficients	
	6i	**6ii**	**6i**	**6ii**
N-1	-0.45	-0.43	0.35	0.37
C-2	0.29	0.36	-0.11	-0.12
N-3	-0.33	-0.35	-0.30	-0.35
C-4	0.26	0.21	0.17	0.18
N-5	-0.30	-0.32	0.30	0.33

The pyrimidinones **5** and **9c-f** appeared to be potential synthons for the synthesis of fused pyrimidinones *via* annelation reactions. Thus, the treatment of 5-isopropenylpyrimidinones ($R^2 = CH_3$) with 85% H_3PO_4 in refluxing toluene resulted in the formation of previously unknown 3-aryl-5,5-dimethyl-2-methylthio/secondaryamino-3,5-dihydro-4*H*-indeno[1,2-*d*]pyrimidin-4-ones **10** (Scheme 4). A similar reaction



Scheme 4

in the presence of $AlCl_3$ in methylene chloride resulted in better yields of same indeno[1,2-*d*]pyrimidinones **10**. However, in case of 5-vinylpyrimidinones ($R^2 = H$), the attempted cyclisation with 85% H_3PO_4 or Lewis acid resulted in an intractable mixture from which no pure product could be isolated. The compounds **10** were characterised on the basis of analytical and spectral data. The compound **10a**, for example, was analysed for $C_{20}H_{18}N_2OS$ and showed a molecular ion peak at *m/z* 334. Its IR spectrum showed a sharp band at 1662 cm^{-1} due to α,β-unsaturated carbonyl group. Its ^1H NMR spectrum showed the absence of isopropenyl functionality and exhibited two sharp singlets due to methylthio (δ 2.59) and two methyl (δ 1.57) groups. Its ^{13}C NMR spectrum was also in agreement with the assigned structure.

Experimental

Melting points were determined with a Toshniwal melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 983 Infrared spectrophotometer using KBr disc. ^{1}H NMR spectra were recorded in deuteriochloroform, with a Varian 390 90 MHz and Bruker AC-F 300 300 MHz spectrometer using TMS as internal standard; *J* values are in Hz.. ^{13}C NMR spectra were also recorded with Bruker AC-F 300 spectrometer in deuteriochloroform using TMS as internal standard. Mass spectra were obtained by electron impact at 70 eV.

Starting Materials:

1,3-Diaza-1,3-butadienes,[1] crotonyl chloride and 3,3-dimethylacryloyl chloride[15] were prepared by the reported procedures.

Reactions of 1,3-diaza-1,3-butadienes with ketenes:

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

5-Isopropenyl-2-methylthio-3,6-diphenylpyrimidin-4(3*H*)-one (5a): 70%; mp 201-203 °C. IR (KBr) ν 1668 cm^{-1} (C=O). ^{1}H NMR δ 2.00 (s, 3H, -CH_3), 2.46 (s, 3H, -SCH_3), 4.87 (br s, 1H, Ha), 5.17 (br s, 1H, Hb), 7.29-7.37 (m, 5H, arom), 7.51-7.53 (m, 3H, arom), 7.70-7.73 (m, 2H, arom). ^{13}C NMR δ 15.13 (-SCH_3), 22.7 (-CH_3), 119.35 (=CH_2), 122.19, 127.61, 128.51, 128.72, 128.83, 129.38, 129.60, 135.71, 138.23 (arom); 138.43 (-C=), 156.47 (C-2), 158.69, 161.42 (C-4). Anal. Calcd for $C_{20}H_{18}N_2OS$: C, 71.86; H, 5.39; N, 8.38. Found: C, 71.81; H, 5.32; N, 8.35. ms *m/z*: 334 (M^+).

5-Isopropenyl-3-(*p*-methylphenyl)-2-methylthio-6-phenylpyrimidin-4(3*H*)-one (5b): 72%; mp 208-210 °C. IR (KBr) ν 1669 cm^{-1} (C=O). ^{1}H NMR δ 2.05 (s, 3H, -CH_3), 2.43 (s, 3H, -CH_3), 2.51 (s, 3H, -SCH_3), 4.88 (br s, 1H, Ha), 5.19 (br s, 1H, Hb), 7.32-7.60 (m, 7H, arom), 7.69-7.72 (m, 2H, arom). ^{13}C NMR δ 15.23 (-SCH_3), 21.32 (-CH_3), 22.73 (-CH_3), 119.63 (=CH_2), 122.25, 127.71, 128.23, 128.82, 128.92, 130.20, 133.17, 138.50, 137.57, (arom); 139.79 (-C=), 160.11; 161.81 (C-4). Anal. Calcd for $C_{21}H_{20}N_2OS$: C, 72.38; H, 5.79; N, 8.04. Found: C, 72.59; H, 5.90; N, 8.06. ms *m/z*: 348 (M^+).

5-Isopropenyl-3-(*p*-methoxyphenyl)-2-methylthio-6-phenylpyrimidin-4(3*H*)-one (5c): 72%; mp 218-220 °C. IR (KBr) ν 1665 cm^{-1}. ^{1}H NMR δ 2.03 (s, 3H, -CH_3), 2.50 (s, 3H, -SCH_3), 3.91 (s, 3H, -OCH_3), 4.89 (br s, 1H, Ha), 5.19 (br s, 1H, Hb), 7.17-7.58 (m, 7H, arom), 7.77-7.95 (m, 2H, arom). ^{13}C NMR δ 15.24 (-SCH_3), 23.19 (-CH_3), 55.20 (-OCH_3), 119.32 (=CH_2), 122.24, 127.60, 128.20, 128.79, 128.94, 130.34,

134.00, 138.64 (arom); 139.84 (-C=); 156.64 (C-2); 160.12; 162.00 (C-4). Anal. Calcd for $C_{21}H_{20}N_2O_2S$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.40; H, 5.61; N, 7.62. ms *m/z*: 364 (M^+).

3-(*p*-Chlorophenyl)-5-isopropenyl-2-methylthio-6-phenylpyrimidin-4(3*H*)-one (5d): 70%; mp 225-226 °C. IR (KBr) ν 1671 cm^{-1} (C=O). ^1H NMR δ 2.00 (s, 3H, $-CH_3$), 2.48 (s, 3H, $-SCH_3$), 4.89 (br s, 1H, Ha), 5.20 (br s, 1H, Hb), 7.28-7.80 (m, 9H, arom). ^{13}C NMR δ 15.24 ($-SCH_3$); 22.74 ($-CH_3$), 119.56 ($=CH_2$), 122.27, 127.78, 128.81, 129.07, 129.85, 130.03, 134.21, 135.95, 138.25 (arom); 138.40 (-C=); 156.73 (C-2); 159.55; 161.48 (C-4). Anal. Calcd for $C_{20}H_{17}ClN_2OS$: C, 65.13; H, 4.65; N, 7.60. Found: C, 65.08; H, 4.55; N, 7.55. ms *m/z*: 368 (M^+).

2-Methylthio-3,6-diphenyl-5-vinylpyrimidin-4(3*H*)-one (5e): 70%; mp 238-239 °C. IR (KBr) ν 1667 cm^{-1} (C=O). ^1H NMR δ 2.45 (s, 3H, -SCH3), 5.37 (dd, J = 11.8 and 2.9, 1H, Ha), 6.17 (dd, J = 17.5 and 2.9, 1H, Hb), 6.59 (dd, J = 17.5 and 11.8, 1H, H), 7.25-7.63 (m, 10H, arom). ^{13}C NMR δ 15.33 ($-SCH_3$); 115.32 ($=CH_2$); 123.41, 128.06, 128.57, 128.84, 129.33, 129.47, 139.27 (-C=), 159.23; 161.60 (C-2); 163.36 (C-4). Anal. Calcd for $C_{19}H_{16}N_2OS$: C, 71.22; H, 5.03; N, 8.74. Found: C, 71.24; H, 5.01; N, 8.72. ms *m/z*: 320 (M^+).

3-(*p*-Methylphenyl)-2-methylthio-6-phenyl-5-vinylpyrimidin-4(3*H*)-one (5f): 72%, mp 219-221 °C. IR (KBr) ν 1662 cm^{-1} (C=O). ^1H NMR δ 2.34 (s, 3H, $-CH_3$), 2.50 (s, 3H, -SCH3), 5.34 (dd, J = 11.8 and 2.9, 1H, Ha), 6.23 (dd, J = 17.4 and 2.9, 1H, Hb), 6.54 (dd, J = 17.4 and 11.8, 1H, H), 7.23-7.69 (m, 9H, arom). ^{13}C NMR δ 15.34 ($-SCH_3$) ; 21.35 ($-CH_3$) ; 116.30 ($=CH_2$) ; 122.23, 128.07, 128.62, 128.89, 129.40, 129.50, 129.82, 129.99, 130.30, 135.99, 138.26 (arom); 139.27 (-C=) ; 158.92; 161.72 (C-2); 163.40 (C-4). Anal Calcd. for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42; N, 8.38. Found : C, 71.82; H, 5.35; N, 8.33. ms *m/z*: 334 (M^+).

3-(*p*-Methoxyphenyl)-2-methylthio-6-phenyl-5-vinylpyrimidin-4(3*H*)-one (5g): 75%; mp 211-212 °C. IR (KBr) ν 1667 cm^{-1}. ^1H NMR δ 2.51 (s, 3H, -SCH3), 3.71 (s, 3H, $-OCH_3$), 5.36 (dd, J = 11.8 and 2.9, 1H, Ha), 6.18 (dd, J = 17.4 and 2.9, 1H, Hb), 6.60 (dd, J = 17.4 and 11.8, 1H, H), 7.23-7.70 (m, 9H, arom). ^{13}C NMR δ 15.29 ($-SCH_3$), 50.15 ($-OCH_3$), 115.83 ($=CH_2$), 123.40, 127.80, 128.06, 128.21, 128.57, 128.76, 128.99, 129.41, 129.65, 130.60, 135.80, 138.30 (arom); 158.64; 161.82 (C-2); 164.00 (C-4). Anal. Calcd for $C_{20}H_{18}N_2O_2S$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.51; H, 5.13; N, 7.98. ms *m/z*: 350 (M^+).

3-(*p*-Chlorophenyl)-2-methylthio-6-phenyl-5-vinylpyrimidin-4(3*H*)-one (5h): 71%; mp 206-208 °C. IR (KBr) ν 1665 cm^{-1} (C=O). ^1H NMR δ 2.50 (s, 3H, $-SH_3$), 5.33 (dd, J = 11.5 and 2.8, 1H, Ha), 6.21 (dd, J = 17.6 and 2.8, 1H, Hb), 6.58 (dd, J = 17.6 and 11.5, 1H, H), 7.10-7.40 (m, 9H, arom). ^{13}C NMR δ 15.50 ($-SCH_3$), 115.41 ($=CH_2$), 122.89, 127.90, 128.55, 129.10, 129.17, 129.22, 129.58, 135.15, 137.83 (arom); 139.09 (-C=); 159.03; 161.71 (C-2); 164.22 (C-4). Anal. Calcd for $C_{19}H_{15}ClN_2OS$: C, 64.31; H, 4.26; N, 7.90. Found:C, 64.30; H, 4.28; N, 7.87. ms *m/z*: 354 (M^+).

Preparation of 1-aryl-4-(*N*-arylamino)-4-phenyl-2-secondaryamino-1,3-diaza-1,3-butadienes: The 1,3-diaza-1,3-butadiene **1** (1 mmol) was refluxed in benzene with secondaryamine (1 mmol) for 5-6 h. It was then washed with water (3 x 50 ml) and dried over anhydrous sodium sulfate. The removal of benzene

under reduced pressure afforded the desired product **6**, which was further recrystallised from a mixture 1:1 of benzene and hexane.

1-(*p*-Methylphenyl)-4-phenyl-4-(*N*-phenylamino)-2-pyrrolidino-1,3-diaza-1,3-butadiene (6a): 92%; mp 162-164 °C. IR (KBr) ν 1552 cm^{-1} (C=N). ^1H NMR δ 1.85-1.89 (m, 4H, $-CH_2-CH_2-$), 2.27 (s, 3H, $-CH_3$), 3.42-3.46 (m, 4H, $-CH_2-N-CH_2-$), 6.72-7.34 (m, 15H, arom). Anal. Calcd for $C_{25}H_{26}N_4$: C, 78.50; H, 6.85; N, 14.65. Found: C, 78.69; H, 6.89; N, 14.49. ms *m/z*: 382 (M^+).

1-(*p*-Methylphenyl)-4-{*N*-(*p*-methylphenylamino)}-4-phenyl-2-pyrrolidino-1,3-diaza-1,3-butadiene (6b): 93%; mp 167-169 °C. IR (KBr) ν 1555 cm^{-1} (C=N). ^1H NMR δ 1.82-1.86 (m, 4H, $-CH_2-CH_2-$), 2.34 (s, 3H, $-CH_3$), 2.26 (s, 3H, $-CH_3$), 3.38-3.42 (m, 4H, $-CH_2-N-CH_2-$), 6.68-7.34 (m, 13H, arom). Anal. Calcd for $C_{26}H_{28}N_4$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.93; H, 7.07; N, 14.03. ms *m/z*: 396 (M^+).

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

3,5,6-Triphenyl-2-pyrrolidinopyrimidin-4(3*H*)-one (9a): 80%; mp 130-131 °C. IR (KBr) ν 1653 cm^{-1} (C=O). ^1H NMR δ 1.73-1.77 (m, 4H, $-CH_2-CH_2-$), 3.13-3.17 (m, 4H, $-CH_2-N-CH_2-$), 7.13-7.25 (m, 8H, arom), 7.38-7.48 (m, 7H, arom). ^{13}C NMR δ 25.44 ($-CH_2-CH_2-$), 49.99 ($-CH_2-N-CH_2-$), 113.62, 126.38, 127.50, 127.65, 127.75, 128.24, 128.57, 128.91, 129.31, 130.03, 131.50, 135.45, 137.74, 139.29 (arom); 152.91 (C-6); 159.42 (C-2); 163.98 (C-4). Anal. Calcd for $C_{26}H_{23}N_3O$: C, 79.36; H, 5.89; N, 10.68. Found: C, 79.37; H, 5.82; N, 10.68. ms *m/z*: 393 (M^+).

3-(*p*-Methylphenyl)-5,6-diphenyl-2-pyrrolidinopyrimidin-4(3*H*)-one (9b): 82%; mp 204-205 °C. IR (KBr) ν 1652 cm^{-1} (C=O). ^1H NMR δ 1.73-1.77 (m, 4H, $-CH_2-CH_2-$), 2.37 (s, 3H, $-CH_3$), 3.14-3.17 (m, 4H, $-CH_2-N-CH_2-$), 7.14-7.24 (m, 12H, arom), 7.44-7.47 (d, 2H, arom). ^{13}C NMR δ 21.21 ($-CH_2-CH_2-$), 25.41 ($-CH_3$), 49.95 ($-CH_2-N-CH_2-$), 113.45, 119.81, 126.31, 127.48, 127.61, 128.53, 128.94, 129.13, 129.40, 129.55, 130.02, 131.51, 134.95, 135.51, 138.20, 139.32 (arom); 152.98 (C-6); 159.42 (C-2); 164.12 (C-4). Anal. Calcd for $C_{27}H_{25}N_3O$: C, 79.59; H, 6.18; N, 10.32. Found: C, 79.58; H, 6.13; N, 10.27. ms *m/z*: 407 (M^+).

3,6-Diphenyl-3-pyrrolidino-5-vinylpyrimidin-4(3*H*)-one (9c): 76%; mp 190-192 °C. IR (KBr) ν 1659 cm^{-1} (C=O). ^1H NMR δ 1.68-1.72 (m, 4H, $-CH_2-CH_2-$), 3.07-3.10 (m, 4H, $-CH_2-N-CH_2-$), 5.19 (dd, J = 11.8 and 2.9, 1H, Ha), 6.29 (dd, J = 17.5 and 2.9, 1H, Hb), 6.50 (dd, J = 17.5 and 11.7, 1H, H), 7.25-7.68 (m, 10H, arom). ^{13}C NMR δ 25.38 ($-CH_2-CH_2-$), 49.99 ($-CH_2-N-CH_2-$), 109.12 (C-5), 115.56 ($=CH_2$), 127.91, 128.43, 128.99, 129.07, 129.75, 130.45, 137.64 (arom); 139.27 (-C=); 159.23, 161.64 (C-2); 163.30 (C-4). Anal. Calcd for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.95; H, 6.11; N, 12.21. ms *m/z*: 343 (M^+).

3-(*p*-Methylphenyl)-6-phenyl-2-piperidino-5-vinylpyrimidin-4(3*H*)-one (9d): 73%; mp 188-189 °C. IR (KBr) ν 1660 cm^{-1} (C=O). ^1H NMR δ 1.65-1.69 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.28 (s, 3H, $-CH_3$), 3.14-3.17 (m, 4H, $-CH_2-N-CH_2-$), 5.34 (dd, *J* = 11.6 and 2.8, 1H, Ha), 6.23 (dd, *J* = 17.5 and 2.8, 1H, Hb), 6.44 (dd, *J* = 17.6 and 11.5, 1H, H), 7.13-7.59 (m, 9H, arom). ^{13}C NMR δ 21.14 ($-CH_3$); 25.03 (-CH2-CH2-), 50.1 ($-CH_2-N-CH_2-$); 115.21 ($=CH_2$); 127.70, 127.93, 128.82, 129.33, 129.60, 129.87, 137.96 (arom); 139.26 (-C=); 158.67; 161.29 (C-2); 163.00 (C-4). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.50; H, 6.72; N, 11.29. ms *m/z*: 371 (M^+).

5-Isopropenyl-3-(*p*-methylphenyl)-6-phenyl-2-pyrrolidinopyrimidin-4(3*H*)-one (9e): 71%; mp 210-211 °C. IR (KBr) ν 1663 cm^{-1} (C=O). ^1H NMR δ 1.63-1.66 (m, 4H, $-CH_2-CH_2-$), 2.03 (s, 3H, $-CH_3$), 2.34 (s, 3H, $-CH_3$), 3.14-3.17 (m, 4H, $-CH_2-N-CH_2-$), 4.85 (br s, 1H, Ha), 5.17 (br s, 1H, Hb), 7.34-7.89 (m, 9H, arom). ^{13}C NMR δ 21.14 ($-CH_3$); 24.22 ($-CH_2-CH_2-$); 25.15 ($-CH_3$); 50.02 (-CH2-N-CH_2-); 118.55 ($=CH_2$); 123.20, 127.34, 127.89, 128.35, 128.63, 128.70, 129.29, 134.88, 137.58, 138.56 (arom); 139.89 (-C=); 157.43 (C-2); 160.20; 163.50 (C-4). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.60; H, 6.78; N, 11.31. Found: C, 77.60; H, 6.69; N, 11.28. ms *m/z*: 371 (M^+).

5-Isopropenyl-3-(*p*-methylphenyl)-6-phenyl-4-piperidinopyrimidin-4(3*H*)-one (9f): 76%; mp 204-206 °C. IR (KBr) ν 1662 cm^{-1}. ^1H NMR δ 1.62-1.65 (m, 6H, $-CH_2-CH_2-CH_2-$), 2.01 (s, 3H, $-CH_3$), 2.39 (s, 3H, $-CH_3$), 3.13-3.16 (m, 4H, $-CH_2-N-CH_2-$), 4.84 (br s, 1H, Ha), 5.11 (br s, 1H, Hb), 7.35-7.76 (m, 9H, arom). ^{13}C NMR δ 21.21 ($-CH_3$); 24.21 ($-CH_2-CH_2-$); 25.04 ($-CH_3$); 49.59 ($-CH_2-N-CH_2-$); 118.77 ($=CH_2$); 122.23, 127.59, 128.18, 128.80, 128.92, 130.21, 134.03, 138.27, 138.65 (arom); 139.86 (-C=); 157.43 (C-2); 160.20; 163.49 (C-4). Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 77.90; H, 6.98; N, 10.88. ms *m/z*: 385 (M^+).

***Cyclization reactions of pyrimidinones;* General Procedure:**

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

3,5-Dihydro-5,5-dimethyl-2-methylthio-3-phenyl-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10a): 95%; mp 229-231 °C. IR (KBr) ν 1662 cm^{-1}. ^1H NMR δ 1.57 (s, 6H, 2 x $-CH_3$), 2.59 (s, 3H, $-SCH_3$), 7.33-7.94 (m, 9H, arom). ^{13}C NMR δ 15.55 ($-SCH_3$); 23.58 (2 x $-CH_3$); 46.19; 121.70, 122.67, 126.73, 127.07, 129.84, 130.32, 134.34, 135.89 (arom); 137.04; 156.29 (C-6); 159.06; 160.29 (C-2); 164.01 (C-4). Anal. Calcd for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42; N, 8.38. Found: C, 71.72; H, 5.35; N, 8.33. ms *m/z*:334 (M^+).

3,5-Dihydro-5,5-dimethyl-3-(*p*-methylphenyl)-2-methylthio-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10b): 94%; mp 262-264 °C. IR (KBr) ν 1663 cm^{-1} (C=O). ^1H NMR δ 1.55 (s, 6H, 2 x $-CH_3$), 2.44 (s, 3H,

-CH_3), 2.58 (s, 3H, -SCH_3), 7.24-7.69 (m, 5H, arom), 7.90-8.19 (m, 3H, arom). Anal. Calcd for $C_{21}H_{20}N_2OS$: C, 72.38; H, 5.79; N, 8.04. Found: C, 72.37; H, 5.70; N, 8.00. ms *m/z*: 348 (M^+).

3,5-Dihydro-3-(*p*-methoxyphenyl)-5,5-dimethyl-2-methylthio-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10c): 92%; mp 228-230 °C. IR (KBr) ν 1668 cm^{-1} (C=O). ^1H NMR δ 1.56 (s, 6H, 2 x -CH_3), 2.58 (s, 3H, -SCH_3), 3.87 (s, 3H, -OCH_3), 7.01-7.90 (m, 8H, arom). ^{13}C NMR δ 15.57 (-SCH_3); 23.53 (2 x -CH_3); 46.14 (C-5); 55.25 (-OCH_3); 114.75, 121.61, 122.03, 126.97, 128.34, 129.68, 129.93 (arom); 137.01 (C-5); 156.31 (C-6); 159.60; 160.33 (C-2); 164.85 (C-4). Anal. Calcd for $C_{21}H_{20}N_2O_2S$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.30; H, 5.45; N, 7.66. ms *m/z*: 364 (M^+).

3,5-Dihydro-3-(*p*-chlorophenyl)-5,5-dimethyl-2-methylthio-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10d): 94%; mp 227-228 °C. IR (KBr) ν 1660 cm^{-1} (C=O). ^1H NMR δ 1.55 (s, 6H, 2 x -CH_3), 2.59 (s, 3H, -SCH_3), 7.25-7.90 (m, 8H, arom). ^{13}C NMR δ 15.50 (-SCH_3); 23.51 (2 x -CH_3); 46.19; 121.70, 122.07, 126.73, 127.07, 129.84, 130.32, 134.34, 135.89 (arom); 137.04; 156.29 (C-6); 159.06; 160.29 (C-2); 164.01 (C-4). Anal. Calcd for $C_{20}H_{17}ClN_2OS$: C, 65.12; H, 4.65; N, 7.59. Found: C, 65.07; H, 4.56; N, 7.55. ms *m/z*: 368 (M^+).

3,5-Dihydro-5,5-dimethyl-3-(*p*-methylphenyl)-2-pyrrolidino-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10e): 78%; mp 236-238 °C. IR (KBr) ν 1665 cm^{-1} (C=O). ^1H NMR δ 1.54 (s, 6H, 2 x -CH_3), 1.64-1.68 (m, 4H, -CH_2-CH_2-), 2.30 (s, 3H, -CH_3), 7.24-7.89 (m, 8H, arom). Anal. Calcd for $C_{24}H_{25}N_3O$: C, 77.63; H, 6.78; N, 11.31. Found: C, 77.60; H, 6.71; N, 11.27. ms *m/z*: 371 (M^+).

3,5-Dihydro-5,5-dimethyl-3-(*p*-methylphenyl)-2-piperidino-4*H*-indeno[1,2-*d*]pyrimidin-4-one (10f): 79%, mp 242-243 °C. IR (KBr) ν 1663 cm^{-1} (C=O). ^1H NMR δ 1.56 (s, 6H, 2 x -CH_3), 1.62-1.65 (m, 6H, -CH_2-CH_2-CH_2-), 2.40 (s, 3H, -CH_3), 3.13-3.15 (m, 4H, -CH_2-N-CH_2-), 7.35-7.76 (m, 8H, arom). Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.91. Found: C, 77.90; H, 7.00; N, 10.88. ms *m/z*: 385 (M^+).

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References

1. Dey, P.D.; Sharma, A.K.; Rai, S.N.; Mahajan, M.P. *Tetrahedron*, **1995**, *51*, 7459.
2. Kametani, T.; Hibino, S. *Advances in Heterocyclic Chemistry*, Academic Press, New York, **1987**, *42*, 246.
3. Overman, L.E.; Petly, C.B.; Ban, T.; Huang, G.T. *J. Am. Chem. Soc.*, **1983**, *40*, 261.
4. Bremer, M.L.; Weinreb, S.M. *Tetrahedron*, **1983**, *40*, 261.
5. Boger, D.L.; Panek, J.S. *J. Org. Chem.*, **1983**, *48*, 621.
6. Boger, D.L. *Tetrahedron*, **1983**, *39*, 2869.

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

8. Gusman, A.; Romero, M.; Talamas, F.X.; Villena, R.; Greenhouse, R.; Muchowski, J.M. *J.Org. Chem.*, **1996**, *61*, 2470.

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

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

11. Mazumdar, S.N.; Mukherjee, S.; Sharma, A.K.; Sengupta, D.; Mahajan, M.P. *Tetrahedron*, **1994**, *50*, 7579.

12. Oshiro, Y.; Komatsum, M.; Uesaka, M.; Agawa, T. *Heterocycles*, **1984**, *22*, 549.

13. (a) Bose, A.K.; Spiegelman, G.; Manhas, M.S. *Tetrahedron Lett.*, **1971**, 3167. (b) Bose, A.K.; Krishanan, L.; Wagle, D.R.; Manhas, M.S. *Tetrahedron Lett.*, **1986**, *27*, 5955. (c) Manhas, M.S.; Ghosh, M.; Bose, A.K. *J.Org. Chem.*, **1990**, *55*, 575.

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

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

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

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

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

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

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