CHAPTER IV

ISOLATION AND TRANSFORMATIONS OF CYANOVINYLAMIDINES

Isolation of Cyanovinylamidines

Introduction

Primary pyrimidine syntheses involving the condensation of 1,3-dicarbonyl compounds or their analogues with amidines are presumed to proceed through nonisolable, open-chain vinylamidine intermediates. In fact, there are only a few reports on the isolation of these hypothetical intermediates in the condensation of 1,3-dicarbonyl analogues with amidines.6,40-42,71

Present Work, Results and Discussion

The condensation of amidine with carbethoxycyanoketene S,N-acetal 447 in the presence of excess of base, in refluxing ethanol, yields 5-cyanopyrimidin-4(3H)-one 448 as the only isolable product of the reaction, as described in Chapter III.

\[
\begin{align*}
\text{H}_5\text{C}_2\text{O}_2\text{C} & \quad \text{CN} \\
R_1-\text{N} & \quad \text{SCH}_3 \\
\text{R}_2 & \\
447 \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{NH} \\
R_3 & \\
\rightarrow \\
\text{NC} & \quad \text{O} \\
\text{R}_2 & \quad \text{N} \\
\text{R}_3 & \\
448 \\
\end{align*}
\]
However, the ketene S,N-acetal 285, when allowed to stand together with benzamidine, liberated from its hydrochloride by treatment with equimolar amount of base in ethanol, at room temperature, yielded a colorless crystalline solid, m.p. 180-182°C, analysing for C_{19}H_{18}N_4O_2. The product was different in physical and chemical properties from the high melting 5-cyanopyrimidin-4-one 365. Though the product exhibited N-H stretching absorption at 3430, 3340, and 3240 cm^{-1} in the I.r. spectrum, the presence of strong C≡N absorption strongly suggested that the compound is not the o-aminooester 462 which could have, otherwise, formed through an alternative mode of cyclization involving the cyano group.

The I.r. spectral observations together with the \textsuperscript{1}H N.m.r. and the mass spectral data proved that the compound obtained is the N-(carbethoxycyanovinyl)benzamidine 454, the presumed intermediate in the pyrimidine cyclization.
This serendipitous isolation of the intermediate 454 in the condensation of \( S,N \)-acetal 285 with benzamidine could be attributed, at least in part, to the mild reaction conditions employed, such as stirring the reactants at room temperature and also the use of stoichiometric amount of base needed for the in situ liberation of the amidine from its salt. It was found that the vinylamidine 454 is stable enough to be stirred at room temperature in ethanol for any length of time without undergoing any appreciable chemical and physical changes.

There are only three reports which describe the successful isolation of open-chain \( N \)-(cyanovinyl)amidine intermediates of the type 450. These involve the condensation of ethyl ethoxymethylenecyanoacetate 449 with acetamidine or benzamidines.40-42

\[
\begin{align*}
\text{449} & \quad \text{450} \\
\text{H}_5\text{C}_2\text{O}_2\text{C} & \quad \text{H}_5\text{C}_2\text{O}_2\text{C} \\
\text{HOC}_2\text{H}_5 & \quad \text{H}_2\text{N} \\
& \quad \text{NH}_2 \\
\rightarrow & \\
& \quad \text{R} = \text{CH}_3, \text{C}_6\text{H}_5, \text{o(CH)}_3\text{CHOC}_6\text{H}_4
\end{align*}
\]
Therefore, an attempt was made to isolate the vinyl-amidine intermediates in the reactions of cyano- and dicyanoketene S,N-acetals with amidines which were earlier found to yield pyrimidines.

Thus, cyanoketene S,N-acetals 287-290, 292 when treated with benzamidine, liberated from its hydrochloride by treatment with an equivalent of sodium hydroxide in ethanol, at room temperature, afforded N-(cyanovinyl)benzamidines 455-459 in 60-70% yield (Scheme XXX) (Table XI).

\[
\text{H}_5\text{C}_2\text{O}_2\text{C} \quad \text{CN} \quad + \quad \text{NH} \quad \xrightarrow{\text{C}_2\text{H}_5\text{OH}} \quad \text{H}_5\text{C}_2\text{O}_2\text{C} \quad \text{CN} \quad \text{NH}_2 \\
\text{H}_2\text{N} \quad \text{C}_6\text{H}_5 \quad \text{H}_2\text{N} \quad \text{C}_6\text{H}_5 \\
\text{SCH}_3 \quad \text{R} \quad \text{R}
\]

287, 455; \( R = 2-\text{CH}_3 \)  
288, 456; \( R = 3-\text{CH}_3 \)  
289, 457; \( R = 4-\text{CH}_3 \)  
290, 458; \( R = 2-\text{CH}_2\text{O} \)  
292, 459; \( R = 4-\text{Cl} \)

Scheme XXX

However, attempts to isolate cyanovinylbenzamidines 451 and 452 by the reaction of N-alkyl ketene S,N-acetals
282, 474 with benzamidine, under similar conditions, did not meet with success. Therefore, an alternate procedure employing sodium hydride in dimethylformamide as the base for the in situ liberation of benzamidine from its hydrochloride, followed by its reaction with S,N-acetals 282, 474 was attempted. Dilution of the reaction mixture with water, indeed, was found to give the cyanovinylbenzamidines 451 and 452 in good yields.

\[
\begin{align*}
\text{H}_2\text{C}=\text{O} & \quad \text{CN} \\
\text{H}_2\text{N} & \quad \text{NH} \\
\text{SCH}_3 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

Similarly, acetamidine, liberated from acetamidine hydrochloride by treatment with sodium hydride in dimethylformamide, reacted with the S,N-acetal 285 to afford good yields of the cyanovinylacetamidine 453.
However, attempts to condense cyanoketene S,N-acetals 285 and 290 with morpholinocarboxamidine sulfate employing sodium hydride in dimethylformamide as the base met with failure.

Earlier, the cyanoketene acetals were found to condense with morpholino- and piperidinocarboxamidines, liberated from their salts by treatment with sodium ethoxide in ethanol, to afford the pyrimidines 358, 374. Therefore, it was thought that morpholinocarboxamidine could be liberated from its sulfate salt by treatment with sodium ethoxide in ethanol and condensed with carbethoxycyanoketene S,N-acetals 285 and 290 to obtain N-(cyanovinyl)morpholinocarboxamidines. This method was, indeed, found successful and the N-(cyanovinyl)amidines 460 and 461 could be isolated in 40-50% yield.

\[
\begin{align*}
\text{285, 290} & \quad + \quad \text{H}_2\text{C}_2\text{O}_2\text{C}^\text{CN} \quad \overset{\text{C}_2\text{H}_5\text{OH}}{\longrightarrow} \quad \text{H}_5\text{C}_2\text{O}_2\text{C}^\text{CN} \\
285, 460; \quad \text{R} = \text{H} & \quad \text{460, 461} \\
290, 461; \quad \text{R} = 2-\text{CH}_3\text{O} & \quad \text{290, 461}; \quad \text{R} = 2-\text{CH}_3\text{O}
\end{align*}
\]
However, all attempts to isolate the vinylamidine 475 in the reaction of carbethoxycyanoketene S,N-acetal 371a with benzamidine were futile. Instead the condensation was found to yield, directly, the 5-cyanopyrimidin-4(3H)-one 371 as the isolable product of the reaction.

Similarly, failures were met with in the attempted isolation of vinylamidines in the reactions of dicyanoketene S,N-acetal 284 and α-phenylcyanoketene S,N-acetal 296 with benzamidine and guanidine. These condensations, when attempted at very low temperatures yielded only the starting cyanoketene S,N-acetal as the isolable product. However, at temperatures sufficient to bring about methanethiol elimination, the pyrimidines 345, 351 and 356 were obtained. Thus, it seems likely that the condition required for the addition-elimination reaction at C-1 of the S,N-acetals 284, 296 are too severe and result in the immediate
cyclization of the intermediates; thereby rendering the vinylamidine isolation difficult.

Spectral Characterization of Vinylamidines

The U.v. spectral characteristics of vinylamidines 451-456 and 458-460 synthesized in the present study are presented in the Table XII. The U.v. spectra of alkylaminovinylamidines 451, 452 exhibit a longer wavelength absorption at around 280 nm (log $\varepsilon \sim 4.3$). The N-benzyl derivative 452 shows an additional low intensity absorption at around 256 nm (log $\varepsilon \sim 4.21$).
The spectra of N-(arylamino vinyl)amidines 453-456, 459 and 460 exhibit a longer wavelength absorption at around 305 nm (log ε 4.2 - 4.5), thereby indicating that the aryl substituent on the nitrogen atom of the vinylamine contributes to the bathochromie shift of the longer wavelength absorption observed at 280 nm in the alkynaminovinylamidines. Ortho substitution by a methoxy group on the N-phenyl moiety results in a further increase in the longer wavelength absorption from 305 nm to 322 nm (log ε 4.15). In addition to the absorption at 305 nm, a high intensity absorption at around 225 nm (log ε 4.32 - 4.37) is observed in all the N-(arylamino vinyl)amidines synthesized in the present study. While N-(arylamino vinyl)benzamidines 454-456, 458, 459 exhibit low intensity absorptions as shoulders at around 265 nm, the vinylacetamidine 453 and the morpholinocarboxamidine 460 are devoid of any absorption in this region.

The U.v. absorption spectra of vinylamidines 451, 455 and 459 show no significant change in 0.1 N hydrochloric acid. The absorption pattern of vinylamidines in 0.1 N sodium hydroxide was found to be time dependent. The spectrum of N-methyl vinylamidine 451 in 0.1 N sodium
hydroxide was characterised by the appearance of a shoulder at 250 nm which gradually increased in intensity. However, no change was observed in the longer wavelength absorption at 280 nm.

The spectrum of N-aryl vinylamidine 459 taken immediately after the addition of 0.1 N sodium hydroxide exhibited low intensity absorptions at 255, 270 and 305 nm. At the end of 60 minutes, the spectrum exhibited strong absorptions at 255 and 270 nm. The longer wavelength absorption of the spectrum shifted to 302 nm. That the changes in the spectral pattern is due to the cyclization of the vinylamidine 459 to the pyrimidin-4-one 369 was indicated by the similarity in the spectral pattern of 459 to that of 5-cyanopyrimidin-4-one 369 in 0.1 N sodium hydroxide.

Due to the presence of three potentially tautomersizable hydrogen atoms, the vinylamidines 451-461 can be expected to exist in a variety of tautomeric and stereoisomeric forms. Therefore, it was thought of interest to establish the tautomeric nature of these vinylamidines and their preferable configuration through i.r. and $^1$H n.m.r. characteristics.
All the carbethoxycyanovinylamidines synthesized exhibit a strong C≡N absorption at around 2200 cm⁻¹ due to the conjugated cyano group. The C=O absorption of these vinylamidines appears at 1670 cm⁻¹. This shift in the carbonyl stretching frequency to a lower wave number can be attributed to the involvement of the carbonyl function in the intramolecular hydrogen bonding. In the I.r. spectrum, the vinylamidines show three to four prominent N-H stretching absorptions, around 3430, 3330 and 3230 cm⁻¹, characteristic of primary amino group (Table XIII).

The ¹H N.m.r. spectra of the vinylamidines 451-454, 456-461 were devoid of any one proton signal in the region δ 4.5 - 5.0. Earlier, such absence of one proton signal at δ 4.7 - 5.0 has been taken as a proof for the existence of cyanoketene S,N-acetals in the S,N-acetal form.²⁷⁷ Thus, the I.r. spectral data, absence of a one proton signal at δ 4.5 - 5.0 and the presence of signals which can be expected of protons residing on the nitrogen atom indicate that the vinylamidines exist as the cyanoketene aminals 479 or 480 and not as carbethoxycyanoacetamidines 476-478.
The vinylamidines exhibit two D$_2$O exchangeable singlets corresponding to three protons. Of these, a singlet corresponding to two protons appears at $\delta$ 5.7 - 6.9 in vinylamidines 451-453, 456, 460 and 461, and at $\delta$ 7.0 - 7.6 in amidines 454, 457-459, thus indicating the existence of the amidine moiety in the amino-azomethine form. The two proton singlet in vinylamidines 454, 457-459 at $\delta$ 7.0 - 7.6 is found to overlap the aryl proton signals occurring in this region (Table XIII).

The N-H signals of the N-methyl and N-benzylamino-vinylamidines 451 and 452 appear as poorly resolved quartet and triplet at $\delta$ 9.33 and $\delta$ 9.8, respectively, indicating the residence of the proton on the alkyl substituted nitrogen. The corresponding methyl and methylene signals are observed as doublets at $\delta$ 2.87 and 4.47, respectively, thereby indicating the mutual coupling of the N-H proton.
with the adjacent CH$_3$ and CH$_2$ protons. These observations suggest that the vinylamidines exist in the aminomethylene-carbethoxycyanoketene aminal form 481a or 482.

The secondary amino N-H absorption in the N-(arylaminovinyl)amidines 453, 454, 456, 458-461 appears as a sharp singlet in the region δ 11.0 - 11.2. This large downfield shift in the N-H absorptions can be attributed to the presence of these amidine derivatives in the intramolecularly hydrogen bonded γ form 481.
A large downfield shift in the N-H proton signal has, earlier, been adduced to as the evidence for the presence of hydrogen bonding in a variety of enaminocarbonyl compounds and analogues.277,281-283

**Transformations of Cyanovinylamidines.**

Vinylamidines have been presumed to be the intermediates in the primary pyrimidine syntheses involving the condensation of 1,3-dicarbonyl compounds or analogues with amidines. Therefore, isolated vinylamidines should, in principle, cyclize to pyrimidines under appropriate conditions. However, due to the presence of two non-equivalent groups at C-2 the cyanovinylamidines synthesized in the present study can be expected to exhibit two different modes of cyclizations. Therefore, an investigation on the cyclization of cyanovinylamidines, under different conditions, was undertaken.

The base catalysed condensation of carbethoxycyanoketene S,N-acetals with amidines has been shown to yield the 5-cyanopyrimidin-4-ones as the products. Therefore, cyanovinylamidines could also be expected to cyclize to pyrimidin-4-ones under the influence of a base. Thus,
heating an ethanolic solution of cyanovinylamidines 451, 453, 454, 457 and 459, in the presence of sodium ethoxide was, indeed, found to yield the 5-cyanopyrimidin-4(3H)-ones 362, 364, 365, 367 and 370, as the products (Scheme XXXI) (Table XIV).

Earlier, Foldi and Salamon\(^{40}\) have reported the cyclization of N-(cyanovinyl)acetamidine 483 to 4-aminopyrimidine 484 employing dilute acetic acid as a catalyst.

However, in the present study, attempted cyclization of N-(cyanovinyl)amidine 454 employing dilute acetic acid was not successful.
Since the amidine 454 failed to cyclize in acetic acid, it was thought that the use of a stronger acid such as p-toluenesulfonic acid or hydrogen chloride may bring about the cyclization. Thus, the cyclization of the amidine 454 was attempted by heating an equimolar mixture of 454 and p-toluenesulfonic acid in refluxing benzene. The product obtained on work-up was found to be the 4-amino-5-carbethoxypyrimidine 462. The cyanovinylamidines 457 and 459 could also be cyclized to 4-amino-5-carbethoxypyrimidines 463 and 464 under similar conditions (Scheme XXXII) (Table XV).

\[
\begin{align*}
\text{Scheme XXXII} \\
\text{454, 462; } R=\text{H} \\
\text{457, 463; } R=\text{4-CH}_3 \\
\text{459, 464; } R=\text{4-Cl}
\end{align*}
\]

However, attempted cyclization of vinylamidine 453 to 4-aminopyrimidine by treatment with p-toluenesulfonic
acid in refluxing benzene led only to the isolation of aminal 465 by the elimination of acetonitrile from the amidine.

Hydrogen chloride is known to enhance the reactivity of CEN in a variety of reactions undergone by nitriles and this fact has been utilized in the hydrogen chloride catalysed reaction of nitriles with o-aminocarbonyl compounds for the synthesis of condensed pyrimidines. The acid catalysed pyrimidine cyclization has been presumed to proceed via o-amidinocarbonyl intermediate. Therefore, it was thought of interest to study the effect of hydrogen chloride on the cyclization of cyanovinylamidines synthesized in the present study. Thus, a stream of dry hydrogen chloride was passed through a solution of the vinylamidine 454 in dioxane for 4-5 hours and the reaction mixture was allowed to stand at room temperature for 12 hours. The work-up of the reaction mixture yielded a pale yellow crystalline solid, m.p. 132-134°C, as the only product, which was different from the closely melting 4-aminopyrimidine 462 (m.p. 135-37°C). The I.r. spectrum of the product was devoid of CEN stretching absorption at around
2200 cm$^{-1}$, indicating the participation of the nitrile function in the cyclization. However, the I.r. and $^1$H N.m.r. spectra of the product indicated the absence of a primary amino group. The mass spectrum of the product exhibited a prominent molecular ion peak at m/e 353 and an intense M+2 peak at m/e 355, strongly hinting at the presence of chlorine in the molecule. Moreover, the compound analysed for C$_{19}$H$_{16}$ClN$_3$O$_2$. Based on these observations the product was assigned the structure as 5-carbethoxy-4-chloro-6-phenylamino-2-phenylpyrimidine 467. The vinylamidines 453, 457-459 were also found to cyclize to the corresponding 4-chloropyrimidines 466, 468-470 in a similar manner, on treatment with dry hydrogen chloride (Scheme XXXIII) (Table XVI).

![Scheme XXXIII](image_url)
However, the attempted cyclization of cyanovinylamidines 451 and 460 to the corresponding 4-chloropyrimidines was not successful. Unchanged cyanovinylamidines 451 and 460 were found to be the isolable products in these reactions.

There does not seem to be any report on such a direct synthesis of 4(6)-chloropyrimidines, in the literature. A plausible mechanism for this interesting novel transformation is presented in the Scheme XXXIV and bears a formal resemblance to the mechanism for the direct formation of condensed 4-chloropyrimidines in the reactions of o-amino-nitriles with certain nitriles under the influence of dry hydrogen chloride gas. 300
Though the precise stage at which the chlorine atom gets incorporated is not certain, it is reasonable to assume a concerted mechanism for the formation of 4-chloropyrimidines. The protonated amidine $485$ may undergo chloride attack on the nitrile group and concomitant cyclization with the elimination of ammonia to yield the pyrimidine $487$ (path a).

In view of the known tendency of the nitriles to form imidoyl chlorides, the formation of an amidino-imidoyl intermediate $486$ also appears plausible. The amidino-imidoyl chloride $486$ can undergo cyclization with the elimination of ammonia to yield the 4-chloropyrimidine $487$ (path b).

The formation of a cyanovinylimidoyl chloride $488$ through protonation of the cyanovinylamidine $481$ and the displacement of ammonia by chloride ion, followed by cyclization can also be conceived as an alternate reaction pathway for the formation of 4-chloropyrimidine $487$. 
However, the intermediacy of such cyanovinylimidoyl chloride 488 seems unlikely due to the absence of any reports on the conversion of amidines into imidoyl chlorides under the influence of hydrogen chloride. Moreover, there does not seem to be any report on the synthesis of imidoyl chlorides of the type 488.

However, a solitary report describes the isolation of dicyanovinylimidoyl chloride of the type 490 as stable product in the reaction of dicyanovinylamine 489 with acid chlorides in refluxing acetone. It has been suggested that the reaction involves an unusual mode of condensation between the amino group of the O,N-acetal 489 and the acid chloride with the elimination of water, though, in the normal course, the reaction would be expected to yield the amide 491.

\[
\begin{array}{c}
\text{H}_2\text{C} = \text{N} - \text{O} - \text{C} - \text{R} \\
\text{489}
\end{array}
\text{R}^2\text{COCl} \rightarrow
\begin{array}{c}
\text{H}_2\text{C} = \text{N} - \text{Cl} - \text{O} - \text{R} \\
\text{490}
\end{array}
\]

In the light of the present observations that a cyanovinylamidine prefers to cyclize to 4-chloropyrimidine in the presence of hydrogen chloride, it appears likely
that the intermediate acylaminonitrile of the type 491 could, possibly, undergo analogous mode of cyclization, especially in the presence of acid chloride and the hydrogen chloride formed during the reaction, to a 4-chloropyrimidine.

However, the spectral and chemical evidence presented for the structure of the compounds proposed as imidoyl chlorides by Mower and Dickinson is not unequivocal to confirm the imidoyl chloride structure 490. Moreover, the presented spectral and chemical evidence is insufficient to distinguish between the imidoyl chloride structure 490 and the alternative possibility of an isomeric pyrimidine 492, which seems to have been overlooked by these workers.

\[
\begin{align*}
\text{490} & \quad \begin{array}{c}
\text{Cl} \\
\text{R}^1 \text{O} \\
\text{NC} \\
\text{CN}
\end{array} \\
\text{R}^2 \\
\end{align*}
\begin{align*}
\text{492} & \quad \begin{array}{c}
\text{Cl} \\
\text{R}^1 \text{O} \\
\text{NC} \\
\text{N}
\end{array} \\
\text{R}^2 \\
\end{align*}
\]

In fact, the compound obtained by reacting the O,N-acetal 493 with acetyl chloride according to the method reported by Mower and Dickinson was found to be identical in all respects with an authentic sample of 4-chloro-5-cyano-6-ethoxy-2-methylpyrimidine 471, prepared from 4,6-dichloro-5-cyano-2-methylpyrimidine 471a.
It follows from these observations that the compounds described as the cyanovinylamide derivatives 490, 491 by Mower and Dickinson301 are, in fact, the corresponding pyrimidines 492, 494.

A plausible mechanism for the formation of 4-chloropyrimidines in the reaction of cyanovinylamines with acid chlorides is presented in the Scheme XXXV. The 4-chloropyrimidine formation, probably, proceeds through O-acyl cyanovinyl imidoyl derivative 495 formed by the acylation
of cyanovinylamide 491. The O-acyl derivative 495, in the presence of hydrogen chloride, liberated during the acylation, undergoes cyclization either through a concerted mechanism or through an imidoyl chloride intermediate to form 4-chloropyrimidine 492.

\[
\begin{align*}
\text{NC-} & \quad \text{CH} \\
\text{R} & \quad \text{COCl} \\
\text{Cl} & \quad \text{NH} \\
\text{R}^1 & \quad \text{O-} \quad \text{N-} \quad \text{R}^2 \\
\text{R}^1 & \quad \text{O-} \quad \text{C-} \quad \text{R}^2
\end{align*}
\]

This sequence of reactions suggested that acid chloride could be used as reagent for the direct cyclization of cyanovinylamines to 4-chloropyrimidines. In fact, the reaction of cyanoketene S,N-acetal 472a with acetyl
chloride was found to yield, directly, the 2-methyl-4-chloropyrimidine 472 as the product indicating, thereby, the generality of the reaction.

Thus, the cyclization of cyanovinylimidoyl derivatives with hydrogen chloride appears to be a facile route to the synthesis of 4-chloropyrimidines. The method offers an attractive alternative for the preparation of 6-substituted amino-4-chloropyrimidines which are otherwise difficultly accessible.

Physical and Spectral Properties of Vinylamidines and Pyrimidines

The cyanovinylamidines 451-461, the 4-amino-6-aryl-amino-5-carbethoxypyrimidines 462-464 and 4-chloro-5-carbethoxy- and 5-cyanopyrimidines 466-472 are crystalline solids. While the cyanovinylamidines, 4-hydroxy- and the 4-aminopyrimidines are colourless compounds, the 4-chloropyrimidines are pale yellow. Among the vinylamidines and the vinylamidine derived pyrimidines, the melting points are
in the order: 5-cyanopyrimidin-4-ones > vinylamidines > 4-amino-5-carbethoxypyrimidines > 4-chloro-5-carbethoxypyrimidines.

The vinylamidines 451-461 are moderately soluble in benzene, ethanol, and dichloromethane, while the 4-chloropyrimidines 466-470 are freely soluble in most of the organic solvents except hexane from which they are recrystallized. The 4-amino-5-carbethoxypyrimidines 462-464, on the other hand, are moderately soluble only in polar solvents, such as ethanol. 5-Cyanopyrimidin-4-ones, derived by the base catalysed cyclization of vinylamidines, are moderately soluble in dimethylformamide and dimethyl sulfoxide. The vinylamidines are moderately soluble in dilute hydrochloric acid.

The base catalysed cyclization of vinylamidines to 5-cyanopyrimidin-4-ones results in the disappearance of primary N-H stretching bands in the I.r. spectrum without affecting the C= N and C=O absorption to any significant extent.

The 4-amino-5-carbethoxypyrimidines 462-464 exhibit three prominent N-H stretching bands in the region 3500-3300 cm⁻¹. The C=O absorption in these pyrimidine derivatives appears
at a lower wave number of 1670-1650 cm$^{-1}$, indicating the presence of intramolecular hydrogen bonding involving the carbonyl group (Table XVII).

The 4-chloro-5-carbethoxypyrimidines, on the other hand, exhibit a weak N-H band at around 3250 cm$^{-1}$. The C=O stretching absorptions in these pyrimidine derivatives are observed at around 1680-1670 cm$^{-1}$ (Table XVIII).

In the U.v. spectrum the 5-cyanopyrimidin-4-one 365 and the 4-amino-5-carbethoxypyrimidines 462-464 show similar absorption pattern. Thus, while the pyrimidine-4-one 365 exhibits longer wavelength absorption at 255 nm (log $\varepsilon$ 4.27), 263 (log $\varepsilon$ 4.27) and 305 (log $\varepsilon$ 3.89), the aminopyrimidine 362 exhibits the absorption at around 250 nm (log $\varepsilon$ 4.5), 260 (log $\varepsilon$ 4.5), and 310 (log $\varepsilon$ 4.0). 4-Amino-5-carbethoxypyrimidines, however, show an additional absorption as a shoulder at around 235 nm (log $\varepsilon$ 4.25). Thus, the cyclization of vinylamidines to 4-hydroxy- and 4-amino-pyrimidines results in an increase in the intensity of absorption at around 265 nm and a decrease in the intensity of the absorption at 310 nm.

The 4-chloro-5-carbethoxypyrimidines 467, 468 and 470 exhibit an entirely different pattern than the 4-hydroxy- and
and 4-aminopyrimidines with the appearance of a single absorption maxima at 280 nm ($\log \varepsilon = 4.55$).

The cyanovinylamidines $451-454$, $459$ and $460$ exhibit intense molecular ion peaks under electron impact. In the higher mass region, the vinylamidines exhibit ion peaks $496a-499a$, corresponding to the loss of $\text{C}_2\text{H}_5\text{O}^+$, $\text{C}_2\text{H}_5\text{OH}$, $\text{CO}_2\text{C}_2\text{H}_4$ and $\text{CO}_2\text{C}_2\text{H}_5^+$ from the molecular ion. The radical cation at $M-46$ can also be formulated as $497a$, attributable to the ionization of 5-cyanopyrimidin-4-one, formed by the thermal cyclization of vinylamidine. Similarly, alternative structures can be formulated for the loss of $\text{C}_2\text{H}_5\text{O}^+$, $\text{C}_2\text{H}_5\text{OH}$, $\text{CO}_2\text{C}_2\text{H}_4$ and $\text{CO}_2\text{C}_2\text{H}_5^+$ from the molecular ion.

The fragmentation pattern of cyanovinylacetamidine $453$ and the -benzamidines $451$, $452$, $454$ and $459$ is presented in the Scheme XXXVI. The spectra show, in addition to the loss of $\text{EtO}^+$, $\text{EtOH}$, $\text{CO}_2\text{C}_2\text{H}_4$ and $\text{CO}_2\text{C}_2\text{H}_5^+$, a moderately intense peak at $M-112$ which can be assigned to the nitrilium ion $500$ formed by the loss of $\text{NC-CH}^\text{NH} \text{CO}_2\text{C}_2\text{H}_5$ from the molecular ion. The vinylamidines also exhibit the loss of $\text{CH}_3\text{CN}$ or $\text{NH}_2$ or $\text{C}_6\text{H}_5\text{CN}$ and $\text{CH}_3\text{CN}$ or $\text{NH}_2$ or $\text{C}_6\text{H}_5\text{CN}$ from the molecular ion.
The ions m/e 120 and 147 corresponding to 501a and 417, respectively characterize the degradation of all the cyanovinylbenzamidines. Similarly, the cyanovinylacetamidine 452 exhibits moderately intense peak at m/e 85 corresponding to 501b. Interestingly, the formation of the cation 417 was also observed in the spectra of 2-phenylpyrimidin-4-ones 365, 367 and 370. Therefore, it appears that a fraction of the vinylamidine undergoes cyclization to 5-cyanopyrimidin-4-one during the process of ionization.

\[ \begin{align*}
501a, \text{ m/e 120} & \quad 417, \text{ m/e 147} & \quad 501b, \text{ m/e 85}
\end{align*} \]

The 1-arylamino vinylacetamidine 453 and -benzamidines 454 and 459 exhibit intense ion peaks at m/e 118, 180 and 214 formulated as 502a, 502b and 502c, respectively. The formation of these N-arylnitrilium ions 502a-c can be rationalized by the mechanism shown in the Scheme XXXVII.
Scheme XXXVI
The methylaminovinylbenzamidine 451 exhibits additional ion peaks due to the decomposition of the radical cation 503a or 503b formed by the loss of CH₂=NH from the molecular ion.

**Scheme XXXVII**

The methylaminovinylbenzamidine 451 exhibits additional ion peaks due to the decomposition of the radical cation 503a or 503b formed by the loss of CH₂=NH from the molecular ion.
The spectrum of the (cyanovinyl)morpholinocarboxamidine 460 exhibits many intense ion peaks in the higher mass region which arise by the fragmentation of the morpholine moiety. The spectrum also exhibits the loss of \( \text{NCOCH}_2\text{C}_2\text{H}_5 \) and \( \text{OCN}^- \) from the molecular ion to yield moderately intense peaks at m/e 231 and 257, respectively. The ion m/e 231 can also be assigned to the radical cation 504 arising by the loss of \( \text{OCN}^-\text{-CN} \) from the molecular ion.

The fragmentation pattern of the vinylamidine 460 is presented in the Scheme XXXVIII. The spectrum also exhibits the ions m/e 185, 184, 143, and 142 in the lower mass region.

The mass spectral degradation of 4,6-diamino-5-carbethoxypyrimidine 462 is presented in the Scheme XXXIX. The spectrum exhibits intense \( M_+ \) and \( M-1 \) peaks at m/e 334 and 333, respectively. McLafferty rearrangement and loss of \( \text{C}_2\text{H}_5\text{OH} \) from \( M_+ \) and \( M-1 \) leads to ions m/e 288 and 287.
Scheme XXXVIII
respectively. The decomposition of the radical cation m/e 288 with the loss of CO and C₆H₅CN yields ions m/e 260 and 185. The ion peak m/e 184, which is as intense as m/e 185, probably, arises by the loss of C₆H₅CN from ion m/e 287, as well as the loss of H⁺ from m/e 185.

The loss of NH₂⁺, CO and NH₂CN from the radical cation m/e 185 yields the cation at m/e 169 and the radical cations m/e 157 and 143. The lower mass region of the spectrum also shows ions m/e 131, 118, 104 and 103.

\[
\begin{align*}
\text{m/e 131} & \quad \text{m/e 118} \\
\text{m/e 104} & \quad \text{m/e 103}
\end{align*}
\]

The spectrum of 6-p-tolylamino-5-carbethoxypyrimidine 463 is characterised by an analogous fragmentation pattern.
Scheme XXXIX
The 4-chloropyrimidines 466-468, 471 and 472 exhibit intense molecular ion peaks and are characterised by the appearance of M+2 peaks, about 30% as intense as the M⁺ peaks. 5-Carbethoxy-4-chloro-6-anilinopyrimidine 467 shows an intense ion peak at m/e 307 which can be attributed to the McLafferty rearrangement and the loss of C₂H₅OH from the molecular ion. The loss of Cl⁻ from the radical cation 506 (m/e 307) leads to the cation m/e 272 as a moderately intense peak. The ion peak at m/e 244 can be formulated as 507 obtained by the stepwise loss of CO and Cl⁻ from the radical cation m/e 307. Major decomposition pathway of the ions m/e 307, 279, 272 and 244 appears to be the loss of neutral molecule of C₆H₅CN to yield the ions m/e 204, 176, 169 and 141, respectively (Scheme XL). Similar fragmentation pattern was observed in the spectra of 5-carbethoxy-4-chloropyrimidines 466 and 468.

6-Ethoxy-5-cyano-4-chloropyrimidine 471 exhibits a base peak at m/e 169 due to the radical cation 508a or 508b, formed by the McLafferty rearrangement and elimination of ethylene from the molecular ion. Moderately intense ion at m/e 153 can be attributed to the loss of CH₃CHO.
Scheme XL
from the molecular ion. Loss of CO from the radical cation m/e 169 leads to ion m/e 141.

Loss of Cl\(^+\) from the molecular ion does not seem to be an important pathway in 4-chloropyrimidine 471. The spectrum of 471 shows the loss of Cl\(^+\) from radical cation m/e 153 as a moderately intense peak. Ions at m/e 92 and 93 are attributed to the loss of ClCN and CH\(_3\)CN from m/e 153 and 134, respectively (Scheme XLI).

\[\text{Scheme XLI}\]
The spectrum of 4-chloro-5-cyano-6-methylthiopyridine exhibits an intense molecular ion peak at m/e 199. Loss of Cl from the molecular ion yields an intense peak at m/e 164. Moderately intense ion peak at m/e 152 is possibly due to the loss of CH$_3$S from the molecular ion. The appearance of a more intense ion peak at m/e 154 may be attributed to the loss of CHS from molecular ion to yield the cation. The loss of HCN from the molecular ion yields a moderately intense peak at m/e 172. This loss, possibly, involves a cyclization and ring cleavage of the molecular ion to yield.

The cation m/e 164, formed by the loss of Cl, eliminates CH$_3$CN to yield an intense ion peak at m/e 123. The formation of an abundant ion m/e 108 can only be explained by the loss of CH$_3$ from the cation. The fragmentation pattern observed in the spectrum is depicted in the Scheme XLII.
Scheme XLII
Table XI

N- (2-carbethoxy-2-cyano-1-aminovinyl) amidines

<table>
<thead>
<tr>
<th>No.</th>
<th>R¹</th>
<th>R²</th>
<th>M.P. °C</th>
<th>YIELD %</th>
<th>Sol.</th>
<th>Mol. Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>451</td>
<td>CH³</td>
<td>C₆H₅</td>
<td>150-153</td>
<td>70</td>
<td>DM-H</td>
<td>C₁₄H₁₆N₂O₂</td>
</tr>
<tr>
<td>452</td>
<td>C₆H₅CH₂</td>
<td>C₆H₅</td>
<td>144-146</td>
<td>63</td>
<td>B-H</td>
<td>C₂₀H₂₀N₂O₂</td>
</tr>
<tr>
<td>453</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>173-175</td>
<td>70</td>
<td>B-H</td>
<td>C₁₄H₁₆N₂O₂</td>
</tr>
<tr>
<td>454</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>180-182</td>
<td>70</td>
<td>B</td>
<td>C₁₉H₁₈N₂O₂</td>
</tr>
<tr>
<td>455</td>
<td>2-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>180-182 (d)</td>
<td>60</td>
<td>B</td>
<td>C₂₀H₂₀N₂O₂</td>
</tr>
<tr>
<td>456</td>
<td>3-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>166-168 (d)</td>
<td>69</td>
<td>B</td>
<td>C₂₀H₂₀N₂O₂</td>
</tr>
<tr>
<td>457</td>
<td>4-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>186-190</td>
<td>62</td>
<td>B</td>
<td>C₂₀H₂₀N₂O₂</td>
</tr>
<tr>
<td>458</td>
<td>2-CH₃OC₆H₄</td>
<td>C₆H₅</td>
<td>196-198 (d)</td>
<td>70</td>
<td>DC</td>
<td>C₂₀H₂₀N₂O₃</td>
</tr>
<tr>
<td>459</td>
<td>4-CIC₆H₄</td>
<td>C₆H₅</td>
<td>223-225</td>
<td>68</td>
<td>E</td>
<td>C₁₉H₁₇ClN₄O₂</td>
</tr>
<tr>
<td>460</td>
<td>O₆H₅</td>
<td>4-morpho-linyl</td>
<td>218-220 (d)</td>
<td>40</td>
<td>E-C</td>
<td>C₁₇H₂₁N₅O₃</td>
</tr>
<tr>
<td>461</td>
<td>2-CH₃OC₆H₄</td>
<td>4-morpho-linyl</td>
<td>225-227 (d)</td>
<td>56</td>
<td>E-C</td>
<td>C₁₈H₂₃N₅O₄</td>
</tr>
</tbody>
</table>

* B = Benzene, C = Chloroform, DC = 1,2-Dichloroethane, DM = Dichloromethane, E = Ethanol, H = Hexane
TABLE XII

U.v. spectral data of

N-(2-carbethoxy-2-cyano-l-aminovinyl)amidines

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>No.</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>$\lambda_{\text{max}}$ nm (log ε)</th>
</tr>
</thead>
<tbody>
<tr>
<td>451</td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>205(4.59), 214sh(4.43), 279(4.34)</td>
</tr>
<tr>
<td>452</td>
<td>C₆H₅CH₂</td>
<td>C₆H₅</td>
<td>206(4.56), 256(4.21), 282(4.27)</td>
</tr>
<tr>
<td>453</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>206(4.38), 306(4.39)</td>
</tr>
<tr>
<td>454</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>205(4.52), 224(4.32), 268sh(4.16), 308(4.33)</td>
</tr>
<tr>
<td>455</td>
<td>2-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>204(4.50), 222(4.30), 262sh(4.12), 305(4.20)</td>
</tr>
<tr>
<td>456</td>
<td>3-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>205(4.63), 225(4.37), 266sh(4.23), 308(4.38)</td>
</tr>
<tr>
<td>458</td>
<td>2-CH₃OC₆H₄</td>
<td>C₆H₅</td>
<td>204(4.38), 227sh(4.21), 276sh(3.96), 288sh(3.98), 322(4.15)</td>
</tr>
<tr>
<td>459</td>
<td>4-ClC₆H₄</td>
<td>C₆H₅</td>
<td>204(4.66), 229(4.36), 268sh(4.27), 311(4.46)</td>
</tr>
<tr>
<td>460</td>
<td>C₆H₅</td>
<td>4-morpholinyl</td>
<td>210(4.41), 227sh(4.26), 302(4.42)</td>
</tr>
</tbody>
</table>
TABLE XIII
I.r. and $^1$H N.m.r. spectral data of N-(2-carbethoxy-2-cyano-1-aminovinyl)amidines.

![Chemical Structure Diagram]

<table>
<thead>
<tr>
<th>No.</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>$\nu_{max} \text{ cm}^{-1}$</th>
<th>$^1$H N.m.r. (O)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$\text{NH}_2^*$</td>
</tr>
<tr>
<td>451</td>
<td>CH$_3$</td>
<td>C$_6$H$_5$</td>
<td>3420, 3350, 3300, 3230 (NH); 2200 (C=EN); 1670 (C=O)</td>
<td>6.07 (br, s, 2H)</td>
</tr>
<tr>
<td>452</td>
<td>C$_6$H$_5CH_2$</td>
<td>C$_6$H$_5$</td>
<td>3430, 3340, 3300, 3230 (NH); 2200 (C=EN); 1665 (C=O)</td>
<td>5.6 (br, s, 9.8 (t, 1H)</td>
</tr>
<tr>
<td>453</td>
<td>C$_6$H$_5$</td>
<td>CH$_3$</td>
<td>3480, 3320, 3260, 3210 (NH); 2200 (C=EN); 1665 (C=O)</td>
<td>6.5 (br, s, 11.08 (s, 1H)</td>
</tr>
<tr>
<td>454</td>
<td>C$_6$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>3430, 3340, 3240 (NH); 2190 (C=EN); 1670 (C=O)</td>
<td>7.03</td>
</tr>
<tr>
<td>455</td>
<td>2-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>3440, 3350, 3280, 3240 (NH); 2200 (C=EN); 1665 (C=O)</td>
<td>-</td>
</tr>
<tr>
<td>456</td>
<td>3-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>3430, 3340, 3240 (NH); 2200 (C=EN); 1670 (C=O)</td>
<td>6.37 (br, s, 11.15 (s, 1H)</td>
</tr>
<tr>
<td>457</td>
<td>4-CH$_3$C$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>3430, 3350, 3220 (NH); 2200 (C=EN); 1660 (C=O)</td>
<td>7.09</td>
</tr>
<tr>
<td>No.</td>
<td>R1</td>
<td>R2</td>
<td>max cm⁻¹</td>
<td>¹H N, m.p. (°)</td>
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<tr>
<td>-----</td>
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<td>-------------------</td>
<td>-------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>458</td>
<td>2-CH₃OC₆H₄</td>
<td>C₆H₅</td>
<td>3430, 3340, 3230(NH); 2200(CEN); 1670(C=O)</td>
<td>6.7⁺</td>
</tr>
<tr>
<td>459</td>
<td>4-CIC₆H₄</td>
<td>C₆H₅</td>
<td>3420, 3340, 3230(NH); 2200(CEN); 1665(C=O)</td>
<td>7.3⁺</td>
</tr>
<tr>
<td>460</td>
<td>C₆H₅</td>
<td>4-morpholino</td>
<td>3410, 3340, 3230(NH); 2190(CEN); 1665(C=O)</td>
<td>6.93(s, 2H)</td>
</tr>
<tr>
<td>461</td>
<td>2-CH₃OC₆H₄</td>
<td>4-morpholino</td>
<td>3400, 3320, 3220(NH); 2190(CEN); 1665(C=O)</td>
<td>6.8(s, 2H)</td>
</tr>
</tbody>
</table>

* The signals disappear on D₂O exchange

⁺ The signals are overlapped by aryl proton signals
TABLE XIV

5-Cyanopyrimidin-4(3H)-ones prepared by the cyclization of N-(2-carbethoxy-2-cyano-1-aminovinyl)amidines.

![Chemical structure]

<table>
<thead>
<tr>
<th>No.</th>
<th>R¹</th>
<th>R²</th>
<th>M.P. °C</th>
<th>Yield %</th>
<th>Sol.of Crystn*</th>
<th>Mol. Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>362</td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>350-352</td>
<td>71</td>
<td>D-E</td>
<td>C₁₂H₁₀N₄O</td>
</tr>
<tr>
<td>364</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>325-327</td>
<td>62</td>
<td>D-E</td>
<td>C₁₂H₁₀N₄O</td>
</tr>
<tr>
<td>365</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>&gt;360</td>
<td>66</td>
<td>D-E</td>
<td>C₁₂H₁₂N₄O</td>
</tr>
<tr>
<td>367</td>
<td>4-CH₃C₆H₄</td>
<td>C₆H₅</td>
<td>&gt;360</td>
<td>68</td>
<td>DS-E</td>
<td>C₁₈H₁₄N₄O</td>
</tr>
<tr>
<td>370</td>
<td>4-ClC₆H₄</td>
<td>C₆H₅</td>
<td>&gt;360</td>
<td>70</td>
<td>DS-E</td>
<td>C₁₇H₁₁ClN₄O</td>
</tr>
</tbody>
</table>

* D = Dimethylformamide; DS = Dimethyl sulfoxide; R = Ethanol
TABLE XV

4-Amino-5-carbethoxypyrimidines prepared by the cyclization of N-(2-carbethoxy-2-cyanovinyl) amidines.

![Chemical structure]

<table>
<thead>
<tr>
<th>No.</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>m.p. °C</th>
<th>Yield%</th>
<th>Mol. Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>462</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>135-137</td>
<td>54</td>
<td>C&lt;sub&gt;19&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td>463</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>160-162</td>
<td>55</td>
<td>C&lt;sub&gt;20&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td>464</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>183-185</td>
<td>59</td>
<td>C&lt;sub&gt;19&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;ClN&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

*All the compounds were recrystallized from ethanol.*
TABLE XVI

4-Chloro-5-carbethoxypyrimidines prepared by the cyclization of N-2-carbethoxy-2-cyano-1-amino-vinyl)amidines.

\[
\begin{array}{cccccc}
\text{No.} & \text{R}^1 & \text{R}^2 & \text{M.P.} \degree \text{C} & \text{Yield} \% & \text{Mol. Formula} \\
466 & \text{C}_6\text{H}_5 & \text{CH}_3 & 77-79 & 60 & \text{C}_{14}\text{H}_{14}\text{ClN}_3\text{O}_2 \\
467 & \text{C}_6\text{H}_5 & \text{C}_6\text{H}_5 & 132-134 & 50 & \text{C}_{19}\text{H}_{15}\text{ClN}_3\text{O}_2 \\
468 & 4\text{-CH}_3\text{C}_6\text{H}_4 & \text{C}_6\text{H}_5 & 116-118 & 51 & \text{C}_{20}\text{H}_{18}\text{ClN}_3\text{O}_2 \\
469 & 2\text{-CH}_3\text{OC}_6\text{H}_4 & \text{C}_6\text{H}_5 & 117-119 & 52 & \text{C}_{20}\text{H}_{18}\text{ClN}_3\text{O}_3 \\
470 & \text{ClC}_6\text{H}_4 & \text{C}_6\text{H}_5 & 127-129 & 51 & \text{C}_{19}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_2 \\
\end{array}
\]

*All the compounds were recrystallized from n-hexane.*
TABLE XVII

I.r. and U.v. spectral data of 4-amino-5-carbethoxypyrimidines

<table>
<thead>
<tr>
<th>No.</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>( \nu_{\text{max}} \text{ cm}^{-1} ) (selected bands)</th>
<th>( \lambda_{\text{max}} \text{ nm (log } \epsilon \text{)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>462</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3460, 3400, 3350 (NH); 1670 (C=O)</td>
<td>209 (4.55), 237 (4.32), 260 (4.58), 267 (4.59), 308 (4.13)</td>
</tr>
<tr>
<td>463</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3460, 3420, 3360 (NH); 1650 (C=O)</td>
<td>210 (4.47), 236 (4.24), 261 (4.49), 269 (4.49), 310 (3.99)</td>
</tr>
<tr>
<td>464</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3500, 3470, 3320 (NH); 1670 (C=O)</td>
<td>212 (4.40), 240sh (4.27), 261 (4.57), 270 (4.60), 308 (4.16)</td>
</tr>
</tbody>
</table>
TABLE XVIII

I.r. and U.v. spectral data of 4-chloro-5-carbethoxypyrimidines

![Pyrimidine Structure]

<table>
<thead>
<tr>
<th>No.</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>ν&lt;sub&gt;max&lt;/sub&gt; cm&lt;sup&gt;-1&lt;/sup&gt; (selected bounds)</th>
<th>λ&lt;sub&gt;max&lt;/sub&gt; cm&lt;sup&gt;-1&lt;/sup&gt; (log ε)</th>
</tr>
</thead>
<tbody>
<tr>
<td>466</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1660 (C=O)</td>
<td></td>
</tr>
<tr>
<td>467</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3230 (NH); 1675 (C=O)</td>
<td>205 (4.55), 280 (4.57)</td>
</tr>
<tr>
<td>468</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3200 (NH); 1670 (C=O)</td>
<td>205, 280</td>
</tr>
<tr>
<td>469</td>
<td>2-CH&lt;sub&gt;3&lt;/sub&gt;CC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>3240 (NH); 1680 (C=O)</td>
<td></td>
</tr>
<tr>
<td>470</td>
<td>4-ClC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>1670 (C=O)</td>
<td>204, 281</td>
</tr>
</tbody>
</table>
Reaction of ethyl 2-cyano-3-(methylamino)-3-(methylthio)acrylate with benzamidines:

To an ice-cold suspension of 0.96g (0.02 mol) of sodium hydride (50%) in 20ml of dimethylformamide was added portionwise, with stirring, 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate. The mixture was stirred for 30 minutes at room temperature, cooled and treated, dropwise, with a solution of 4.0g (0.02 mol) of ethyl 2-cyano-3-(methylamino)-3-(methylthio)acrylate (282) in 10ml dimethylformamide. The mixture was stirred at 5-10°C for one hour and allowed to stand at room temperature for 12 hours. The reaction mixture was poured into ice-water and the solid obtained was filtered, washed with water and dried. Recrystallization from dichloromethane-hexane yielded 3.8g of colorless crystalline product, m.p. 150-153°C. The product was characterized as N-[2-carbethoxy-2-cyano-1-(methylamino)vinyl]benzamidine (451).

Analysis:

- **IR (KBr)**: 3420, 3350, 3300, 3230 (NH); 1670 (C=O); 1650, 1610, 1580, 1480, 1410, 1350, 1300, 1140, 1050, 980, 785, 770, 700 cm⁻¹
- **UV (MeOH)**: 205nm (log ε 4.59), 214sh (4.43), 279 (4.34)
NMR (CDCl₃) : δ 1.27 (t, 3H, CO₂CH₂CH₃), 2.9 (d, 3H, J=5 Hz, NH-CH₃), 1.17 (q, 2H, CO₂CH₂CH₃), 6.07 (broad s, 2H, NH₂), 7.3-7.9 (m, 5H, Ar-H), 9.33 (q, 1H, NH-CH₃)

NMR (CDCl₃ + D₂O) : δ 1.27 (t, 3H, CO₂CH₂CH₃), 2.9 (s, 3H, NHCH₃), 4.17 (q, 2H, CO₂CH₂CH₃), 7.3-7.9 (m, 5H, Ar-H)

MS, m/e : 272 (M⁺), 243, 227, 226, 199, 160, 147, 124, 121, 120, 104, 103

Reaction of ethyl 3-(benzylamino)-2-cyano-3-(methylthio)acrylate with benzamidine

Ethyl 3-(benzylamino)-2-cyano-3-(methylthio)acrylate 4.14g (0.015 mol) was reacted with 2.9g (0.015 mol) of benzamidine hydrochloride dihydrate in the presence of 0.72g (0.015 mol) of sodium hydride (50%) in 30ml dimethylformamide according to the procedure described for 451. The crude product on recrystallization from benzene-hexane yielded 3.3g of colorless crystalline product, m.p. 144-146°C. The product was characterized as N-[1-(benzylamino)-2-carbethoxy-2-cyanovinyl]benzamidine (452).

Analysis : C₂₀H₂₀N₄O₂ (348.39) Requires C, 68.95; H, 5.79%

Found C, 68.97; H, 5.36%
IR (KBr) : 3430, 3340, 3300, 3230(NH), 2200(C=EN); 1665(C=O); 1640, 1620, 1570, 1400, 1300, 1150, 1060, 1035, 785, 760, 700 cm⁻¹

UV (MeOH) : 206 nm(log ε 4.56), 256(4.21), 282(4.27)

NMR (CDCl₃) : δ 1.27(t, 3H, CO₂CH₂CH₃), 4.17(q, 2H, CO₂CH₂CH₃), 4.47(d, 2H, J=5Hz, NH-CH₂C₆H₅), 5.6(broad s, 2H, NH₂), 7.27-7.83(m, 10H, Ar-H), 9.8(t, 1H, NHCH₂C₆H₅)

NMR (CDCl₃+D₂O) : δ 1.27(t, 3H, CO₂CH₂CH₃), 4.2(q, 2H, CO₂CH₂CH₃), 4.5(s, 2H, NH-CH₂C₆H₅), 7.27-7.83(m, 10H, Ar-H)

MS, m/e : 348(M⁺), 319, 303, 302, 301, 275, 273, 245, 236, 213, 199, 193, 171, 155, 131, 121, 120, 106, 104

Reaction of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)acrylate with acetamidine

To an ice-cold suspension of 0.96g (0.02 mol) of sodium hydride (50%) in 20ml dimethylformamide was added with stirring, 1.9g (0.02 mol) of acetamidine hydrochloride. The mixture was stirred for 30 minutes and treated dropwise, under cooling and stirring, with a solution of 5.25g (0.02 mol)
of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)acrylate (285) in 15ml of dimethylformamide. After allowing to stand at room temperature for 12 hours, the reaction mixture was poured into ice-water. The solid obtained was filtered, washed with water and dried. Recrystallization from benzene-hexane afforded 3.8g of colorless crystalline product, m.p. 173-175°C. The product was identified as N-[2-carbethoxy-2-cyano-1-(phenylamino)viny]acetimid (453).

Analysis: $\text{C}_4\text{H}_6\text{N}_2\text{O}_2$ (272.30) Requires C, 61.75; H, 5.92%; Found C, 61.73; H, 5.76%

IR (KBr): 3480, 3320, 3260, 3210(NH), 2200(C≡N); 1665(C=O), 1650, 1610, 1580, 1500, 1380, 1300, 1230, 1180, 1160, 1050, 780, 750 cm$^{-1}$

UV (MeOH): 206nm (log ε 4.38), 306(4.39)

NMR (CDCl$_3$ + DMSO): $\delta$ 1.32(t, 3H, CO$_2$CH$_2$CH$_3$), 2.02(s, 3H, N≡C-CH$_3$); 4.23(q, 2H, CO$_2$CH$_2$CH$_3$), 6.5(broad s, 2H, NH$_2$); 7.25(m, 5H, Ar-H), 11.08(s, 1H, NH-C$_6$H$_5$).

NMR (CDCl$_3$ + DMSO+D$_2$O): $\delta$ 1.32(t, 3H, CO$_2$CH$_2$CH$_3$), 2.02(s, 3H, CH$_3$); 4.23(q, 2H, CO$_2$CH$_2$CH$_3$), 7.25(m, 5H, Ar-H)

MS, m/e: 272(M$^+$), 230, 214, 199, 186, 185, 169, 160, 158, 157, 142, 119, 118
Reaction of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)acrylate with benzamidine

To a solution of 0.8g (0.02 mol) of sodium hydroxide in 30ml of ethanol was added, with stirring, 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate. After stirring for 30 minutes, precipitated sodium chloride was filtered off and the filtrate was treated portionwise, with stirring, with 5.25g (0.02 mol) of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)acrylate (285). The reaction mixture was stirred for 30 minutes and allowed to stand at room temperature for 12 hours. The solid obtained was filtered, washed with cold ethanol and dried. Recrystallization from benzene yielded 4.7g of colorless crystalline product, m.p. 180-182°C. The product was characterized as N-[2-carbethoxy-2-cyano-1-(phenylamino)vinyl]benzamidine (454).

Analysis: C, H, N, O, (334.37) Requires C, 68.25; H, 5.43% Found. C, 68.25; H, 5.80%

IR (KBr): 3430, 3340, 3240(NH); 2190(C=EN); 1670(C=O);
1660, 1645, 1610, 1570, 1500, 1470, 1435,
1410, 1370, 1350, 1300, 1175, 1150,
1050, 785 cm⁻¹

UV (MeOH): 205nm(log ε 4.52), 224(4.32), 268sh(4.16),
308(4.33)
Reaction of ethyl 2-cyano-3-[(2-methylphenyl)amino]-3-(methylthio)acrylate with benzamidine.

Ethyl 2-cyano-3-[(2-methylphenyl)amino]-3-(methylthio)acrylate (287) 5.5g (0.02 mol) was reacted with benzamidine liberated from 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate by treatment with 0.8g (0.02 mol) of sodium hydroxide in 30ml of ethanol according to the procedure described for 454. The crude product obtained was recrystallized from benzene to obtain 4.1g of colorless crystalline product, m.p. 180-182°C(d). The product was characterized as N-[2-carbethoxy-2-cyano-1-[2-methylphenylamino]vinyl]benzamidine (455).

Analysis : $C_{20}H_{20}N_4O_2$ (348.39) Requires C,68.95; H,5.79%

Found C,69.34; H,5.34%

IR (KBr) : 3440, 3350, 3280, 3240(NH); 2200(C≡N), 1665(C=O); 1650, 1620, 1600, 1575, 1495, 1470, 1460, 1445, 1410, 1350, 1305, 1185, 1150, 1055, 790, 755 cm$^{-1}$

UV (MeOH) : 204nm(log $\varepsilon$ 4.50), 222(4.30), 262sh(4.12), 305(4.2)
Reaction of ethyl 2-cyano-3-[(3-methylphenyl)amino]-3-(methylthio)acrylate with benzamidine

Ethyl 2-cyano-3-[(3-methylphenyl)amino]-3-(methylthio)acrylate (283) 5.5g (0.02 mol) was reacted with benzamidine, liberated from 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate by treatment with 0.8g (0.02 mol) of sodium hydroxide in 30ml ethanol, according to the procedure described for 454. The crude solid on recrystallization from benzene afforded 4.8g of colorless crystalline product, m.p. 166-168°C (d). The product was characterized as N-[2-carbethoxy-2-cyano-1-[(3-methylphenyl)amino]vinyl]-benzamidine (456).

Analysis : C_{20}H_{20}N_{4}O (348.39) Requires C, 68.95; H, 5.79%
            Found   C, 69.30; H, 5.85%

IR (KBr) : 3430, 3340, 3240(NH); 2200(C≡N); 1670(C=O),
           1650, 1620, 1575, 1410, 1370, 1365, 1300,
           1170, 1150, 1050, 780 cm\(^{-1}\)

UV (MeOH) : 205nm(log \(\epsilon\) 4.63), 225(4.37), 266sh(4.23),
            308(4.38)

NMR (CDCl\(_3\) + DMSO) : δ 1.32(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 2.27(s, 3H, Ar-CH\(_3\))
                         4.23(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 6.37(broad s, 2H, NH\(_2\) ),
                         7.06-7.8(m, 9H, Ar-H), 11.15(s, 1H, NH-Ar)

NMR (CDCl\(_3\) + DMSO + D\(_2\)O) : δ 1.32(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 2.27(s, 3H, Ar-CH\(_3\))
                               4.23(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 7.06-7.8(m, 9H, Ar-H)
Reaction of ethyl 2-cyano-3-[{4-methylphenyl}amino]-3-{methylthio}acrylate with benzamidine

Ethyl 2-cyano-3-[{4-methylphenyl}amino]-3-{methylthio}acrylate (289) 5.5g (0.02 mol) was reacted with benzamidine, liberated from 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate and 0.80g (0.02 mol) of sodium hydroxide in 30ml of ethanol according to the procedure described for 454. The crude product on recrystallization from benzene yielded 4.3g of colorless crystalline product, m.p. 188-190°C. The product was characterized as N-[(2-carbethoxy-2-cyano-1-[{4-methylphenyl}amino]vinyl)benzamidine (457).

Analysis : C_{20}H_{20}N_{4}O_{2} (348.39) Requires C, 68.95%; H, 5.79%

Found C, 69.07; H, 5.97%

IR (Nujol) : 3430, 3350, 3220 (NH); 2200 (C=N); 1660 (C=O); 1640, 1600, 1570, 1500, 1190, 1160, 1060, 830, 790, 770 cm

NMR (CDCl₃) : δ 1.33(t, 3H, CO₂CH₂CH₃), 2.29(s, 3H, Ar-CH₃), 4.24(q, 2H, CO₂CH₂CH₃), 7.09-7.70(m, 11H, NH₂ and Ar-H)
Reaction of ethyl 2-cyano-3-[(2-methoxyphenyl)amino]-3-(methylthio)acrylate with benzamidine

Ethyl 2-cyano-3-[(2-methoxyphenyl)amino]-3-(methylthio)acrylate (290) 5.85g (0.02 mol) was reacted with benzamidine, liberated from 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate by treatment with 0.8g (0.02 mol) of sodium hydroxide in 40ml of ethanol, according to the procedure described for 454. The crude solid on recrystallization from 1,2-dichloroethane yielded 5.1g of colorless crystalline product, m.p. 196-198°C(d). The product was characterized as N-[2-carbethoxy-2-cyano-1-[(2-methoxyphenyl)amino]vinyl]benzamidine (458).

Analysis

IR (KBr) : 3430, 3340, 3230(NH); 2200(C=EN); 1670(C=O); 1610, 1570, 1500, 1460, 1440, 1375, 1290, 1260, 1220, 1180, 1150, 1055, 1035, 785, 740 cm\(^{-1}\)

UV (MeOH) : 204nm(log \(\varepsilon\) 4.38), 227sh(4.21), 276sh(3.96), 288sh(3.98), 322(4.15)

NMR (CDCl\(_3\) + DMSO) : \(\delta\) 1.27(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 3.9(s, 3H, Ar-OCH\(_3\)), 4.18(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 6.7-7.9(m, 9H, NH\(_2\) and Ar-H), 11.33(s, 1H, NH-Ar)

NMR (CDCl\(_3\) + DMSO + D\(_2\)O) : \(\delta\) 1.3(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 3.9(s, 3H, Ar-OCH\(_3\)), 4.18(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 6.7-7.9(m, 9H, Ar-H)
Reaction of ethyl 3-[(4-chlorophenyl)amino]-2-cyano-3-(methylthio)acrylate with benzamidine

Ethyl 3-[(4-chlorophenyl)amino]-2-cyano-3-(methylthio)acrylate (292) 5.9g (0.02 mol) was reacted with benzamidine liberated from 3.85g (0.02 mol) of benzamidine hydrochloride dihydrate by treatment with 0.8g of sodium hydroxide in 40ml of ethanol according to the procedure described for 454. The crude solid on recrystallization from ethanol yielded 5.0g of colorless crystals, m.p. 223-225°C. The product was characterized as N-[2-carbethoxy-1-[(4-chlorophenyl)amino]-2-cyanovinyl]benzamidine (459).

Analysis: C_{19}H_{17}ClN_{4}O_{2} (368.82) Requires C, 61.87; H, 4.65%
Found C, 62.24; H, 4.40%

IR (KBr): 3420, 3340, 3230 (NH); 2200 (C=O); 1650, 1610, 1570, 1500, 1480, 1460, 1405, 1375, 1360, 1300, 1170, 1090, 1050, 830, 780 cm\(^{-1}\)

UV (MeOH): 204nm (log \(\varepsilon\) 4.66), 229(4.36), 268sh(4.27), 311(4.46)

NMR (CDCl\(_3\) + DMSO): \(\delta\) 1.3(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 4.2(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 7.3-7.9(m, 9H, Ar-H)

NMR (CDCl\(_3\) + DMSO + D\(_2\)O): \(\delta\) 1.3(t, 3H, CO\(_2\)CH\(_2\)CH\(_3\)), 4.2(q, 2H, CO\(_2\)CH\(_2\)CH\(_3\)), 7.3-7.9(m, 9H, Ar-H)
Reaction of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)-acrylate with morpholinocarboxamidine

To a solution of 0.46g of sodium in 30ml of absolute ethanol was added 3.55g (0.01 mol) of morpholinocarboxamidine sulfate and the mixture was heated at 70°C for 6 hours. Sodium sulfate separated was filtered, and to the filtrate was added, with stirring, 5.25g (0.02 mol) of ethyl 2-cyano-3-(methylthio)-3-(phenylamino)acrylate (285). The mixture was stirred at room temperature for 24 hours and cooled. The solid obtained was filtered, washed with cold ethanol and dried. Recrystallization from ethanol-chloroform yielded 2.75g of colorless crystals, m.p. 218-220°C(d). The product was identified as N-[2-carbethoxy-2-cyano-1-(phenylamino)-vinyl] morpholinocarboxamidine (460).

**Analysis**

- **C, H, N, O** (343.38) Requires C, 59.46; H, 6.16\%
  - Found C, 59.33; H, 6.51\%

**IR (KBr)**

- 3410, 3340, 3230 (NH); 2190 (C=O); 1665 (C=O); 1650, 1610, 1580, 1550, 1500, 1440, 1370, 1350, 1290, 1175, 1120, 780, 750 cm⁻¹

**UV (MeOH)**

- 210nm (log ε 4.41), 227sh(4.26), 302(4.42)

**NMR (CDCl₃ + DMSO)**

- δ 1.27(t, 3H, CO₂CH₂CH₃), 3.3-3.83(m, 8H, CH₂ of morpholino), 4.13(q, 2H, CO₂CH₂CH₃), 6.93(s, 2H, NH₂), 7.13-7.33(m, 5H, Ar-H), 10.9(s, 1H, NH-Ar)
NMR (CDCl₃ + DMSO + D₂O)

6 1.27(t, 3H, CO₂CH₂CH₃), 3.3-3.83(m, 8H, CH₂ of morpholino), 4.13(q, 2H, CO₂CH₂CH₃), 7.0-7.33(m, 5H, C₆H₅).

MS, m/e

343(M⁺), 313, 312, 298, 286, 270, 266, 257, 251, 240, 231, 223, 221, 211, 185, 169, 156, 144, 143, 142

Reaction of ethyl 2-cyano-3-[(2-methoxyphenyl)amino]-3-(methylthio)acrylate with morpholinocarboxamidine

Ethyl 2-cyano-3-[(2-methoxyphenyl)amino]-3-(methylthio)acrylate (290) 5.85g (0.02 mol) was reacted with morpholinocarboxamidine, liberated from 3.55g (0.01 mol) of morpholinocarboxamidine sulfate by treatment with a solution of 0.46g of sodium in 30ml of absolute ethanol according to the procedure described for 460. The crude product on recrystallization from ethanol-chloroform yielded 4.2g of colorless crystals, m.p. 225-227°C(d). The product was characterized as N-[2-carbethoxy-2-cyano-1-[(2-methoxyphenyl)amino]vinyl]morpholinocarboxamidine (461).

Analysis : C₁₈H₂₃N₅O₄ (373.40) Requires C, 57.89; H, 6.21%

Found C, 57.51; H, 6.09%
Cyclization of N-[2-carbethoxy-2-cyano-1-(methylamino)vinyl] benzamidine in the presence of sodium ethoxide.

To a solution of 1.35g (0.005 mol) of N-[2-carbethoxy-2-cyano-1-(methylamino)vinyl] benzamidine (451) in 20ml of absolute ethanol was added, with stirring, a solution of 0.12g of sodium in 10ml of absolute ethanol. The mixture was refluxed for 3 hours, cooled, poured into ice-water, and acidified with dilute hydrochloric acid (10% w/v). The solid obtained was filtered, washed with water and dried. Recrystallization from dimethylformamide-ethanol yielded
0.8g of colorless crystalline product, m.p. 350-352°C. The product was found identical (mp, IR) with 5-cyano-6-(methylamino)2-phenylpyrimidin-4(3H)-one (362).

Cyclization of N-\[2-carbethoxy-2-cyano-1-(phenylamino)vinyl\]-acetamidine in the presence of sodium ethoxide.

To a solution of 1.35g (0.005 mol) of N-\[2-carbethoxy-2-cyano-1-(phenylamino)vinyl\]acetamidine (453) in 20ml of ethanol was added a solution of 0.12g of sodium in 10ml of absolute ethanol. The reaction mixture was refluxed for 3 hours, cooled, poured into ice-water and acidified with dilute hydrochloric acid. The solid obtained was filtered, washed with water and dried. Recrystallization from dimethylformamide-ethanol yielded 0.7g of colorless crystalline product, m.p. 325-327°C. The product was identical (mp, IR) with the 5-cyano-2-methyl-6-(phenylamino)-pyrimidin-4(3H)-one (364).

Cyclization of N-\[2-carbethoxy-2-cyano-1-(phenylamino)vinyl\]-benzamidine in the presence of sodium ethoxide.

To a solution of 1.67g (0.005 mol) of N-\[2-carbethoxy-2-cyano-1-(phenylamino)vinyl\]benzamidine (454) in 20ml of absolute ethanol was added a solution of 0.12g of sodium in 10ml of absolute ethanol. The reaction mixture was
refluxed for 3 hours, cooled and poured into ice-water. The solid obtained on acidification with dilute hydrochloric acid (10% w/v) was filtered, washed with water and dried. Recrystallization from dimethylformamide-ethanol afforded 1.0g of colorless crystalline product, m.p. > 360°C, identical (IR) with 5-cyano-6-(phenylamino)-2-phenylpyrimidin-4(3H)-one (365).

**Cyclization of N-[2-carbethoxy-2-cyano-1-[4-methylphenyl]-amino]vinyl]benzamidine in the presence of sodium ethoxide.**

To a solution of 1.7g (0.005 mol) of N-[2-carbethoxy-2-cyano-1-[4-methylphenyl]amino]vinyl]benzamidine (457) in 20ml of absolute ethanol was added a solution of 0.12g of sodium in 10ml of absolute ethanol and the reaction mixture was treated according to the procedure described for the cyclization of vinylamidine 454 to the pyrimidin-4-one 365. The crude solid on recrystallization from dimethyl sulfoxide-ethanol yielded 1.0g of colorless crystalline product m.p. > 360°C. The product was found identical (IR) with 5-cyano-6-[(4-methylphenyl)amino]-2-phenylpyrimidin-4(3H)-one (367).
Cyclization of $N$-[(2-carbethoxy-1)-(4-chlorophenyl)amino]-2-cyanovinyl]benzamidine with sodium ethoxide.

To a solution of 1.9g (0.005 mol) of $N$-[(2-carbethoxy-1)-(4-chlorophenyl)amino]-2-cyanovinyl]benzamidine (459) in 20ml of ethanol was added a solution of 0.12g of sodium in 10ml of ethanol and the reaction mixture was treated according to the procedure described for the cyclization of vinylamidine 454 to the pyrimidin-4-one 365. The crude solid on recrystallization from dimethyl sulfoxide-ethanol yielded 1.15g of colorless crystalline product, m.p. > 350°C. The product was identical (IR) with $6$-[(4-chlorophenyl)amino]-5-cyano-2-phenylpyrimidin-4(3H)-one (370).

Cyclization of $N$-[(2-carbethoxy-2-cyano-1-)(phenylamino)vinyl]benzamidine in the presence of p-toluenesulfonic acid.

To a solution of 3.34g (0.01 mol) of $N$-[(2-carbethoxy-2-cyano-1)-(phenylamino)vinyl]benzamidine (454) in 60ml of benzene was added 1.9g (0.01 mol) of p-toluenesulfonic acid monhydrate and the mixture was refluxed for 8 hours. Benzene was removed by distillation under reduced pressure. The residue was triturated with 50ml of ice-water and basified with ammonium hydroxide solution (10% w/v). The solid obtained was filtered, washed with water and dried.
Recrystallization from ethanol afforded 1.8g of colorless crystalline product, m.p. 135-137°C. The product was characterised as 4-amino-5-carbethoxy-6-(phenylamino)-2-phenylpyrimidine (462).

Analysis : \[ \text{C}_{19}\text{H}_{18}\text{N}_{4}\text{O}_2 \] (334.37) Requires C, 68.25; H, 5.43%  
Found C, 68.48; H, 5.59%

IR (Nujol) : 3460, 3400, 3350(NH); 1670(C=O); 1600, 1520, 1270, 1190, 1120, 1090, 830, 800, 770 cm\textsuperscript{-1}

UV (MeOH) : 209nm(\epsilon 4.55), 237(4.32), 260(4.58), 267(4.59), 308(4.13)

MS, m/e : 334(M\textsuperscript{+}), 306, 288, 261, 185, 184, 169, 157  
144, 131, 118, 104

Cyclization of \[ \text{N-[2-carbethoxy-2-cyano-1-[(4-methylphenyl)amino]vinyl]benzamidine} \] in the presence of p-toluenesulfonic acid.

A mixture of 1.74g (0.005 mol) of \[ \text{N-[2-carbethoxy-2-cyano-1-[(4-methylphenyl)amino]vinyl]benzamidine} \] (457) and 0.95g (0.005 mol) of p-toluenesulfonic acid monohydrate in 30ml of benzene was refluxed for 8 hours and the reaction mixture was treated according to the procedure described for 462. The crude solid on recrystallization from ethanol yielded 0.95g of colorless crystalline product, m.p. 160-162°C. The product was characterised as 4-amino-5-carbethoxy-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (463).
Analysis : \( C_{20}H_{20}N_{4}O_{2} \) (348.39) Requires C, 68.95; H, 5.79%

Found C, 69.05; H, 5.99%

IR (Nujol) : 3460, 3420, 3360 (NH); 1650 (C=O), 1590, 1520, 1270, 1190, 1120, 830, 800 cm\(^{-1}\)

UV (MeOH) : 210nm (log \( \varepsilon \) 4.47), 236 (4.24), 261 (4.49), 269 (4.49), 310 (3.99)

MS, m/e : 348 (M\(^+\)), 319, 318, 302, 275, 274, 232, 199, 198, 183, 171, 170, 157, 156, 145, 132, 104

Cyclization of \( N-[2\text{-carbethoxy-1-[}(4\text{-chlorophenyl} )amino]-2\text{-cyanovinyl} ]\) benzamidine in the presence of p-toluenesulfonic acid.

A mixture of 1.85g (0.005 mol) of \( N-[2\text{-carbethoxy-1-[}(4\text{-chlorophenyl} )amino]-2\text{-cyanovinyl} ]\) benzamidine (459) and 0.95g (0.005 mol) of p-toluenesulfonic acid monohydrate in 30ml of benzene was refluxed for 8 hours and the reaction mixture was treated according to the procedure described for 462. The crude solid on recrystallization from ethanol afforded 1.1g of colorless crystalline product, m.p. 183-185°C. The product was characterised as 4-amino-5-carbethoxy-6-[\(4\text{-chlorophenyl} )amino]-2-phenylpyrimidine (464).

Analysis : \( C_{19}H_{17}ClN_{4}O_{2} \) (368.82) Requires C, 61.87; H, 4.65%

Found C, 62.18; H, 4.88%
IR (Nujol) : 3500, 3470, 3320 (NH); 1670 (C=O), 1610, 1520, 1270, 1150, 1100, 835, 825, 820, 800 cm⁻¹
UV (MeOH) : 212 nm (log ε 4.40), 240 sh (4.27), 261 (4.57), 270 (4.60), 308 (4.16)

Attempted cyclization of N-[2-carbethoxy-2-cyano-1-(phenyl-
amino)vinyl]acetamidine in the presence of p-toluenesulfonic acid.

To a solution of 2.7g (0.01 mol) of N-[2-carbethoxy-
2-cyano-1-(phenylamino)vinyl]acetamidine (453) in 50ml of benzene was added 1.75g (0.01 mol) of p-toluenesulfonic acid monohydrate and the mixture was refluxed for 4 hours. The reaction mixture was cooled and the solvent was removed under reduced pressure. To the residue was added 50ml of ice-water and the mixture was basified with dilute ammonium hydroxide solution (10% w/v). The solid obtained was filtered, washed with water and dried. Recrystallization from benzene yielded 1.5g of colorless crystalline solid m.p. 170-172°C. The product was characterized as ethyl 3-amino-2-cyano-3-(phenyl-
amino)acrylate (465).

Analysis : C₁₂H₁₃N₃O₂ (231.25) Requires C, 62.32; H, 5.67%
Found C, 62.47; H, 6.01%
IR (KBr) : 3460, 3310, 3220 (NH); 2200 (C=N); 1650 (C=O), 1570, 1500, 1450, 1400, 1370, 1300, 1190, 1120, 1060, 770, 720 cm\(^{-1}\)

MS, m/e : 231 (M\(^+\)), 214, 186, 169, 157, 142, 131, 119, 117, 104, 103, 93

Cyclization of N-[2-carbethoxy-2-cyano-1-(phenylamino)vinyl]-acetamidine in the presence of dry hydrogen chloride gas.

A stream of dry hydrogen chloride gas was passed through an ice-cold solution of 2.7g (0.01 mol) of N-[2-carbethoxy-2-cyano-1-(phenylamino)vinyl]acetamidine (453) in 25ml of dioxane for 6 hours. The reaction mixture was allowed to stand at room temperature for 12 hours and poured into ice-water. The solid obtained was filtered, triturated with saturated sodium bicarbonate solution, filtered, washed with water and dried. Recrystallization from n-hexane yielded 1.75g of colorless crystalline product, m.p. 77-79°C. The product was characterized as 5-carbethoxy-4-chloro-2-methyl-6-(phenylamino)pyrimidine (466).

Analysis : \( \text{C}_{14}\text{H}_{14}\text{ClN}_3\text{O}_2 \) (291.73) Requires C, 57.63; H, 4.84\%

\[
\begin{align*}
\text{Found} & \quad \text{C, 57.82; H, 5.02\%} \\
\end{align*}
\]

IR (Nujol) : 1660 (C=O); 1600, 1550, 1260, 1200, 1160, 1025, 950, 770 cm\(^{-1}\)

MS, m/e : 293, 291 (M\(^+\)), 262, 245, 217, 176, 169, 142, 131, 114
Cyclization of N-[2-carbethoxy-2-cyano-1-(phenylamino)vinyl]benzamidine in the presence of dry hydrogen chloride.

A stream of dry hydrogen chloride gas was passed into an ice-cold solution of 1.7g (0.005 mol) of N-[2-carbethoxy-2-cyano-1-(phenylamino)vinyl]benzamidine (454) in 30ml of dioxane for 5 hours. The mixture was allowed to stand at room temperature for 12 hours and poured into ice-water. The solid obtained was filtered, trituated with saturated sodium bicarbonate solution, filtered, washed with water and dried. Recrystallization from n-hexane yielded 0.9g of a pale yellow crystalline product, m.p. 132-134°C. The product was characterized as 5-carbethoxy-4-chloro-6-(phenylamino)-2-phenylpyrimidine (467).

Analysis: C_{19}H_{16}ClN_{3}O_{2} (353.80) Requires C, 64.50%; H, 4.56%
Found C, 64.97%; H, 4.78%

IR (KBr): 3230 (NH), 1675 (C=O), 1600, 1570, 1540, 1490, 1450, 1410, 1370, 1350, 1325, 1300, 1280, 1210, 1170, 1010, 980, 810, 785 cm^{-1}

UV (MeOH): 205nm (log ε 4.55), 280(4.57)

NMR (CDCl_{3}): δ 1.42 (t, 3H, CO_{2}CH_{2}CH_{3}), 4.46 (q, 2H, CO_{2}CH_{2}CH_{3}), 7.5 (m, 5H, Ar-H), 8.42 (s, 1H, C_{6}H_{5}NH)

MS, m/e: 355, 353 (M^+), 307, 279, 272, 244, 176, 169, 141, 114, 104, 103

A stream of dry hydrogen chloride gas was passed through an ice-cold solution of 1.75g (0.005 mol) of N-[2-carbethoxy-2-cyano-1-[(4-methylphenyl)amino]vinyl]benzamidine (457) in 30ml dioxane for 5 hours and the reaction mixture was treated according to the procedure described for 467. The crude solid on recrystallization from n-hexane yielded 0.9g of a pale yellow crystalline product, m.p. 116-118°C. The product was characterized as 5-carbethoxy-4-chloro-6-(4-methylphenyl)amino-2-phenylpyrimidine (468).

Analysis: $C_{20}H_{18}ClN_3O_2$ (367.83) Requires C, 65.30; H, 4.93%

Found C, 65.41; H, 5.21%

IR (Nujol): 3200(NH); 1670(C=O); 1600, 1540, 1225, 1190, 1090, 1025, 995, 870, 830, 790 cm$^{-1}$

UV (MeOH): $\lambda_{max}$ 205, 280 nm

MS, m/e: 369, 367(M$^+$), 321, 293, 286, 258, 190, 183, 155, 128, 103.

A stream of dry hydrogen chloride was passed through an ice-cold solution of 1.82g (0.005 mol) of N-[2-carbethoxy-2-cyano-1-(2-methoxyphenyl)amino]vinyl]benzamidine (458) in 30ml of dioxane for 5 hours and the reaction mixture was treated according to the procedure described for 467. The crude product on recrystallization from n-hexane yielded 1.0g of a yellow crystalline product, m.p. 117-119°C. The product was characterized as 5-carbethoxy-4-chloro-6-[2-methoxyphenylamino]-2-phenylpyrimidine (469).

Analysis: \[ \text{C}_{20}\text{H}_{18}\text{ClN}_3\text{O}_3 (383.83) \text{ Requires C, 62.58; H, 4.73\%} \]
Found \[ \text{C, 62.89; H, 4.97\%} \]

IR (Nujol): 3240(NH); 1680(C=O), 1600, 1570, 1550, 1280, 1260, 1210, 1110, 1080, 1020, 810, 790 cm\(^{-1}\)
Cyclization of N-[2-carbethoxy-1-[4-chlorophenyl]amino]-2-cyanovinyl]benzamidine in the presence of dry hydrogen chloride gas

A stream of dry hydrogen chloride gas was passed through an ice-cold solution of 1.85g (0.005 mol) of N-[2-carbethoxy-1-[4-chlorophenyl]amino]-2-cyanovinyl]benzamidine (459) in 30ml of dioxane for 5 hrs. and the reaction mixture was treated according to the procedure described for 467. The crude solid on recrystallization from n-hexane gave 1.0g of pale yellow crystalline product, m.p. 127-129°C, characterized as 5-carbethoxy-6-[4-chlorophenyl]amino]-4-chloro-2-phenylpyrimidine (470).

Analysis : C_{19}H_{15}Cl_{2}N_{3}O_{2} (388.25) Requires C, 58.77%; H, 3.89%
            Found   C, 58.50%; H, 4.07%

IR (Nujol) : 1670 (C=O), 1610, 1520, 1250, 1220, 1190, 1085, 995, 830, 820, 800 cm^{-1}

UV (MeOH) : \lambda_{max} 204, 281 nm

4-Chloro-5-cyano-6-ethoxy-2-methylpyrimidine (471).

To an ice-cold solution of 11.0g (0.15 mol) of dimethylformamide in 100ml of chloroform was added with stirring 15.3g (0.1 mol) of phosphorous oxychloride. The mixture was stirred for one hour at room temperature, cooled and treated portionwise with 6.3g (0.05 mol) of
4,6-dihydroxy-2-methylpyrimidine. The mixture was warmed at 50-55°C with stirring for 8 hours, cooled and filtered. The solid was washed with dry chloroform and dried. The dry solid was dissolved in 30ml of ice-cold water, filtered and the clear filtrate was allowed to stand for 12 hours at room temperature. Separated 4,6-dihydroxy-2-methylpyrimidine-5-carboxaldehyde was filtered, washed with water and dried, yield 6g (78%), m.p. 225-230°C (d), (230-240°C (d)).

The crude 4,6-dihydroxy-2-methylpyrimidine-5-carboxaldehyde 4.62g (0.03 mol) was added to a mixture of 4.17g (0.06 mol) of hydroxylamine hydrochloride and 4.92g (0.06 mol) of sodium acetate in 30ml of water. The mixture was stirred for 1 hour and heated at 70°C for 4 hours, and cooled. 4,6-Dihydroxy-2-methylpyrimidine-5-carboxaldoxime obtained was filtered, washed with water and dried, yield 4g (79%), m.p. > 360°C.

To a mixture of 3.4g (0.02 mol) of crude 4,6-dihydroxy-2-methylpyrimidine-5-carboxaldoxime, and 8.2g (0.06 mol) of N,N-dimethylaniline was added, with cooling, 9.2g (0.06 mol) of phosphorous oxychloride. The mixture was heated under reflux for one hour, cooled and poured into ice-water. The solid obtained was filtered, washed with
water and dried. The crude product was extracted with chloroform and the chloroform extract was concentrated under reduced pressure. The residue obtained was recrystallized from hexane to obtain 1.7g (45%) of pale yellow crystals of 4,6-dichloro-5-cyano-2-methylpyrimidine, m.p. 110-113°C (114-115°C). 305

To an ice-cold solution of 1.41g (7.5 mmol) of 4,6-dichloro-5-cyano-2-methylpyrimidine in 30ml of absolute ethanol was added with stirring a solution of 0.17g of sodium in 10ml of absolute ethanol. The reaction was refluxed for 4 hours, cooled and poured into ice-water. The solid obtained was filtered, washed with water and dried. Recrystallization of the crude solid from petroleum ether (60-80) yielded 0.7g (47%) of colorless crystalline product, m.p. 63-65°C (63.5-64°C). 305

\[ \text{IR (KBr)} : 2220(\text{C=\text{N}}); 1580, 1530, 1450, 1420, 1390, 1340, 1210, 1050, 1010, 920, 785 \text{ cm}^{-1} \]

\[ \text{NMR (CDCl}_3) : 6.1.47(\text{t, 3H, OCH}_2\text{CH}_3), 2.67(\text{s, 3H, CH}_3), 4.8(\text{q, 2H, OCH}_2\text{CH}_3) \]

\[ \text{MS, m/e} : 199, 197(M^+), 182, 169, 153, 141, 134, 124, 110, 93, 85 \]
Reaction of 3-amino-2-cyano-3-ethoxyacrylonitrile with acetyl chloride.

To a refluxing solution of 4.11g (0.03 mol) of 3-amino-2-cyano-3-ethoxyacrylonitrile in 100ml of acetone was added 250 ml of acetyl chloride. The mixture was refluxed for 2 hours and excess of acetone was removed by distillation under reduced pressure. The residue on recrystallization from petroleum ether (60-80) yielded 1.5g of colorless crystalline product, m.p. 63-65°C (69-70). The product was identical (mmp, TLC, IR, NMR and mass) with 4-chloro-5-cyano-6-ethoxy-2-methylpyrimidine (471).

4-Chloro-5-cyano-2-methyl-6-(methylthio)pyrimidine (472).

A mixture of 3.6g (0.02 mol) of 5-cyano-2-methyl-6-(methylthio)pyrimidin-4(3H)-one and 35ml of phosphorous oxychloride was refluxed for 8 hours. Excess of phosphorous oxychloride was removed by distillation under reduced pressure. The residue was neutralized with saturated sodium bicarbonate solution. The crude solid obtained was filtered, washed with water and dried. Recrystallization from n-hexane yielded 2.1g (53%) of pale yellow crystals m.p. 122-124°C.
Analysis: C$_7$H$_5$ClN$_3$S (199.67) Requires C, 42.11%; H, 3.03%
Found C, 41.37%; H, 3.30%

IR (KBr): 2220 (C=O); 1540, 1480, 1400, 1345, 1330, 1300 cm$^{-1}$

MS, m/e: 201, 199 (M$^+$), 198, 172, 164, 154, 152, 123, 111, 108, 91

Reaction of 3-amino-2-cyano-3-(methylthio)acrylonitrile with excess of acetyl chloride.

To a refluxing mixture of 2.8g (0.02 mol) of 3-amino-2-cyano-3-(methylthio)acrylonitrile in 100ml of dry acetone was added 25ml of acetyl chloride. The reaction mixture was refluxed for 4 hours and excess of acetone and acetyl chloride were removed by distillation under reduced pressure. The residue on recrystallization from n-hexane afforded 1.0g of colorless crystals m.p. 122-124°C. The product was identical (mmp, TLC, IR) with 4-chloro-5-cyano-2-methyl-6-(methylthio)pyrimidine (472).