IIA: POLARIZED KETENE S,N- AND N,N - ACETALS : A REVIEW

IIB: REACTION OF LITHIOAMINO ANIONS WITH POLARIZED KETENE S,S- ACETALS: AN IMPROVED AND A NEW GENERAL METHOD FOR THE SYNTHESIS OF POLARIZED KETENE S,N- AND N,N -ACETALS.

II A.1. INTRODUCTION

The polarized ketene S,N-1 and N,N-acetals 2 like oxoketene S,S-acetals, are well defined compounds which can be preserved without apparent decomposition. They can be considered as vinylogous amides if they are derived from ketones and as
vinyllogous amines if they are derived from other methylene compounds. The chemistry of enamines derived from various ketones and primary or secondary amines is well documented. They have been extensively used as synthetic intermediates to react with various electrophiles making use of α-carbon. However, these enaminones are found to be more sensitive to moisture and undergo ready hydrolytic cleavage to the starting materials. On the other hand, the ketene S,N- and N,N-acetals are more stable and exhibit properties identical to enamines. They can undergo nucleophilic displacement with various binucleophiles 3-6 (Scheme-1)\(^1,2,6\) followed by intra molecular cyclization with α-oxo functionality. Like enamines the α-carbon in the ketene S,N- and N,N-acetals is nucleophilic enough to react with various electrophilic species so that these reactions can be utilized to construct heterocycles of different structural features.

The behaviour of polarized ketene S,N and N,N-acetals as functionalized enaminones or enamines is manifested in the reaction of 1 and 2 with compounds having activated multiple bonds leading to the synthesis of a wide variety of heterocycles. Few of these transformation for the synthesis of pyrroles 9 via S,N-acetals 8 is shown in Scheme-2\(^7\). Another variation of this method for the synthesis of 2-amino pyrroles 12 starting with ketene S,S-acetals 10 condensed with various amines to give the pyrole via S,N-acetals 11 is also shown in Scheme-3\(^8\).

The doubly activated polarized ketene S,S-acetal 13 underwent smooth displacement reaction at room temperature with aziridine to yield the corresponding S,N-aziridino acetals 14 in excellent yields. These intermediates yielded the corresponding pyrrolines 15 through facile potassium iodide induced rearrangement. (Scheme-4)\(^9\).
Scheme-1

(Ref. 2-6)
Scheme 2

8

HCl/Ether
(0-5°)

[Ref.7]
$\text{ArCO} = \text{CN}$

$\text{MeS} - \text{SMe}$

$\text{R-NH}_2$

$\text{PhCOCI}$

$\text{C}_6\text{H}_5$

$\text{R} = \text{CH}_3, \text{C}_2\text{H}_5, \text{CH}_2\text{C}_6\text{H}_5$

$\text{Ref. 8}$

Scheme 3
Scheme - 4

13, 15, R = CN; R^1 = CONH₂
R = H, CN; R^1 = COOEt

16, 18, R = Ar, Me

(Ref. 9)
The method is extended to accompalish identical transformation to give novel spiro pyrrolines 18 under identical reaction conditions (Scheme-4)\textsuperscript{9}.

It is evident that polarized ketene S,N- and N,N-acetals, in addition to their reactivity as 1,3 electrophilic-3-carbon fragments, they differ from polarized ketene dithioaceta in their enamine reactivity profile providing C-C-N component in the product heterocycles. Based on this reactivity a number of reactions have been done in our laboratory for the synthesis of wide variety of amino and alkyl heterocycles 19-35 (Scheme 5 & 6)\textsuperscript{10-24}.

IIA.2. METHODS OF SYNTHESIS OF KETENE S,N- AND N,N-ACETALS

There are a number of methods described in the literature for the synthesis of ketene S,N- and N,N-acetals and they can be broadly classified in the following categories:

IIA.2.1 Direct method using isothiocyanates.

IIA.2.2 Displacement method.

IIA.2.3 Thioamide method.

IIA.2.4 Miscellaneous methods.

IIA.2.1.1 Direct Synthesis Using Alkyl And Aryl Isothiocyanates.

The reaction of active methylene compounds 36 with alkyl or aryl isothiocyanate in the presence of a base followed by alkylation to yield the ketene S,N-acetals is one of the efficient methods reported in the literature\textsuperscript{25-33}. Thus, when 36 was reacted in the presence of sodium hydride and dimethyl formamide, the sodium salt 37 separated, in situ, was alkylated with appropriate alkyl halides to yield the desired ketene S,N-
Scheme 6
acetals 38 in good to excellent yields (Scheme 7). The methods is particularly useful for the preparation of S,N-acetals exclusively.

IIA.2.1.2. Using thiocarbamoyl chlorides and C-aryl sulfonyl thioformamides:
Active methylene compounds 36 (Scheme 8) have been reacted in the presence of sodium hydride and DMF benzene mixture with thiocarbamoyl chlorides 39a\textsuperscript{34,35} or C-aryl sulfonylthio formamides 39b\textsuperscript{36a} to give the corresponding thiomides 40 which on subsequent alkylation gave S,N-acetals 41.

IIA.2.1.3. Using S-alkyl isothiureas and dithiocarbonic acid diester-imides:
Active methylene compounds 3 are also shown to react with S-methyl isothiureas 39'a-b (Scheme 8b)\textsuperscript{26,36b,36c} in neutral medium to give directly the corresponding ketene N,N-acetals 41'a and S,N-acetals 41'b in good yields.

IIA.2.2. Displacement Method
The ketene S,S-acetals are known to undergo facile displacement reaction with primary or secondary amines to give the corresponding S,N- and N,N-acetals depending upon the reaction conditions and the stoichiometry of the amine used. Thus, the ketene S,S-acetals 42 (Scheme 9)\textsuperscript{26,27,37-41} react with ammonia, primary or secondary (Scheme 7) aliphatic amines 43 and primary aromatic amines 45 in ethanol to give the corresponding ketene S,N-acetals 44 and N,N-acetals 46, or mixtures of S,N- and N,N-acetals. However, their reactivity with aromatic amines in boiling acetic acid is more selective. In most of the cases both S,N- 48 and N,N-acetals 47 are formed as mixtures and column chromatography is necessary to separate them (Scheme-10)\textsuperscript{42}. 
\[
\begin{align*}
X & \quad \text{+} \quad \text{Ph-} \quad \text{N= C=S} \quad \xrightarrow{\text{Base}} \quad \text{X} \quad \text{S} \quad \text{Na^+} \quad \xrightarrow{R- \text{hal}} \quad \text{X} \quad \text{S} \quad \text{R} \\
36 & \quad \xrightarrow{\text{DMF}} \quad 37 & \quad \xrightarrow{\text{NHPh}} \quad 38
\end{align*}
\]

\(X = \text{NO}_2; \ Y = \text{H}; \ R = \text{Me}\)

\(X = \text{NO}_2; \ Y = \text{PhCO}; \ R = \text{CH}_2\text{Ph}, \text{CH}_2\text{NO}_2, \text{CH}_2\text{COMe}, \text{CH}_2\text{COPh}\).

\(X = \text{CN}, \text{COOEt}, \text{CONH}_2, \text{Ph}; \ Y = \text{CN}; \ R = \text{CH}_2\text{CN}, \text{CH}_2\text{COOR}, \text{CH}_2\text{CONH}_2\).

\(X = \text{COOMe}; \ Y = \text{CN}, \text{COOMe}; \ R = \text{Me, allyl, crotyl}\).

\(X = \text{COOEt}; \ Y = \text{COOEt, COMe}; \ R = \text{Me, allyl, crotyl}\).

\(X = \text{COMe}, \ Y = \text{H, COMe}; \ R = \text{Me, allyl}\).

(Ref. 25–33)

\textit{Scheme-7}
\begin{align*}
\text{X} & \quad + \quad Z-C-N-R \\
\text{Y} & \quad \xrightarrow{\text{NaH, DMF-Benzene}} \quad \text{CH-S-N-R} \\
\text{36} & \quad \text{39a-b} \\
\text{39a}, Z = \text{Cl} \\
\text{39b}, Z = \text{SO}_2\text{Ar} \\
\begin{align*}
\text{X} & = \text{Y} = \text{CN}; R = \text{Me} \\
\text{b}, X = \text{Y} = \text{CN}; R = \text{Me} \\
\text{c}, X = \text{Y} = \text{CN}; Y = \text{Ph}; R = \text{Me} \\
\text{d}, X = \text{Y} = \text{CN}; R = \text{CH}_2\text{Ph}
\end{align*}
\end{align*}

\text{(Ref. 34-36)}

\text{Scheme - 8}
Scheme 8B
Scheme 9

42, 44, \( R^1 = \text{CN}; \ R^2 = \text{CN}, \ \text{CO}_2\text{Alk}; \ R^3 = \text{H}, \ R^4 = \text{alkyl, aryl} \).

\( R^1 = \text{MeCO}, \text{ArCO}; \ R^2 = \text{MeCO}, \text{ArCO}, \text{CN}, \text{SO}_2\text{Ar}; \ R^3 = \text{H}, \ R^4 = \text{alkyl, aryl} \).

42, 45, \( R^3 = R^4 = \text{morpholino, pyrrolidino, piperdino, aziridino} \).

\( R^1 = \text{ArCO, MeCO}; \ R^2 = \text{H} \).

(Ref. 26, 27, 37-42)
Scheme 10

\[
\text{R}_1\text{SMe} + \text{ArNH}_2 \xrightarrow{\text{AcOH/\Delta}} \text{R}_1\text{NHAr} + \text{R}_2\text{NHAr}
\]

47, 48  \( R_1 \) = substituted aryl, methyl
47, 48  \( R_2 \) = H, CN, CO\(_2\)Alkyl
47, 48  \( \text{Ar} \) = substituted aryl.

80%  20%
IIA.2.3. **Thioamide method**

The displacement method failed to yield S,N-acetals of piperidine or morpholines, which could also not be prepared by the direct method. But the thioamide 50 (Scheme 11) derived from the corresponding dithioester 49 and amine are reported to be alkylated to the corresponding ketene S,N-acetals 52 in good yields. Similarly, the formation of 54 from 53 is described

IIA.2.4. **New methods developed in the laboratory for the synthesis of ketene S,N- and N,N-acetals**

(a) **Thioamide method**

Recently Junjappa, Ila and co-workers reported a facile preparation of dithioesters 56 (Scheme 12) by reacting ketones with trithiocarbonate in excellent yields. The dithioester 56 thus prepared, underwent smooth condensation with morpholine 57 in boiling ethanol to give the corresponding thioamide 58 which was subsequently alkylated with methyl iodide in the presence of sodium hydride to give 59 in high yield.

(b) **Quaternisation method**

The displacement reaction as mentioned earlier when applied to less reactive a-oxoketene dithioacetal require more vigorous conditions and generally afford a mixture of S,N- and N,N- acetals. Therefore, an alternative method of preparation of ketene S,N-acetals by displacement method involves the reaction of dimethyl sulfonium salts derived from the respective dithioacetals. Thus, the dimethyl sulfonium perchlorate 61 on reaction with amines in the presence of anhydrous potassium carbonate in acetone afforded the corresponding ketene S,N-acetals 62-63 in moderate to high yields (Scheme 13).
Scheme-11

(Ref. 39, 43-46)
Scheme-12

Ref. 47
\[ \text{Scheme 13} \]

\[ R^1 = \text{C}_6\text{H}_6, 4\text{ClC}_6\text{H}_4, 4\text{MeOC}_6\text{H}_4, R^2 = \text{H} \]
\[ R^1 - R^2 = -(\text{CH}_2)_4- \]
\[ R^3 = \text{Me} \]

(Ref. 48, 49)
(c) Using Lithioamino anions

Attempts to prepare functionalized ketene S,N-acetals like 3- methylthio-3-(2-pyridylamino)-2-aryl-2-propene-1-ones 68 by using the methods reported earlier were unsuccessful. But recently we have developed a new method for the preparation of ketene S,N-acetals 66, 68, 70 by displacement method using the lithioamino anions 71, 73, 75 (Scheme 14). The preliminary study on these preparations and the scope of this new approach developed is discussed in detailed in part II of this chapter.
\[ \text{Scheme -14} \]

\[ \text{Ref. 56} \]
REFERENCES


REACTION OF LITHIOAMINO-ANIONS WITH $\alpha$-OXOKETENE DITHIOACETALS:

AN IMPROVED AND A NEW GENERAL METHOD FOR THE SYNTHESIS OF $\alpha$-OXOKETENE S,N- AND N,N- ACETALS.

IIB.1. In the preceding part of the chapter a brief literature survey on the methods of the preparation of S,N and N,N- acetals is described. Although the preparation of S,N- acetals by reacting enolate anions with isothiocyanates and the reaction of amines with dithioates followed by alkylation to give the corresponding S,N-acetals appears to constitute the good methods for the preparation of S,N-acetals, the preparation of isothiocynates from amino heterocycles is not very satisfactory. Since $\alpha$-oxoketene dithioacetals of wide structural diversity are available in large
quantities, it was considered of interest to examine the reaction of aromatic amines (aniline, 2-chloroaniline, 4-chloroaniline, 4-methyl aniline and 4-methoxy aniline) and amino-heterocycles (2-amino pyridine and 3-amino pyridine) with the α-oxoketene dithioacetals in the presence of n-butyl lithium.

The results of these investigations are described in this chapter. In an optimized reaction condition, the lithio-amino anion 2a was generated by deprotonation at amino group of aniline by n-butyllithium in dry tetrahydrofuran (THF) at 25°C under an efficient atmosphere of nitrogen. The α-oxoketene dithioacetal 1a was added as a THF solution over a period of 30 minutes. The reaction mixture, after work-up and purification, yielded the corresponding S,N-acetals (3a) as 3-Methylthio-3-(phenylamino)-1-phenyl-2-propen-1-one as bright yellow needles (CHCl₃-ether), m.p. 57°C. The structure of S,N-acetals 3a was fully established from its spectral and analytical data. The overall yield of 3a was 89% and the structure was further confirmed by comparing its properties with the authentic sample prepared by the other reported methods₁,² (mixed m.p. superimposable IR and NMR). Similarly, the α-oxoketene dithioacetals 1b-f were reacted with aniline in the presence of n-butyllithium (1 eqv) at 25°C to yield the corresponding α-oxoketene S,N-acetals 3b-f in 80-89% overall yields (Scheme-1).

Substituted anilines 2-chloroaniline, 4-chloro-aniline, 4-methyl aniline and 4-methoxy aniline also reacted with 1a in the presence of n-butyl lithium under the same reaction conditions to yield the corresponding S,N-acetals 3g-j in 80-83% overall yield (Scheme-1 and Table-1). The structure of the unreported S,N-acetal 3g was fully established on the basis of the spectral and analytical data which is given in the experimental section.
\[
\begin{align*}
\text{1a-f} & \quad \text{2a-e} \\
1a, R = \text{C}_6\text{H}_5, R^1 = \text{H} & \quad 2a, R^2 = \text{H} \\
b, R = \text{4-MeOC}_6\text{H}_4, R^1 = \text{H} & \quad b, R^2 = \text{2-Cl} \\
c, R = \text{4-ClC}_6\text{H}_4, R^1 = \text{H} & \quad c, R^2 = \text{4-Cl} \\
d, R = \text{4-BrC}_6\text{H}_4, R^1 = \text{H} & \quad d, R^2 = \text{4-Me} \\
e, R = R^1 = \text{4-Cl} & \quad e, R^2 = \text{4-MeO} \\
f, R = R^1 = \text{4-Br} & \quad f, R = R^1 = \text{4-MeO} \\
g, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{2-Cl} & \\
h, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-Cl} & \\
i, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-Me} & \\
j, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-MeO} & \\
\end{align*}
\]

\[
\begin{align*}
\text{3a-j} \\
3a, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{H} \\
b, R = \text{4-MeOC}_6\text{H}_4, R^1 = \text{H}, R^2 = \text{H} \\
c, R = \text{4-ClC}_6\text{H}_4, R^1 = \text{H}, R^2 = \text{H} \\
d, R = \text{4-BrC}_6\text{H}_4, R^1 = \text{H}, R^2 = \text{H} \\
e, R = R^1 = \text{4-Cl} & \quad e, R^2 = \text{4-Me} \\
f, R = R^1 = \text{4-Br} & \quad f, R = R^1 = \text{4-MeO} \\
g, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{2-Cl} & \\
h, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-Cl} & \\
i, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-Me} & \\
j, R = \text{C}_6\text{H}_5, R^1 = \text{H}, R^2 = \text{4-MeO} & \\
\end{align*}
\]

Scheme-1

(See Table-1)
Table 1

Polarised Ketene $S, N$-acetals prepared by direct displacement using metallated amines.

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Product 3</th>
<th>$R$</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>a</td>
<td>$C_6H_5$</td>
<td>H</td>
<td>H</td>
<td>89</td>
</tr>
<tr>
<td>2.</td>
<td>b</td>
<td>4-MeOC$_6H_4$</td>
<td>H</td>
<td>H</td>
<td>90</td>
</tr>
<tr>
<td>3.</td>
<td>c</td>
<td>4-ClC$_6H_4$</td>
<td>H</td>
<td>H</td>
<td>85</td>
</tr>
<tr>
<td>4.</td>
<td>d</td>
<td>4-BrC$_6H_4$</td>
<td>H</td>
<td>H</td>
<td>80</td>
</tr>
<tr>
<td>5.</td>
<td>e</td>
<td>$\text{[Structure]}$</td>
<td>H</td>
<td>H</td>
<td>80</td>
</tr>
<tr>
<td>6.</td>
<td>f</td>
<td>$\text{[Structure]}$</td>
<td>H</td>
<td>H</td>
<td>80</td>
</tr>
<tr>
<td>7.</td>
<td>g</td>
<td>$C_6H_5$</td>
<td>H</td>
<td>2-ClC$_6H_4$</td>
<td>82</td>
</tr>
<tr>
<td>8.</td>
<td>h</td>
<td>$C_6H_5$</td>
<td>H</td>
<td>4-MeC$_6H_4$</td>
<td>80</td>
</tr>
<tr>
<td>9.</td>
<td>i</td>
<td>$C_6H_5$</td>
<td>H</td>
<td>4-MeC$_6H_4$</td>
<td>82</td>
</tr>
<tr>
<td>10.</td>
<td>j</td>
<td>$C_6H_4$</td>
<td>H</td>
<td>4-MeOC$_6H_4$</td>
<td>85</td>
</tr>
</tbody>
</table>

3a-f, 3h-j reported earlier
Interestingly, when 1a was reacted under similar reaction conditions with 2- lithio- aminopyridine 4, the corresponding 3- methylthio-3- (2- pyridyl amino)-1- phenyl-2 propene 1-one 5a was obtained in 92% yield. The S,N acetal 5a was not reported in the literature and its structure was established on the basis of analytical and spectral data. The compound was analysed for the molecular formula C₁₅H₁₄N₂O₂S with a molecular weight 270.1.

It's IR (KBr) spectrum showed bands for γNH associated with intra molecular hydrogen bonding with carbonyl oxygen at 3351 cm⁻¹. The very low frequency carbonyl stretching at 1588 cm⁻¹ was attributed to the enamino form. (See Scheme-6). The other absorption at 1537 (c= N), 1244 cm⁻¹ were also noted. The structure of 5a was further confirmed by its ¹H NMR (CDCl₃) spectrum (Fig.1). The singlet at ppm 2.37 was assigned to the three SMe protons. The vinylic proton appeared as a singlet at (15.93. The signal due to -NH proton associated with intramolecular hydrogen with carbonyl oxygen appeared at δ14.64. The aromatic protons appeared at δ7.38-7.42 (m,3H, ArH), 7.86-7.89 (m,1H, ArH) and the 4-pyridyl protons show clearly ABMX system at δ6.85 (m,1H, 5-H) 6.93 (d,1H,3H), 7.53 (ddd,1H,4-H) and 8.27 (ddt,1H,6-H) with the coupling constants, J₃₄=8.7, J₄₅=0.3 J =6.0, J₅₆ = 0.01 3.4 4.6 5,6 3,5Hz. ¹³CNMR spectrum of compound 5a was also in conformity with the assigned structure (Fig.2). ¹³CNMR (75.5MHz, CDCl₃) δppm.15.9(SCH₃), 90.63 (=CH), 113.6, 118.0 (C=5 and C-3 of pyridyl), 127.0, 128.5. 131.4 (C-2,C-3 & C-4 of Ar), 137.6 (C-4pyridyl 139.8 (C-1 Ar), 146.6 (C-6 pyridyl), 151.2, 185.67 for carbonyl carbon.

Similarly, 2-lithio aminopyridine was reacted with various α-oxoketene dithioacetals 1b-j under the described reaction conditions to yield the corresponding S,N- acetals 5b-j in 80-93% overall yield (Scheme-2). The structure of all these compounds were
Scheme 2

1, 5, a, R = C₆H₅, R¹ = H
b, R = 4- MeOC₆H₄, R¹ = H
c, R = 4- Cl C₆H₄, R¹ = H
d, R = 4- MeC₆H₄, R¹ = H
e, R = 2- furyl, R¹ = H
f, R = 2- thienyl, R¹ = H
g, R = R¹ = -(CH₂)₄-
h, R = R¹ = [Ring]
i, R = R¹ = [Ring]
j, R = C₆H₅ -CH=CH, R¹ = H
fully established by their analytical and spectral data which are described in the experimental section.

Under similar reaction conditions, 3- lithio- amino pyridine 6 also reacted with α-oxoketene dithioacetals 1a-e to yield the corresponding S,N-acetals 7a-e in 60-70% over all yields. (Scheme -3). The structures of 7a-e were fully established by their analytical and spectral data and were in agreement with the assignment (see in experimental section).

It is interesting to note that when 2- equimolar quantity of 2- lithioamino pyridine was reacted with 1- equimolar quantity of 1a and refluxed for three hours yielded the corresponding N,N-acetals 8a in 79% yield. (Scheme-4). Similarly 8b was also obtained in 80% yield. The analytical and spectral data of both 8a and 8b are described in experimental section.

Also, in a typical experiment, S,N-acetal 5a was refluxed in methanol in the presence of sodium methoxide (1eqv), the corresponding S,N-acetal 10a was formed in 61% yield.(Scheme-5). This reaction is unusual since such displacement of methylthio group of S,N-acetals is not reported in earlier literature. In all the S,N-acetals described in Scheme -1 did not undergo such displacement reactions even on prolonged heating of methanol under identical conditions.

However, the 2- amino pyridine moiety because of the electron deficient character of the pyridine ring makes C-4 more electrophilic thus facilitating the displacement of methylthio group by methoxy group.
Scheme-3

1,6,7, a, R = C₆H₅, R¹ = H
b, R = 4-MeOC₆H₄, R¹ = H
c, R = 4-MeC₆H₄, R¹ = H
d, R = H₅C₂O⁻, R¹ = CN
e, R = 2-furyl, R¹ = H
Scheme-4

1, 8, a, R^1 = C_6H_5, R^2 = H

b, R^1 = 4-MeOC_6H_4, R^2 = H
Scheme 5
The O,N- acetal **10a** was also alternatively prepared in 81% yield by reacting O,S-acetals **9a** with 2-lithio amino pyridine (Scheme-5) (The required O,S-acetals **9a-b** were prepared by earlier reported method). Similarly the O,S-acetals **9b** was reacted with 2 lithio-amino pyridine to yield the corresponding O,N-acetal **10b** in 81% yield. The analytical and spectral data of both **10a** and **10b** are described in experimental section.
IIB.2. SPECTRAL STUDIES AND CONFIGURATIONAL ASSIGNMENTS.

All the S,N- acetals formed 3a-j, 5a-j and 7a-e displayed the formation of only one stereoisomer which was evident from their sharp melting points. The chemical shift values of SMe and vinylic protons appeared as sharp singlets in all the cases indicating the purity of their geometrical isomerism. The geometry of the S,N-acetals thus formed, was assigned E- configuration on the basis of IR and NMR data.

Polarized keten- S,N- acetals are known to exist in tautomeric equilibrium between enamino A and imino form B (Scheme-6) which can be easily distinguished with the help of IR and NMR spectroscopy. The spectral studies on α- oxoketene S,N-acetals 3a-j (Scheme-1), 5a-j (Scheme-2) and 7a-e (Scheme-3) prepared for the present investigation, indicated that all of them exist in the enamino form A which supports the E- configuration. The IR spectrum strongly indicate the hydrogen bonded NH stretching, vibration at 3330-3350cm\(^{-1}\) suggesting its position with the intramolecularly associated hydrogen. The carbonyl stretching vibration in these compounds was merged with bands around and below 1600 cm\(^{-1}\) reflecting characteristic conjugation effect of the amino group and strong intramolecular hydrogen bonding. In \(^1\)HNMR spectrum, the downfield shift of the - NH proton signal at δ13-15 ppm was attributed to its intramolecular hydrogen bonding. It is interesting to note that all the S,N- acetals were found to be exclusively in E- configuration and the corresponding isomers were not formed in any of the experiments.

Apparently it appears that the strong intramolecular hydrogen bonding directs the overall configuration of the S,N-acetals (Scheme-6).
All E-configuration

Scheme 6
IIB.3. CONCLUSION

A new efficient method for the synthesis of various S,N-acetals involving α-oxoketene dithioacetals and lithio-amino anions has been developed. The examples, examined in these studies demonstrate that the method is very versatile since the reaction conditions are mild and the displacement is highly stereoselective (E- configuration). The hitherto unreported S,N- acetals derived from amino pyridines could also be prepared by this method in improved yields. The S,N- acetals derived from 2- amino pyridines 5a-j displayed characteristic properties undergoing easy displacement of the methylthio group by alkoxy group while others do not undergo these displacement reactions under similar reaction conditions.
II B.4. EXPERIMENTAL SECTION

Melting points were determined on a “Thomas-Hoover” capillary melting point apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 297 and Perkin-Elemer 983 spectrometers. $^1$H NMR (90 MHz) were recorded on Varian EM-390 high resolution $^1$H NMR (300 MHz) and $^{13}$C NMR (75.5 MHz) spectra were recorded on Brucker ACF 300 spectrometer. The chemical shifts (δ ppm) and the coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethyl silane or DMSO-d$_6$ in $^{13}$C NMR. The following abbreviations are used to describe peak patterns when appropriate : br=broad, s=singlet, d=doublet, d=double doublet, dt = double triplet, t=triplet, q=quartet, m=multiplet. Mass measurements were carried out with Jeol JMS D-300 spectrometer. Masses (MS) are reported in unit of mass over charge (m/z), the molecular or base peaks and relative intensities are indicated by (M) and (%) respectively. Elemental analysis were performed on a Heracus CHN-O-Rapid Analyzer. Dry benzene was obtained by washing with concentrated sulphuric acid followed by azeotropic distillation and stored over sodium wire. Dry ether was obtained by keeping over calcium chloride (fused) and stored over sodium wire. Lithium Ingot (Aldrich) were cut into smaller pieces and washed with dry ether twice before use. n-Butyl lithium was prepared according to the reported procedure.

Starting materials:

Commercially available ketones p-methoxybenzaldehyde acetophenone, 4-chloroacetophenone, 4-methoxy acetophenone, acetone, cyclohexanone and cycloheptanone were purified either by simple distillation/distillation under reduced pressure or crystallization before use. 2-Acetyl furan & 6 methoxy tetralone
was purchased from Aldrich and used as such 1-tetralone bp 140°-150°C (10 mm), 2-acetyl thiophene bp 214°C, were prepared according to the earlier reported procedures. Aniline, O-chloroaniline, p-chloroaniline were distilled prior to use. p-Toludine, p-anisidine and p-bromoaniline, 2-aminopyridine, 3-aminopyridine were recrystallised before use. α-Oxoketene S,S-acetals required for the present investigation were prepared according to the earlier reported literature procedures which are given below.

General procedure for the preparation of oxoketene dithioacetal (1a-f of Scheme-1, 1a-i of Scheme-2, 1a-e of Scheme-3) using sodium tert.butoxide. A mixture of ketone (0.2 mol) and carbon disulphide (0.2 mol) was added dropwise to an ice-cold and well stirred suspension of sodium t-butoxide (0.4 mol) in dry benzene (200 ml) and the reaction mixture was allowed to stir at room temperature for 5-6 hours. Acid free dimethyl sulphate (0.2 mol) was then gradually added with stirring and cooling and the reaction mixture was allowed to stir at room temperature for 6-10 hours. The reaction mixture was poured over aqueous saturated ammonium chloride solution (250 ml) and the layers were separated. The aqueous layer was extracted with benzene (100 ml) and combined benzene extracts were washed with water (4×250 ml), dried (Na₂SO₄) and evaporated. Trituration of the oil residue with hexane gave the dithioacetals as yellow crystalline solid in good yields. Liquid dithioacetals were purified by passing through silica gel column using hexane-ethylacetate (9:1 to 8:2) as eluent. All the known dithioacetals were characterized by comparison of their melting points, NMR, IR spectra with those of reported data and of authentic sample.
Condensation of -acylketene dithioacetals with aldehydes: General procedure for the preparation of 5-aryl, 1-bis(methylthio) 1,4-pentadiene-3-ones (1j Scheme-2). To a cooled and stirred solution of sodium ethoxide in ethanol, prepared by dissolving sodium (0.06 mol) in ethanol (30 ml), a solution of the -acylketene dithioacetal (0.03 mol) and aldehyde (0.03 mol) in minimum ethanol was added dropwise over a period of 5 minutes. The reaction mixture was brought to room temperature over a period of 20 minutes and further stirred at room temperature for 4-5 hr. The mixture was diluted with cold water (100 ml) and solid separates out was filtered, washed with water (4x50 ml) and dried.

General procedure for the generation and reaction of 1-lithioamino benzenes and substituted 1-lithioamino benzenes with α-oxoketene dithioacetal: preparation of S,N-acetals (3a-j). To a stirred solution of 1-aminobenzene (aniline) or substituted aniline (10 mmol) in dry THF (20 ml) n-butyllithium was added under dry and inert atmosphere, over 20 minutes at room temp. (25°C). The reaction mixture was stirred for 30 minutes at the same temp. The lithiation was indicated by the appearance of reddish brown colour. A solution of oxoketene S,S-acetal (10 mmol) in dry THF (25 ml) was added. The contents were stirred at room temperature for 5-6 hours. In case of S,N-acetals (3é-g), after addition of oxoketene S,S-acetals the reaction mixture was refluxed with stirring at 60°C for 2-3 hours to complete the reaction. Then it was brought to room temperature, worked up by pouring into saturated aqueous NH₄Cl solution (100 ml), extracted with chloroform (2x50 ml) and the combined extracts were washed with water (2x50 ml), dried (Na₂SO₄) and evaporated to give the crude product, which was purified by crystallization from chloroform-hexane mixture or by passing through column of silica gel using...
ethylacetate - hexane (1:9) as eluent (3e-g). Analytical and spectral data of the hitherto unreported S, N-acetal 3h is given below:

3-Methylthio-3-(2-chlorophenylamino)-1-phenyl-2-propen-1-one (3h) was isolated as light yellow crystals (chloroform-hexane) m.p. 110°C; yield 2.50g (82%). $\nu_{\text{max}}$ (KBr) : 3320 (NH), 1603, 1592, 1240 cm$^{-1}$. $\delta_H$ (300 MHz, CDCl$_3$): 2.38 (s, 3H, SCH$_3$), 5.93 (s, 1H, vinylic), 7.15 [(ddd, 1H, $J = 17$Hz (J3,4+ J4,5+ J4,6)], 7.23 [(ddd, 1H, $J = 16.5$ Hz (J4,8+J5,6 +J 3,5), H-5], 7.39-7.45 (m, 4H, H-6 & ArH, 7.50 (m, 2H, ArH), 7.92 (dd, 1H, $J = 9.6$ Hz, H-3), 13.4769 (s, 1H, NH, exchanges D$_2$O). $\delta_C$ (75.5 MHz, CDCl$_3$) : 14.77 (SCH$_3$), 89.69 (=CH), 126.90 (C-6 anil), 127.1 (C-2'Ar), 127.46, 128.29 (C-3'Ar), 129.7 (C-4Am) 130.0 (C-5anil), 131.07 (C-3aniline) 135-77 (C-2 aniline) 139.80 (C-1'Ar), 167-06 (=C), 186.30 (C=O). Anal. Calcd. for C$_{16}$H$_{14}$Cl NOS (303.5), C 63.26, H 4.6, N 4.6. Found. C 63.37, H 4.5, N 4.80.

Generation of 2-lithio-amino pyridine and its reaction with $\alpha$-oxoketene dithioacetal: General procedure for the preparation of ketene S,N-acetals 5a-j. To a stirred solution of 2-aminopyridine (0.94g, 10 mmol) in anhydrous tetrahydrofuran (THF) (20 ml), n-butyllithium (15 mmol) was added with stirring and maintaining the temperature at 0°C. The lithiation was indicated by the appearance of reddish brown colour. The reaction mixture was stirred at the same temperature for 30 minutes. A solution of oxoketene dithioacetal (10 mmol) in dry THF (25 ml) was added and stirred for 30-45 minutes (0°C) and then allowed to warm to room temperature. The reaction mixture was further stirred at the same temperature for one hour, worked up by pouring into saturated aqueous NH$_4$Cl solution 50ml) extracted with chloroform (2x50 ml) and the combined extracts were washed with water (2x50 ml), dried (Na$_2$SO$_4$) and evaporated to give the crude product, which
was purified by crystallization from chloroform/hexane mixture or by passing through silica gel column using ethylacetate-hexane (1:9) as eluent (5g-j). The structures (5a-j) were fully established from their spectral and analytical data which are given below:

3-Methylthio-3-(2-pyridyl amine)-1-phenyl-2-propene-1-one (5a) was isolated as light yellow crystals (chloroform-hexane), yield 12.50g (92%), m.p. 90°C. \( \nu_{\text{max}} \) (KBr) \( \delta_{\text{H}} \) (300 MHz, CDCl\(_3\)):\ 2.37 (s, 3H, SCH\(_3\)), 5.93 (s, 1H, vinylic), 6.85 (m, 1H, 5-H pyridyl), 6.93 (d, 1H, \( J = 9 \) Hz, 3-H pyridyl), 7.38-7.42 (m, 3H, ArH), 7.53 (ddd, 1H, \( J=15.6 \) Hz, 4-H pyridyl), \( 7.86-7.89 \) (m, 2H, ArH), 8.27 (dt, 1H, \( J = 6.6 \) Hz), 6-H pyridyl), 14.64 (s, 1H, NH, exchanges D\(_2\)O). [3-H, 5-H, 4-H and 6-H pyridyl = ABMX system; from first order analysis, \( J_{3,4} = 8.7, J_{4,6} = 0.3, J_{5,6} = 6.0, J_{3,5} = 0.01 \) Hz] \( \delta_{C} \) (75.5 MHz, CDCl\(_3\))=15.9 (SCH\(_3\)), 90.63 (=CH), 113.6, 118.0 (C-5 and C-3 of pyridyl), 127.0, 128.5, 131.4 (C-2', C-3' & C-4' of Ar), 137.6 (C-4 pyridyl), 139.8 (C-1'Ar), 146.6 (C-6 pyridyl), 152.2 (=C), 165.8 (=C), and 185.67 (C=O).


3-Methylthio-(2-pyridylamino)-1-(4-methoxypnveyl)-2-propene-1-one (5b) was isolated as yellow crystals, yield 2.80g (93%), m.p. 105°C. \( \nu_{\text{max}} \) (KBr) \( \delta_{\text{C}} \) (300 MHz, CDCl\(_3\)) : 6.91 (d, 2H, \( J = 9 \) Hz, ArH), 6.93-6.98 (m, 2H, 6-H & 3-H pyridyl), 7.59 (ddd, 1H, \( J_{4,5}, J_{4,6}, J_{4,3} = 17.3 \) Hz, 4-H pyridyl) \( 7.88-7.91 \) (d, 2H, \( J = 9 \) Hz, ArH), 8.32 (dt, 1H, 6-H pyridyl), 14.56 (s, 1H, NH, exchanges D\(_2\)O). \(^{13}\)CNMR (75.5 MHz, CDCl\(_3\)) : 16.10 (SCH\(_3\)), 55.3 (OCH\(_3\)), 90.5 (=CH), 113.61 (C-2' of Ar), 113.84, 118.13
(C-5 and C-3 pyridyl), 129.08 (C-3' of Ar), 132.46 (C-1' of Ar), 137.96, 146.81 (C-4 & C-6 pyridyl) 152.50 (=C), 162.19 (C-9' Ar), 165.13 (=C) and 185.25 (C=O). Anal. Calcd. for C_{16}H_{16}N_{2}O_{2}S (300.1) C 63.97, H 5.33, N 9.33. Found: C 63.95, H 5.29, N 9.50.

3-Methylthio-3-(2-pyridyl amino)-1-(4-chlorophenyl)-2-propene-1-one (5c) was isolated as bright yellow crystals (chloroform-hexane) m.p. = 116°C, yield 2.75g (90%). \( \nu_{\text{max}} \) (KBr): 3498, 3347(NH), 1579, 1538, 1248 cm\(^{-1}\). \( \delta_{11} \) (90 MHz, CDCl\(_3\)) : 2.38 (s, 3H, SCH\(_3\)), 5.91 (s, 1H, vinylic), 6.91-7.10 (m, 2H, 5-H & 3-H pyridyl), 7.49 (d, 2H, J = 9Hz, ArH), 7.59 (ddd, 1H, J\(_{4,5}\) J\(_{4,6}\) J\(_{4,3}\) = 17.5 Hz, 4-H pyridyl) 8.00 (d, 2H, J = 9Hz, ArH), 8.32 (dt, 1H, J = 6.9 Hz, 6-H pyridyl), 14.60 (s, 1H, NH). \( \delta_{c} \) (75 MHz, CDCl\(_3\)) : 16.1 (SCH\(_3\)), 114.01, 118.5 (C-5, C-3 pyridyl), 128.5, 128.59, 137.28 (C-2', C-3' and C-1' of Ar), 138.03 (C-4 pyridyl), 138.35 (C-4' Ar), 146.0 (C-6 pyridyl), 152.2 (=C), 166.58 (= C), 184.52 (C=O). Anal. Calcd. for C\(_{15}\)H\(_{13}\)N\(_{2}\)O\(_{2}\)Cl (304.6), C 59.06, H 4.2, N 9.12. Found : C 59.13, H 4.1, N 9.10.

3-Methylthio-3-(2-pyridyl amino)-1-(4-methylphenyl)-2-propene-1-one (5d) was isolated as yellow solid (chloroform-hexane) m.p. 110°C yield 2.56g (90%). \( \nu_{\text{max}} \) (KBr) : 3487, 3320 (NH), 1748, 1522, 14556, 1250 cm\(^{-1}\). \( \delta_{11} \) (90 MHz, CDCl\(_3\)) : 2.58 (s, 3H, CH\(_3\)), 2.60 (s, 3H, SCH\(_3\)), 5.99 (s, 1H, vinylic), 7.15 (m, 1H, 5-H pyridyl), 7.25 (d, 1H, J = 9Hz, 3-H pyridyl), 7.45 (d, 2H, J = 8.9 Hz, ArH), 7.75 (ddd, 1H, J = 17.3 Hz (J\(_{4,5}\) J\(_{4,6}\) J\(_{4,3}\)), 4-H pyridyl) 8.05 (d, 2H, J = 8.9 Hz, ArH), 8.51 (dt, 1H, J = 6.9 Hz, H-6 pyridyl), 14.95 (s, 1H, NH, exchanges D\(_2\)O). Anal. Calcd. for C\(_{16}\)H\(_{16}\)N\(_{2}\)O\(_{2}\)Cl (284.1) C 67.60, H 5.6, H 5.7, N 9.75.

3-Methylthio-3-(2-pyridylamino)-1-(2-furyl)-2-propene-1-one 5e was isolated as yellow crystals (EtOAc - hexane); m.p. 120°C, yield 2.30g (88%). \( \nu_{\text{max}} \) (KBr) : 3460, 3247 (NH), 1678, 1599, 1230 cm\(^{-1}\). \( \delta_{11} \) (300 MHz, CDCl\(_3\) d (ppm) : 2.40 (s, 3H, SCH\(_3\)),
5.92 (s, 1H, vinylic), 6.51 (dd, 1H, H-4' furyl, J = 4.5 Hz), 6.82 (m, 1H, H-5 pyridyl), 6.88 (d, 1H, J = 9 Hz, H-3 pyridyl), 7.10 (d, 1H, J = 4.5 Hz, H-3' furyl), 7.48 (d, 1H, J = 3 Hz, H-5' furyl), 7.00 (ddd, 1H, J = 16.6 Hz, H-4 pyridyl), 8.30 (dt, 1H, J = 6.9 Hz, H-6 pyridyl), 14.80 (s, 1H, NH). Anal. Calcd. for C_{13}H_{12}N_{2}O_{2}S (260.1), C 59.99, H 4.6, N 10.76. Found: C 59.8, H 4.70, N 10.71.

3-Methylthio-3-(2-pyridylamino)-1-(2-thienyl)-2-propene-1-one 5f was isolated as light yellow solid (EtOAc-hexane) m.p. 109°C, yield 2.17g (89%). ν\text{max} (KBr) : 3386, 3343 (NH), 175, 1591, 1281 cm\textsuperscript{-1}. δ\textsubscript{11} (300 MHz, CDCl\textsubscript{3}) : 2.51 (s, 3H, SCH\textsubscript{3}), 5.91 (s, 1H, vinylic), 6.98 (m, 1H, H-5 pyridyl), 7.14 (dd, 1H, J = 8 Hz, H-4' thienyl), 7.25 (d, 1H, J = 8.9 Hz, H-3 pyridyl), 7.60 (d, 1H, J = 4.5 Hz, H-3' thienyl), 7.75 (d, 1H, J = 6.0 Hz, H-5' thienyl), 7.80 (ddd, 1H, J = 16.5 Hz, H-4 pyridyl), 8.50 (dt, 1H, J = 6.9 Hz, H-6 pyridyl). Anal. Calcd. for C\textsubscript{13}H\textsubscript{12}N\textsubscript{2}O\textsubscript{2}S (276); C 56.52, H 4.3, N 10.4. Found: C 56.50, H 4.2, N 10.21.

2-Methylthio-2-(2-pyridylamino)methylene cyclohexanone 5g was isolated as viscous oil, yield 1.50g (60.4%). ν\text{max} (CCl\textsubscript{4}) : 3460, 3335 (NH), 1661, 1628, 1521 cm\textsuperscript{-1}. δ\textsubscript{11}(90 MHz, CCl\textsubscript{4}); d ppm : 1.86-2.03 (m, 4H, 2xCH), 2.30 (s, 3H, SCH\textsubscript{3}), 3.12-3.24 (m, 4H, 2xCH\textsubscript{2}), 7.03 (m, 1H, H-5 pyridyl), 7.42-7.48 (m, 2H, H-3 & H-4 pyridyl), 9.08 (d, 1H, J = 9 Hz, H-6 pyridyl), 14.00 (brs, 1H, NH, exchanges D\textsubscript{2}O). Anal. Calcd. for C\textsubscript{13}H\textsubscript{16}N\textsubscript{2}O\textsubscript{2}S (248); C 62.9, H 6.4, N 11.2. Found C 62.7, H 6.1, N 11.5.

2-[Methylthio-(2-pyridylamino)]methylene tetralone 5h was isolated as viscous yellow oil (3h), yield 2.6g (91%). ν\text{max} (CCl\textsubscript{4}) : 3382, 1675, 1609, 1586, 1236 cm\textsuperscript{-1}. δ\textsubscript{11}(90 MHz, CCl\textsubscript{4}); 2.15 (s, 3H, SCH\textsubscript{3}), 2.80-2.95 (m, 4H, 2xCH\textsubscript{2}), 7.00 (ddd, 1H, J = 16 Hz, H-5 pyridyl), 7.20-7.31 (m, 3H, ArH), 7.40-7.50 (m, 2H, H-3 and H-4 pyridyl), 8.09 (m, 1H, ArH), 8.43 (dd, 1H, J = 8.9 Hz, H-6 pyridyl), 13.1 (brs, 1H, NH,
2-[Methylthio-(2-pyridylamino)methylene-6-methoxy-1-tetralone (5i) was isolated as an oil yield 2.50g (76.6%). $\nu_{\text{max}}$ (CCl₄) : 3382, 3066, 1634, 1598, 1490, 1270 cm⁻¹. $\delta_{\text{IR}}$(90 MHz, CCl₄): 2.67 (s, 3H, SCH₃), 3.90 (s, 3H, OCH₃), 3.90-3.93 (m, 4H, 2xCH₂), 7.20 (ddd, 1H, J=15.6 Hz, H-5 pyridyl), 7.31 (m, 2H, H-3 & H-4 pyridyl), 7.40-7.45 (m, 2H, ArH), 7.89 (s, 1H, ArH), 8.55 (dd, 1H, J = 9Hz, H-6 pyridyl), 13.00 (brs, 1H, NH). Anal. Calcd. for C₁₈H₁₈N₂O₂S. C 66.2, H 5.5, N 8.4. Found: C 66.2, H 5.5, N 8.2.

1-Methylthio-1-(2-pyridyl amino)-3-oxo-5(4methoxy phenyl)-1,4-pentadiene (5j) was isolated as yellow crystals(chloroform-Hexane), m.p 120°C yield 2.77g (85%). $\nu_{\text{max}}$ (KBr):3414, 3370, 1606, 1545, 1476 cm⁻¹. $\delta_{\text{IR}}$(300MHz, CDCl₃): 2.41(s,3H, SCH₃), 3.82 (s,3H, OCH₃) ,5.43(s,1H,H-2vinylc), 6.64 (d,1H,J=15Hz,H-4) ,6.8(d,2H,J=9Hz, ArH 6.92-6.97 (m,1H-3, H-4 pyridyl), 7.5 (d, 2H, J=9Hz,ArH), 7.56 (d,1H1, J = 15Hz, H-5),7.62(ddd,1H,J= 15.6Hz,H-5 pyridyl),8.32 (dd,1H,J= 9Hz, H-6 pyridyl, 14.7 (s,1H,NH),exchanges D₂O.(75MHz) d: 16.05 (SCH₃),55.26 (OCH₃), 113.84, 114.1 13CNMR CHAr), 118.13, 125.7, 128.2 (CH,Ar), 129.5,137.9, 139, 146.7, 152.5, 160.8, 165.5,183.84 (C=O).Anal : Calcd for C₁₈H₁₈N₂O₂S (326): C 66.5, H. 5.6, N 8.4. Found: C 66.2,H 5.5,N 8.2.

**Generation of 3-lithio-aminopyridine and it's reaction with $\alpha$-oxoketene dithioacetals:** General procedure for the preparation of S,N-acetals (7a-e). To a solution of 3-aminopyridine (1.41g, 15 mmol) in dry THF (25 ml) n-butyllithium (15 mmol) was added under nitrogen and inert atmosphere with stirring at room temperature. The reaction mixture was gradually warm upto 45°C and stirred for 30
minutes at the same temperature. Then it was brought to room temperature (25°C) and a solution of S,S-acetal (10 mmol) in dry THF (25 ml) was added. The reaction mixture was further stirred for 5 hours at ambient temperature. It was then quenched with saturated NH₄Cl solution (50 ml) and extracted with chloroform (2x50 ml). The combined extracts were washed with water (2x50 ml), dried (Na₂SO₄) and evaporated to give the crude product which were chromatographed on silica gel using ethylacetate-hexane (2:8) as eluent.

3-Methylthio-3-(3-pyridylamino)-1-phenyl-2-propene-1-one (7a) was isolated as low melting solid, yield 2.00g (70%). IR v max (CCl₄): 3416, 3034, 1693, 1549, 1256 cm⁻¹. ¹H NMR (90 MHz, CDCl₃): 2.31 (s, 3H, SCH₃), 5.91 (s, 1H, vinyl), 7.20-7.26 (m, 1H, H-5 pyridyl), 7.29-7.35 (m, 1H, H-4Py) 7.35-7.50 (m, 3H, ArH), 7.91-8.12 (m, 2H, ArH) 8.45 (dd, 1H, J = 9.6Hz, H-6pyridyl), 8.62 (s, 1H, H-2 pyridyl), 14.01 (1H, NH, exchanges D₂O). Found : C 66.69, H 5.15, N 10.38.

3-Methylthio-3-(3-pyridylamino)-1-(4-methoxyphenyl)-2-propene-1-one (7b) isolated as yellow crystal m.p. 95°C, yield 2.10g (70%). IR v max (KBr) : 3421, 3055, 1603, 1541, 1246 cm⁻¹. ¹H NMR (90 MHz, CDCl₃) : 2.34 (s, 3H, SCH₃), 3.75 (s, 3H, OCH₃), 5.83 (s, 1H, vinylic), 6.84 (d, 2H, J = 9Hz, ArH), 7.19 (dd, 1H, J = 9Hz, H-5 pyridyl), 7.56 (dd, 1H, J = 9Hz, H-5 pyridyl), 7.81 (d, 2H, J = 9Hz, ArH), 8.35 (dd, 1H, J = 8.5Hz, H-6 pyridyl), 8.36 (s, 1H, H-2 pyridyl), 13.44 (s, 1H, NH). Anal. Calcd. for C₁₁H₁₆N₂O₅ (300.1) C 63.97, H 5.33, N 9.33. Found : C 63.95, H 5.30, N 9.50.

3-Methylthio-3-(3-pyridylamino)-1-(4-methylphenyl)-2-propene-1-one (7c) was isolated as low melting solid, yield 1.95g (68%). IR v max (CCl₄): 3385, 3049, 1609, 1544, 1184 cm⁻¹. ¹H NMR (90 MHz, CDCl₃): 2.35 (s, 3H, SCH₃), 5.81 (s, 1H, vinylic), 7.01 (d, 2H, J = 9Hz, ArH), 7.45-7.50 (dd, 1H, H-5 pyridyl), 7.55 (dd, 1H, H-3 pyridyl), 7.65
(d, 2H, J = 9Hz, ArH), 8.35 (dd, 1H, J = 8Hz, H-6 pyridyl), 8.56 (s, 1H, H-2Py), 14.0 (1H, NH). Anal. Calcd. for C_{16}H_{16}N_{2}O_{2}S (284.1) C 67.60, H 5.61 N 9.81. Found: C 67.50, H 5.7 N 9.75.

1-(3-pyridylamino)-2-carboethoxy-2-cyano-1-methylthiomethylene (7d) was isolated as colourless solid, m.p. 110°C, yield 2.40g (91.2%). $\nu_{\text{max}}$ (KBr): 3302, 2264, (C=N) 1670, 1621 cm$^{-1}$. $\delta_{\text{H}}$ (90 MHz, CDCl$_3$): 1.30 (t, 3H, CH$_2$CH$_3$, J = 7Hz), 2.30 (s, 3H, SCH$_3$), 4.36 (q, 2H, CH$_2$CH$_3$, J = 7 Hz), 7.40 (dd, 1H, J = 9.6 Hz, H-5 pyridyl), 7.75 (d, 1H, J = 8Hz, H-4 pyridyl), 8.65 (m, 2H, s and d overlapped, H-2 & H-6 pyridyl), 12.10 (brs, 1H, NH). Anal. Calcd. for C$_{12}$H$_{13}$N$_3$O$_2$S (263) C 54.75, H 4.9, N 15.96. Found: C 54.66, H 4.7, N 16.10.

3-Methylthio-3-(3-Pyridylamino)-1-(2-furyl)-2-propen-1-one (7e) was isolated as yellow solid m.p. 105°C, yield 1.65g (62%). $\nu_{\text{max}}$ (KBr) : 3436, 3104, 1723, 1670, 1017 cm$^{-1}$. $\delta_{\text{H}}$ (90 MHz, CDCl$_3$) : 2.50 (s, 2H, SCH$_3$), 5.91 (s, 1H, vinylic), 6.60 (dd, 1H, J = 4.5 Hz, H-3' furyl), 7.30 (dd, 1H, J = 5.5 Hz, 1'-'-4' furyl), 7.50 (dd, 1H, J$_{4,5}$ =9Hz, J$_{4,6}$ =1.8Hz, H-4 pyridyl), 7.52 (dd, 1H, J$_{5,4}$ =9Hz, J$_{5,6}$ =6Hz), H-5 pyridyl) 7.70 (d, 1H, J=3Hz, H-5' furyl), 8.40 (dd, 1H, J$_{6,5}$ =6Hz, J$_{6,4}$ =1.8Hz, H-6pyridyl), 8.60 (s, 1H, H-2 pyridyl). Anal. Calcd. for C$_{13}$H$_{12}$N$_3$O$_2$S (260.1) C 59.9, H 4.6, N 10.76. Found : C 59.8, H 4.70, N 10.71.

**General procedure for the preparation of N,N-acetals (8a-b):** To a solution of 2-amino pyridine (1.88g, 20 mmol) in anhydrous THF (25 ml), n-butyllithium (20 mmol) was added under dry and inert atmosphere, over 20 minutes with stirring at room temperature (25°C). After 30 minutes, a solution of oxoketene dithioacetal (10 mmol) in dry THF (25 ml) was added and continued stirring for another 1 hr at the same temperature. Then the reaction mixture was refluxed for 5 hours at 60°C
(monitored by TLC). After cooling to room temperature, the reaction mixture was quenched with saturated NH4Cl solution (100 ml), extracted with chloroform (2x50 ml) and the combined extracts were washed with water (2x50 ml), dried (Na2SO4) and evaporated to give the crude product, which was purified by column chromatography (silica gel) using ethylacetate-hexane (2:8) as eluent.

3,3-Bis(2-pyridyl amino)-1-(phenyl)-2-propen-1-one (8a) was isolated as yellow crystals (EtoAc-hexane), yield 2.50g (79%) m.p.125°C ν̇max (KBr) : 3427, 1653, 1611, 1592, 1545 cm⁻¹ δ̇H (90 MHz, CDCl3): 6.95-7.35 (m, 5H, olefinic, ArH, & H-5 pyridyl), 7.50 (m, 2H, H-3, pyridyl), 7.65-8.10 (m, 5H, ArH, 2xH-4, H-5) 8.40 (d, 1H, J = 6.9Hz, H-6 pyridyl), 8.60 (d, 1H, J = 6.9Hz, H-6 pyridyl), 13.30 (brs, 1H, NH), 14.63 (brs, 1H, NH). Anal. Calcd. for C19H16N4O (316), C 72.1~, H 5.09, N 17.72. Found : C 72.25, H 5.09, N 17.61.

3,3-Bis(2-pyridylamino)-1-(4-methoxyphenyl)-2-propen-1-one (8b) was isolated as yellow coloured solid, yield 2.80g (80.9%), m.p.130°C ν̇max (KBr): 3401, 1659, 1608, 1589, 1532 cm⁻¹ δ̇H(CDCl3): 3.80 (s, 3H, OCH3), 6.90-7.30 (m, 5H, olefinic, ArH, 2xH-5 pyridyl), 7.60 (m, 4H, 2xH-3 & 2xH-4 pyridyl), 8.00 (d, 2H, J = 9Hz, ArH), 8.25 (d, 1H, J = 9Hz, H-6 pyridyl), 8.55 (d, 1H, J = 6.9 Hz, H-6 pyridyl), 13.20 (brs, 1H, NH), 14.80 (brs, 1H, NH). Anal. Calcd. for C20H18N4O2 (346) C 69.36, H 5.20, N 16.18. Found : C 69.40, H 5.12, N 16.21.

General procedure for the preparation of O,N-acetals (10 a-b)

Method A: (N,S-acetal as precursor): To a cooled and stirred solution of sodium alkoxides (prepared by dissolving sodium, 0.01 mol, in 20 ml of respective alcohol) in the respective alcohol (10 ml), the ketone S,N-acetal (0.01 mol) was added and stirred for 10-15 minutes. The reaction mixture was refluxed for 8-10 hours
(monitored by TLC). The solvent was distilled under reduced pressure and the residue was quenched in crushed ice. It was extracted with chloroform (2x50 ml), washed (H2O), dried (Na2SO4) and distilled off to give the crude O,N-acetals which were purified either by crystallization or chromatography on silica gel using EtOAc-hexane (1:2) as eluent.

**Method B**: (O,S-acetal as precursor): To a solution of 2-aminopyridine (0.94g, 10 mmol) in anhydrous THF (20 ml), n-butyllithium (15 mmol) was added under dry and inert atmosphere at ambient temperature. After stirring for 30 minutes, a solution of α-oxoketene O,S-acetal (prepared by reported procedure) in dry THF (25 ml) was added and stirred for another 1 hour at the same temperature. The reaction mixture was quenched with sat. NH4Cl solution (100 ml), extracted with chloroform (2x50 ml) and the combined extracts were washed with water (100 ml), dried (Na2SO4) and evaporated to give the crude O,N-acetals, which were purified by column chromatography.

**3-Methoxy-3-(2-pyridylamino)-1-phenyl-2-propene-1-one (10a)** was isolated as light yellow crystals (chloroform-hexane), yield 1.56g (61.4%), m.p. 130°c \( \nu_{\text{max}} \) (KBr) : 3918, 3258, 1627, 1599, 1339 cm\(^{-1}\). \( \delta_{\text{H}} \) (90 MHz, CDCl3) : 3.63 (s, 3H, OCH3), 5.30 (s, 1H, vinylic), 6.70 (ddd, J = 15.4 Hz, H-5 pyridyl), 7.10-7.50 (m, 4H, 3-arH & H-3), 7.80-8.15 (m, 3H, 2 ArH), 8.35 (td, 1H, J = 8.0 Hz, H-6), 14.0 (brs, 1H, NH, exchanges D2O). Anal. Calcd. for C15H14N2O2 (254) C 70.86, H 5.51, N 11.02. Found : C 70.65, H 5.60, N 11.20.

**3-Methoxy-3-(2-pyridylamino)-1-(4-chlorophenyl)-2-propene-1-one (10b)** was isolated as light yellow crystals (CHCl3 -hexane), m.p. 137°c yield 1.80g (62%).\( \nu_{\text{max}} \) (KBr) : 3417, 1617, 1589, 1213 cm\(^{-1}\). \( \delta_{\text{H}} \) (90 MHz, CDCl3) : 3.90 (s, 3H, OCH3), 5.60 (s,
REFERENCE:


2. A. Rahman, Ph.D. *Thesis submitted to Department of Chemistry, NEHU, Shillong*, June, 1984, Chapter-II.


