The synthesis of α-oxoketene S,S-acetals of the general formula 1 was first reported by Kelber and coworkers\textsuperscript{1} in 1910. This class of compounds can be easily prepared from a wide variety of active methylene ketones and carbon disulfide in the presence of a suitable base followed by alkylation. Many experimental variations of this method are now available in the literature\textsuperscript{2}. They are also called as polarized ketene S,S-acetals. The polarized ketene S,S-acetals possess 1,3-electrophilic centers with differing electrophilicity and, therefore, are excellent class of 3-carbon synthons. They have been extensively used to construct various carbocycles and heterocycles by reacting them with various 1,2- or 1,3-binucleophiles. A brief review on their utility as 3-carbon fragment has been shown in Scheme 1.

The polarized ketene S,S-acetals can be converted into corresponding polarized ketene S,N- and N,N-acetals\textsuperscript{2} and\textsuperscript{3} respectively by reacting them with appropriate amines under different conditions\textsuperscript{5-7}. These S,N- and N,N-acetals, in turn, are excellent enamines and have been used to synthesize various heterocycles. They can be considered as vinylogous amides if they are derived from ketones and as vinylogous amines if they are derived from other active methylene compounds. They also possess 1,3-electrophilic centers and have been used to construct various heterocycles. Their various transformations have been briefly shown in Scheme 2.
\[
\begin{align*}
R_1\text{CHO} & \quad = \quad (R^3)_2\text{Cu} \\
\text{or} & \\
\beta - \text{Ketoaldehyde} & \\
\text{polyene esters} & \quad < \quad 1,2-\text{Hydride} \text{ or } \text{organometallic} \\
& \quad \text{addition and} \quad 1,3-\text{Carbonyl} \\
& \quad \text{transposition} \\
\text{double bond} & \quad \text{reactivity} \\
\text{Bromination} & \\
\end{align*}
\]
Scheme 2

2, 3. $X = \text{SMe, NHR}^{\#}$

$Y = \text{NHR}^{\#}$
In the present study it was proposed to explore the enamine behaviour of the polarized ketene S,N- and N,N-acetals. Thus, they are shown to react with maleic anhydride in refluxing acetonitrile to afford various pyrrolin-3-acetic acids in excellent yields (Scheme 3). Alternately, they yield various pyranopyrroles when reacted with maleic anhydride in the presence of acetic anhydride in refluxing acetonitrile (Scheme 3). It is also shown that the pyrrolin-3-acetic acids are cyclized to the corresponding pyranopyrroles when heated with acetic anhydride (Scheme 3). Similarly, the cyclic S,N- and N,N-acetals also react with maleic anhydride in refluxing acetonitrile to yield various pyrrolothiazoles and pyrroloimidazoles in good yields (Scheme 4). However, these pyrrolothiazoles and pyrroloimidazoles failed to cyclize in the presence of acetic anhydride. As a model reaction, the S,N-acetals 2a and 2d are shown to react with maleimide in refluxing acetonitrile to yield the corresponding pyrrolin-3-acetamides in good yields (Scheme 5). The corresponding pyrrolopyridines were obtained when the refluxing time was increased (Scheme 5). Few N,N-acetals are also shown to react with maleic anhydride and maleimide in refluxing acetonitrile to yield the corresponding pyrrolin-3-acetic acids and pyrrolin-3-acetamides in good yields (Scheme 6). However, and failed to cyclize in acetic anhydride. The scope and limitations of this method are discussed in detail in the second chapter.
Scheme 3
Scheme 4

\[ R\text{-}J \overset{4\text{ h}}{\underset{82-91\%}{\rightarrow}} \text{MeCN, } \Delta, 2h \]

\[ X = O, NH \]

Scheme 5

\[ R_1\text{-}CONH}_2 \rightarrow \text{MeCN, } \Delta, 2h, 85-88\% \]

\[ R_2 \]

\[ 10a, 10d \]

\[ 11a, 11d \]

\[ R_1\text{-}CONH}_2 \rightarrow \text{MeCN, } \Delta, 2h, 70-82\% \]

\[ R_2 \]
\[ \text{Ar} = \text{C}_6\text{H}_5 \]
\[ \text{Ar} = 4-\text{MeC}_6\text{H}_4 \]

3 a. \( \text{Ar} = \text{C}_6\text{H}_5 \)
3 b. \( \text{Ar} = 4-\text{MeC}_6\text{H}_4 \)

\[ R^3 = \text{H} \]

Scheme 6
In the third chapter, it was proposed to react various polarized ketene S,N-acetals with bromoacetdehyde diethylacetal. Thus, are shown to react with in refluxing DMF, to yield the corresponding 1,2,3-trisubstituted pyrroles in good to excellent yields (Scheme 7). The cyclic S,N-acetals also reacted with to yield various pyrroloimidazoles in good yields (Scheme 8). Similarly, also reacted with propargyl bromide in the presence of refluxing dioxan, to yield the corresponding 5-methyl-1,2,3-trisubstituted pyrroles in good to excellent yields (Scheme 9). The cyclic S,N-acetals also reacted with to yield various pyrroloimidazoles in good yields (Scheme 10). The scope and limitations of this method are also described in this chapter.

Thus, it has been shown, in the second and third chapter, that the polarized ketene S,N- and N,N-acetals can be conveniently used as enamines to construct various heterocycles.

In continuation of our study on the polarized ketene S,S-acetals, it was proposed to react them with azaallyl cations. Thus, the S,S-acetals are shown to react with 2-lithiomethylquinoline to yield the corresponding carbinol acetals in quantitative yields (Scheme 11). These carbinol acetals are conveniently cycloaromatized, in the presence of borontrifluoride etherate, to yield the corresponding benzo[c]quinolizinium and condensed
Scheme 7

<table>
<thead>
<tr>
<th></th>
<th>R¹</th>
<th>R²</th>
<th></th>
<th>R¹</th>
<th>R²</th>
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</thead>
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<tr>
<td>a</td>
<td>Me</td>
<td>Et</td>
<td>b</td>
<td>Me</td>
<td>PhCH₂</td>
</tr>
<tr>
<td>c</td>
<td>Ph</td>
<td>Me</td>
<td>d</td>
<td>Ph</td>
<td>Et</td>
</tr>
<tr>
<td>e</td>
<td>Ph</td>
<td>n-Pr</td>
<td>f</td>
<td>4-ClC₆H₄</td>
<td>i-Pr</td>
</tr>
<tr>
<td>g</td>
<td>Ph</td>
<td>n-Bu</td>
<td>h</td>
<td>Ph</td>
<td>Ph</td>
</tr>
<tr>
<td>i</td>
<td>Ph</td>
<td>PhCH₂</td>
<td></td>
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</tbody>
</table>

2 a-i → 14

DMF/120°C 4-8 hr

15A

15 a-i
Scheme 8

R₁
\[ \text{O} \]
H
R₁
\[ \text{O} \]
\[ \text{S} \]
\[ \text{NH} \]
\[ \text{O} \]
\[ \text{EtO} - \text{O} \]
\[ \text{Et} \]
\[ \text{Br} \]
\[ \text{DMF/120°C} \]
\[ 4 \text{ - 8hr} \]
\[ 61 \text{- 73%} \]
\[ \text{g. R₁} = \text{Me} \]
\[ \text{b. R₁} = 4 \text{- ClC₆H₄} \]
\[ \text{c. R₁} = \text{Ph} \]

7 a-c

14

16 a-c
Scheme 9
Scheme 10

CuBr/dioxane, 110°C

R1 = Me
R1 = Ph

R'1 = 4-ClC6H4

19a-c

2a-c
Scheme - 12
derivatives 22 in good to excellent yields (Scheme 11). The scope and limitations of this method have been discussed in detail in the fourth chapter.

In continuation of our study on the synthetic utility of polarized ketene S,S-acetals, it was proposed to prepare the hitherto unknown S,S-acetal 23 from the 3-methyl ether of estrone, a potent female sex hormone. The estrone molecule has been greatly modified synthetically to design some compounds which can separate the antifertility property from estrogenic property. While much of the literature is devoted to the construction of rings on the A ring of estrone, there is virtually no attempt to construct aromatic ring on the D ring. In the fifth chapter various carbocycles and heterocycles have been prepared by reacting the estrone S,S-acetal 23 with various binucleophiles (Scheme 12). The details of all these transformations have been described in the fifth chapter.

REFERENCES