Ylides (1) are zwitterionic compounds in which an anion is covalently bonded to a positively charged heteroatom, and are considered as resonance hybrids of two limiting structures, the ylide form (1a) and the ylene form (1b). One of these, the ylide form (1a) emphasizes the dipolar zwitterionic nature involving an onium centre at element like nitrogen, phosphorus or arsenic, next to a carbanionic function, which may at least partially be delocalized into suitable substituents. On the other hand, in the ylene form (1b), a true double bond is postulated between the onium centre and the ylidic carbon, thus reducing or even eliminating the formal charges at these atoms. The application of modern physical techniques and the results of sophisticated theoretical calculations have made increasingly clear that the ylide form predominates in the ground state. Most of the early investigations successfully used this description for most of their problems of structures, reactivity and for the rationalization of reaction mechanism. Therefore, it is with justification that the term ylide is used now-a-days exclusively in the literature.
The reactivity of these ylides depends both on the properties of the carbanion and the possible involvement of the heteroatom. These compounds vary widely in stability, depending on the symmetry of the molecules and the extent of π - δ bonding. A quantitative comparison of the stability of the ylides, formed by different elements have been made using the rates of alkali catalysed exchange of the α-hydrogen atom of the corresponding salts. The acidity of salt and, hence, the stability of the ylide are greatly affected by the change in structure.

Ylides have been classified in two main groups on the basis of stability and the ease with which they undergo reaction with a variety of electrophilic substrates. The first and the larger group comprises the ylides so called "non-stabilized ylides" which are generated in the solution from their precursors but could not be isolated due to lack of the stabilizing factors and undergo reactions 'in situ'. These ylides may further be divided into two categories depending upon the attachment of alkyl or aryl-alkyl groups with the heteroatom. The arylalkylidene ylides, sometime designated as semi-stabilized ylides which could not be isolated but persisted in solution for a considerable period in contrast to the alkylidene ylides which are very short-lived. The second and smaller group consists of "stabilized ylides" and is taken to imply an ylide which may be isolated, purified, usually stored in atmosphere and used in subsequent reactions. The
stability of these ylides may be attributed to the attachment of the electron withdrawing groups with the ylidic carbanion.

In recent years, synthetic applications of ylides have been realized and studies on these reactive intermediates have been expanded in many directions which led to the exploration of the ylides of nitrogen, phosphorus, arsenic and sulfur as evidenced by research monographs and comprehensive review articles. The involvement of a particular heteroatom results into marked differences in the chemical and physical behaviour of different types of ylides.

The development of the chemistry of nitrogen ylides began with the early attempts to prepare organic derivatives containing pentavalent nitrogen. To this purpose, Schlenk and Holtz treated tetramethylammonium chloride with sodium triphenylmethylide(2) and isolated a red product, insoluble in organic solvent, to which they assigned structure (Scheme VI.1).

Later Hager and Marvel attempted to prepare analogous compounds in which all the five groups around nitrogen were more equivalent. These workers found that the reaction of triethylbenzylammonium bromide with ethyl lithium did not produce tetraethylammonium benzylide, thus ruling out the existence of any intermediate in which all the five groups bound to the nitrogen approached equivalency. From this observation, Hager and Marvel concluded that the material prepared by Schlenk and Holtz was
Scheme VI.1

\[ \text{Scheme VI.1} \]

\[ (\text{Ph})_3 \text{C} \text{Na} + (\text{CH}_3)_4 \text{N} \cdot \text{Cl} \rightarrow (\text{CH}_3)_4 \text{N} \cdot \text{C}(\text{Ph})_3 + \text{NaCl} \]

Scheme VI.2

\[ \text{Scheme VI.2} \]
tetraalkylammonium salt of relatively stable triphenylmethyl carbanion (3) rather than derivative of pentavalent nitrogen.

In 1944, Witting and Pelletschin\textsuperscript{26} began a reinvestigation of the pentavalent nitrogen problem and succeeded in isolating a red powder by the treatment of 9-fluorenylidenetrimethylammonium bromide (4) with phenyllithium in ether. However, since benzene was isolated from the reaction mixture the compound could not be pentavalent nitrogen derivative and was assigned an ylide structure on the basis of its reaction with water, methyl iodide, iodine and benzyl bromide (Scheme VI.2). Following this initial preparation of a stable material having an ylide structure, a variety of nitrogen ylides have been prepared, characterized and their chemistry has been reviewed.

The N-ylides have been classified according to the onium group structure into: ammonium-ylides (5), cycloammonium-ylides (6), immonium-ylides (7), cycloimmonium-ylides (8), nitrile-ylides (9) and diazonium-ylides (10). The cycloimmonium-ylides have been further divided into five-membered cycloimmonium-ylides and six-membered cycloimmonium-ylides, which include pyridinium (11) and benzopyridinium-ylides (12).

Neglecting the Coulombic interaction as a minor contribution to stability, the N-ylide stability is determined by two important factors: the structure of the Onium group and the anionic part. N-ylides due to absence of d-orbital overlap do not contribute the ylene form and the only stabilizing factor involved
electrostatic interaction between two charges localized on adjacent nitrogen and carbon atom, if no other strong delocalizing group is present.

Ammonium and cycloammonium groups lack stability due to the absence of stabilizing factors. An increase of molecular stability is observed in the cycloimmonium-ylides in which the nitrogen atom being involved into N-heteroaromatic ring. The main subject of our studies is the pyridinium and benzopyridinium ylides - a class of cycloimmonium ylides in which the cationic part is involved in the heteroaromatic ring.

The stability of pyridinium and benzopyridinium-ylides may be attributed to an extensive delocalization of positive charge on the system, as represented by their various contributing structures (13,14) (Scheme VI.3) and to the carbanion participation in the resonance of heteroaromatic ring (14a-c) (Scheme VI.4). The Coulombic interactions, which are also responsible for the stability of some ammonium ylides, are less important in case of cycloimmonium-ylides so far as the stability is concerned and if it is assumed that there is only an electrostatic interaction between the carbanion and the onium group, as represented in the structure (15b), the electron pair of sp\(^3\) hybridized ylidic carbanion would be involved in a \(\pi d\) type of molecular orbital with the sp\(^2\) hybridized nitrogen atom of heteroaromatic ring. However, overlapping is more effective, if we consider the resonating form (15c) in which there is an interaction of the bielectronic
Scheme VI.3
p-orbital with the \( \pi \)-electrons of the heteroaromatic ring and therefore, ylides afford stability.\(^{27}\) The stability has also been found to be influenced by the nature of substituents \( R^1 \) and \( R^2 \) attached to the ylide carbanion. If these groups are electron withdrawing additional resonance structures occur determining a marked sp\(^2\) hybridization of the ylide carbon through charge delocalization.\(^{27}\)

The reactivity of cycloiminonium-ylides depends on the properties of the carbanion as well as possible involvement of heteroatom. Usually the alkylidenecycloiminonium-ylides of less stability show high reactivity, whereas highly stabilized cycloiminonium-ylides show less reactivity. The reactivity of cycloiminonium-ylides is influenced by delocalization of positive charge over heteroaromatic ring, coulombic attractive strength between the aromatic positive cyclic nitrogen and the negative carbon and delocalization of charge on the carbon ylide by electron withdrawing groups i.e., \( R^1 \) and \( R^2 \). Thus, the nucleophilic character of the cycloiminonium-ylides decreases while the stability increases if the lone pair of electrons on the \( \alpha \)-carbon atom of the form 14a is delocalized. The electron withdrawing substituents \( R^1 \) and \( R^2 \) tend to stabilize the negative charge and, consequently, reduces the reactivity of the ylide. On the other hand, when there is no such interaction, an extremely reactive ylide is formed.
VI.1 PREPARATION OF CYCLOIMMONIUM YLIDES

1.1 Ylides from Quaternary Salt (Salt Method)

This remains the most common method of preparing cycloimmonium-ylides and involves the reaction of quaternary cycloimmonium salts with a base which is strong enough to abstract a proton from the α-carbon. In principle, any cycloimmonium salt (16) carrying at least one α-hydrogen is convertible into an ylide (17) (Scheme VI.5).\(^\text{28, 29}\) Cycloimmonium salt (16) are prepared by the quaternization of substituted alkyl halides with respective tertiary bases viz., pyridine, picoline, quinoline and isoquinoline etc. (Scheme VI.5). Quaternization may also be performed by the treatment of tertiary base with an active methylene derivative and iodine. This method was first reported by Ortoleva\(^\text{30, 31}\) and widely applied in a great number of cases by King\(^\text{32-34}\) and others,\(^\text{35}\) known as King-Ortoleva method and results in the formation of the quaternary iodide salt of type 18 (Scheme VI.6).

The strength of base necessary for the dehydrohalogenation of the corresponding salt depends on the acidity of α-hydrogen atom which, in turn, depends on the nature of substituents present on the α-carbon atom. Most common bases used for the purpose are aqueous solution of alkali carbonates\(^\text{35}\) or amines in anhydrous aprotic solvents.\(^\text{36-38}\) Sometime, the use of sodium hydride in dimethylformamide has found to be advantageous, particularly for unisolable ylides which are to be used in subsequent reactions. A wide number of cycloimmonium-ylides are incapable of being
Scheme VI. 4

\[
\begin{align*}
15\text{a} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \\
15\text{b} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \\
15\text{c} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet}
\end{align*}
\]

M.O. of 15c

Scheme VI. 5

\[
\begin{align*}
\text{N} + \text{X-CH} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \\
\text{N} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet}
\end{align*}
\]

Scheme VI. 6

\[
\begin{align*}
2 \text{N:} + \text{I}_2 + \text{CH}_3\text{COR} & \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \\
\text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet} \quad \text{\textbullet}
\end{align*}
\]
isolated due to their sensitivity towards atmospheric components and, therefore, generated in anhydrous media under inert atmosphere and used as such in subsequent reactions. Such reactions are usually carried out in nonpolar solvents, though some time more polar solvents are advantageous.39,40

1.2 Ylides from Azaheterocycles and Ethylene Oxide

Linn et al.41 and others42 have reported the formation of many dicyanomethylide (21), which are highly stable, by the reaction of tetracyanoethylene oxide (20) with azaheterocycles (19) at 0°C (Scheme VI.7).

1.3 Ylides from Diazocompounds

Pyridinium ylides (23) have also been prepared by the irradiation of triphenyl or tetraphenyldiazocyclopentadiene (22) in pyridine under nitrogen with a high pressure of mercury lamp through a pyrex filter43 (Scheme VI.8).

1.4 Ylides from N-Heterocycles and Carbene

Cycloimmonium-ylides (25) have also been prepared by the reaction of carbene (24) on azaheterocycles44 (Scheme VI.9).

1.5 Synthesis of Disubstituted Ylides

Disubstituted ylides (27,28) have been synthesized from monosubstituted ylide (26) directly by treatment with acylating reagent,45 isocyanates46,47 and isothiocyanates48,49 (Scheme VI.10).
Scheme VI.7

![Diagram of chemical reaction](image1)

Scheme VI.8

![Diagram of chemical reaction](image2)

Scheme VI.9

![Diagram of chemical reaction](image3)

Scheme VI.10

![Diagram of chemical reaction](image4)
Recently, Leonte and Zugravescu\textsuperscript{50} have synthesized dicyano-
pyridiniummethylide (30) by heating cyanocarbamylpyridinium-
methylide (29) with POC\textsubscript{3} in the presence of sodium pyrosulfite. 
But when acetic anhydride was used as dehydrating agent instead 
of POC\textsubscript{3}, cyanoacetylpyridinium-methylide (31) was formed. The 
ylide (31) was also prepared by acetylation of ylide (32). Alter-
natively, ylide (30) could be synthesized by the reaction of 
bromocyaano-acetic ester (33) with carbalkoxypyridinium-ylide (34) 
(Scheme VI.11).

1.6 Synthesis of Polyyldes

Although numerous methods have been devised from time to 
time to enable the synthesis of mono- and disubstituted ylides\textsuperscript{45-50} 
as described in the previous section, however, no attention has 
been paid towards synthesizing poly-ylides for nearly two and a 
half decade since the inception of pyridinium ylides. It was 
during early seventies that Berlin et al.\textsuperscript{51,52} and others\textsuperscript{53} shared 
the credit for synthesizing poly-ylides by dehydrohalogenation of 
poly(4-methylpyridinium chloride) (35) in the presence of aqueous 
ammonia and demonstrated the formation of poly-ylide (36) by 
appearance of a dark coloured water insoluble polymeric product 
(Scheme VI.12).
Scheme VI.11

\[ \begin{align*}
C_5H_5N-C&\overset{POCl_3}{\rightarrow} C_5H_5N-C \overset{Ac_2O}{\rightarrow} C_5H_5N-C \\
&\overset{\text{Na}_2S_2O_5}{\rightarrow} C_5H_5N-C \overset{\text{Ac}_2O}{\rightarrow} C_5H_5N-C
\end{align*} \]

Scheme VI.12

\[ \begin{align*}
\text{Py-CH} &\overset{\text{Cl}}{\rightarrow} \text{Py-CH} \overset{(n+1)\text{HCl}}{\rightarrow} \text{Py-CH} \\
&\overset{\text{Cl}}{\rightarrow} \text{Py-CH} \overset{\text{Cl}}{\rightarrow} \text{Py-CH}
\end{align*} \]

Scheme VI.13

\[ \begin{align*}
\text{COC}_6H_5 &\overset{\text{Py-CH}_3}{\rightarrow} \text{COC}_6H_5 \overset{\text{CH}_3}{\rightarrow} \text{COC}_6H_5 \\
&\overset{\text{Py-CH}_3}{\rightarrow} \text{COC}_6H_5 \overset{\text{CH}_3}{\rightarrow} \text{COC}_6H_5
\end{align*} \]
Two. REACTIONS OF CYCLOIMMONIUM YLIDES

2.1 Thermolysis

The thermal stability of cycloimmonium-ylides considered as a criterion of molecular stability was not studied in adequate experimental conditions. Cook et al.\textsuperscript{54} isolated dibenzoylethylen (37) by sublimation of pyridinium-ylide (12) at 150° in high vacuo condition. The former product (37) seemed to have been resulted from dimerization of carbene intermediate formed by the heterolytic cleavage of ylide bond, however, the reaction took another course when the same ylide (12) was heated in benzene in presence of copper or copper oxide to afford 1,3-dibenzoylindolizine (38)\textsuperscript{55} unexpectedly. The mechanism of the reaction is still obscure (Scheme VI.13).

Zugravescu et al.\textsuperscript{56} have studied the thermal decomposition of mono- and disubstituted isoquinolinium-ylides (39) and reported the formation of isoquinoline and cyclopropane derivatives (41), formed by trimerization of carbene intermediate (40) (Scheme VI.14).

2.2 Photochemistry

The existing literature reveals that no considerable amount of work has been done on the photolytic conversions of pyridinium-ylides.\textsuperscript{57,58} However, these ylides in the presence of ultraviolet radiations usually follow two different courses: (i) the cleavage of C\textsuperscript{-}-N\textsuperscript{+} bond with the formation of the heterocycles and disubstituted carbene which, in turn, add on benzene to give benzene-
norcaradiene (44). This is usually the main reaction and (ii) the photochemical isomerisation of the ylide, involving either contraction or expansion of heteroaromatic ring (Scheme VI.15).

2.3 Alkylation

Cycloimmonium-ylides having active methylene group are capable of undergoing substitution reaction with alkyl halides to afford carbanion disubstituted ylides (46), presumably via intermediacy of salt (45) which in the presence of base loses hydracid molecule and converted into the ylide (46)59 (Scheme VI.16). However, the method was found to be of little worth in the syntheses of disubstituted ylides owing to the fact that they undergo decomposition.

If alkylation is carried out without using dehydrohalogenating reagent, the overall process is rather complex. Thus, by treating pyridiniumbenzoyl-methylide (12) with phenacyl bromide, owing to the possible interactions between the intermediates and the initial ylide (12), and to the transylidation reaction and bond cleavage, gave several products (47-51)60 (Scheme VI.17).

Henerick et al.61 reported the preparation of a wide range of ketones (54) by the reduction of salt (53) with zinc and acetic acid, formed by the alkylation of ylide (52) (Scheme VI.18).
Scheme VI.14

\[
\begin{align*}
\text{[Image: reaction scheme]} \\
\text{R} & = \text{H, -CO}_2\text{Et} \\
3(40) & \rightarrow \\
\text{Et}_2\text{C} & \text{R} \\
\text{R} & = \text{H, -CO}_2\text{Et}
\end{align*}
\]

Scheme VI.15

\[
\begin{align*}
\text{[Image: reaction scheme]} \\
\text{42} & \text{[hv]} \rightarrow \\
\text{43} & \text{[image: product scheme]} \\
\text{44} & \text{[image: product scheme]}
\end{align*}
\]

Scheme VI.16

\[
\begin{align*}
\text{[Image: reaction scheme]} \\
\text{[image: product scheme]} & \text{[image: product scheme]}
\end{align*}
\]

Scheme VI.17

\[
\begin{align*}
\text{[Image: reaction scheme]} \\
\text{[image: product scheme]} \\
\text{[image: product scheme]}
\end{align*}
\]
Scheme VI.17 (contd)

\[ \begin{align*}
12 + 49 & \rightarrow C_5H_5N-CH-CO_C_6H_5 \quad \text{cleavage} \\
& \rightarrow \quad C_5H_5N-CH-CO_C_6H_5 \\
& \rightarrow \quad \text{H}_5C_6O_C_5H_5 \\
& \rightarrow \quad \text{C}_5H_5N-CH-CO_C_6H_5 \\
\end{align*} \]

Scheme VI.18

\[ \begin{align*}
C_5H_5N-CH-CO_R & \xrightarrow{R'X} C_5H_5N-CH-CO_R \\
& \xrightarrow{\text{Red.-HX}} R'CH_2C=CH + C_5H_5N \\
\end{align*} \]

Scheme VI.19

\[ \begin{align*}
N-CH-CO_R + R'COX & \rightarrow N-CH-CO_R \\
& \xrightarrow{\text{base}} N-CH-CO_R \\
\end{align*} \]

Scheme VI.20

\[ \begin{align*}
C_5H_5N-CH=C-SCH_3 & \xrightarrow{\text{PhCO}_2O} C_5H_5N-CH=C-SCH_3 \\
& \xrightarrow{\text{base}} C_5H_5N-CH=C-SCH_3 \\
& \xrightarrow{\text{PhCO}_2O} C_5H_5N-CH=C-SCH_3 \\
\end{align*} \]

Scheme VI.21

\[ \begin{align*}
\text{C}_5H_5N-CH=COC_6H_5 + \text{(C}_6H_5CO)_2O & \rightarrow \text{C}_5H_5N-CH=COC_6H_5 \\
& \xrightarrow{\text{base}} \text{C}_5H_5N-CH=COC_6H_5 \\
& \xrightarrow{\text{PhCO}_2O} \text{C}_5H_5N-CH=COC_6H_5 \\
& \xrightarrow{\text{PhCO}_2O} \text{C}_5H_5N-CH=COC_6H_5 \\
& \xrightarrow{\text{PhCO}_2O} \text{C}_5H_5N-CH=COC_6H_5 \\
\end{align*} \]
2.4 Acylation

Cycloimmonium-ylides (55), due to strong nucleophilicity of the ylide carbanion, can be easily acylated by a suitable acylating agent (Scheme VI.19). However, the course of the reaction varies with the nature of acylating agent used. Thus, pyridinium-ylide (56) with benzoyl chloride led to the O-acylated (57) and S-acylated products (58), whereas with benzoic anhydride only C-acylated products (59) are obtained (Scheme VI.20).

Similarly, the interaction of the isoquinolinium-ylides (60) with benzoic anhydride led to the formation of C-acylated products (61) (Scheme VI.21).

2.5 Arylation

Unlike alkylation reactions, the arylation of cycloimmonium-ylides is comparatively difficult due to diminished reactivity of aryl halides. However, Reusching and Krohnke reported that quinolininium-ylides (62) when subjected to arylation by picryl chloride (63) forms through an intermediate (64) a red coloured product to which structure is assigned. The same on treatment with concentrated sulfuric acid undergoes debenzoylation resulting in the formation of 8,10-dinitrosoindolo(2,1-a)-quinoline (66) (Scheme VI.22).

Similarly, pyridinium and isoquinolinium-ylides (67a,b) also react 'in situ' with picryl chloride (63) in alkaline media
Scheme VI.22

62 + 63 → base → 64
- HBr - HCl

Scheme VI.23

67a-b + (O₂)₃ C₆H₂ Cl → 63

67a = C₅H₂N
b = C₉H₇N (isoq.)

Piperidine

- HNO₂

69a-b
to afford deep coloured products to which structures $68a, b$ were assigned. Furthermore, it was observed that the products $(68a, b)$ on their treatment with piperidine lose a molecule of nitrous acid, thus leading to the formation of indolizines $69a, b$ (Scheme VI.23).

2.6 Reaction with Aldehydes

Pyridinium-ylides react with aldehydes to afford aldol type products as a pyridinium ethanolic salt (70) \textsuperscript{66, 67} (Scheme VI.24). Howe and Ratts \textsuperscript{68} reported the deuterium exchange studies in the piperidine catalyzed condensation of N-methylpyridinium iodide (71) with aromatic aldehydes and observed that N-(2-hydroxy-2-phenylethyl)pyridinium iodide (73) is formed along with 2-(α-hydroxybenzyl)-1-methylpyridinium iodide (72) (Scheme VI.25).

Pyridinium-ylides, generated from pyridinium salt (74) having strong electron withdrawing groups readily react with aromatic aldehyde in the presence of pyridine to afford vinylpyridinium salts (75) \textsuperscript{69} (Scheme VI.26).

Pyridinium-ylides, when treated with aromatic aldehydes in the presence of ammonia, undergo Mannich type of condensation to afford pyrimidines. Thus, phenacylidene pyridinium-ylide (76) reacts with aromatic aldehydes in the presence of glacial acetic acid and ammonia to afford triarylpyrimidines (77) \textsuperscript{69} (Scheme VI.27).

Unlike pyridinium-ylide, there are very few reports concerning the reaction of aromatic aldehydes with isoquinolininium-ylides.
Scheme VI.24

\[
\text{C}_5\text{H}_5\text{N} - \text{CH} - R' + \text{Ar} \cdot \text{CHO} \rightleftharpoons \text{C}_5\text{H}_5\text{N} - \text{CH} = \text{CH} - \text{Ar} \quad 70
\]

Scheme VI.25

\[
\text{C}_5\text{H}_5\text{N} - \text{CH}_2R + \text{Ar} \cdot \text{CHO} \rightleftharpoons \text{C}_5\text{H}_5\text{N} - \text{C}=\text{CHAr} \quad 75
\]

Scheme VI.26

\[
\left[ \begin{array}{c}
\text{R} = -\text{CN} \text{ or } -\text{CH}_3
\end{array} \right]
\]

Scheme VI.27

\[
\text{C}_5\text{H}_5\text{N} - \text{CH} + 2\text{Ar} \cdot \text{CHO} + 2\text{NH}_3 \xrightarrow{\text{AcOH}} \text{H}_6\text{C}_6 \quad 77
\]
However, Ahlbrecht et al. were first to report the reaction of semistabilized isoquinolinium-ylide (78) with aromatic aldehydes to afford corresponding isoquinolinium ethanols (80) via intermediacy of compound 79 (Scheme VI.28).

2.7 Reaction with Ketones

The reactions of cycloimmonium-ylides with carbonyl functions are not only restricted to the aldehydes but the same are also found to be quite reactive towards ketones as evidenced by their reactions with tropone, 1,2-diketone and quinone etc. However, the mode of reaction depends upon the nature of the ylide as well as on the ketone employed for the purpose. Thus, phenacylidenepyridinium-ylide (81) reacts with tropone to afford 2-hydroxy-2-phenyl-3-phenacyl-2H-cyclohepta(b)furan (82) (Scheme VI.29).

Contrary to this, pyridinium-ylides may take a different course when they are made to react with 1,2-diketone. This approach was proved to be highly indispensable in the syntheses of heterocycles. Noteworthy in this respect, is the synthesis of 2,3-disubstituted dehydroquinolizinium salt (84) through the condensation of 2-picolinium salt (83), carrying an activated N-pyridinoylmethyl group, with 1,2-diketone in the presence of weak base (Scheme VI.30). This reaction in the later stage proved to be highly useful for the comprehensive synthesis of quinolizine ring particularly useful in building up of alkaloid
Scheme VI. 28

\[
R^1 = -C_6H_5; -C_6H_4\cdot NO_2 (4)
\]

Scheme VI. 29

Scheme VI. 30

Scheme VI. 31
nucleus. Pyridinium-ylides were also found to undergo reaction with quinone resulting in the formation of heterocycles, which, in turn, depends, upon the cyclization agent. Thus, pyridinium-ylide reacts 'in situ' with 2-chloro-1,4-naphthoquinone following Michael type of addition to afford an intermediate (85) which on cyclization in the presence of zinc and acetic acid gives benzocoumarine (86). However, benzocinnone (87) is the exclusive product of the reaction when hydrazine hydrate is employed for bringing about aza ring closure of the intermediate product (85)\(^73,74\) (Scheme VI.31).

2.8 Reaction with \(\alpha,\beta\)-Unsaturated Ketones

A variety of N-heterocycles as well as aromatic hydrocarbons may be synthesized by the reaction of cycloiminonium-ylides with \(\alpha,\beta\)-unsaturated ketones owing the different course of the reaction, which, in turn, depends both upon the experimental conditions as well as on the nature of ylide employed for the purpose. Thus phenacylidene pyridinium-ylide and their isoquinolinium counterparts (88a,b), generated 'in situ' from their respective precursors, readily add on \(\alpha,\beta\)-unsaturated ketones to afford pentane 1,5-dionylpyridinium and isoquinolinium derivatives (89a-b) which on treatment with a mixture of glacial acetic acid and ammonium acetate undergo aza ring closure to afford 2,4,6-trisubstituted pyridines (90)\(^71,75,76\) (Scheme VI.32) whereas -pyridones\(^77\) were the exclusive products of Michael addition
followed by cyclization of N-(aminoformylmethylene)pyridinium-ylide (91) onto \(\alpha, \beta\)-unsaturated ketones (Scheme VI.33). Krohnke et al.\(^75\) have applied this method in the syntheses of a variety of useful pyridines and pyridones.

Pyridinium salts (93) with active methylene group, when treated with substituted benzalacetophenones (94) in the presence of anhydrous zinc chloride, afforded polycyclic aromatic hydrocarbons (95)\(^{74,78}\) (Scheme VI.34).

2.9 Reaction with Nitroso Compounds

Krohnke et al.\(^79-80\) were first to report that the cycloimmonium-ylides are capable of undergoing reaction with nitroso compounds to afford nitrone derivatives. Thus, the pyridinium phenacylides and their isoquinolinium counterparts (96a,b) generated from their precursors, on reaction with nitroso benzene afforded similar product, \(\alpha\)-benzoyl-N-phenyl-nitrone (97) in spite of different onium centre (Scheme VI.35).

The reaction of 4-bromophenacylpyridinium ylide (98) with \(\alpha\)-nitroso-\(\beta\)-napthol and \(\alpha\)-nitroso-\(\beta\)-naphthylamine was found to afford naphthoxazole derivative (99) and benzoquinoxaline-N-oxide derivative (100) respectively\(^81\) (Scheme VI.36).

2.10 Reaction with Carbon-Sulfur Bond

Phenacylidenepyridinium-ylide (101) reacts with carbon disulfide to afford S-betaine (102) which on treatment with
Scheme VI.32

\[ R^1 \text{X} + \text{RCO}_2 \text{R}^3 \rightarrow [\text{R}^1 \text{X}] + \text{R}^1 \text{X} - \text{R}^3 \]

88 a-b

88 89 a X = C_5H_5N
b X = C_9H_7N

Scheme VI.33

C_5H_5N\text{CH} - \text{CONH}_2 + C_6H_5\text{CH} = \text{CH} - \text{C}_6H_5 \rightarrow \text{92}

Scheme VI.34

H_5C_5N\text{CH}_2 + \text{ArCH} - \text{C}_6H_5 \rightarrow \text{ZnCl}_2 \text{200°C} \rightarrow \text{95}

Scheme VI.35

\[ \text{X-CH-CO}_2 \text{C}_6H_5 + \text{Ar-N}=\text{O} \rightarrow [\text{X-CH-CO}_2\text{C}_6H_5] \]

96 a-b

96 a X = C_5H_5N
b X = C_9H_7N (isoq.)
methyl iodide gives S-alkylated product (103)\textsuperscript{82,83} (Scheme VI.37). On the other hand, phenacylideneisoquinolinium-ylide (104) reacts with carbon disulfide in alkaline medium to afford 2-mercapto-3-benzoylthiazolo [2,3-a] isoquinolinium ring system (105) proving stronger positivation of 1st position in comparison to the above mentioned pyridinium-ylide (Scheme VI.38).\textsuperscript{84}

2.11 Reaction with Nitrile-imine

It has been observed that reaction of cycloimmonium-ylides with dipolar species takes an interesting course mainly due to the fact that they are polarisable molecules and their reactions are markedly influenced by the nature of solvent and base employed for their generation. Thus, pyridinium phenacyllyde, when generated 'in situ' from sodium methoxide in dioxane-methanol medium, reacts with nitrile imine to afford the adduct (106). On the other hand, reaction follows an entirely different course when triethylamine in chloroform is used as base and gives a mixture of products (107) and (108) (Scheme VI.39).

2.12 Reaction with Nitromethane

Keil and Krohnke\textsuperscript{86} studied the cyclization reaction of isoquinolinium-ylides (109a) generated 'in situ' from the respective precursors by using sodium carbonate as dehydro-halogenating agent and reported the formation of two products (113a) and (114) via intermediacy of (112), formed by dehydration of another intermediate (111), formed by the internal
Scheme VI.36

\[
\begin{align*}
\text{N-CH-COC}_6\text{H}_4\text{Br}^{98} + \text{C}_10\text{H}_6\text{ON} &\rightarrow \text{C}_10\text{H}_6\text{ON-CH-COC}_6\text{H}_4\text{Br}^{100} \\
\text{N-CH-COC}_6\text{H}_4\text{Br}^{98} + \text{C}_10\text{H}_6\text{NOH} &\rightarrow \text{C}_10\text{H}_6\text{NOH-CH-COC}_6\text{H}_4\text{Br}^{100} \\
\text{N-CH-COC}_6\text{H}_4\text{Br}^{99} + \text{C}_10\text{H}_6\text{NH}_2 &\rightarrow \text{C}_10\text{H}_6\text{NH}_2-\text{CH-COC}_6\text{H}_4\text{Br}^{100}
\end{align*}
\]

Scheme VI.37

\[
\begin{align*}
\text{C}_10\text{H}_5\text{N-CH-COC}_6\text{H}_5^{101} + \text{C}_10\text{H}_6\text{CS=S} &\rightarrow \text{C}_10\text{H}_5\text{N-CH-\text{COC}_6\text{H}_5}^{102} \\
\text{C}_10\text{H}_5\text{N-CH-COC}_6\text{H}_5^{101} + \text{C}_10\text{H}_6\text{NSSCH}_3 &\rightarrow \text{C}_10\text{H}_5\text{N-CH-COC}_6\text{H}_5^{103}
\end{align*}
\]

Scheme VI.38

\[
\begin{align*}
\text{C}_10\text{H}_7\text{N-CH-COC}_6\text{H}_5^{104} + \text{CS}_2 &\rightarrow \text{C}_10\text{H}_7\text{N-CH-COC}_6\text{H}_5^{105} \\
\text{C}_10\text{H}_7\text{N-CH-COC}_6\text{H}_5^{105} -2[\text{H}] &\rightarrow \text{C}_10\text{H}_7\text{N-CH-COC}_6\text{H}_5^{105}
\end{align*}
\]
aldolization of primary reaction product (110). However, the compound (113b) was the exclusive product of the reaction of nitromethane and isoquinolinium-ylide when triethylamine was used as dehydrohalogenating agent instead of sodium carbonate (Scheme VI.40).

It is interesting to note that neither N-acetonyl nor N-phenacylidene pyridinium-ylides, themselves, are capable of undergoing similar cyclization reactions with nitromethane as isoquinolinium-ylides, but the substitution of cyano-group at position 3 in the pyridinium ring makes the pyridinium-ylide as reactive as isoquinolinium-ylide. Thus pyridinium-ylide (115) reacted with nitromethane resulting in the formation of indolizine derivative (166) following the same reaction sequence (Scheme VI.41).

2.13 Reaction with Diazonium Salts

Substituted aroylmethylene pyridinium-ylides (101) are capable of undergoing reaction 'in situ' with diazonium salts, obtained from aromatic acids to afford 1,4-dihydro-1,2,4,5-tetrazines (117) in the presence of sodium acetate (Scheme VI.42).

2.14 Reaction with Amino Compounds

Cycloimmonium-ylides are capable of undergoing reaction with amino-compounds in a variety of ways depending on the chemical nature of amino-compounds and ylide employed for the purpose.
Scheme VI. 39

\[
\begin{align*}
\text{Et}_3 \text{N} & \quad \text{CHCl}_3 \\
\text{CH}_3 \text{COO} & \text{C}_\text{N} \text{H}_2 \text{COR} \quad \text{Ph} \\
\text{CH}_3 \text{COO} & \text{C} \text{N} \text{N} \text{NH} \text{Ph} \\
\text{CH}_3 \text{COO} & \text{C} \text{N} \text{NH} \text{Ph} \\
\end{align*}
\]

Scheme VI. 40

\[
\begin{align*}
\text{Br} & \quad \text{base} \\
\text{Ph} & \quad \text{CH}_2 \text{COR} \\
\text{CH}_3 \text{NO}_2 & \\
\text{H} & \quad \text{HOH} \\
\end{align*}
\]
Thus, pyridinium-ylide (118a) with aliphatic amines forms respective imidopyridinium salt (119). On the other hand, 3-cyanosubstituted pyridinium-ylide (118b) due to strong positive charge at α-position, undergoes cyclization reactions with hydrazine hydrate to afford cyclopyridinotriamine (120) (Scheme VI.43).

Aroylmethylenepyridinium-ylides and their isoquinolininium counterparts (96a-b) react 'in situ' with aromatic amines to afford indole derivatives (121) in the presence of N,N-dimethylaniline under reflux temperature. However, ylides when treated with o-phenylenediamine in boiling acetic acid affords 2-phenylbenzimidazole derivatives (122) (Scheme VI.44).

On the other hand, phenacylidenequinolininium-ylides (123) on their reaction with aromatic amines and o-phenylenediamine follow a different course of reaction due to the presence of strong positive charge at α-position and thus give rise to the formation of dihydroimidazo[1,2a]quinolinium system (124a,b) (Scheme VI.45). However, isoquinolininium ylides (125) reacts 'in situ' with hydrazine hydrate to afford triazinophenantridine derivatives (126) (Scheme VI.46).

Phenacylideneisoquinolininium-ylides (127) and their quinolinium counterparts (128) are capable of undergoing cyclization reactions with ammonia or ammonium acetate in glacial acetic acid to afford 2-phenyl-2,3-dihydroimidazoisoquinoline (129) and
Scheme VI. 41

\[ \text{Scheme VI. 42} \]

\[ \text{Scheme VI. 43} \]

\[ \text{Scheme VI. 44} \]
2-phenyl-1,2-dihydroimidazo[1,2a]quinoline (130) showing strong positivation of onium groups in comparison to that of pyridinium ylides (Scheme VI.47).

2.15 Reaction with Isocyanates and Isothiocyanates

Aroylmethyleneopyridinium, quinolinium and isoquinolinium-ylides, due to strong nucleophilic character of the ylide carbanion, afforded respective carbanion disubstituted ylide (133) on reaction with phenylisocyanate and isothiocyanate (131a,b) via intermediacy of betaine derivative (132)\textsuperscript{55,96} (Scheme VI.48).

Later on, Soto and Ohta\textsuperscript{96} reported that toluene solution of betaine derivative (134a,b), formed by the reaction of phenacylideneisoquinolinium-ylide with phenylisocyanate and phenylisothiocyanate (131a,b), when heated under reflux for a longer time in the presence of air gave the mesionic adducts (135a,b) via a dehydrogenating cyclization. The compounds (135a,b) could easily be methylated with methyl iodide to afford respective methyl derivatives (136a,b) (Scheme VI.49).

2.16 Cycloaddition Reactions of Cycloimmonium Ylides

Pyridinium, quinolinium and isoquinolinium-ylides undergo various types of cycloaddition reactions to afford heterocyclic compounds which are difficult to prepare via other synthetic routes.
Scheme VI.45

\[ \text{Scheme VI.45} \]

\[
\begin{align*}
\text{123} & \quad \text{+} \quad \text{124a} \quad \text{124b} \\
\text{123} & \quad \text{CH COPh} \quad \text{NH}_2 \quad \text{NH}_2 \\
\end{align*}
\]

Scheme VI.46

\[ \text{Scheme VI.46} \]

\[
\begin{align*}
\text{125} & \quad \text{NH}_2 \cdot \text{NH}_2 \cdot \text{H}_2\text{O} \\
\end{align*}
\]

Scheme VI.47

\[ \text{Scheme VI.47} \]

\[
\begin{align*}
\text{127} - \text{128} & \quad \text{130} \\
\end{align*}
\]
(i) **Dimerization reaction**

Isoquinolinium salts (137) in basic tetrahydrofuran or chloroform are converted into dimers (139). The formation of these dimers are attributed into a (3+3) cycloaddition of intermediate ylide (138) showing 1,3 dipolar nature (Scheme VI.50).

(ii) **(3 + 2) Dipolar cycloaddition reactions**

(a) **Reactions of monosubstituted ylides with acetylenic derivatives** - Monosubstituted pyridinium ylides (140) undergo cycloaddition reactions with acetylenic dipolarophiles (141) giving indolizines (143). The primary addition product (142) easily aromatise either by hydrogen transfer to the dipolarophile or by dismutation (Scheme VI.51).

The isoquinolinium-methylene (144) react almost in a similar manner with acetylenic dipolarophiles and given benzoindolizines (147) formed by the aromatization of the intermediates dihydroindolizines (145, 146) (Scheme VI.52). The mono-substituted quinolinium-ylides behave in exactly similar manner to that of pyridinium-ylides.

(b) **Reaction of disubstituted ylides with acetylenic dipolarophiles** - The disubstituted ylides give (3+2) type of cycloaddition reactions because of the remaining negative charge on the ylide carbon. Previously it has been reported that in disubstituted ylides, the negative charge of the ylide carbon atom is
Scheme VI.48

\[ \text{N-CHCOR} + \text{C}_6\text{H}_5\text{-N=C=X} \rightarrow \text{N-CHCOR} \]

\[ \text{C}_6\text{H}_5\text{-N=C=X} \]

\[ \text{N-CHCOR} \]

Scheme VI.49

\[ \text{127} + \text{131} \rightarrow \text{Isoq-CH-COPh} \]

\[ \text{C}_6\text{H}_5\text{N-C=X} \]

\[ \text{134a-b} \]

\[ \Delta -2[H] \]

\[ \text{135a-b} \]

\[ \text{CH}_3 \]

\[ \text{136a-b} \]

Scheme VI.50

\[ \text{2} \]

\[ \text{137} \]

\[ \text{138} \]

\[ \text{139} \]

Scheme VI.51

\[ \text{140} + \text{141} \]

\[ \text{142} \]

\[ \text{143} \]
delocalized on the substituents but according to theoretical calculations, some negative charge remains on the atom. This explains which ylidic compounds give (3+2) type of cycloadditions.

The pyridinium-methylides (148) react with DMAD and lead to the formation of indolizines (150) by the loss of a hydrogen and an ylide substituent from intermediate (149) (Scheme VI.53). Isoquinolinium-methylides (151) also react with acetylenic derivatives giving indolizine derivative (154). Dihydroindolizines 152 and 153 are the isolable reaction intermediates (Scheme VI.54). The quinolinium-ylide (155), generated 'in situ', on reaction with DMAD in the presence of sodium hydride gives (3+2) cycloadduct (156) (Scheme VI.55).

(c) Reaction with ethylenic compounds- Mono- and dicarbethoxy isoquinolinium methylides (157 & 159) react with olefins in the presence of methanol, leading to the formation of tetrahydroindolizines (160) with the elimination of an alkyl carbonate molecule from the intermediate (158) (Scheme VI.56).

(iii) (5+2) Dipolar cycloaddition reactions

The charge distribution of highly electron withdrawing disubstituted ylide is such that they give a 1,5-dipole system (161). Zugravescu et al. have isolated oxazepinic derivatives (162) during the reaction of dicarbethoxyisoquinolinium methylides (161) with DMAD in benzene (Scheme VI.57).
Scheme VI. 52

\[
\begin{align*}
\text{C}_9\text{H}_7\text{N}^+\text{CHR} & \xrightarrow{\text{R}^1\text{C}≡\text{C}-\text{R}^2} [\text{145}] \\
& \xrightarrow{146a} [\text{146b}] \xrightarrow{147}
\end{align*}
\]

Scheme VI. 53

\[
\begin{align*}
\text{C}_{5}\text{H}_{5}\text{N}^+\text{CHR} & \xrightarrow{\text{DMAD}} [\text{149}] \\
& \xrightarrow{-\text{H},\text{R}^1} [\text{150}]
\end{align*}
\]

Scheme VI. 54

\[
\begin{align*}
\text{151} & \xrightarrow{\text{R}^1\text{C}≡\text{C}-\text{R}^2} [\text{152}] \\
& \xrightarrow{\text{153}} [\text{154}]
\end{align*}
\]
(iv) **Dipolar cycloaddition reactions**

Cyanocarbethoxy or carbomethoxy pyridinium ylides (163) react with DMAD in the presence of acetonitrile to give ylide (164)\(^{112}\) (Scheme VI.58).

(v) **Cycloaddition involving intermediate formation of an aziridine**

The dicarbomethoxyisoquinolinium-methyldiene (165), on its reaction with dicyanoacetylene or DMAD, afford the product (166) in very low yield. The formation of (168a-b) from the aziridine intermediate (167)\(^{113-115}\) is the main part of the reaction (Scheme VI.59).

2.17 **Metallation Reactions of Cycloimmonium Ylides**

Pyridinium ylides, a class of cycloimmonium ylides, being the versatile ligands for metals in their various oxidation states, coordinate with metal ions as neutral ligands to form a C-bond between the ylide carbon and the metal atom and thus lead to the formation of ylide-metal complexes.\(^{116}\)

The mode of reaction and the formation of complexes depend upon the reaction conditions (solvent and reagents). For example, pyridinium-phenacyllyde on its reaction with various metal halides affords ylide metal complexes (169) (Scheme VI.60).
Scheme VI.55

\[ \text{R} = \text{CO}_{\text{Me}}, \text{COPh} \]

Scheme VI.56

\[ \text{R} = \text{OH} \]

Scheme VI.57

\[ \text{DMAD} \]

Scheme VI.58

\[ \text{DMAD} \]
2.18 Some Spectral Properties of Pyridinium Ylides

Krohnke and Bohlmann\textsuperscript{117} classified as C-betaines, the ylides having maxima at 440-460 m\(\mu\) and as O-betaines those with maxima 300-330 m\(\mu\). They concluded that the O-betaines included pyridinium dibenzoyl methylylide and the C-betaines included all phenacylides. The spectra of pyridinium cyclopentadienylylide in several solvents have been studied.\textsuperscript{118}

Similarly, the visible absorption band of pyridinium ylide is attributed to an intramolecular charge-transfer transition (Scheme VI.61).

(a) IR Spectra

IR spectra of the ylides have been measured in chloroform solution. The spectra are complex but also show strong ylide carbonyl absorption\textsuperscript{119-123} at low frequency. Thus the ylide (170 (R=R'=Ph) absorbs near 1490 cm\(^{-1}\) and the ylide (171) (R=Ph) near 1500 cm\(^{-1}\). This presumably indicates the structure (172) makes notable contribution to the resonance hybrids.

The ylides (173) and (174) absorbed strongly at 2166 cm\(^{-1}\) and 2185 cm\(^{-1}\) respectively which clearly indicates that structure (174 & 176), respectively contribute to the resonance hybrids.

(b) NMR Spectra

The most interesting feature of the NMR spectra of the pyridinium ylides is the variation in the chemical shift of
Scheme VI.59

\[ \text{R}^1\text{C} \equiv \text{C} \rightarrow \text{R}^2 \rightarrow \text{H}_3\text{C} \text{O}_2\text{C} \]

\[ \text{Me}_2\text{C} \]

\[ \text{R}^1 = \text{R}^2 = \text{CN} \]

\[ \text{R}^1 = \text{R}^2 = \text{CO}_2\text{CH}_3 \]

Scheme VI.60

\[ \text{C}_5\text{H}_5\text{N} + \text{CHCOC}_6\text{H}_5 + \text{HgCl}_2 \rightarrow \text{Hg}_2 \left( \text{C}_5\text{H}_5\text{N} - \text{CH} \cdot \text{CO}_2\text{C}_6\text{H}_5 \right)_2 \text{Cl}_4 \]

Scheme VI.61

\[ \text{DIPOLE} \]

\[ \text{R} - \text{CO} - \text{C} - \text{COR}^1 \]

\[ \text{R} - \text{CO} - \text{C} - \text{Py} \]

\[ \text{Ph} - \text{CO} - \text{C} - \text{Py} \]

\[ \text{Ph} - \text{CO} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]

\[ \text{EtOOC} - \text{C} - \text{Py} \]
-proton of the pyridine ring. In the perchlorate salt of \(177\), these protons absorb at \(\delta \ 9.21\) (d\(_6\)-dimethylsulfoxide) but at \(\delta \ 8.63\) (deutero chloroform) in the corresponding ylide:

\[
\text{EtOOC-CH-COOEt} \\
\text{Py}^+ \text{ClO}_4^-
\]

Similar values were observed for \(\alpha\)-protons in the ylide \(170\) \((R=\text{Me}, R'=\text{Ph})\) and \(172\) \((R=R'=\text{Ph})\). This shift is to be expected because of the overall increase in electron density. However, in the cyano-ylides \(173\) and \(175\), the \(\alpha\)-proton absorbed well downfield at \(\delta \ 9.23\) and \(\delta \ 9.31\) respectively but the \(\beta\)- and \(\gamma\)-protons are not deshielded. This effect may also be explicable in terms of contribution of the structures \(174\) and \(176\).

2.19 **Some Important Physical Properties of Cycloimmonium Ylides**

Surpateanu and Rucinschi\(^{124}\) have shown that some isoquinolinium ylides are highly sensitive acid-base indicator which works on basis of the reversibility of the conversion reaction of deeply coloured ylide to the colourless quaternary isoquinolinium salts.

Surpateanu et al.\(^{125,126}\) have also studied the semiconducting properties of some isoquinolinium ylides. The electrical conductivity of organic semiconductors is expressed by the
equation:

\[ \sigma = \sigma_0 e^{-\left(\frac{ET}{kT}\right)} \]

where \( \sigma \) is the electrical conductivity corresponding to the absolute temperature \( T \) at which measurement was performed. \( \sigma_0 \) is electrical conductivity for \( T \rightarrow \infty \), \( k \) is Boltzmann's constant, \( ET \) is so called thermal activation energy. The dependence of the electrical conductivity upon temperature for ylidic compounds proves the semiconducting character.
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