UNIT 9 CARBENES, NITRENES AND BENZYNES

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9.1 INTRODUCTION

In the earlier units in this course, you have learnt that certain organic reactions proceed via electron-deficient intermediates (carbocations) while in others, electron-rich intermediates (carbanions) are involved. In this unit, we will study some other types of intermediates which are commonly encountered in molecular rearrangements, namely the carbenes, nitrenes and benzyynes. Carbenes and nitrenes are electron-poor species having a sextet of electrons on carbon or nitrogen. The simplest benzyne, benzyne (C₈H₆) is dehydrobenzene which is postulated as an intermediate in nucleophilic substitution of aryl halides. These are all highly reactive intermediates. Their reactions are often marked by selectivity and interesting from the mechanistic view. Still another type of reaction intermediates, the free radicals will be taken up in the next unit.

Objectives

After studying this unit, you should be able to:

- outline different methods for generation of carbenes, nitrenes and benzyynes,
- discuss the structures and stabilities of carbenes, nitrenes and benzyynes, and
- explain the reactivity of these reaction intermediates and discuss their important reactions.

9.2 CARBENES

Carbenes are neutral tervalent carbon intermediates with only a sextet on carbon. The simplest carbene is methylene (CH₂), in which the carbon atom has only six electrons, two each in the two carbon-hydrogen covalent bonds and two unshared. As such, methylene is electrically neutral as there is no formal charge on carbon (compare with carbocations and carbanions). However, with only a sextet on the carbon, of which two are unshared electrons, carbenes are expected to be intensely reactive.
One or both hydrogen atoms in methylene may be replaced by halogen, alkyl, phenyl or acyl groups. The reactions of dichlorocarbene (dichloromethylene) are quite common and would be described later in this unit. The species (CH₂)₂C is known as dimethylcarbene or isopropylidene. Dimethylcarbene is isoelectronic with boron trimethyl. The central carbon and boron atom in each is electron-deficient with only a sextet. Therefore both of them act as electrophiles.

### 9.2.1 Generation

Since carbenes are highly reactive, they are generated in situ, i.e., in the reaction itself. The following methods for their generation are common:

1. **Photolysis or thermolysis of diazomethane or ketene:***
   
   \[
   [\text{CH}_2\equiv\text{N}=\text{N}] \underset{\text{hv or } \Delta}{\longrightarrow} \text{CH}_2\equiv\text{N} + \text{N}_2
   \]

   \[
   \text{CH}_2\equiv\text{C} \equiv \text{O} \underset{\text{hv or } \Delta}{\longrightarrow} \text{CH}_2 + \text{CO}
   \]

   You would notice that diazomethane and ketene are isoelectronic as are N₂ and CO.

2. **Elimination or 1,1-elimination from haloalkanes:** This happens when a haloalkane is treated with a very strong base like potassium tert-butoxide (2-methyl propoxide) or n-butyl lithium.

   \[
   \text{CHCl}_3 + \text{tert-BuOK} \xrightarrow{\text{DSMO}} \text{CCl}_2 + \text{tert-BuOH} + \text{KCl}
   \]

   \[
   \text{CH}_2\text{Cl}_2 + n-\text{BuLi} \xrightarrow{} \text{CHCl} + n-\text{BuH} + \text{LiCl}
   \]

   In the above reactions, both a proton and a chloride ion are lost from the same carbon atom. Hence such reactions are called as α-elimination or 1,1-elimination, (compare with β-elimination or 1,2-elimination described in Unit 7).

3. **Treatment of (methylene iodide) with zinc, in the presence of copper or silver, in ether solution:**

   \[
   \text{CH}_2\text{I}_2 + \text{Zn} \xrightarrow{\text{Cu or Ag}} \text{I}^-\text{CH}_2^-\text{Zn}^-\text{I} \xrightarrow{} \text{CH}_2 + \text{ZnI}_2
   \]

   This is known as Simmons-Smith reaction. The organic compound CH₂ZnI₂ having a masked carbene is called a carbenoid, i.e., carbene like.

4. **Thermal decomposition of sodium trichloroacetate:**

   \[
   \text{CCl}_3\text{COO}^+\text{Na}^- \xrightarrow{} \text{CO}_2 + \text{Na}^+\text{CCl}_3 - \text{NaCl} \xrightarrow{} \text{CCl}_2
   \]

   This is known as dichlorocarbene.
v) Thermal or photochemical decomposition of alkali metal salts of
p-toluene sulphonylhydrazones of aldehydes and ketones.

\[ R_2C \equiv N - NaSO_2Ar \xrightarrow{\text{Heat or Light}} R_2C \quad + \quad N_2 \quad + \quad NaSO_2Ar \]

sodium salt of
p-toluene sulphonyl
hydrazone

\[ \text{sodium benzene sulphonate} \]

9.2.2 Structure and Stability

The electronic spectra of carbenes show that there are two forms of carbenes: the singlet and the triplet. Let us see how we can account for this. As you know carbon has four low-energy orbitals, one 2s, and three 2p. In a carbene, two of these are used for bonding. Therefore, there are two low-energy orbitals available to accommodate the unshared electrons. If both these electrons go into one orbital, the spins must pair. If these two electrons go into different orbitals they will have parallel or unpaired spins. A carbene in the latter state would have a permanent magnetic moment and would exist in three closely grouped energy states, if it were placed in a magnetic field. Such a state is called the triplet state. The state, in which the electrons are paired, has no magnetic moment and exists in a single energy state when placed in a magnetic field. Hence it is called the singlet state. Singlet carbene is generated initially in photolysis of diazomethane, as in the preparation (i) above. It is usually formed in the liquid phase. Singlet carbene is less stable of the two. It has higher energy than the triplet carbene due to electron repulsion arising from pairing the two electrons in a single orbital. Singlet carbene is supposed to have a bent shape with RCR bond angle around 103-105°. Here the carbon is sp² hybridized.

\[ \text{Triplet carbene is formed in gas phase photolysis in the presence of an inert gas like nitrogen or argon. Since in triplet carbene, the unshared electron pair is not spin-paired, the two electrons with parallel spins are in separate p-orbitals. So triplet carbene behaves as a diradical. It is nearly linear in shape, with RCR bond angle around 136-180°, and the carbon atom is sp hybridised.} \]

\[ \text{Changeover from singlet to triplet state is called inter system crossing.} \]

\[ \text{Atoms with unshared pairs of electrons like halogen atoms stabilise carbenes. We can visualise the following type of resonance, which would stabilise a carbene.} \]

\[ \text{Phenyl groups can, similarly stabilise a carbene through resonance.} \]
9.2.3 Reactions

Carbenes usually undergo two types of reactions. These are cycloadditions and insertions.

Cycloaddition-Formation of a Ring

Reactions in which a reagent adds across a multiple bond to give a cyclic product are called cycloadditions. Thus, the reaction of bromoform with potassium tert-butoxide in the presence of trans 2-butene forms trans-dimethyl dibromocyclopropane. cis-2-Butene affords the corresponding cis-cyclopropane derivative under the same conditions. Here dibromocarbene is generated by the reaction of bromoform with tert-butoxide which then adds at the C=C bond of the alkenes.

\[
\text{CHBr}_3 + \text{tert-} \text{BuOCH}_2 \xrightarrow{+ \text{Br}_2} \text{CHBr}_3 + \text{tert-} \text{BuOH} + \text{KBr}
\]

The cycloaddition reactions also support the existence of two forms of carbene. For instance, it has been observed that photolysis of diazomethane in the presence of cis-2 butene gives only the cis-1,2-dimethylcyclopropane. It is presumed that in this reaction, the singlet methylene which is generated, attacks simultaneously both the double-bonded carbon atoms of the alkene in a concerted or nearly concerted manner. The overlap of the \(\pi\)-cloud of alkene with empty \(p\) orbital of methylene results in the formation of the cyclic intermediate (I). This results in a stereospecific addition, i.e. the cyclopropane formed has the same stereochemistry as the alkene. In this case both have cis-geometry. This reaction is an example of cis or syn addition, meaning that both the new bonds are formed on the same side or face of the alkene.

\[
\text{CH}_2\text{N}_2 \xrightarrow{\text{hv}} \text{CH}_2 + \text{N}_2 \\
\text{H} \quad \text{H} \quad \| \quad \text{CH}_3 \quad \text{CH}_3
\]

If the above reaction is carried out in the presence of an inert gas, the singlet methylene generated initially gets converted to the triplet state. This occurs due to intermolecular collisions. Triplet carbene acts as a diradical and adds to the alkene in two steps. The initial addition of the triplet carbene to one of the carbon atoms of the alkene gives an intermediate diradical. The latter has a life-time long enough to permit rotation about the central carbon-carbon bond. Collapse of the two types of intermediates \(a\) and \(b\) would give a mixture of cis and trans-1,2-dimethylcyclopropanes. It is clear that in this case stereospecificity would be lost. Compare this with stereospecific addition of singlet methylene which occurs in one step, in a concerted manner as described above.
The \textit{sym} addition of a carbene to a cyclic alkene gives a bicyclic product having \textit{cis} stereochemistry at the bridge-head. An illustrative example is the addition of chlorocarbene to cyclohexene.

\[
\text{CH}_2\text{Cl}_2 + n-\text{BuLi} \rightarrow \text{CHCl}_2
\]

\[
\text{dichloromethane} \quad \text{chlorocarbene}
\]

In some cases, the initial cycloaddition of carbene to cyclic molecules is followed by a ring opening process. The bond common to both rings of the bicyclic addition product gets cleaved. This process, thus, leads to ring expansion. A common example is the reaction of pyrrole with trichloromethane (chloroform) and caustic potash to give 3-chloropyridine, where a five membered ring gets expanded to a six-membered one.

\[
\text{CHCl}_3 + \text{KOH} \rightarrow \text{CCl}_2 + \text{KCl} + \text{H}_2\text{O}
\]

The conversion of a six-membered ring to a seven-membered ring product occurs in the formation of cycloheptatriene carboxylate from the photolysis of diazoacetic ester in the presence of benzene.

\[
\text{N}_2\text{CHCO}_2\text{C}_2\text{H}_5 \xrightarrow{\text{hv}} \text{CHCO}_2\text{C}_2\text{H}_5
\]
SAQ 1

It is interesting to note that when photolysis of diazomethane is carried out in liquid cis or trans 2-butene, the addition is stereoselective and stereospecific. On the other hand when photolysis is carried out in gaseous 2-butene, the addition is non-stereoselective and non-stereospecific. Explain.

Insertions

It has been observed that the activated carbenes generated by photolysis of diazomethane or ketene undergo insertion reactions with alkanes. Methylene, for example, gets inserted into the carbon-hydrogen bond of methane to give ethane.

\[
\text{CH}_2\text{N}_2 \xrightarrow{\text{hv}} :\text{CH}_2 \\
\text{N}_2 \\
\text{CH}_3\text{H} + :\text{CH}_2 \xrightarrow{\text{hv}} \text{CH}_3\text{H} \xrightarrow{\text{hv}} \text{CH}_3\text{CH}_3
\]

With propane, a mixture of butane and 2-methylpropane is formed. Carbene, in this case, may be generated by photolysis of ketene,

\[
\text{CH}_2\text{C}==\text{O} \xrightarrow{\text{hv}} :\text{CH}_2 \\
\text{CO} \\
:\text{CH}_2 + \text{CH}_3\text{CH}_2\text{H} \xrightarrow{\text{hv}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 \\
65\% \\
:\text{CH}_2 + \text{CH}_3\text{CH}==\text{CH}_3 \xrightarrow{\text{hv}} \text{CH}_3\text{CH}==\text{CH}_3 \\
37\%
\]

Such insertion reactions with higher alkanes lead to a complex mixture of isomeric products.

It is supposed that the back lobe of the C-H bond is involved in insertion reactions leading to an inversion of configuration.

\[
\text{CH}_2 \xrightarrow{\text{hv}} \text{CH}_3\text{CH}_3
\]

This is elegantly illustrated by photolysis of diazomethane in the diacetate of trans-1,2-cyclopentanediol. In the product, the two acetate groups have a cis configuration. Obviously inversion of configuration has taken place during the insertion reaction.
Methylene also inserts into benzene to form cycloheptatriene.

\[
\text{cycloheptatriene}
\]

Insertion of carbenes also occurs into oxygen-hydrogen bonds of alcohols and acids. In fact this is one of the most convenient methods for preparing methyl ethers or esters. The alcohol or acid has just to be treated with an ethereal solution of diazomethane.

\[
\begin{align*}
\text{CH}_3\text{N}_2 & \rightarrow \text{CH}_2 + \text{N}_2 \\
\text{RCH}_2\text{O} - \text{H} + \text{CH}_2 & \rightarrow \text{RCH}_2\text{O} - \text{CH}_3 \\
\text{RCH}_2\text{COOH} + \text{CH}_2 & \rightarrow \text{RCH}_2\text{COOCH}_3
\end{align*}
\]

Unlike the C-H bond O-H bond is a polar bond and the reaction is supposed to proceed by the following mechanism.

i) \( \text{R}-\text{C} \overset{\text{O}}{\text{O}} - \text{H} + \text{CH}_2\text{N} \equiv \text{N} \rightarrow \text{R}-\text{C}^- \overset{\text{O}}{\text{O}} + \text{CH}_3\text{N} \equiv \text{N} \)

\( \text{ii)} \)

Similar insertion products are formed from alkyl halides. However, insertion reactions of dichlorocarbene and methylene obtained by Simmons-Smith reaction have not been observed.

SAQ 2

Predict the products in the following reactions.

\[
\begin{align*}
\text{i)} & \quad \text{CH}_3 + \text{:CH}_2 + \text{CH}_3\text{CH} - \text{CH}_2 - \text{CH}_3 \\
\text{ii)} & \quad \text{C}_6\text{H}_5\text{C}_6\text{H}_5 + \text{CH}_3\text{OH} \\
\text{iii)} & \quad \text{H} \rightarrow \text{CH}_2\text{N}_2
\end{align*}
\]

Some of the common and synthetically useful reactions occurring through carbene intermediates are described below:

Rieimr - Tiemann Reaction: Involves heating a phenol with chloroform and aqueous sodium hydroxide to give a hydroxyaldehyde. Thus phenol reacts with chloroform and aqueous sodium hydroxide to give o-hydroxybenzaldehyde.

\[
\begin{align*}
\text{CHCl}_3 + \text{KOH} & \rightarrow \text{CCl}_2 + \text{H}_2\text{O} + \text{KCl} \\
\text{C}_6\text{H}_5\text{OH} + \text{OH}^- & \rightarrow \text{C}_6\text{H}_5\text{OH} + \text{H}_2\text{O} \\
\text{C}_6\text{H}_5\text{OH} + \text{CCl}_2 & \rightarrow \text{C}_6\text{H}_5\text{OCCl}_2 \rightarrow \text{C}_6\text{H}_5\text{Cl}_2 \rightarrow \text{C}_6\text{H}_5\text{CHO}
\end{align*}
\]
Carbylamine Reaction: On heating a mixture of a primary amine, chloroform and caustic potash, an isocyanide or nitrile, having a bad smell is formed. This is one of the tests for the presence of a p-amino group in a compound.

\[
\begin{align*}
CHCl_3 & \quad + \quad KOH \quad \rightarrow \quad nCl_2 & \quad + \quad H_2O & \quad + \quad KCl \\
RNH_2 & \quad + \quad nCl_2 \quad \rightarrow \quad [RNH_2\text{C}l_2] & \quad \rightarrow & \quad RNH\text{C}l_2 & \quad \rightarrow & \quad RN=\text{C}l \\
& \quad \downarrow & \quad \text{-cL} \quad \downarrow & \quad \text{R}\text{-N}\equiv\text{C}: & \quad \end{align*}
\]

Dichlorocarbene (generated as above) reacts with ethanol to give ethyl orthoformate. This reaction is used in industrial preparation of orthoformate ester.

\[
\begin{align*}
nCl_2 & \quad + \quad C_2H_5OH \quad \rightarrow \quad C_2H_5OCHCl_2 & \quad \rightarrow & \quad (C_2H_5O)_2CH & \quad + \quad 2Cl^- \\
\end{align*}
\]

Dichlorocarbene is hydrolysed readily to form formate ion.

\[
\begin{align*}
H_2O & \quad + \quad nCl_2 \quad \rightarrow \quad [H_2O\text{C}l_2] \quad \rightarrow \quad HO-\text{C}HCl_2 \\
& \quad \downarrow & \quad \text{-OH}\quad \downarrow \\
& \quad \text{HO-}\quad \text{C}\quad & \quad \text{O}
\end{align*}
\]

Wittig Reaction: Dichlorocarbene reacts with triphenylphosphine to give an ylide intermediate which on treatment with ketones gives 1,1-dichloroalkanes.

\[
\begin{align*}
(C_6H_5)_3P^+ & \quad + \quad nCl_2 \quad \rightarrow \quad (C_6H_5)_3P\text{C}l_2 \\
\text{Triphenylphosphine} & \quad \text{ylide} \\
(C_6H_5)_3P\text{C}l_2 & \quad + \quad R_2=O \quad \rightarrow \quad (C_6H_5)_3P\text{C}l_2 \\
& \quad \rightarrow & \quad (C_6H_5)_3P=O \quad + \quad R_2=\text{C}l_2
\end{align*}
\]

Wolff Rearrangement: A carbene intermediate is formed when α-diazoketones are either treated with silver oxide or irradiated with light. Migration of a group, attached to the carbonyl function, to the electron-deficient carbon gives rise to a ketene. This isomerisation is known as the Wolff rearrangement. The ketene rapidly reacts with protic solvents to form addition products. Carboxylic acids, esters or acid amides are the final products formed with water, ethanol or ammonia, respectively.

\[
\begin{align*}
\text{O} & \quad \rightarrow & \quad \text{C}_6\text{H}_5-\text{C}=\text{CH}=\text{N}=\text{N}^{-} \\
& \quad \downarrow & \quad \text{+Ag}_2O \\
\text{N}_2 & \quad + \quad [C_6\text{H}_5-\text{C}=\text{C}] & \quad \rightarrow & \quad C_6\text{H}_5-\text{C}=\text{CH}=\text{C}=\text{O} \\
\text{phenyl ketene} & \quad \rightarrow & \quad \text{C}_6\text{H}_5\text{CH}_2\text{COOH} & \quad \text{phenyl acetic acid} \\
& \quad +\text{H}_2\text{O} & \quad \text{C}_6\text{H}_5\text{CH}_2\text{COOH} \quad \rightarrow \quad \text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{C}_6\text{H}_5 \\
& \quad \text{phenyl acetic acid} & \quad \text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{C}_6\text{H}_5 & \quad \text{phenyl acetic acid} \\
& \quad \rightarrow & \quad \text{C}_6\text{H}_5\text{CH}_2\text{CONH}_2 & \quad \text{phenyl acetic acid}
\end{align*}
\]
The above reaction is used to convert carboxylic acids, via acid chlorides, to their higher homologues in Arndt-Eistert synthesis.

SAQ 3

How will you affect the following conversions?

i) 

\[
\begin{array}{c}
\text{OH} \\
\text{OH} \\
\end{array} \rightarrow \begin{array}{c}
\text{COOH} \\
\end{array}
\]

ii) 

\[
\begin{array}{c}
\text{CH}_3 \text{C} = \text{O} \\
\text{CH}_3 \\
\end{array} \rightarrow \begin{array}{c}
\text{CH}_3 \text{C}=\text{Cl}_2 \\
\text{CH}_3 \\
\end{array}
\]

iii) 

\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{COOH} \\
\end{array} \rightarrow \begin{array}{c}
\text{C}_6\text{H}_5\text{CH}_2\text{COOH} \\
\end{array}
\]

9.3 NITRENES

Nitrenes, like carbenes, are neutral species in which the nitrogen atom has only a sextet of valence electrons and thus, like the carbon atom in carbenes, it is electron-deficient. Nitrenes are highly unstable intermediates with a very short life time, of the order of a few microseconds. They are either trapped with suitable reagents or may form stable molecules by rearrangement.

The parent species, :NH, is known as imidogen or azene or imene. It is formed when hydrazoic acid is irradiated with UV light. Cycloaddition occurs in the presence of ethene to give ethene imine or aziridine.

\[
\begin{array}{c}
\text{HN}_3 \\
\text{HN} \\
\text{CH}_2=\text{CH}_2 + :\text{NH} \rightarrow \text{CH}_2=\text{CH}_2 \\
\text{aziridine} \\
\end{array}
\]

In the absence of a reagent, dimerisation of imidogen to diimide takes place.

\[
2 :\text{NH} \rightarrow \text{HN}=\text{NH}
\]

9.3.1 Generation

The common method for generation of nitrenes is thermolysis or photolysis of azides.

\[
\text{R}-\overline{\text{N}}-\text{N}=\text{N} \xrightarrow{\text{hv or } \Delta} \text{R}-\text{N}: + \text{N}_2
\]

Nitrene intermediates are formed in thermal or photochemical decomposition reactions of most alkyl, aryl or sulphonyl azides and azido formates with loss of nitrogen.

Alkyl nitrenes are highly reactive and either immediately isomerise to imines by 1, 2-H migration or form primary amines by intermolecular hydrogen abstraction.
Hydrogen abstraction

\[ R-\text{CH}_2-N_3 \xrightarrow{+2H} RCH_2\text{NH}_2 \]

Alkenyl nitrenes generally rearrange to imines which are tautomeric with nitriles.

\[ R-\text{CH}=\text{CH}-N_3 \rightarrow R-\text{CH}=\text{C}=\text{NH} \iff RCH_2-\text{C}=\text{N} \]

Alkynyl nitrenes have not yet been prepared. However the analogous cyanonitrene has been well characterised during the decomposition of cyanogen azide;

\[ \text{NCN}_3 \rightarrow \text{NC}+\text{N}_2 \]

Or \[ \text{[N≡C--N=N=N]} \rightarrow \text{N≡C=N=N]→ N≡C--N} \]

Decomposition of aryl azides in a variety of solvents has been studied. In inert solvents like hydrocarbons the main products are azo compounds and amines. The amines, as we will discuss later, are formed from azo compounds by hydrogen abstraction.

Thermolysis or photolysis of a phenyl azide in aniline solution can be a good route to derivatives of 2-phenylamino-3H-azepine. It has been proposed that the reaction involves generation of a nitrene in the initial step followed by the sequences given below:

9.3.2 Structure and Stability

Nitrenes, like methylenes, can exist either in a singlet or triplet state. In the singlet state, there are two pairs of electrons and a low lying empty \( \pi \) orbital, while in the triplet state, there is one electron pair and two unpaired electrons with parallel spins.

As said earlier, the unshared lone pair on nitrene is generally not shown.

Electron spin resonance studies have shown that in nitrenes, like in methylenes, the triplet state is the ground state. Experimental evidence from a variety of reactions indicates that nitrenes are initially formed in singlet state. However, this may change to the lower energy triplet state by collisional deactivation with inert gas or solvent molecules.

The two forms differ in their chemical reactions. As would be expected, the singlet species adds to multiple bonds in a stereospecific manner, whereas in the case of the triplet species which behaves more like a diradical, the addition would be non-stereospecific. Further, the
singlet nitrene inserts into C—H bonds while the triplet species abstracts hydrogen. These reactions are described in the following subsection.

9.3.3 Reactions

The highly reactive nitrenes formed in any reaction stabilise themselves in a number of ways. Some of these are:

**Coupling:** Two nitrene species may unite to form an azo compound. This reaction is observed only in flash photolysis in inert solvents where a high nitrene concentration is produced.

\[ 2[R-N:] \rightarrow R-N=N-R \]

**Hydrogen abstraction:** It has been postulated that hydrogen abstraction probably involves triplet nitrene. Abstraction reactions of nitrenes, in a way, can be taken as an indication of the presence of triplet species.

Triplet nitrenes abstract hydrogen from a C—H bond to produce primary amines. The first step of the reaction is supposed to be abstraction of hydrogen by triplet nitrene from the substrate to form an amino and a carbon radical. The two radicals produced would have parallel spins and, therefore, cannot couple unless their spins are reversed. The time required for this reversal is enough to allow the radicals to drift apart. The amino radical, meanwhile, would abstract another hydrogen to form a primary amine.

\[
\begin{align*}
\text{ArN}_3 & \xrightarrow{\text{hv}} \text{Ar-N} : \xrightarrow{\text{Ar-})}  \\
\text{Ar-} \text{N} : + \text{H-C} & \rightarrow \text{[Ar-N-H + C-]}  \\
& \text{radicals with parallel spins}  \\
\text{Ar-} \text{N-H} + \text{H-C} & \rightarrow \text{Ar-NH}_2 + \text{C-}
\end{align*}
\]

Following are some examples illustrating hydrogen abstraction by nitrenes.

\[
\begin{align*}
\text{RO-C-N}_3 \xrightarrow{\Delta} \text{RO-C-N} : \xrightarrow{\text{alkyl azido formate}} \text{RO-C-NH}_2 \xrightarrow{\text{alkyl carbamate}} \\
\text{C}_6\text{H}_5-C-N_3 \xrightarrow{\Delta} \text{C}_6\text{H}_5-C-N : \xrightarrow{\text{bromide}} \text{C}_6\text{H}_5-C-NH_2 \xrightarrow{\text{benzamide}}
\end{align*}
\]

**Rearrangement**

Nitrenes frequently undergo a rearrangement in which an alkyl, aryl or H migrates from α-carbon to the nitrogen, in a 1,2-shift. The group migrates with its electron pair from carbon to the electron-deficient nitrogen. The mechanism of this rearrangement is very similar to that of carbocations which you will study later in this block.

\[
\begin{align*}
\text{C} & \xrightarrow{\text{R}} \text{N} : \xrightarrow{\text{1,2-alkyl shift}} \text{C-N-R}  \\
\text{C} & \xrightarrow{\text{N}} \text{R} \xrightarrow{\text{shift}} \text{C-N-R}
\end{align*}
\]
Gas phase pyrolysis of tert-butyl azide and photosensitized decomposition of triphenylmethyl azide given below illustrate this type of rearrangement.

\[
\begin{align*}
\text{CH}_3\text{C}-\text{N}_3 \rightarrow \text{CH}_3\text{C}-\text{N}^- \rightarrow \text{CH}_3\text{C} \equiv \text{N} \equiv \text{CH}_3 \\
\text{tert- butyl azide}
\end{align*}
\]

The name tetrazole indicates a five membered ring with four nitrogen atoms. Benzimidazole indicates a five membered ring containing two nitrogen atoms fused to a benzene ring. Notice the numbering starts with the saturated hetero atom going round the ring as shown.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C}-\text{N}_3 \rightarrow \text{C}_6\text{H}_5\text{C}-\text{N}^- \rightarrow \text{C}_6\text{H}_5\text{C} \equiv \text{N} \equiv \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 \rightarrow \text{C}_6\text{H}_5 \rightarrow 1,5\text{-diphenyl tetrazole}
\end{align*}
\]

Such 1,2 shifts of nitrenes are of great synthetic utility in heterocyclic chemistry. For example, benzophenone diazide on photolysis gives a tetrazole and a benzimidazole on rearrangement of the nitrene intermediates.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C}-\text{N}_3 \rightarrow \text{C}_6\text{H}_5\text{C}-\text{N}^- \rightarrow \text{C}_6\text{H}_5\text{C} \equiv \text{N} \equiv \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 \rightarrow 2\text{-phenyl benzimidazole}
\end{align*}
\]

Acyl nitrenes, formed during photolysis or thermolysis of dilute solutions of acyl azides, undergo rearrangement to give isocyanates:

\[
\begin{align*}
\text{O} & + \rightarrow \text{R}-\text{C} \equiv \text{N} \equiv \text{N} \equiv \text{N} \\
& \text{hv or } \Delta \rightarrow \text{R}-\text{C} \equiv \text{N}^- \rightarrow \text{R}-\text{N} \equiv \text{C} \equiv \text{O}
\end{align*}
\]

An important example of the above is Hofmann rearrangement in which an acid amide is reacted with bromine and aqueous sodium hydroxide to give a primary amine. In this reaction an acyl nitrene intermediate is formed through N-bromamide, which immediately rearranges to an isocyanate. Hydrolysis of the isocyanate gives the primary amine with loss of carbon dioxide. The amine would therefore have one carbon atom less than the acid. We will take up details of this reaction in Unit 11.
**2NaOH + Br₂ → NaBr + NaOBr + H₂O**

\[
\begin{align*}
0 & \xrightarrow{(i)} \text{bromamide} \\
\text{R—C—NH₂ + 0Br} & \xrightarrow{(ii)} \text{R—C—N—H + OH} \\
& \xrightarrow{(iii)} \text{R—C—N₂} \quad \text{(unstable)} \\
& \xrightarrow{(iv)} \text{RNH₂ + CO₂}
\end{align*}
\]

As you will study later, there is a similarity in Hofmann, Schmidt and Curtius rearrangements. Mechanistically, in each of these an acyl nitrene seems to be involved.

**Insertion:**

Nitrenes insert into various C—H bonds:

\[
\text{R—N⁺} + \text{R'—H} \rightarrow \text{R'—H} \rightarrow \text{R'—NH—R}
\]

Thermolysis of cyanogen azide at temperatures, 586-600K, proceeds with conservation of spin to yield singlet nitrene, which inserts stereo — specifically into tertiary C—H bonds of cis and trans 1,2-dimethylcyclohexane.

\[
\text{N₃CN} \xrightarrow{\text{heat}} \text{C—CN}
\]

**SAQ 4**

Write down various steps involved in the following conversions. Give the mechanism where possible.

i) \[ \text{CH₃CH₂COOH} \rightarrow \text{CH₃CH₂NH₂} \]

ii) \[ \text{CH₃CH₂COOH} \rightarrow \text{CH₃CH₂NHCOO—C—CH₃} \]

**1,3-Dipolar cyclo-additions**

You are familiar with 1,2-dipolar additions across multiple bonds like the addition of Br₂ to C=C. In 1,3-dipolar cycloadditions a neutral three-atom 4π electron unit (addendum) adds to a multiple bond. The term dipolar refers to the necessary formal charges in the Lewis structure of the 4-π component. Examples of such system are:

\[
\text{ozone} \quad \text{R—N==N=N} \quad \text{azide}
\]
The products of such reactions are five-membered ring systems. You may recall ozonolysis of alkenes which starts with addition of ozone to the >C=C<

Photolysis of ethyl azidoformate in benzonitrile giving 1,3,4-oxadiazole is an example of a 1,3-dipolar addition in which the carboethoxy nitrene formed as an intermediate adds across the -C=N-

Additions to alkenes

Nitrenes add to alkenes to form aziridines. As in the insertion reaction singlet nitrenes add stereospecifically while the triplet ones non-stereospecifically. Nitrene initially formed as singlet species may slowly decay into the triplet one:

Thus photolysis of methyl azidoformate, N₂COOCH₃ in cis- and trans-2-butene gives 87% cis and 13% trans aziridine in the former case and 8% cis and 92% trans aziridine in the latter.
As you can see the addition is stereospecific, which implies that the singlet nitrene formed adds to the double bond before it has time to change to the triplet state.

SAQ 5

Photo decomposition of cis-triazoline gave the cis- and trans- aziridines in the following proportion. How do you explain this?

\[
\begin{align*}
\text{cis} & \quad \text{trans} \\
\text{C}_6\text{H}_5 - & \quad \text{C}_6\text{H}_5 - \\
\text{CH}_3 & \quad \text{CH}_3 \\
\hline
\text{65\%} \quad & \quad \text{17\%}
\end{align*}
\]

9.4 BENZYNES

Another type of intensely reactive reaction intermediates are benzynes, or the 1,2-dehydrobenzenes. Benzynes or arynes have been postulated as intermediates in nucleophilic substitutions of aryl halides which have no activating groups. In such reactions, the bases required are stronger than those normally used. The most interesting aspect of these reactions is that the incoming group does not always take the position vacated by the leaving group. That the latter statement is true was elegantly demonstrated by the reaction of 1-\(^{14}\)C-chlorobenzene with potassium amide in liquid ammonia.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{Cl} & \quad \text{NH}_2/\text{NH}_3 \\
\hline
\text{47\%} \quad & \quad \text{53\%}
\end{align*}
\]

The product consisted of aniline, half of which was labelled in 1-position and the other half in 2-position. This is possible only if there is a symmetrical intermediate, like benzynie, which can be attacked by ammonia in either of the two positions.

Other strong bases like tert-butoxide ion can be used in place of amide ion. Evidence for the formation of benzynie as an intermediate also comes from the reaction of p-chlorotoluene with potassium amide and liquid ammonia. The product is a mixture of \(m\)- and \(p\)-toluidines. This can only be explained on the basis of 3:4-benzynie as an intermediate, since direct replacement of the halogen would give only \(p\)-toluidine. Addition of an amide ion to a 3,4 benzynie intermediate and subsequent abstraction of a proton from ammonia by the anions can account for the formation of two products:
Let us look into the mechanistic details of a substitution reaction involving benzyne as an intermediate. We can take the reaction of chlorobenzene with potassium amide in liquid ammonia as an example. In such replacements mechanistic route is supposed to involve two stages, elimination followed by addition of the nucleophile. The elimination stage, in which benzyne is formed, is again presumed to involve two steps: abstraction of proton by the amide ion to form a carbanion which then loses the halide ion to form benzyne. The first step in this reaction, the loss of proton is the slow, rate determining step.

Thus elimination can be shown as:

\[ \text{benzyne} \]

As you can see, the geometry of benzene ring would permit only a cis coplanar elimination (though not concerted).

The addition stage, in which benzyne reacts with the nucleophile, may again be a two step process:

\[ \text{benzyne} \]

Such elimination-addition reactions proceeding through a benzyne intermediate are also called "Cline Substitution". Further confirmation of this mechanism comes from the observation that 2,6-disubstituted aryl halides which do not have hydrogens ortho to the halogen do not react with amide ion in liquid ammonia, e.g., 2-chloro-3-methyl-xylene and 2-bromo-3-methyl-anisole:

Another interesting observation is that o-deutero bromobenzene reacts more slowly than bromobenzene with amide ion in liquid ammonia. It is known that carbon-deuterium bond is stronger than carbon hydrogen bond. Since, as said above, loss of proton is the rate-determining step in this reaction, the slower rate in case of o-deutero bromo-benzene can be explained on the basis of isotope effect.
You can now differentiate cine substitution from an ordinary nucleophilic substitution. In an ordinary nucleophilic substitution, the incoming group is expected to occupy the position vacated by the leaving group. Further, whether or not an ortho hydrogen is present would make no difference.

Orientation

However, in reactions involving benzyne intermediates, there are two factors which affect the position of the incoming group. One of these is related to the acidity of the hydrogen which is removed, and the other to the stability of the carbanion formed on addition of the nucleophile. Both these are briefly discussed below:

i) Acidity of hydrogen being removed

When there are groups ortho or para to the leaving group, X, there is no choice and benzyne is formed only in one way e.g.,

But when a meta group is present, the benzyne may form in two different ways:

In such cases, the more acidic hydrogen is removed. Since acidity is related to the inductive effect of Z, it may be stated that the electron attracting Z favours removal of the ortho hydrogen while an electron donating Z favours removal of the para hydrogen.

ii) Stability of carbanion formed

The benzyne, once formed, may be attacked at two positions. The favoured position for nucleophilic attack is the one which leads to the more stable carbanion intermediate, and

Since the electron pair in the carbanions involved in both the stages is out of the plane of the \( \pi \) -cloud, there is no resonance interaction between these electrons and the \( \pi \)-cloud. Only inductive effect working along bonds or through space is operative. This would be stronger in ortho than in para position.
Reaction Intermediates and Molecular Rearrangements

this in turn is also dependent on the inductive effect of Z.

For-I groups the more stable carbanion is the one in which the negative charge is closer to the substituent.

The above principles are illustrated by the reaction of o-bromoanisole and m-bromoanisole with sodamide. Both yield the same product, namely, m-aminoanisole (m-anisidine).

It is obvious that for both of them to yield the same product, the benzyne intermediate would have to be the same in both the cases. Let us go into the orientation in the elimination as well as in the addition stage and see if we can justify these experimental observations. Remember, methoxy group has an electron-withdrawing, -I, inductive effect.

o-Bromoanisole would yield, 2,3-benzyne as shown because there is only one option.

\[ \text{OCH}_3 \quad \text{Br} \xrightarrow{\text{NH}_2} \quad \text{OCH}_3 \quad \text{NH}_2 \xrightarrow{} \quad \text{OCH}_3 \]

2,3-benzyne

In the case of m-bromoanisole, the more acidic ortho hydrogen is removed, leading to the same benzyne. The carbanion formed would obviously be also the more stable one, due to -I effect of both ortho OCH\(_3\) and Br. The para hydrogen is less acidic, the carbanion formed would be stabilised only by the -I effect of ortho bromine, and so it is not formed. The ortho carbanion loses Br to give 2,3-benzyne as shown.

In the second stage, addition of NH\(_2\) to the benzyne, carbanion ortho to the methoxy group would be stabilised by the -I effect, whereas the one at the meta position is not. So you can see why m-anisidine would be the predominant product.

9.4.1 Generation

You have studied above aromatic substitution reactions in which benzyynes have been postulated as intermediates. There is spectroscopic and other evidence for the formation of benzyynes in the following reactions.
This involves sideways overlap of \( sp^2 \) orbitals of the two carbon atoms, one originally holding the helogen and the other hydrogen, to form an additional \( \pi \)-bond which is out of the plane of the aromatic \( \pi \)-cloud. This new bond orbital lies along the side of the ring and has little interaction with the \( \pi \)-cloud lying above and below the ring. However, the additional bond involves considerable deformation of the bond angles concerned, from \( 180^\circ \) to \( 120^\circ \), and is therefore weak. Try to visualise this structure. It is like the formation of a triple bond between \( C_1 \) and \( C_2 \). If it were an open chain compound, the two \( sp \) orbitals would be linear with an angle of \( 180^\circ \). However, in this six-membered ring structure, these \( sp \) carbons have to be bonded on either side with \( sp^2 \) carbon atoms, reducing the bond angle to nearer \( 120^\circ \). This would imply that this bond would have to be bent, setting in severe strain, something like in cyclopropene. The unstable nature of benzyne and its high reactivity can be easily explained on the basis of this structure.

### 9.4.2 Structure and Stability

Although no benzyne have been isolated, spectroscopic evidence for the transient existence of benzyne has been obtained. It is generally agreed that the aromatic character of the cyclic system in the benzyne intermediate is undisturbed. On this presumption two alternate structures can be written. One structure of benzyne has been postulated as:

This involves sideways overlap of \( sp^2 \) orbitals of the two carbon atoms, one originally holding the helogen and the other hydrogen, to form an additional \( \pi \)-bond which is out of the plane of the aromatic \( \pi \)-cloud. This new bond orbital lies along the side of the ring and has little interaction with the \( \pi \)-cloud lying above and below the ring. However, the additional bond involves considerable deformation of the bond angles concerned, from \( 180^\circ \) to \( 120^\circ \), and is therefore weak. Try to visualise this structure. It is like the formation of a triple bond between \( C_1 \) and \( C_2 \). If it were an open chain compound, the two \( sp \) orbitals would be linear with an angle of \( 180^\circ \). However, in this six-membered ring structure, these \( sp \) carbons have to be bonded on either side with \( sp^2 \) carbon atoms, reducing the bond angle to nearer \( 120^\circ \). This would imply that this bond would have to be bent, setting in severe strain, something like in cyclopropene. The unstable nature of benzyne and its high reactivity can be easily explained on the basis of this structure.
In the dipolar structures, which can be considered as resonance structures of the above, the benzene ring is again essentially undisturbed except for the removal of two hydrogens. There would be a partial overlap between adjacent \( sp^2 \) orbitals with the formation of a weak bond, which is consistent with observed reactivity.

![Lewis structure](image)

It is argued that if this were the case, \( C_1-C_5 \) distance should be less; as this would provide a better overlap of weakly interacting \( sp^2 \) orbitals. As a result, \( C_1-C_5 \) and \( C_1-C_6 \) bond lengths are consistent with this stipulation as you can see in the above diagram.

### 9.4.3 Reactions

In addition to amination and hydrolysis of halobenzenes about which you have studied above, benzyne intermediates have also been postulated in the following reactions:

**Ring closure reactions:** Benzyne is an electron-deficient species and, therefore, we may expect it to behave as an electrophile. In case an atom, which can donate a pair of electrons is suitably placed, intramolecular addition leading to cyclisation can occur.

This provides a new general method for the synthesis of cyclic systems. N-Methyl 1-2-(m-chlorophenyl)-ethylamine, for example, gives N-methyl-indoline on treatment with phenyl lithium:

![Chemical structure](image)

**Addition Reactions:** As powerful dienophiles, benzyynes react with conjugated systems to give Diels-Alder adducts. For example, o-bromofluorobenzene on treatment with magnesium or Li/Hg was trapped by furan or anthracene:

![Chemical structure](image)

This, in fact, is taken as an evidence for the formation of benzyne intermediate.

In the absence of a reagent, the benzyne formed undergoes dimerisation to give diphenylene.

![Chemical structure](image)

**SAQ 6**

Give the Products in the following cases:
9.5 SUMMARY

Carbenes, nitrenes and benzyynes are intensely reactive reaction intermediates. They are unstable species and have not been isolated. Their existence has been shown either by spectroscopic studies or by chemical reactions. While carbenes and nitrenes have been postulated as intermediates in molecular rearrangements, nucleophilic substitution of aryl halides which do not have any activating groups is supposed to proceed via benzyne mechanism.

In this unit various methods for the generation of these transient reaction intermediates have been described and their structure and stability discussed. Carbenes and nitrenes are electron-deficient species. They act as electrophiles in chemical reactions. Their typical reactions are insertion, cycloadditions, and rearrangement. Carbenes and nitrenes react with alkenes to give three-membered ring products. Rearrangement reactions of carbenes and nitrenes lead to a variety of products. Benzyne acts as dienophiles and participate in Diels-Alder reaction.

9.6 TERMINAL QUESTIONS

1) Predict the product(s) in the following and give mechanism.

\[
\text{Cyclohexene} + \text{CH}_2\text{J}_2 \xrightarrow{\text{Zn-Cu}} \text{(C}_2\text{H}_5)_2\text{O} \]

\[
\text{Z-2-pentene} + \text{CHCl}_3 \xrightarrow{\text{tret-BuO}^-\text{K}^+} 
\]

\[
\text{Fluorobenzene with } \xrightarrow{\text{C}_2\text{H}_5\text{Li}} \text{ with labelled } \xrightarrow{\text{(C}_2\text{H}_5)_2\text{O}} \text{a-carbon} 
\]

2) Give the steps involved in the following conversions:

a) \[
\text{\begin{array}{c}
\text{COOH} \\
\end{array}} \xrightarrow{\text{}} \text{\begin{array}{c}
\text{CH}_2\text{COOH} \\
\end{array}}
\]

b) \[
\text{\begin{array}{c}
\text{COOH} \\
\end{array}} \xrightarrow{\text{}} \text{\begin{array}{c}
\text{OCCOC}_6\text{H}_5 \\
\end{array}}
\]

c) \[
\text{\begin{array}{c}
\text{C}_6\text{H}_5\text{COCH}_3 \\
\end{array}} \xrightarrow{\text{}} \text{\begin{array}{c}
\text{C}_6\text{H}_5-\text{NH}-\text{COCH}_3 \\
\end{array}}
\]
3) Write down the predicted product and the corresponding intermediate in each of the following cases:

a) ![Chemical Structure]

b) ![Chemical Structure]

c) ![Chemical Structure]

9.7 ANSWERS

Self-Assessment Questions

1) In the liquid phase, singlet carbene produced adds stereospecifically to the alkenes. In the gaseous phase, singlet carbene first produced changes to triplet state, which adds in a non-stereospecific mode.

2) ![Chemical Structure]

3) i) Reimer-Tiemann reaction on phenol with CCl₄/KOH.
ii) Wittig reaction with (C₆H₅)₂PCCI₂
iii) Conversion of diazocetophenone and Wolff rearrangement.

4) i) Conversion to azide and then rearrangement of acyl nitrile in the presence of water.
ii) Rearrangement of acyl nitrile in the present of tert-butylalcohol.

5) Triazoline undergoes photodecomposition to give the intermediate singlet diradical which undergoes ring closure to aziridine more rapidly than bond rotation.
Terminal Questions

1) a) Cycloaddition of methylene to give norcarane. No insertion of methylene occurs.
   b) Syn addition of dichlorocarbene on the alkene. No insertion product is observed.
   c) Two types of biphenyl. One in which the α-carbon and other in which the β-carbon is labelled.

2) a) Arndt-Eistert synthesis
   
   ![Chemical Reaction Diagram]

   b) Ammonolysis
   
   ![Chemical Reaction Diagram]

   c) 
   
   ![Chemical Reaction Diagram]

3) 

   a) 
   
   ![Chemical Reaction Diagram]

   b) 
   
   ![Chemical Reaction Diagram]

   c) 
   
   ![Chemical Reaction Diagram]

This can be justified on the basis of the -I effect of Cl in determining the orientation at elimination and addition stage.