

### 3.4. Organic Reactive Intermediates

#### 3.4.1. Reactive Intermediates

- The chemical species having less energy, but more stability compared to activated complex is known as reactive intermediate.

#### 3.4.2. Some salient features of a reactive intermediate are .....

- It is the intermediate stage of a chemical reaction.
- Reactive intermediates are real species having very short lifetime.
- Once it is formed, must be exhausted before end of the reaction.
- Most stable reactive intermediate leads to formation of major product.

#### 3.4.3. Types of reactive intermediates:

(a) Carbocation, (b) Carbanion, (c) Free radical, (d) Carbene, (e) Nitrene and (f) Benzyne.

##### (a) Carbocation:

- Positively charged species having six electrons in the outer orbit.
- Highly electron deficient species
- Highly reactive and easily gets converted into more stable molecule.

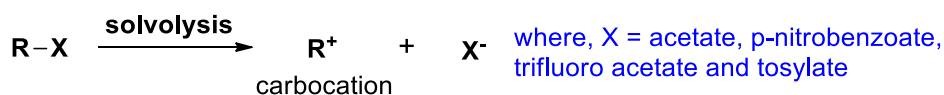
##### ❖ Division of carbocation:

These are divided into two main categories

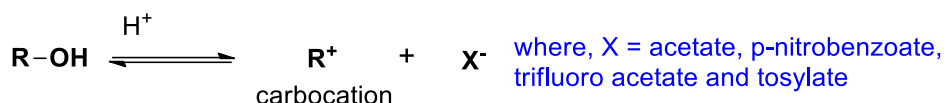
- Classical carbocation (carbenium ion): These are trivalent carbocation having  $sp^2$  hybridized atom which is planar.
- Non-classical carbocation (carbenium ion): These are tetra or penta coordinated carbocation ( $C^+$ ), however, the pentavalent carbocations are much rare than carbenium ions.

##### ❖ Generation of carbocations:

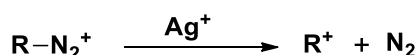
- Heterolytic cleavage of C-hetero atom bond:



- By heterolysis of onium salt



- By the heterolysis of diazonium salts



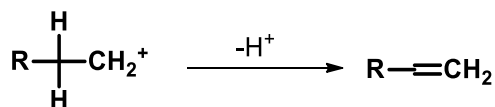
### ❖ Stability of carbocations

The carbocations may be stabilized by (a) Inductive effect (+I), (b) Hyperconjugative effect and (c) Resonance.

- Alkyl carbocations are stabilized by +I effect and hyperconjugative effect as the alkyl group has electron releasing capability. 3° carbocation is more stable than 2° carbocation and 2° carbocation is more stable than 1° carbocation.
- A vinyl group stabilizes a carbocation more than methyl group as vinyl group is an effective electron releasing substituent. Vinyl cation is more stable than methyl cation.
- The stability of a carbocation can also be established with the help of resonance; more the number of canonical structure for a particular carbocation, greater will be the stability of the carbocation. e.g. benzyl carbocation is more stable than allyl carbocation.
- Cyclopropenyl cation is also stable because of aromatization.
- The stability carbocation is also increased due to the presence of hetero atom containing unshared pair of electrons, e.g oxygen, nitrogen or halogen. In those cases the carbocation is stabilized by resonance.

### ❖ Reactions of carbocations:

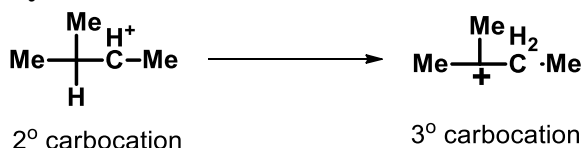
- (i) **Elimination of proton:** A carbocation may lose a proton to afford alkene, alkyne etc



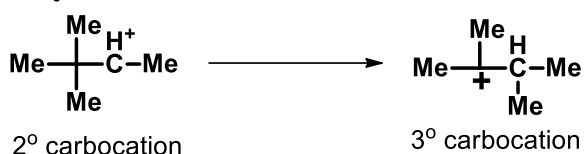
(ii) **Molecular rearrangements:**

A carbocation may undergo molecular rearrangement to afford a more stable carbocation by the means of the following ways.....

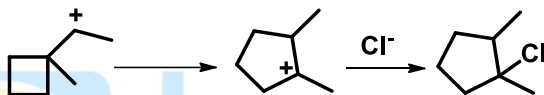
(a) **Hydride shift:** A 2° carbocation is converted into a 3° carbocation by hydride shift.



(b) **Alkyl shift:** A 2° carbocation is converted into a 3° carbocation by alkyl shift.



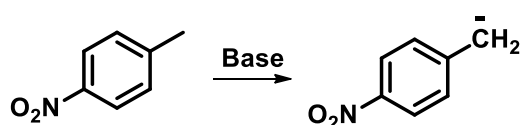
(c) **Ring expansion:** Small rings (cyclopropyl or cyclobutyl) where angle strain is high get stabilized by ring expansion.

(b) **Carbanion:**

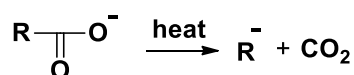
- The intermediates which have carbon atom with negative charge
- Carbon atom has eight electrons in the outer orbit.
- These are strong Lewis base and strong nucleophile.

❖ **Preparation**

(a) By the elimination of H<sup>+</sup> from certain organic compounds



(b) By decomposition of anions



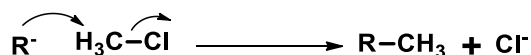
## ❖ Stability

The carbanions are electron rich species and thereby react very readily with electrophiles (electron deficient species).

- The stability of a carbanion increases if an electron withdrawing/attracting atom or group is present in the molecule
- The stability of a carbanion decreases if an electron donating/releasing atom or group is present in the molecule.

## ❖ Reaction of carbanion

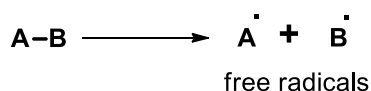
- (i) Reactions with electrophiles: Carbanions sometimes may act as nucleophile and react with electrophilic species.



- (ii) Addition reactions: Carbanions add to the carbonyl compounds. The addition reaction with aldehyde affords aldol.

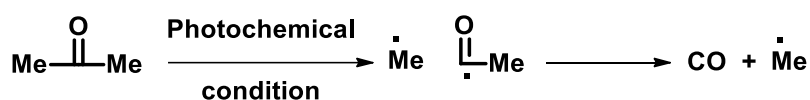
(c) *Free Radicals:*

These are the reactive intermediates having an unpaired electron on one of the atom. These are obtained by the hemolytic cleavage of a covalent bond.

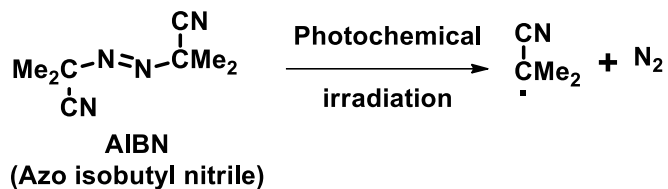
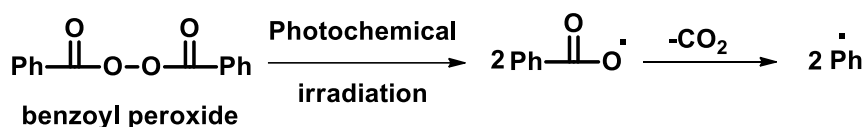


## ❖ Generation of free radicals:

- (i) By photolysis of compounds:



- (ii) By thermolysis of organic compounds:



Peroxides and AIBN are usually used as free radical generators from other molecules.

- Strong bonds that are difficult to cleave by thermolysis, can easily be cleaved by photolysis.
- Photolysis is the specific method for the hemolytic cleavage than pyrolysis or thermolysis.

➤ **Stability of free radicals:**

- The sequence of stability of alkyl free radicals are as follows



This order can be explained by the fact that alkyl groups have electron releasing power and hence increases the stability of electronically poor free radicals.

- The free radicals are also stabilized by conjugation

Reactions of free radical:

- (i) Coupling reactions



## (ii) Disproportionation reactions

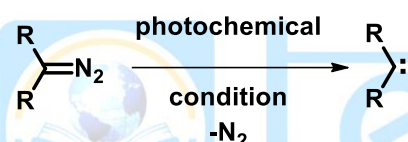
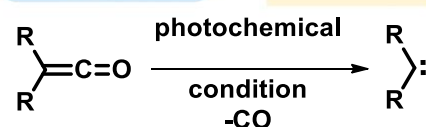
When the temperature is high, then alkyl radical undergoes disproportionation to form alkene and alkane.



## (d) Carbenes:

- Carbenes are divalent, neutral carbon intermediate.
- The carbon atom two unpaired electron
- The carbene carbon contains six electron, and hence act as strong electrophile.

## ➤ Generation of Carbenes

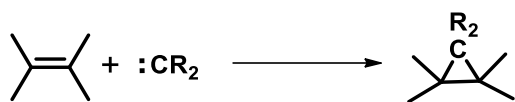
(i) *Photolysis of diazo compounds*(ii) *Thermolysis or photolysis of ketenes:*❖ *Stability of Carbenes*

- If the atom or groups attached with carbene carbon is electron releasing, then its stability would be more.
- Triplet carbenes are more stable than singlet carbenes.

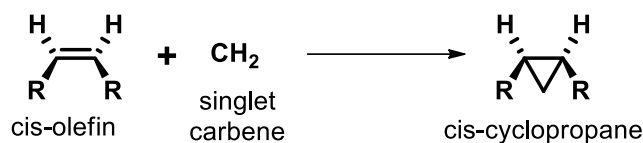
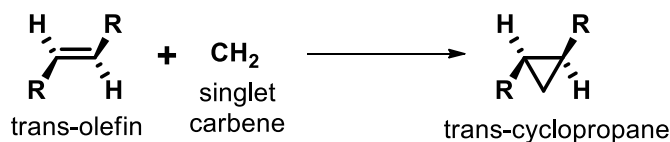
❖ *Reactions of Carbenes*

- Carbenes are very unstable and reactive intermediates, singlet carbenes are more reactive than triplet carbenes.

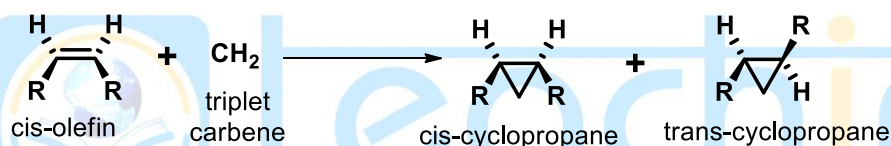
(1) **Addition reaction:** Carbenes undergoes addition reaction with alkenes to form cyclic compounds.



(a) In liquid state reactive species is singlet carbene and it adds on alkene in a stereo specific way to form cis-cyclopropane from cis alkene and trans cyclopropane from trans alkene.

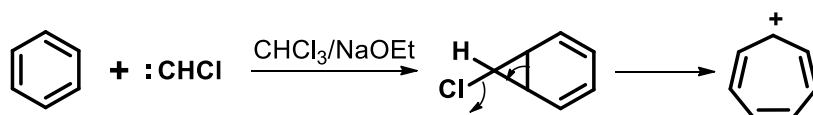


(b) In gaseous state reactive species is triplet carbene and it adds on alkene in a non-stereo specific way to form a mixture of cis- and trans-cyclopropane from cis alkene.



## (2) Ring expansion reactions:

Ring expansion reaction is used to happen by the addition of a halogenocarbene to a double bond followed by rearrangement.

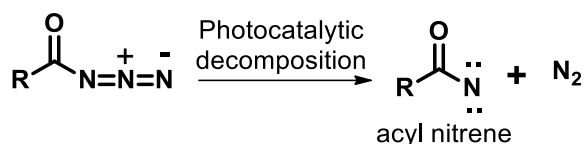
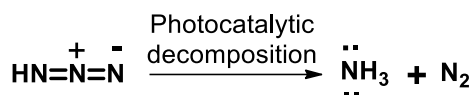


## (e) Nitrenes:

- Nitrenes are highly reactive, neutral reaction intermediates.
- Electron deficient monovalent nitrogen species.

❖ **Stereochemistry:**

Like carbene, nitrenes also exist in two states, (i) singlet state (where two non bonded electrons are antiparallel to each other) and (ii) triplet state (where two non bonded electrons are parallel to each other).

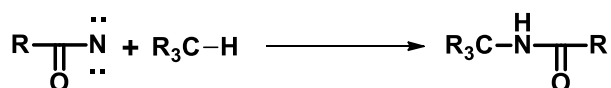
❖ **Generation of nitrenes:**(a) **Thermal or photocatalytic decomposition of azides:**(b) **Photolysis of hydrazoic acid:**(c) **Photolysis of alkyl isocyanates**❖ **Stability of nitrenes:**

- (i) Nitrenes are very reactive.
- (ii) It can not be isolated.
- (iii) It can be trapped by reaction with carbon monoxide to yield an isocyanate.
- (iv) It can also be trapped in presence of ethylene to afford aziridine.

❖ **Reaction of Nitrenes:**

- (i) Insertion reactions: Singlet nitrene undergoes insertion reaction to produce 2° amine.

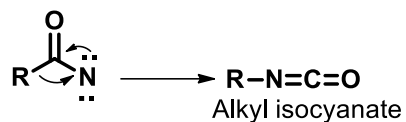
Acyl- and sulfonyl nitrenes can also undergoes insertion reaction.





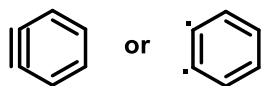
## (ii) Rearrangement reactions:

Alkyl nitrenes undergo rearrangement reaction and produces alkyl isocyanate which is the key intermediate of Hofmann, Lossen and Curtius rearrangement.



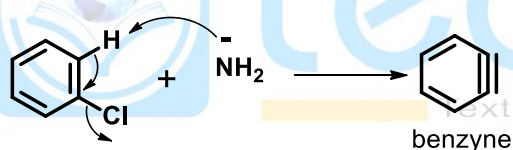
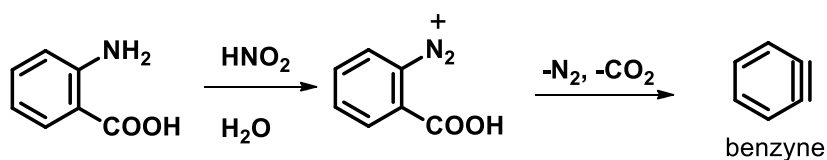
## (f) Benzyne:

Benzyne is a neutral, highly reactive intermediates. It can be represented as the following structure.



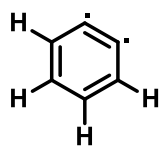
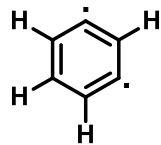
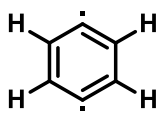
## ❖ Generation of benzyne:

## (i) From aryl halides

(ii) From *o*-amino benzoic acid

❖ **Stability of benzyne:**

There are three structures of diradical didehydrobenzenes as 1,2-, 1,3- and 1,4-didehydrobenzene respectively. The energy of these three molecules in silico are 106, 122 and 138 Kcal/mole.

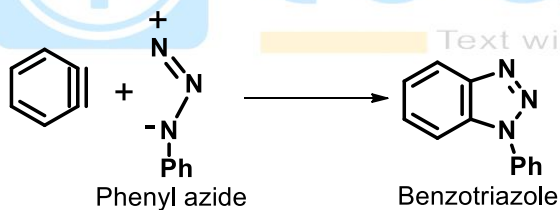
1,2-didehydro  
benzene1,3-didehydro  
benzene1,4-didehydro  
benzene❖ **Reactions of benzyne:**

(i) Cycloaddition reactions

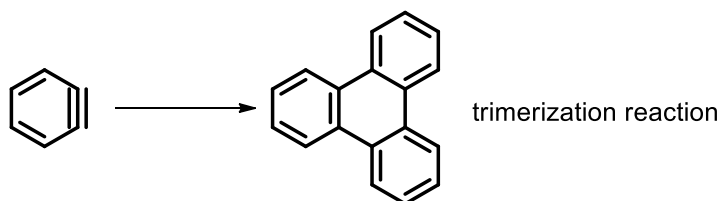
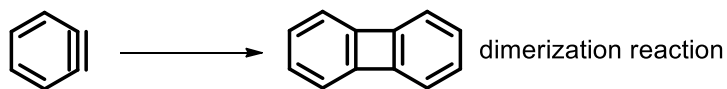
(a) [2+2]-cycloaddition



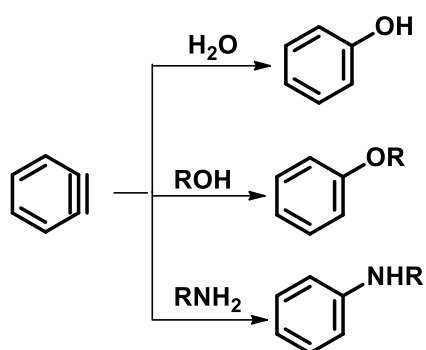
(b) [2+3]-cycloaddition



(ii) Dimerization and trimerization reactions



## (iii) Reactions with nucleophiles



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