

### Chapter 3: “Organic reactions and synthesis of a drug molecule”

#### *Introduction to intermediates*

*Reactions involving substitution, addition, elimination,*

*Oxidation- reduction, Diels elder cyclization and epoxide ring openings reactions.*

*Synthesis of a commonly used drug molecule like aspirin.*

#### • Introduction to intermediates

Intermediates are organic species which are formed for a short live during the reaction and further final product is formed from that intermediate. As we all know that it is very difficult to isolate intermediates, only few stale intermediates can be isolated.

Types of intermediates.

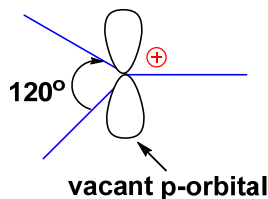
**Carbocation**

**Carbanion**

**Free radical**

Organic Species having 6 electrons paired having positive charge on central carbon.

In Carbocation central carbon is  $sp^2$  hybridized, Planar (means every atoms on the single page) with a vacant p-orbital, which will be perpendicular to the plane (means above at  $90^\circ$  to the page)

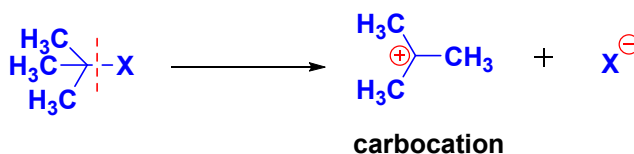


There are two types of carbocation:

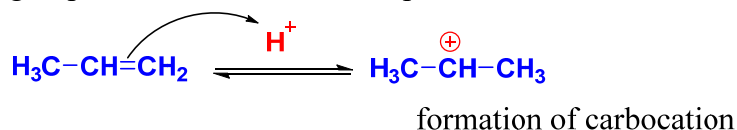
- Short lived:  $C^+$   $(CH_3)_3C^+$ ,  $(CH_3)_2CH^+$
- Stable  $C^+$ :  $(Ph)_3C^+$ ,  $(Ph)_2CH^+$

Formation of  $C^+$  by Heterolytic cleavage:

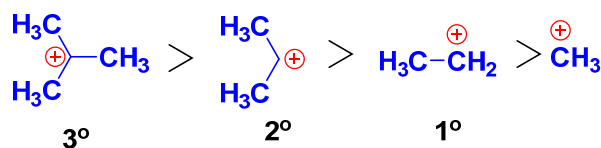
- By direct breaking of C-X bond in presence of highly polar solvent.



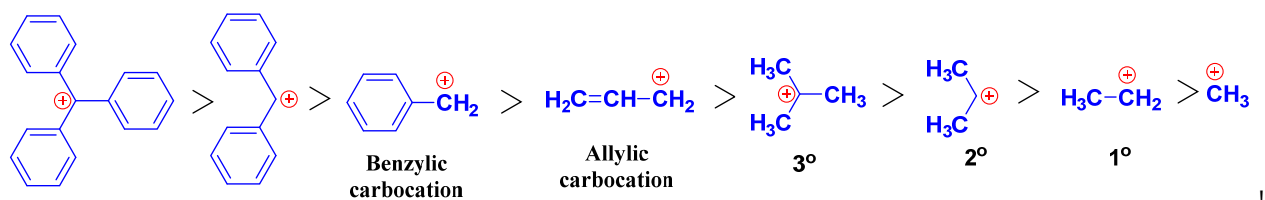
- By adding of proton to unsaturated comp.



Stability Order:



Normal stability order of carbocation

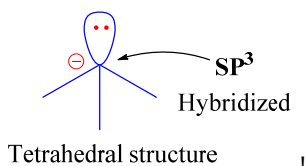


Over all stability order of carbocation

Here Carbocation stability order is due resonance as the positive charge is delocalized on various carbon atoms, whereas  $\text{CH}_3^+$  is least stable, as in this case the positive charge is not delocalized. It is fully present on a single carbon atom.

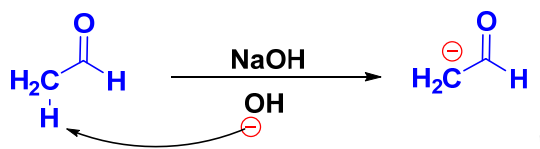
## Carbanion

Organic species with negative charge on the central carbon atom having one pair of electron present in the  $\text{SP}^3$  orbital. In carbanion there is 3 covalent bonds present.

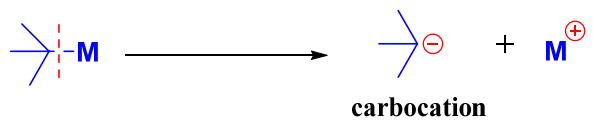


It is formed by different ways

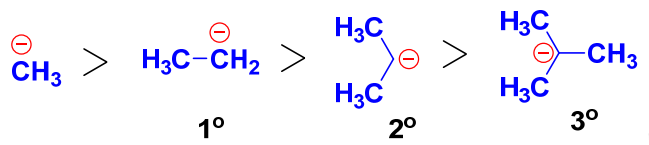
- i) Formation of  $\text{C}^-$  by Heterolytic cleavage of C-H bond.



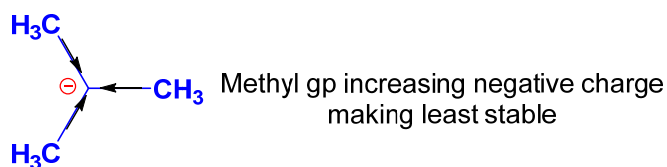
- ii) By breaking of C-M (M= Metal) bond.



Stability Order of Carbanion

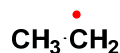


$3^\circ$  is least stable as there are three methyl group which donate electron to the central carbanion so on that carbon negative charge is more compared to other, making it least stable. As more charge less stable.

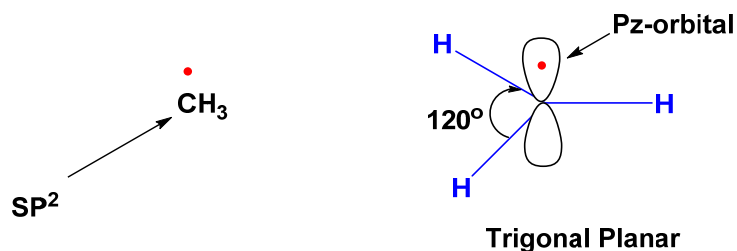


### Free radical:

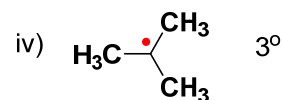
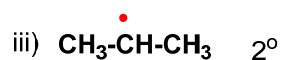
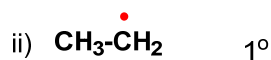
A species having a C-atom with one free electron and no charge is called as free radical.



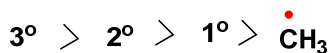
Structure: Free radicals are generally  $\text{SP}^2$  hybridized



➤ Stability:



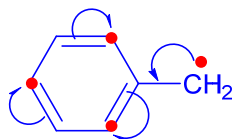
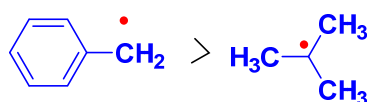
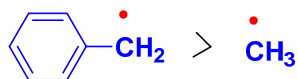
Among alkyl radical generally S.O is



Donor Increases  
Acceptor decreases

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➤ !



This is stable, as the radical is moving to 3 carbons so charge is not present at a particular carbon i.e. dispersion of charge

2<sup>nd</sup> Lecture will be on

“Reactions involving substitution, addition, elimination.”

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