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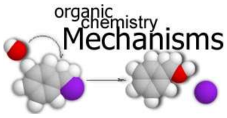

# CHEM 344
# ORGANIC REACTION MECHANISM

## FOR CHEMISTRY' STUDENTS, COLLEGE OF SCIENCE

PRE-REQUISITES COURSE; CHEM 241
CREDIT HOURS; 2 (2+0+0)

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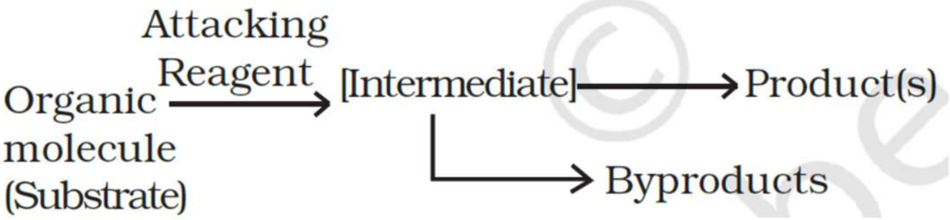
# INTRODUCTION

## Fundamental Principles

## FUNDAMENTAL CONCEPTS IN ORGANIC REACTION MECHANISM

- The general reaction is depicted as follows :



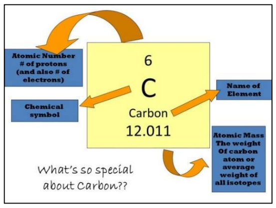
- Substrate; A molecule whose carbon is involved in new bond formation
- and the other one is called reagent.

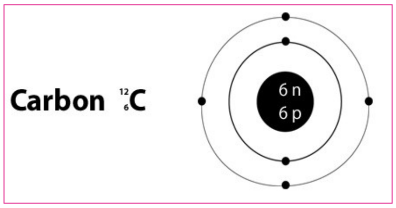
## DEFINITION

- A ***mechanism*** is the actual process by which a reaction takes place:
  - Which bonds are broken, in what order;
  - How many steps are involved;
  - The relative rate of each step, etc.
- A detailed study of the sequence of steps which are involved in the conversion of reactants into product(s) is known as ***reaction mechanism***.
- In order to state a mechanism completely, we should have to specify the *position of all atoms*, including those in *solvent molecules*, and the *energy of the system*, at every point in the process

# ATOMIC ORBITALS

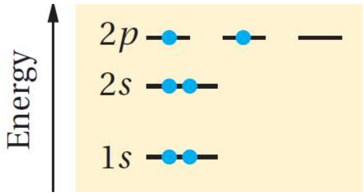
- The element carbon (atomic number 6)



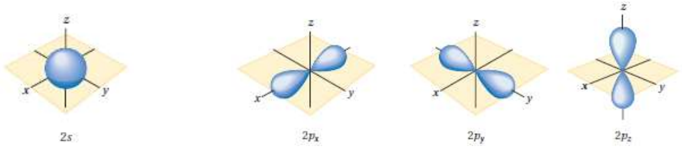


- The electronic configuration of carbon (*atomic number 6*) can be represented as

$1s^2 2s^2 2p^1_x 2p^1_y$ or $1s^2 2s^2 2p^2$

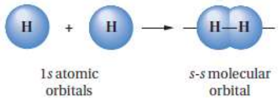


- **s orbital** is spherically shaped electron cloud with the atom's nucleus and its center.
- **p orbital** is a dumbbell-shaped electron cloud with the nucleus between the two lobes.



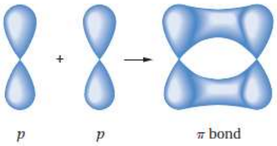
# SIGMA (σ) AND pi (π) BONDS

- Sigma bonds (σ bonds) can be formed from
  - The overlap of two s atomic orbitals.



  - The end-on overlap of two *p* atomic orbitals.
  - The overlap of two an s atomic orbital with a p atomic orbital.

- pi bonds (π bonds) can be formed from
  - The side-side overlap between two *p* atomic orbitals.

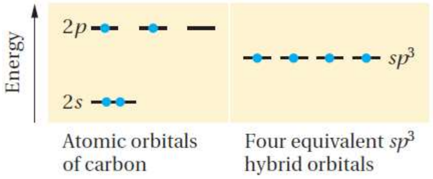


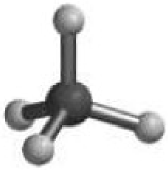
## HYBRIDIZATION

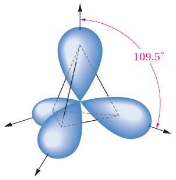
### CARBON *sp*³ HYBRID ORBITALS

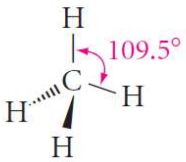
- The angle between any two of the four bonds formed from *sp*³ orbitals is approximately 109.5° with Regular tetrahedral geometry.

*$1s^2 2s^2 2p_x^1 2p_y^1$ Equivalent to* $:\dot{\mathrm{C}}\cdot$









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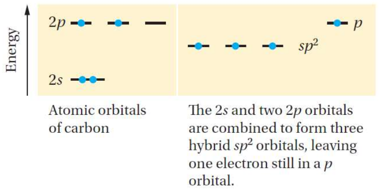
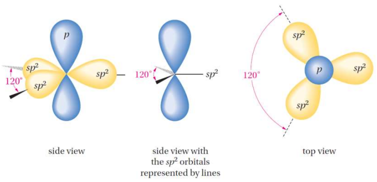
## HYBRIDIZATION

### CARBON *sp*² HYBRID ORBITALS

- Combine only three of the orbitals, to make three equivalent *sp*²-hybridized orbitals (called *sp*² because they are formed by combining one s and two p orbitals)
- The angle between them is 120° with A trigonal carbon

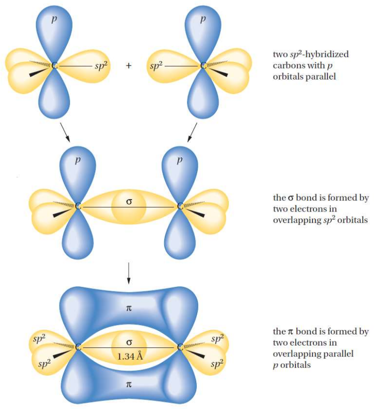




side view

side view with the *sp*² orbitals represented by lines

top view

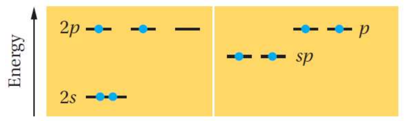


Schematic formation of a carbon–carbon double bond. Two *sp*² carbons form a sigma (s) bond (end-on overlap of two *sp*2 orbitals) and a pi (p) bond (lateral overlap of two properly aligned *p* orbitals).

# HYBRIDIZATION

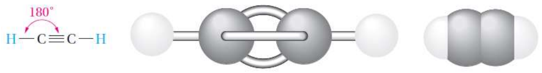
## CARBON *sp* HYBRID ORBITALS

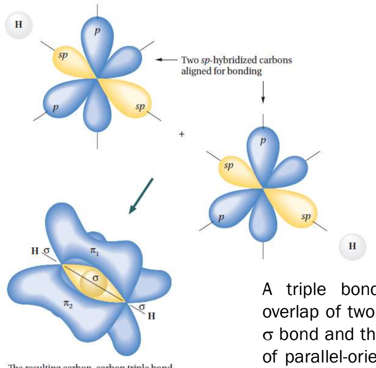
- The carbon atom of an acetylene is connected to only *two* other atoms. Therefore, we combine the 2s orbital with only one 2*p* orbital to make two *sp*-hybrid orbitals
- The angle between the two hybrid orbitals is 180° and Linear



Atomic orbitals of carbon

The 2*s* and one 2*p* orbital are combined to form two hybrid *sp* orbitals, leaving one electron in each of two *p* orbitals.





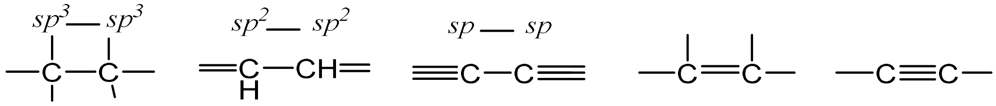
The resulting carbon–carbon triple bond, with a hydrogen atom attached to each remaining *sp* bond. (The orbitals involved in the C—H bonds are omitted for clarity.)

A triple bond consists of the end-on overlap of two *sp*-hybrid orbitals to form a σ bond and the lateral overlap of two sets of parallel-oriented *p* orbitals to form two mutually perpendicular π bonds.

# BONDING IN CARBON COMPOUNDS

## CARBON-CARBON BONDS

- The combination of two carbons results from the axial overlap of two $sp^3$ atomic orbitals
- With increasing the s component, the bond length decreases as the electron in s orbital in held closer and tightly by the nucleus.

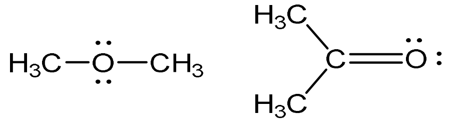


| | $sp^3$— $sp^3$ | $sp^2$— $sp^2$ | $sp$ — $sp$ | | |
|---|---|---|---|---|---|
| Bond length (A) | 1.54 | 1.47 | 1.38 | 1.33 | 1.20 |
| Bond energy (kJ) | 347 | | | 598 | 812 |

## BONDING IN CARBON COMPOUNDS

### CARBON-OXYGEN BONDS

- The electronic configuration of oxygen atom is $1s^2 2s^2 2p_x^2 2p_y^1 2p_z^1$
- **C – O –C ;** the oxygen atom could use four $sp^3$ hybrid orbitals: two to form sigma bonds by overlap with an $sp^3$ orbital of each of the two carbon atoms and the other two to accommodate its two lone pairs of electrons.
- **C = O ;** the oxygen atom could use three $sp^2$ hybrid orbitals: one to form sigma bonds by overlap with an $sp^2$ orbital of the carbon atom and the other two to accommodate its two lone pairs of electrons.
- *Leaves an unhybridized p orbital on both oxygen and carbon to form pi bond.*



| | | |
|---|---|---|
| Bond length (A) | 1.42 | 1.22 |
| Bond energy (kJ) | 360 | 750 |

- *Bond energy is greater than twice due to the stability in C=O as the lone pairs on oxygen are further apart.*

## BONDING IN CARBON COMPOUNDS

### CARBON-NITROGEN BONDS

- The electronic configuration of nitrogen atom is $1s^2 2s^2 2p_x^1 2p_y^1 2p_z^1$

| | $C-\ddot{N}$ | $C=\ddot{N}$ | $C\equiv\ddot{N}$ |
|---|---|---|---|
| Bond length (A) | 1.47 | 1.29 | 1.16 |
| Bond energy (kJ) | 305 | 616 | 893 |

# ELECTRON DISPLACEMENT EFFECTS IN COVALENT BONDS

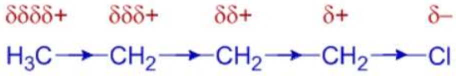
- The electron displacement in an organic molecule may take place either in
  - The ground state under the influence of an atom or a substituent group cause permanent polarization of the bond (*Inductive effect and resonance effects*).

  Or

  - in the presence of an appropriate attacking reagent.
  - Temporary electron displacement effects (*electromeric effect or polarizability effect*).

# INDUCTIVE EFFECT

- *Inductive effects are electronic effects that occur through sigma σ bonds caused by electronegativity differences of atoms.*



$$\overset{\delta\delta\delta+}{H_3C} \rightarrow \overset{\delta\delta\delta+}{CH_2} \rightarrow \overset{\delta\delta+}{CH_2} \rightarrow \overset{\delta+}{CH_2} \rightarrow \overset{\delta-}{Cl}$$

- *Types of inductive effect:*

  1) **Negative inductive effect (-I):**
     - This is the electron-withdrawing inductive effect, also known as the *-I* effect

       $NH_3^+ > NO_2 > CN > SO_3H > CHO > CO > COOH > COCl > CONH_2 >$
       $F > Cl > Br > I > OH > OR > NH_2 > C_6H_5 > H$

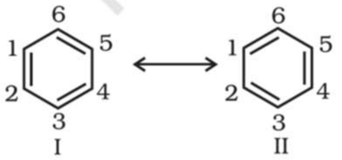
  2) **Positive inductive effect (+I):**
     - This is electron releasing character and is indicated by the *+I* effect

       $C(CH_3)_3 > CH(CH_3)_2 > CH_2CH_3 > CH_3 > H$

## RESONANCE STRUCTURE

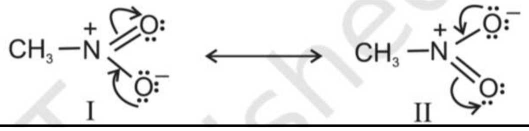
- The resonance structures are hypothetical and individually do not represent any real molecule.
- An example:

  Benzene; Its cyclic structure containing alternating C–C single and C=C double bonds



- An example:

  Nitromethane ($CH_3NO_2$); It is therefore a resonance hybrid of the two canonical forms I and II.



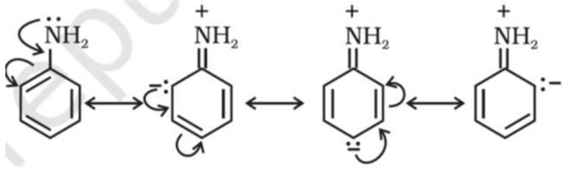
## RESONANCE OR MESOMERIC EFFECT

- The resonance effect is defined as ‘the polarity produced in the molecule by the interaction of two π-bonds or between a π-bond and lone pair of electrons present on an adjacent atom’.

  (i) Positive Resonance Effect (+R effect):

  *The transfer of electrons is away from an atom or substituent group attached to the conjugated system.*

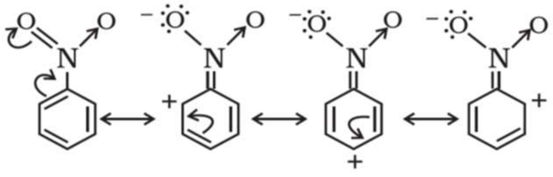
  *Examples; – halogen, –OH, –OR, –OCOR, –$NH_2$, –NHR, –$NR_2$, –NHCOR,*



  (ii) Negative Resonance Effect (- R effect):

  *The transfer of electrons is towards the atom or substituent group attached to the conjugated system.*

  *Examples; – COOH, –CHO, >C=O, – CN, –$NO_2$*

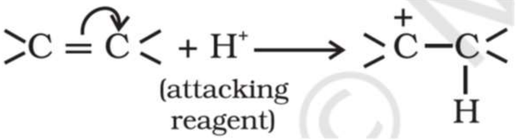


## ELECTROMERIC EFFECT (E EFFECT)

- The organic compounds having a multiple bond (a double or triple bond) show this effect in the presence of an attacking reagent only.
- The complete transfer of a shared pair of π-electrons to one of the atoms joined by a multiple bond on the demand of an attacking reagent.

(i) Positive Eelctromeric Effect (+E effect):

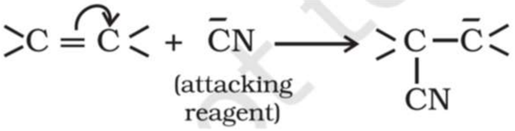
*the π–electrons of the multiple bond are transferred to that atom to which the reagent gets attached.*



$>C=C< + H^{+} \longrightarrow >\overset{+}{C}-\underset{H}{C}<$

(ii) Negative Electromeric Effect (–E effect):

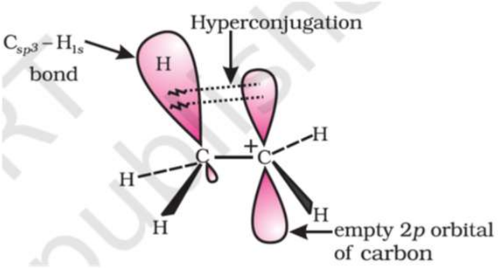
*the π - electrons of the multiple bond are transferred to that atom to which the attacking reagent does not get attached.*

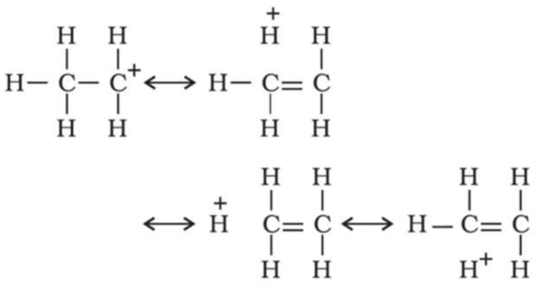


$>C=C< + \bar{C}N \longrightarrow >\underset{CN}{C}-\bar{C}<$

## HYPERCONJUGATION

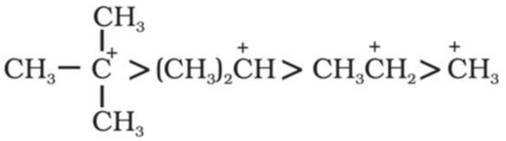
- It involves delocalization of σ electrons of C—H bond of an alkyl group directly attached to an atom of unsaturated system or to an atom with an unshared *p* orbital.
- $CH_3CH_2^+$ (ethyl cation); the positively charged carbon atom has an empty *p* orbital. One of the C-H bonds of the methyl group can align in the plane of this empty *p* orbital and the electrons constituting the C-H bond in plane with this *p* orbital can then be delocalized into the empty p orbital.





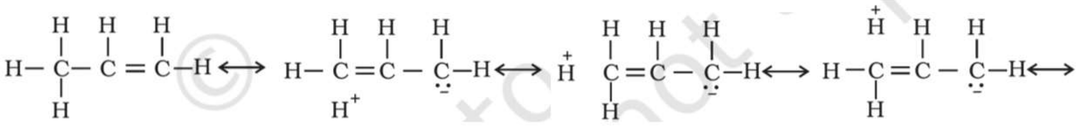
## HYPERCONJUGATION

- This type of overlap stabilizes the carbocation because electron density from the adjacent σ bond helps in dispersing the positive charge.
- In general, greater the number of alkyl groups attached to a positively charged carbon atom, the greater is the hyperconjugation interaction and stabilization of the cation.



$$CH_3-\overset{+}{C}(CH_3)_2 > (CH_3)_2\overset{+}{C}H > CH_3\overset{+}{C}H_2 > \overset{+}{C}H_3$$

- Hyperconjugation is also possible in alkenes and alkylarenes.



## TYPES OF ORGANIC REACTIONS

1) Substitution Reactions

   *a. Nucleophilic substitution*

   *b. Electrophilic substitution*

   *c. Free-radical substitution*

2) Addition Reactions

   *a. Nucleophilic addition*

   *b. Electrophilic addition*

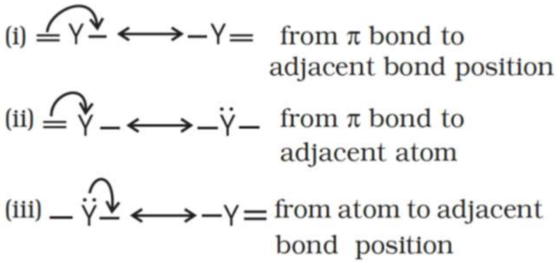
   *c. Free-radical addition*

3) Elimination Reactions

4) Rearrangement reactions

## ELECTRON MOVEMENT IN ORGANIC REACTIONS: THE ARROW NOTATION

- The movement of electrons in organic reactions can be shown by curved-arrow notation.



(i) from π bond to adjacent bond position

(ii) from π bond to adjacent atom

(iii) from atom to adjacent bond position

- Movement of single electron is indicated by a single barbed 'fish hooks' (i.e. *half headed curved arrow*).

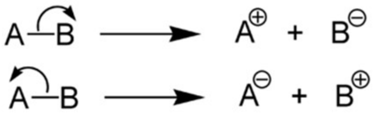
$CH_3-Cl \longrightarrow \dot{C}H_3 + \dot{C}l$

## HOW DO THESE REACTIONS OCCUR?

## NOTATIONS FOR BOND BREAKING

- There are two types of mechanisms depending on the way bonds are broken and made:

**1) Heterolytic bond fission**

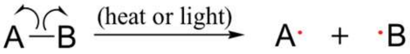


$A-B \longrightarrow A^{\oplus} + B^{\ominus}$

$A-B \longrightarrow A^{\ominus} + B^{\oplus}$

- The bonds are broken in such a way that the bond electron pair is assigned completely to one fragment.
- These reactions are also called *ionic reactions*, since ionic reactants, products, or intermediates are usually involved.

**2) Homolytic bond fission**



$A-B \xrightarrow{\text{(heat or light)}} A\cdot + \cdot B$

- The bonds are broken in such a way that one bond electron remains with one fragment and the other one bond electron with the other atom.
- Free radical intermediates are therefore involved and these transformations are consequently called *radical reactions*.

## HOW DO THESE REACTIONS OCCUR?

### NOTATIONS FOR BOND MAKING

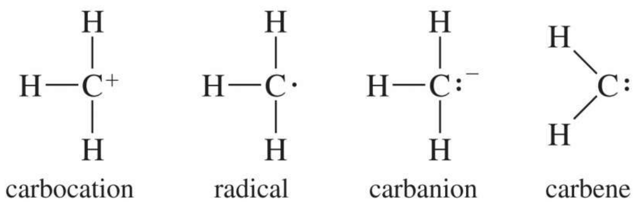
- Symmetrical bond-making (radical):
  *one bonding electron is donated by each reactant*

- Unsymmetrical bond-making (polar):
  *two bonding electrons are donated by one reactant*

## REACTIVE INTERMEDIATE

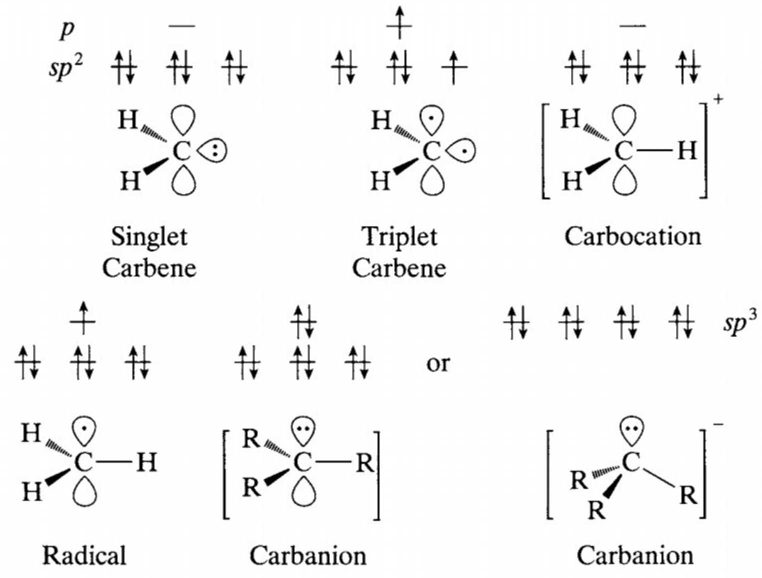
- There are four types of organic species;
  *very short-lived and exist only as intermediates that are quickly converted to more stable molecules*

### Carbon Reactive Intermediates



- Nitrenes (*nitrogen analogs of carbenes*) $\mathbf{R-\overline{\underline{N}}}$

## REACTIVE INTERMEDIATE



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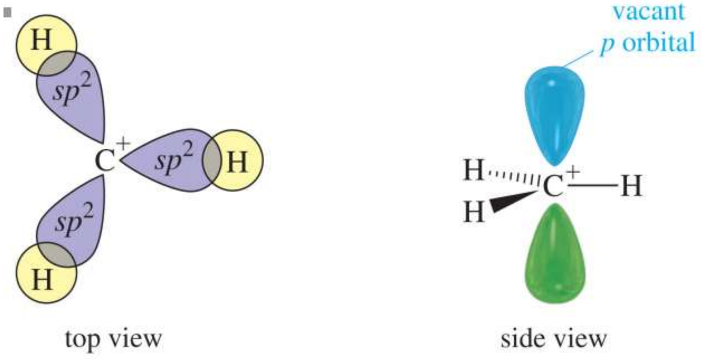
## REACTIVE INTERMEDIATE

### CARBOCATION

**Carbocation Structure**

- Carbon has 6 electrons, positively charged.
- Carbon is $sp^2$ hybridized with vacant *p* orbital



# REACTIVE INTERMEDIATE

## CARBOCATION

### Methods of Forming Carbocation

(A) Heterolytic fission of neutral species

- Simple ionization; *the electron pair remains with departing group, which is called leaving group and tertiary butyl group carries positive charge.*

$$Me_3C{-}Br \rightleftharpoons Me_3C^{\oplus}\,Br^{\ominus}$$

- Ionization may also be induced by Lewis acids, e.g. $BF_3$, $AlCl_3$ to yield in this case an acyl cation.

$$MeCOF + BF_3 \rightleftharpoons MeCO^{\oplus}\,BF_4^{\ominus}$$

- With antimony pentaflouride ($SbF_5$) as a Lewis acid, with either liquid $SO_2$ or excess $SbF_5$ as solvent,

$$R{-}F + SbF_5 \rightleftharpoons R^{\oplus}SbF_6^{\ominus}$$

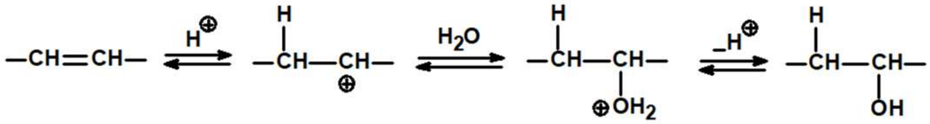
# REACTIVE INTERMEDIATE

## CARBOCATION

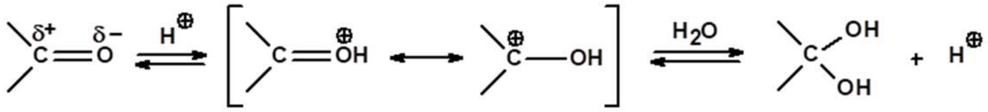
### Methods of Forming Carbocation

(B) Addition of cations to neutral species

- The most common cation is $H^+$, adding to unsaturated linkages, i.e. protonation, in for example the acid-catalyzed hydration of alkenes:



- Protonation can also occur on oxygen in a carbon-oxygen double bond,



## REACTIVE INTERMEDIATE

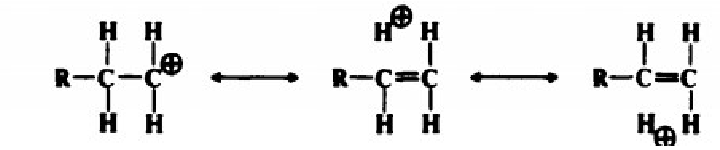
## CARBOCATION

### Stability and Structure of Carbocation

- The simple alkyl carbocation have already been seen to follow the stability sequence,

$$Me_3C^{\oplus} > Me_2CH^{\oplus} > MeCH_2^{\oplus} > CH_3^{\oplus}$$

- The stability order can be explained by hyperconjugation and inductive effect
- Quantum mechanical calculations for simple alkyl cations do indeed suggest that the planar (*sp*$^2$) configuration is more stable than the pyramidal (*sp*$^3$) by ≈ 84 kJ (20 kcal) mol$^{-1}$.



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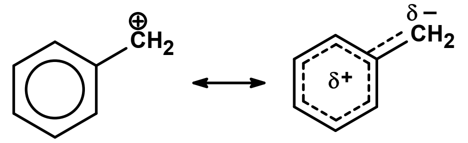
## REACTIVE INTERMEDIATE

## CARBOCATION

### Stability and Structure of Carbocation

- The possibility of delocalizing the charge, particularly where this can involve π orbitals:

$$CH_2{=}CH{-}\overset{\oplus}{C}H_2 \longleftrightarrow \overset{\oplus}{C}H_2{-}CH{=}CH_2$$



$$Me{-}O{-}\overset{\oplus}{C}H_2 \longleftrightarrow Me{-}\overset{\oplus}{O}{=}CH_2$$

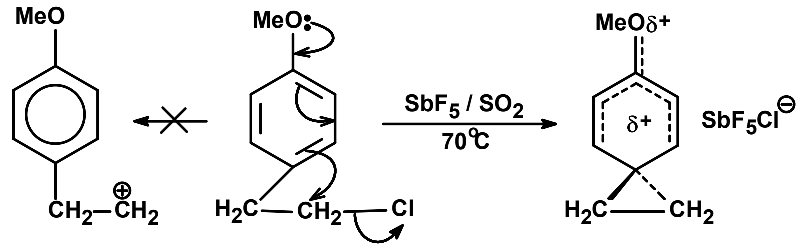
REACTIVE INTERMEDIATE

## CARBOCATION

### Stability and Structure of Carbocation

- Stabilization can also occur, again by delocalization, through the operation of a neighboring group effect resulting in the formation of a 'bridged' carbocation.

*Thus the action of $SbF_5$ in liquid $SO_2$ on p-$MeOC_6H_4CH_2CH_2Cl$ (1) results in the formation of (2) rather than the expected cation (3), phenyl acting as a neighboring group:*



(3) (1) (2)

---

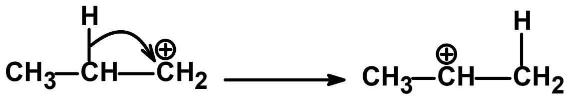
REACTIVE INTERMEDIATE

## CARBOCATION

### Carbocation Rearrangements

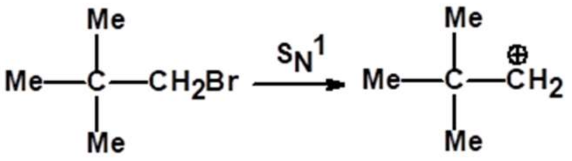
- Without change in carbon skeleton;

*1-propyl cation rearranged to the 2-propyl cation by the migration of a hydrogen atom, with its electron pair (i.e. as $H^-$), from $C_2$ to the carbocationic $C_1$, a 1,2-hydride shift:*



$$CH_3-\overset{H}{C}H-\overset{\oplus}{C}H_2 \longrightarrow CH_3-\overset{\oplus}{C}H-\overset{H}{C}H_2$$

- With change in carbon skeleton; Neopentyl rearrangements



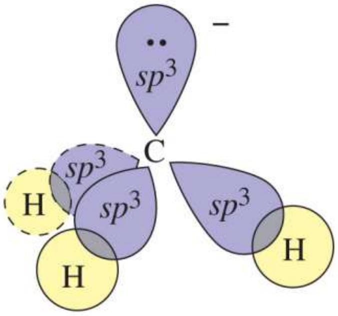
$$Me-\underset{Me}{\overset{Me}{C}}-CH_2Br \xrightarrow{S_N1} Me-\underset{Me}{\overset{Me}{C}}-\overset{\oplus}{C}H_2$$

## REACTIVE INTERMEDIATE

## CARBANION

### Carbanion Structure

- *Eight electrons on carbon: 6 bonding plus one lone pair.*
- *Carbon has a negative charge.*
- *Destabilized by alkyl substituents.*



methyl anion

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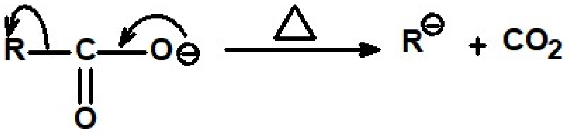
## REACTIVE INTERMEDIATE

## CARBANION

- *Carbanion* possess an unshared pair of electrons and is therefore a base.
- Carbanion can be formed by
  - *Removal of a proton*

$$R_3C—H + B\!: \rightleftharpoons R_3C^{\ominus} + BH^{\oplus}$$

  - *Removal of $CO_2$ from decarboxylation of $RCO_2^-$*



$$R—\underset{\underset{O}{\|}}{C}—O^{\ominus} \xrightarrow{\Delta} R^{\ominus} + CO_2$$

  - *Removal of Cl from $Ph_3C$-Cl*

$$Ph_3C—Cl \xrightarrow{Na\ /\ Hg} Ph_3C^{\ominus}\,Na^{\oplus}$$

REACTIVE INTERMEDIATE

## CARBANION

### Stability of Carbanion

- The main features that serve to stabilize carbanions are
  - *increase in s character at the carbanion carbon*

$$CH_3{-}CH_3 < CH_2{=}CH_2 < HC{\equiv}CH$$

  - *electron-withdrawing inductive effects*

$^{-}CF_3$ and $^{-}C(CF_3)_3$ by electron-withdrawal.

*The destabilizing influence of the electron-donating inductive effect of alkyl groups is seen in the observed carbanion stability sequence:*

$$CH_3^{\ominus} > RCH_2^{\ominus} > R_2CH^{\ominus} > R_3C^{\ominus}$$

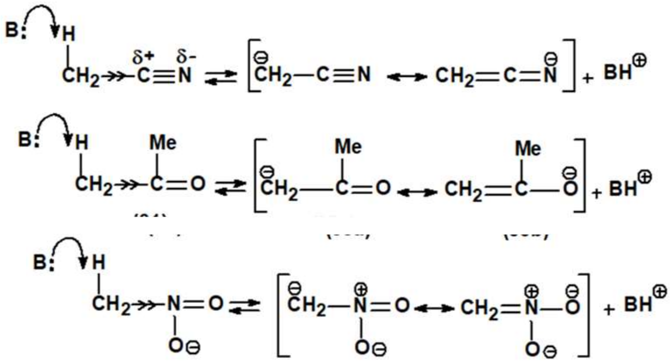
REACTIVE INTERMEDIATE

## CARBANION

### Stability of Carbanion

- The main features that serve to stabilize carbanions are
  - *conjugation of the carbanion lone pair with a polarized multiple bond*

*the most common stabilizing feature, e.g. with CN, C=O, $NO_2$*



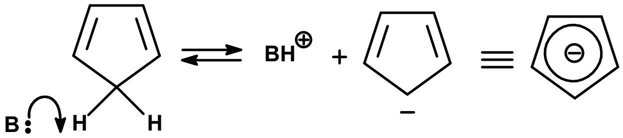
## REACTIVE INTERMEDIATE

### CARBANION

#### Stability of Carbanion

- The main features that serve to stabilize carbanions are
  - *aromatization*

the cyclopentadienyl anion, being a 6π electron delocalized system, The 6 electrons can be accommodated in three stabilized π molecular orbitals, like benzene, and the anion thus shows quasi-aromatic stabilization; it is stabilized by *aromatization*:



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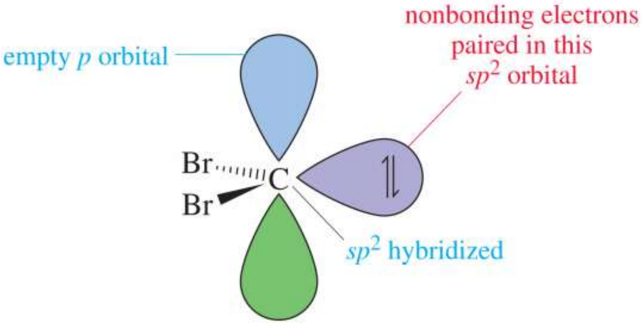
## REACTIVE INTERMEDIATE

### CARBENES AND NITRENES

#### Carbenes Structure

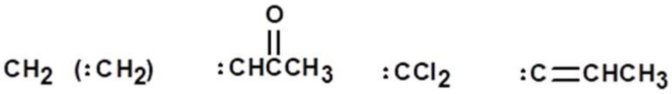
- Carbon is neutral
- Vacant p orbital, so can be electrophilic
- Lone pair of electrons, so can be nucleophilic



## REACTIVE INTERMEDIATE

### CARBENES AND NITRENES

- *Carbenes* (also called methylenes) are highly reactive species.
- *Carbenes* are molecules containing divalent carbon atoms.
- Each divalent carbon has two unshared electrons, which are often shown when writing the structures of carbenes.
- However, carbenes are neutral molecules, not carbanions.



$CH_2$ $(:CH_2)$ $:CH\overset{\overset{\displaystyle O}{\|}}{C}CH_3$ $:CCl_2$ $:C{=}CHCH_3$

- *Nitrenes* are compounds, such as $:NC_6H_5$, that contain monovalent nitrogen atoms.

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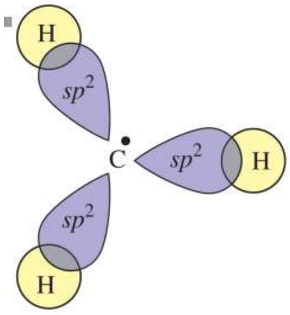
## REACTIVE INTERMEDIATE

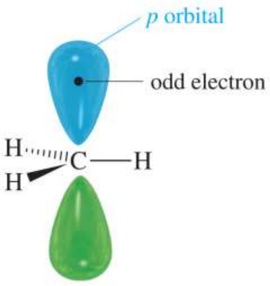
### FREE RADICALS

Free radical Structure

- Electron-deficient
- Stabilized by alkyl substituents.
- Order of stability: 3° > 2° > 1°.



top view



side view

## REACTIVE INTERMEDIATE

### FREE RADICALS

- Radicals are species that contain one or more unpaired electrons.
- Many radicals are produced by homolytic cleavage of bonds.

$$Cl_2 \xrightarrow{h\nu} 2Cl^{\cdot}$$

- Hydrogen abstraction; many radicals can remove hydrogen atoms from organic molecules to form carbon radicals.

$$F\cdot + CH_4 \longrightarrow HF + \cdot CH_3$$

## NUCLEOPHILES AND ELECTROPHILES

### ELECTROPHILES

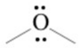
- Electrophile ($E^+$); (electron-loving) are electron-deficient species and tend to attack the substrate at a site of high electron density and the reaction is called *electrophilic*.
- Examples of electrophiles include
  - Positively charged species as exemplified by proton ($H^+$), cations (such as $Cl^+$, $NR_4^+$) and carbocations ($^+CH_3$) and
  - Neutral species as exemplified by Lewis acids (such as $BF_3$, $AlCl_3$, $ZnCl_2$) and carbenes ($Cl_2C:$) or neutral molecules having functional groups like carbonyl group (>C=O) or alkyl halides ($R_3C$-X, where X is a halogen atom).
- They have six valence electrons (except $H^+$) and can accept an electron pair from a nucleophile to acquire the stable octet.
- For example, hydroxide ion combines with a proton to give water.

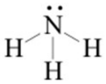
$$H^{\oplus} + \overset{\ominus}{O}H \longrightarrow H{-}O{-}H$$

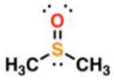
## NUCLEOPHILES AND ELECTROPHILES

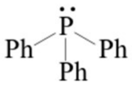
### NUCLEOPHILES

- Nucleophile (Nu:); a reagent that brings an electron pair to the reactive site and the reaction is then called *nucleophilic*.
- Some examples of nucleophiles are
  - the negatively charged ions with lone pair of electrons such as hydroxide ($HO^-$), cyanide ($NC^-$) ions and carbanions ($R_3C:^-$).
  - Neutral molecules having nonbonding lone pair(s) of electrons such as water, ammonia, alcohols, dimethylsulfide and triphenylphosphine


water


ammonia


dimethylsulfide

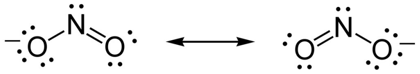

triphenylphosphine

- Nucleophilic reagents tend to attack the electron deficient species (electrophiles).

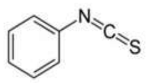
## NUCLEOPHILES AND ELECTROPHILES

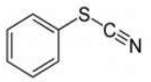
### NUCLEOPHILES

- The nucleophiles which have more than one (generally two) suitable atoms through which they can attack the substrate are known as ambident nucleophiles.
- *An ambident nucleophile is an anionic nucleophile whose negative charge is delocalized by resonance over two unlike atoms or over two like but non-equivalent atoms.*
- Some examples are
  - Cyanide, isothiocyanate and nitrite ions are some examples of ambident nucleophiles, since they have more than one reactive site.




*isothiocyanate* binds through N   *thiocyanate* binds through S

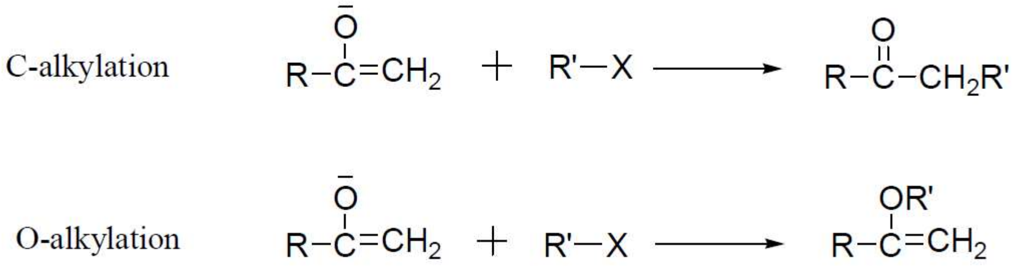

phenyl isothiocyanate


phenyl thiocyanate

## NUCLEOPHILES AND ELECTROPHILES

### NUCLEOPHILES

- Example
  - Alkylation of enolate can either occur at C or O. since most negative charge of an enolate is on the Oxygen atom, the O-alkylated product is dominated.



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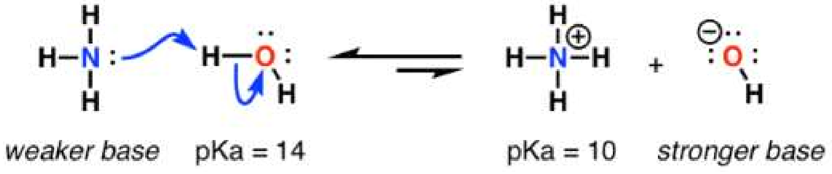
## NUCLEOPHILES AND ELECTROPHILES

### NUCLEOPHILICITY AND BASICITY?

- ***Basicity:*** nucleophile attacks hydrogen (proton).
- ***Nucleophilicity:*** nucleophile attacks any atom other than hydrogen (e.g. carbon).

Most species can participate in reversible acid-base reactions.
*Basicity can be measured by the position of an equilibrium (e.g. stability is a thermodynamic property.*

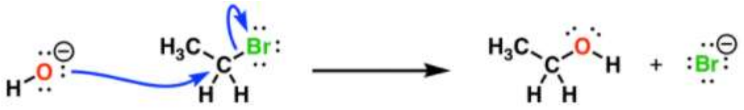


## NUCLEOPHILES AND ELECTROPHILES

### NUCLEOPHILICITY AND BASICITY?

- *Basicity:* nucleophile attacks hydrogen (proton).
- *Nucleophilicity:* nucleophile attacks any atom other than hydrogen (e.g. carbon).

Reactions of nucleophiles with carbon are irreversible and are not in equilibrium (e.g. A bond forms, a bond breaks, and that's the end of the reaction).
*e.g. the nucleophilicity is measured by the rate of the reaction.*



*irreversible reaction*

## NUCLEOPHILES AND ELECTROPHILES

### FACTORS AFFECTING NUCLEOPHILICITY

- *Charge:* the conjugate base is always a stronger nucleophile as the nucleophilicity increases with increasing electron density on an atom.

$HO^{-}$ > $H_2O$     $H_2N^{-}$ > $NH_3$     $HS^{-}$ > $H_2S$

- *Electronegativity:* nucleophilicity increases with decreasing electronegativity as the less electronegative the atom, the less "tightly held" those electrons will be.

$H_3C^{-}$ > $H_2N^{-}$ > $HO^{-}$ > $F^{-}$

$H_3N$ > $H_2O$ > $HF$

These two factors correlate strongly with basicity.

## NUCLEOPHILES AND ELECTROPHILES

### FACTORS AFFECTING NUCLEOPHILICITY

- *solvent:* in *polar protic solvents*, nucleophilicity increases going down the periodic table (solvation).

*strongest* *weakest* (In polar protic solvents)

- *solvent:* in *polar aprotic solvents*, nucleophilicity increases going up the periodic table (solvation).

*strongest* *weakest* (In polar aprotic solvents)

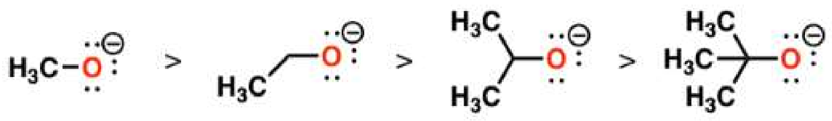
Nucleophilicity is essentially correlated with basicity.

---

## NUCLEOPHILES AND ELECTROPHILES

### FACTORS AFFECTING NUCLEOPHILICITY

- *Steric Hindrance "Bulkiness":* in *polar protic solvents*, nucleophilicity increases going down the periodic table (solvation).



best nucleophile
(least bulky)

worst nucleophiles
(most bulky)

## NUCLEOPHILES AND ELECTROPHILES

### NUCLEOPHILICITY AND BASICITY?

Strong Bases/Strong Nucleophiles

A good base is usually a good nucleophile. So, strong bases — substances with negatively charged O, N, and C atoms — are strong nucleophiles.

Examples are: $RO^-$, $OH^-$, RLi, $RC{\equiv}C:^-$, and $NH_2^-$.

Strong Bases/Poor Nucleophiles

Some strong bases are poor nucleophiles because of steric hindrance.

Examples are $t$-$BuO^-$, $t$-BuLi, and $LiN[CH(CH_3)_2]$

Weak Bases/Good Nucleophiles

$I^-$ is a weak base, but it is a good nucleophile because the large electron cloud is highly polarizable.

## WHY DO THESE REACTIONS OCCUR?

### THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

- When we look at an organic reaction we have to take into account two main concepts:
    - The equilibrium
    - The rate of the reaction.

- The conversion between reactants and products is governed by the reaction free energy ΔG (*free energy of the products) – (free energy of the reactants*).
    - A reaction is thermodynamically allowed when the free energy of the products is lower than that of the reactants (i.e. ΔG is negative).
    - When ΔG = zero, the equilibrium is reached and an equilibrium constant $K_{eq}$ of the reaction can be defined as a function of $\Delta G°$, the variation in the standard free energies.

*The equilibrium constant $K_{eq}$ is the ratio between the equilibrium concentration of the products and that of the reactants.*

## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

- When we look at an organic reaction we have to take into account two main concepts:

  (1) The equilibrium (2) The rate of the reaction.

- The conversion between reactants and products is governed by the reaction free energy ΔG (*free energy of the products) – (free energy of the reactants*).
- The reactants must be supplied with enough *activation energy* to enable the reaction to proceed in the forward direction.
- All organic reactions will reach equilibrium that favors the more stable side.

For a reaction:

$$aA + bB \rightleftharpoons dD + eE$$

$K_{eq}$ = [products] / [reactants] = $[D]^d\,[E]^e / [A]^a\,[B]^b$

---

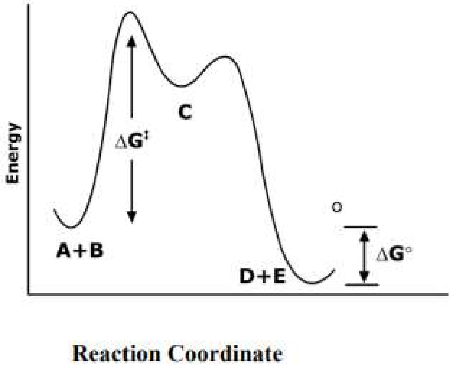
## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

Energy profile for reaction A + B $\longrightarrow$ C $\longrightarrow$ D + E

$\Delta G^o$ = *(free energy of products) – (free energy of reactants)*

$\Delta G^‡$ = *(free energy of transition state) – (free energy of reactants)*



*Any quantity that refers to the transition state is represented by the doubledagger superscript (‡ )*

## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

The thermodynamic stability is indicated by $\Delta G^o$:

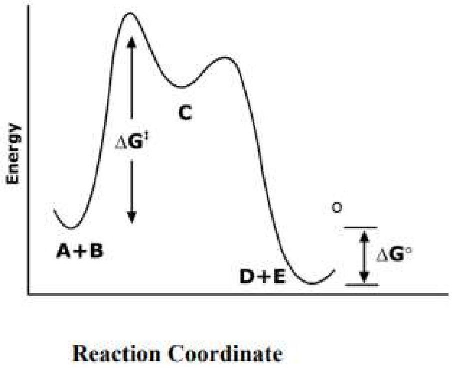
If $\Delta G^o$ is negative the product is **thermodynamically stable** compared to reactant and the reaction is said to be ***exergonic reaction***.

If $\Delta G^o$ is positive the product is **thermodynamically unstable** compared to reactant and the reaction is said to be **endergonic reaction.**

The kinetic stability of a component is indicated by $\Delta G^‡$ :

If $\Delta G^‡$ is large, the compound (the reactant) is **kinetically stable** i.e., it does not undergo that reaction rapidly.

If $\Delta G^‡$ is small, the compound (the reactant) is **kinetically unstable** i.e., it undergoes the reaction rapidly.



## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

- For a reaction to take place spontaneously;
  *the free energy of the products must be lower than the free energy of the reactants; i.e., ΔG must be negative.*
- The Gibbs standard free-energy (ΔG) change has an enthalpy component and an entropy component, which are related by the following equation:

$$\Delta G^o = -RT \ln K_{eq} = \Delta H - T \Delta S$$

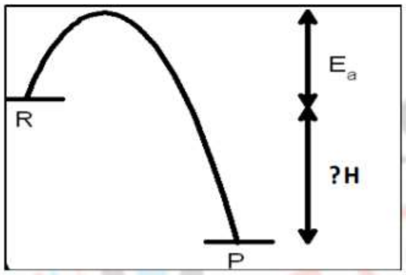
The enthalpy term (ΔH);

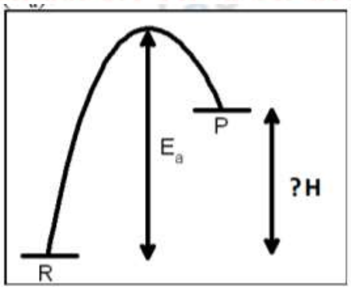
*When new bonds are formed, heat is given off and when bonds are broken, heat is consumed.*
*Thus, ΔH is a measure of the bond-making and bond-breaking processes that occur as reactants are converted into products.*

Entropy (ΔS) is defined as the degree of disorder of a system.

## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION





**Exothermic/spontaneous Reactions**

- More energy will be released to the surrounding.
- $\Delta H$ will be negative.
- The products are thermodynamically stable than the reactants ($-\Delta G$).
- The equilibrium constant for the reaction will be large ($K_{eq}>1$).

**Endothermic/nonspontaneous Reactions**

- More energy will be absorbed from the surrounding.
- $\Delta H$ will be positive.
- The reactants are thermodynamically stable than the products ($+\Delta G$).
- The equilibrium constant for the reaction will be small ($K_{eq}<1$).

## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

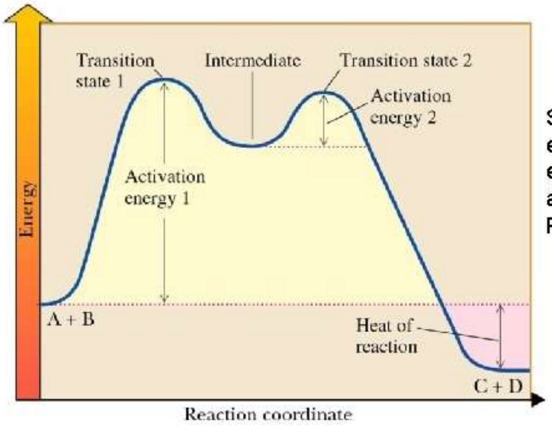
### Multi-Step Reactions

Step 1: A + B → Intermediate

Step 2: Intermediate → C + D

Step 1 is the "slow step", the rate determining step.

Step 1: endergonic, high energy of activation. Slow process

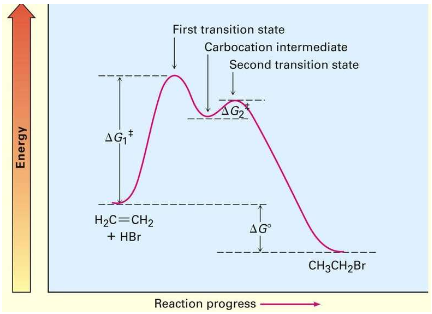


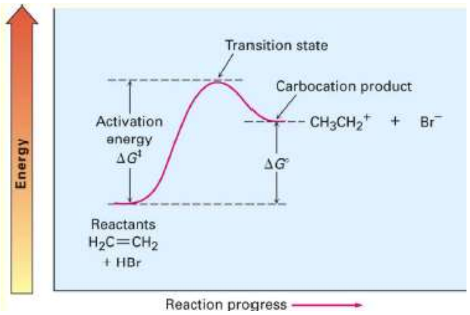
Step 2: exergonic, small energy of activation. Fast Process.

## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

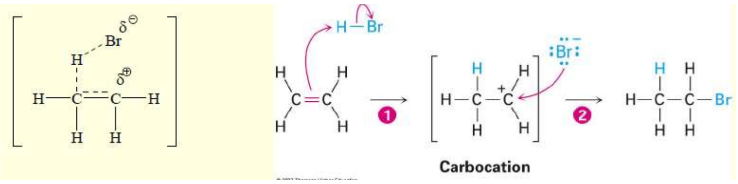
### Energy diagram for the reaction of Ethylene with HBr





- If a reaction occurs in more than one step, it must involve species that are neither the reactant nor the final product.
- These are called reaction *intermediates*.
- Each step has its own free energy of activation

- The energy needed to go from reactant to transition state is the *activation energy (ΔG‡).*
- The highest energy point in a reaction step is called the *transition state*



## WHY DO THESE REACTIONS OCCUR?

## THERMODYNAMIC AND KINETIC REQUIREMENT OF A REACTION

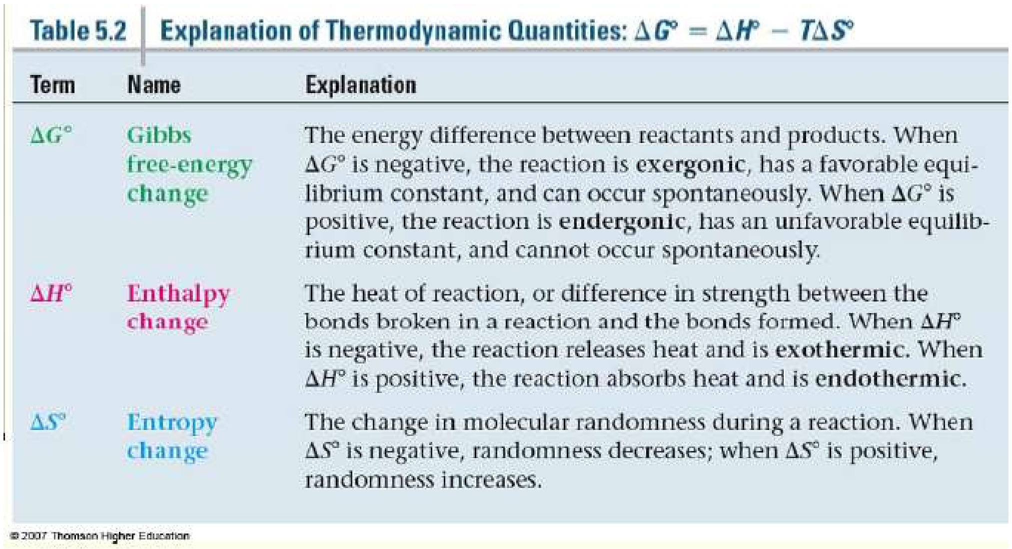


**Table 5.2** Explanation of Thermodynamic Quantities: $\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$

| Term | Name | Explanation |
|---|---|---|
| $\Delta G^{\circ}$ | Gibbs free-energy change | The energy difference between reactants and products. When $\Delta G^{\circ}$ is negative, the reaction is **exergonic**, has a favorable equilibrium constant, and can occur spontaneously. When $\Delta G^{\circ}$ is positive, the reaction is **endergonic**, has an unfavorable equilibrium constant, and cannot occur spontaneously. |
| $\Delta H^{\circ}$ | Enthalpy change | The heat of reaction, or difference in strength between the bonds broken in a reaction and the bonds formed. When $\Delta H^{\circ}$ is negative, the reaction releases heat and is **exothermic**. When $\Delta H^{\circ}$ is positive, the reaction absorbs heat and is **endothermic**. |
| $\Delta S^{\circ}$ | Entropy change | The change in molecular randomness during a reaction. When $\Delta S^{\circ}$ is negative, randomness decreases; when $\Delta S^{\circ}$ is positive, randomness increases. |

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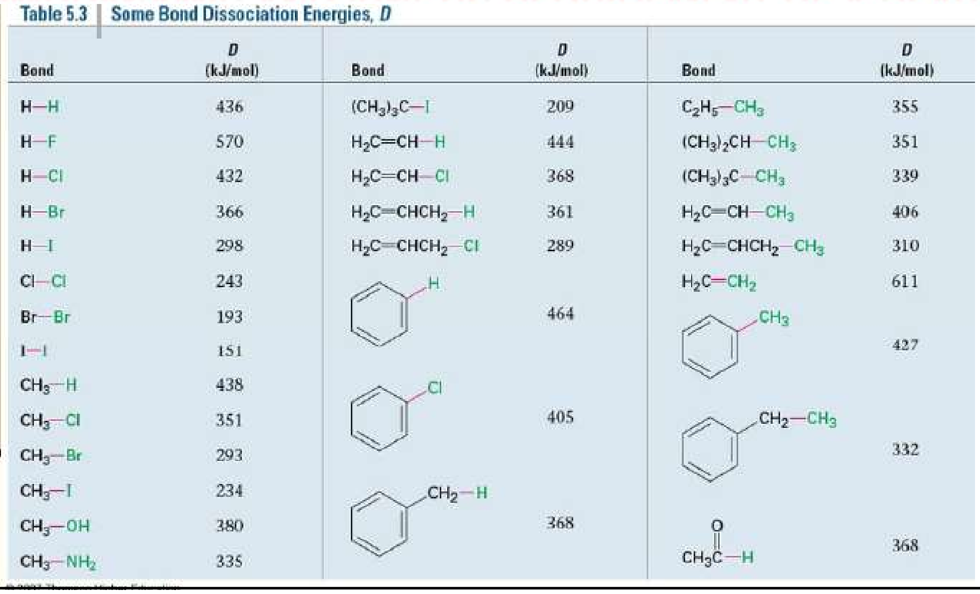

**Table 5.3 | Some Bond Dissociation Energies, *D***

| Bond | *D* (kJ/mol) | Bond | *D* (kJ/mol) | Bond | *D* (kJ/mol) |
|---|---|---|---|---|---|
| $H{-}H$ | 436 | $(CH_3)_3C{-}I$ | 209 | $C_2H_5{-}CH_3$ | 355 |
| $H{-}F$ | 570 | $H_2C{=}CH{-}H$ | 444 | $(CH_3)_2CH{-}CH_3$ | 351 |
| $H{-}Cl$ | 432 | $H_2C{=}CH{-}Cl$ | 368 | $(CH_3)_3C{-}CH_3$ | 339 |
| $H{-}Br$ | 366 | $H_2C{=}CHCH_2{-}H$ | 361 | $H_2C{=}CH{-}CH_3$ | 406 |
| $H{-}I$ | 298 | $H_2C{=}CHCH_2{-}Cl$ | 289 | $H_2C{=}CHCH_2{-}CH_3$ | 310 |
| $Cl{-}Cl$ | 243 | | | $H_2C{=}CH_2$ | 611 |
| $Br{-}Br$ | 193 | H | 464 | | |
| $I{-}I$ | 151 | | | $CH_3$ | 427 |
| $CH_3{-}H$ | 438 | | | | |
| $CH_3{-}Cl$ | 351 | Cl | 405 | | |
| $CH_3{-}Br$ | 293 | | | $CH_2{-}CH_3$ | 332 |
| $CH_3{-}I$ | 234 | | | | |
| $CH_3{-}OH$ | 380 | $CH_2{-}H$ | 368 | | |
| $CH_3{-}NH_2$ | 335 | | | $CH_3\overset{O}{\overset{\Vert}{C}}{-}H$ | 368 |

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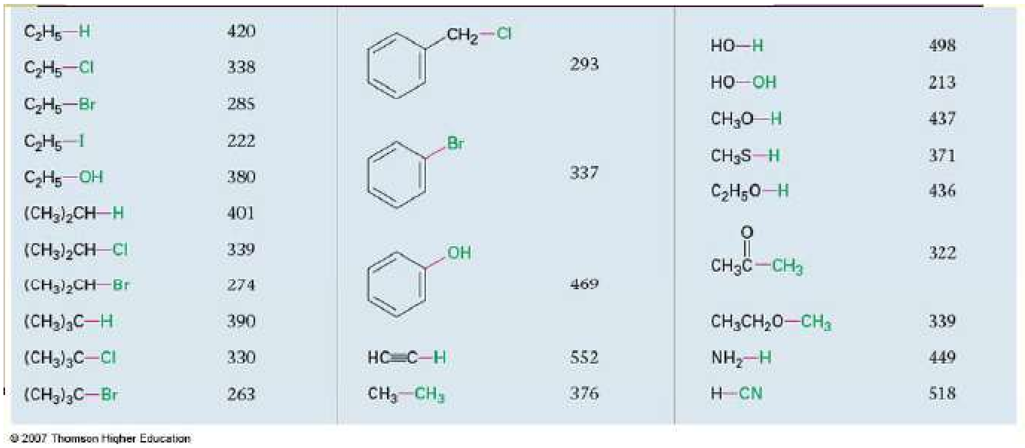

| | | | | | |
|---|---|---|---|---|---|
| $C_2H_5{-}H$ | 420 | | | $HO{-}H$ | 498 |
| $C_2H_5{-}Cl$ | 338 | $CH_2{-}Cl$ | 293 | $HO{-}OH$ | 213 |
| $C_2H_5{-}Br$ | 285 | | | $CH_3O{-}H$ | 437 |
| $C_2H_5{-}I$ | 222 | | | $CH_3S{-}H$ | 371 |
| $C_2H_5{-}OH$ | 380 | Br | 337 | $C_2H_5O{-}H$ | 436 |
| $(CH_3)_2CH{-}H$ | 401 | | | | |
| $(CH_3)_2CH{-}Cl$ | 339 | | | $CH_3\overset{O}{\overset{\Vert}{C}}{-}CH_3$ | 322 |
| $(CH_3)_2CH{-}Br$ | 274 | OH | 469 | | |
| $(CH_3)_3C{-}H$ | 390 | | | $CH_3CH_2O{-}CH_3$ | 339 |
| $(CH_3)_3C{-}Cl$ | 330 | $HC{\equiv}C{-}H$ | 552 | $NH_2{-}H$ | 449 |
| $(CH_3)_3C{-}Br$ | 263 | $CH_3{-}CH_3$ | 376 | $H{-}CN$ | 518 |

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Kinetics Overview; The smaller the $E_a$ the faster is the reaction:

- If the activation energy is low then the reaction will be fast even at low temperatures. Such reactions do increase their rates with increasing temperature as well
- If the activation energy is high then at low temperatures the reaction will be slow. It can be made faster by increasing the temperature

For the reaction:

First order reaction

$$A \longrightarrow B$$

Rate = k [A]

*If the rate of a reaction depends on the concentration of only one reactant,*

Second-order reaction:

$$A + B \longrightarrow C + D$$

Rate = k [A] [B]

*A reaction whose rate depends on the concentrations of two reactants*