



Kayhan

Introduction to Organic Reactions

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February 2020

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Electron arrays of some basic elements

Valence Electrons

H (Hydrogen): $1s^1$ → 1

C (Carbon): $1s^2 2s^2 2p^2$ → 4

N (Nitrogen): $1s^2 2s^2 2p^3$ → 5

O (Oxygen): $1s^2 2s^2 2p^4$ → 6

F (Fluorine) : $1s^2 2s^2 2p^5$ → 7

Valence electrons are the electrons present in the outermost shell of an atom.

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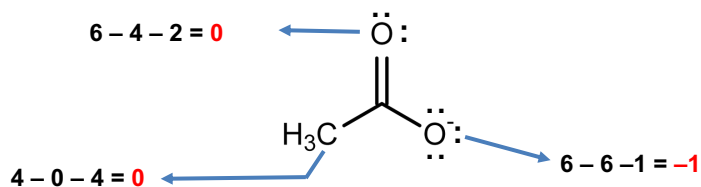
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Formal Charges

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$$\text{Formal Charge} = \boxed{\text{Number of Valence Electrons}} - \boxed{\text{Number of Unpaired Electrons}} - \boxed{\text{Number of Covalent Bonds (Number of paired electrons/2)}}$$



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Introduction to reaction mechanism

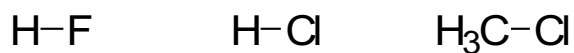
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In all chemical reactions
in common \longrightarrow **Electron Exchange**

Bond electrons can be evenly distributed between two atoms:



If one of the atoms forming the bond tends to attract more electrons than the other, the distribution of electrons in the bond will be polarized, such bonds are called **polar covalent bonds**.



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Partial Charge ($\delta = \text{delta}$)

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Partial positive = $\delta+$

Partial negative = $\delta-$

Electronegativity is a measure of an atom's ability to attract the shared electrons of a covalent bond to itself.

- Bond formed due to equal sharing of electrons is known as covalent bond. If bond is formed between two atoms having different electronegativities, then electron pair is not equally shared.
- More electronegative atom tends to attract shared pair towards itself and hence acquires partial negative charge. And other atom having less electronegativity acquires partial positive charge.
- Thus due to difference in electronegativity, opposite charges get developed, this is known as **polarisation of a covalent bond**.

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Electronegativity

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Electronegativities increase from left to right and from bottom to top in the periodic table.

electropositive elements

Metals of Group I and Group II tends to give electrons

IA	IIA	IIIA	IVA	VA	VIA	VIIA
H 2.3						
Li 1.0	Be 1.5	B 2.0	C 2.5	N 3.0	O 3.5	F 4.0
Na 0.9	Mg 1.2	Al 1.5	Si 1.8	P 2.2	S 2.5	Cl 3.0
K 0.8						Br 2.8
Rb 0.8						I 2.5
Cs 0.7						

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Inductive Effect

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Effect on electron density in one portion of a molecule due to electron-withdrawing or electron-donating groups elsewhere in the molecule.

Substituents with -I inductive effects

If an element is more electronegative from hydrogen, the inductive effect of the element is (-) and is shown as -I.

$-\text{NH}_3^+$	$-\text{F}$
$-\text{NR}_3^+$	$-\text{Cl}$
$-\text{NO}_2$	$-\text{Br}$
$-\text{CN}$	$-\text{OH}$
$-\text{COOH}$	$-\text{OR}$
$-\text{COOR}$	$-\text{SH}$
$-\text{CHO}$	$-\text{SR}$
$-\text{C}=\text{CH}_2$	$-\text{C}\equiv\text{CH}$

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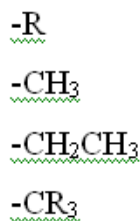


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Alkyl groups and alkali metals (Li, Mg) show **positive inductive effect (+I)**.

Less electronegative than hydrogen (electropositive)

Substituents with +I inductive effects



An **inductive effect** is an electronic effect due to the polarisation of only **sigma (σ) bonds** within a molecule or ion.

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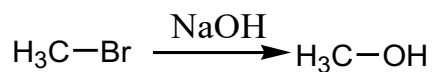
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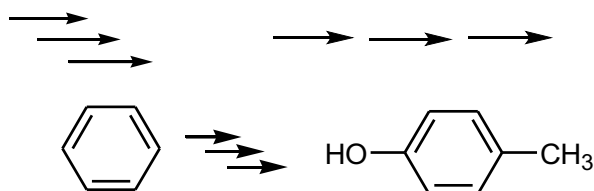
Various Arrow Used in Organic Chemistry

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1) For a one-step reaction



2) In order to achieve the final product in more than one step,



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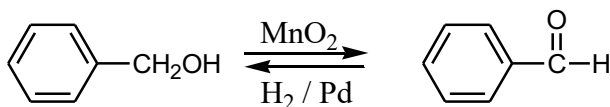
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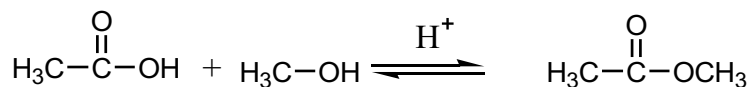


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3) In order to show that the final product can be synthesized from starting compound or the starting compound can be obtained from final product by using different reagents in a one-step reaction equation.



4) In the equilibrium reactions



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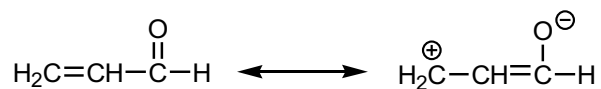
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5) Mesomers (Resonance)



6) Direction of movement of an electron



7) Direction of movement of two electrons



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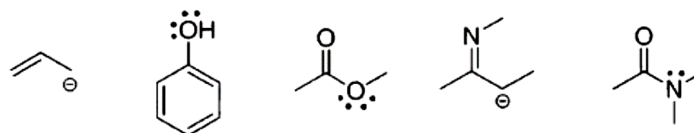
Mesomerism (Resonance)

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1) Compounds with conjugated π bonds



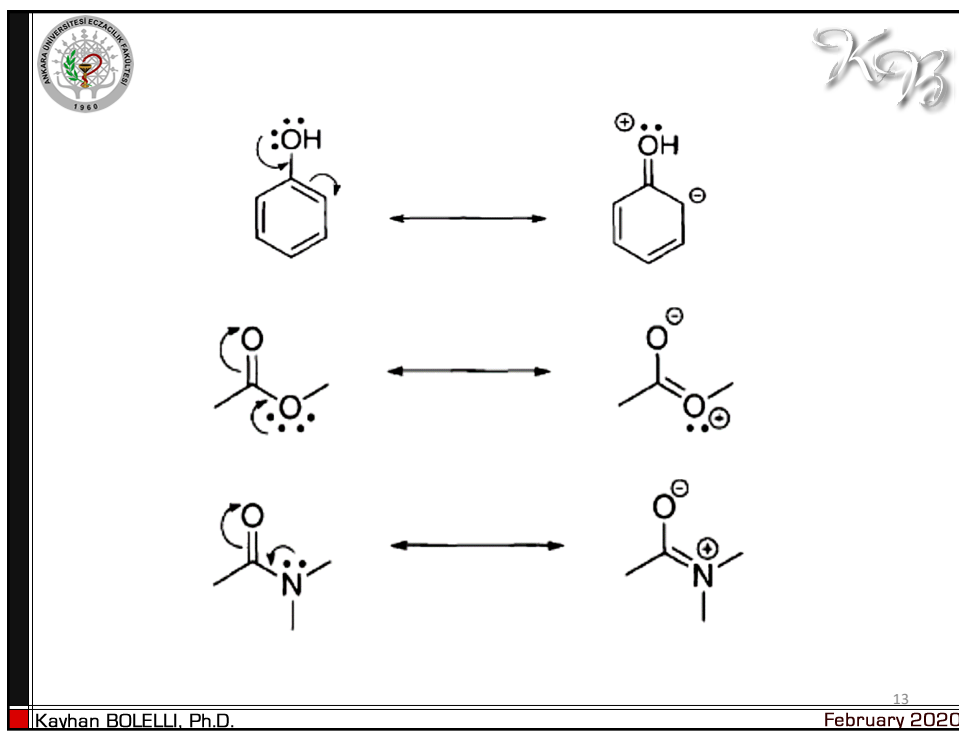
2) Compounds bearing the unshared electron pair on the atom adjacent to the π bond



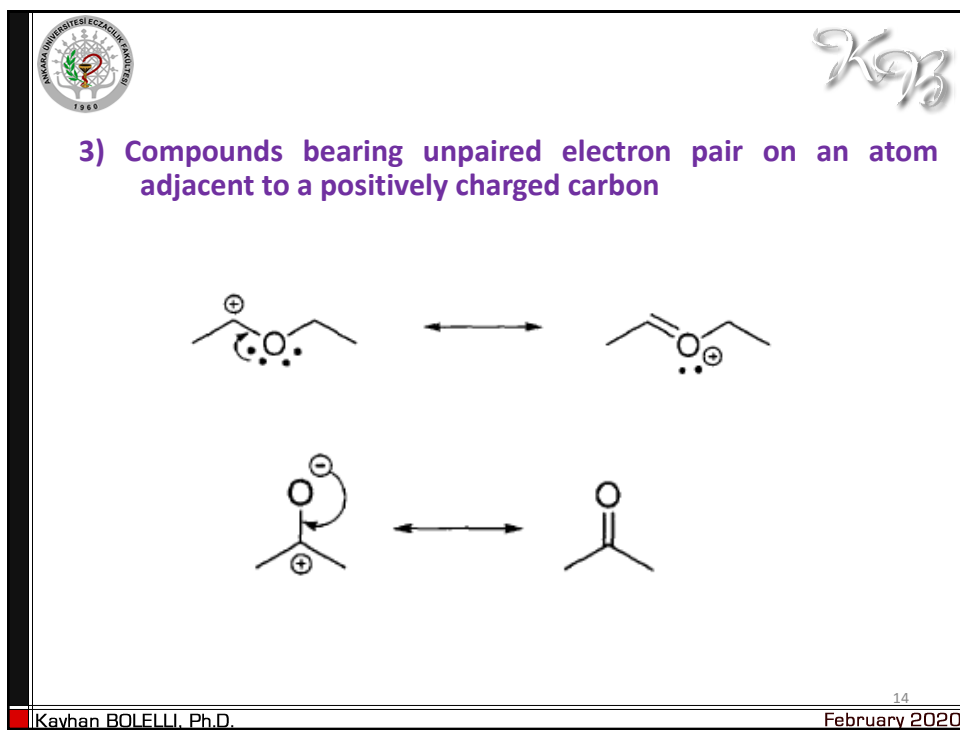
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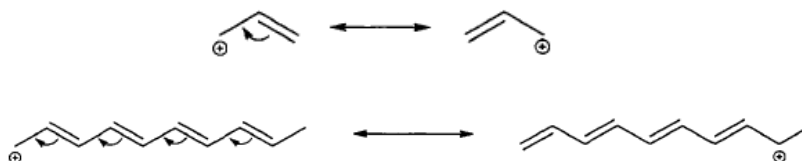


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4) The presence of a π bond (or conjugate π bonds) adjacent to the positive charge



5) The presence of a π bond between two different atoms



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Mesomeric effect

The **mesomeric effect** (or **resonance effect**) is the movement of π electrons toward or away from a substituent group.

– M acting substituents

Since the group withdraw electrons from the conjugated system it shows – M effect. These substituents deactivate the ring and orient the reaction towards the *meta* position.

+ M acting substituents

If the group donates electrons to the conjugated system it shows + M effect. These substituents activate the ring and orient the reaction towards the *orto/para* position.

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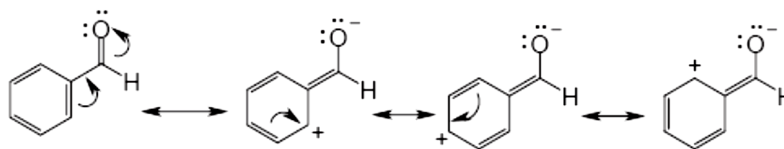
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Benzaldehyde molecule:

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– M effect

the electrophilic substitution reaction takes place at the position of *meta*

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Substituents with - M Effect

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$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{H} \end{array}$	$\begin{array}{c} \text{NH} \\ \parallel \\ -\text{C}-\text{H} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{R} \end{array}$	$\begin{array}{c} \text{C} \equiv \text{N} \\ \\ -\text{C}-\text{H} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{Cl} \end{array}$	$\begin{array}{c} \oplus \\ \\ \text{N} \\ \\ \text{O} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{OH} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{S}-\text{CH}_3 \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{OR} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{S}-\text{OH} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NH}_2 \end{array}$	

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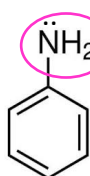
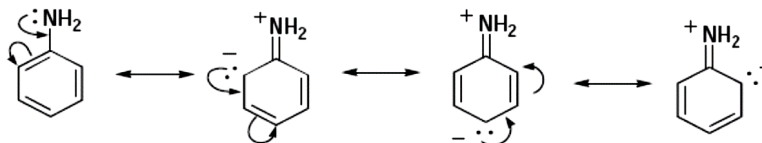
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Substituents with - M Effect

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Inductive Effect $-I$

(Nitrogen withdraw the electrons with inductive effect)

Mesomeric Effect $+M$

The mesomeric effect is dominant from the inductive effect and the electrophilic substitution reaction occurs in *ortho*, *para* positions.

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Substituents with +M Effect

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Active groups with + M effect are usually heteroatoms with free electrons in their outer shell.


-OH	-F
-OR	-Cl
-NH ₂	-Br
-SH	-I
-SR	

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Ethyl alcohol

$$\text{H}_3\text{C}-\text{CH}_2-\ddot{\text{O}}\text{H}$$

Hydroxyethene

$$\text{H}_2\text{C}=\text{CH}-\ddot{\text{O}}\text{H}$$




Since the electronegativity of oxygen atom is greater than carbon, the inductive effect of the hydroxyl substituent is - I effect, respectively.

There is no mesomeric effect since there is no π bond or empty p orbital.


Since a pair of unpaired electrons on the O atom are jointly used with the π bond, the mesomeric effect is + M

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Nucleophiles



Nucleophile is a chemical species that donates an electron pair to an electrophile to form a chemical bond in relation to a reaction.


a) Anion: An anion may be defined as an atom or molecule that is negatively charged.

$\text{F}^{\ominus} \quad \text{Cl}^{\ominus} \quad \text{Br}^{\ominus} \quad \text{HO}^{\ominus} \quad \text{HS}^{\ominus} \quad \text{RCOO}^{\ominus} \quad \text{CH}_3^{\ominus}$

b) Lewis bases: A Lewis base is a compound that has an electron pair.

$\text{NH}_3 \quad \text{H}_3\text{C}-\text{NH}_2 \quad \text{H}_3\text{C}-\text{OH} \quad \text{H}_3\text{C}-\text{SH}$

c) Double bond between carbon-carbon

$\text{H}_2\text{C}=\text{CH}_2$


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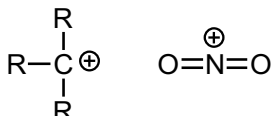


Electrophile

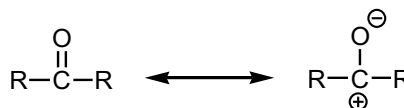
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Electrophiles are positively charged or neutral species having vacant orbitals that are attracted to an electron rich centre. It participates in a chemical reaction by accepting an electron pair in order to bond to a nucleophile.

a) Cations:



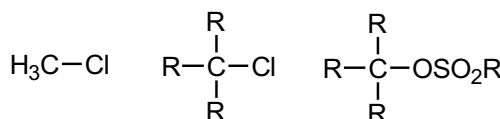
c) Carbon of carbonyl:



b) Lewis acid:



d) Compounds with bond polarisation



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Primary, Secondary, Tertiary and Quaternary Terms

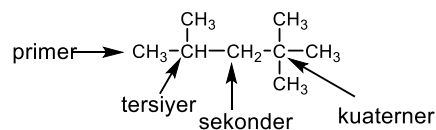
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If the carbon atom bound to one carbon atom, it is **primer**,

If the carbon atom bound to two carbon atom, it is **secondary**,

If the carbon atom bound to three carbon atom, it is **tertiary**,

If the carbon atom bound to four carbon atom, it is **quaternary**,



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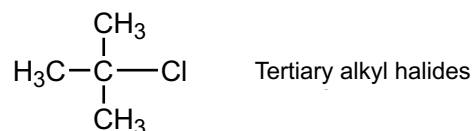
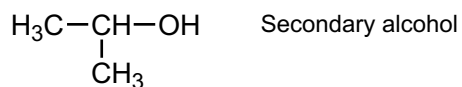
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Primary, Secondary, Tertiary and Quaternary Terms

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In alkyl halides and in alcohols, the number of alkyl groups attached to the carbon atom to which the substituent is attached is checked.



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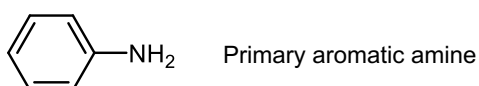
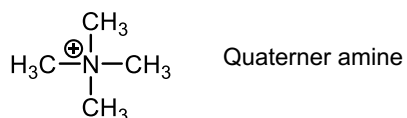
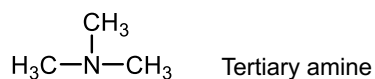
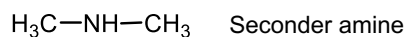
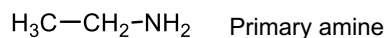
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Primary, Secondary, Tertiary and Quaternary Terms

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- In amines, the number of alkyl groups attached to the nitrogen is checked.



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Classification of Organic Reactions

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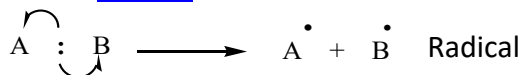


Classification of Organic Reactions

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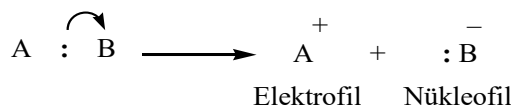
a) Homolytic cleavage [Radical Reactions]:

In homolytic cleavage, the two electrons in the bond are divided equally between the products. Homolytic cleavage often produces radicals.



b) Heterolytic cleavage [Ionic Reactions]:

In heterolytic cleavage, one atom gets both of the shared electrons. Heterolytic cleavage produces nucleophile and electrophile.



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Organic reactions are classified as following:

A) Radical Reactions

- a- Radical substitution (S_R)
- b- Radical addition (A_R)

B) Ionic Reactions

- a- Substitution reactions (S)
- b- Addition reactions (A)
- c- Elimination reactions (E)

C) Transposition Reactions

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Substitution Reactions (S)

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Substitution reaction is a chemical reaction during which one functional group in a chemical compound is replaced by another functional group. There are two types, electrophilic and nucleophilic.

Electrophilic Substitution (SE)

These reactions are usually substitutions in aromatic structures and occur in three steps.

1. Formation of electrophilic unit
2. Addition of electrophilic unit to aromatic ring and re-aromatisation of ring
3. Neutralisation of leaving proton

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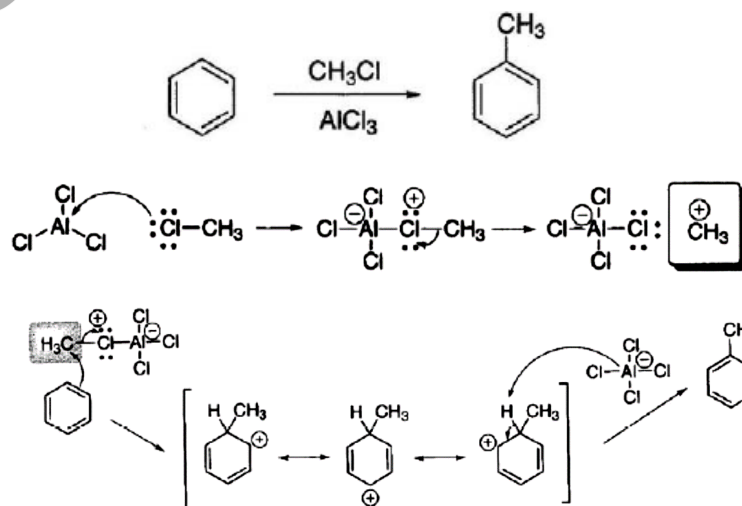
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Friedel-Crafts Alkylation

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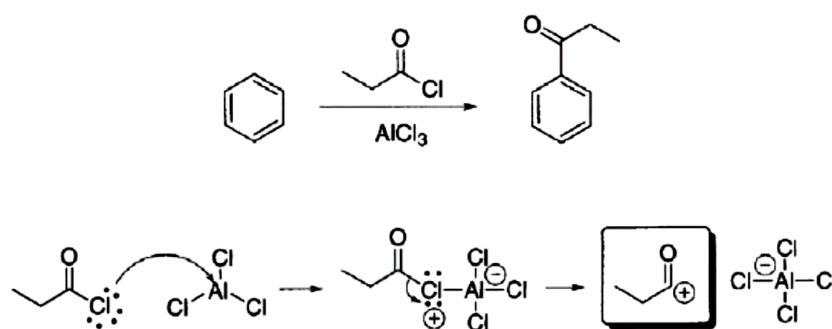
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Friedel-Crafts Acylation

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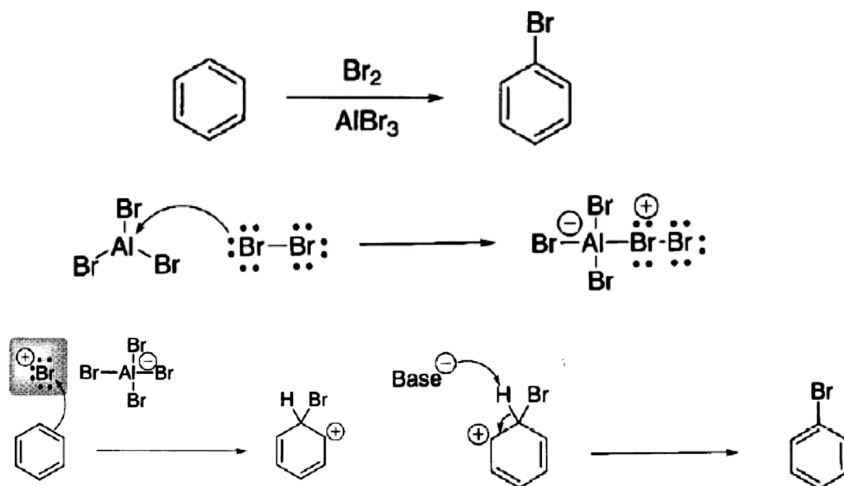
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Synthesis of Bromobenzene

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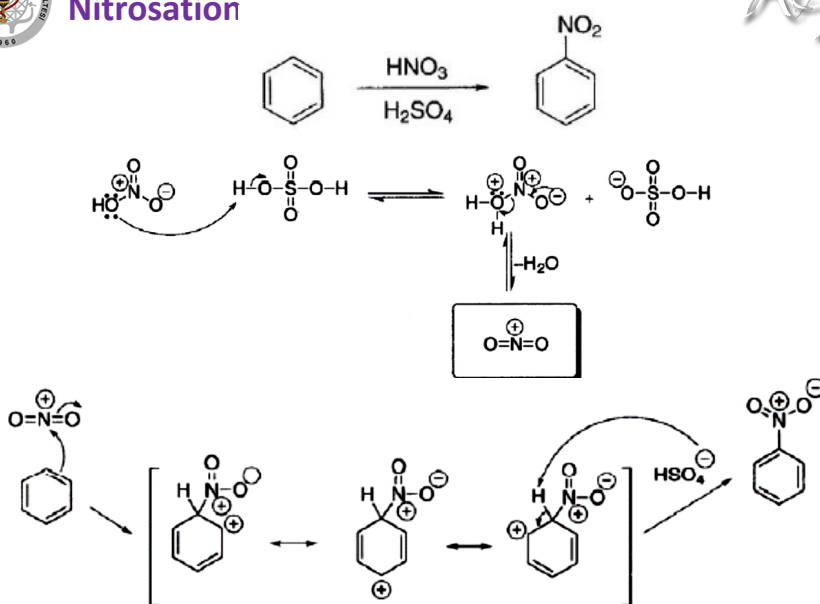
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Nitrosation

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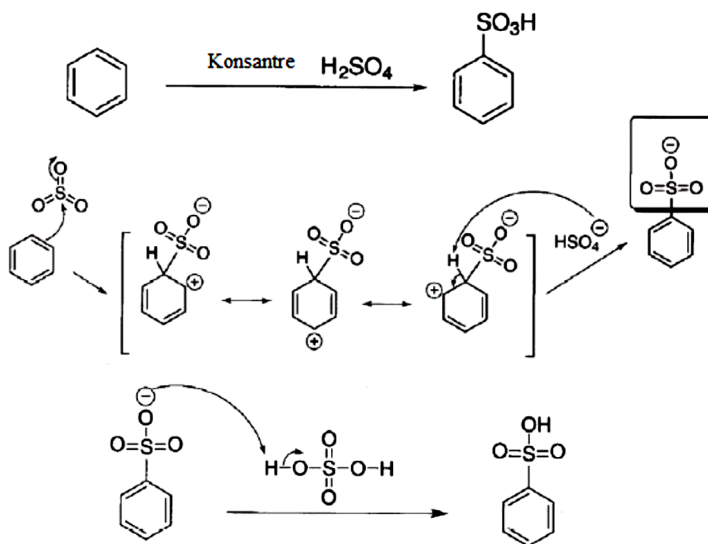
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Sülfonation

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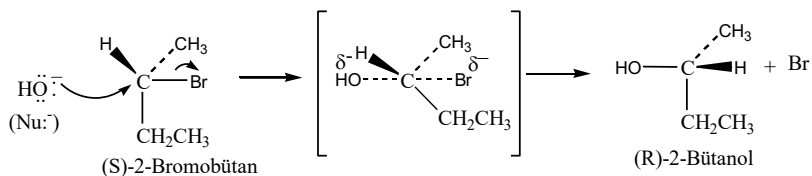


Nucleophilic Substitution (S_N)

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S_N2 : The S_N2 reaction is concerted. The S_N2 occurs in one step.

- Both the nucleophile and substrate are involved in the rate determining step. Therefore the rate is dependent on **both** the concentration of substrate and that of the nucleophile.
- In the S_N2 reaction, the big barrier is **steric hindrance**. Since the S_N2 proceeds through a backside attack, the reaction will only proceed if the empty orbital is accessible. The more groups that are present around the vicinity of the leaving group, the slower the reaction will be. That's why the rate of reaction proceeds from primary (fastest) > secondary >> tertiary (slowest)



$Nu^- = H^-, ^-CN, I^-, Br^-, Cl^-, ^-OH, ^-NH_2, CH_3O^-, CH_3O_2^-, HS^-, H_2O, NH_3$ vs.

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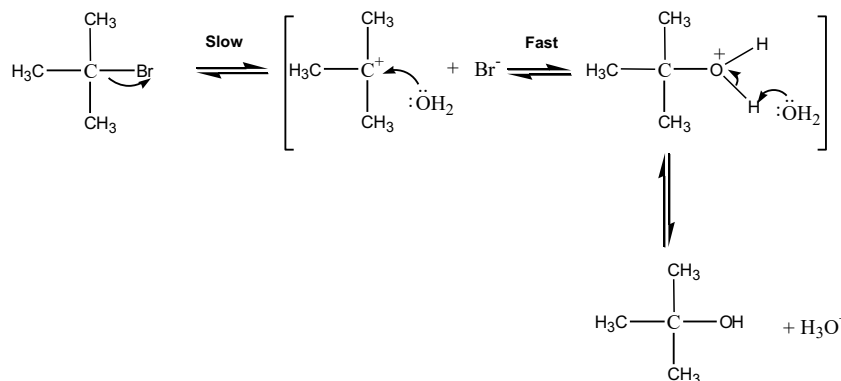
Nucleophilic Substitution (S_N)

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S_{N1} : The S_{N1} reaction proceeds stepwise.

The leaving group first leaves, whereupon a carbocation forms that is attacked by the nucleophile.

- Since the first step of the S_{N1} reaction is **loss of a leaving group** to give a carbocation, the rate of the reaction will be proportional to the stability of the carbocation.
- Carbocation stability increases with increasing substitution of the carbon (tertiary > secondary > primary) as well as with resonance.



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Don't forget!!

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- S_{N1} and S_{N2} reactions only occur for alkyl halides (and related compounds like tosylates and mesylates). If the leaving group is directly attached to an alkene or alkyne, S_{N1} or S_{N2} will not occur!
- The S_{N2} tends to proceed with **strong** nucleophiles; by this, generally means negatively charged nucleophiles such as CH_3O^- , CN^- , RS^- , N_3^- , HO^- , and others.
- The S_{N1} tends to proceed with **weak** nucleophiles – generally *neutral* compounds such as solvents like CH_3OH , H_2O , $\text{CH}_3\text{CH}_2\text{OH}$, and so on.
- The S_{N2} reaction is favored by polar aprotic solvents – these are solvents such as acetone, DMSO, acetonitrile, or DMF that are polar enough to dissolve the substrate and nucleophile but do not participate in hydrogen bonding with the nucleophile.
- The S_{N1} reaction tends to proceed in polar protic solvents such as water, alcohols, and carboxylic acids. These also tend to be the nucleophiles for these reactions as well.

<http://www.masterorganicchemistry.com/2012/08/08/comparing-the-sn1-and-sn2-reactions/>

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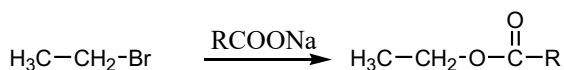
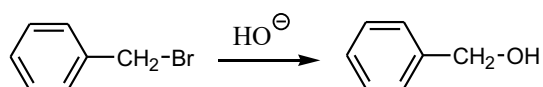
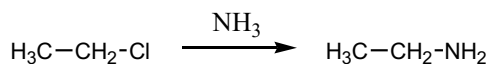
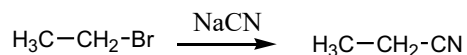
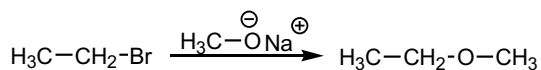
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Nucleophilic Substitution Reactions

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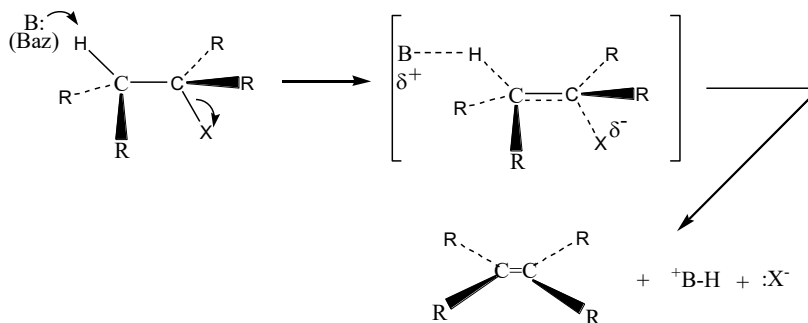


Elimination Reactions (E):

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It is the formation of an unsaturated compound from saturated molecule. There are two types, E_1 ve E_2 according to reaction kinetics. These reactions are parallel to the SN_1 and SN_2 reactions.

E2 Reactions:



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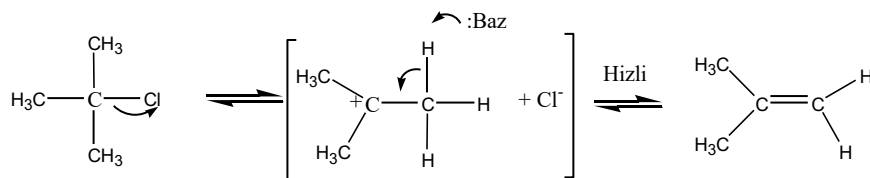
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E₁ Reactions:

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Reaction	Structure of RX	Reactivity of Nu:	Conc. Of Nu:	Solvent
SN2	1>2>3 Only this reaction and E2 will most likely react with a primary RX	Strong nucleophile favors reaction	High concentration of nucleophile favors reaction	Aprotic polar solvent favors a SN2 reaction if <i>either</i> of the reactants is charged ex: DMF DMSO Acetone
E2	3>2>1 Major product is more substituted alkene unless *the base is large *the alkyl halide is an alkyl fluoride *the alkyl halide contains one or more double bonds	Strong Base favors reaction	High concentration of base favors reaction	Aprotic polar solvent favors a E2 reaction if <i>either</i> of the reactants is charged ex: DMF DMSO Acetone
SN1	3>2>1 Forms a carbocation	Not effected by strength of nucleophile but a weak nucleophile favors it by not favoring a SN2 reaction	Not effected but low concentration disfavors a SN2 reaction	Protic polar favors a SN1 reaction if the reactant is not charged. Ex: H2O, CH3OH, etc.
E1	3>2>1 Forms a carbocation	Weak base favors E1 reaction by disfavoring E2 reaction	Not effected but a low concentration of base favors E1 by disfavoring a E2 reaction	Protic polar favors a E1 reaction if the reactant is not charged. Ex: H2O, CH3OH, etc.

<http://users.wfu.edu/wrightmw/chm122/handouts/sn1sn2e1e2%20summary.pdf>

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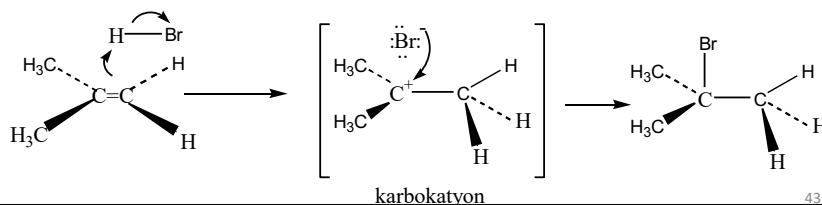


Addition Reactions (A):

Kar3

It is the formation of a saturated compound from unsaturated molecule via addition of some small molecules.

Electrophilic Addition (A_E): The substrate is usually hydrocarbon structures containing unsaturation. **Electrophilic addition** reactions are an important class of reactions that allow the interconversion of $C=C$ and $C\equiv C$ into a range of important functional groups including alkyl halides and alcohols. **Electrophilic addition** provides a products which give more thermodynamic stable carbocation according to Markovnikov rule.



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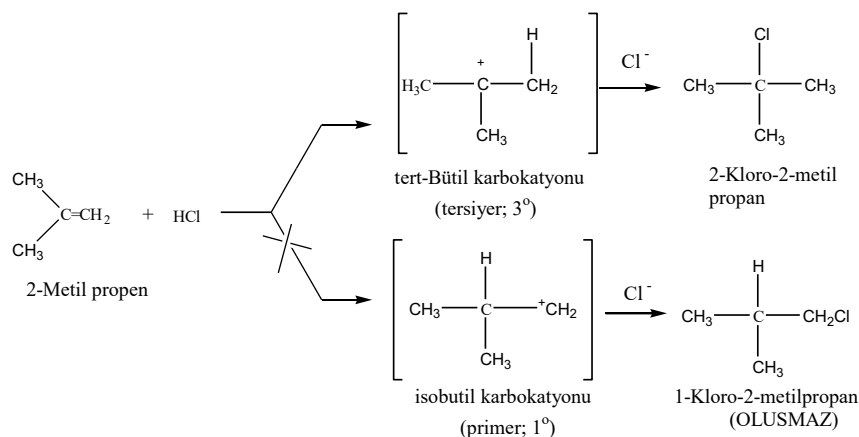
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Electrophilic Addition(A_E):

Kar3



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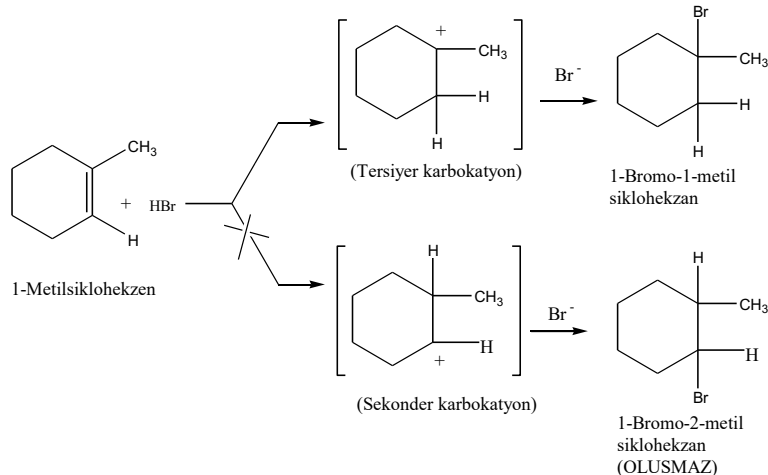
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Electrophilic Addition (A_E):

Kap



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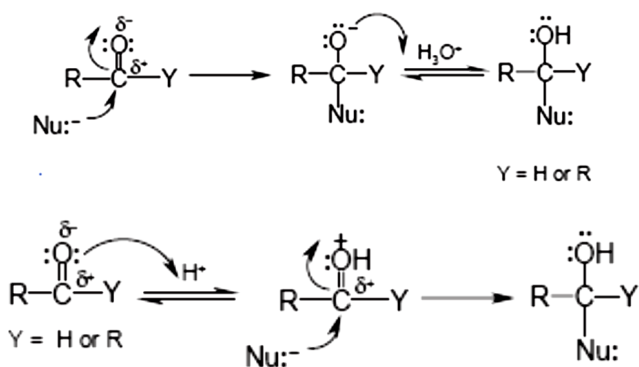
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Nucleophilic addition (A_N):

Kap

Nucleophilic addition reactions are an important class of reactions that allow the interconversion of $\text{C}=\text{O}$ into a range of important functional groups.



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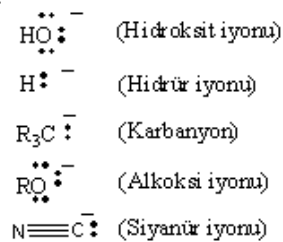
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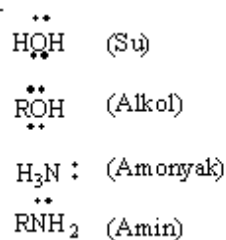
Nucleophiles involved in Nucleophilic addition reactions:

Kap

Nucleophiles with negative charges



Neutral Nucleophiles



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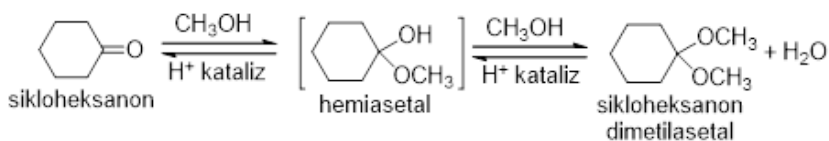
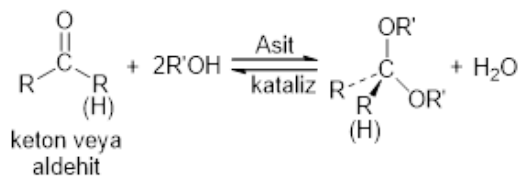
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Kap

Addition of alcohol to aldehyde give hemiacetal and acetal and hemiketale and ketale are obtained with the same reaction with ketone.



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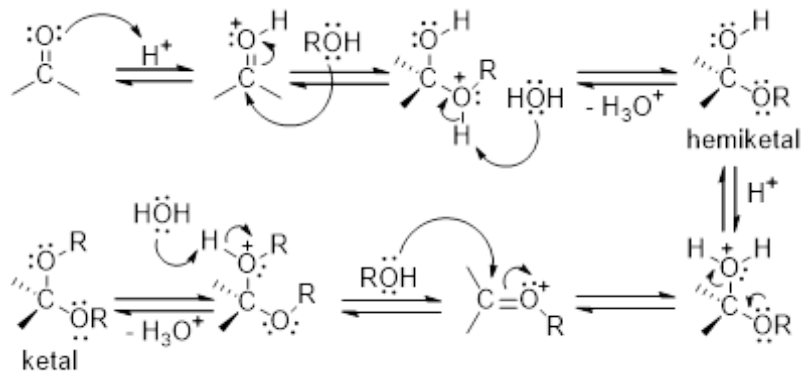
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Reaction mechanism

KaB



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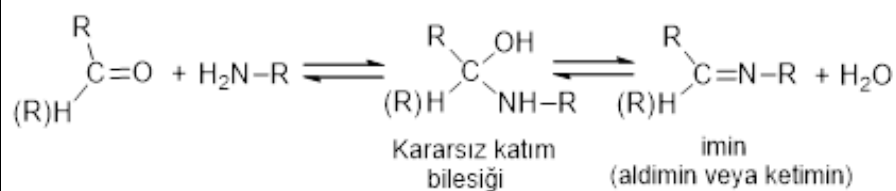
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Imine ve enamine formation

KaB

Addition of primary amines to aldehyde and ketone give imine ($R_2C=NR$), while addition of secondary amine give enamine compounds.



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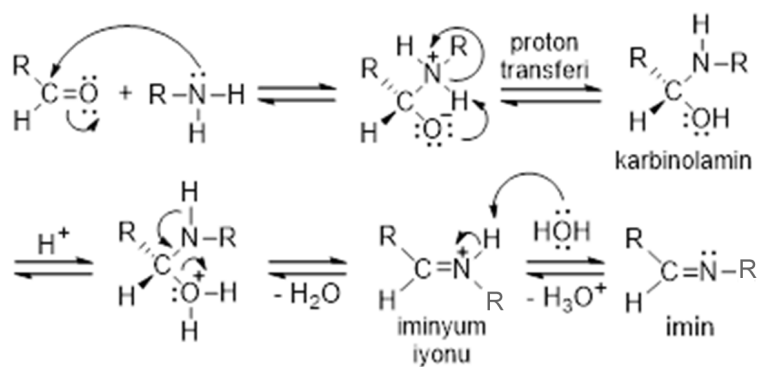
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Mechanism of imine formation

KaB



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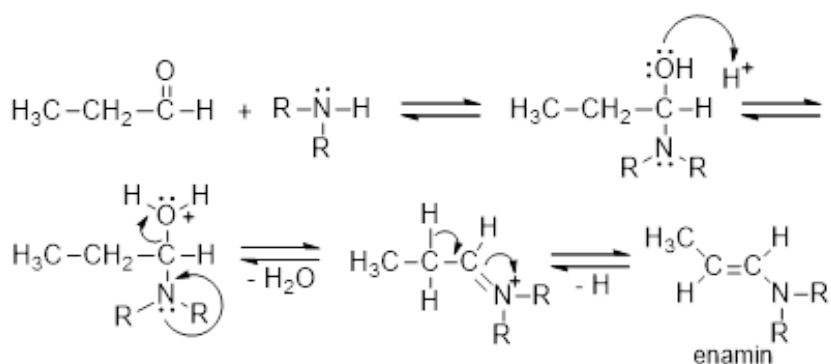
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Mechanism of enamine formation

KaB



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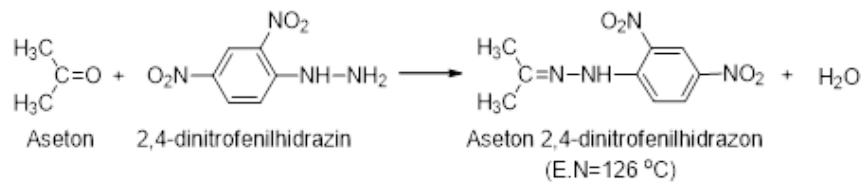
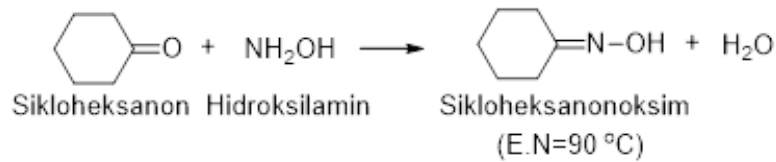
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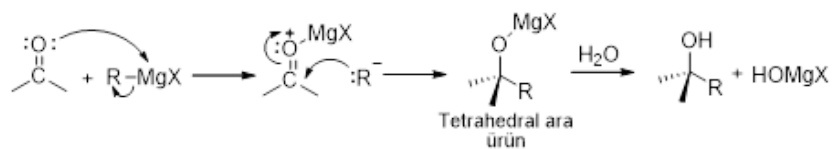
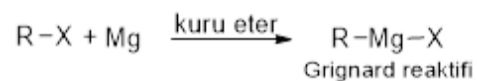
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Mechanism of grignard reaction formation



Nucleophilic addition

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