مذكرة الكيمياء العضوية
لطلاب كلية التربية- الفرقة الاولي
طبيعية وكيمياء
برنامج اللغة الانجليزية

اعداد وتجميع

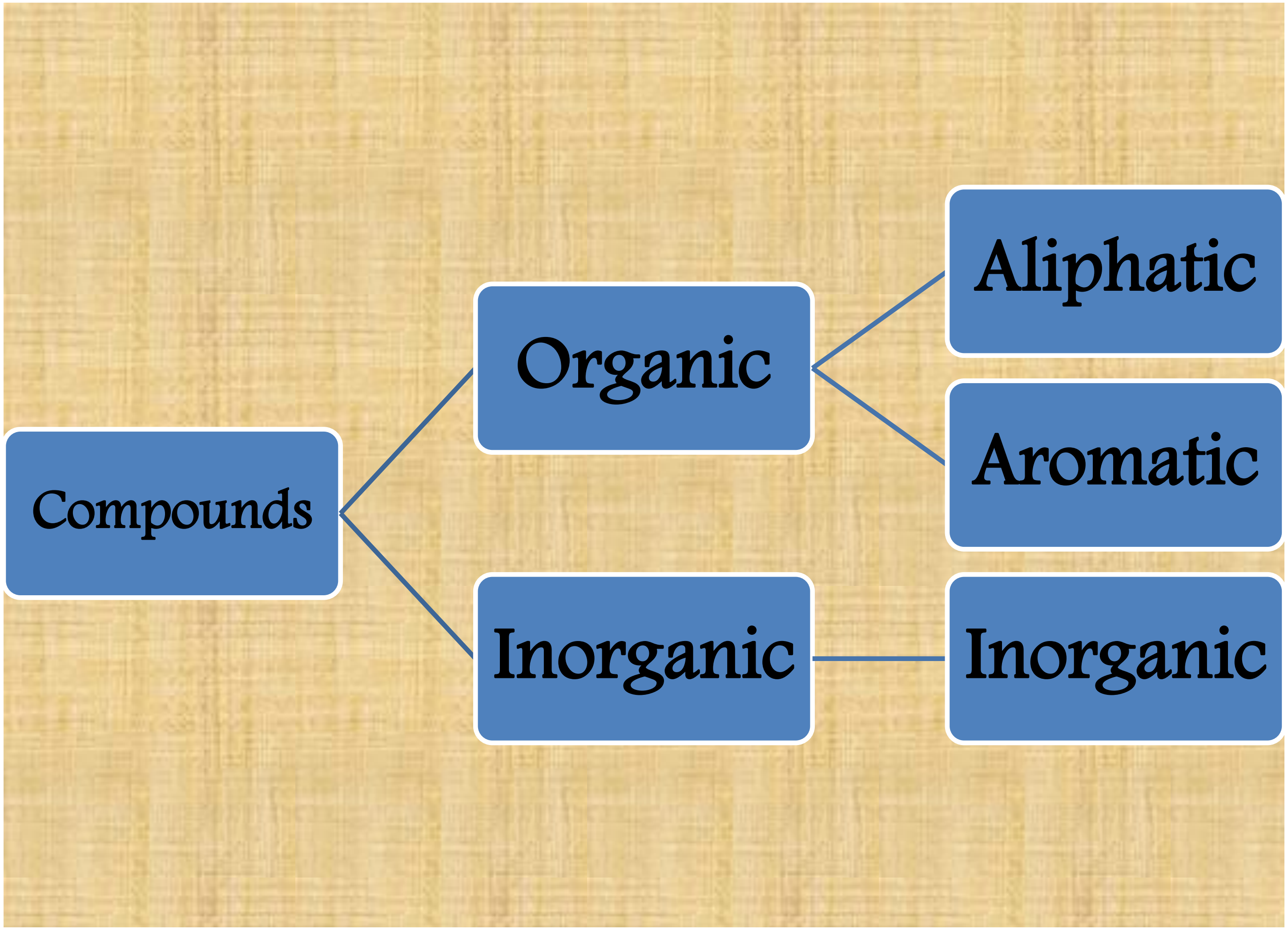
د. محمد مبارك طه

د. ابوبكر هريدي عبد المنصف

ORGANIC CHEMISTRY

Aliphatic Compounds

Classification of compounds



Compounds

Organic

Inorganic

Aliphatic

Aromatic

Inorganic

Introduction to Organic Chemistry

- ❑ Organic chemistry is the study of the structure, properties, composition, reactions, and preparation of carbon-containing compounds. Most organic compounds contain carbon and hydrogen, but they may also include any number of other elements (e.g., nitrogen, oxygen, halogens, phosphorus, silicon, sulfur).
- ❑ Organic chemistry plays an important part in our daily life because food, clothes, paper, ink, rubber, soap, perfumes, medicines etc. are indispensable to us for proper living. Organic compounds are important constituents of many products e.g., paint, food, plastic, explosive, medicine, petrochemical, pesticide etc.

* Classification of organic compounds

1- Hydrocarbons (C,H)

2- Alcohols (C,H,O)

3- Aldehydes (C,H,O)

4- Ketones (C,H,O)

5- carboxylic acids (C,H,O)

6-Esters (C,H,O)

7- Amines (C,H,N)

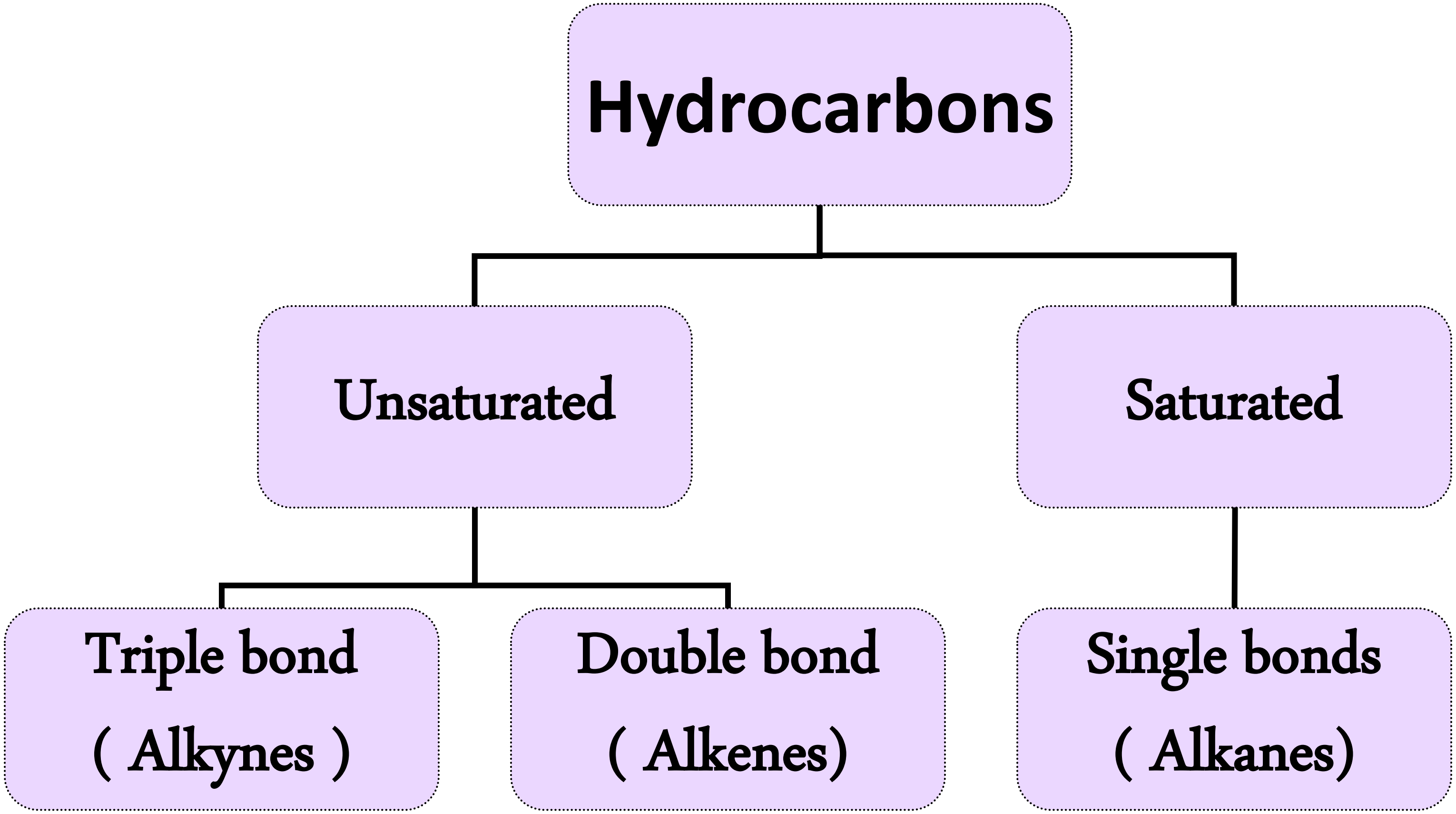
8- Amides (C,H,O,N)

9- Imides (C,H,O,N)

Hydrocarbons

What are hydrocarbons?

Hydrocarbons are compounds comprised exclusively of carbon and hydrogen.



Hydrocarbons

Unsaturated

Saturated

Triple bond
(Alkynes)

Double bond
(Alkenes)

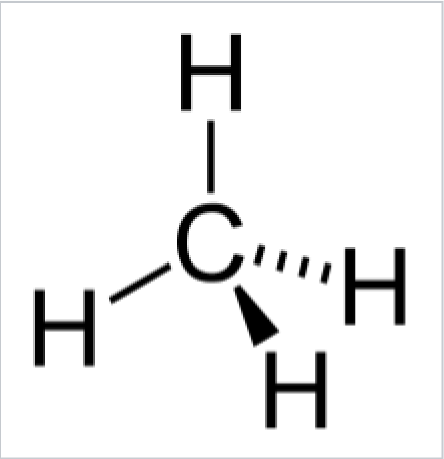
Single bonds
(Alkanes)

Alkanes
C_nH_{2n+2}

What are Alkanes? Alkanes are organic compounds that consist of single-bonded carbon and hydrogen atoms. The formula for Alkanes is C_nH_{2n+2}, subdivided into three groups – chain alkanes, cycloalkanes, and the branched alkanes.

List of Alkanes

Methane (CH_4)
Ethane (C_2H_6)
Propane (C_3H_8)
Butane (C_4H_{10})
Pentane (C_5H_{12})
Hexane (C_6H_{14})
Heptane (C_7H_{16})
Octane (C_8H_{18})

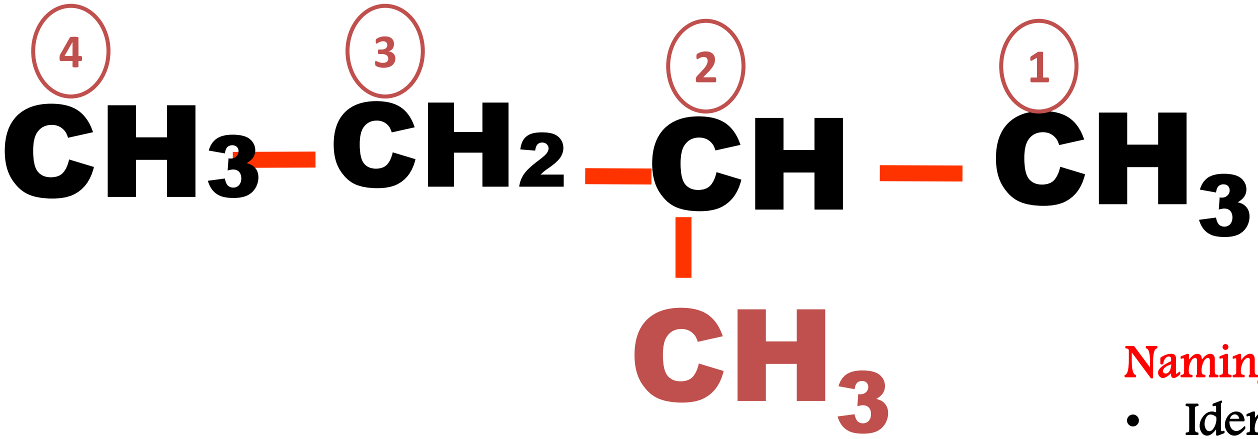


Chemical structure of methane, the simplest alkane

Tetrahedral shape with angles 109.5°

Alkane	Formula	Boiling point [°C]	Melting point [°C]	Density [kg/m^3] (at 20 °C)	Isomers
Methane	CH_4	−162	−182	0.656 (gas)	1
Ethane	C_2H_6	−89	−183	1.26 (gas)	1
Propane	C_3H_8	−42	−188	2.01 (gas)	1
Butane	C_4H_{10}	0	−138	2.48 (gas)	2
Pentane	C_5H_{12}	36	−130	626 (liquid)	3
Hexane	C_6H_{14}	69	−95	659 (liquid)	5
Heptane	C_7H_{16}	98	−91	684 (liquid)	9
Octane	C_8H_{18}	126	−57	703 (liquid)	18
Nonane	C_9H_{20}	151	−54	718 (liquid)	35
Decane	$C_{10}H_{22}$	174	−30	730 (liquid)	75
Undecane	$C_{11}H_{24}$	196	−26	740 (liquid)	159
Dodecane	$C_{12}H_{26}$	216	−10	749 (liquid)	355
Tridecane	$C_{13}H_{28}$	235	−5.4	756 (liquid)	802
Tetradecane	$C_{14}H_{30}$	253	5.9	763 (liquid)	1858
Pentadecane	$C_{15}H_{32}$	270	10	769 (liquid)	4347
Hexadecane	$C_{16}H_{34}$	287	18	773 (liquid)	10,359
Heptadecane	$C_{17}H_{36}$	303	22	777 (solid)	24,894
Octadecane	$C_{18}H_{38}$	317	28	781 (solid)	60,523
Nonadecane	$C_{19}H_{40}$	330	32	785 (solid)	148,284
Icosane	$C_{20}H_{42}$	343	37	789 (solid)	366,319

Nomenclature of alkane



$$CH_3-CH_2-\underset{\underset{CH_3}{|}}{CH}-CH_3$$

Naming rule

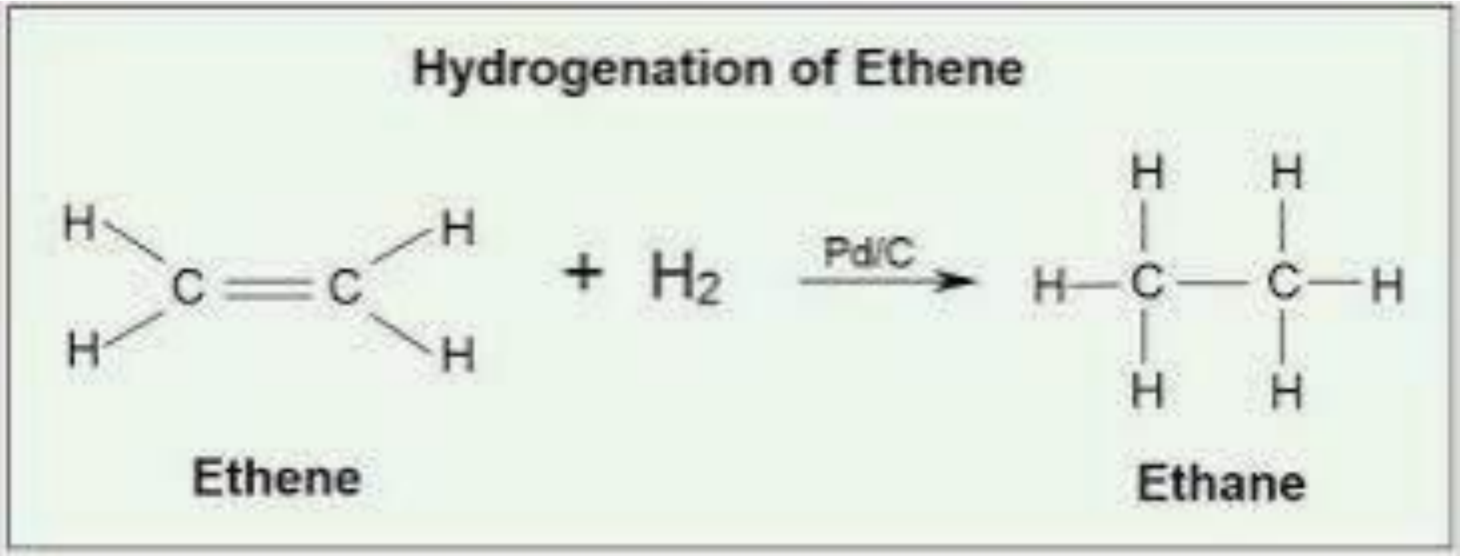
- Identify longest chain
- Branch will take the lowest number

2-methylbutane

Preparation of alkanes

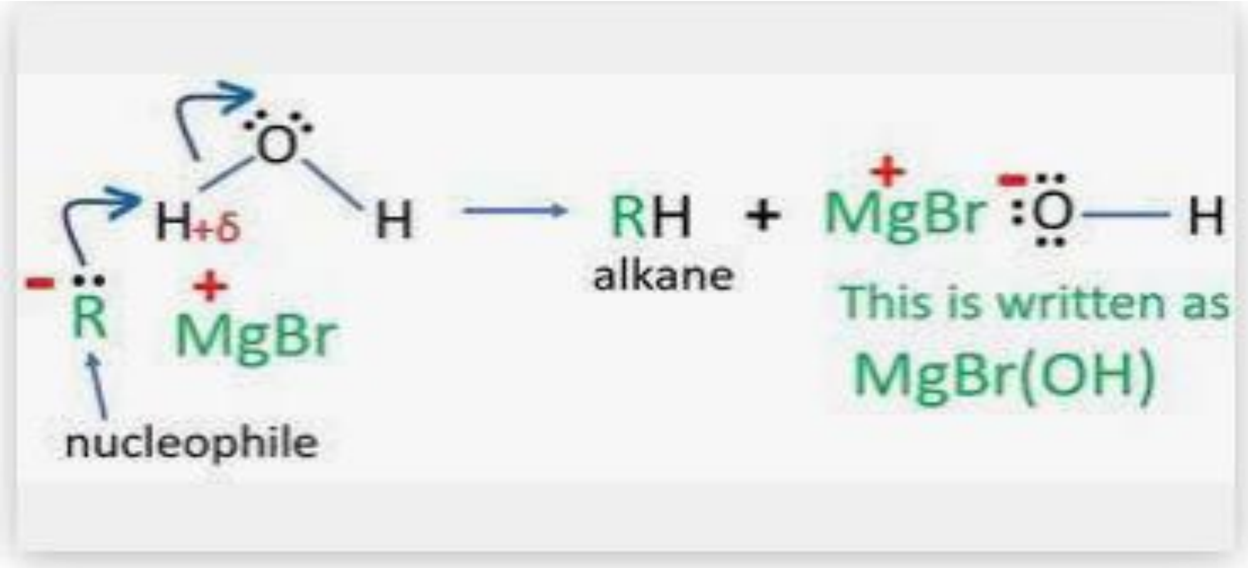
1- Hydrogenation of alkene

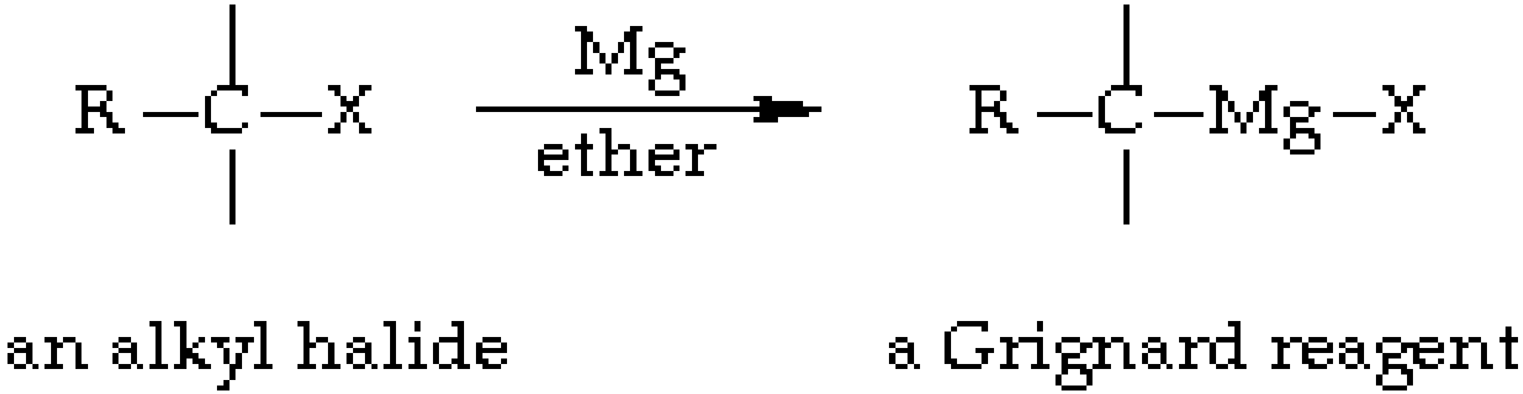
In a hydrogenation reaction, two hydrogen atoms are added across the double bond of an alkene, resulting in a saturated alkane. Hydrogenation of a double bond is a thermodynamically favorable reaction because it forms a more stable (lower energy) product.

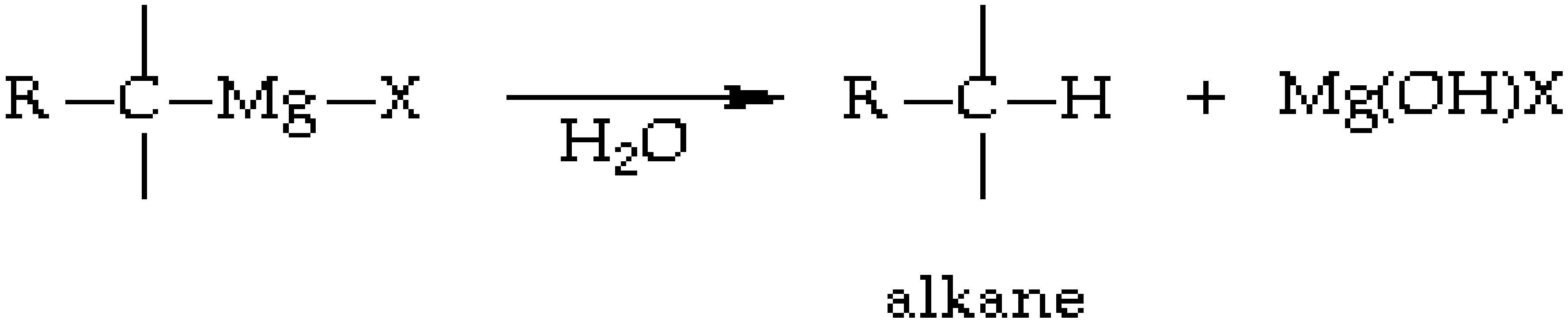


2- Hydrolysis of Grignard reagent

The Grignard reagent is very unstable in water and **hydrolyzes to create an alkane compound**. The Grignard reagent should be produced in dry media for this reason (without water or moisture). The alkane is used to preserve the number of carbon atoms in the Grignard reagent.

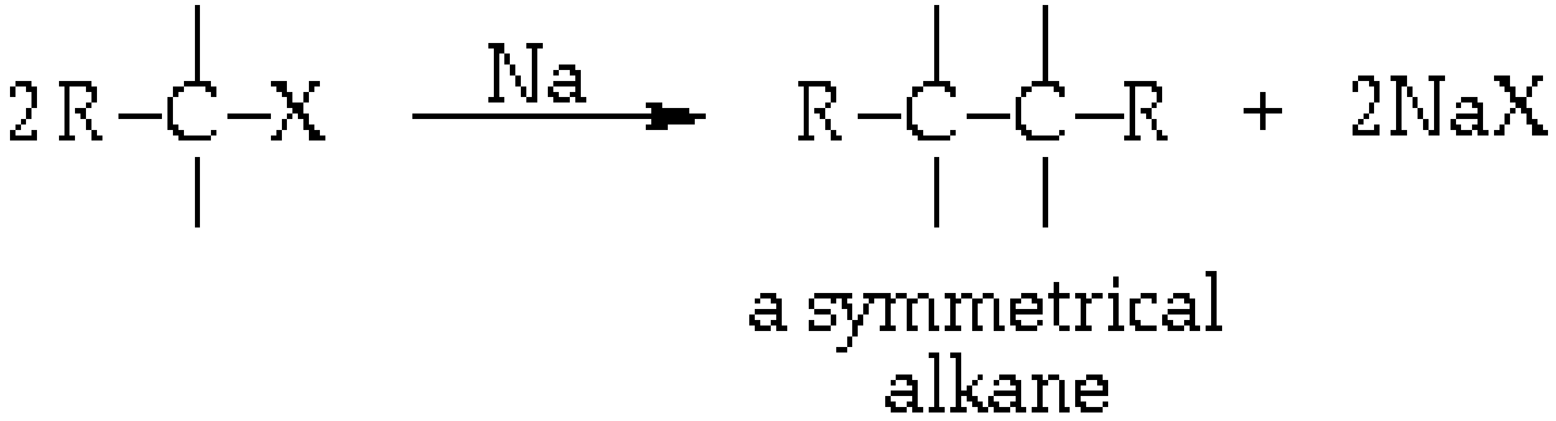



$$R-\overset{|}{\underset{|}{C}}-X \xrightarrow[\text{ether}]{Mg} R-\overset{|}{\underset{|}{C}}-Mg-X$$


$$R-\overset{|}{\underset{|}{C}}-Mg-X \xrightarrow[H_2O]{} R-\overset{|}{\underset{|}{C}}-H + Mg(OH)X$$

3) Wurtz Reaction

It used for the synthesis of alkanes with even number of carbon atoms



$$2\,R-C-X \xrightarrow{Na} R-C-C-R + 2NaX$$

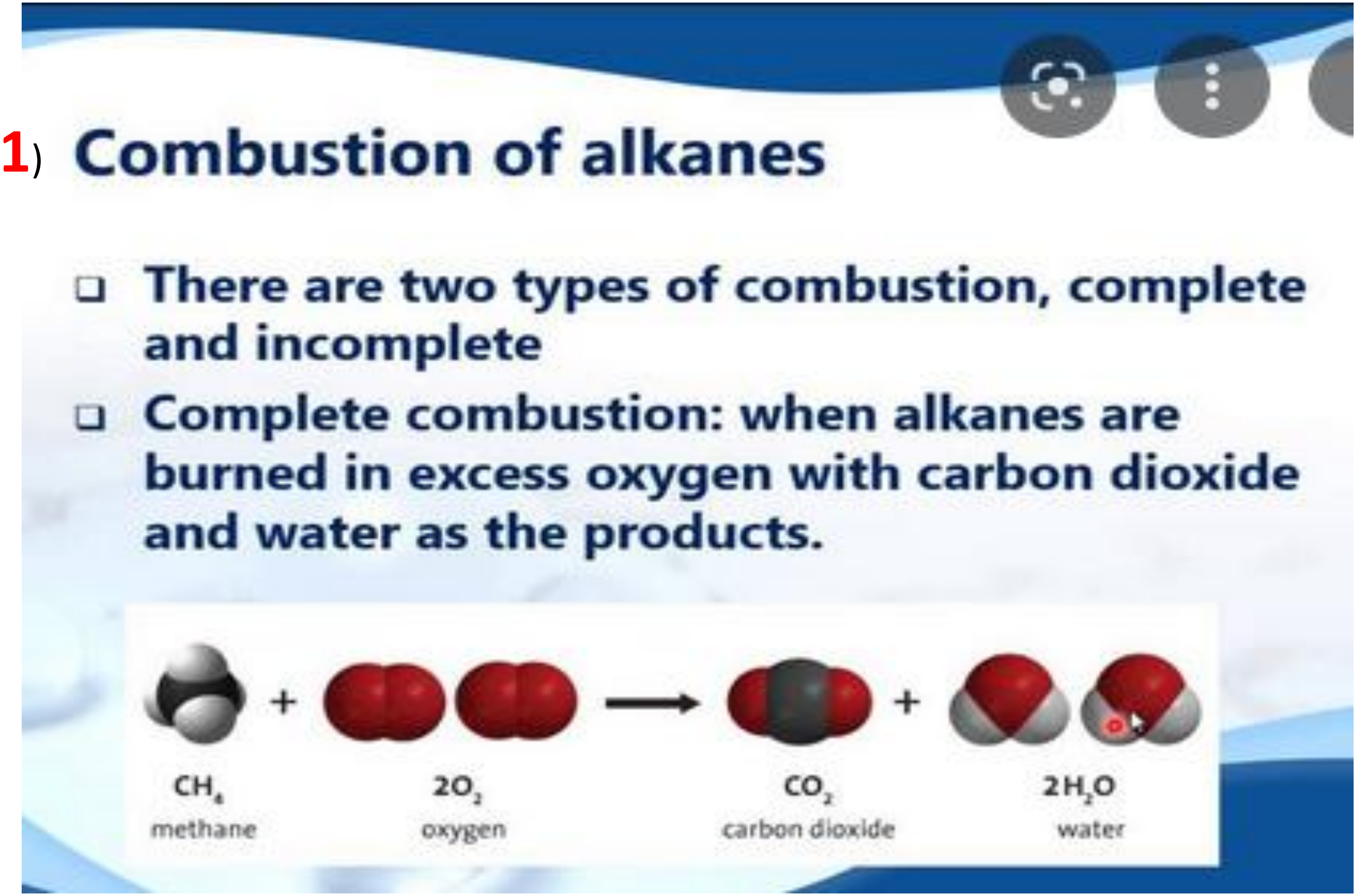
$$2\ CH_3-CH_2-CH_2-Br + 2\ Na \longrightarrow CH_3-CH_2-CH_2-CH_2-CH_2-CH_3$$

Propyl bromide

$+\ 2\ NaBr$

hexane

Reactions of alkanes

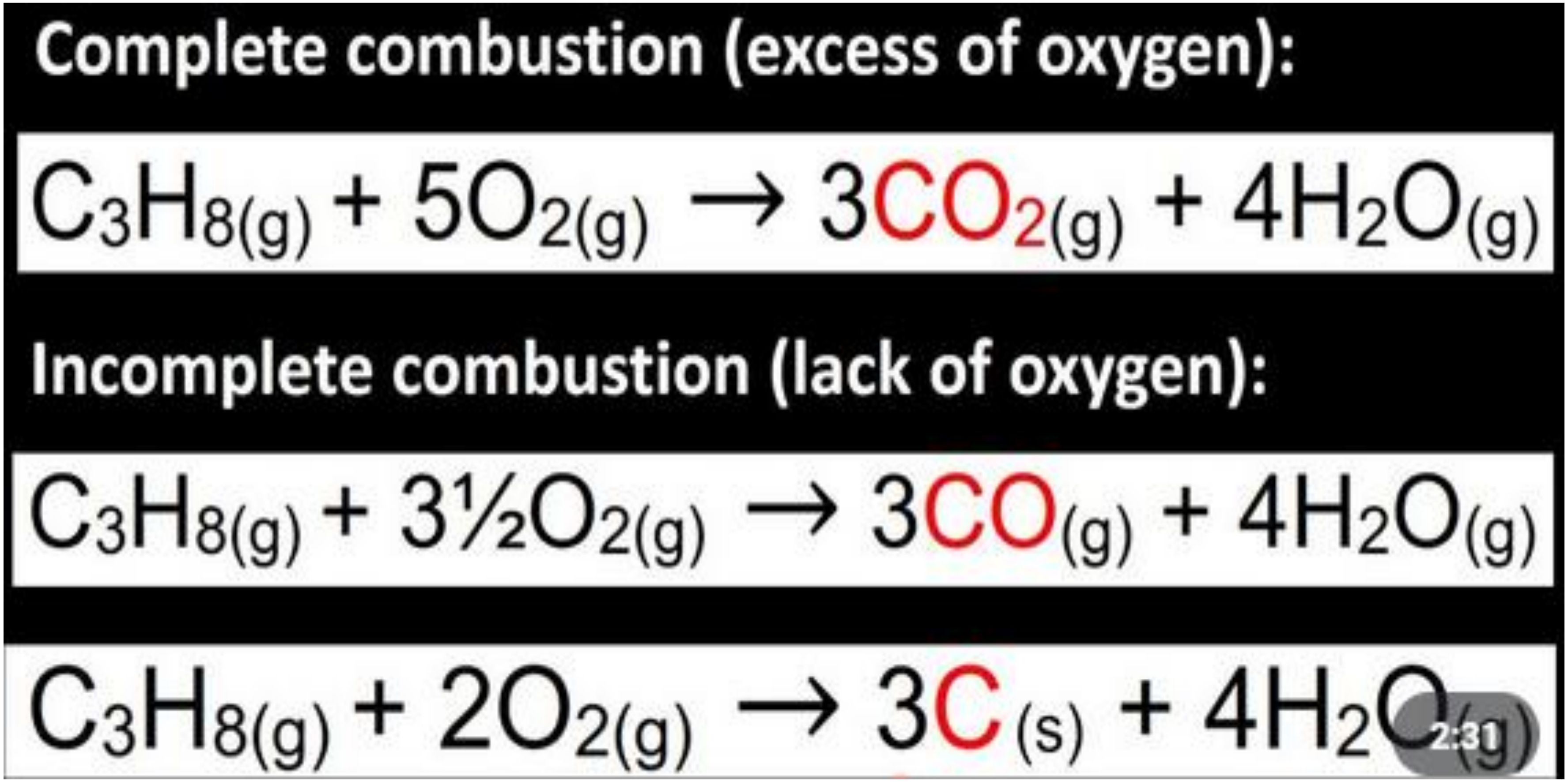


1) Combustion of alkanes

- There are two types of combustion, complete and incomplete
- Complete combustion: when alkanes are burned in excess oxygen with carbon dioxide and water as the products.

CH_4 + $2O_2$ → CO_2 + $2H_2O$

methane, oxygen, carbon dioxide, water



Complete combustion (excess of oxygen):

$$C_3H_{8(g)} + 5O_{2(g)} \rightarrow 3CO_{2(g)} + 4H_2O_{(g)}$$

Incomplete combustion (lack of oxygen):

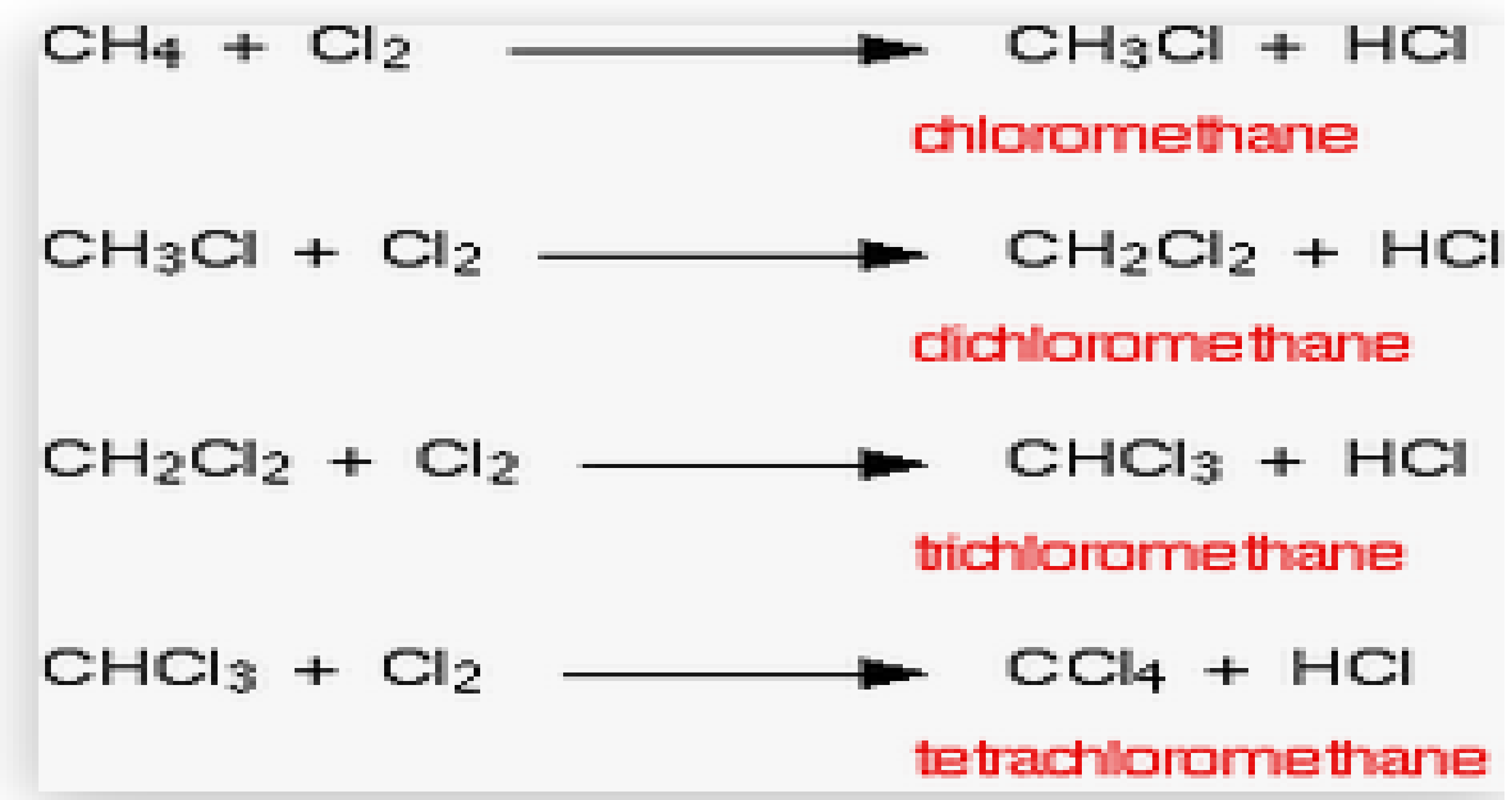
$$C_3H_{8(g)} + 3\tfrac{1}{2}O_{2(g)} \rightarrow 3CO_{(g)} + 4H_2O_{(g)}$$

$$C_3H_{8(g)} + 2O_{2(g)} \rightarrow 3C_{(s)} + 4H_2O_{(g)}$$

2- Replacement reaction

Halogenation

What is Halogenation of Alkanes? Halogenation of an alkane produces a hydrocarbon derivative in which one or more halogen atoms have been substituted for hydrogen atoms. Alkanes are notoriously unreactive compounds because they are non-polar and lack functional groups at which reactions can take place.



$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$

chloromethane

$CH_3Cl + Cl_2 \longrightarrow CH_2Cl_2 + HCl$

dichloromethane

$CH_2Cl_2 + Cl_2 \longrightarrow CHCl_3 + HCl$

trichloromethane

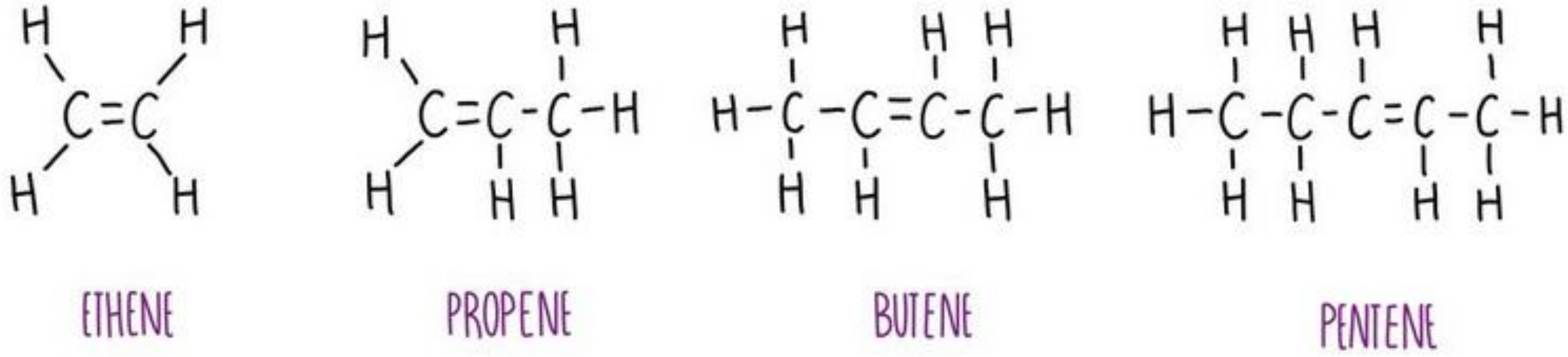
$CHCl_3 + Cl_2 \longrightarrow CCl_4 + HCl$

tetrachloromethane

Alkenes
CnH2n

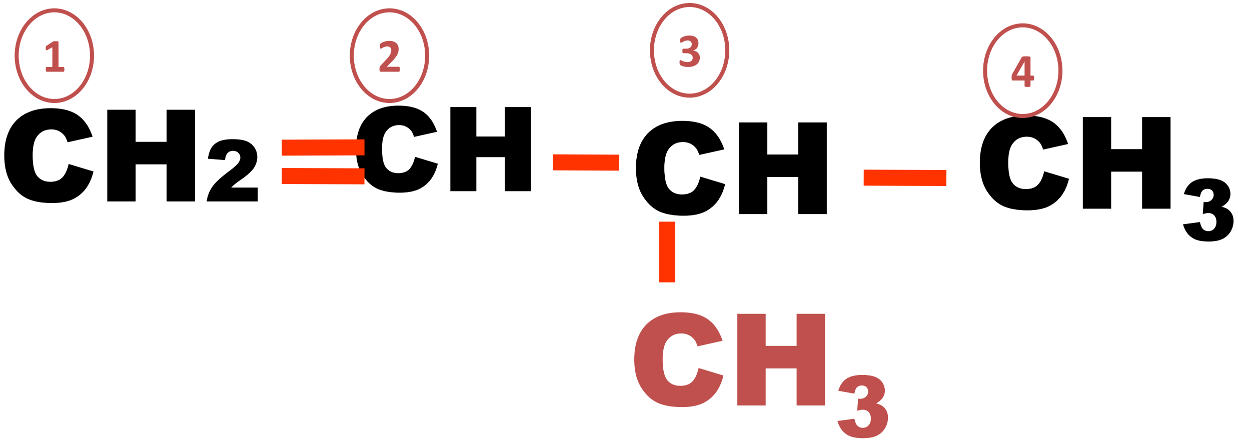
Alkenes are a class of hydrocarbons (e.g, containing only carbon and hydrogen) unsaturated compounds with at least one carbon-to-carbon double bond. Another term used to describe alkenes is olefins. Alkenes are more reactive than alkanes due to the presence of the double bond.

The first four members of the alkene homologous series are called **ethene, propene, butene and pentene.**



Angles 120°

Nomenclature of alkene



$$\overset{1}{C}H_2=\overset{2}{C}H-\underset{CH_3}{\overset{3}{C}H}-\overset{4}{C}H_3$$

3-methyl-1-butene

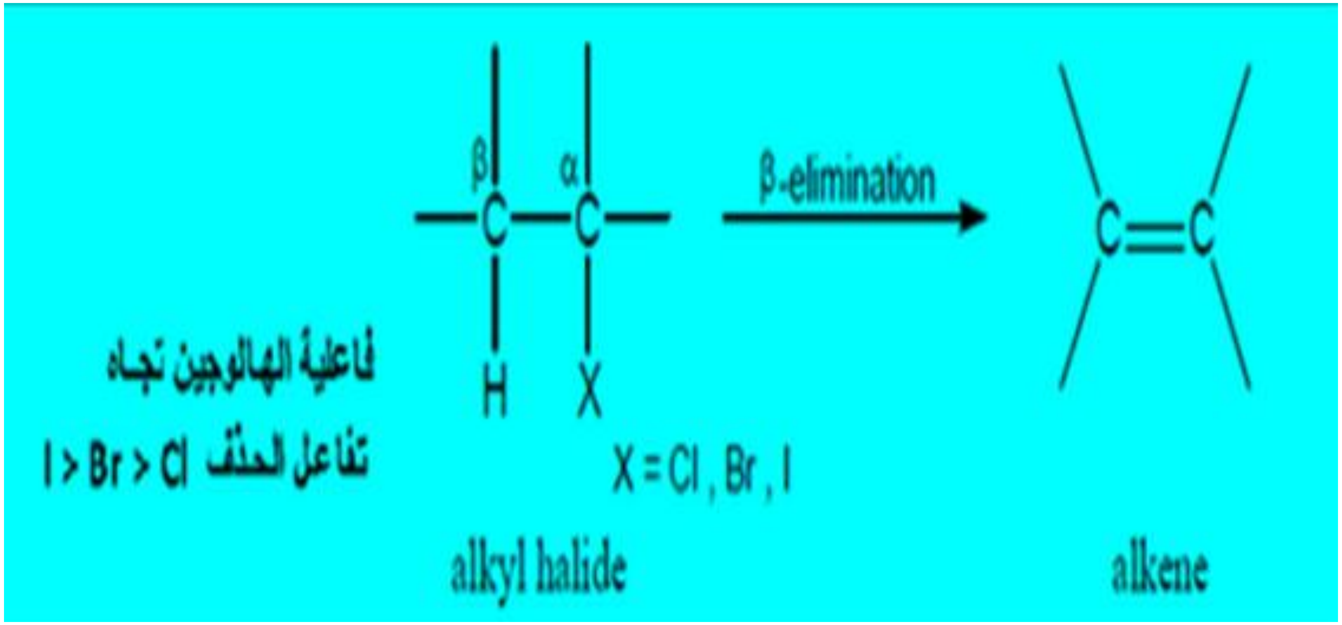
Naming rule

- Identify longest chain contains double bond
- Double bond will take the lowest number

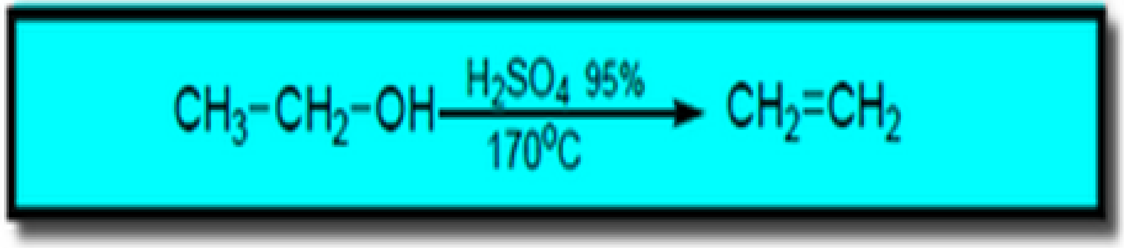
Preparation of Alkenes

(1) Dehydrohalogenation of alkyl halides

When an alkyl halide is heated with concentrated solution of KOH, a molecule of hydrogen halide eliminated and an alkene forms. This reaction is called dehydrohalogenation.

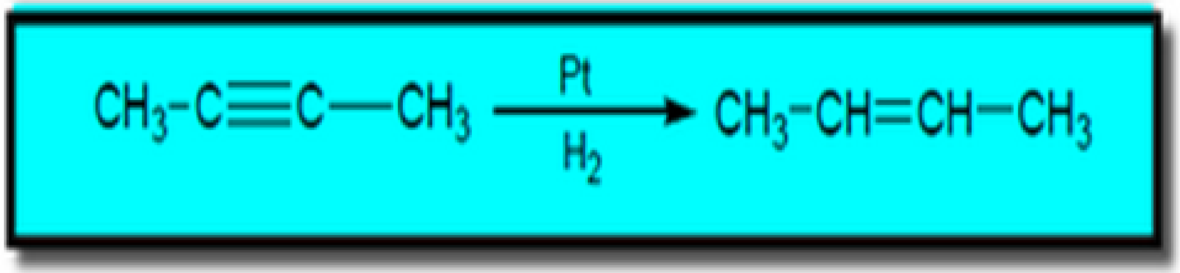


- من الكحول Dehydration of alcohols



$$CH_3-CH_2-OH \xrightarrow[170^oC]{H_2SO_4\ 95\%} CH_2=CH_2$$

- من الألكاينات Reduction of alkynes



$$CH_3-C\equiv C-CH_3 \xrightarrow[H_2]{Pt} CH_3-CH=CH-CH_3$$

Chemical reactions of Alkenes

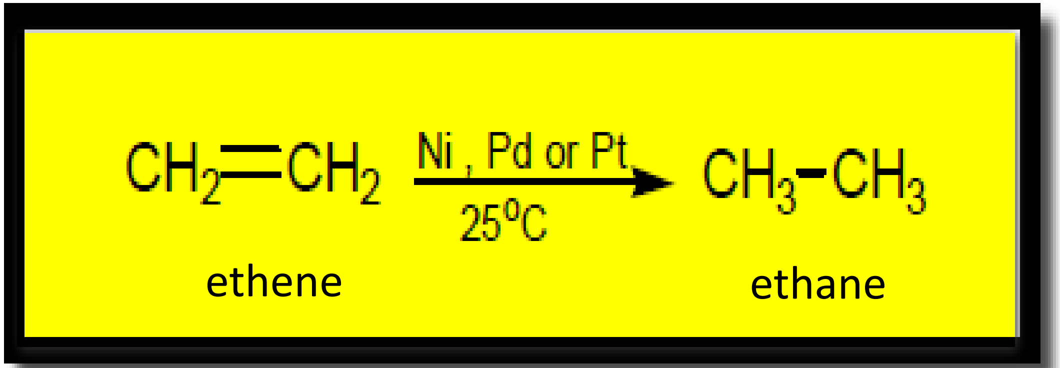
أولا / إضافة المتفاعلات المتماثلة

Addition of symmetric reactants such as H_2 or X_2

هي إضافة شقين متماثلين على الرابطة الزوجية .

أـ إضافة الهيدروجين (الهدرجة Hydrogenation)

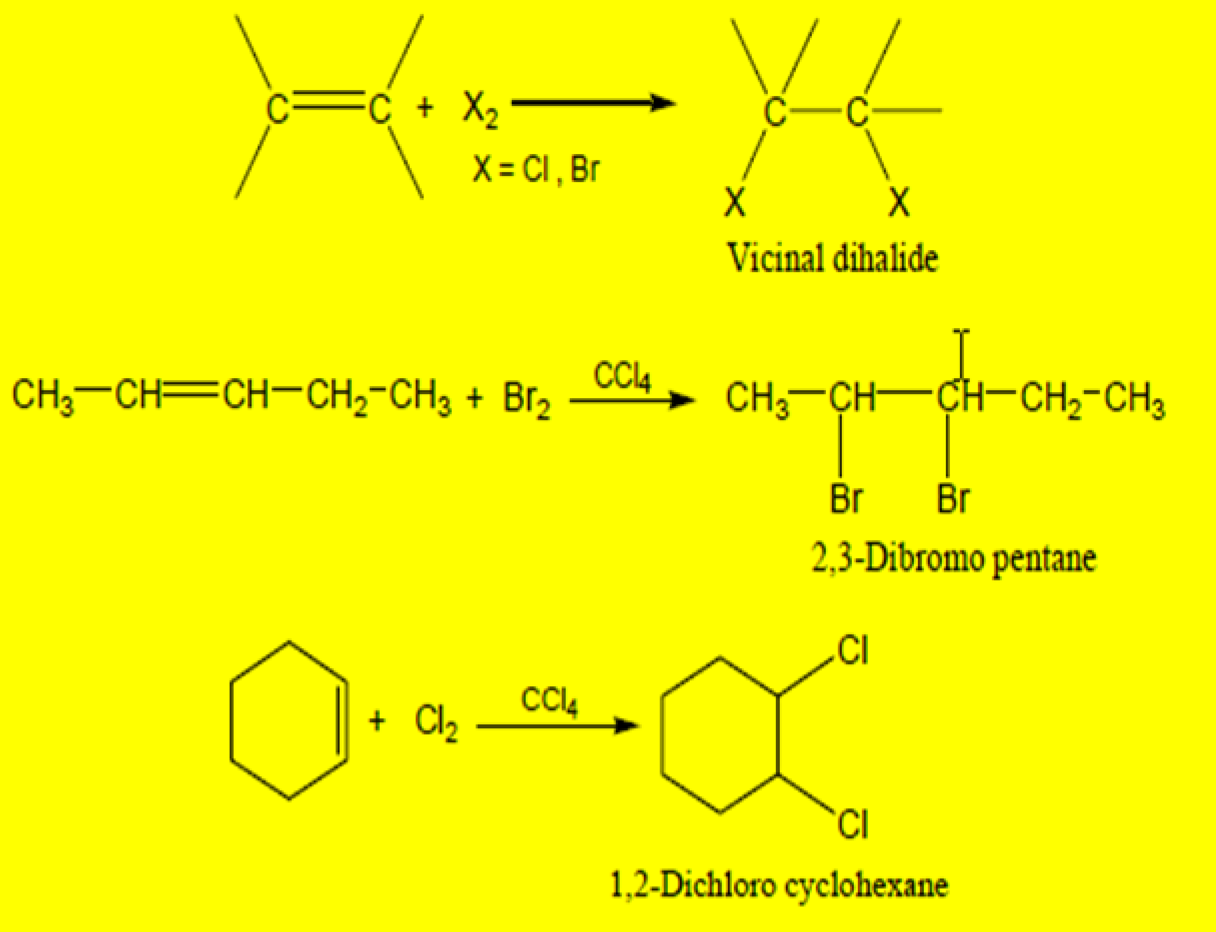
حيث يضاف الهيدروجين إلى الرابطة الثنائية في وجود عوامل حفازة وينتج الألكان المقابل .



$$CH_2{=}CH_2 \xrightarrow[25^{o}C]{Ni\text{ , }Pd\text{ or }Pt} CH_3{-}CH_3$$

ethene ethane

ب - إضافة الهالوجينات **Addition of halogen** (Halogenation الهلجنة)



ثانيا / إضافة المتفاعلات غير المتماثلة

Addition of asymmetric reactants such as H_2O or HX

تعتمد إضافة متفاعل غير متماثل للألكين على تماثل أو عدم تماثل الألكين فإذا كان الألكين غير متماثل فأن إضافة الشقين غير المتماثلين تخضع لقاعدة ماركونيكوف .

What is Markovnikov's rule? Markovnikov's rule states that when an asymmetrical reagent is added to an asymmetrical alkene, then the negative half of the reagent will attach to the carbon atom containing fewer hydrogen atoms.

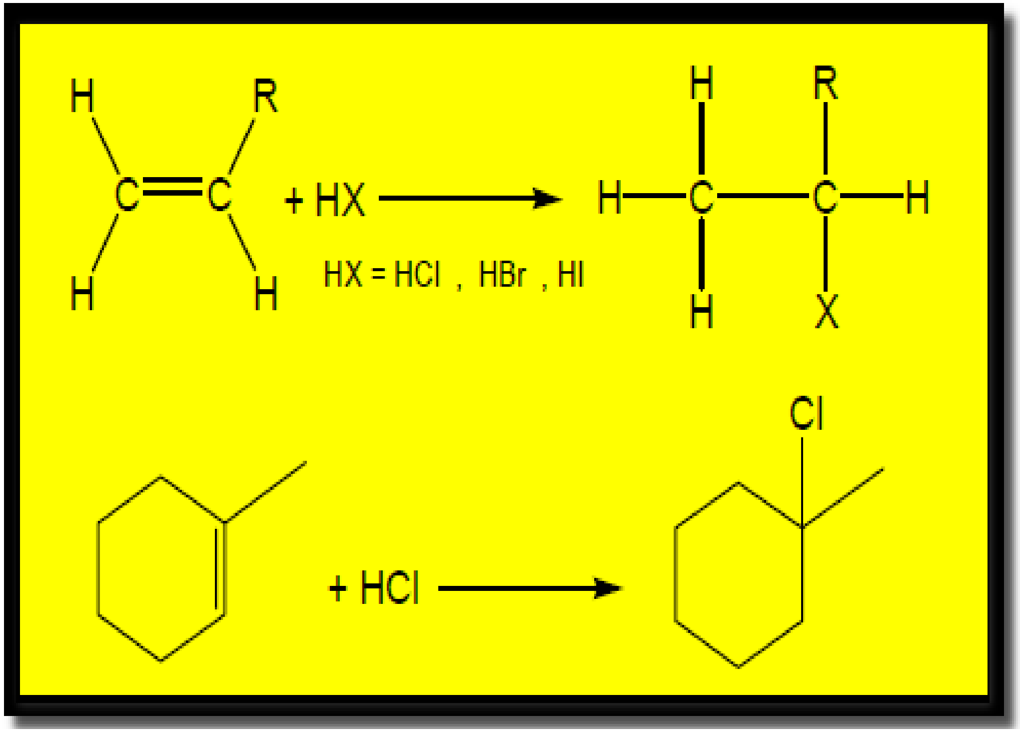
قاعدة ماركونيكوف Markovnikov,s rule

توصل العالم الروسي Vladimir V. Markovnikov سنة 1869م إلى آلية إضافة المتفاعل غير المتماثل للألكين غير المتماثل حيث تنص على : "عند الإضافة الأيونية لمتفاعل غير متماثل إلى ألكين غير متماثل فأن الشق الموجب يضاف إلى ذرة الكربون المتصلة بأعلى عدد من ذرات الهيدروجين بينما يتجه الشق السالب لذرة الكربون المتصلة بأقل عدد من ذرات الهيدروجين."

1- الإضافة حسب قاعدة ماركونيكوف Markovnikov addition

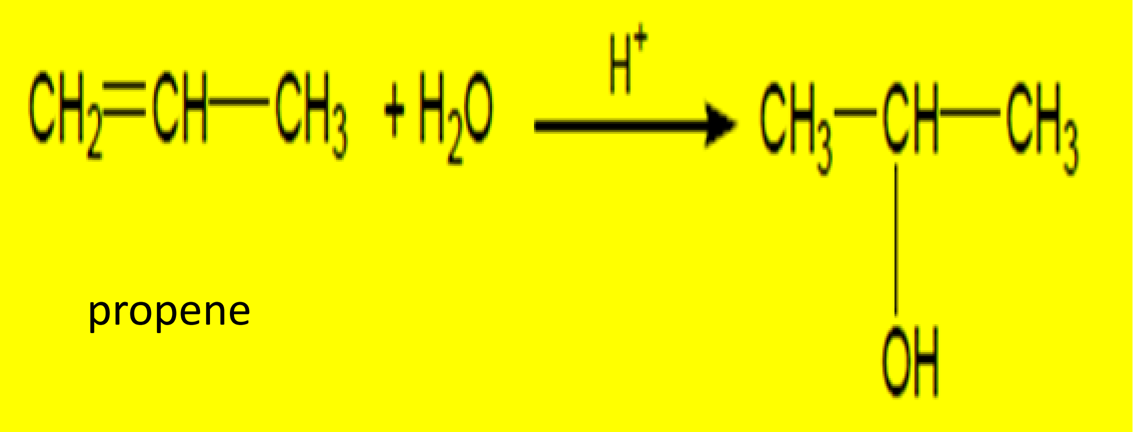
أ ـ إضافة هاليدات الهيدروجين Addition of hydrogen halides

لإجراء هذا التفاعل يستخدم الهاليد الغازي بإمراره مباشرة فى الألكين الذي يقوم بعمل المذيب أو عن طريق إذابة هاليد الهيدروجين فى حمض الخليك ثم يخلط مع الألكين .



b) Hydration (addition of H_2O)

Addition of water is carried out according to Markovnikov's rule



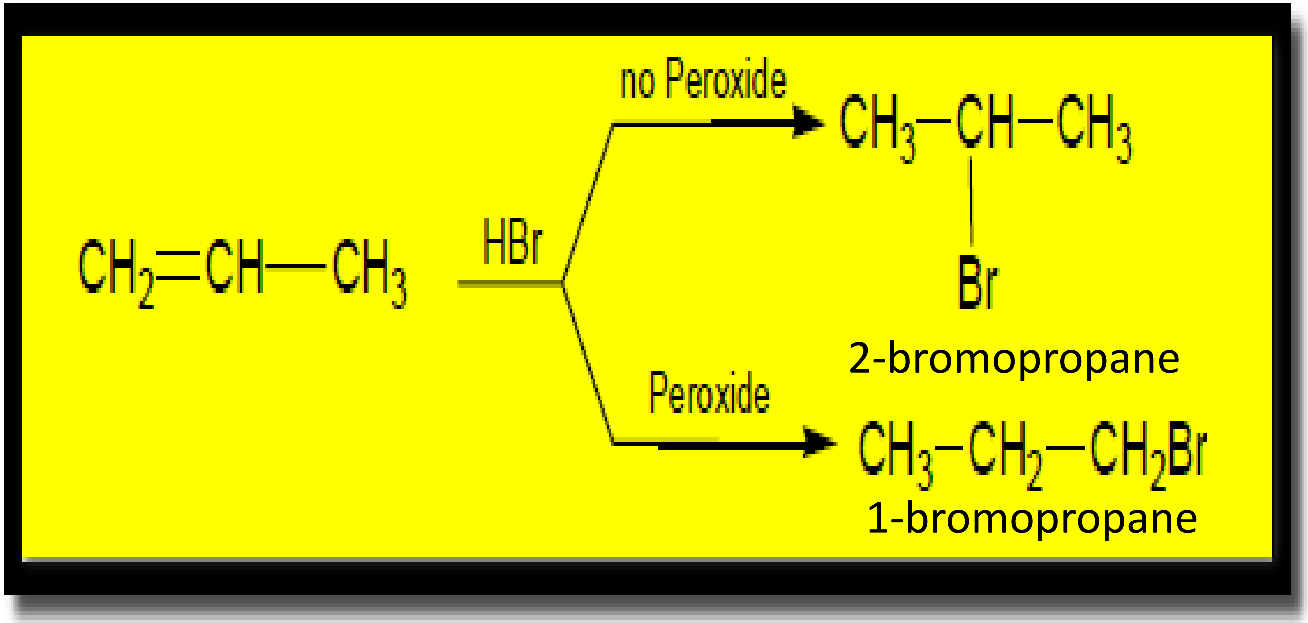
$$CH_2{=}CH{-}CH_3 + H_2O \xrightarrow{H^+} CH_3{-}\underset{\displaystyle OH}{\underset{|}{CH}}{-}CH_3$$

2-propanol

2- الإضافة عكس قاعدة ماركونيكوف Anti-Markovnikov addition

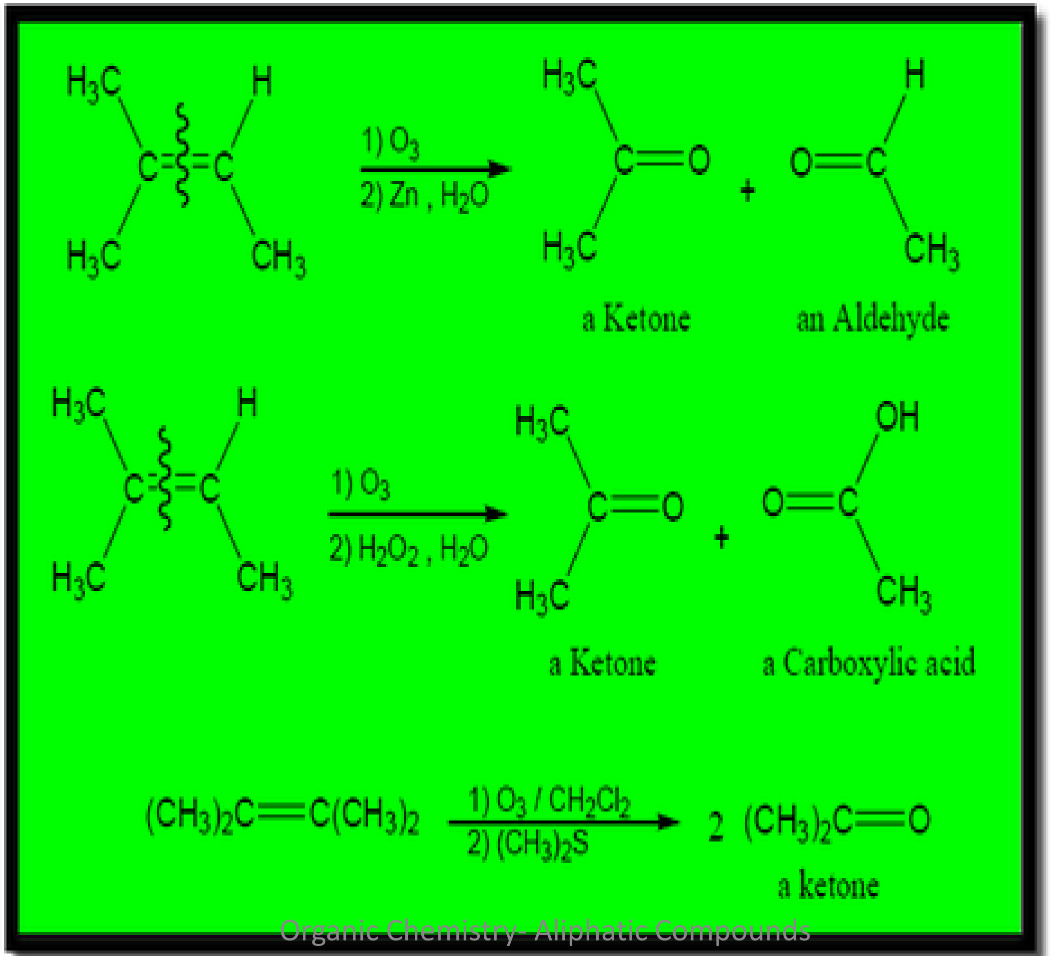
أ ـ إضافة هاليدات الهيدروجين Addition of hydrogen halides

عند إضافة هاليد الهيدروجين في وجود البيروكسيد فأن الإضافة تتم عكس قاعدة ماركونيكوف

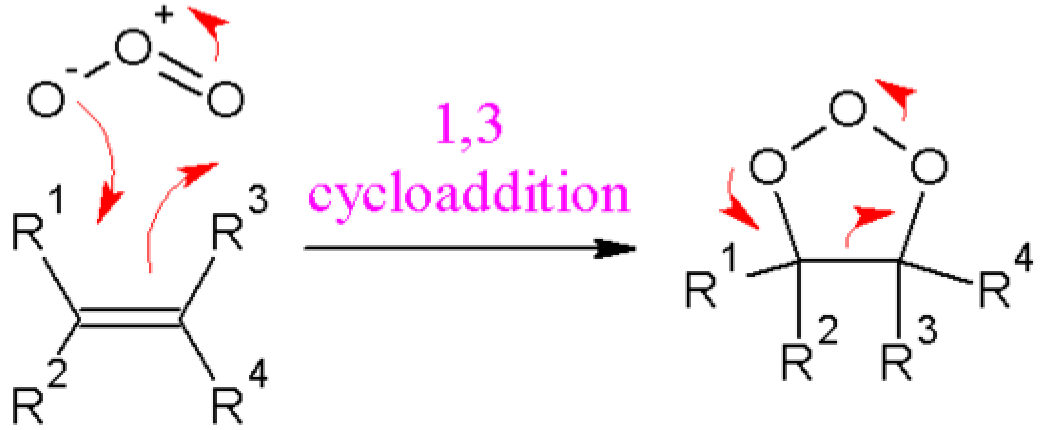


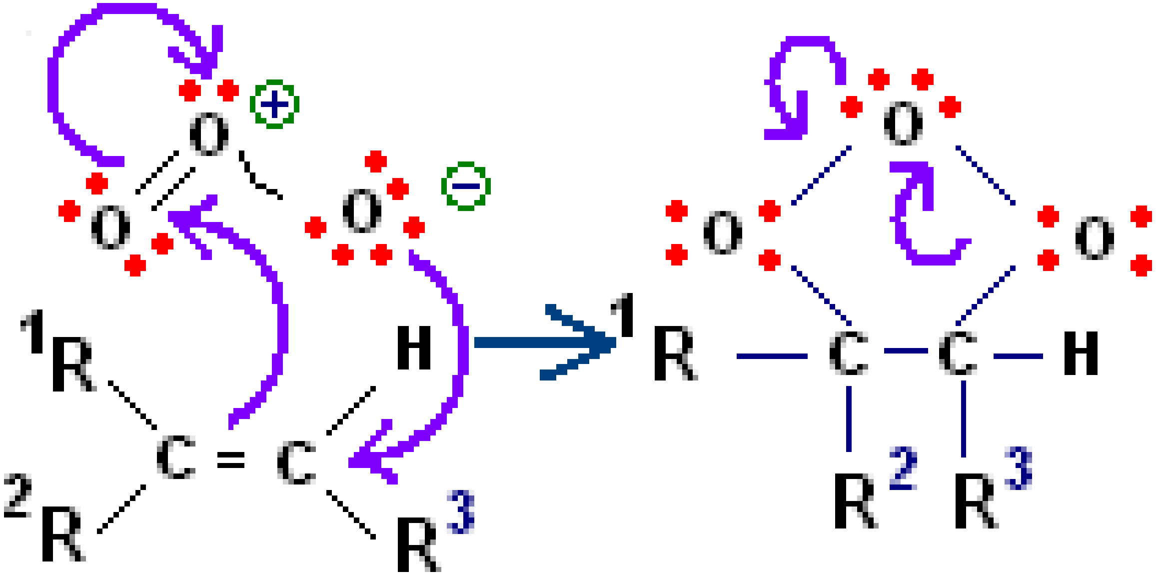
أ- التفاعل مع الأوزون Ozonization :

يتفاعل الأوزون بقوة مع الألكين ويعطي مركبات تسمى أوزونايد Ozonide التي يتم اختزالها بالخارصين Zn أو dimethyl sulfide $(CH_3)_2S$ إلى الدهيدات أو كيتونات وعند إعادة أكسدة مركبات الأوزونايد باستخدام H_2O_2 يتم تحويلها إلى أحماض كربوكسيلية وكيتونات.



Oxidation by Ozone





Alkynes CnH2n-2

Alkynes are hydrocarbons which contain carbon-carbon triple bonds. Their general formula is C_nH_{2n-2} for molecules with one triple bond (and no rings). Alkynes undergo many of the same reactions as alkenes, but can react twice because of the presence of the two p-bonds in the triple bond.

Alkynes are **hydrocarbons which contain carbon-carbon triple bonds.**

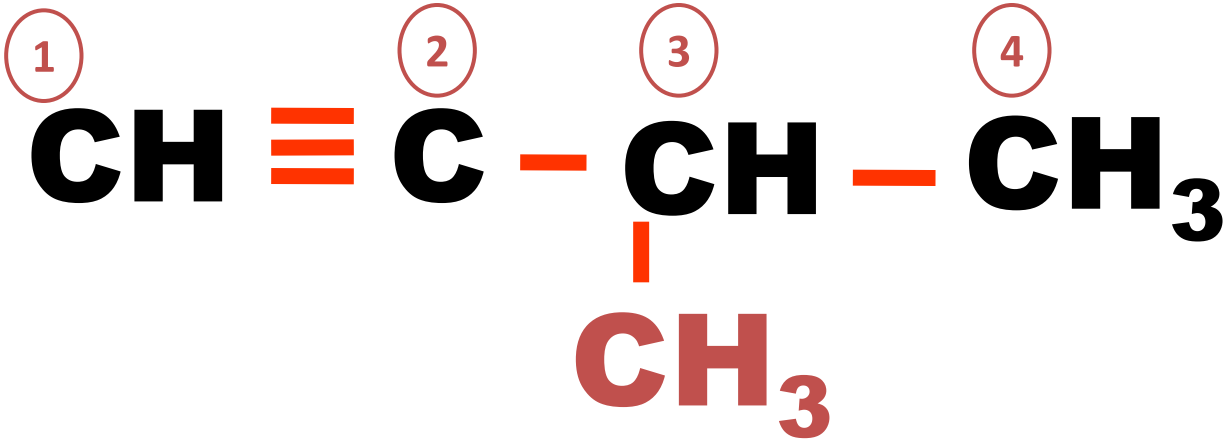
Simplest alkyne is Ethyne or Acetylene

$H-C\equiv C-H$

Angles 180°

General formula: C_nH_{2n-2}

Nomenclature of alkyne



$$\overset{1}{CH} \equiv \overset{2}{C} - \underset{CH_3}{\overset{3}{CH}} - \overset{4}{CH_3}$$

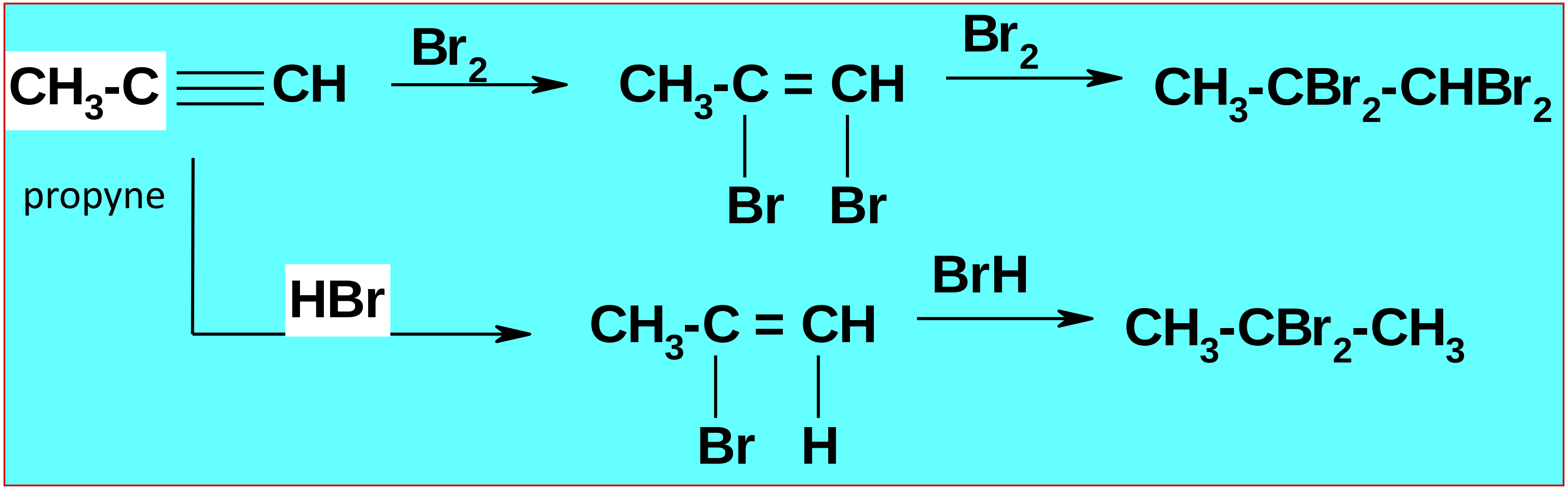
3-methyl-1-butyne

Naming rule

- Identify longest chain contains double bond
- Triple bond will take the lowest number

Reactions of Alkynes

Bromonation Br_2 / Addition of HBr



$$CH_3\text{-}C\equiv CH \xrightarrow{Br_2} CH_3\text{-}\underset{Br}{C}=\underset{Br}{CH} \xrightarrow{Br_2} CH_3\text{-}CBr_2\text{-}CHBr_2$$

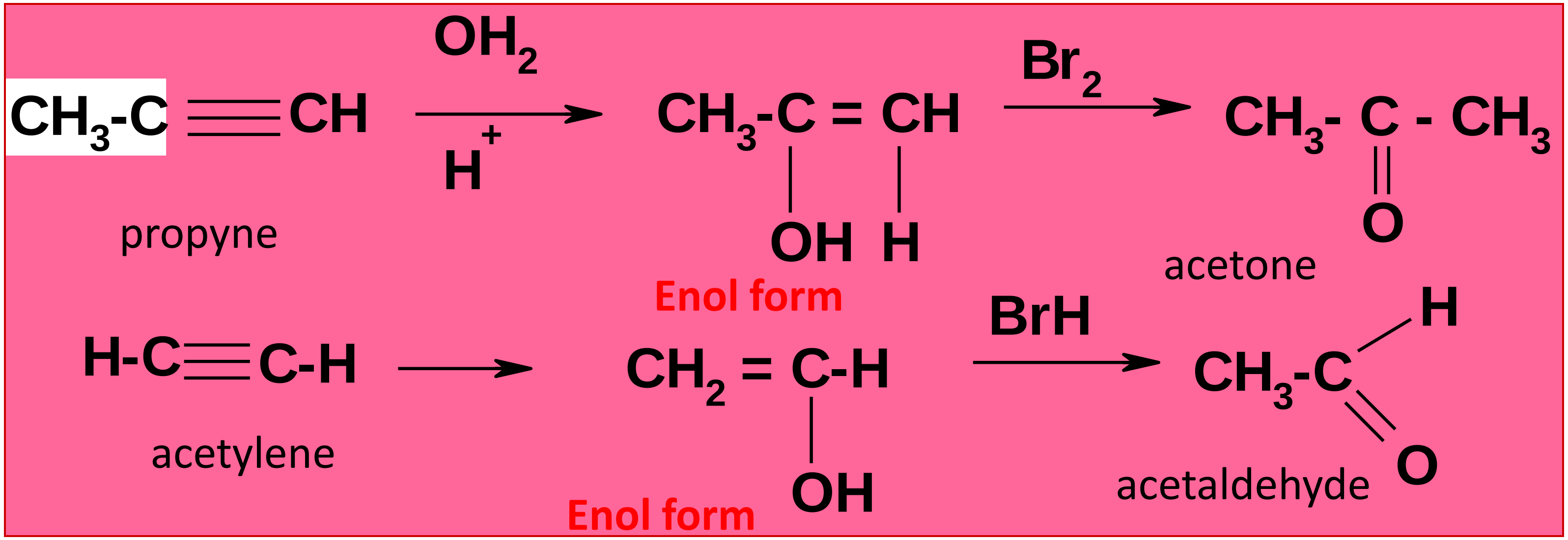
propyne

$$CH_3\text{-}C\equiv CH \xrightarrow{HBr} CH_3\text{-}\underset{Br}{C}=\underset{H}{CH} \xrightarrow{BrH} CH_3\text{-}CBr_2\text{-}CH_3$$

Hydration (addition of H_2O) Markovnikov addition

Hydration of alkyne gives aldehyde or ketone

Firstly, it gives an enol form (unstable) which convert to a keto form (stable) via Tautomerizaton process.



$$CH_3\text{-}C\equiv CH \xrightarrow[H^+]{OH_2} CH_3\text{-}\underset{OH}{\underset{|}{C}} = \underset{H}{\underset{|}{CH}} \xrightarrow{Br_2} CH_3\text{-}\underset{O}{\underset{\|}{C}}\text{-}CH_3$$

propyne

Enol form

acetone

$$H\text{-}C\equiv C\text{-}H \longrightarrow CH_2 = \underset{OH}{\underset{|}{C}}\text{-}H \xrightarrow{BrH} CH_3\text{-}C\overset{H}{\underset{O}{\lessgtr}}$$

acetylene

Enol form

acetaldehyde

Alcohols

ALCOHOLS

- TYPES OF ALCOHOLS
- NOMENCLATURE
- SYNTHESIS
- REACTIONS

TYPES OF ALCOHOLS

According to number of –OH group

1- Mono-hydric
2- Di
3- Tri

According to position of –OH group

1- Primary
2- Secondary
3-Tertiary

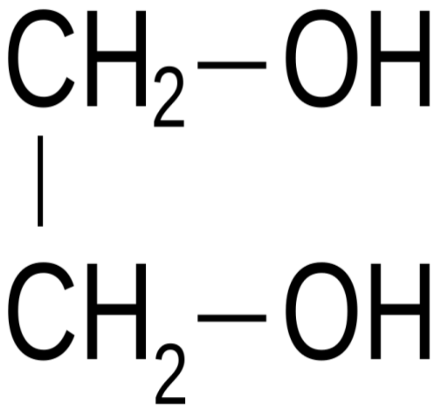
According to number of –OH group

CH_3OH

methanol

CH_3CH_2OH

ethanol

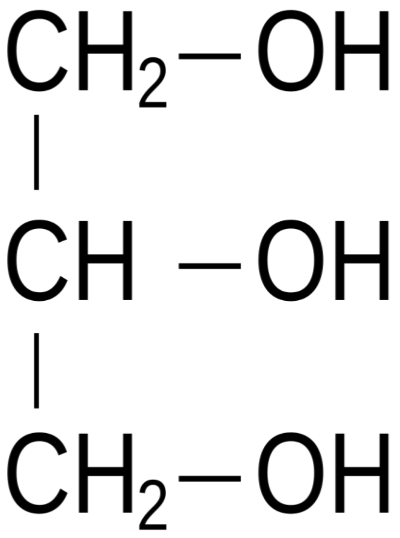


$$\begin{array}{l} CH_2-OH \\ | \\ CH_2-OH \end{array}$$

Ethylene glycol

1,2-dihydroxyethane

Ethane-1,2-diol



$$\begin{array}{l} CH_2-OH \\ | \\ CH-OH \\ | \\ CH_2-OH \end{array}$$

Glycerol

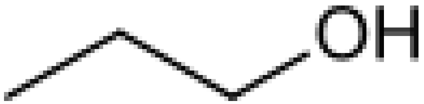
1,2,3-trihydroxypropane

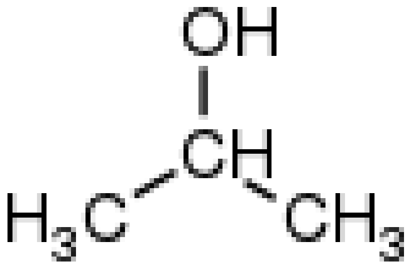
propane-1,2,3-triol

According to position of –OH group

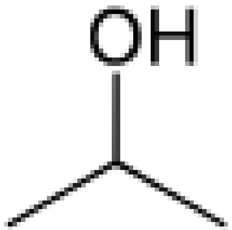
$CH_3CH_2CH_2OH$

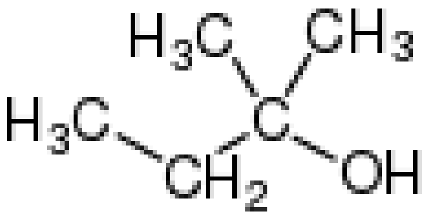
Primary



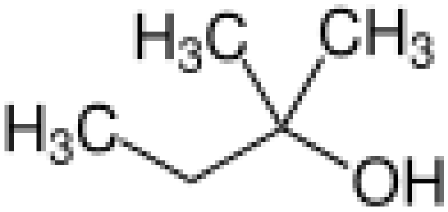


Secondary





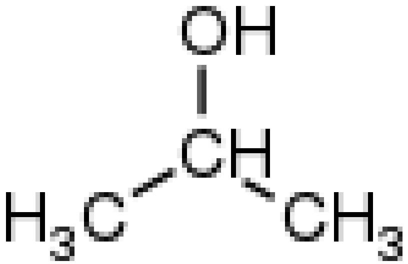
Tertiary



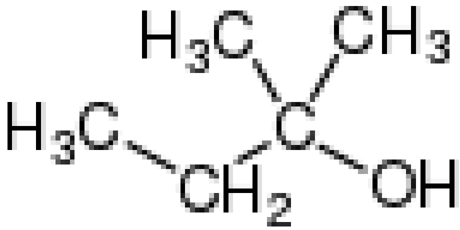
NOMENCLATURE OF ALCOHOLS

CH_3OH

Methanol /
Methyl alcohol



2-propanol/
Isopropanol



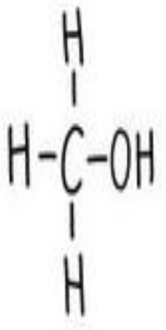
2-methyl-2-butanol

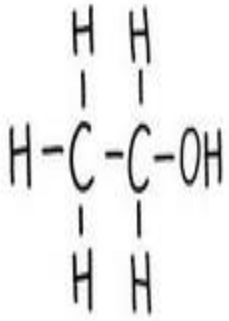
CH_3CH_2OH

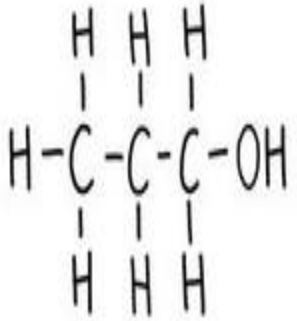
Ethanol /
Ethyl alcohol

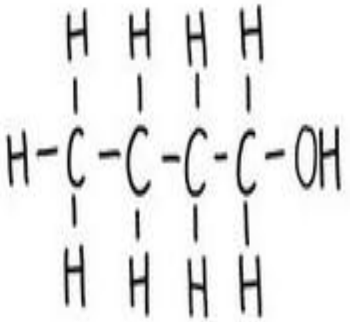
Naming rule

- Identify longest chain contains functional group
- Carbon of functional group will take the lowest number


METHANOL


ETHANOL


PROPANOL


BUTANOL

SYNTHESIS OF ALCOHOLS

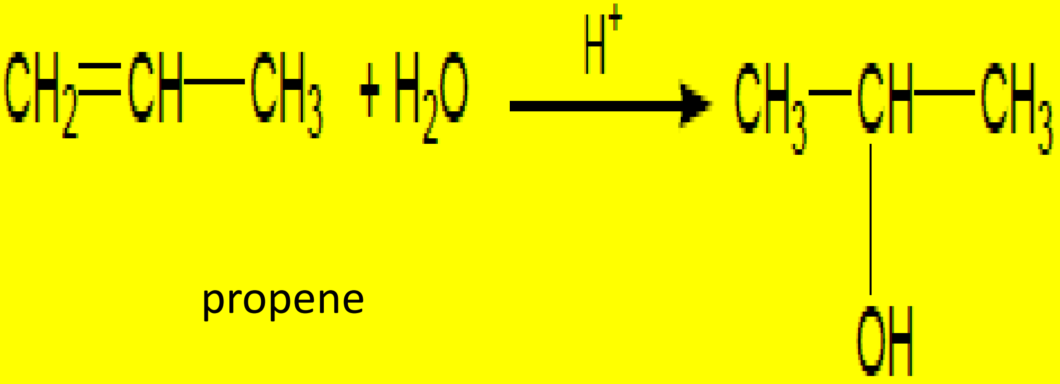
1) Hydrolysis of Alkyl Halides

This is a nucleophilic substitution reaction.

$$\text{R-X} + \text{KOH}_{aq} \rightarrow \text{R-OH}$$

2) Hydration - Addition of water (الإماهة) ب- إضافة الماء

Markincove's rule



$$CH_2{=}CH{-}CH_3 + H_2O \xrightarrow{H^+} CH_3{-}\underset{\large OH}{\underset{|}{CH}}{-}CH_3$$

propene

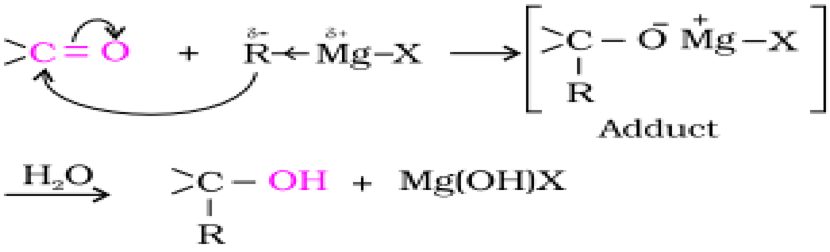
2-propanol

3) Preparation of Alcohols from Grignard Reagent

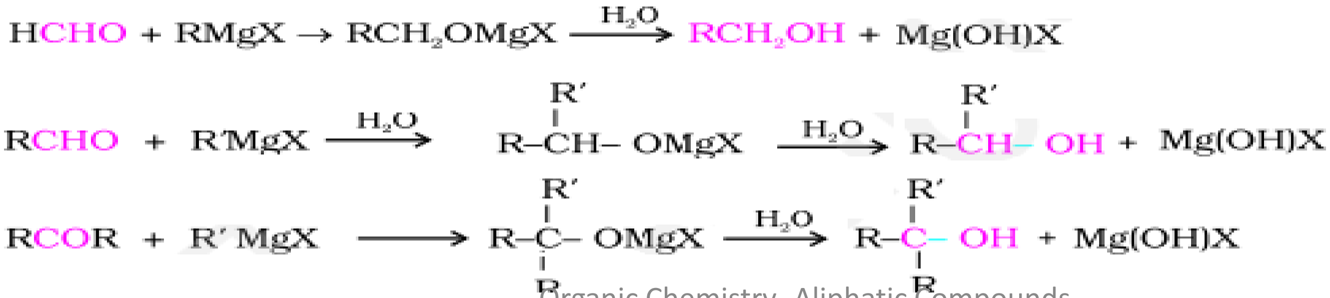
$$CH_3I + Mg \xrightarrow{Ether} CH_3MgI$$

$$CH_3CH_2Br + Mg \xrightarrow{Ether} CH_3CH_2MgBr$$

Ethyl bromide Ethylmagnesium bromide



$$>C=O + \overset{\delta-}{R} \leftarrow \overset{\delta+}{Mg}-X \longrightarrow \left[\underset{R}{>C} - \bar{O}\,\overset{+}{Mg}-X \right] \xrightarrow{H_2O} \underset{R}{>C}-OH + Mg(OH)X$$

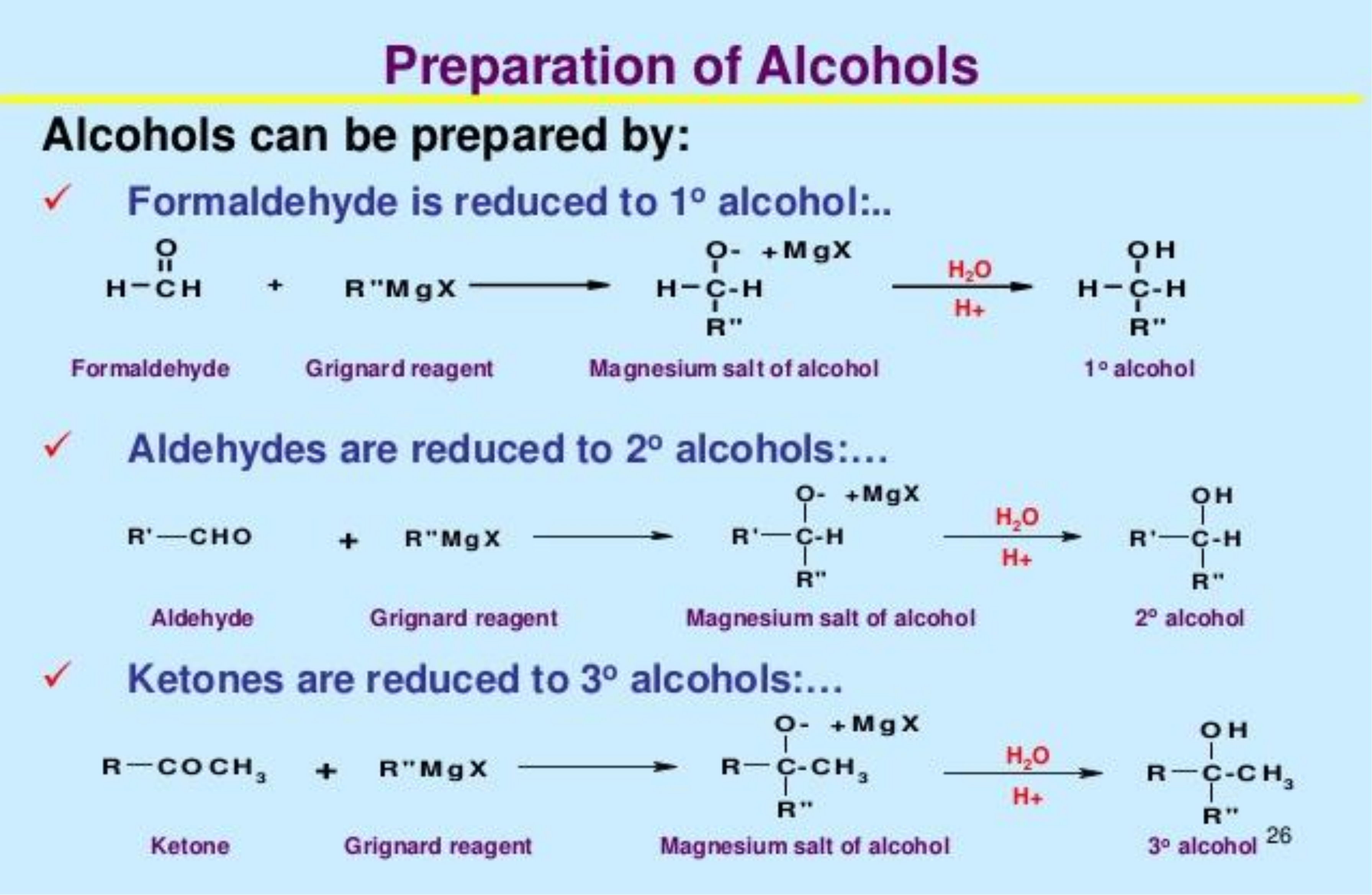


$$HCHO + RMgX \rightarrow RCH_2OMgX \xrightarrow{H_2O} RCH_2OH + Mg(OH)X$$

$$RCHO + R'MgX \xrightarrow{H_2O} R-\overset{R'}{CH}-OMgX \xrightarrow{H_2O} R-\overset{R'}{CH}-OH + Mg(OH)X$$

$$RCOR + R'MgX \longrightarrow R-\underset{R}{\overset{R'}{C}}-OMgX \xrightarrow{H_2O} R-\underset{R}{\overset{R'}{C}}-OH + Mg(OH)X$$

The Grignard reagent : an organometallic compound



Preparation of Alcohols

Alcohols can be prepared by:

- ✓ Formaldehyde is reduced to 1° alcohol:..

$$H-\overset{O}{\overset{\|}{C}}H + R''MgX \longrightarrow H-\underset{R''}{\overset{O^- \; {}^{+}MgX}{C}}-H \xrightarrow[H^+]{H_2O} H-\underset{R''}{\overset{OH}{C}}-H$$

Formaldehyde, Grignard reagent, Magnesium salt of alcohol, 1° alcohol

- ✓ Aldehydes are reduced to 2° alcohols:…

$$R'-CHO + R''MgX \longrightarrow R'-\underset{R''}{\overset{O^- \; {}^{+}MgX}{C}}-H \xrightarrow[H^+]{H_2O} R'-\underset{R''}{\overset{OH}{C}}-H$$

Aldehyde, Grignard reagent, Magnesium salt of alcohol, 2° alcohol

- ✓ Ketones are reduced to 3° alcohols:…

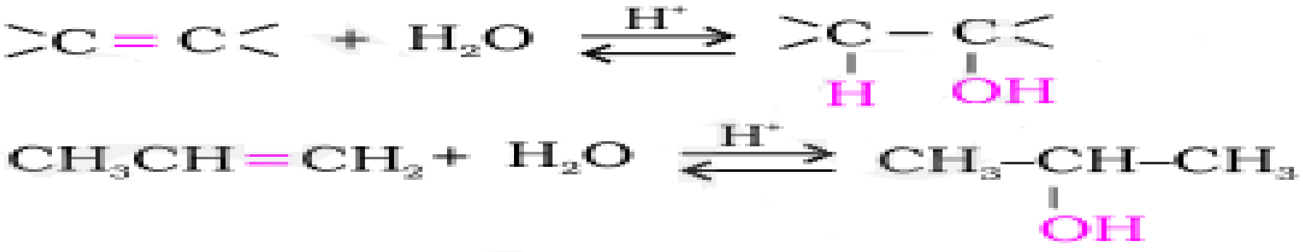
$$R-COCH_3 + R''MgX \longrightarrow R-\underset{R''}{\overset{O^- \; {}^{+}MgX}{C}}-CH_3 \xrightarrow[H^+]{H_2O} R-\underset{R''}{\overset{OH}{C}}-CH_3$$

Ketone, Grignard reagent, Magnesium salt of alcohol, 3° alcohol

26

Hydration of Alkenes

This is electrophilic addition of H_2O to alkenes.



$$>C=C< + H_2O \xrightleftharpoons{H^+} >\underset{H}{C}-\underset{OH}{C}<$$

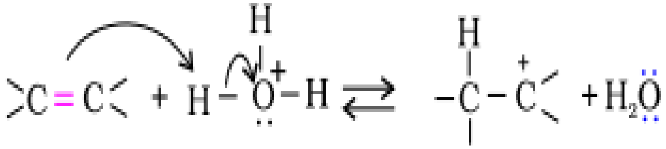
$$CH_3CH=CH_2 + H_2O \xrightleftharpoons{H^+} CH_3-\underset{OH}{CH}-CH_3$$

by application of Markincove's rule: 2-propanol

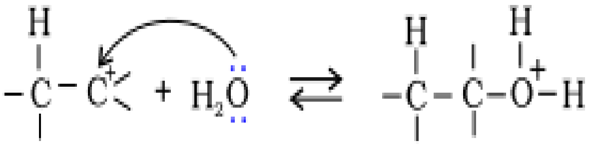
by application of anti- Markincove's rule: 1-propanol

Mechanism of Hydration of alkenes:

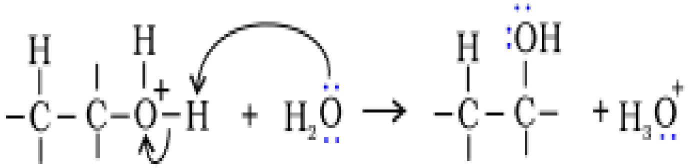
Protonation of alkene to form carbocation by electrophilic



Nucleophilic attack of water on carbocation.



Deprotonation to form an alcohol.



Except ethyl alcohol no other primary alcohol can be obtained by this method, however hydroboration of terminal alkenes give primary alcohols.

Alcohols from Carbonyl Compounds: Reduction

- Reduction of a carbonyl compound gives an alcohol
  - Addition of H to a C=O bond

where [H] is a reducing agent

A carbonyl compound **An alcohol**

- Reduction of aldehydes gives primary alcohols
- Reduction of ketones gives secondary alcohols

An aldehyde **A primary alcohol**

A ketone **A secondary alcohol**

REACTIONS OF ALCOHOLS

1- Elimination R. (Dehydration)

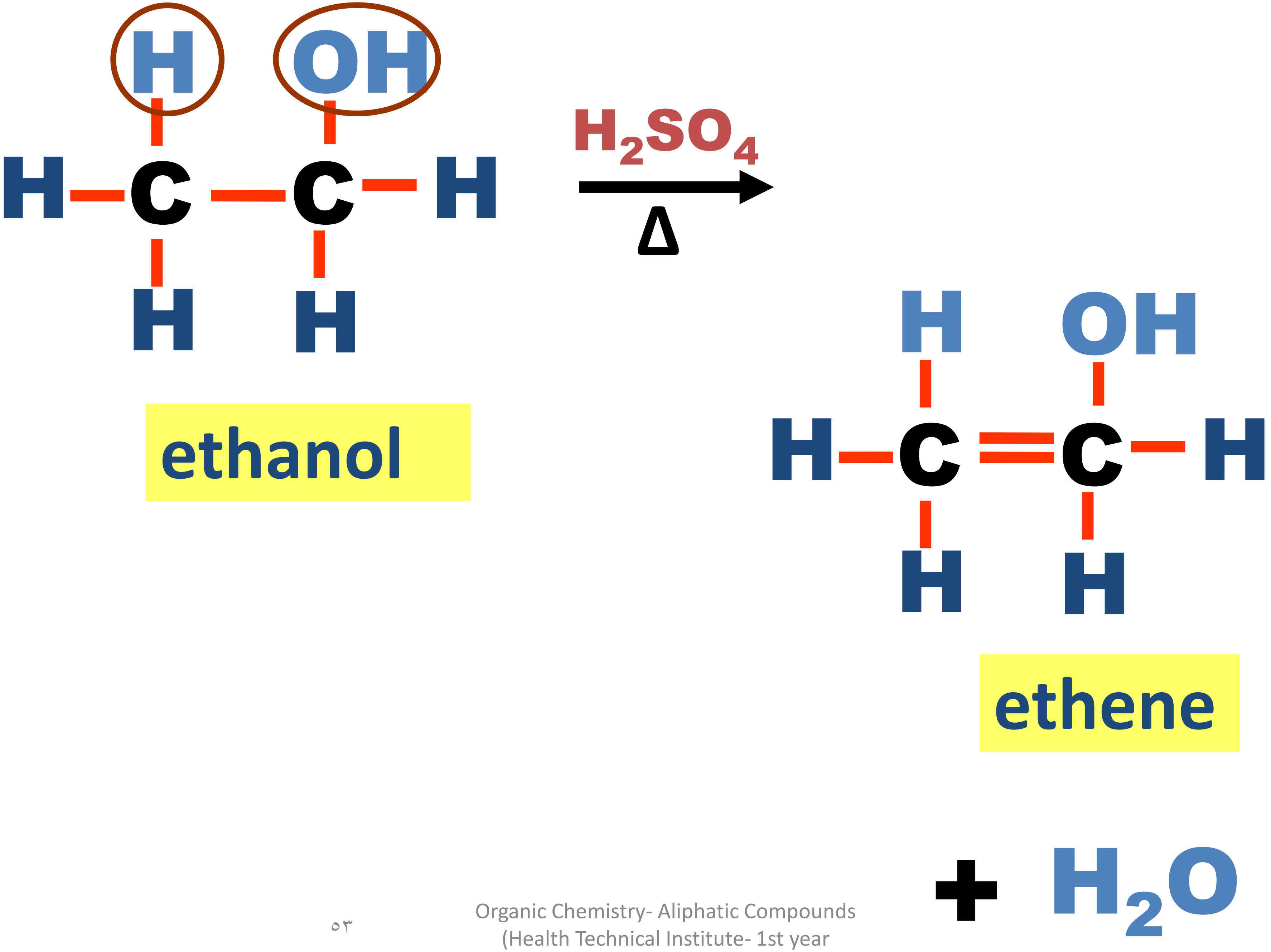
$$RCH_2-CH_2OH \xrightarrow[-\,H_2O]{Al_2O_3,\ 623\,K} RCH{=}CH_2$$

alcohol alkene

For example,

$$C_2H_5OH \xrightarrow[-\,H_2O]{Al_2O_3,\ 623\,K} CH_2{=}CH_2$$

ethanol ethene

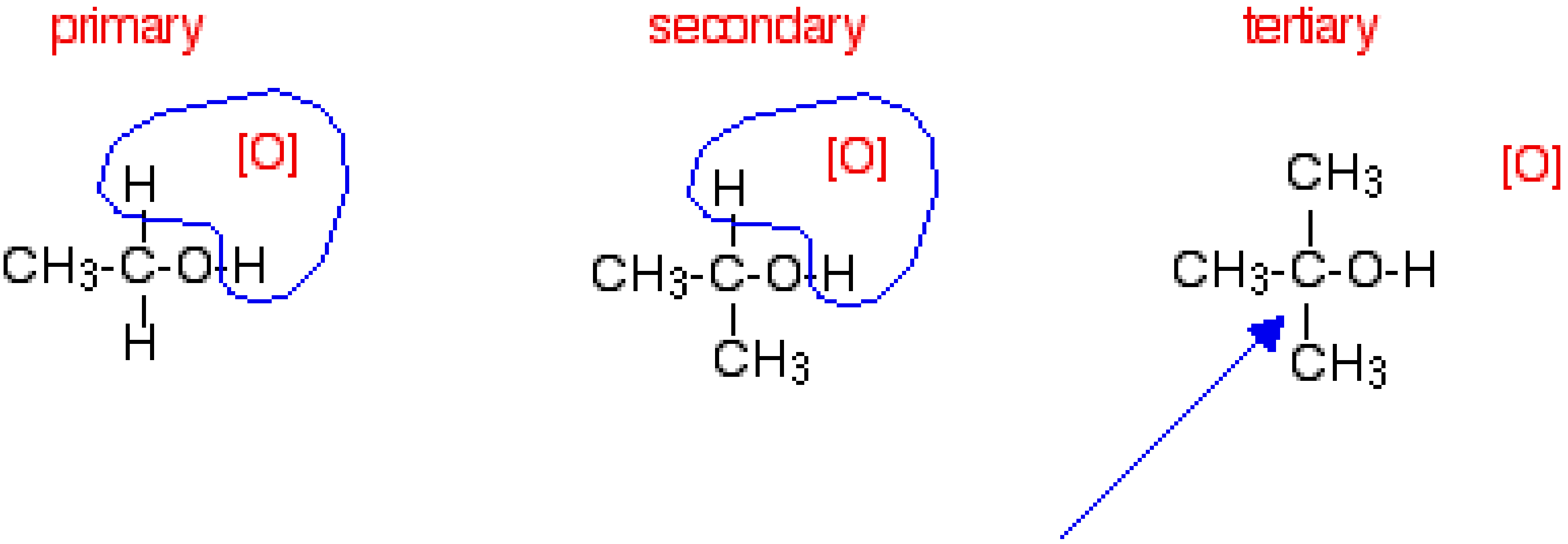

H
OH
H—C—C—H
H H
H_2SO_4
Δ
ethanol
H
OH
H—C=C—H
H H
ethene
+ H_2O

2- Oxidation

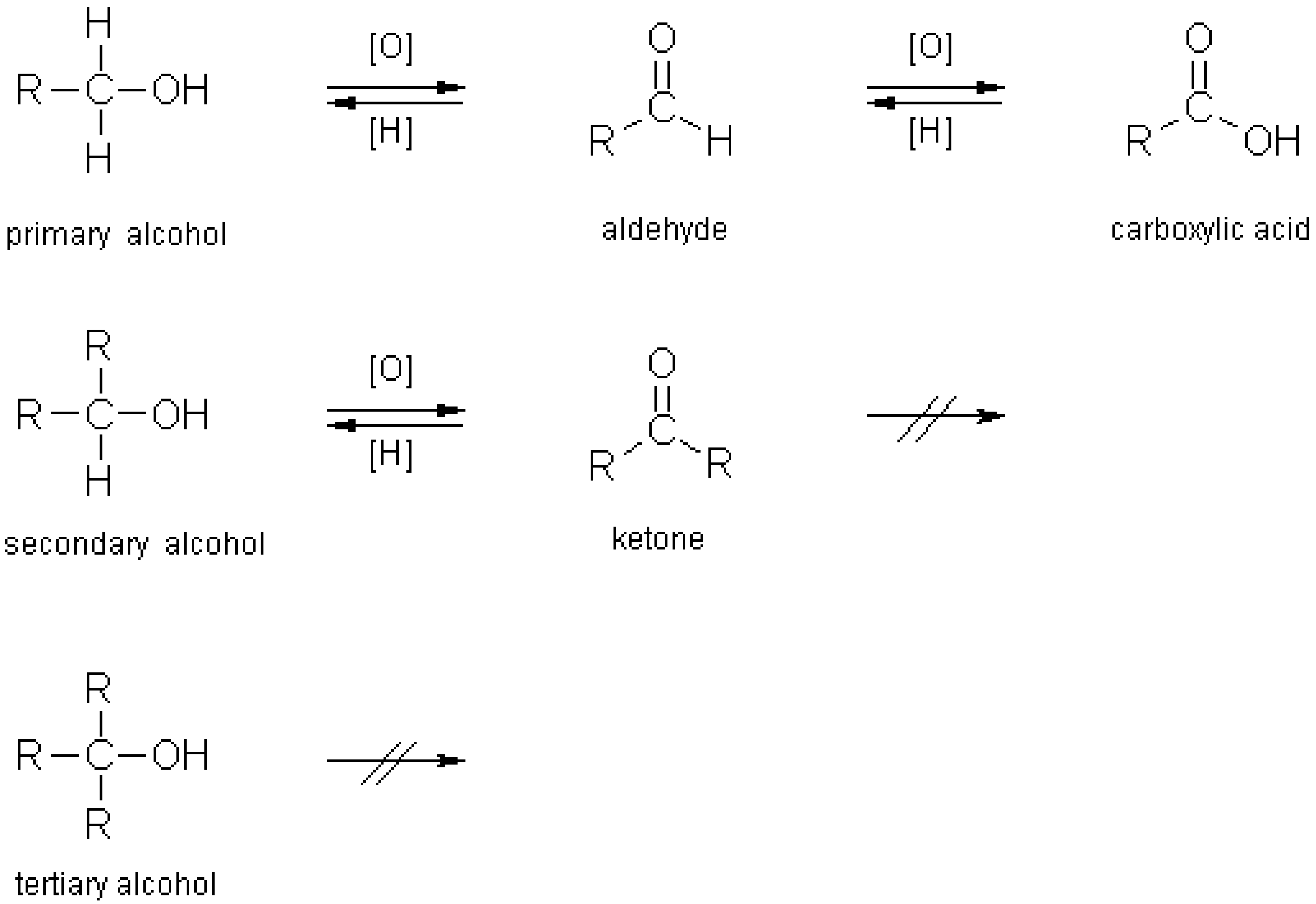
Primary alcohol $\xrightarrow{[O]}$ Aldehyde

Secondary alcohol $\xrightarrow{[O]}$ Ketone

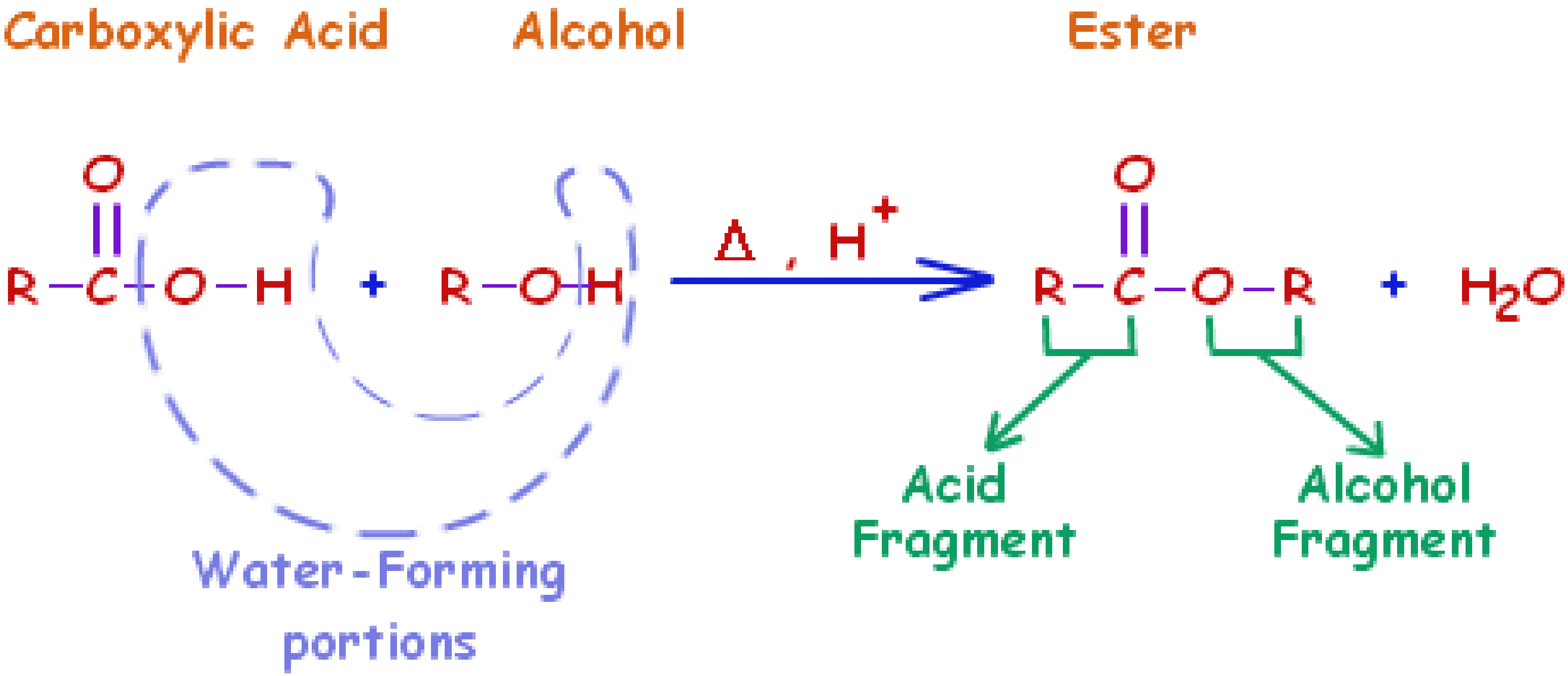
Tertiary alcohols $\xrightarrow{[O]}$ No oxidation

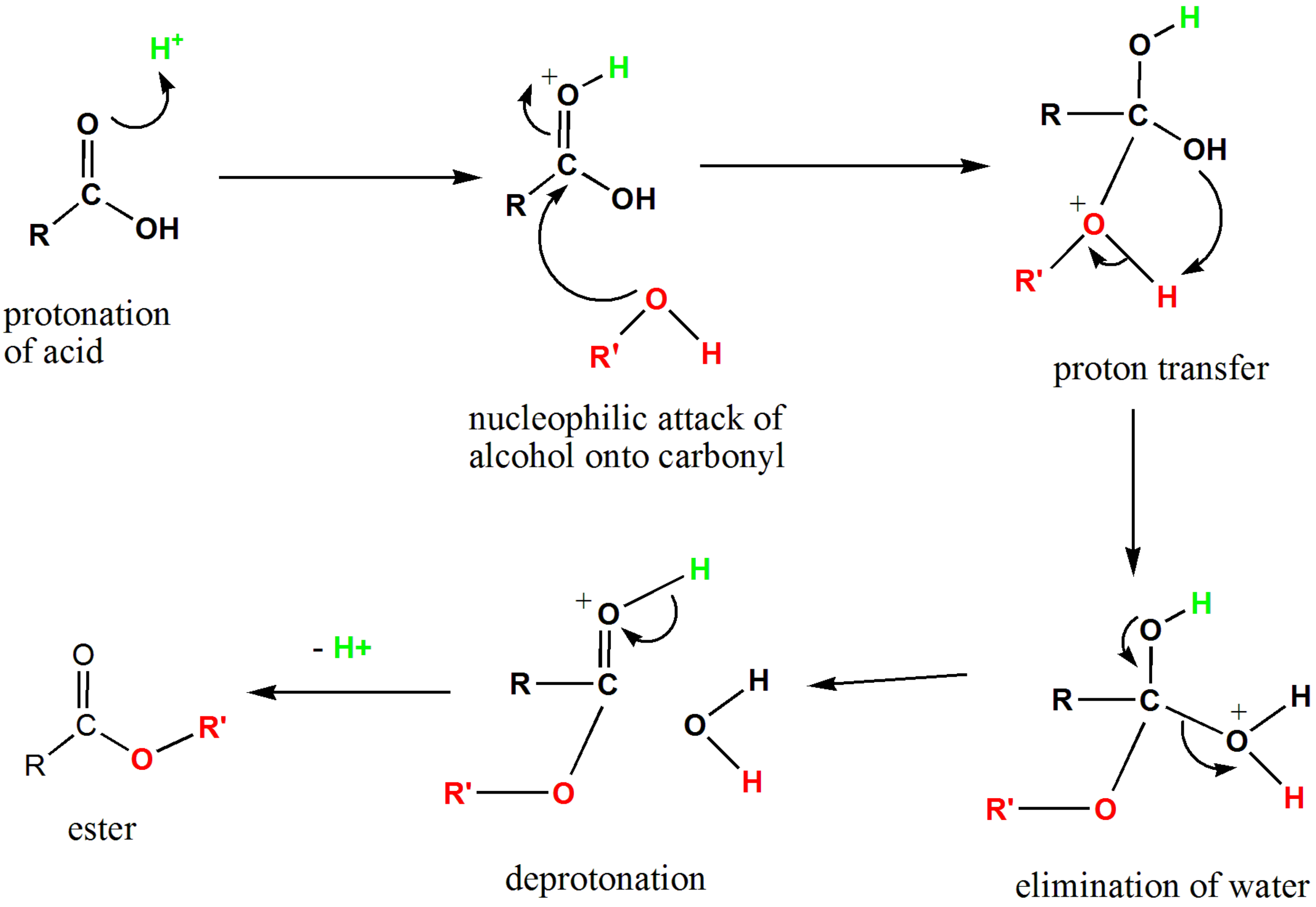


There is no hydrogen attached to this carbon for the oxygen to remove.


[O]
[H]
primary alcohol
aldehyde
carboxylic acid
secondary alcohol
ketone
tertiary alcohol

3-Esterfication





protonation of acid

nucleophilic attack of alcohol onto carbonyl

proton transfer

elimination of water

deprotonation

ester

Aldehydes and Ketones

ALDEHYDES & KETONES

(ALKANALS & ALKANONES)

ALDEHYDES AND KETONES

Properties

Nomenclature

Preparation

Reactions

Carbonyl Functional Groups

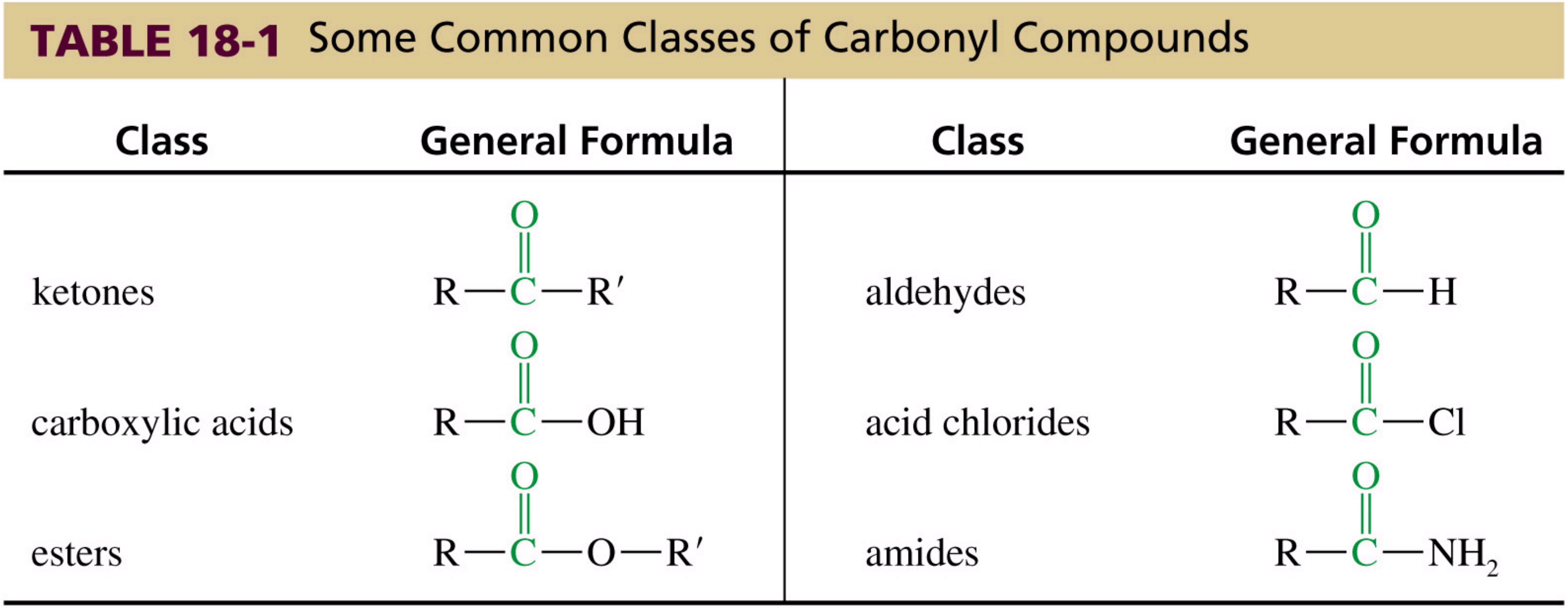
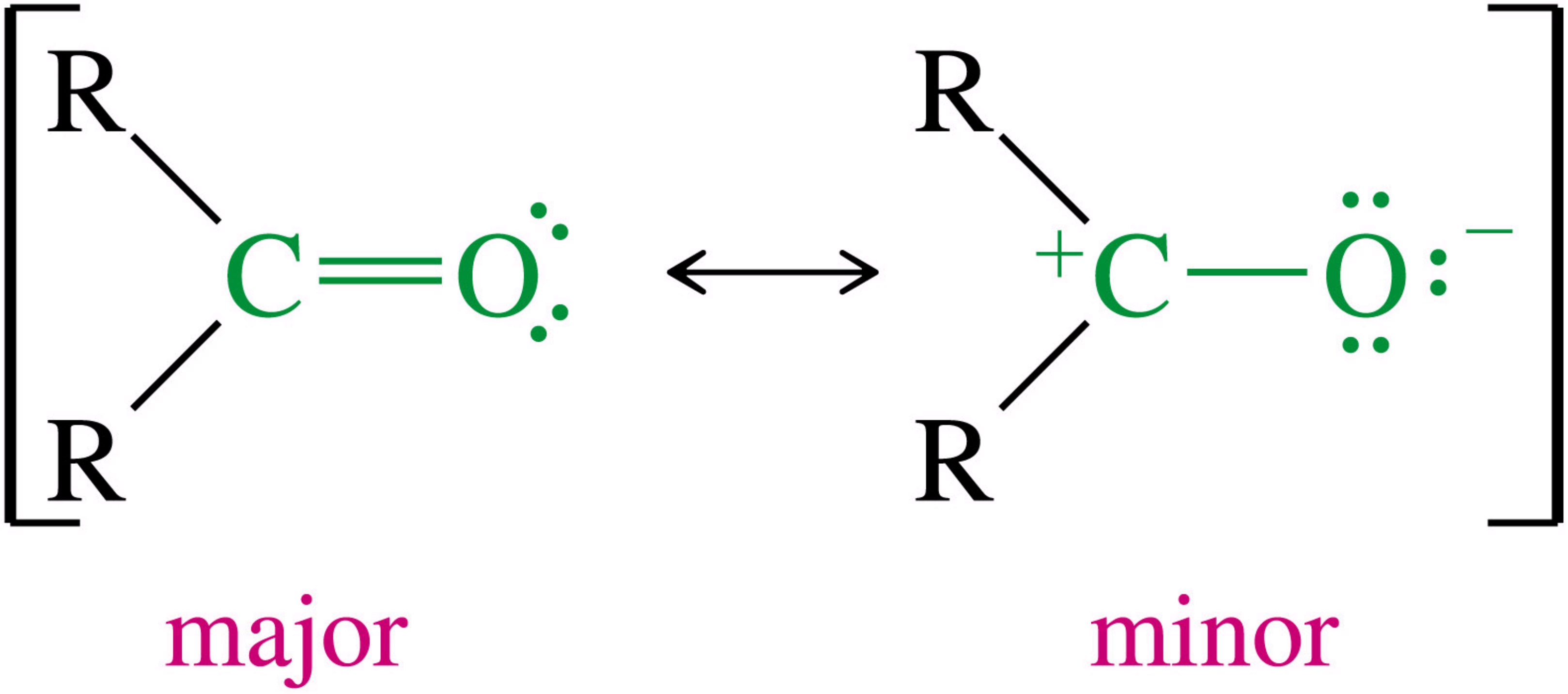


TABLE 18-1 Some Common Classes of Carbonyl Compounds

Class	General Formula	Class	General Formula
ketones	$R-\overset{O}{\overset{\Vert}{C}}-R'$	aldehydes	$R-\overset{O}{\overset{\Vert}{C}}-H$
carboxylic acids	$R-\overset{O}{\overset{\Vert}{C}}-OH$	acid chlorides	$R-\overset{O}{\overset{\Vert}{C}}-Cl$
esters	$R-\overset{O}{\overset{\Vert}{C}}-O-R'$	amides	$R-\overset{O}{\overset{\Vert}{C}}-NH_2$

Large Dipole Controls Properties and Reactivity



Boiling Points

Dipole-Dipole Interactions

$CH_3CH_2CH_2CH_3$

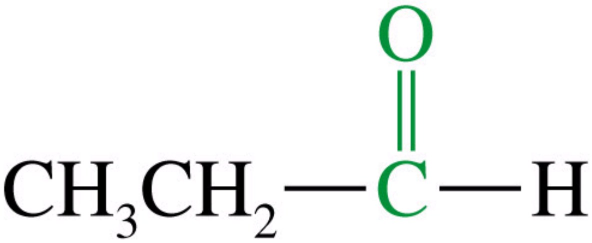
butane

bp 0°C

$CH_3—O—CH_2CH_3$

methoxyethane

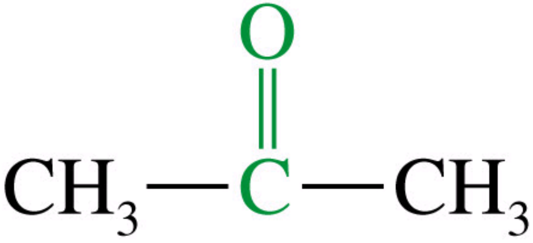
bp 8°C



$CH_3CH_2—\overset{\overset{\displaystyle O}{\|}}{C}—H$

propanal

bp 49°C



$CH_3—\overset{\overset{\displaystyle O}{\|}}{C}—CH_3$

acetone

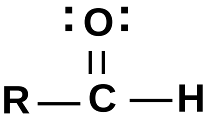
bp 56°C

$CH_3CH_2CH_2—OH$

1-propanol

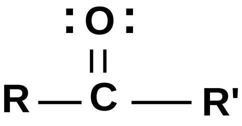
bp 97°C

ALDEHYDES & KETONES (ALKANALS & ALKANONES)



$$R-\overset{:O:}{\overset{\|}{C}}-H$$

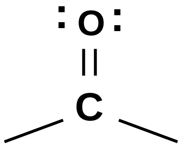
aldehyde



$$R-\overset{:O:}{\overset{\|}{C}}-R'$$

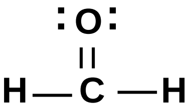
ketone

Aldehydes & ketones both contain the carbonyl group.



carbonyl group

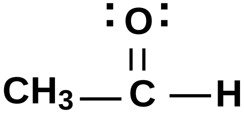
- The simplest aldehyde is formaldehyde (CH_2O). It is the only aldehyde without an alkyl group attached to the carbonyl C.



$$H-\overset{:O:}{\overset{\|}{C}}-H$$

formaldehyde

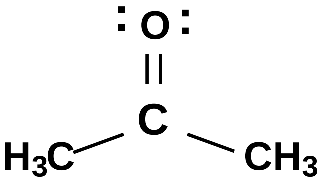
All other aldehydes, such as acetaldehyde (CH_3CHO), have one alkyl group and one H attached to the carbonyl C.



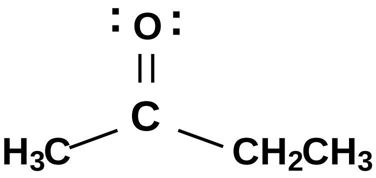
$$CH_3-\overset{:O:}{\overset{\|}{C}}-H$$

acetaldehyde

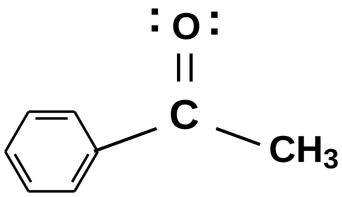
- All ketones have two alkyl groups attached to the carbonyl C.



dimethyl ketone (acetone)



methyl ethyl ketone (MEK)



methyl phenyl ketone (acetophenone)

Classical Aldehyde Nomenclature

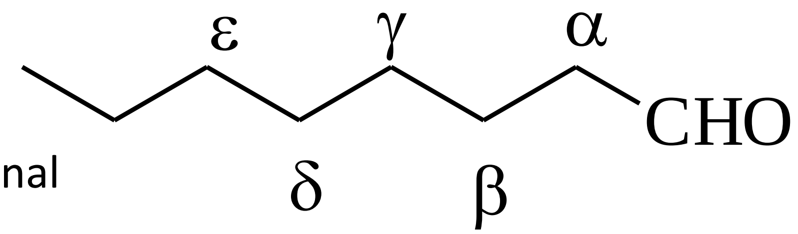
Naming rule

- Identify longest chain contains functional group
- Carbon of functional group will take the lowest number

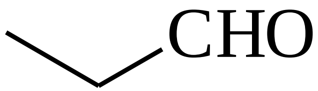
Prefix

form $HCHO$ Formaldehyde/ methanal

acet CH_3CHO Acetaldehyde/ ethanal

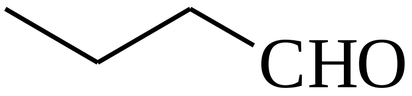


propion

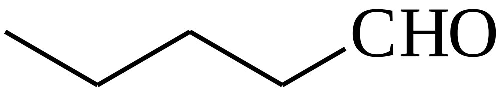


propanal

butyr



valer

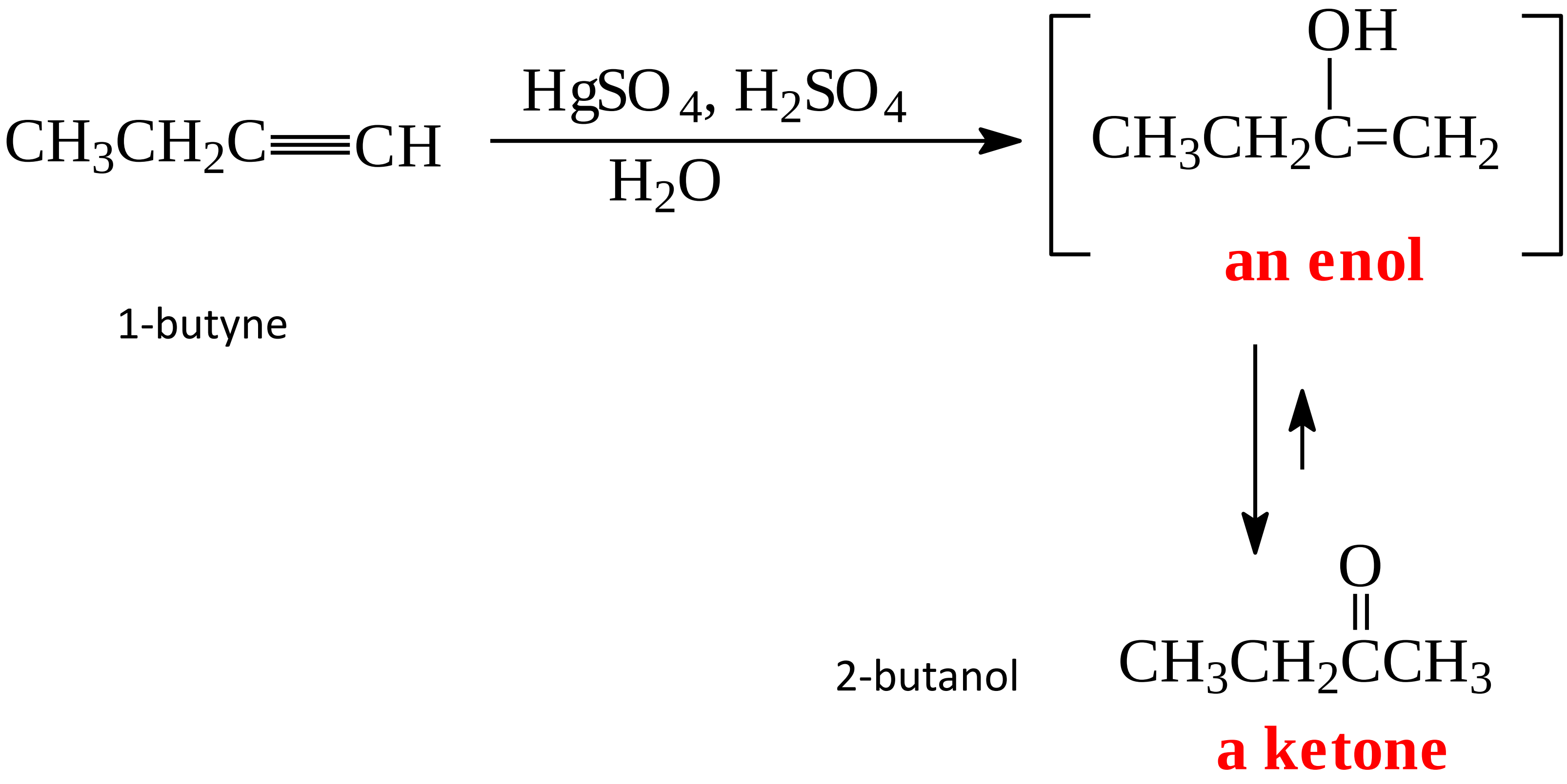


Preparation of Ketones and Aldehydes

1. Hydration of Alkynes (ketones with oxymercuration, aldehydes with hydroboration)
2. Ozonolysis of Alkenes (aldehydes and ketones depending on substitution)
3. Oxidation of alcohols
4. Reduction of acids

1- Hydration of alkyne

a) Markovnikov's rule



$$CH_3CH_2C\equiv CH \xrightarrow[H_2O]{HgSO_4,\ H_2SO_4} \left[CH_3CH_2\overset{OH}{\overset{|}{C}}=CH_2 \right]$$

an enol

1-butyne

$$\downarrow\uparrow$$

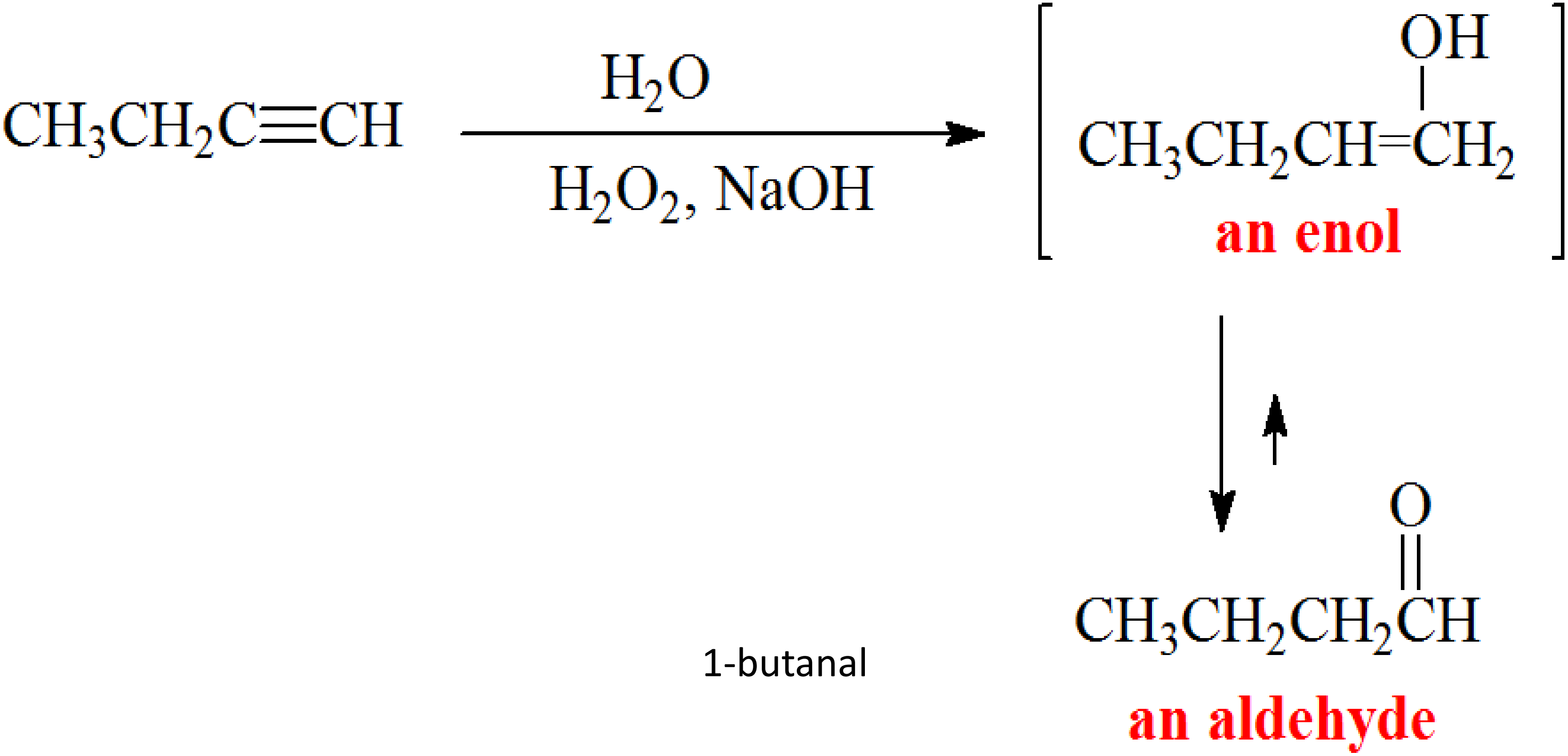
$$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3$$

2-butanol

a ketone

Hydration

b) Anti- Markovnikov's rule



$$CH_3CH_2C\equiv CH \xrightarrow[H_2O_2,\ NaOH]{H_2O} \left[CH_3CH_2CH=\overset{OH}{\overset{|}{C}}H_2 \right]$$

an enol

$$\rightleftharpoons$$

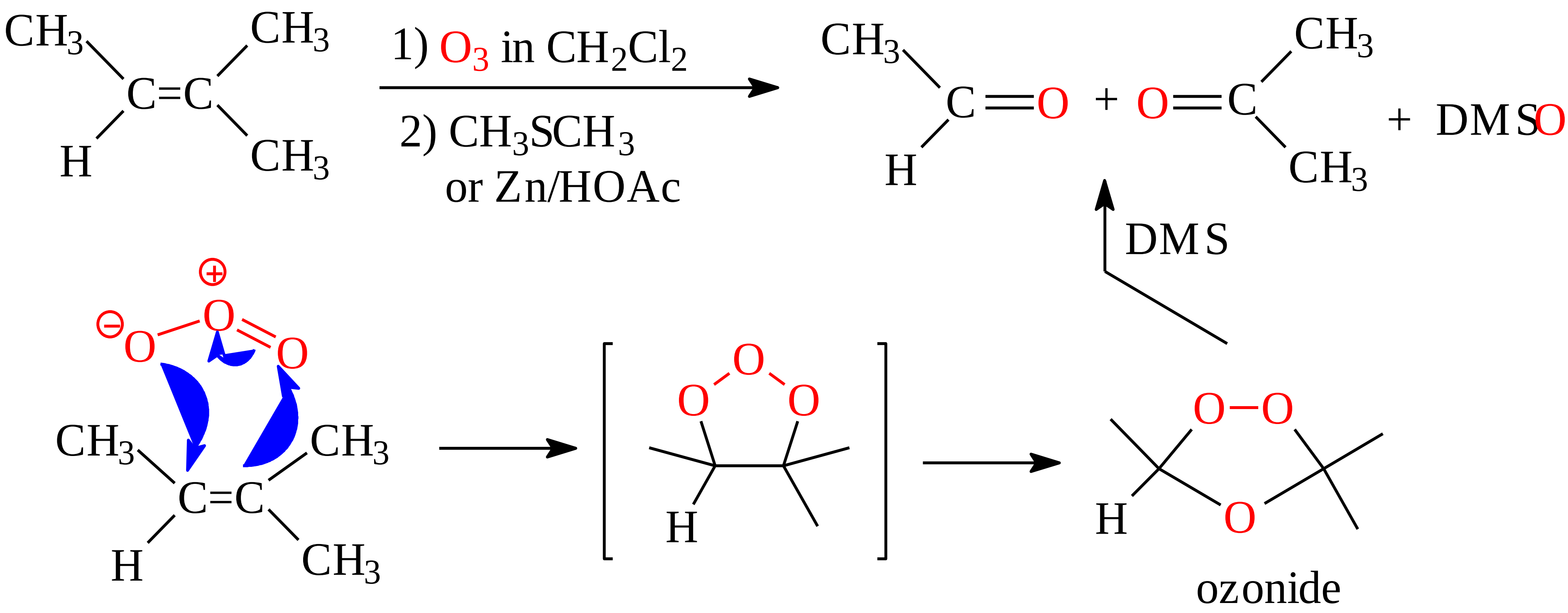
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$$

an aldehyde

1-butanal

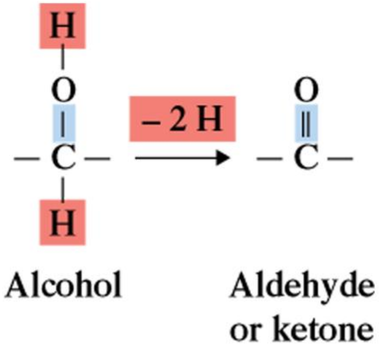
2- Ozonolysis

Alkene Cleavage

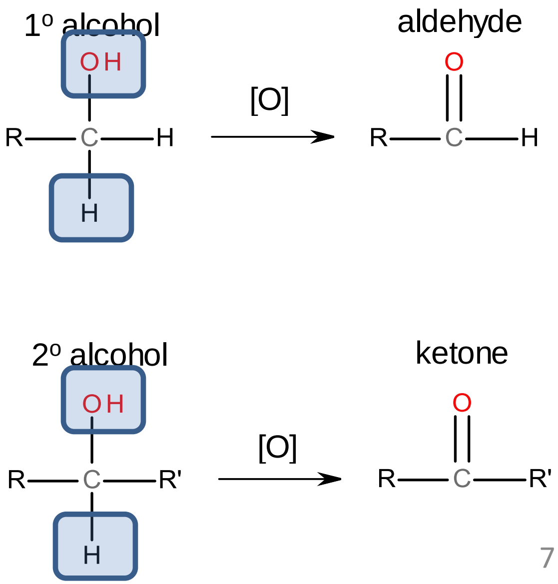


3- Oxidation of alcohols

- alcohols can be oxidized to form aldehydes and ketones.
- Primary (1º) alcohols are oxidized to aldehydes (and subsequently to carboxylic acids)
- Secondary (2º) alcohols are oxidized to ketones

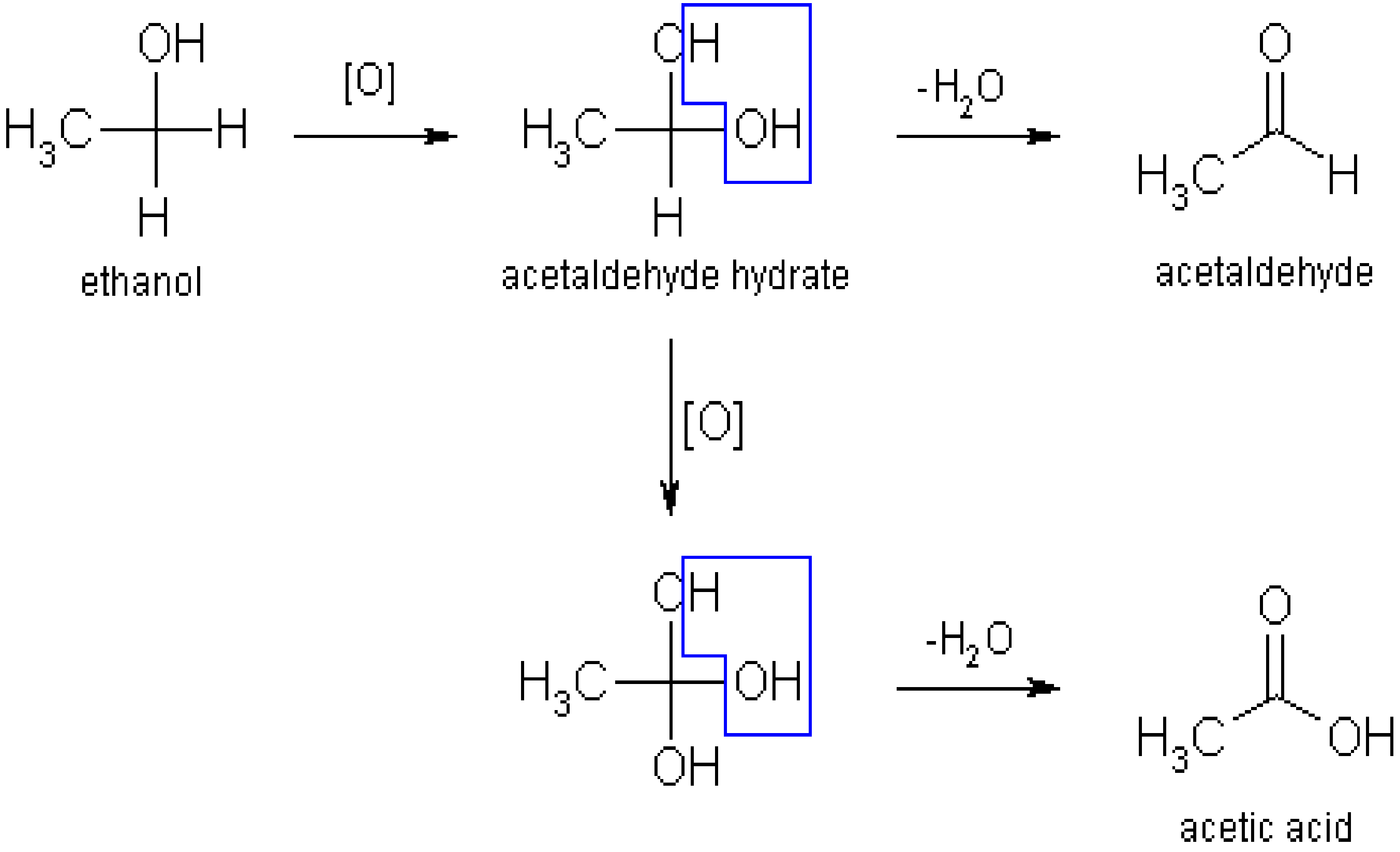


(a)



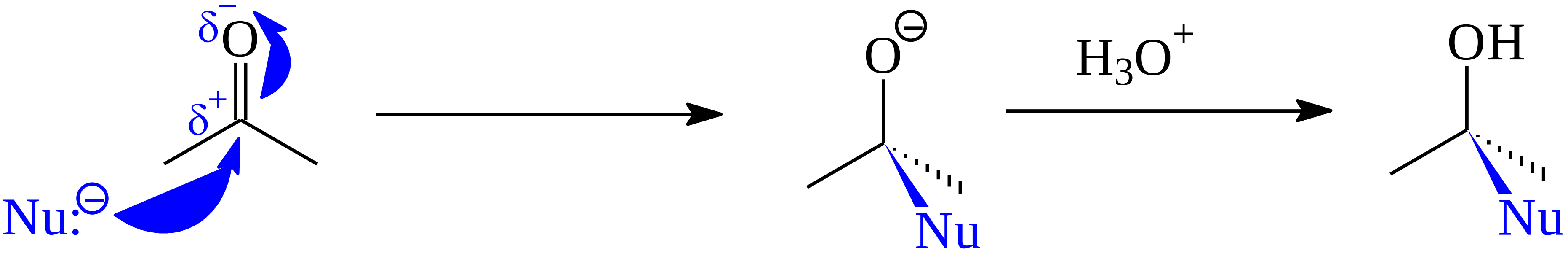
[O] = $KMnO_4$ or $K_2Cr_2O_7$

Contd. Oxidation of alcohols



Nucleophilic Addition Reactions:

Strong Nucleophiles

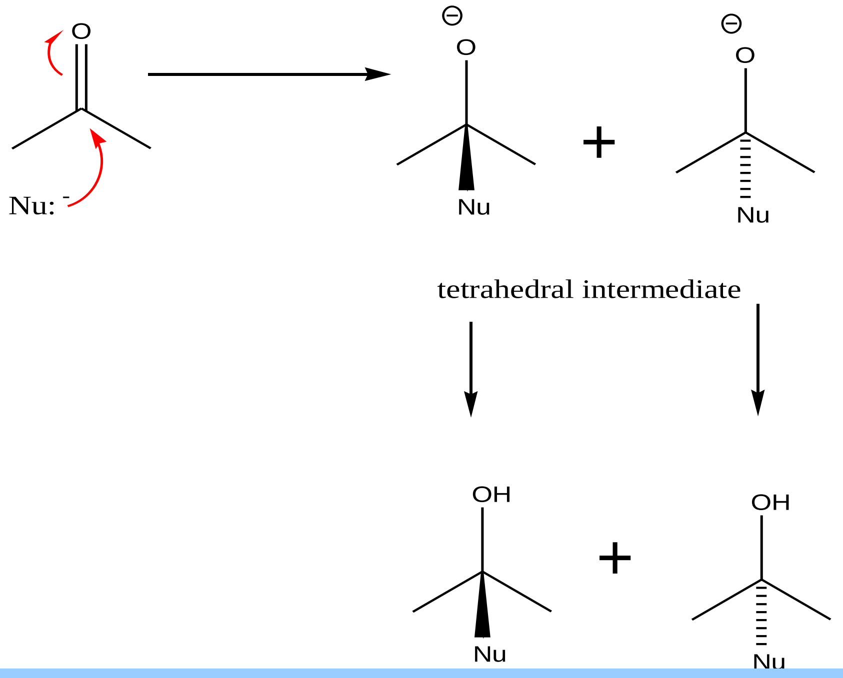


Basic nucleophiles: RMgX, RLi, $LiAlH_4$, $NaBH_4$, RC≡CNa

Nonbasic nucleophiles: CN^-

Addition of a nucleophile: Nucleophilic Addition

Good nucleophile, usually basic



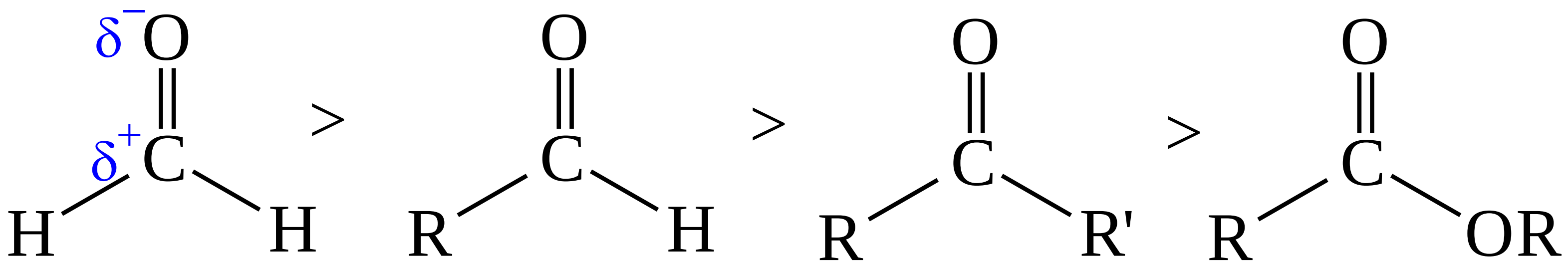
Attack of nucleophile occurs on both sides of carbonyl group.

Produces

Overall: H – Nu was added to carbonyl group double bond.

Notice that the CO bond order was reduced from 2 to 1. The addition reduced the bond order. We will use this idea later.

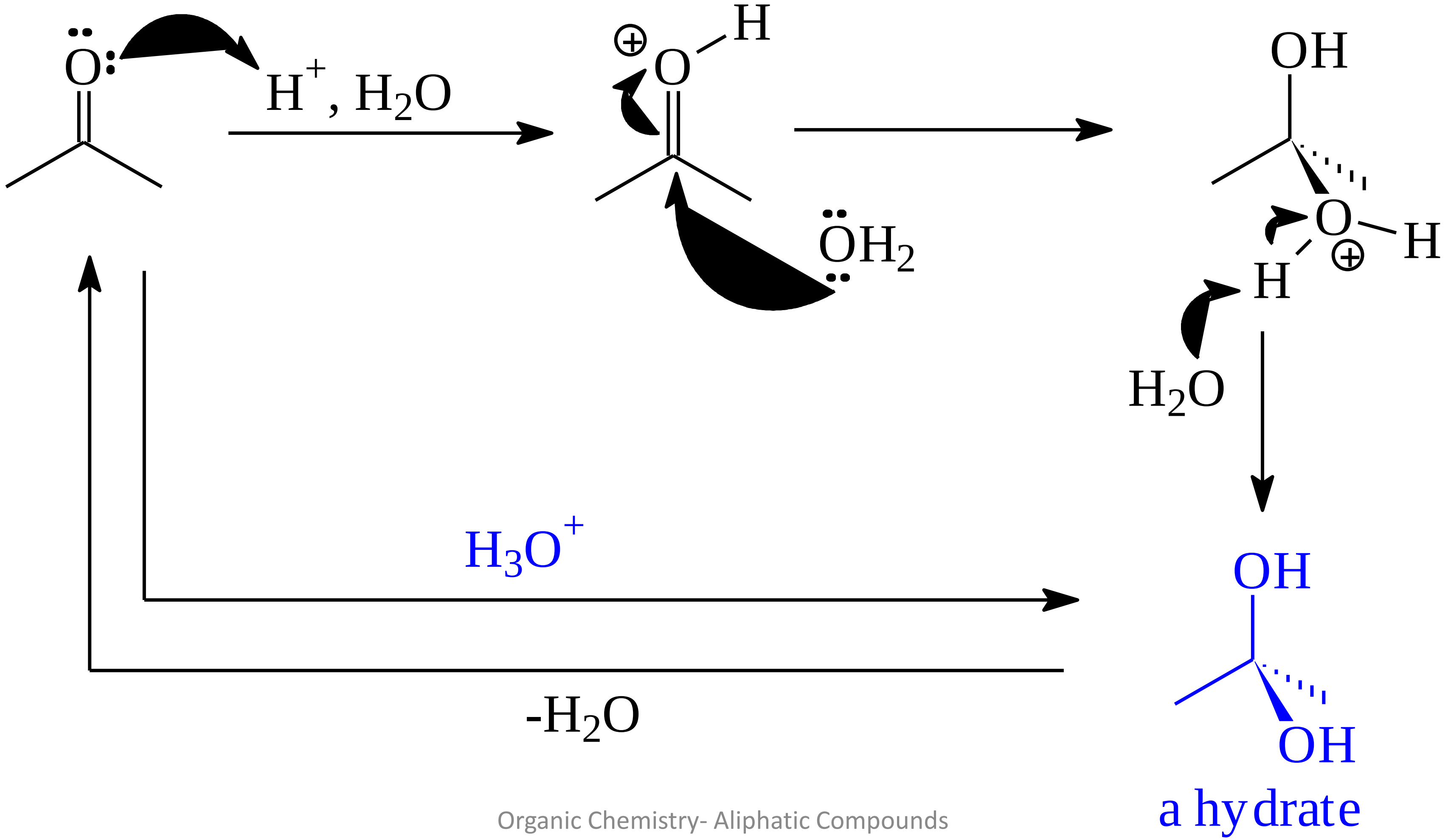
Carbonyl Compounds Reactivity



decreasing rate of reaction with nucleophile →

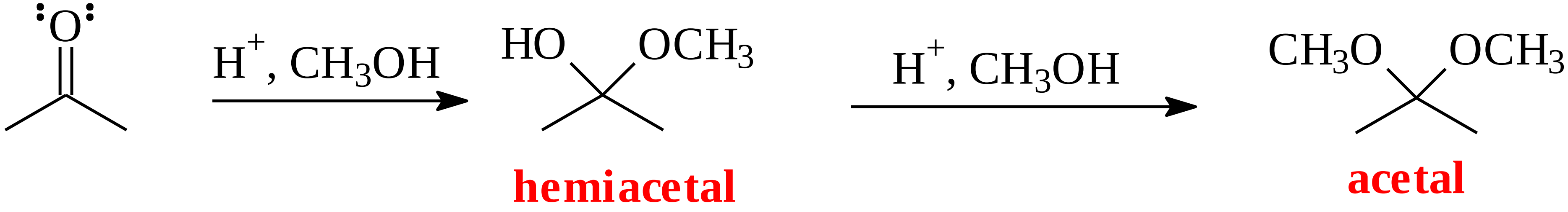
Nucleophilic Addition Reactions:

Weak Nucleophiles

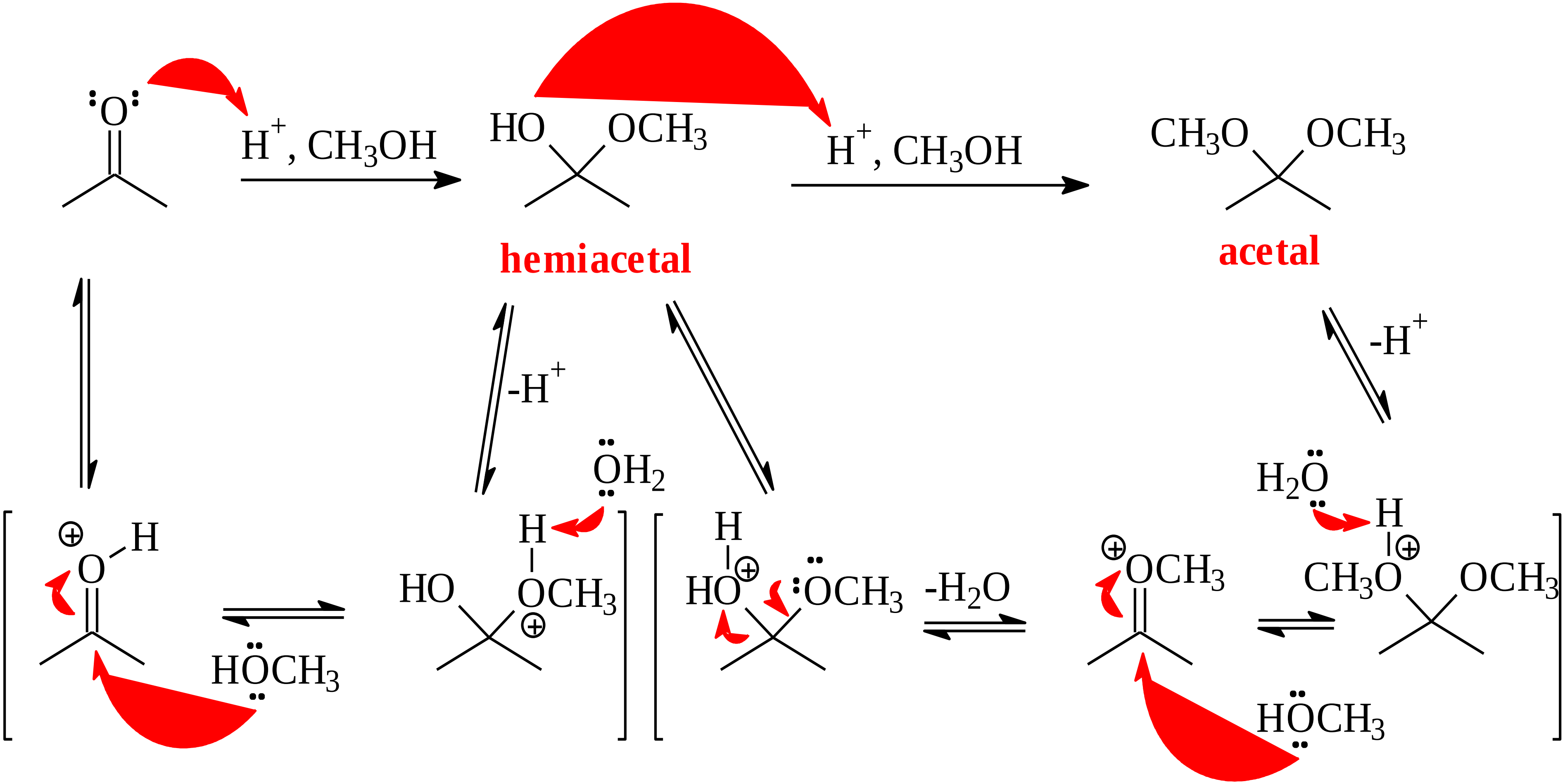


Acetal Formation

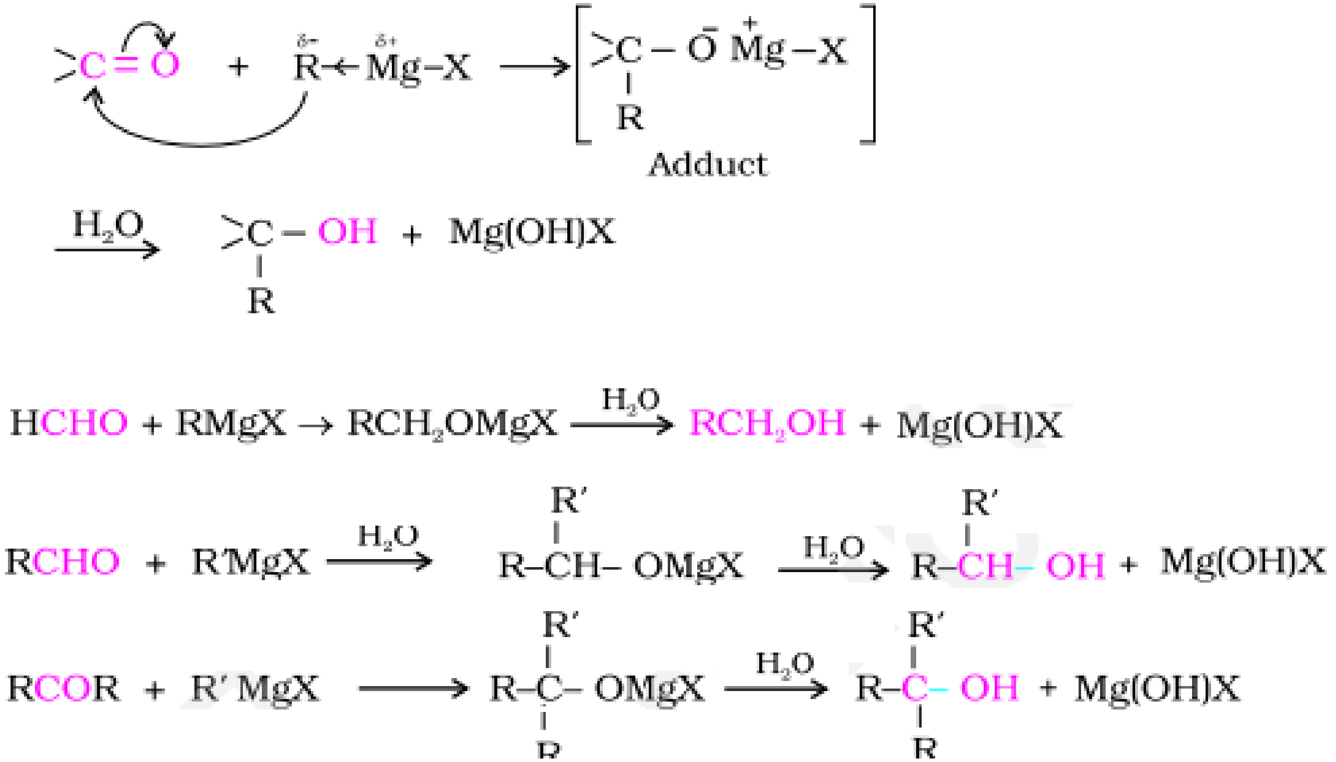
Carbonyl compound reacts with two molecules of alcohol to give acetal



Acetal mechanism



Preparation of alcohols from Grignard Reagent



$$>C=O \;+\; \overset{\delta-}{R}\leftarrow\overset{\delta+}{Mg}-X \longrightarrow \left[\,>\underset{\displaystyle R}{\underset{|}{C}}-\bar{O}\,\overset{+}{Mg}-X\,\right]$$

Adduct

$$\xrightarrow{H_2O} \; >\underset{\displaystyle R}{\underset{|}{C}}-OH \;+\; Mg(OH)X$$

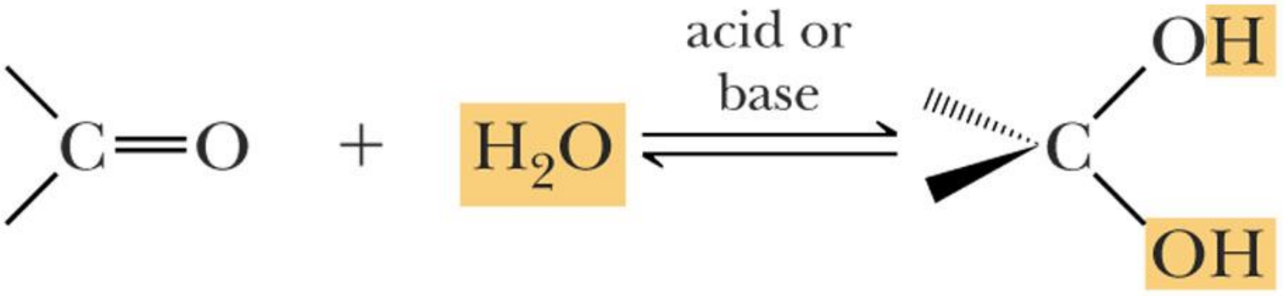
$$HCHO + RMgX \rightarrow RCH_2OMgX \xrightarrow{H_2O} RCH_2OH + Mg(OH)X$$

$$RCHO + R'MgX \xrightarrow{H_2O} R-\overset{\displaystyle R'}{\overset{|}{C}H}-OMgX \xrightarrow{H_2O} R-\overset{\displaystyle R'}{\overset{|}{C}H}-OH + Mg(OH)X$$

$$RCOR + R'MgX \longrightarrow R-\underset{\displaystyle R}{\underset{|}{\overset{\displaystyle R'}{\overset{|}{C}}}}-OMgX \xrightarrow{H_2O} R-\underset{\displaystyle R}{\underset{|}{\overset{\displaystyle R'}{\overset{|}{C}}}}-OH + Mg(OH)X$$

The Grignard reagent : an organometallic compound

Formation of Hydrates, carbonyls and water.



Carbonyl group of an aldehyde or ketone

A hydrate (a gem-diol)

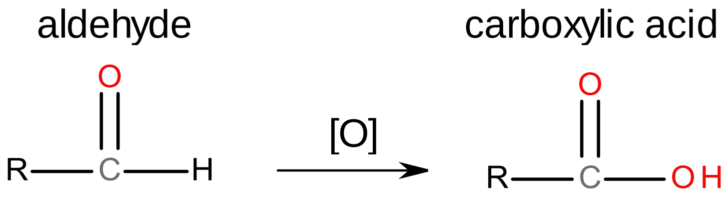
© 2006 Brooks/Cole - Thomson

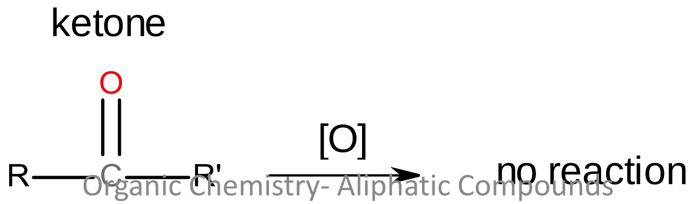
Carbonyl side of equilibrium is usually favored.

Oxidation and reduction of aldehydes and ketones

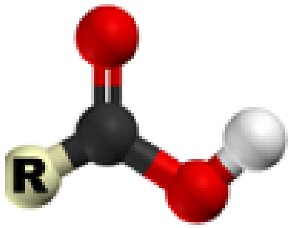
Oxidation reactions

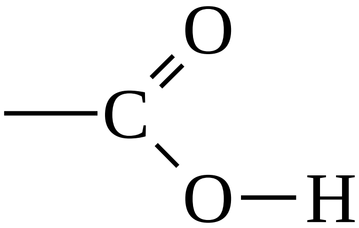
- Aldehydes can be oxidized easily to carboxylic acids
- Ketones are resistant to oxidation.





Carboxylic Acids





- Carboxylic acids are strong organic acids which contain the carboxyl group (-COOH, $-CO_2H$)

- Carboxylic acids are classified as aliphatic or aromatic depending on whether R or an Ar is attached to the carboxylic group
R-COOH or Ar-COOH

Nomenclature of carboxylic acids

Formula	IUPAC alkan -oic acid	Common prefix – ic acid
HCOOH	methanoic acid	formic acid
CH_3COOH	ethanoic acid	acetic acid
CH_3CH_2COOH	propanoic acid	propionic acid
$CH_3CH_2CH_2COOH$	butanoic acid	butyric acid

Naming Rules

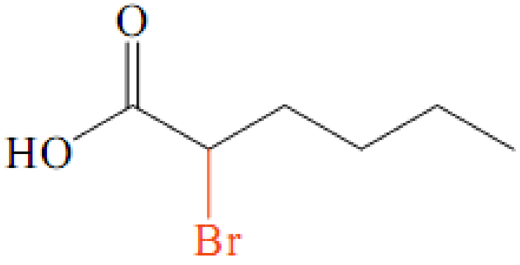
- Identify longest chain
- (IUPAC) Number carboxyl carbon as 1
- (Common) Assign α, β, γ, δ to carbon atoms adjacent to carboxyl carbon

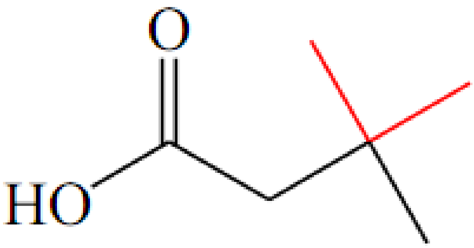
5 4 3 2 1

C—C—C—C—C=O

δ γ β α ← used in common names

Examples:-



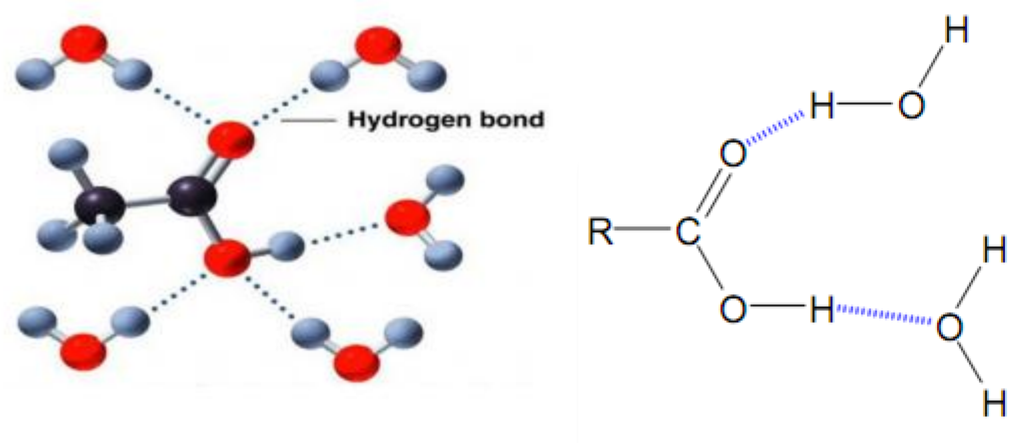


IUPAC:	2- bromohexanoic acid	3,3-dimethylbutanoic acid
Common:	α- bromohexanoic acid	β,β-dimethylbutyric acid

Physical Properties of Carboxylic Acids

1. Solubility

- The carboxylic acid are highly polar organic compounds.
- This polarity results from the presence of a strongly polarized carbonyl (C=O) group and hydroxyl (O-H) group.

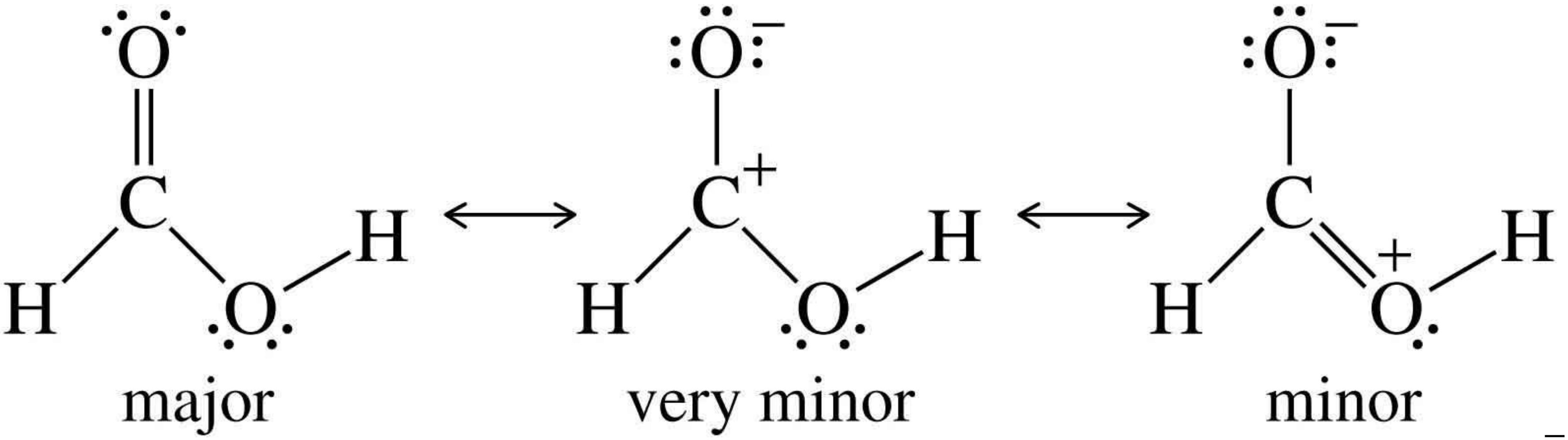


Water Solubility:
Carboxylic acid
Alcohols
Aldehydes/Ketones
Ethers
Alkanes

- As the number of carbons in a carboxylic acid series becomes greater, the solubility in water decreases.
- Aromatic carboxylic acids are insoluble in water.

Structure of Carboxyl

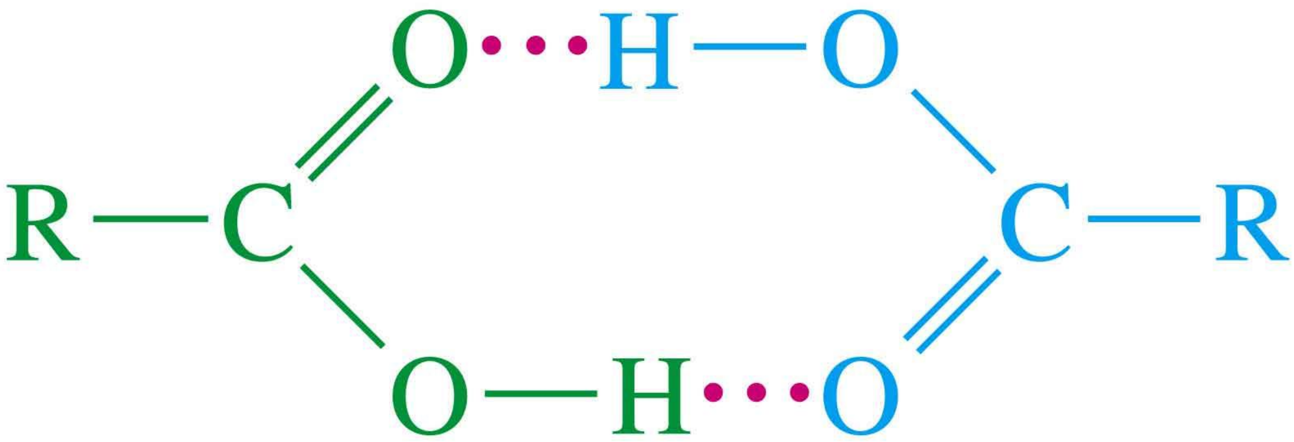
- Carbon is *sp*^{2} hybridized.
- Bond angles are close to 120°.
- O-H eclipsed with C=O, to get overlap of π orbital with orbital of lone pair on oxygen.



=>

Boiling Points

Higher boiling points than similar alcohols, due to dimer formation.



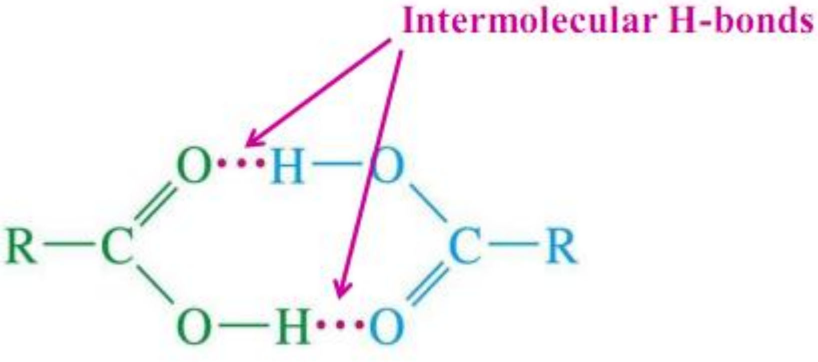
hydrogen-bonded acid dimer

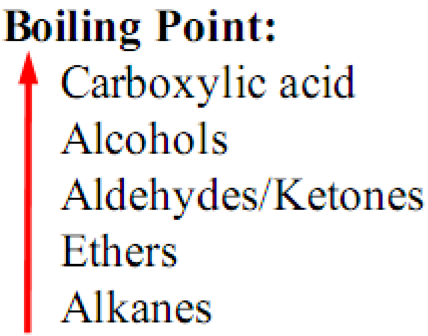
Acetic acid, b.p. 118°C

=>

2. Boiling Point

Carboxylic acids are polar compounds and form very strong intermolecular hydrogen bonds to form a dimer.





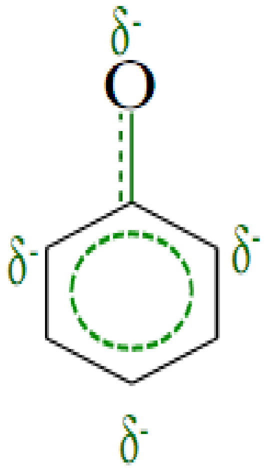
Boiling Point:

- Carboxylic acid
- Alcohols
- Aldehydes/Ketones
- Ethers
- Alkanes

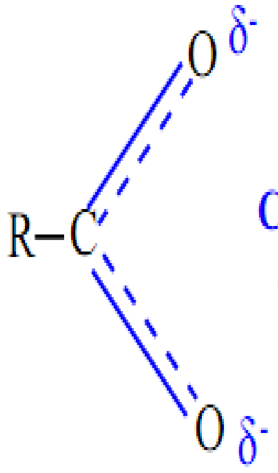
- ➢ As the number of carbons in a carboxylic acid series becomes greater, the boiling point increases.

Acidity and Acid Strength

- The most important chemical property of carboxylic acids chemistry is their acidic nature.
- The mineral acids (HCl, HBr, HI, H_2SO_4, H_3PO_4) are defined as "strong acids" because they undergo complete dissociation.
- Carboxylic acids are strong organic acids , they are much more acidic than alcohols.
- Carboxylic acids are stronger acids than phenols.



Phenoxide ion
(Less stable)



Carboxylate ion
(More stable)

Preparation of Carboxylic acids

1. Oxidation:

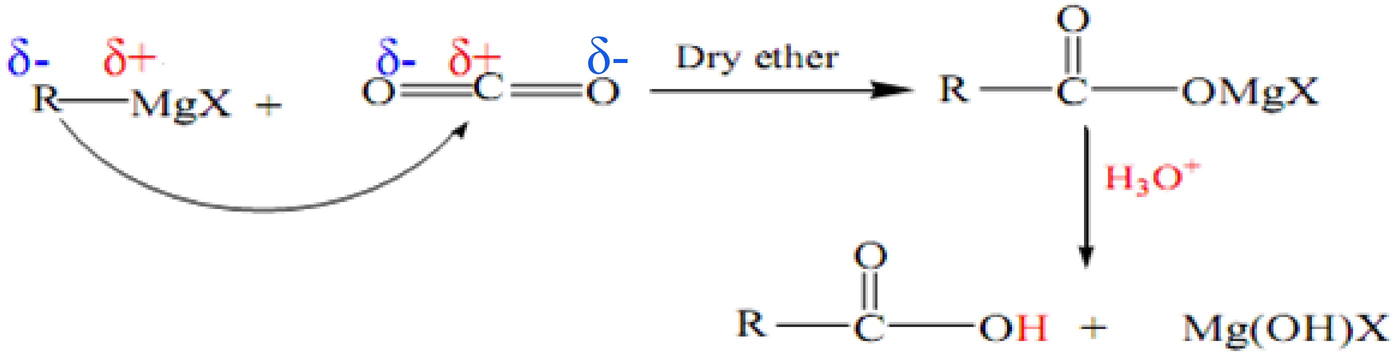
A. Oxidation of primary alcohols and aldehydes

$$\underset{\text{Ethyl alcohol}}{CH_3CH_2OH} \xrightarrow[\text{or}K_2Cr_2O_4/\,H^+]{KMnO_4/\,H^+/\,\Delta} \underset{\text{Acetic acid}}{CH_3\mathbf{COOH}}$$

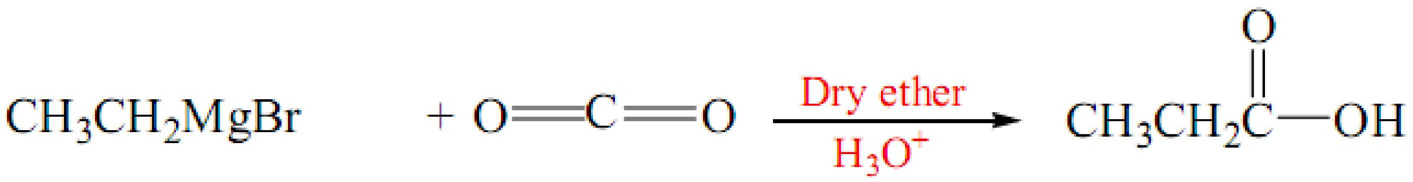
$$\underset{\text{Acetaldehyde}}{CH_3CHO} \xrightarrow{[O]} \underset{\text{Acetic acid}}{CH_3\mathbf{COOH}}$$

2. Carbonation of Grignard Reagents:

The addition of Grignard reagents to CO_2 in form of dry ice gives an acid with one more carbon more than the original Grignard reagent.



Example:



$$CH_3CH_2MgBr + O{=}C{=}O \xrightarrow[H_3O^+]{\text{Dry ether}} CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}{-}OH$$

3. Hydrolysis of Nitriles:

Nitriles:

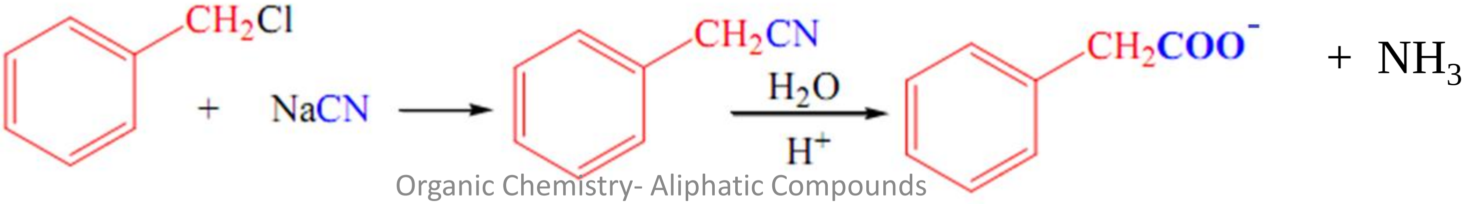
$RC\equiv N$ or $ArC\equiv N$

- They are prepared by reacting a 1° or 2° alkyl halide with cyanide salt.
- Acid hydrolysis of a nitriles yields a carboxylic acids.

$$\underset{\text{Alkyl halide}}{RX} + \underset{\text{Cyanide salt}}{NaC\equiv N} \longrightarrow \underset{\text{Nitriles}}{RC\equiv N} \xrightarrow[H^+]{H_2O} \underset{\text{Carboxylic acids}}{RCOO^-} + NH_3$$

Examples:

$$CH_3CH_2Cl + NaCN \longrightarrow CH_3CH_2CN \xrightarrow[H^+]{H_2O} CH_3CH_2COO^- + NH_3$$



Reactions of Carboxylic acids

1. Reaction with Bases : Salt formation

The carboxyl hydrogen is replaced by metal ion, M^+

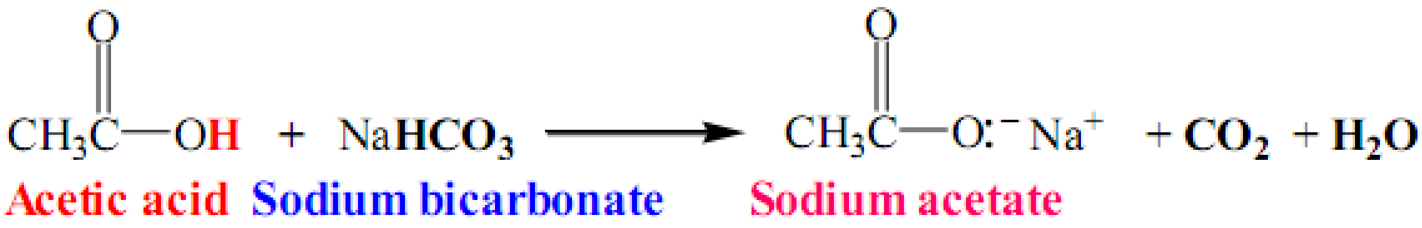
A) With strong base:

$$HCOOH + KOH \longrightarrow HCOO\!:^{-} K^{+} + H_2O$$

Formic acid

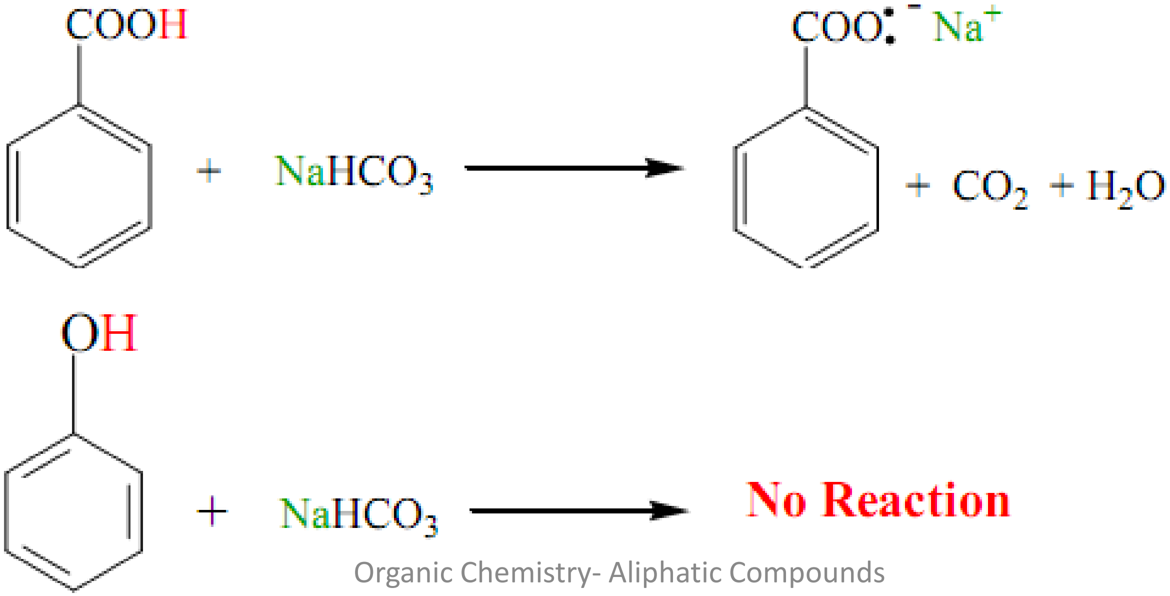
Potassium formate

B) With weak base



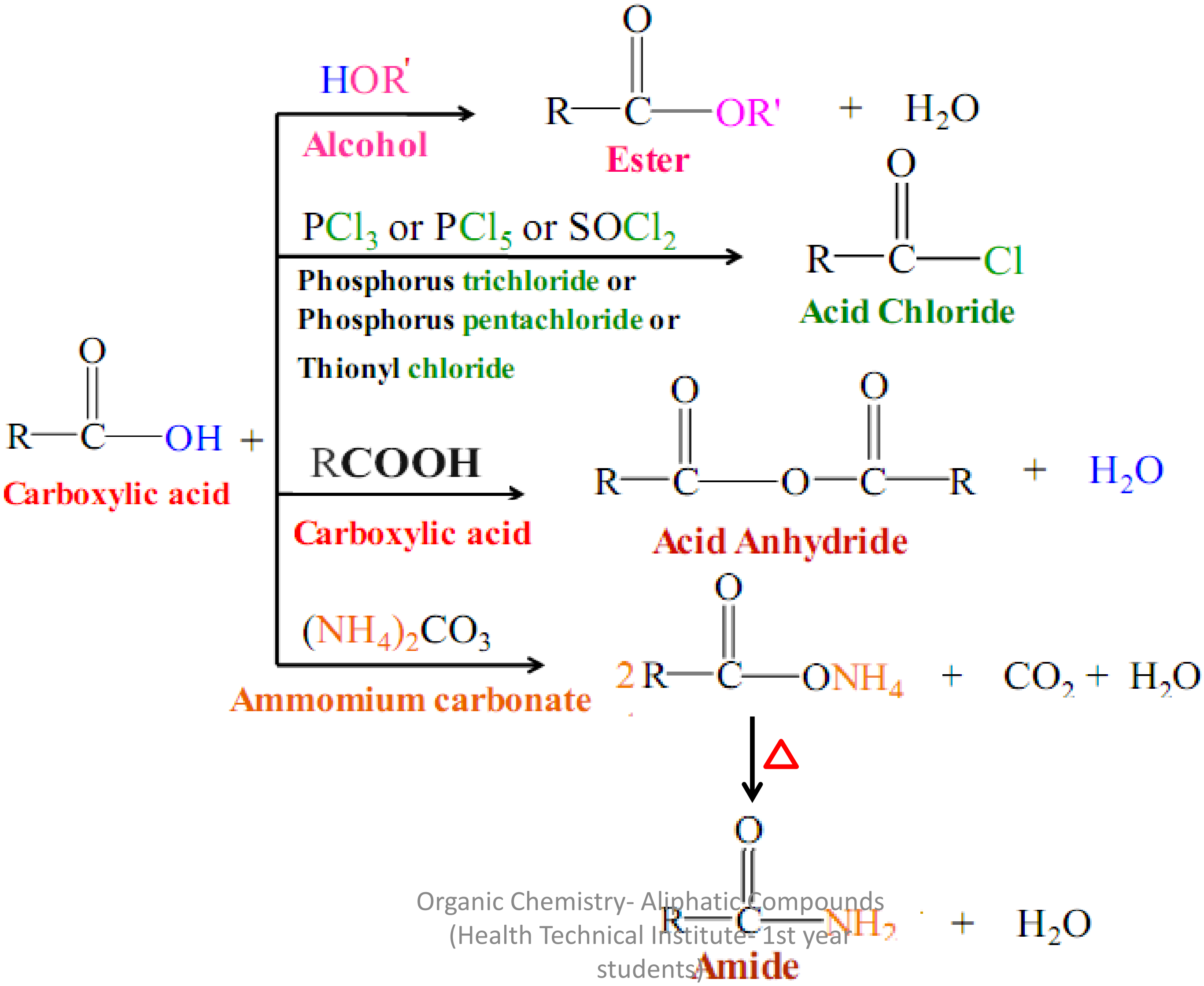
$$CH_3C(=O)-OH + NaHCO_3 \longrightarrow CH_3C(=O)-O:^{-}Na^{+} + CO_2 + H_2O$$

- Weaker acids like phenols react only with strong bases like (NaOH or KOH) and will not react with $NaHCO_3$



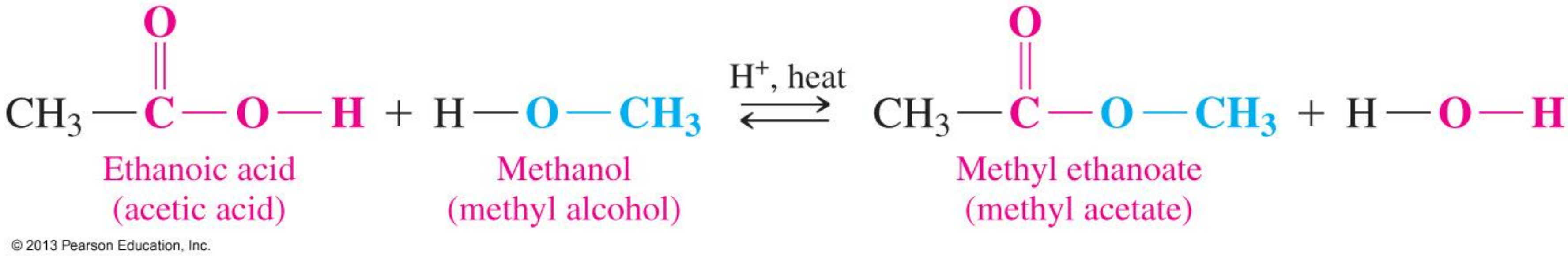
2. Reaction with Nucleophiles to form acid derivatives:

- When the OH of a carboxylic acid is replaced by a nucleophile, :Nu , a carboxylic acid derivative is produced.



ESTERIFICATION

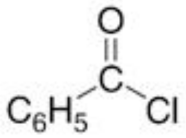
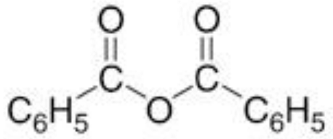
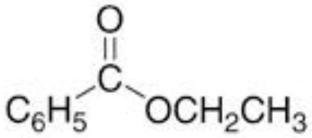
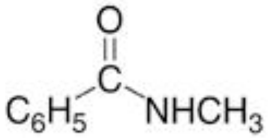
Esterification is the reaction of a carboxylic acid and alcohol in the presence of an acid catalyst to produce an ester.



$$CH_3-\overset{\overset{O}{\|}}{C}-O-H + H-O-CH_3 \xrightleftharpoons{H^+,\ heat} CH_3-\overset{\overset{O}{\|}}{C}-O-CH_3 + H-O-H$$

© 2013 Pearson Education, Inc.

Derivatives of Carboxylic acids

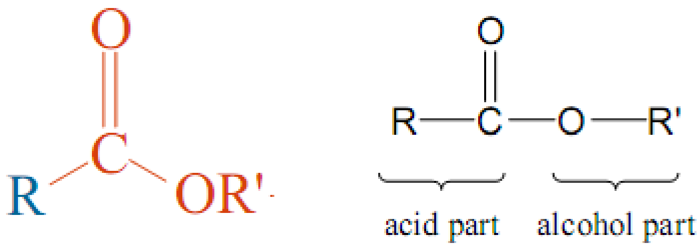
Compound	Name ending	Example	Name
acid chloride	**-yl chloride** or **-carbonyl chloride**		benzoyl chloride
anhydride	**anhydride**		benzoic anhydride
ester	**-ate**		ethyl benzoate
amide	**-amide**		*N*-methylbenzamide

Nomenclature

Nomenclature: the functional derivatives' names are derived from the common or IUPAC names of the corresponding carboxylic acids.

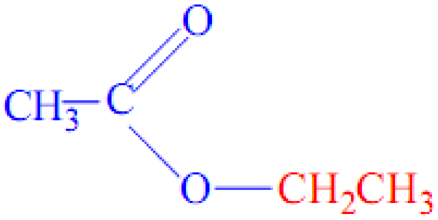
1. Esters:

alkyl alkanoate

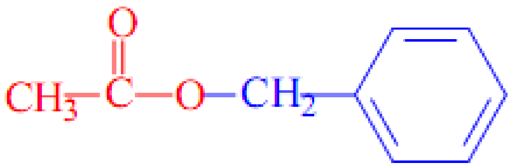


Change –ic acid to –ate preceded by the alkyl is derived from the alcohol, R'OH.

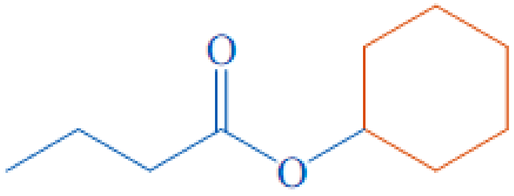
Examples:



Ethylethanoate

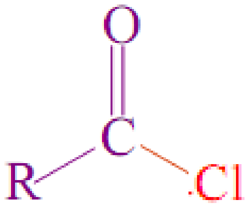


Benzyl ethanoate



Cyclohexyl butanoate

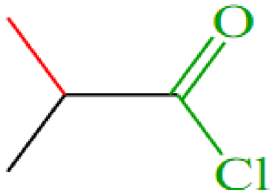
2. Acid Chlorides:



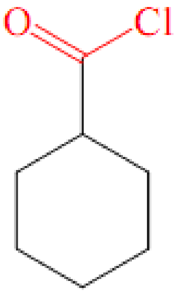
Change –ic acid to –yl chloride

Alkanoyl chloride

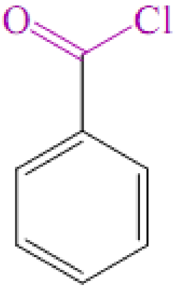
Examples:



2-methylpropanoyl chloride

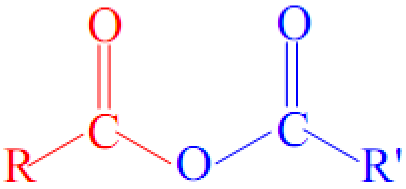


cyclohexanoyl chloride



Benzoyl chloride

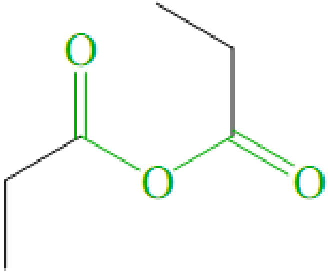
3. Acid Anhydride:



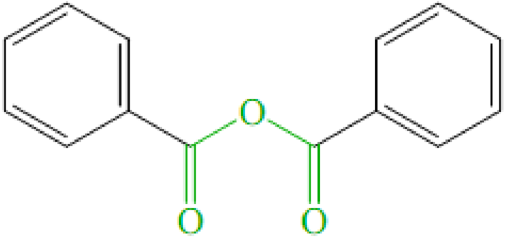
Change acid to anhydride

alkanoic anhydrides

Examples:

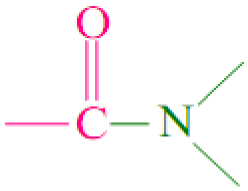


Propanoic anhydride



Benzoic anhydride

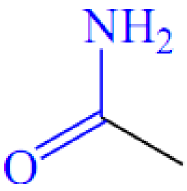
4. Amides:



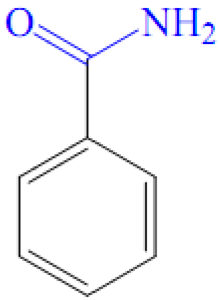
Change -oic acid to –amide

alkanamide

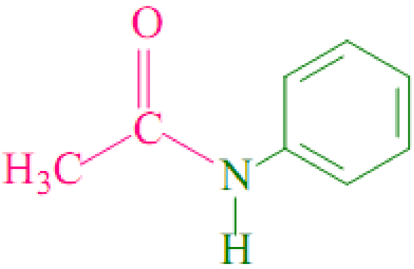
Examples:



Acetamide
Ethanamide

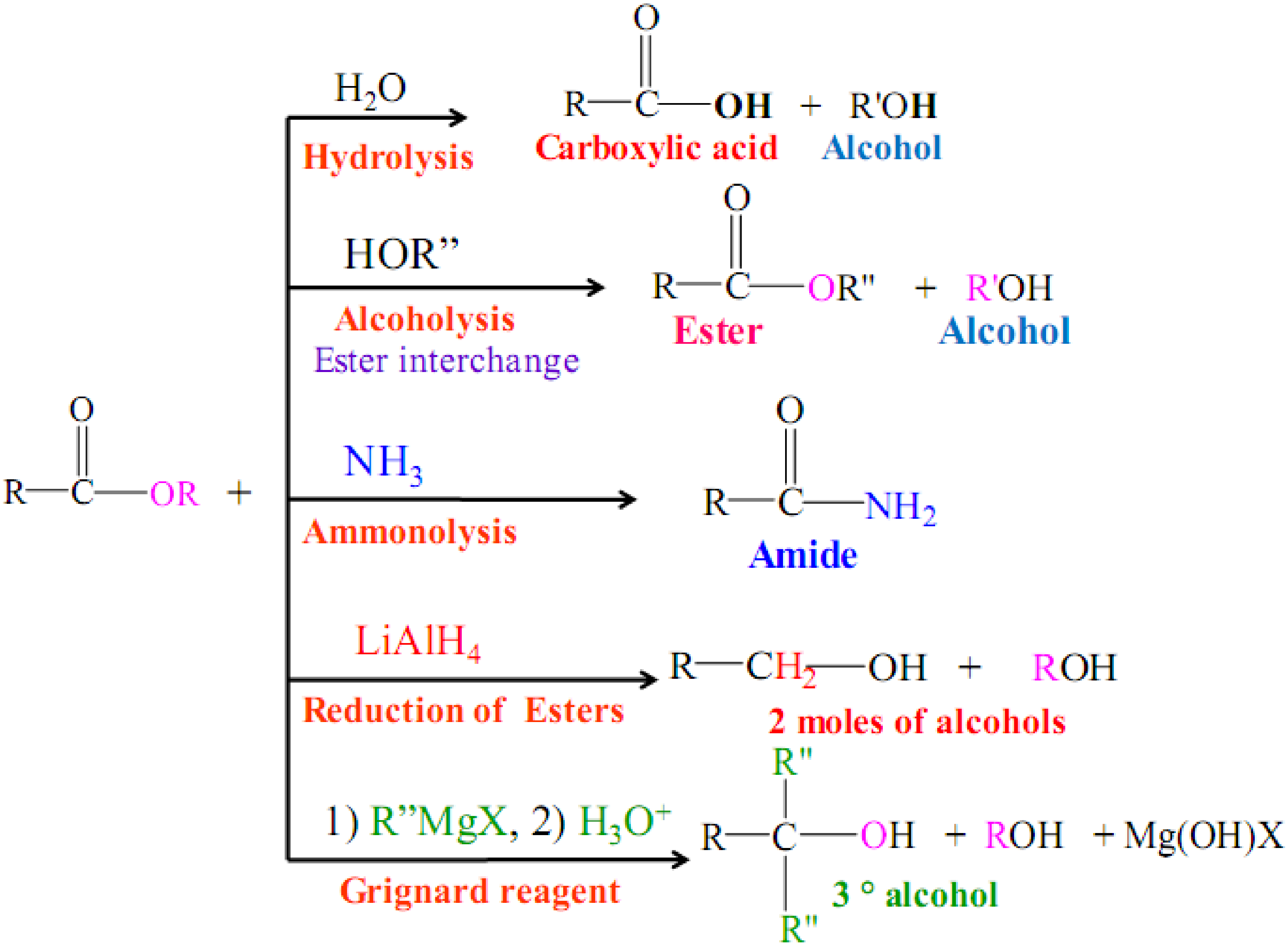


Benzamide

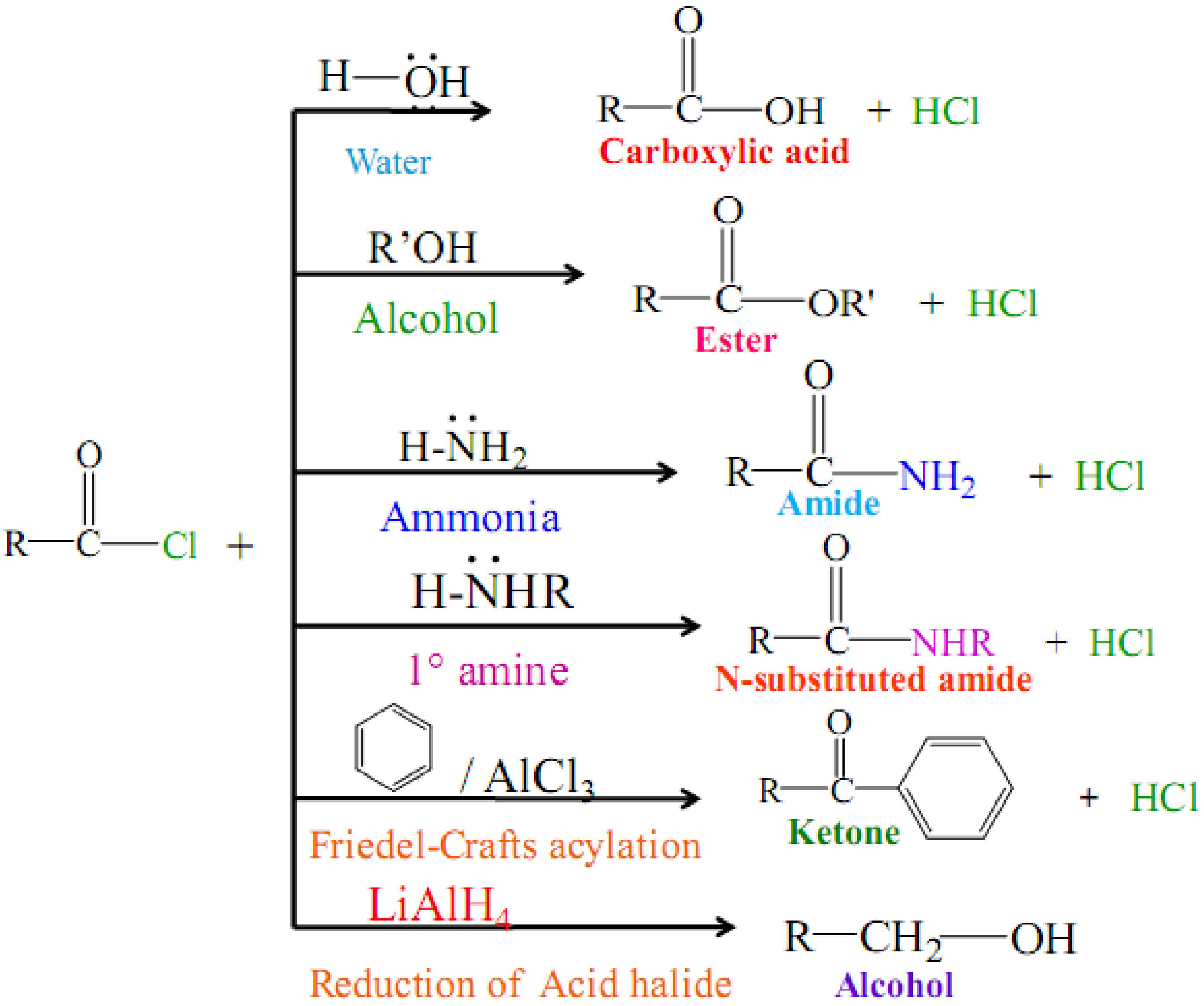


Acetanilide
N-phenylethanamide

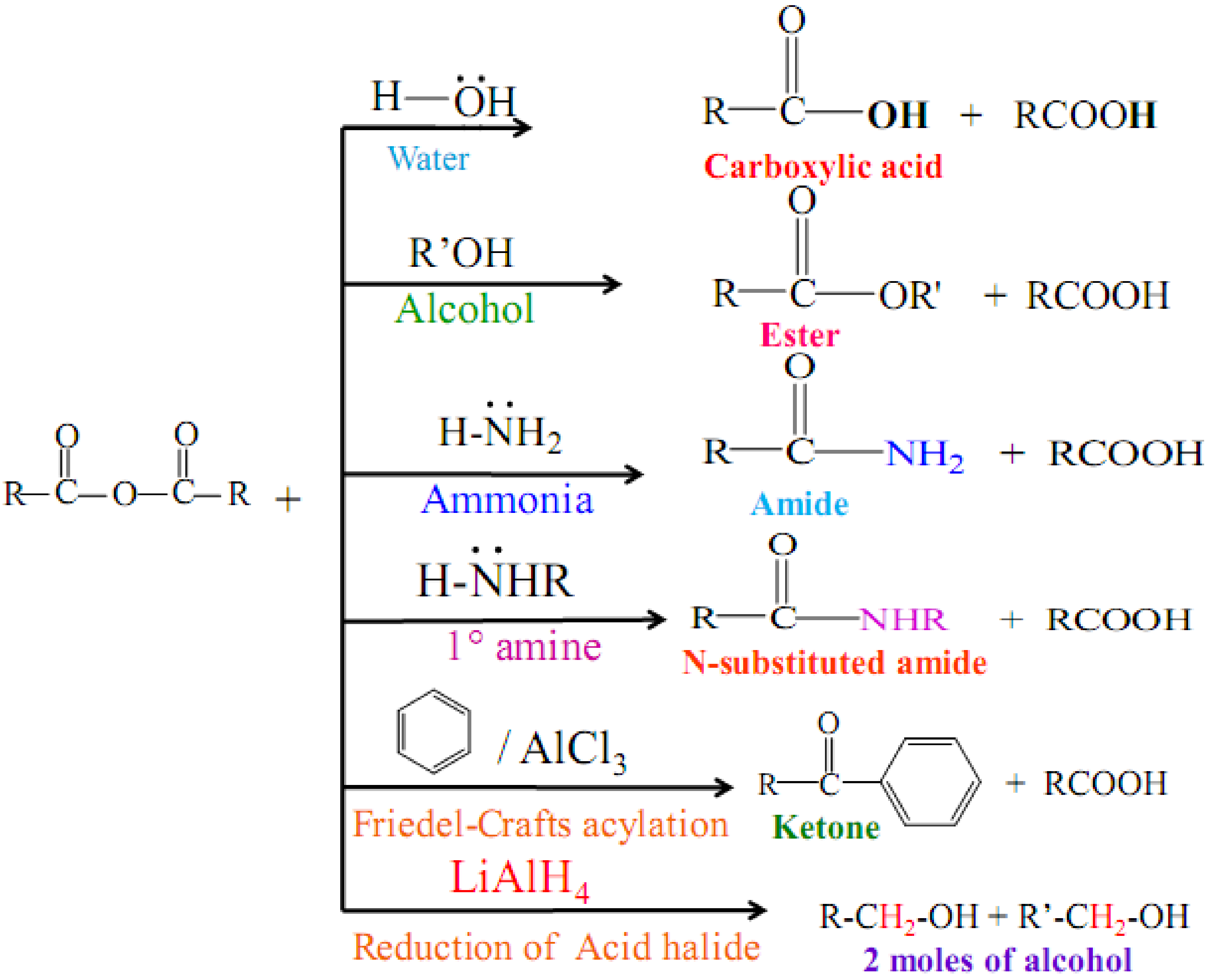
Esters Reactions:



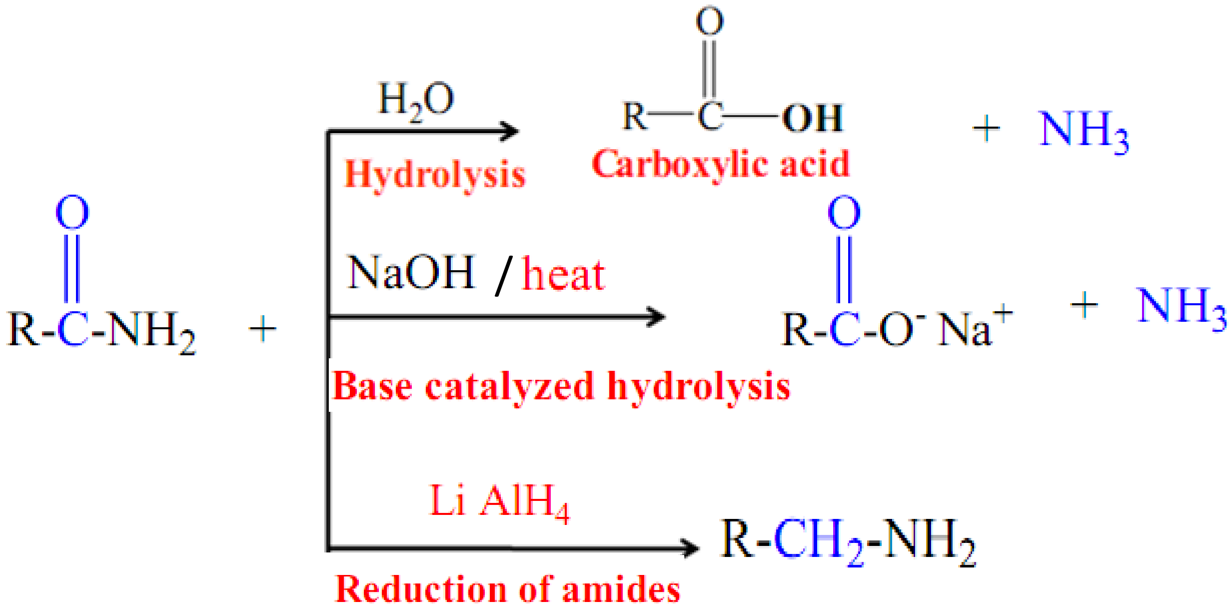
Acid Chlorides Reactions:



Acid Anhydride Reactions:



Amides Reactions:



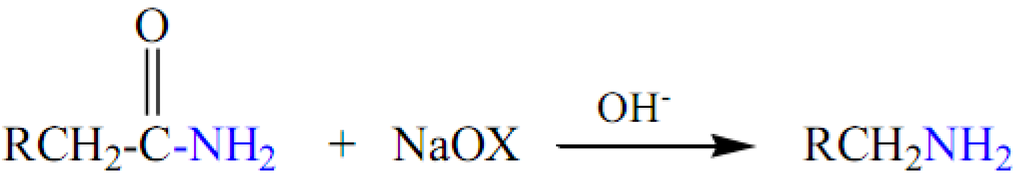
$$R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2 + \xrightarrow[\text{Hydrolysis}]{H_2O} R-\overset{\overset{\displaystyle O}{\|}}{C}-OH + NH_3$$

$$R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2 + \xrightarrow[\text{Base catalyzed hydrolysis}]{NaOH\ /\ \text{heat}} R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}O^- Na^+ + NH_3$$

$$R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2 + \xrightarrow[\text{Reduction of amides}]{Li\ AlH_4} R\text{-}CH_2\text{-}NH_2$$

4- Reaction of amides with alkaline hypohalite solution:

Reduced to amines containing one less carbon atom



$$RCH_2\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2 + NaOX \xrightarrow{OH^-} RCH_2NH_2$$

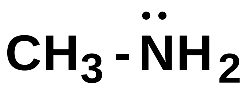
An amine with one less carbon

Amines

The organic bases

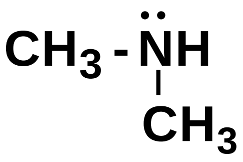
Structure & Classification

- Amines are classified as:
  - 1°, 2°, or , 3° amines: Amines in which there are 1, 2, or 3 alkyl or aryl groups.



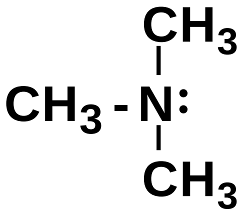
$CH_3-\ddot{N}H_2$

Methylamine
(a 1° amine)



$CH_3-\ddot{N}H(CH_3)$

Dimethylamine
(a 2° amine)



$CH_3-\ddot{N}(CH_3)_2$

Trimethylamine
(a 3° amine)

Categorizing Amines

- Amines are categorized by the number of alkyl groups attached to nitrogen:

1º (primary amine)	RNH_2
2º (secondary amine)	R_2NH
3º (tertiary amine)	R_3N
4º (quaternary amine salt)	R_4N^+

Naming simple amines

- Simple 1º amines are named as “alkylamine”
  - Examples:
    - methylamine CH_3NH_2
    - ethylamine $CH_3CH_2NH_2$
    - butylamine $CH_3CH_2CH_2CH_2NH_2$

- Symmetrical 2º or 3º amines are named as “dialkylamine” or “trialkyamine”
  - Examples:
    - diethylamine $(CH_3CH_2)_2NH$; trimethylamine $(CH_3)_3N$

Naming more complex amines

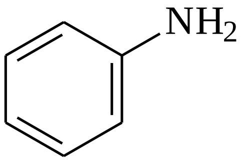
- Amines with more than one type of alkyl group may be named as N-substituted primary amines. The longer alkyl chain determines the base name.
  - Examples
    - N-methylpropylamine $CH_3NHCH_2CH_2CH_3$
    - N,N-dimethylethylamine $(CH_3)_2NCH_2CH_3$

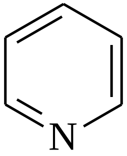
Naming more complex amines

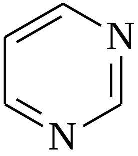
- Amines that have more than one functional group may be named using “amino” as a substituent on the parent molecule.
  - Examples:
    - 2-aminoethanol $H_2NCH_2CH_2OH$
    - 4-aminobutanoic acid $H_2NCH_2CH_2CH_2CO_2H$

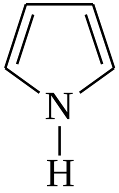
Heterocyclic amines

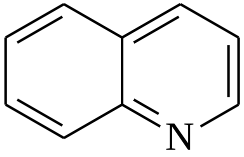
- Some amines have a nitrogen as part of a ring. These generally have common (non-systematic) names, which should be memorized:

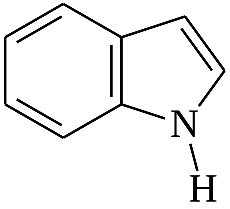

aniline

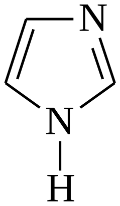

pyridine

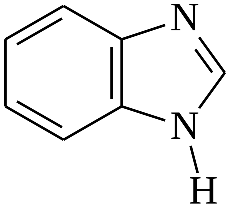

pyrimidine


pyrrole


quinoline

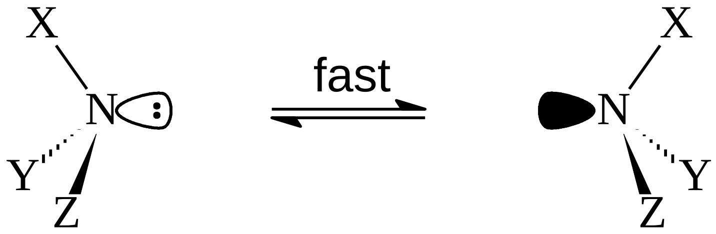

indole


imidazole


benzimidazole

Structure of amines

- Amines have an sp^3 hybridized nitrogen
- In principle, tertiary amines with three different R groups should be **chiral** (i.e., have a stereocenter).
- However, rapid **pyramidal inversion** of the amine nitrogen prevents isolation of the enantiomers except where the nitrogen is part of a ring or has other geometrical constraint.



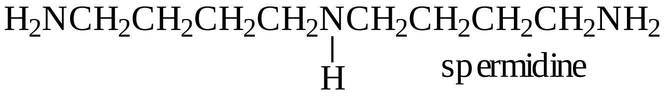
Properties of amines

- Amines are moderately polar and are capable of hydrogen bonding.
- Low MW amines (up to about C_5) are soluble in water; higher MW amines will dissolve in acidic solution (as their conjugate acid).
- Amines are weak bases.

Example of biologically active amines

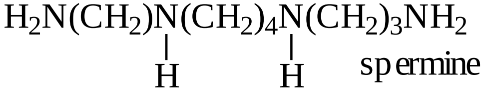
$H_2NCH_2CH_2CH_2CH_2NH_2$ putrescine

$H_2NCH_2CH_2CH_2CH_2CH_2NH_2$ cadaverine



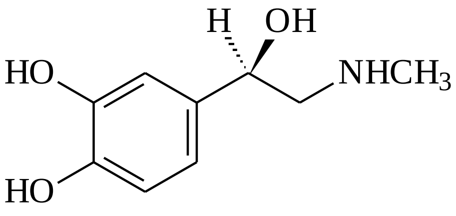
$H_2NCH_2CH_2CH_2CH_2\underset{\displaystyle H}{\underset{|}{N}}CH_2CH_2CH_2CH_2NH_2$

spermidine

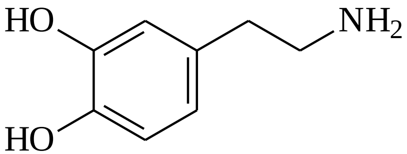


$H_2N(CH_2)\underset{\displaystyle H}{\underset{|}{N}}(CH_2)_4\underset{\displaystyle H}{\underset{|}{N}}(CH_2)_3NH_2$

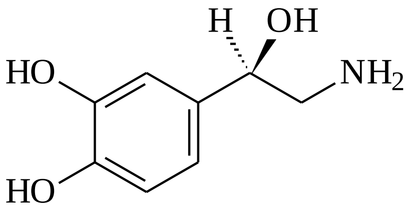
spermine



epinephrine
(adrenaline)



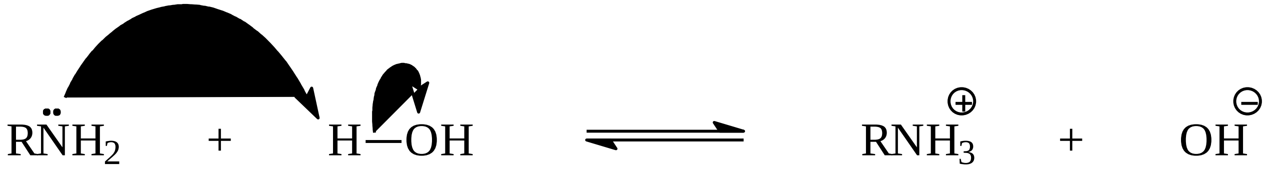
dopamine



norepinephrine
(noradrenaline)

Basicity of amines

- Amines are slightly basic. This because they have a lone pair of electrons to donate to a proton. This same feature makes them nucleophiles.



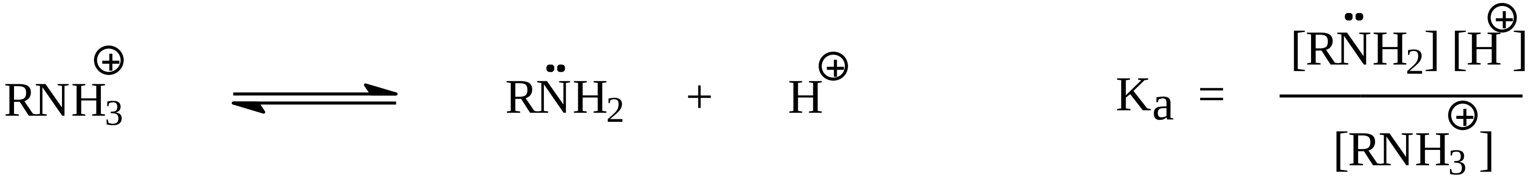
$$R\ddot{N}H_2 + H{-}OH \rightleftharpoons RNH_3^{\oplus} + OH^{\ominus}$$

$$K_b = \frac{[RNH_3^{\oplus}]\,[OH^{\ominus}]}{[RNH_2]}$$

- Typical amines have K_b values = 10^{-3} to 10^{-4}

Basicity of amines…

- However, instead of measuring an amine’s basicity using the above equilibrium, chemists usually refer to the acidity of the conjugate acid of the amine. The weaker the conjugate acid, the stronger the base strength of the amine.

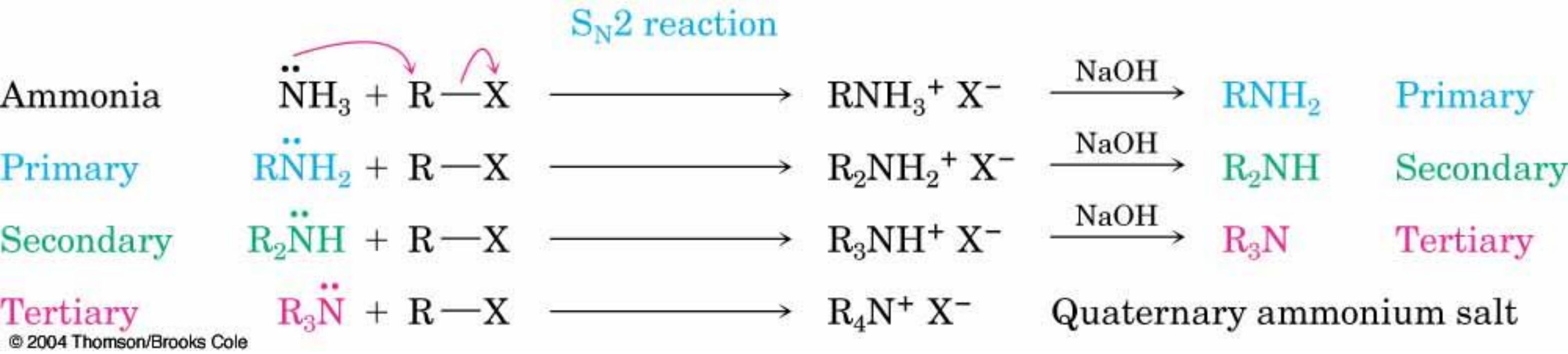


$$RNH_3^{\oplus} \rightleftharpoons R\ddot{N}H_2 + H^{\oplus} \qquad K_a = \frac{[R\ddot{N}H_2][H^{\oplus}]}{[RNH_3^{\oplus}]}$$

- Typical amines have K_a values (of their conjugate acids) of 10^{-10} to 10^{-11} (pK_a values of 10 to 11.)

SN2 Reactions of Alkyl Halides

- Ammonia and other amines are good nucleophiles



© 2004 Thomson/Brooks Cole

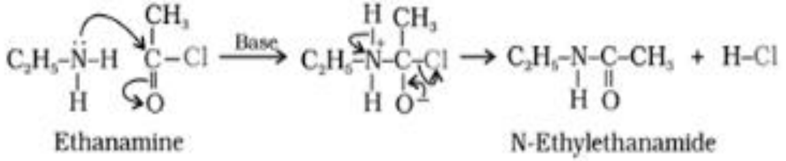
1) Alkylation

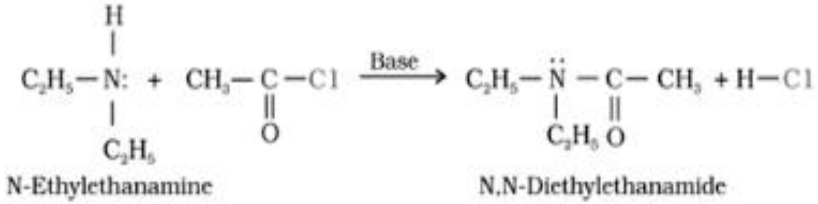
Alkylation of 1^0 amine generates 2^0 amine, 3^0 amine and finally the quaternary salts.

$$RNH_2 \xrightarrow{RX} R_2NH \xrightarrow{RX} R_3N \xrightarrow{RX} R_4N^+X^-$$

2) Acylation

Acylation is the reaction with acid chlorides, anhydrides and esters. These occur by nucleophilic substitution reactions. The reaction is proceeded by the replacement of hydrogen atom of –NH_2 or >N–H group by the acyl group (RCOX).

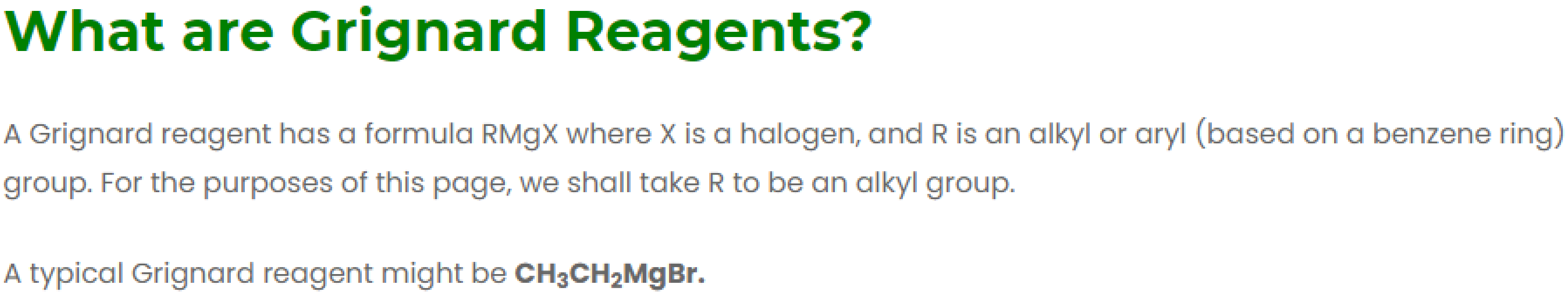




We cannot acylate Tertiary (3^o) amine. This is because there is no Hydrogen bonded to nitrogen.

Grignard's reagent

Grignard Reagent



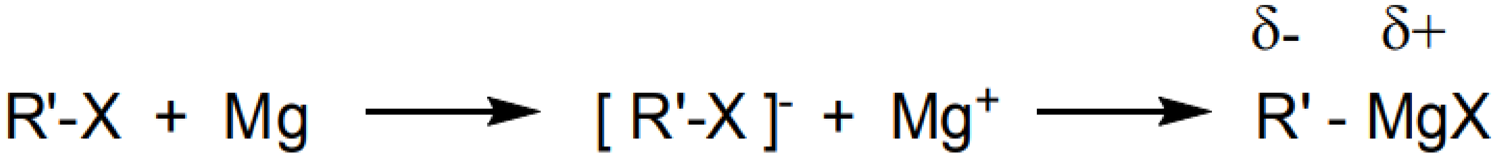
What are Grignard Reagents?

A Grignard reagent has a formula RMgX where X is a halogen, and R is an alkyl or aryl (based on a benzene ring) group. For the purposes of this page, we shall take R to be an alkyl group.

A typical Grignard reagent might be **CH_3CH_2MgBr.**

Background

- **<u>Grignard reagents</u>** are highly reactive organometallic reagents generated by treating alkyl or aryl halides with magnesium metal in the presence of an anhydrous ether.
- The reaction proceeds like a strong base reaction.



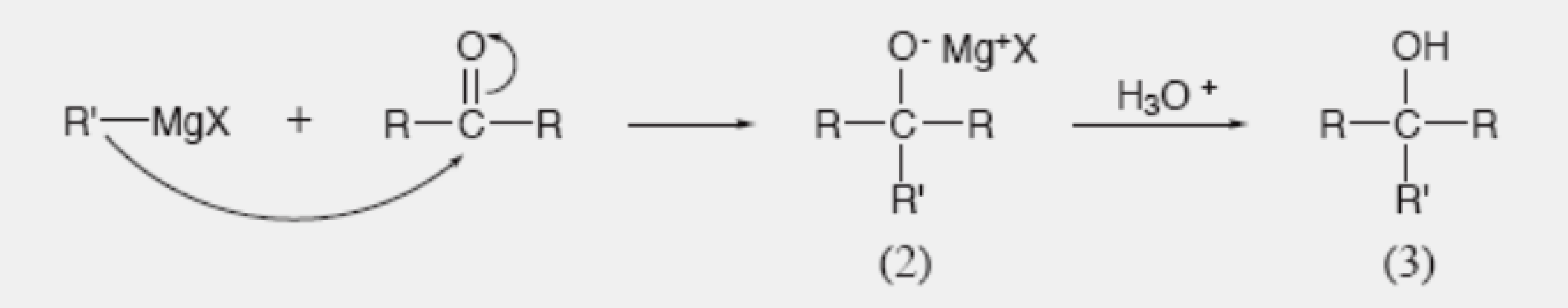
$$R'\text{-}X + Mg \longrightarrow [R'\text{-}X]^{-} + Mg^{+} \longrightarrow \overset{\delta-}{R'} - \overset{\delta+}{MgX}$$

- This reagent was discovered by ***Victor Grignard*** around 1900.

Background

- A Grignard reagent is capable of reacting with many different substrates such as carbonyl compounds, alkyl halides and other organometallic reagents.

- The addition of **Grignard reagents to carbonyl compounds** such as aldehydes, ketones, and esters yields the corresponding **secondary and tertiary alcohols**.

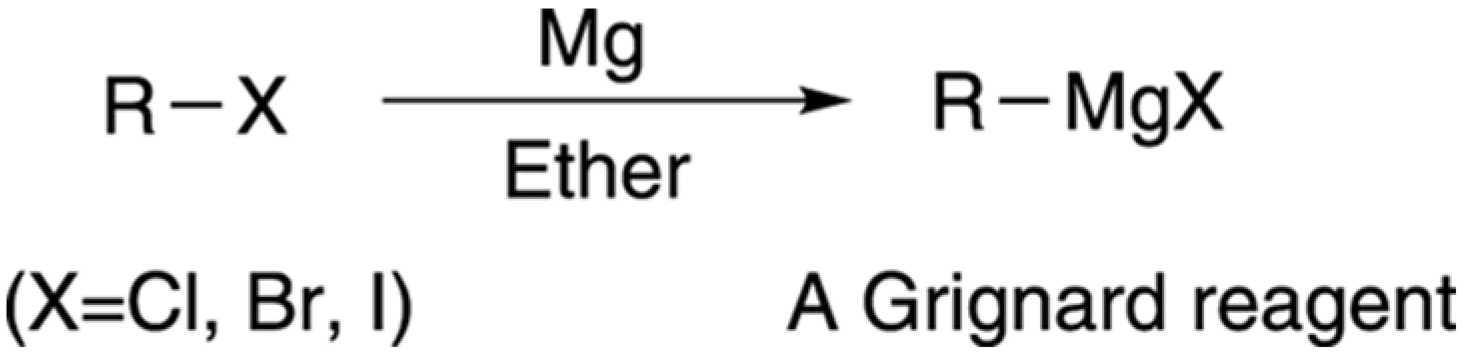


- The ***Grignard reaction*** results in the formation of a ***carbon-carbon bond***.

- **Grignard reagents** are extremely strong bases that can react violently with hydroxylic compounds such as water or alcohols:

$$\mathrm{R{-}MgBr} + \mathrm{H{-}OH} \longrightarrow \mathrm{R{-}H} + \mathrm{HOMgBr}$$

The Preparation of a Grignard Reagent:



$$R-X \xrightarrow[Ether]{Mg} R-MgX$$

The Preparation of a Grignard Reagent:

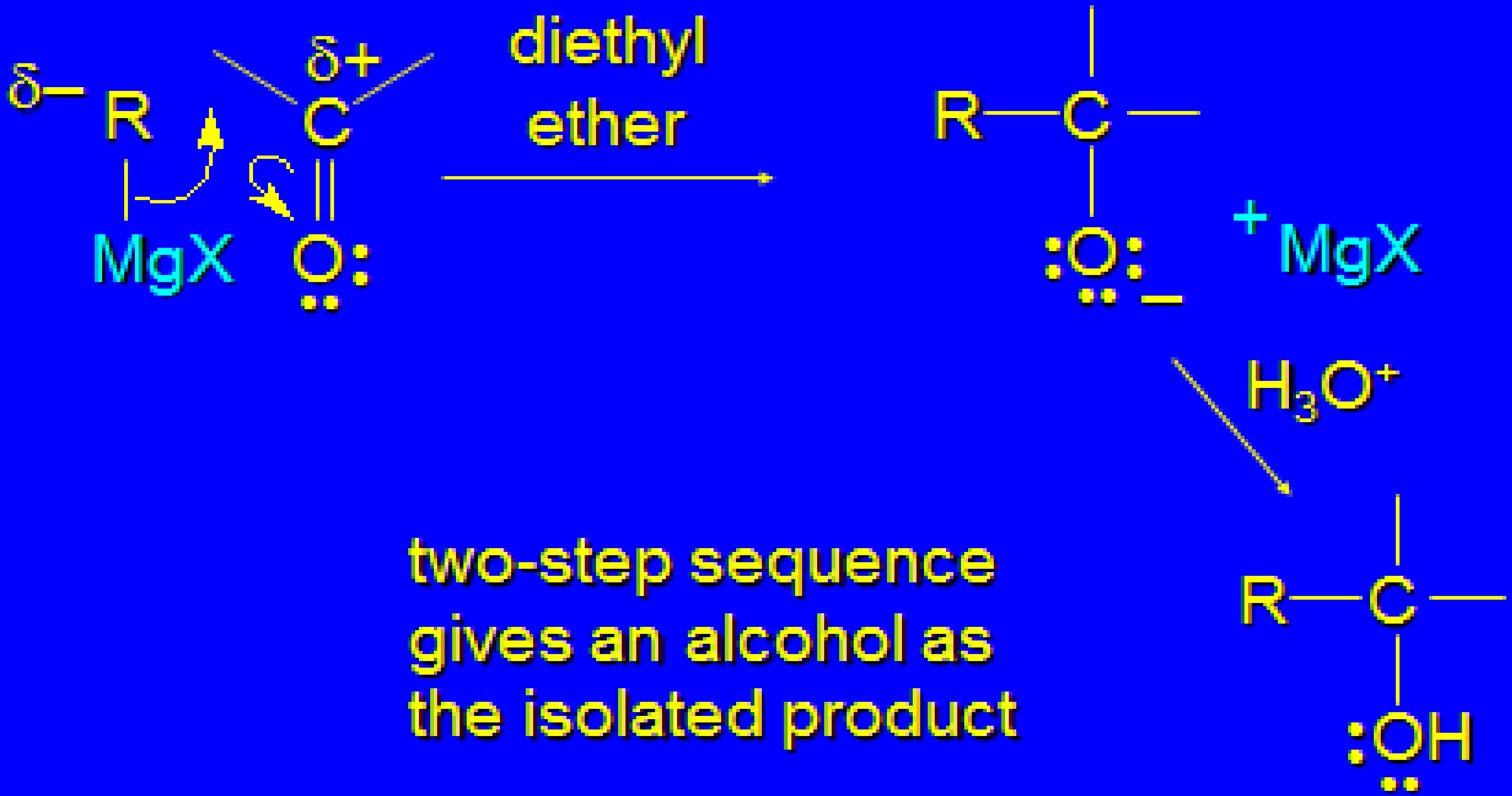
Grignard reagents are made by adding the halogenoalkane to small bits of magnesium in a flask containing ethoxyethane (commonly called diethyl ether or just "ether"). The flask is fitted with a reflux condenser, and the mixture is warmed over a water bath for 20 – 30 minutes.

$$CH_3CH_2Br + Mg \xrightarrow{ethoxyethane} CH_3CH_2MgBr$$

Everything must be perfectly dry because Grignard reagents react with water (see below).

Any reactions using the Grignard reagent are carried out with the mixture produced from this reaction. You can't separate it out in any way.

Grignard reagents act as nucleophiles toward the carbonyl group



two-step sequence gives an alcohol as the isolated product

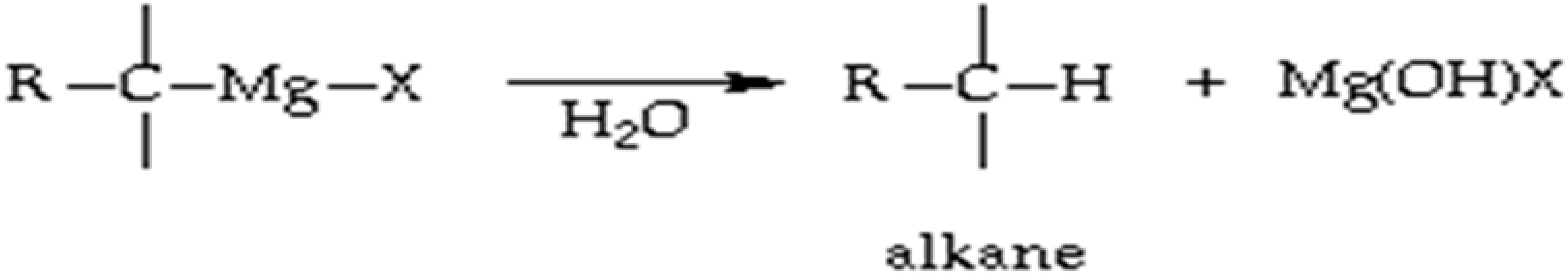
Grignard Reagents and Water:

Grignard reagents react with water to produce alkanes. This is the reason that everything has to be very dry during the preparation above.

For example:

$$CH_3CH_2MgBr + H_2O \longrightarrow CH_3CH_3 + Mg(OH)Br$$

The inorganic product, Mg(OH)Br, is referred to as a “basic bromide”. You can think of it as a sort of half-way stage between magnesium bromide and magnesium hydroxide.



$$R-\overset{|}{\underset{|}{C}}-Mg-X \xrightarrow[H_2O]{} R-\overset{|}{\underset{|}{C}}-H + Mg(OH)X$$

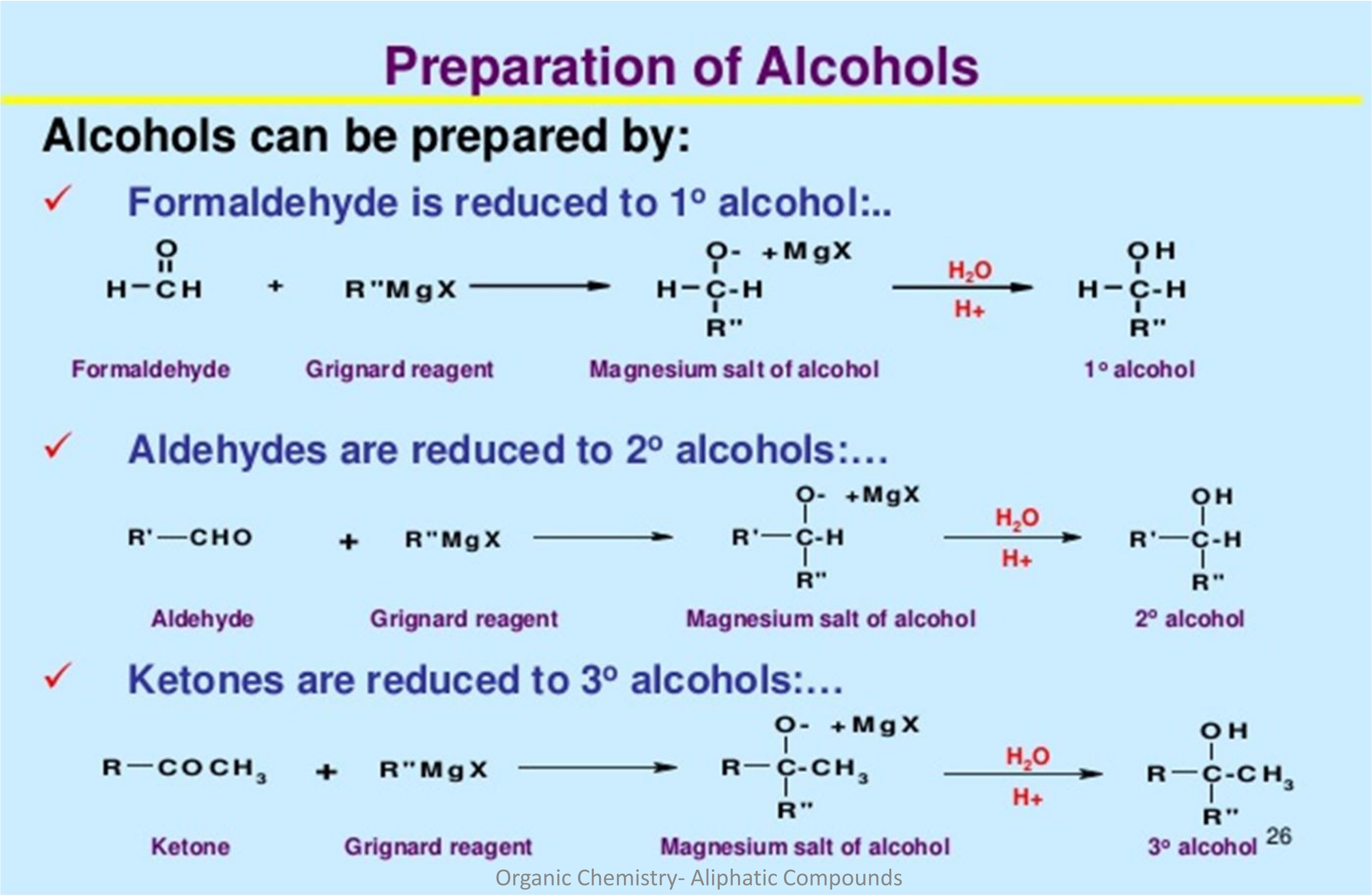
Grignard reagents react with:

formaldehyde to give primary alcohols

aldehydes to give secondary alcohols

ketones to give tertiary alcohols

esters to give tertiary alcohols



Preparation of Alcohols

Alcohols can be prepared by:

- ✓ Formaldehyde is reduced to 1° alcohol:..

$$H-\overset{\overset{O}{\|}}{C}H + R''MgX \longrightarrow H-\underset{\underset{R''}{|}}{\overset{\overset{O^-\ \ {}^+MgX}{|}}{C}}-H \xrightarrow[H+]{H_2O} H-\underset{\underset{R''}{|}}{\overset{\overset{OH}{|}}{C}}-H$$

Formaldehyde, Grignard reagent, Magnesium salt of alcohol, 1° alcohol

- ✓ Aldehydes are reduced to 2° alcohols:…

$$R'-CHO + R''MgX \longrightarrow R'-\underset{\underset{R''}{|}}{\overset{\overset{O^-\ \ {}^+MgX}{|}}{C}}-H \xrightarrow[H+]{H_2O} R'-\underset{\underset{R''}{|}}{\overset{\overset{OH}{|}}{C}}-H$$

Aldehyde, Grignard reagent, Magnesium salt of alcohol, 2° alcohol

- ✓ Ketones are reduced to 3° alcohols:…

$$R-COCH_3 + R''MgX \longrightarrow R-\underset{\underset{R''}{|}}{\overset{\overset{O^-\ \ {}^+MgX}{|}}{C}}-CH_3 \xrightarrow[H+]{H_2O} R-\underset{\underset{R''}{|}}{\overset{\overset{OH}{|}}{C}}-CH_3$$

Ketone, Grignard reagent, Magnesium salt of alcohol, 3° alcohol

Mechanism

$$>C=O + \overset{\delta-}{R} \leftarrow \overset{\delta+}{Mg}-X \longrightarrow \left[>\underset{R}{\underset{|}{C}} - \bar{O}\,\overset{+}{Mg}-X \right]_{\text{Adduct}} \xrightarrow{H_2O} >\underset{R}{\underset{|}{C}} - OH + Mg(OH)X$$

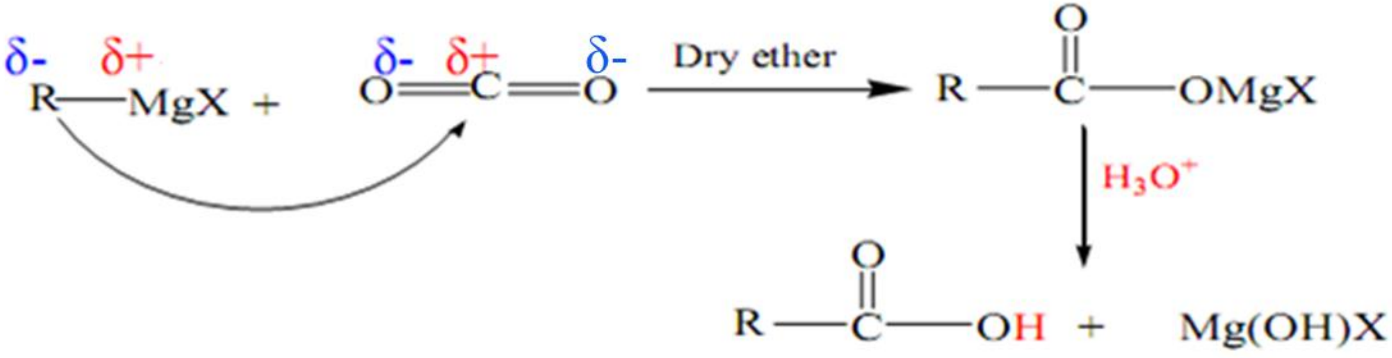
$$HCHO + RMgX \rightarrow RCH_2OMgX \xrightarrow{H_2O} RCH_2OH + Mg(OH)X$$

$$RCHO + R'MgX \xrightarrow{H_2O} R-\overset{R'}{\overset{|}{C}}H-OMgX \xrightarrow{H_2O} R-\overset{R'}{\overset{|}{C}}H-OH + Mg(OH)X$$

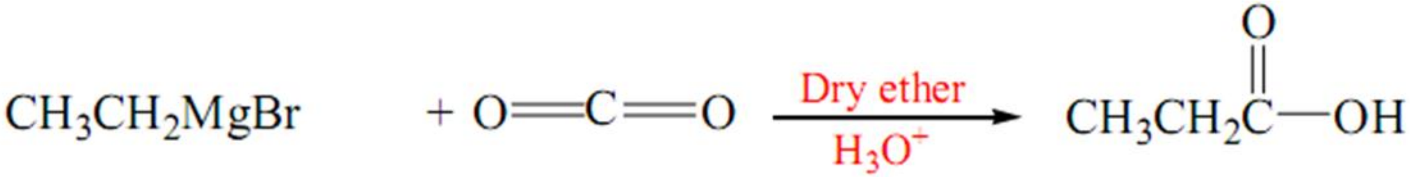
$$RCOR + R'MgX \longrightarrow R-\underset{R}{\underset{|}{\overset{R'}{\overset{|}{C}}}}-OMgX \xrightarrow{H_2O} R-\underset{R}{\underset{|}{\overset{R'}{\overset{|}{C}}}}-OH + Mg(OH)X$$

The Grignard reagent : an organometallic compound

Grignard Reagents and Carbon Dioxide:



Example



$$CH_3CH_2MgBr + O{=}C{=}O \xrightarrow[H_3O^+]{\text{Dry ether}} CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}{-}OH$$

Chemical Reactions

Chemical Reaction

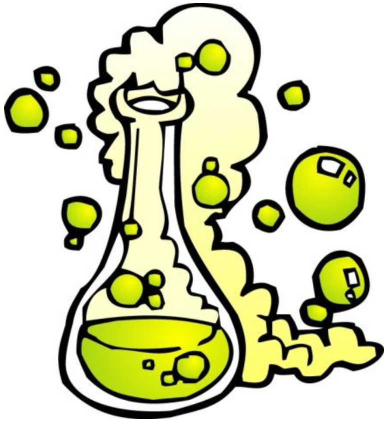
parts are mixed together to make something new.

General: $A + B \rightarrow AB$

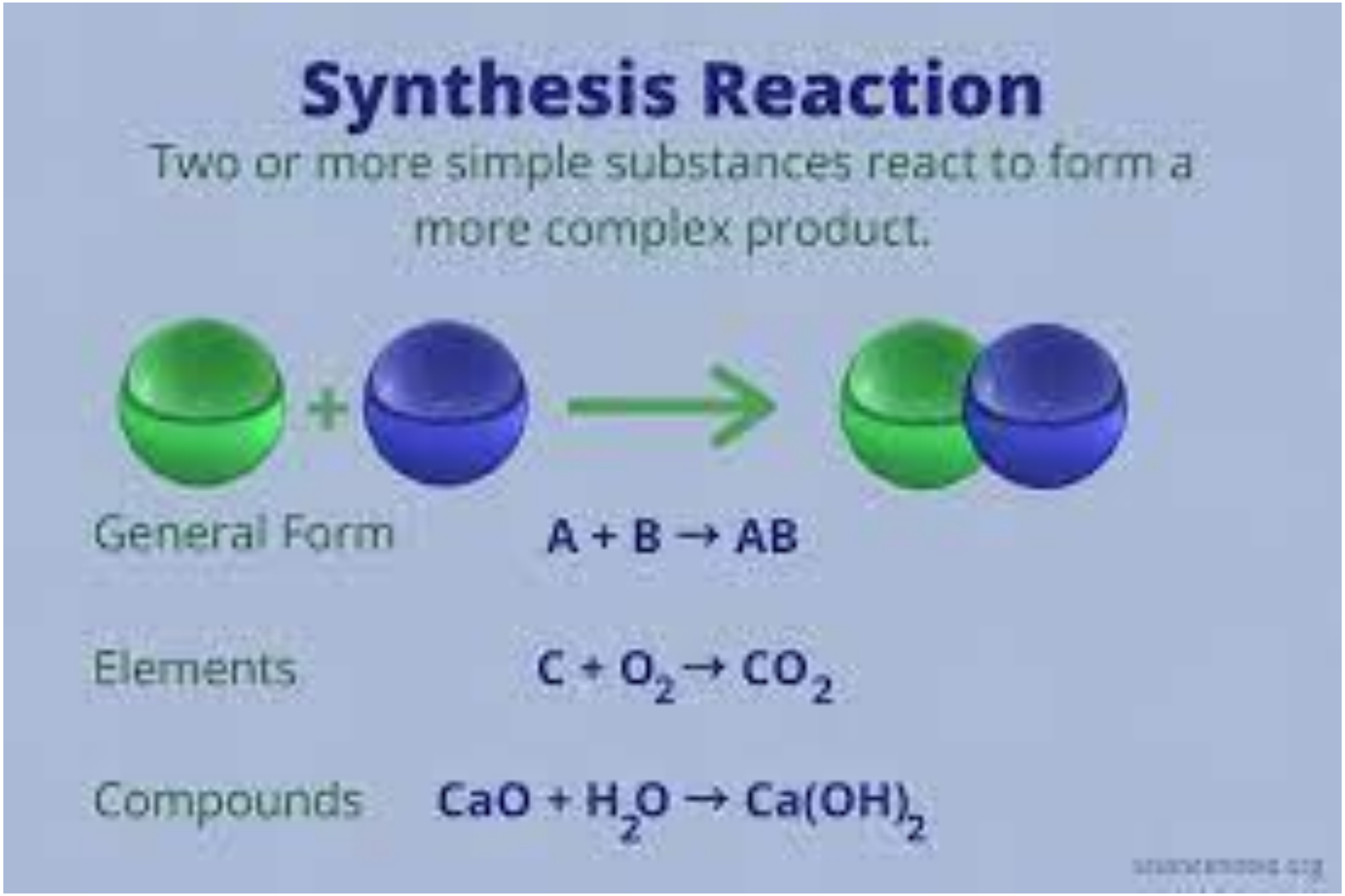
Types of Reactions

1. Synthesis reactions
2. Decomposition reactions
3. Substitution reactions
4. Addition reactions
5. Elimination reactions

You need to be able to identify each type.



1. Synthesis



Synthesis Reaction

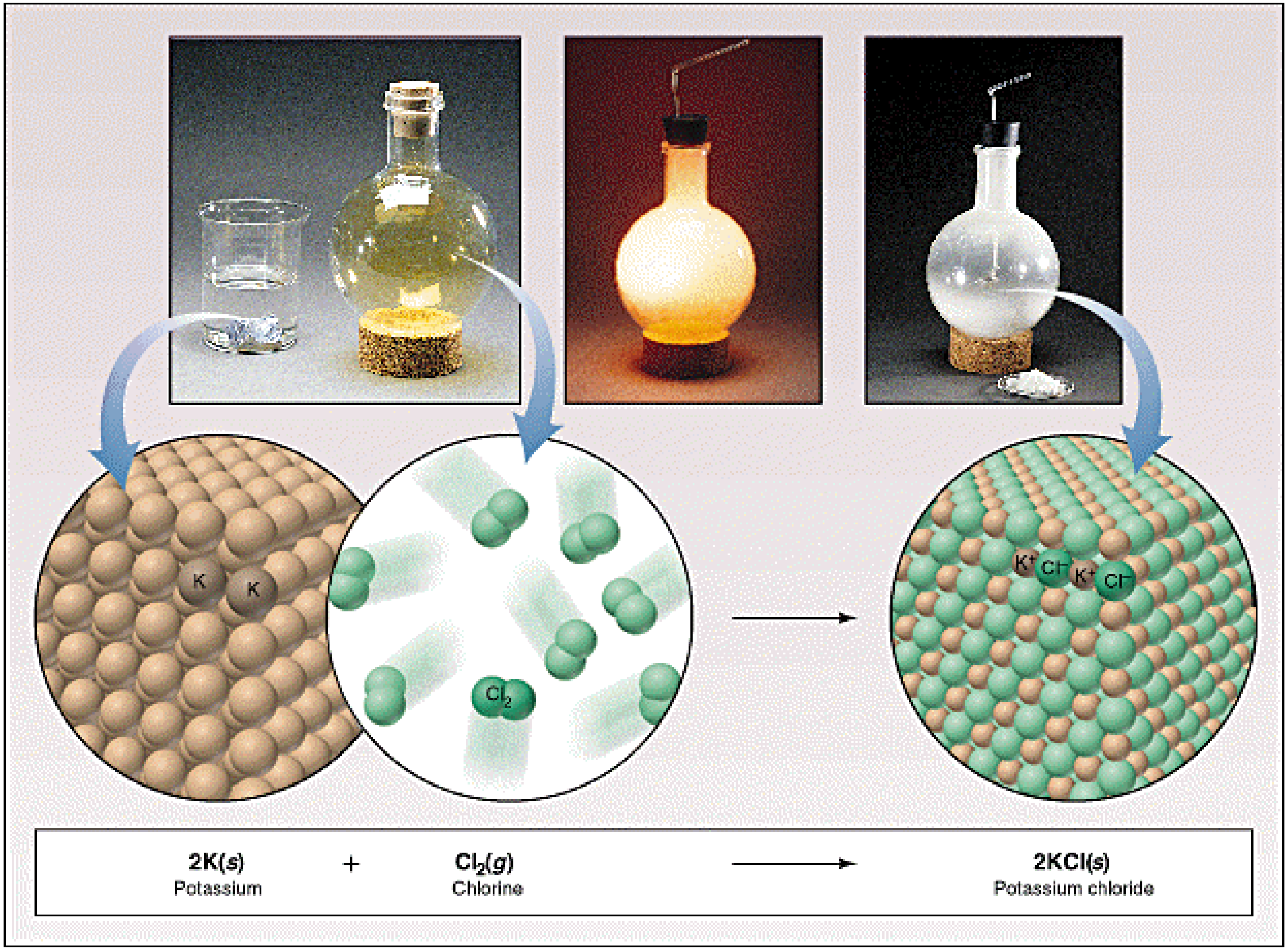
Two or more simple substances react to form a more complex product.

General Form $A + B \rightarrow AB$

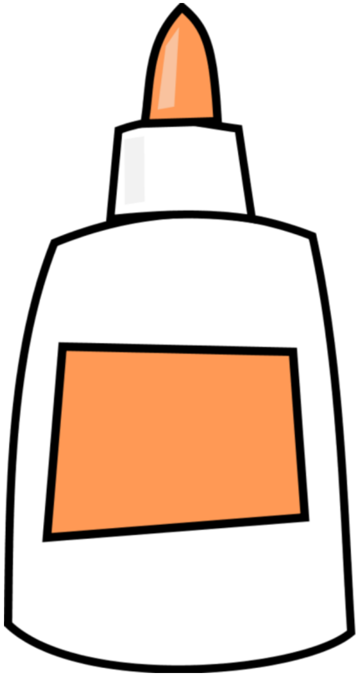
Elements $C + O_2 \rightarrow CO_2$

Compounds $CaO + H_2O \rightarrow Ca(OH)_2$

Ex. Synthesis Reaction



Synthesis



- Predict the products.

$2Na_{(s)} + Cl_{2(g)} \rightarrow 2\ NaCl_{(s)}$

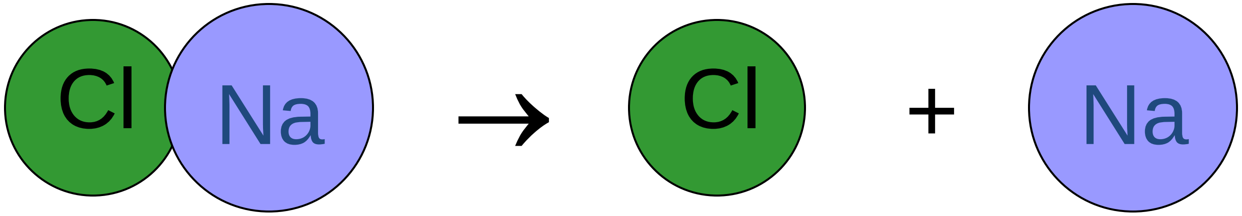
$Mg_{(s)} + F_{2(g)} \rightarrow MgF_{2(s)}$

$2\ Al_{(s)} + 3F_{2(g)} \rightarrow 2\ AlF_{3(s)}$

Synthesis = join together

2. Decomposition

Example: NaCl



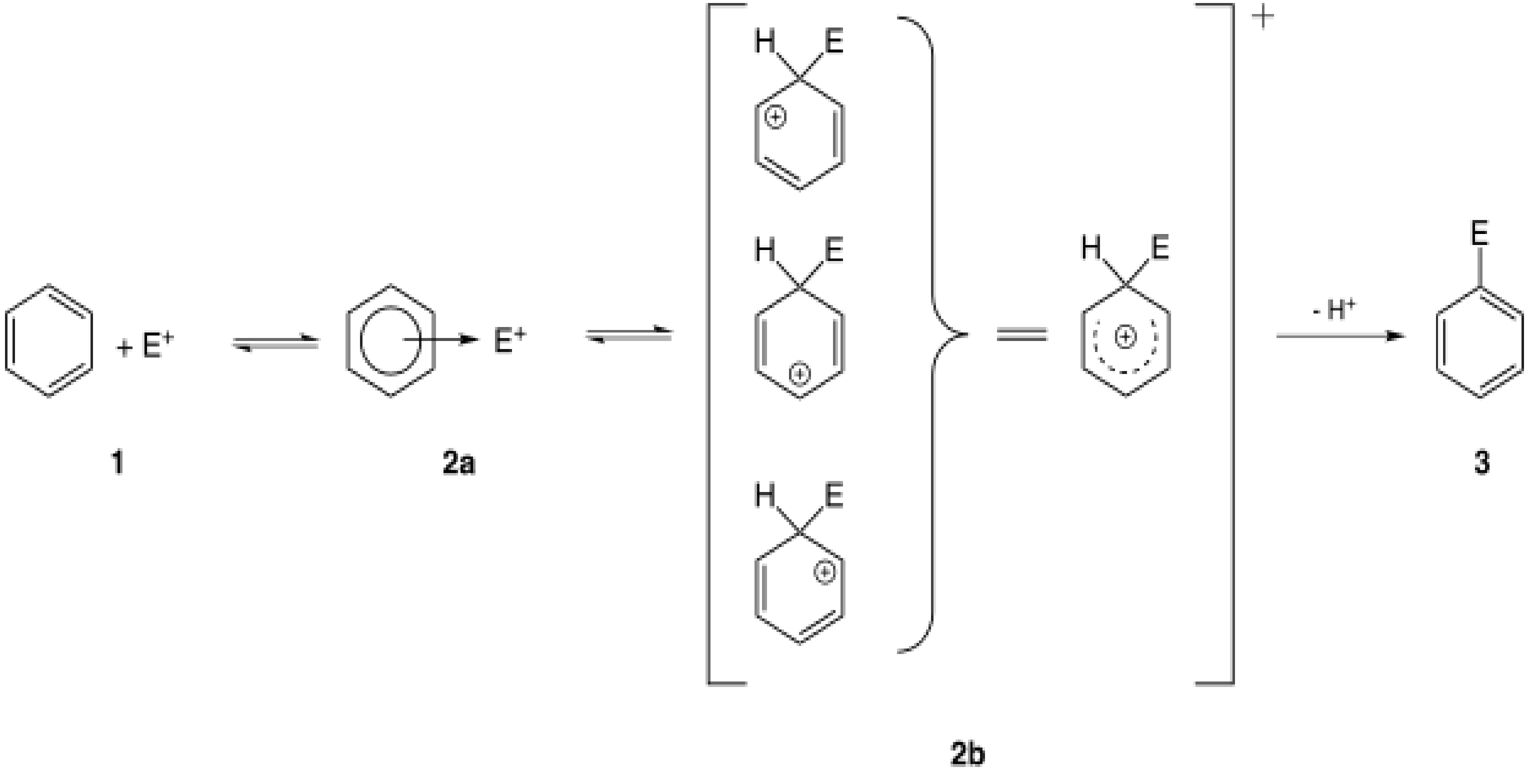
General: $AB \rightarrow A + B$

3. Substitution reaction

a- Nucleophilic reaction

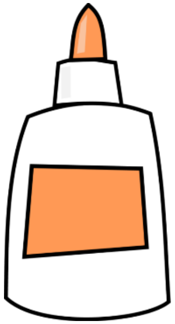
b- Electrophilic reaction

$R\text{-}Br + OH^- \rightarrow R\text{-}OH + Br^-$



+ E⁺
E⁺
H
E
+
- H⁺
E
1
2a
2b
3

Synthesis



join together

A + B → AB

Decomposition

split apart

AB → A + B

Single Replacement

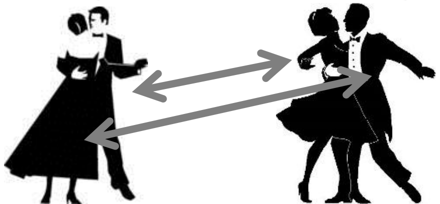
trade 1 place

AB + C → AC + B

Double Replacement

trade 2 places

AB + CD → AC + BD



REFERENCES

1- *Silberberg, Martin (2004). Chemistry: The Molecular Nature Of Matter and Change. New York: McGraw-Hill Companies. ISBN 0-07-310169-9.*

2- Berthelot & Houdas 1893, vol. I, pp. 138-139.

3- *Smith, Michael B.; March, Jerry (2007), Advanced Organic Chemistry: Reactions, Mechanisms, and Structure (6th ed.), New York: Wiley-Interscience, ISBN 978-0-471-72091-1*

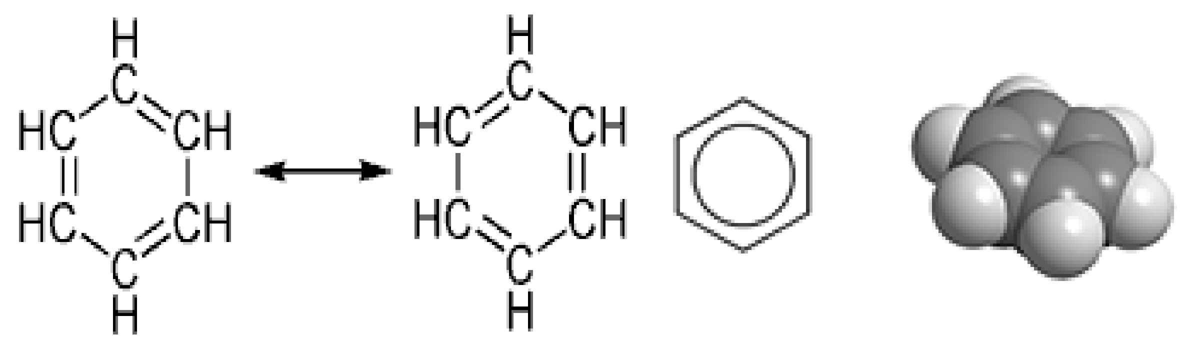
4- Organic Chemistry IUPAC Nomenclature. Rules C-4 Carboxylic Acids and Their Derivatives.

Aromatic Compounds

- **Benzene – a remarkable compound**
- **Discovered by Faraday 1825**
- **Formula C6H6**
- **Highly unsaturated, but remarkably stable**
- **Whole new class of benzene derivatives – called**
- **aromatic compounds**

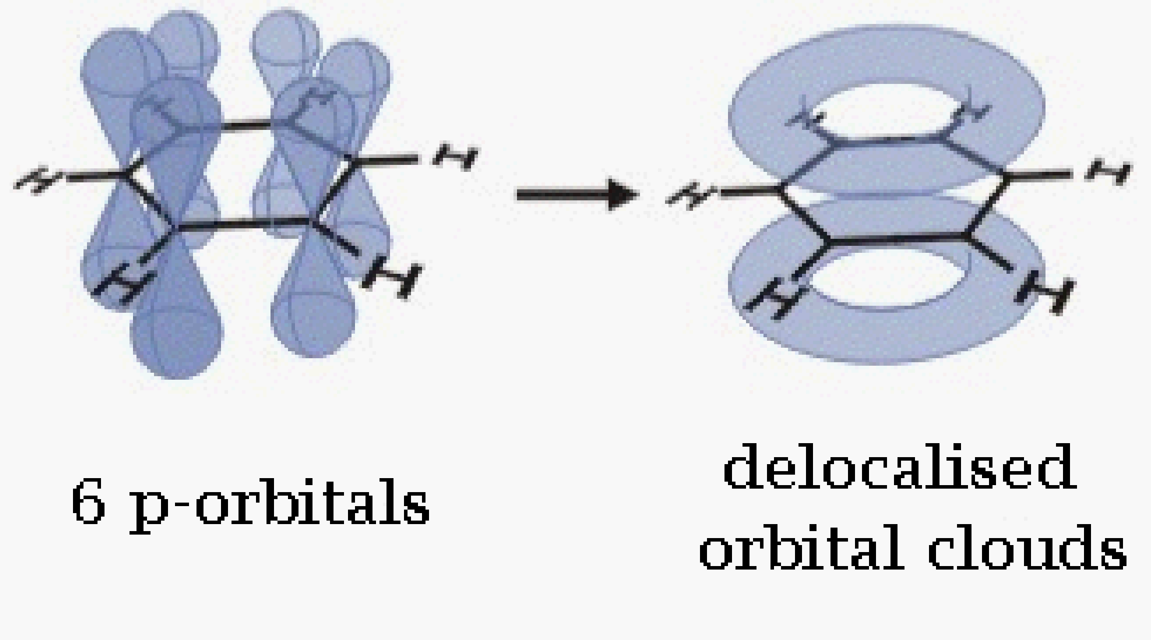
BENZENE : Resonance description

- Later spectroscopic evidence showed all bond lengths in benzene to be **equal** and intermediate between single and double bond lengths (1.39 Å).
- Resonance instead considers such molecules to be an intermediate or average (called a **resonance hybrid**) between several structures that differ only in the placement of the valence electrons



Benzene-orbitals

It was also found that benzene was a flat (planar) molecule.



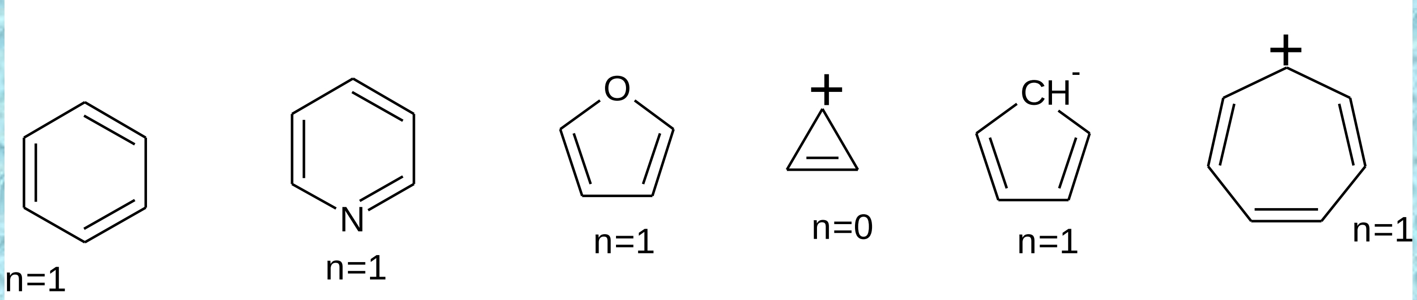
Characteristics of aromatic compounds

1. A delocalized conjugated π system, most commonly an arrangement of alternating single and double bonds : **Conjugated**
2. Coplanar structure, with all the contributing atoms in the same plane
3. Contributing atoms arranged in one or more rings
4. A number of π delocalized electrons that is, $4n + 2$ number of π electrons, where $n=0, 1, 2, 3$, and so on. This is known as Hückel's Rule.

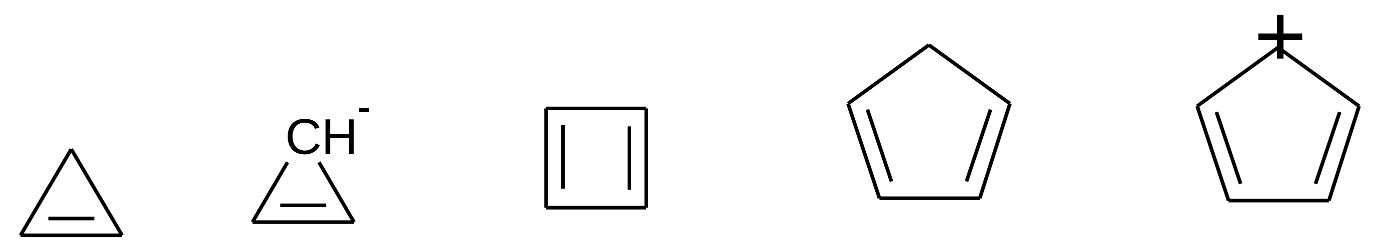
Huckel's Rule: The 4n+2 Rule

- **Planar monocyclic rings with a continuous system of *p***
- **orbitalsand 4n + 2p electrons are aromatic(n = 0, 1, 2, 3 etc)**
- **Aromatic means substantial resonance stabilization**
- **Benzene is aromatic:**
- **planar**
- **Cyclic**
- **orbital at every carbon 6 p electrons (n=1)**
- **Benzene has 3 bonding and 3 antibonding orbitals**
- **All the bonding orbitals are full and there are no electrons in antibonding orbitals; benzene has a closed shell of delocalized electrons and is very stable**

Aromatic compounds



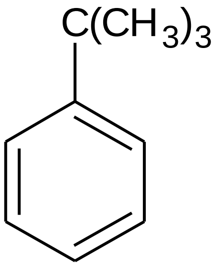
Non Aromatic compounds



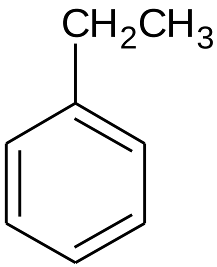
Nomenclature of Aromatic Compounds

1. Monosubstituted Benzenes

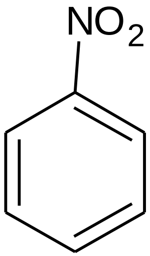
a. IUPAC name



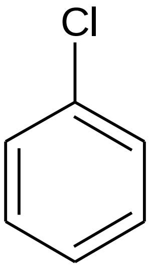
t-Butylbenzene



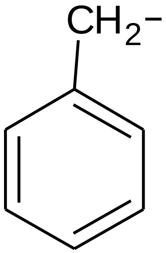
Ethylbenzene



Nitrobenzene

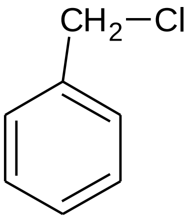


Chlorobenzene

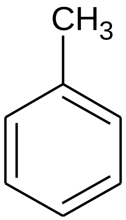


Benzyl group

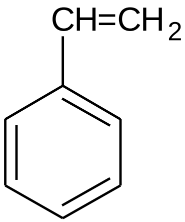
b. Common name



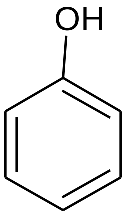
Benzyl chloride



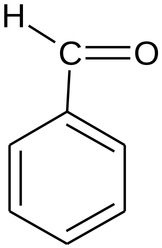
Toluene



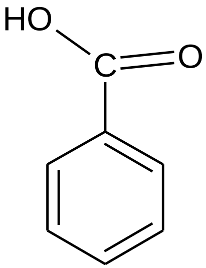
Styrene



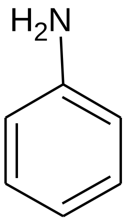
Phenol



Benzaldehyde



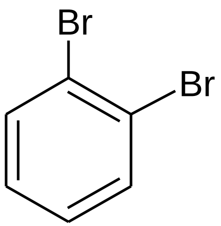
Benzoic acid



Aniline

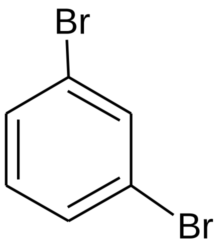
2. Disubstituted Benzenes

All disubstituted benzenes, can give rise to three possible isomers. The differentiate between the isomers, the relative positions of the substituents are designated by number or, more commonly, by the prefixes ortho (o: 1,2), meta (m:1,3) or para (p:1,4).



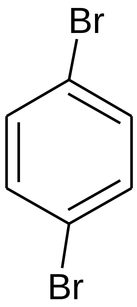
1,2-Dibromobenzene

o-Dibromobenzene



1,3-Dibromobenzene

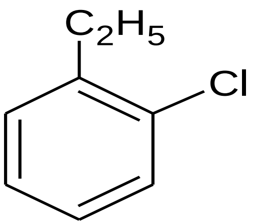
m-Dibromobenzene



1,4-Dibromobenzen

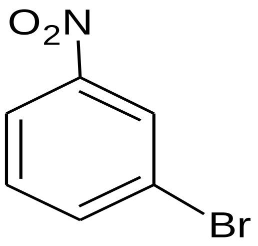
p-Dibromobenzene

When the substituents are different, they are listed in alphabetical order



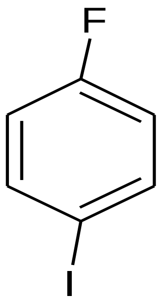
1-Chloro-2-ethylbenzene

o-Chloroethylbenzene



1-Bromo-3-nitrobenzene

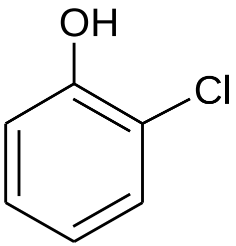
m-Bromonitrobenzene



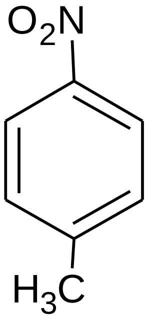
1-Fluoro-4-iodobenzen

p-Fluoroiodobenzene

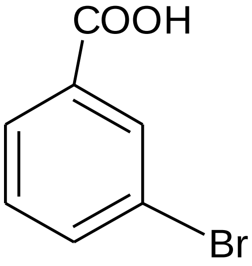
If one of the substituents is part of a parent compound, then the disubstituted benzene is named as a derivative of the parent compound.


2-Chlorophenol

o-Chlorophenol

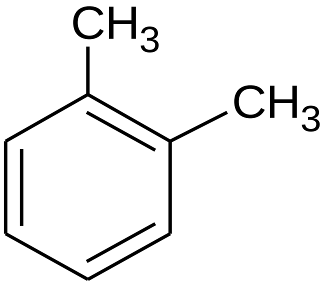

4-Nitrotoluene

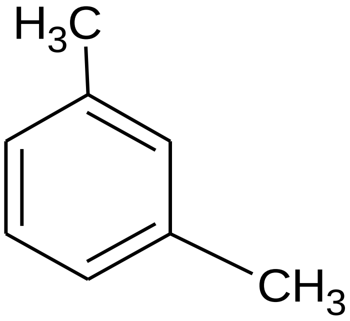
p-Nitrotoluene

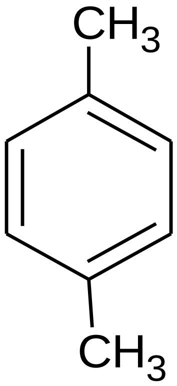

3-Bromobenzoic acid

m-Bromobenzoic aci

Certain disubstituted benzenes are referred to by their common names.

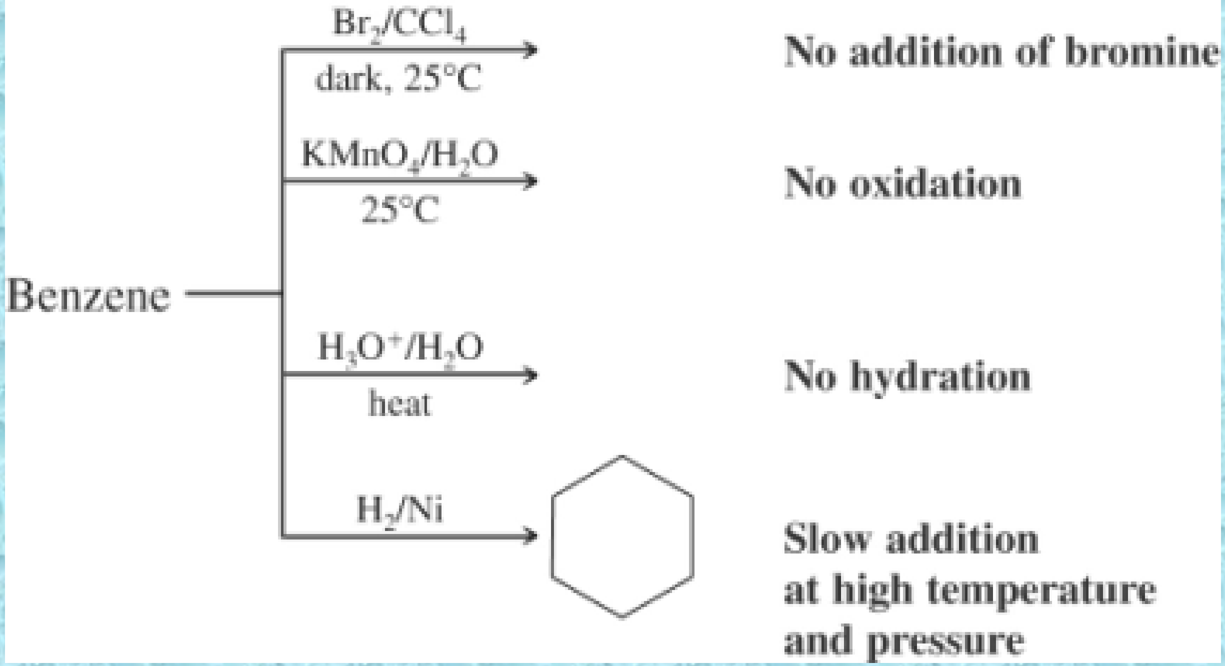

o-Xylene


m-Xylene


p-Xylene

Reactions of Benzene

- **Even though benzene is highly unsaturated, it does not**
- **undergo any of the regular reactions of alkenes**



Reactions of Benzene

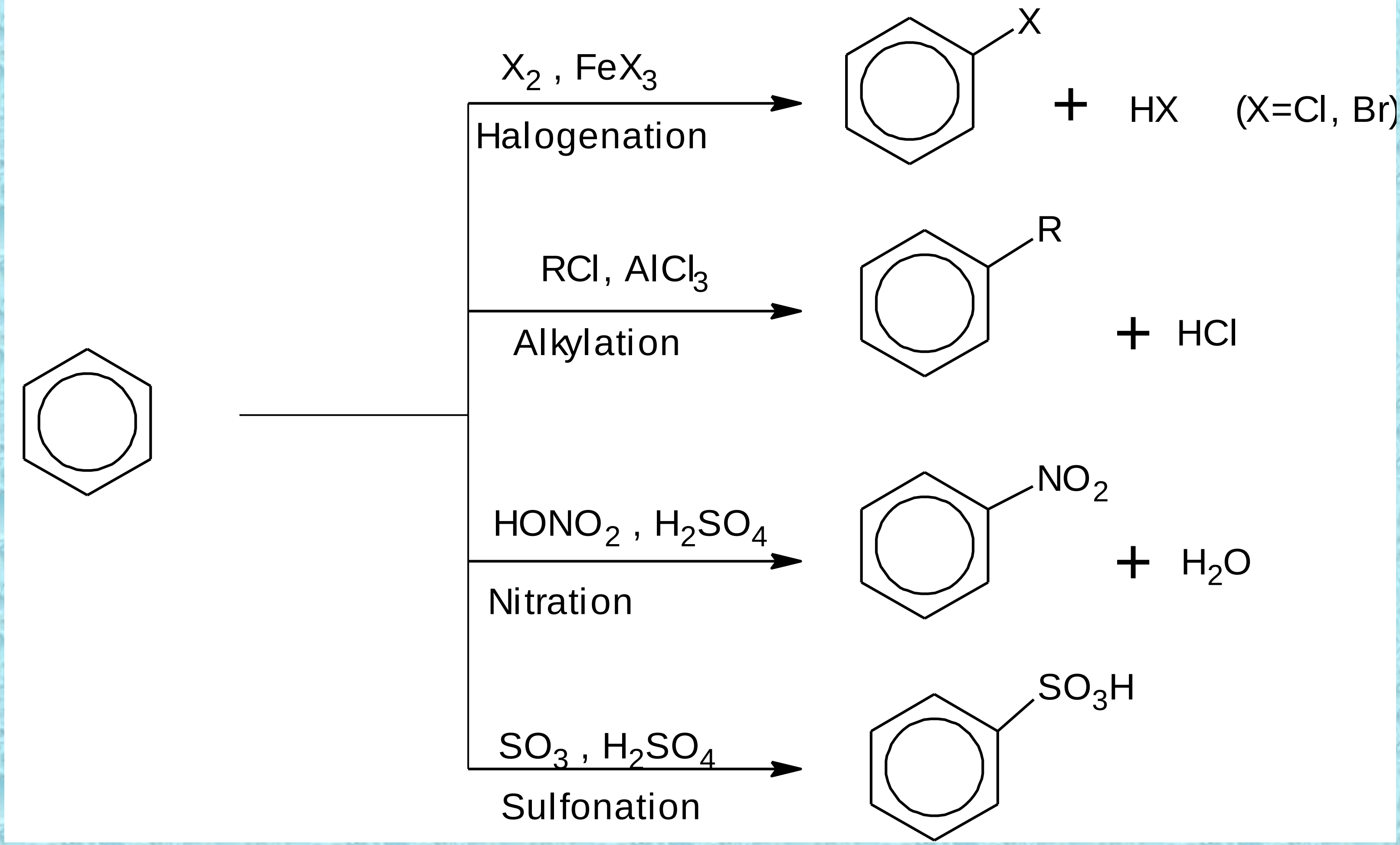
- **Benzene can be induced to react with bromine if a Lewis acid catalyst is present**
- **The reaction is a *substitution* and not an addition!**

$$C_6H_6 + Br_2 \xrightarrow{FeBr_3} C_6H_5Br + HBr \qquad \text{Observed}$$

$$C_6H_6 + Br_2 \not\longrightarrow C_6H_6Br_2 + C_6H_6Br_4 + C_6H_6Br_6 \qquad \text{Not observed}$$

Benzene produces only one monobrominatedcompound
All 6 carbon-hydrogen bonds are equivalent in benzene

Specific Electrophilic Aromatic : Substitution Reactions



X_2 , FeX_3

Halogenation

X

+ HX (X=Cl, Br)

RCl, $AlCl_3$

Alkylation

R

+ HCl

$HONO_2$, H_2SO_4

Nitration

NO_2

+ H_2O

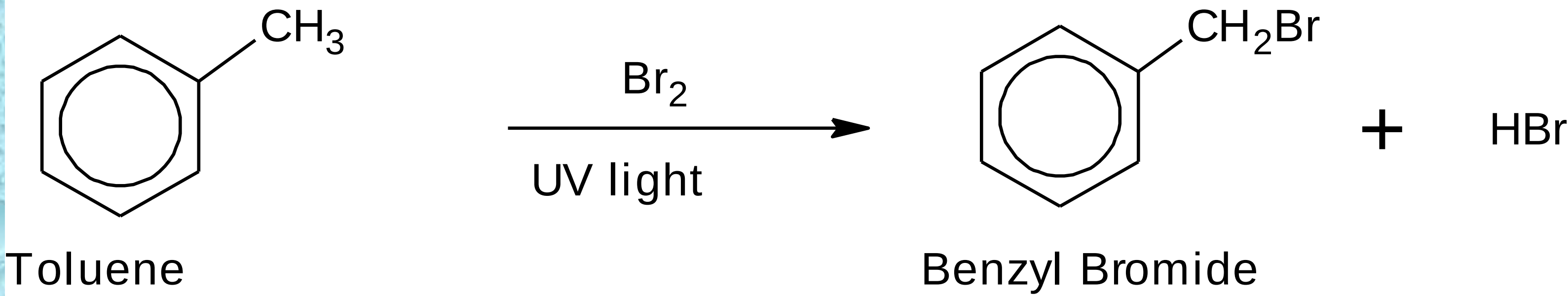
SO_3 , H_2SO_4

Sulfonation

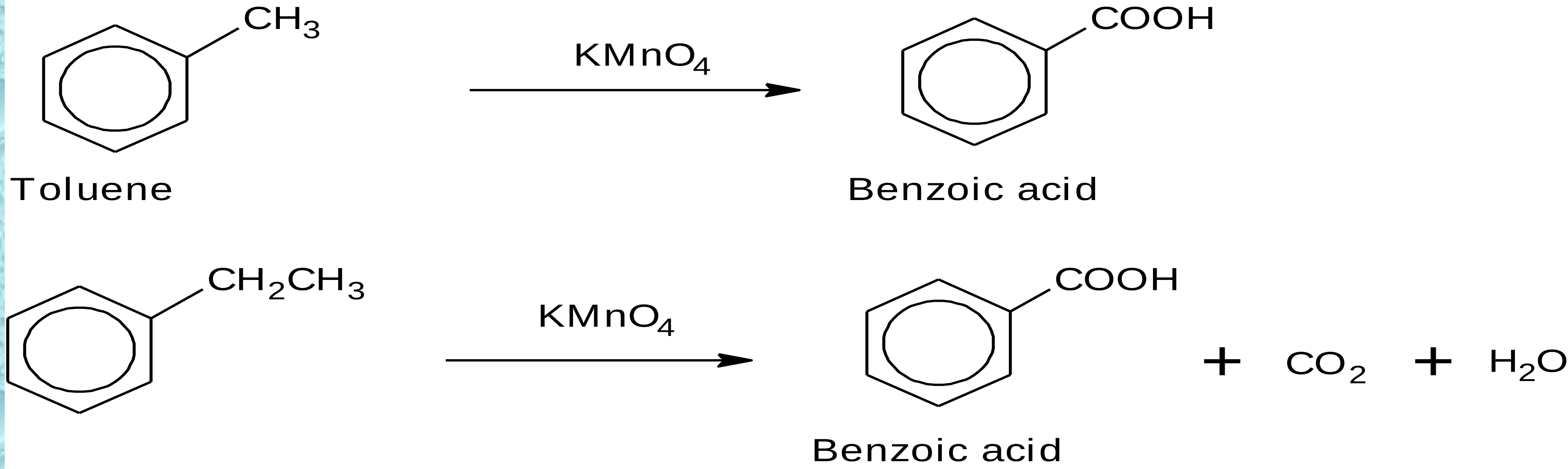
SO_3H

Side-Chain Reactions of Aromatic Compounds

a. Halogenation of an Alkyl Side Chain



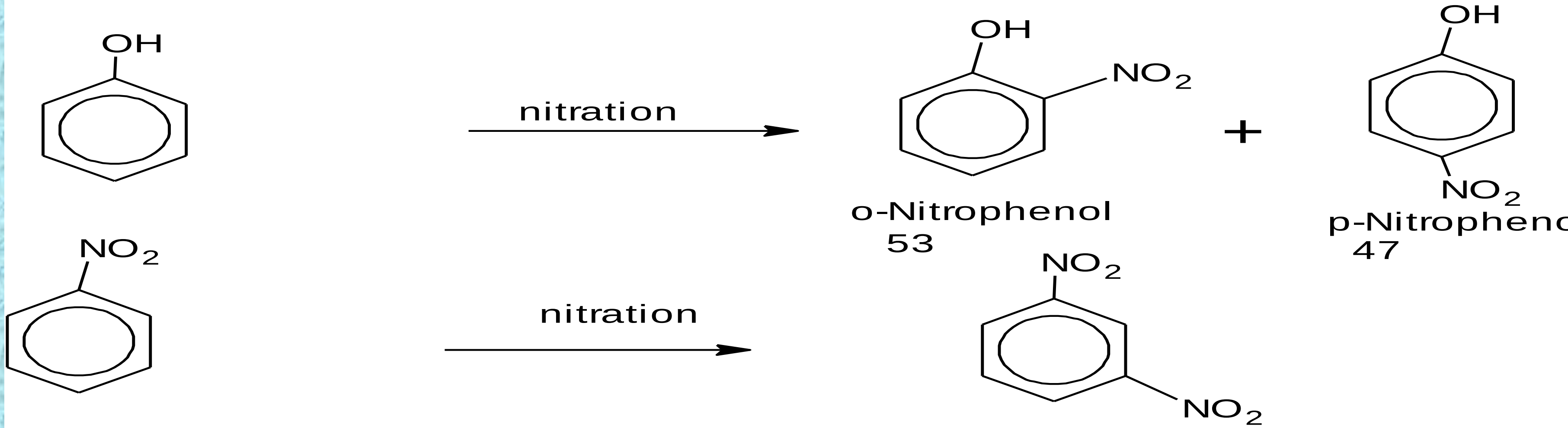
b. Oxidation of an Alkyl Side Chain



Disubstituted Benzenes : Orientation

Orientation Effects of Substituents in Electrophilic Aromatic Substitution :

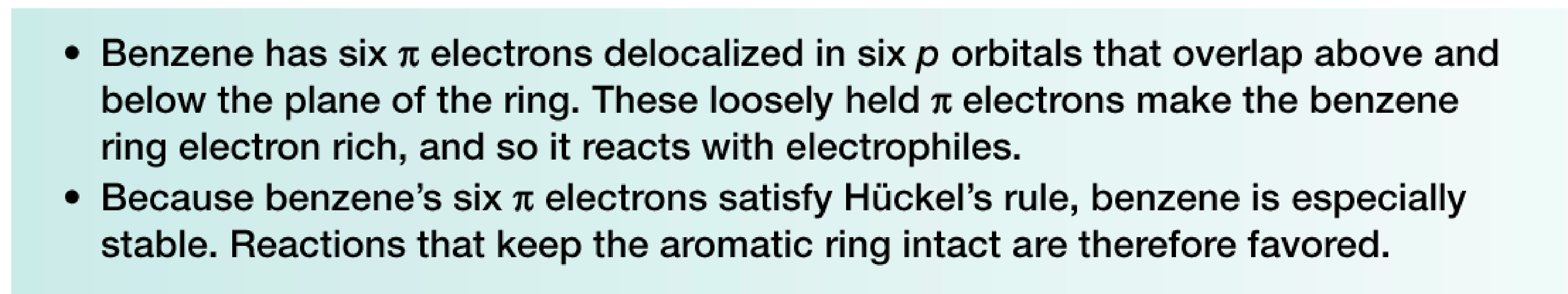
Ortho , para directors	Meta directors
$-OH$, $-OR$ $-NH_2$, $-NHR$, $-NR_2$ $-C_6H_5$ $-CH_3$, $-R$ (alkyl) $-F$, $-Cl$, $-Br$, $-I$	$-NO_2$ $-SO_3H$ $-COOH$, $-COOR$ $-CHO$, $-COR$ $-CN$



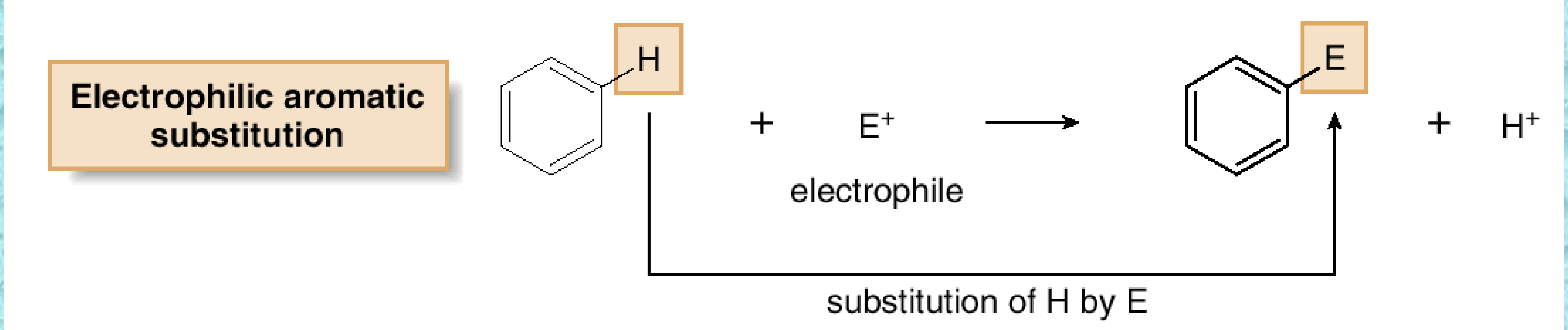
Electrophilic Aromatic Substitution

Background

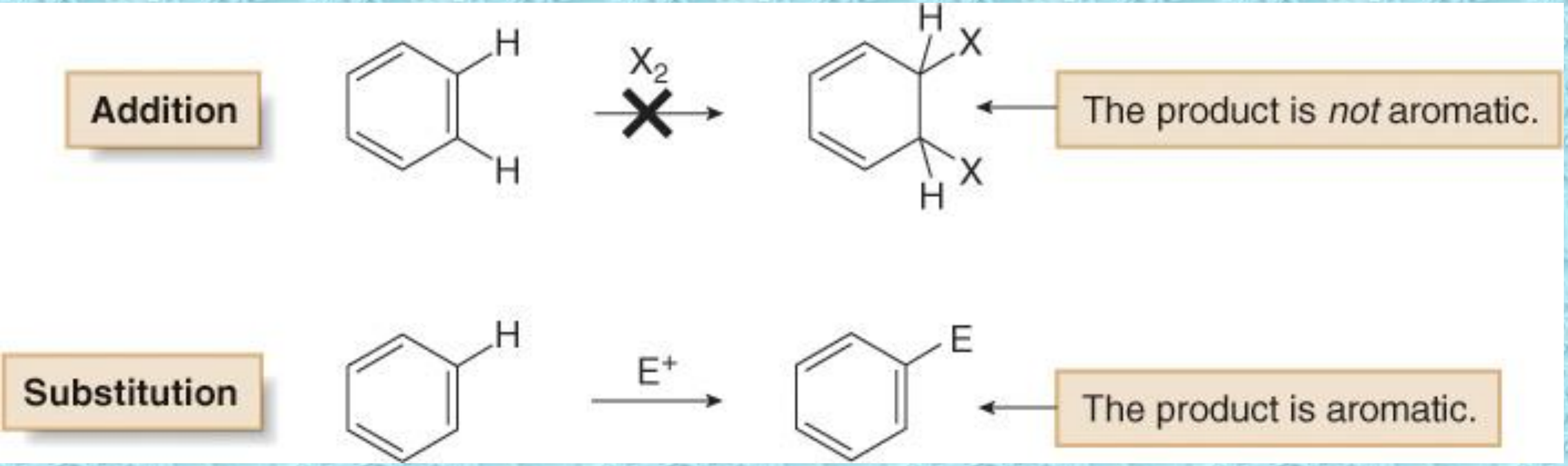
- The characteristic reaction of benzene is electrophilic aromatic substitution—a hydrogen atom is replaced by an electrophile.

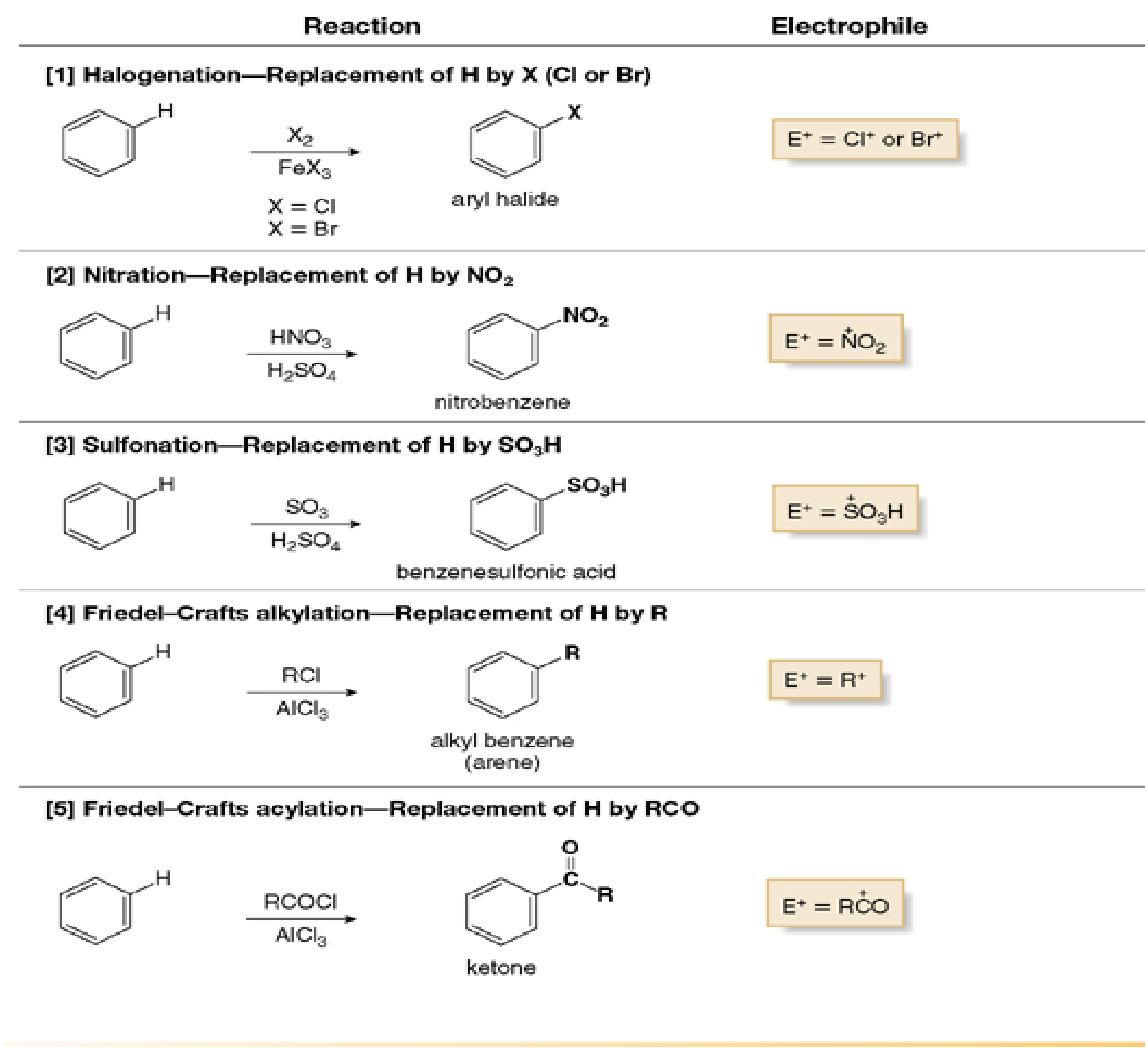


- Benzene has six π electrons delocalized in six *p* orbitals that overlap above and below the plane of the ring. These loosely held π electrons make the benzene ring electron rich, and so it reacts with electrophiles.
- Because benzene's six π electrons satisfy Hückel's rule, benzene is especially stable. Reactions that keep the aromatic ring intact are therefore favored.



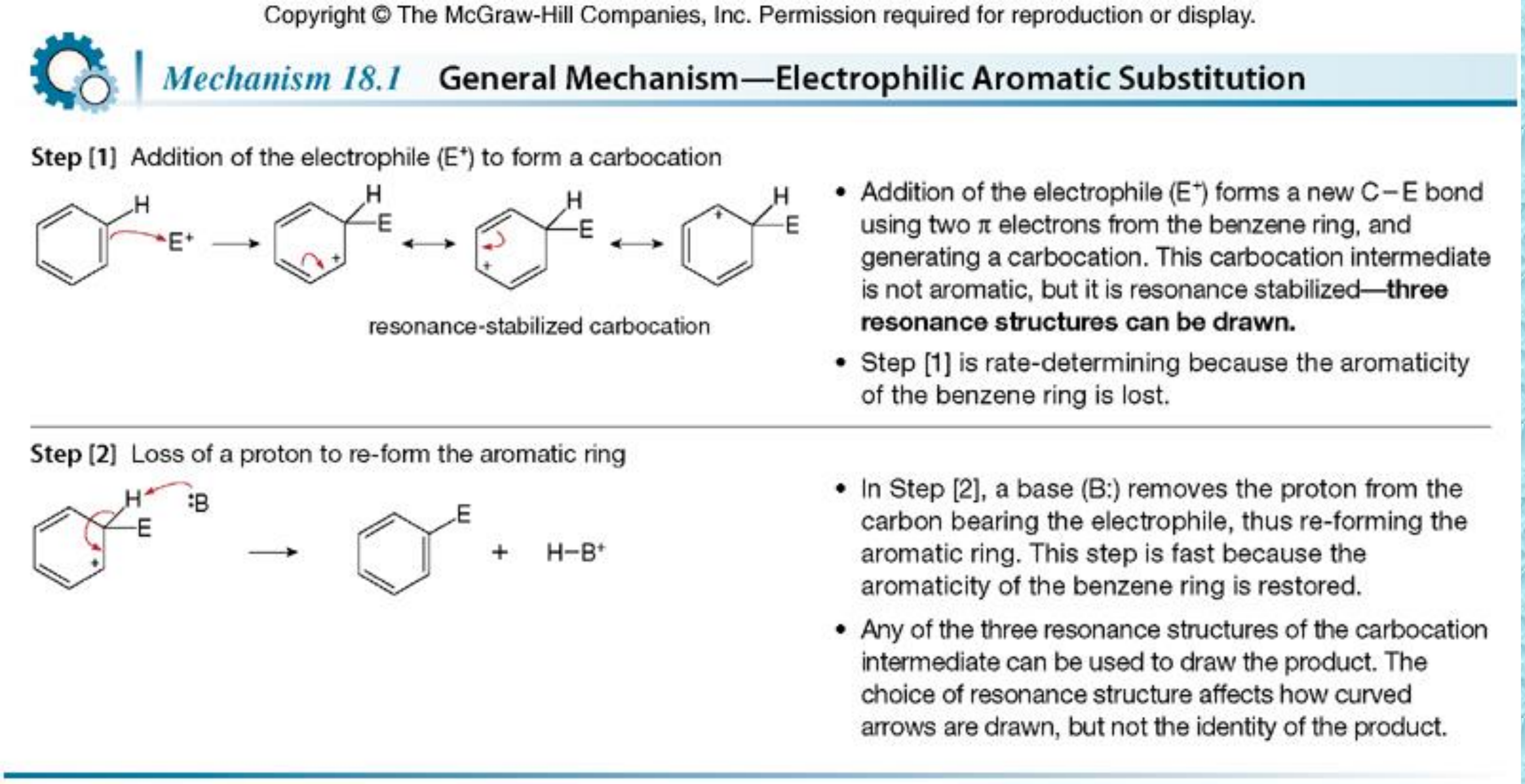
- **Benzene does not undergo addition reactions like other unsaturated hydrocarbons, because addition would yield a product that is not aromatic.**
- **Substitution of a hydrogen keeps the aromatic ring intact.**
- **There are five main examples of electrophilic aromatic substitution.**





Reaction	Electrophile
[1] Halogenation—Replacement of H by X (Cl or Br) $\xrightarrow[\text{FeX}_3]{X_2}$ aryl halide X = Cl X = Br	$E^+ = Cl^+$ or Br^+
[2] Nitration—Replacement of H by NO_2 $\xrightarrow[H_2SO_4]{HNO_3}$ nitrobenzene	$E^+ = \overset{+}{N}O_2$
[3] Sulfonation—Replacement of H by SO_3H $\xrightarrow[H_2SO_4]{SO_3}$ benzenesulfonic acid	$E^+ = \overset{+}{S}O_3H$
[4] Friedel–Crafts alkylation—Replacement of H by R $\xrightarrow[AlCl_3]{RCl}$ alkyl benzene (arene)	$E^+ = R^+$
[5] Friedel–Crafts acylation—Replacement of H by RCO $\xrightarrow[AlCl_3]{RCOCl}$ ketone	$E^+ = R\overset{+}{C}O$

- **Regardless of the electrophile used, all electrophilic aromatic substitution reactions occur by the same two-step mechanism—addition of the electrophile E^+ to form a resonance-stabilized carbocation, followed by deprotonation with base, as shown below:**



Mechanism 18.1 **General Mechanism—Electrophilic Aromatic Substitution**

Step [1] Addition of the electrophile (E^+) to form a carbocation

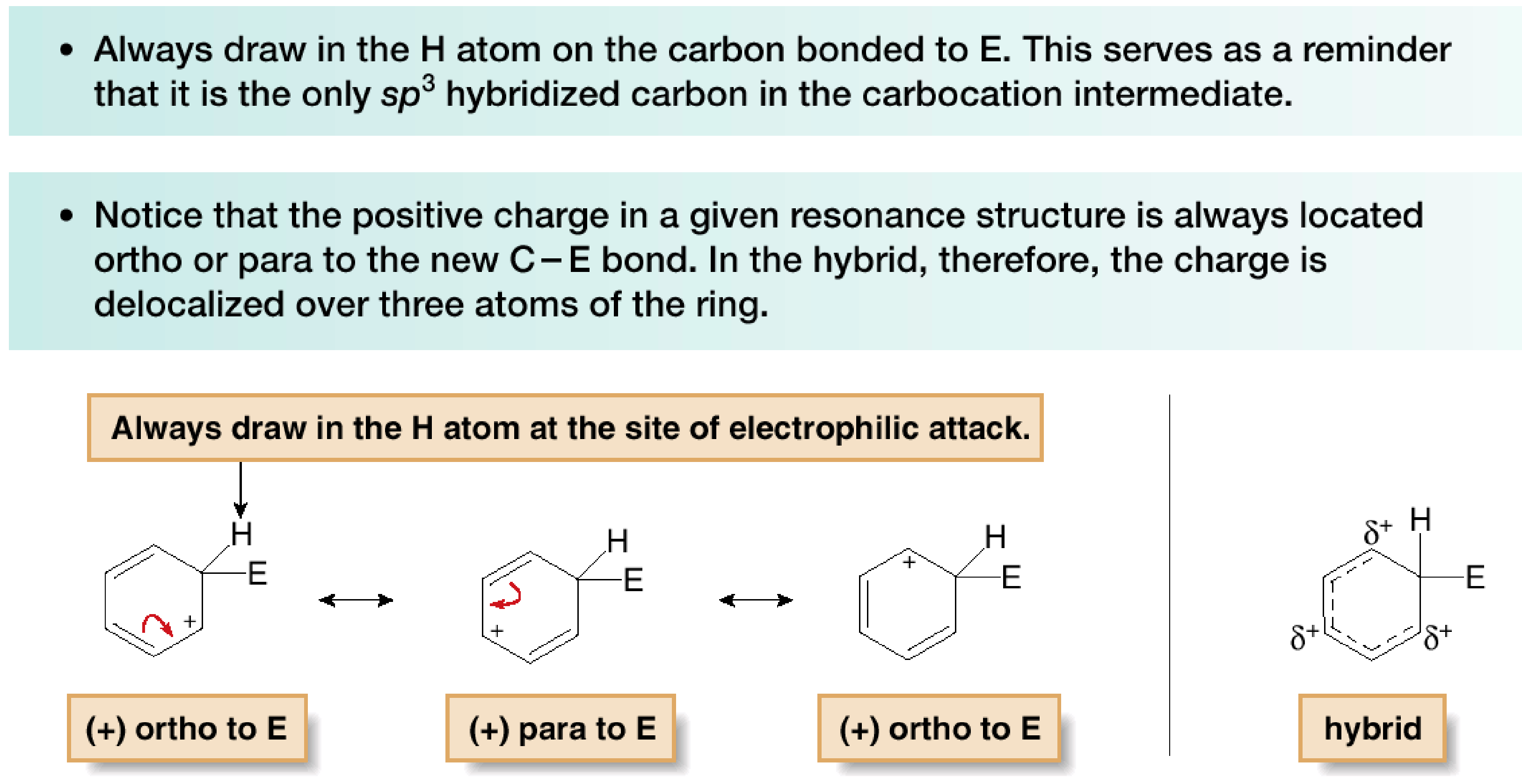
resonance-stabilized carbocation

- Addition of the electrophile (E^+) forms a new C–E bond using two π electrons from the benzene ring, and generating a carbocation. This carbocation intermediate is not aromatic, but it is resonance stabilized—**three resonance structures can be drawn.**
- Step [1] is rate-determining because the aromaticity of the benzene ring is lost.

Step [2] Loss of a proton to re-form the aromatic ring

- In Step [2], a base (B:) removes the proton from the carbon bearing the electrophile, thus re-forming the aromatic ring. This step is fast because the aromaticity of the benzene ring is restored.
- Any of the three resonance structures of the carbocation intermediate can be used to draw the product. The choice of resonance structure affects how curved arrows are drawn, but not the identity of the product.

- **The first step in electrophilic aromatic substitution forms a carbocation, for which three resonance structures can be drawn. To help keep track of the location of the positive charge:**



- Always draw in the H atom on the carbon bonded to E. This serves as a reminder that it is the only *sp*^{3} hybridized carbon in the carbocation intermediate.

- Notice that the positive charge in a given resonance structure is always located ortho or para to the new C – E bond. In the hybrid, therefore, the charge is delocalized over three atoms of the ring.

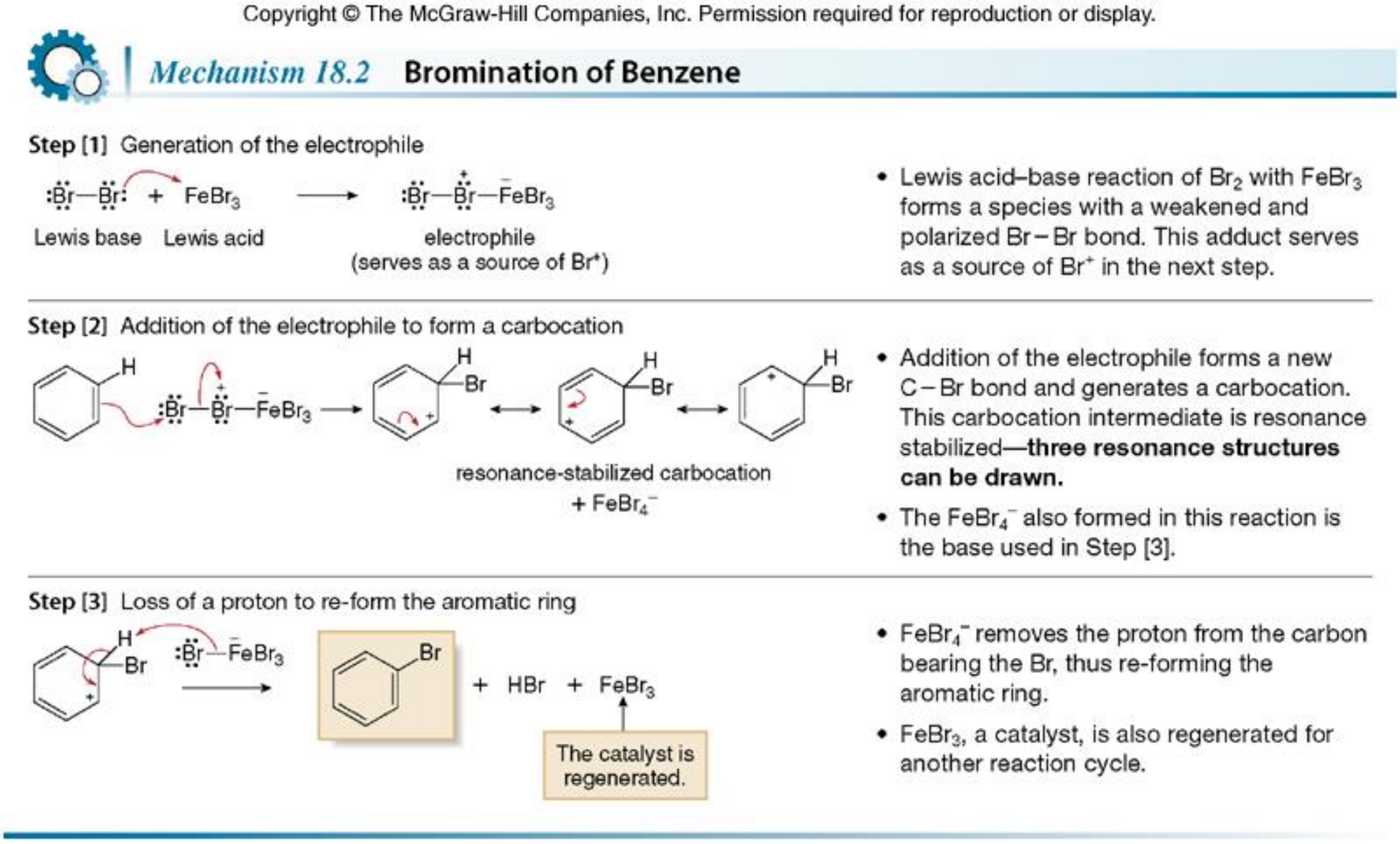
Always draw in the H atom at the site of electrophilic attack.

Halogenation

- In **halogenation**, benzene reacts with Cl_2 or Br_2 in the presence of a Lewis acid catalyst, such as **$FeCl_3$** or **$FeBr_3$**, to give the aryl halides chlorobenzene or bromobenzene respectively.
- Analogous reactions with I_2 and F_2 are not synthetically useful because I_2 is too unreactive and F_2 reacts too violently.

This image cannot currently be displayed.

Chlorination proceeds by a similar mechanism. •



Mechanism 18.2 Bromination of Benzene

Step [1] Generation of the electrophile

- Lewis acid–base reaction of Br_2 with $FeBr_3$ forms a species with a weakened and polarized Br – Br bond. This adduct serves as a source of Br^+ in the next step.

Step [2] Addition of the electrophile to form a carbocation

- Addition of the electrophile forms a new C – Br bond and generates a carbocation. This carbocation intermediate is resonance stabilized—**three resonance structures can be drawn.**
- The $FeBr_4^-$ also formed in this reaction is the base used in Step [3].

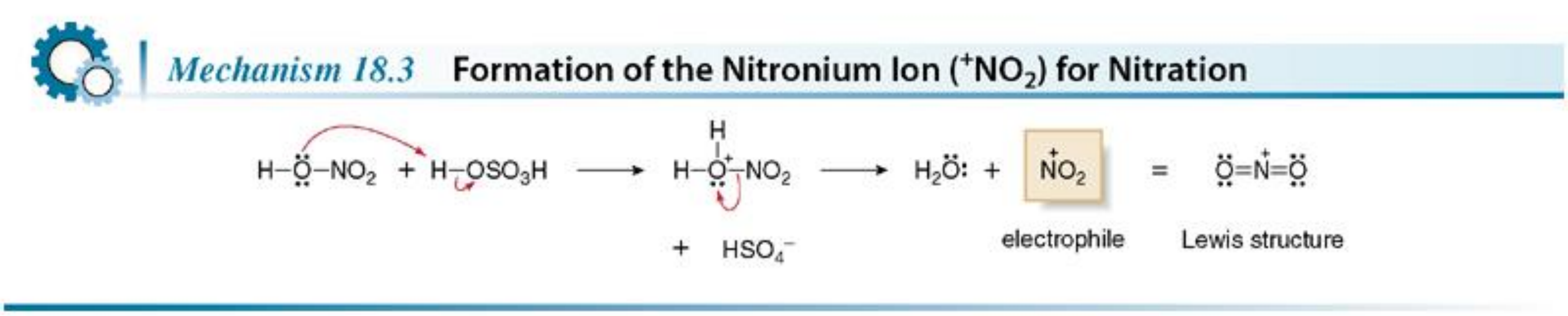
Step [3] Loss of a proton to re-form the aromatic ring

- $FeBr_4^-$ removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.
- $FeBr_3$, a catalyst, is also regenerated for another reaction cycle.

Nitration and Sulfonation

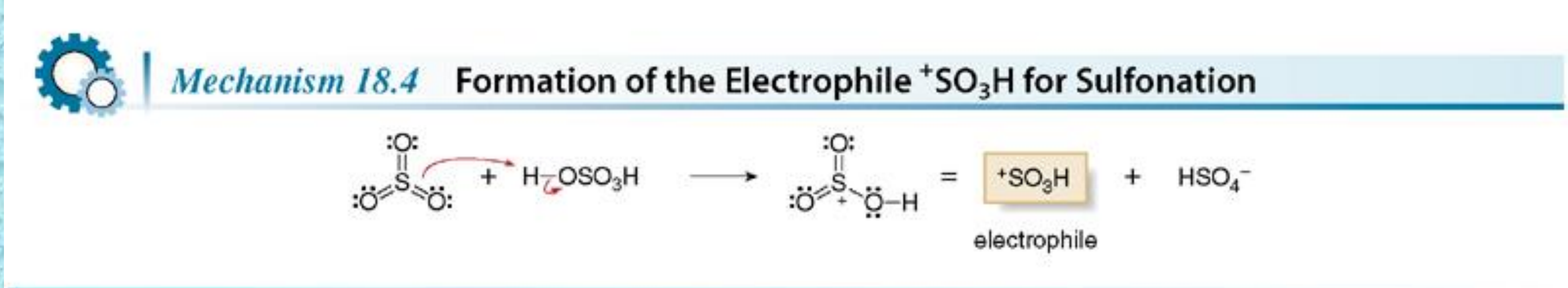
- **Nitration** and **sulfonation** introduce two different functional groups into the aromatic ring.
- **Nitration is especially useful because the nitro group can be reduced to an NH_2 group.**

- **Generation of the electrophile in nitration requires strong acid.**



Mechanism 18.3 Formation of the Nitronium Ion ($^+NO_2$) for Nitration

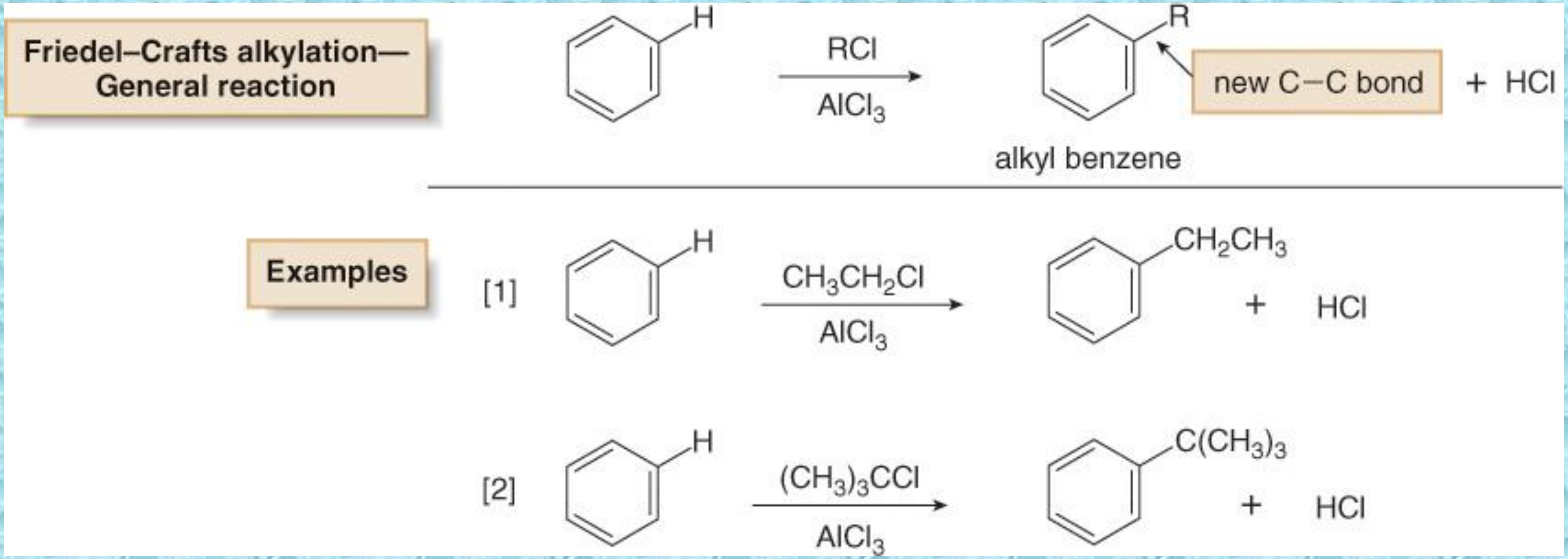
Generation of the electrophile in sulfonation requires • strong acid.



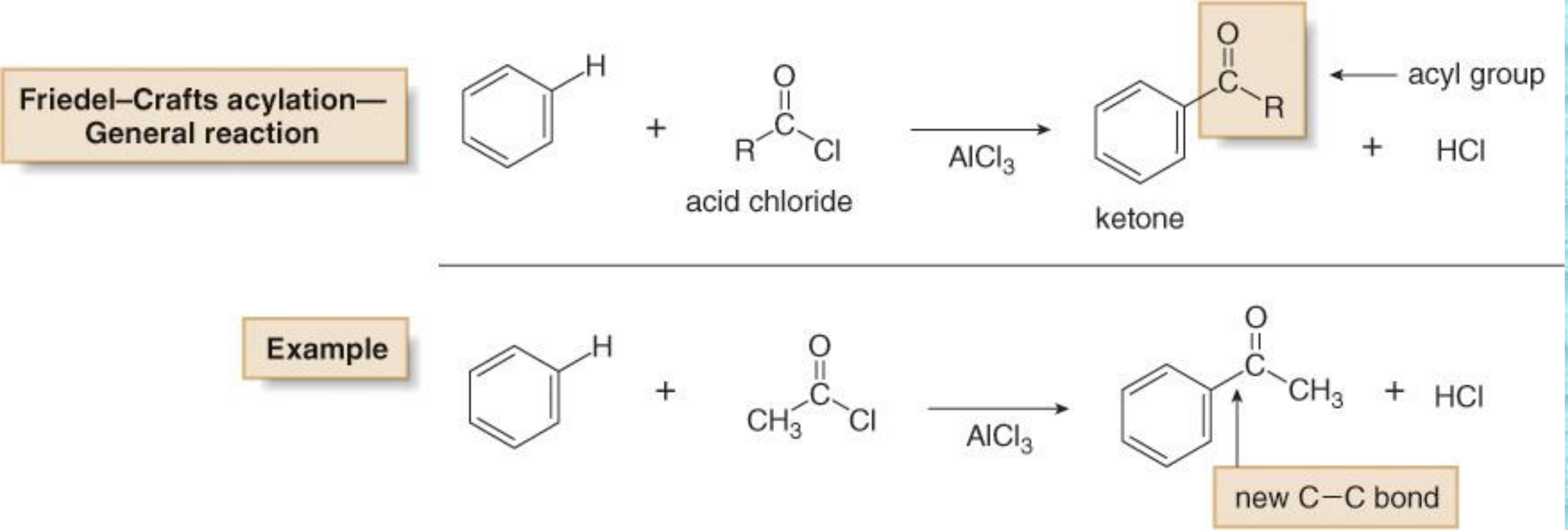
Mechanism 18.4 **Formation of the Electrophile $^{+}SO_3H$ for Sulfonation**

Friedel-Crafts Alkylation and Friedel-Crafts Acylation

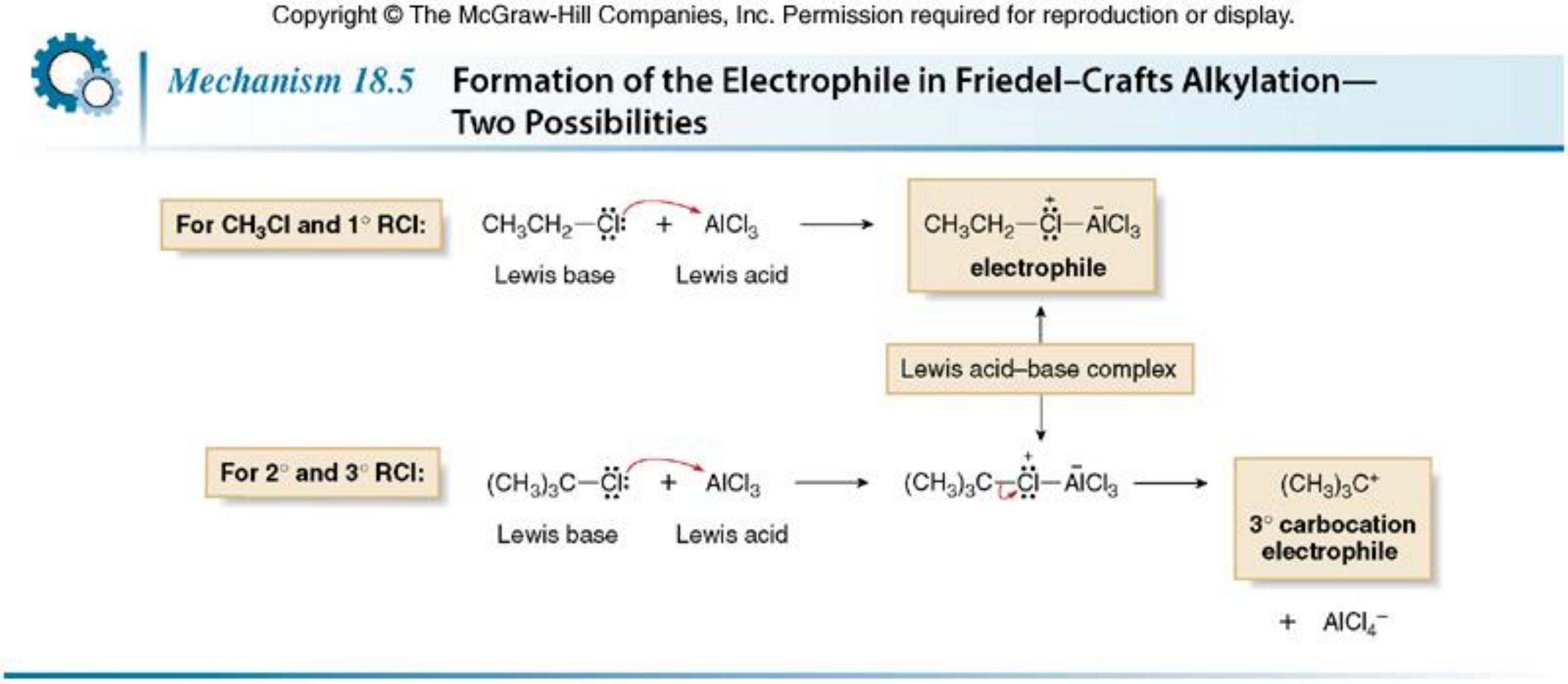
- In Friedel-Crafts alkylation, treatment of benzene with an alkyl halide and a Lewis acid ($AlCl_3$) forms an alkyl benzene.



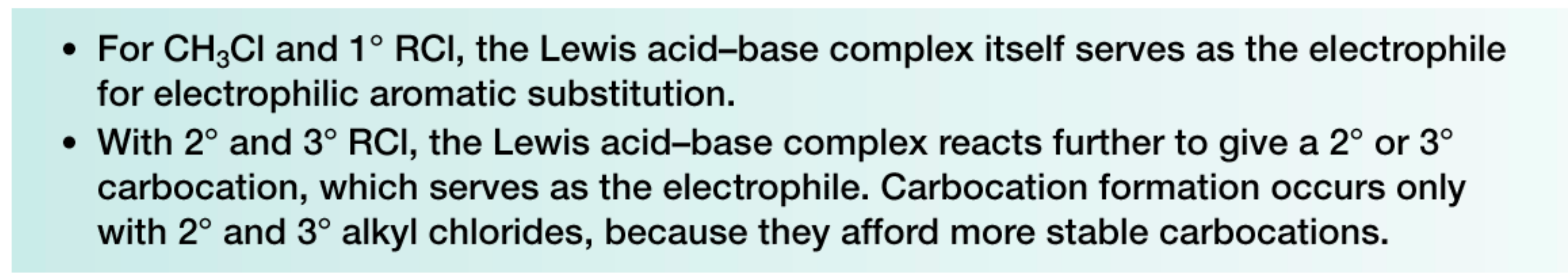
- In **Friedel-Crafts acylation**, a benzene ring is treated with an acid chloride (RCOCl) and $AlCl_3$ to form a ketone.
- Because the new group bonded to the benzene ring is called an **acyl group**, the transfer of an acyl group from one atom to another is an acylation.



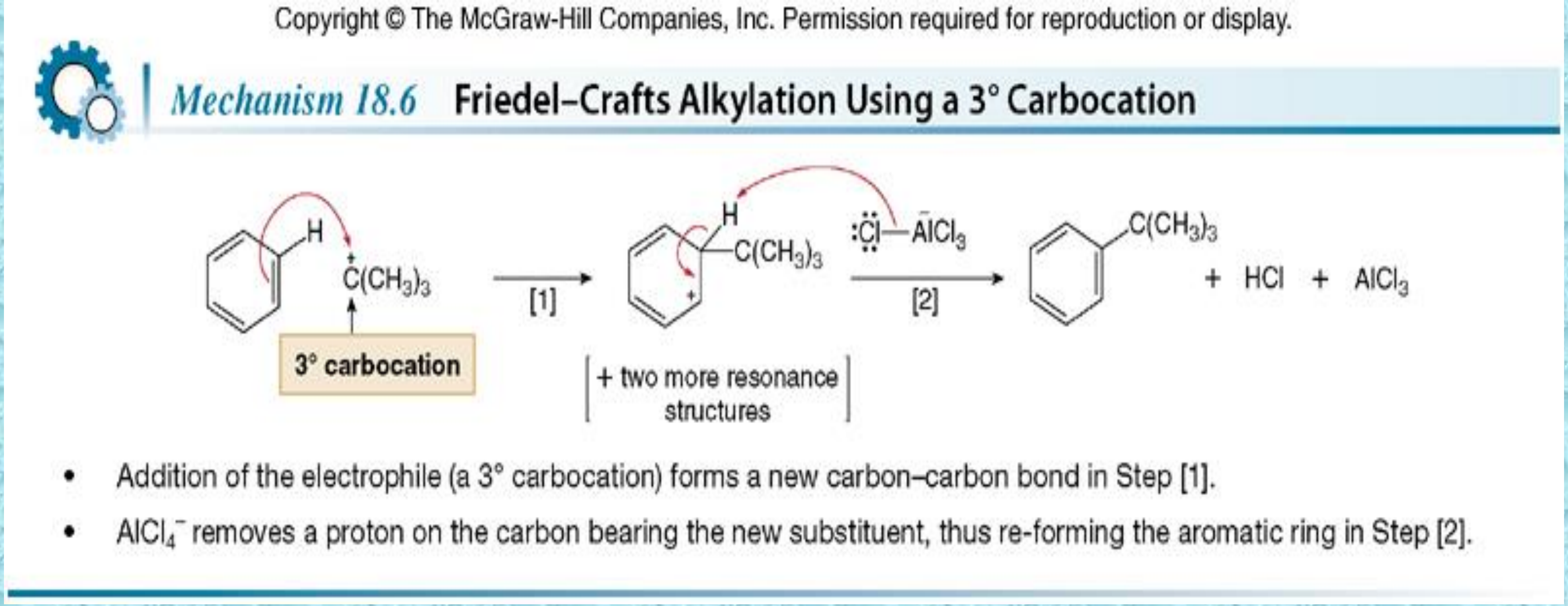
Friedel-Crafts Alkylation and Friedel-Crafts Acylation



Mechanism 18.5 **Formation of the Electrophile in Friedel–Crafts Alkylation—Two Possibilities**



- For CH_3Cl and 1° RCl, the Lewis acid–base complex itself serves as the electrophile for electrophilic aromatic substitution.
- With 2° and 3° RCl, the Lewis acid–base complex reacts further to give a 2° or 3° carbocation, which serves as the electrophile. Carbocation formation occurs only with 2° and 3° alkyl chlorides, because they afford more stable carbocations.

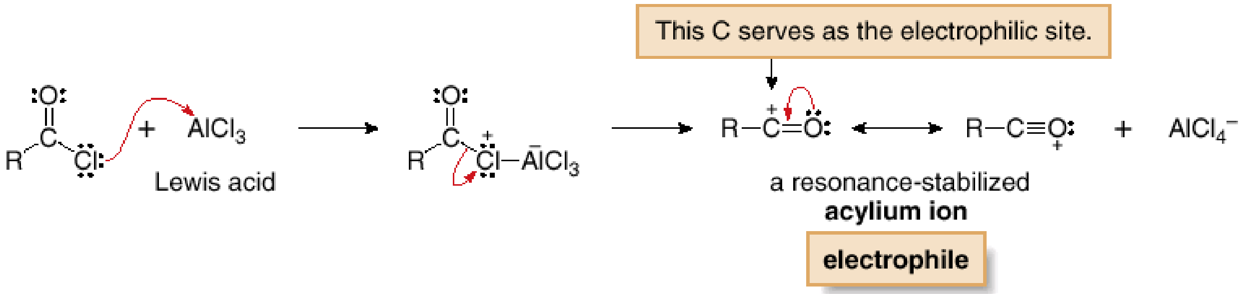


Mechanism 18.6 Friedel–Crafts Alkylation Using a 3° Carbocation

- Addition of the electrophile (a 3° carbocation) forms a new carbon–carbon bond in Step [1].
- $AlCl_4^-$ removes a proton on the carbon bearing the new substituent, thus re-forming the aromatic ring in Step [2].

- In Friedel-Crafts acylation, the Lewis acid $AlCl_3$ ionizes the carbon-halogen bond of the acid chloride, thus forming a positively charged carbon electrophile called an acylium ion, which is resonance stabilized.
- The positively charged carbon atom of the acylium ion then goes on to react with benzene in the two step mechanism of electrophilic aromatic substitution.

Mechanism 18.7 Formation of the Electrophile in Friedel–Crafts Acylation


This C serves as the electrophilic site.

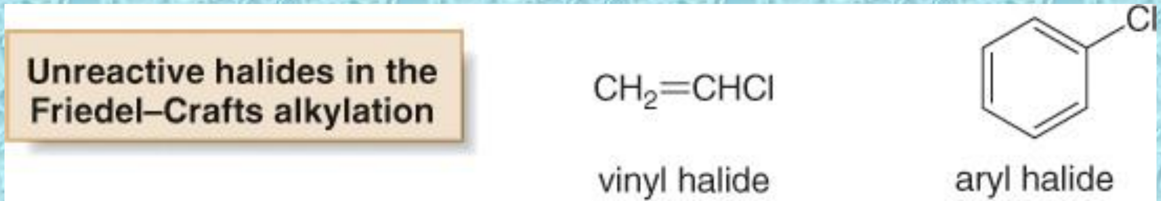
Lewis acid

a resonance-stabilized **acylium ion**

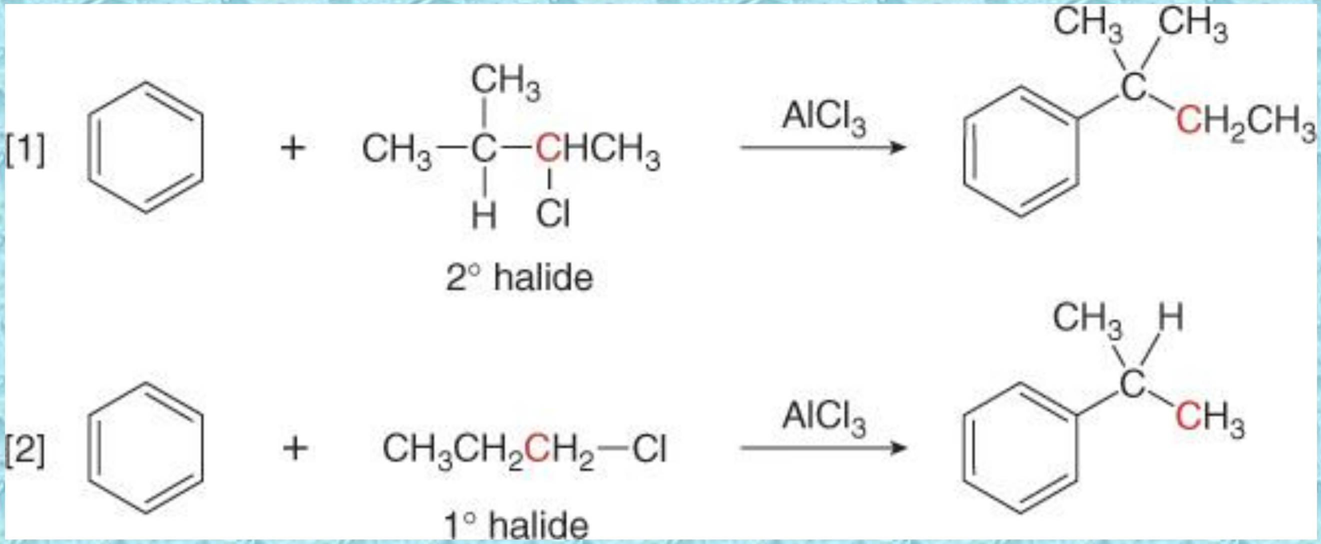
electrophile

Three additional facts about Friedel-Crafts alkylation should be kept in mind.

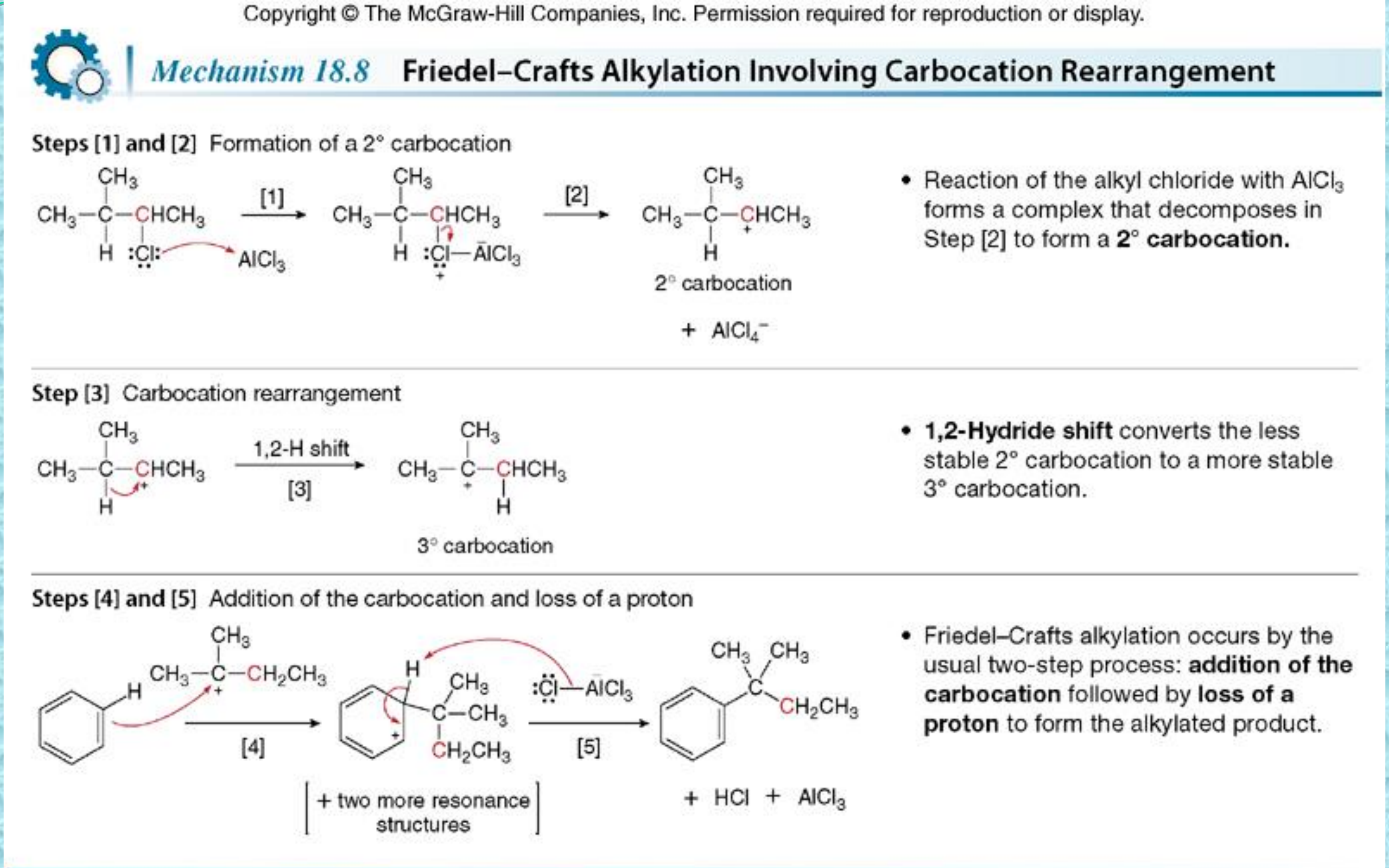
[1] Vinyl halides and aryl halides do not react in Friedel-Crafts alkylation.



Rearrangements can occur. [2]



These results can be explained by carbocation rearrangements.



Mechanism 18.8 Friedel–Crafts Alkylation Involving Carbocation Rearrangement

Steps [1] and [2] Formation of a 2° carbocation

- Reaction of the alkyl chloride with $AlCl_3$ forms a complex that decomposes in Step [2] to form a **2° carbocation.**

Step [3] Carbocation rearrangement

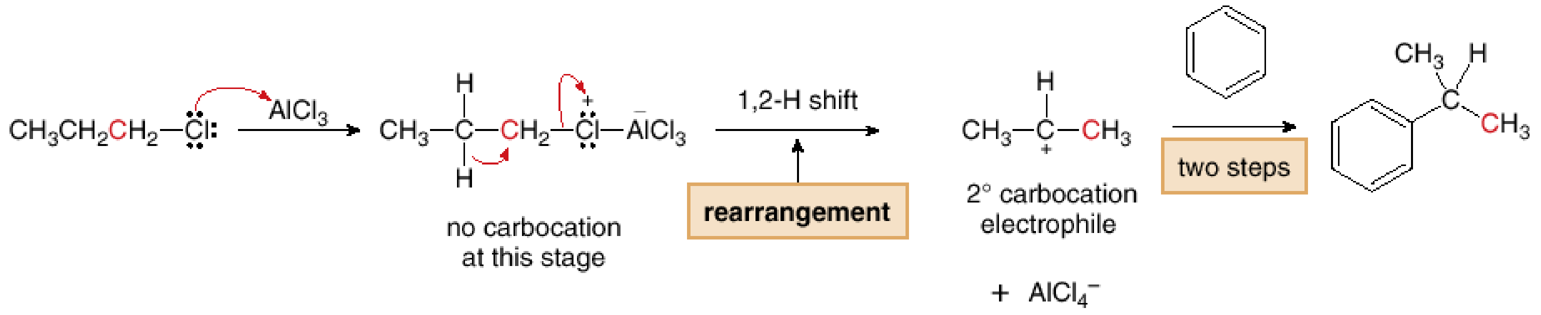
- **1,2-Hydride shift** converts the less stable 2° carbocation to a more stable 3° carbocation.

Steps [4] and [5] Addition of the carbocation and loss of a proton

- Friedel–Crafts alkylation occurs by the usual two-step process: **addition of the carbocation** followed by **loss of a proton** to form the alkylated product.

Rearrangements can occur even when no free carbocation is formed initially.

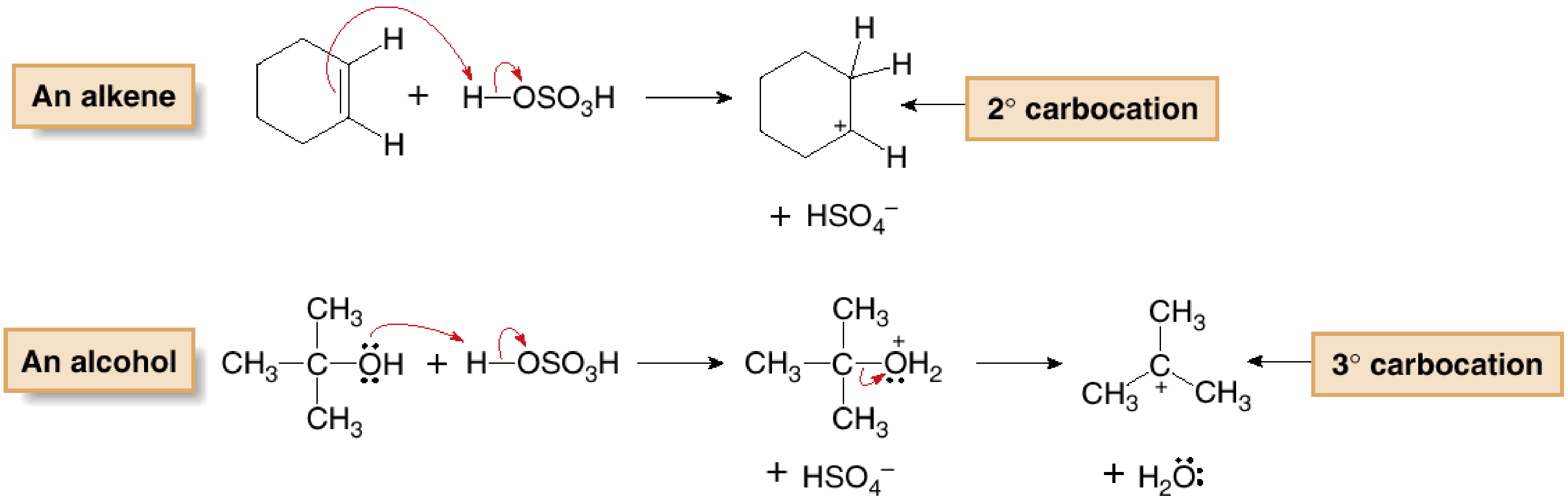
Mechanism 18.9 **A Rearrangement Reaction Beginning with a 1° Alkyl Chloride**



Other functional groups that form carbocations can also be used as starting materials. [3]

- Protonation of an alkene forms a carbocation, which can then serve as an electrophile in a Friedel–Crafts alkylation.

- Protonation of an alcohol, followed by loss of water, likewise forms a carbocation.



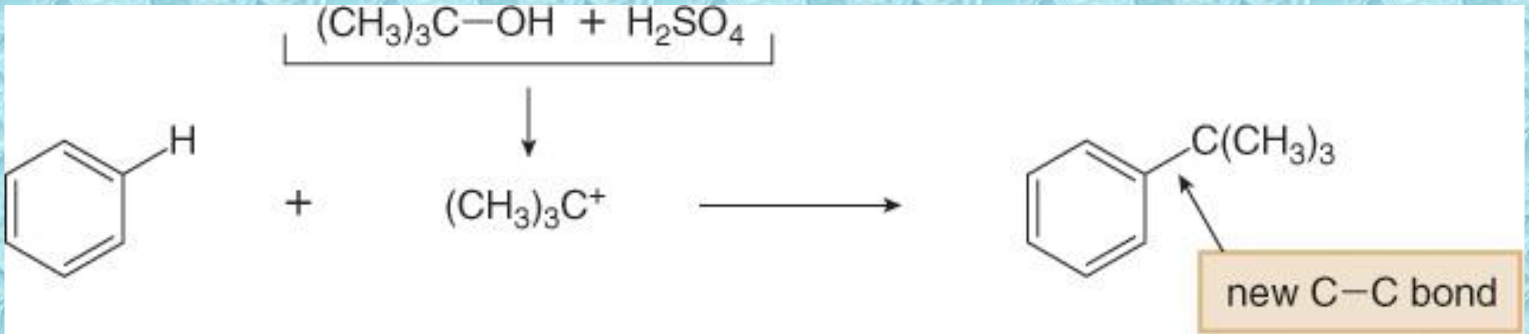
An alkene

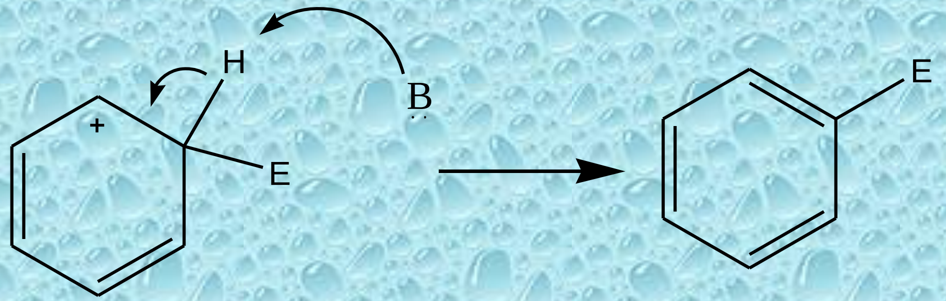
2° carbocation

An alcohol

3° carbocation

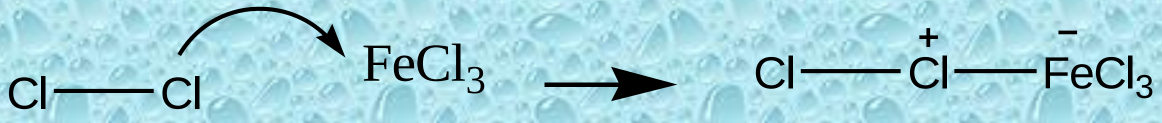
Each carbocation can then go on to react with benzene to form a product of electrophilic aromatic substitution. For example:



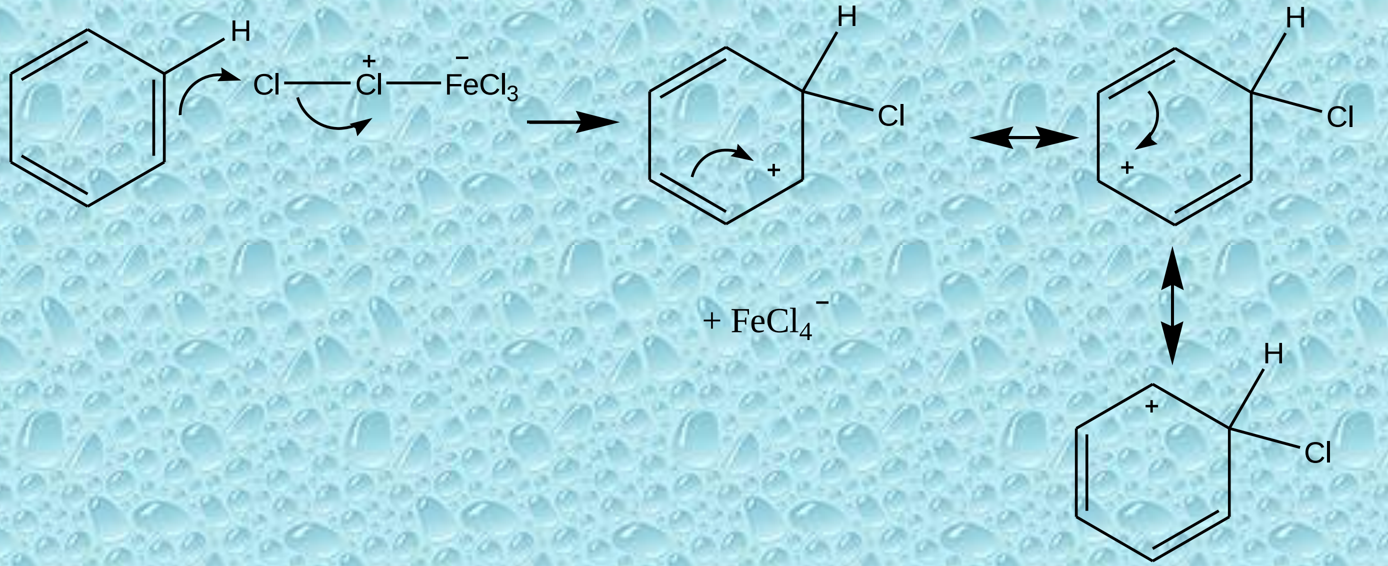

H
E
B
E
+

3) Draw a detailed mechanism of the chlorination of benzene.

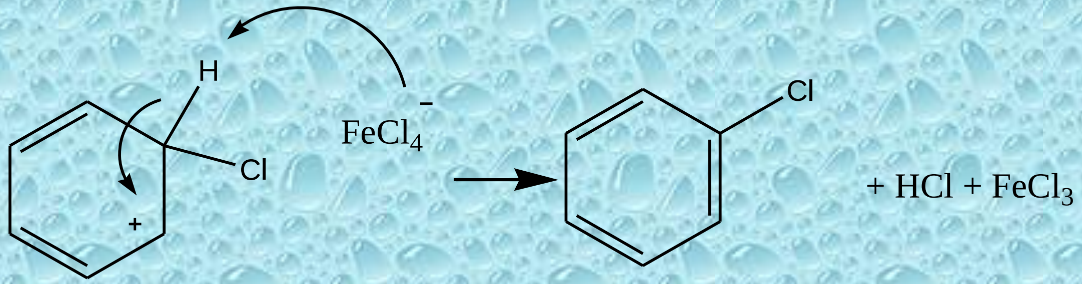
Formation of Electrophile



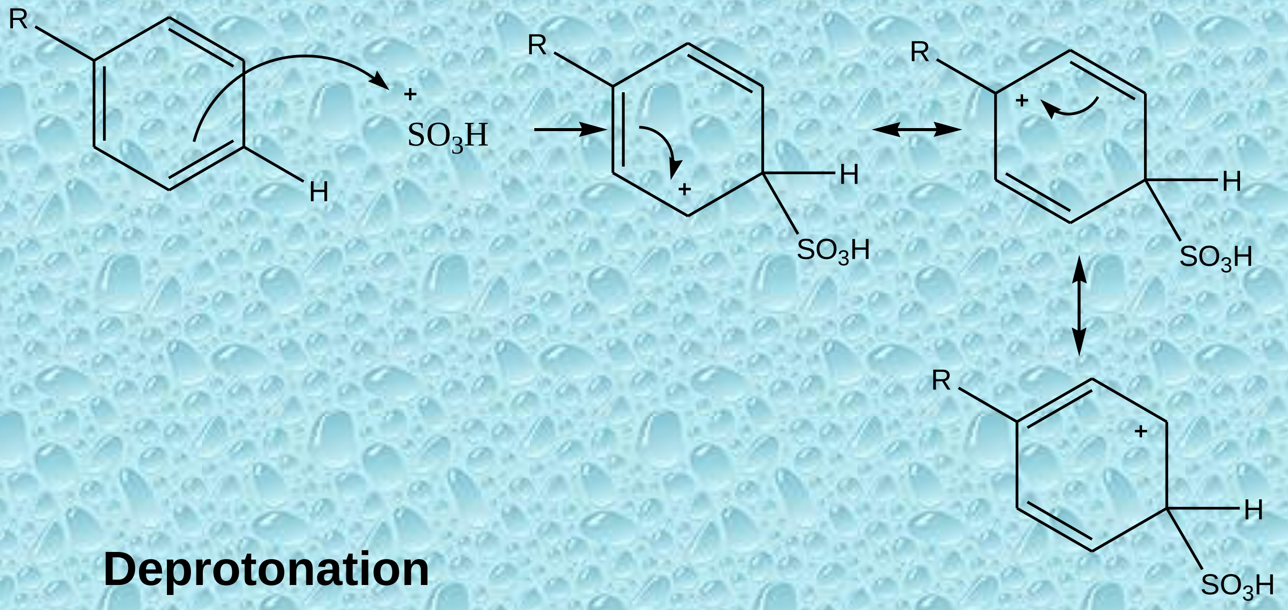
Electrophillic Additon



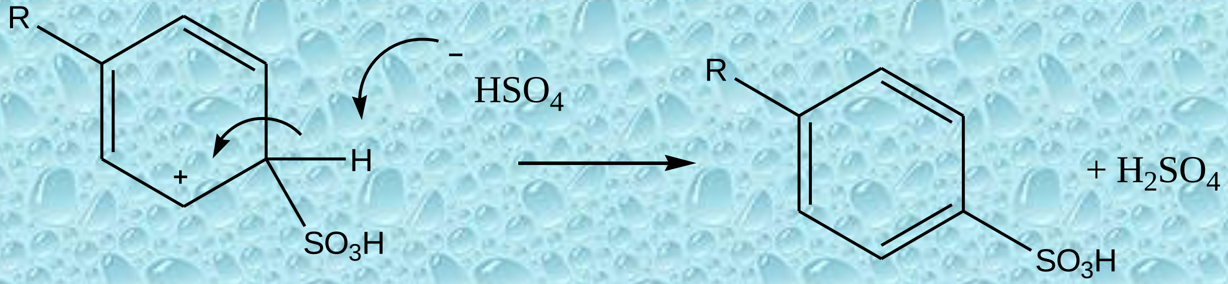
Deprotonation



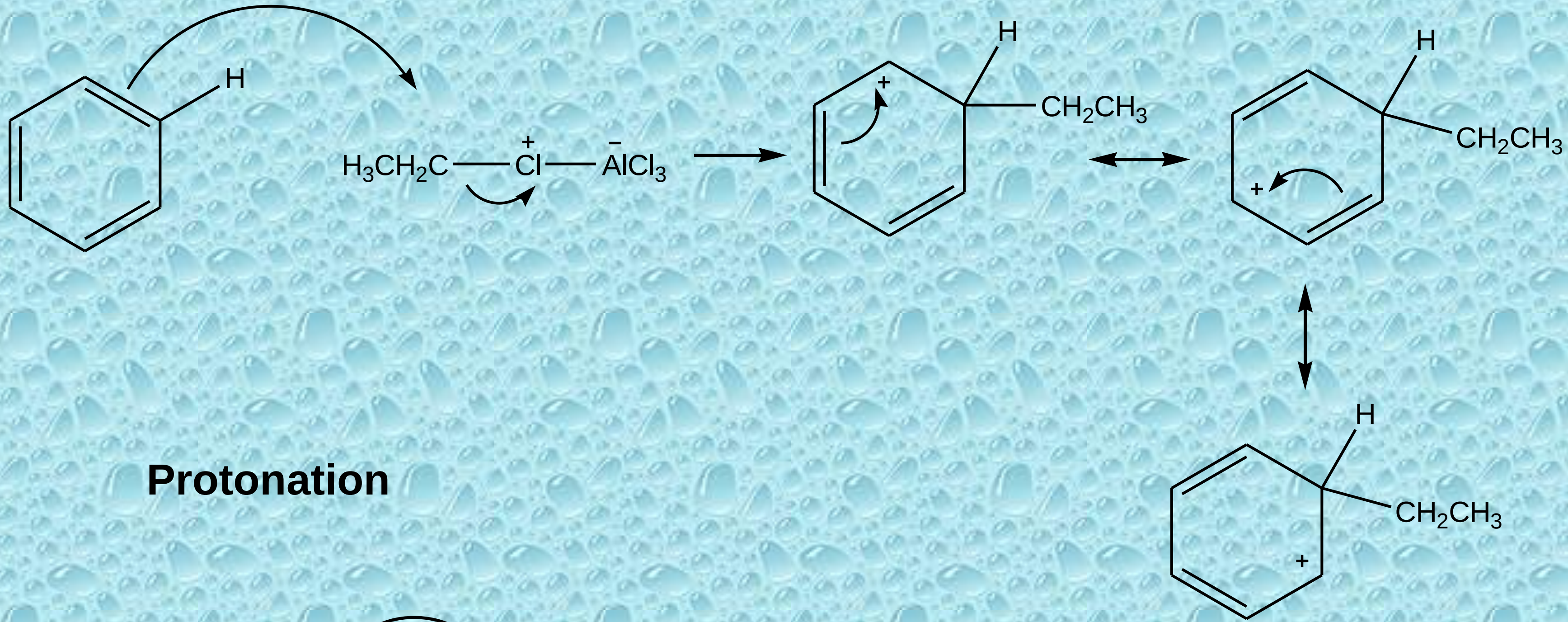
Electrophillic Addition



Deprotonation



Electrophillic Additoon



Protonation