Pharmaceutical Organic Chemistry "2"

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Al-Azhar University-Gaza
College of Pharmacy
Course outline

Organic Chemistry (2) for Pharmacy Students
Sep 2020

- Course name :- Organic Chemistry 2
- Course Code :- PHCH 2306
- Prerequisite :-
    1. General Chemistry (CHEM 1301)
    2. Organic Chemistry 1 (PHCH 1303)
- Lecturer :- Dr:- Kana'n Mahmoud Al Wuhaidi
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- Office Hours will be announced on the door of my room at 7th floor

Text book:-

- Organic Chemistry by ***John E. McMurry***
- Organic Chemistry by ***Jonathan Clayden***
- Synthesis of Essential Drugs by ***R.S. Vardanyan and V.J. Hruby***
- Writing Reaction Mechanisms in Organic Chemistry by ***Audrey Miller***

Week 1- (Benzene and Aromaticity)

- The main criteria for aromaticity
- Aromaticity and drugs
- Heterocycles and aromaticity
- Effect of aromaticity on polarity
- Effect of aromaticity on acidity
- Effect of aromaticity on basicity
- Inductive and mesomeric effects
- Aromaticity in drugs (Aromatic containing drugs)

Week 2 (Reactions of benzene and aromatic compounds)

- Electrophilic aromatic substitution
- Nucleophilic aromatic substitution
- Reactivity and Orientation
- Oxidation of benzene
- Reductions of benzene (Birch reduction)
- Poly nuclear aromatic hydrocarbon synthesis (Naphthalene, Anthracene and Phenanthrene).
- Drug synthesis including Electrophilic and nucleophilic aromatic substitution reactions

Week 3- Nomenclature

- Nomenclature of monofunctional group compounds such as amine, aldehyde, ketone, carboxy acid, ester, acid halide, amide and nitrile.
- Nomenclature of polyfunctional group compounds (matching of two or more of the above functionality)

Week 4-5 (Aldehydes and Ketones) Nucleophilic Additions

- Physical properties of aldheydes and ketones
- Acidity of aldheydes and ketones (α-hydrogen acidity)
- Preparation of aldheydes
- Preparation of ketones
- Feature of carbonyl group
- Nucleophilic addition and Relative reactivity of aldheydes and ketones
- Nucleophilic addition reactions
    a. With Water [Geminal diols)]
    b. With HCN [Cyanohydrins formation]
    c. With Grignard reagent[Alcohol formation]
    d. With Alcohol [Hemi- and Acetal formation]
    e. With Primary amines [Imine formation]
    f. With Secondary amines[Enamine formation]
    g. With Hydrazine in acidic media [Hydrazone formation]
    h. With Hydrazine in basic media '' Wolff-Kishner reaction [Alkane formation]
    i. With Hydroxylamine [Oxime formation]
    j. With Semicarbazide [Semicarbazone formation]
    k. With hydrides [Alcohol formation]
    l. With Phosphorous " Wittig Reaction" [alkene formation]
    m. With NaOH" Cannizzaro Reaction" [Disproportionation product]
- Nucleophilic addition to α,β-unsaturated carbonyl groups
- Some biological Nucleophilic addition reactions
- Drug synthesis including Nucleophilic addition reactions
- Aldehydes and ketones containing drugs

Week 6 (Carbonyl condensation reactions)

- α-carbanions as nucleophiles
- Self and mixed aldol condensation reactions
- Intramolecular aldol condensation reactions
- Self and mixed ester condensation [Claisen condensation]
- Intramolecular Claisen condensations [Dieckmann Cyclization]
- Biological carbonyl condensation
- Drug synthesis including Nucleophilic addition reactions

Week 7-8 (Carboxylic acids and derivatives)

- Physical properties of carboxylic acids
- Substituent effects on acidity of carboxylic acids
- Preparation of carboxylic acids
    a. Hydrolysis of nitriles
    b. Hydrolysis of esters
    c. Hydrolysis of amides
    d. Carboxylation of Grignard reagents
    e. Oxidation of alkyl benzene
    f. Oxidative cleavage of alkenes and alkynes
    g. Oxidation of primary alcohols
- Reactions of carboxylic acids (Derivatives)
    a. Chemistry of esters (reactions and preparations)
    b. Chemistry of acid anhydrides (reactions and preparations)
    c. Chemistry of amides (reactions and preparations)
    d. Chemistry of acid halides (reactions and preparations)
    e. Chemistry of Nitriles (reactions and preparations)
- Polyamides and polyesters [Chain-growth and step-growth polymers]
- Biological carboxylic acids (thiol ester)
- Drug containing carboxylic acids and derivatives

Week 9 (Carbonyl α-Substitution Reactions)

- Acidity of Alpha hydrogenatoms [Enolate ion formation]
- Keto-enol Tautomerism
- Alpha-Halogenation of ketones and aldehydse
- Alpha-Halogenation of Carboxylic acids [Hell-Volhard-Zelinski reaction]
- Halogenation of enolate ions[Haloform reactions]
- Alkylation of enolate [Malonic ester alkylation]
- Drug synthesis via carbonyl alpha-substitution reactions

Week 10-11 (Aliphatic, aromatic amines and phenols)

- Physical properties
- Morphine alkaloids and rule
- Amine basicity and relative basicity of aromatic and aliphatic amines
- Preparation of aliphatic and aromatic amines
    a. S_N2 reactions of alkyl halides with amines
    b. Gabriel Synthesis
    c. Reduction of nitriles and amides using $LiAlH_4$
    d. Reductive amination of aldheydes and ketones
    e. Hofmann and Curtis Rearrangements
    f. Reduction of nitro compounds

- Reactions of Amines
    a. Alkylation
    b. Acylation
    c. Hofmann Elimination
    d. N-Oxidation
    e. Amines and sulfonamide [Sulfa drugs]
    f. Diazonium salts and Sandmeyer reaction
    g. Azo compounds and dyes
- Amines containing drugs
- Physical properties [Solubility, antiseptic and disinfectant features] of phenols
- Phenols acidity
- Preparation of phenols
    a. Alkali fusion of aromatic sulfonates
    b. Hydrolysis of arenediazonium salts
- Reactions of phenols
    a. Alcohol-like reactions [Nucleophilic substitutions and esterification]
    b. Electrophilic aromatic substitution [Kolbe-Schmitt Carboxylation]
    c. Oxidation of phenols
    d. Claisen rearrangement

Week 12-14 (Biomolecules- Short preview)

- Lipids
- Amino acid and Proteins
- Carbohydrates
- Applications

What is pharmacy science?

WHAT IS PHARMACY

"It's the science and technique of preparing & dispensing medication"

Pharmacy combines the study of biology & chemistry to ensure safe consumption of medication & drugs

Example:

Pharmacists give advice on the best and most suitable medication for you

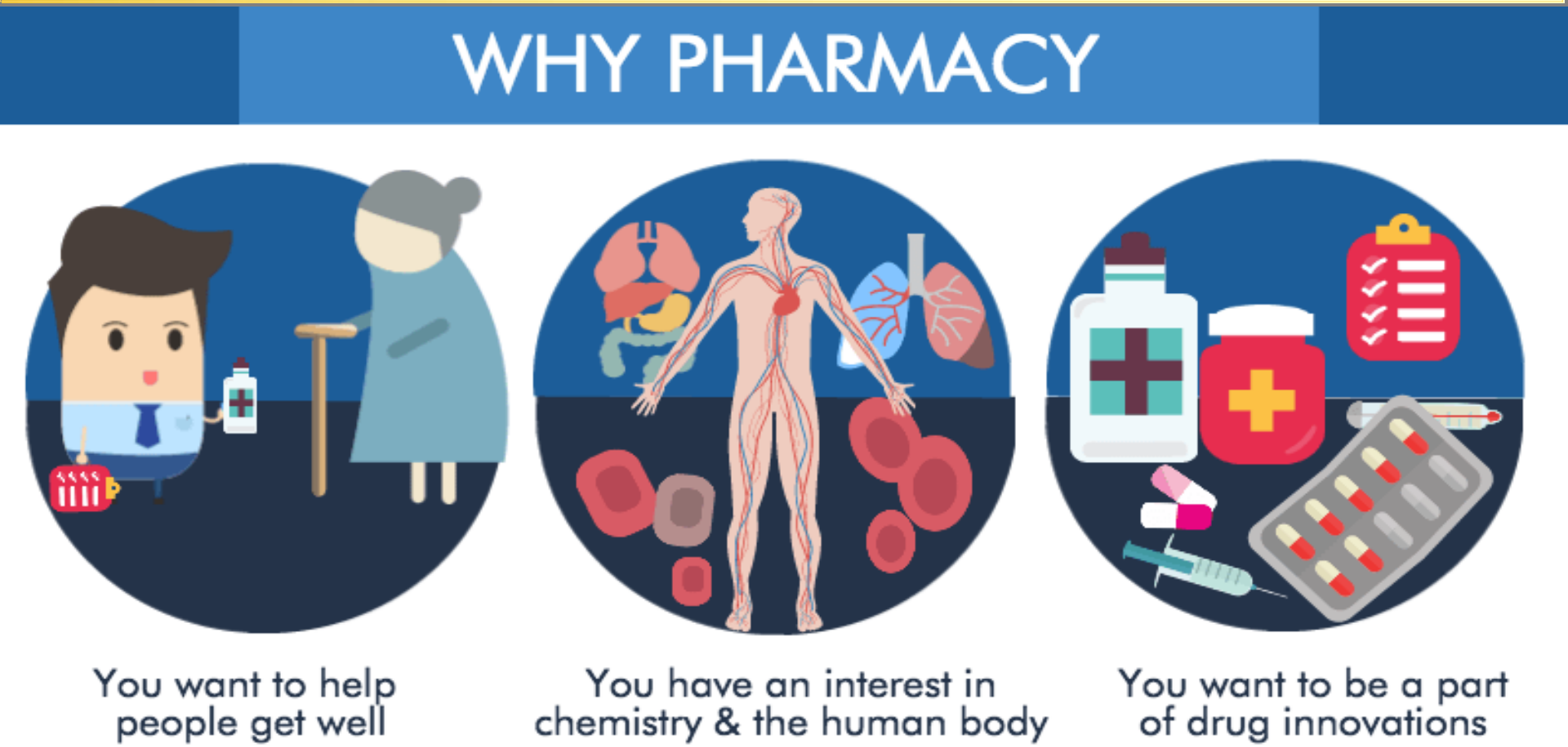
The field of Pharmacy combines the study of :-

a- Biology
b-Chemistry

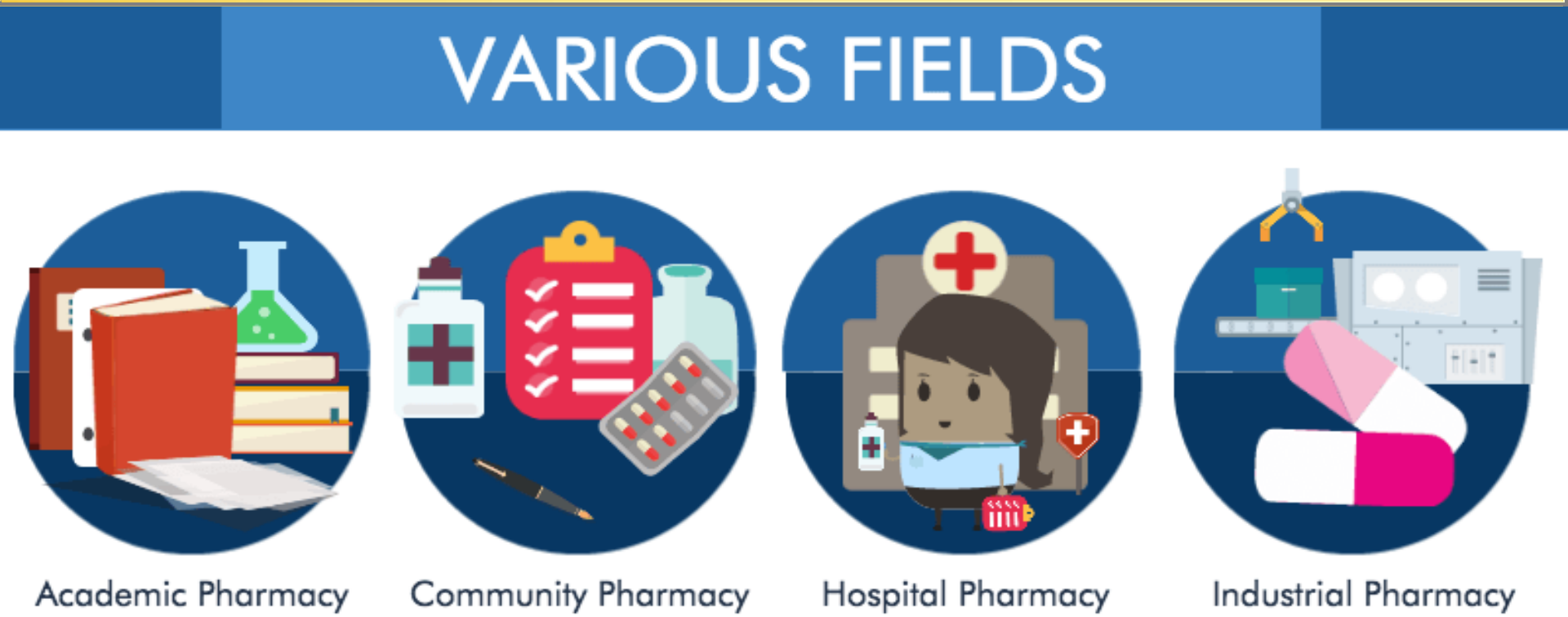
to ensure that the medication and drugs that we consume are safe and effective.

Pharmacists aren't just there to count pills and dispense medicine. Whenever you pop a pill to ease your headache, know that the manufacturing and drug composition of that pill was carefully monitored by a qualified person "pharmacist".

Why you choose to be a pharmacist ?

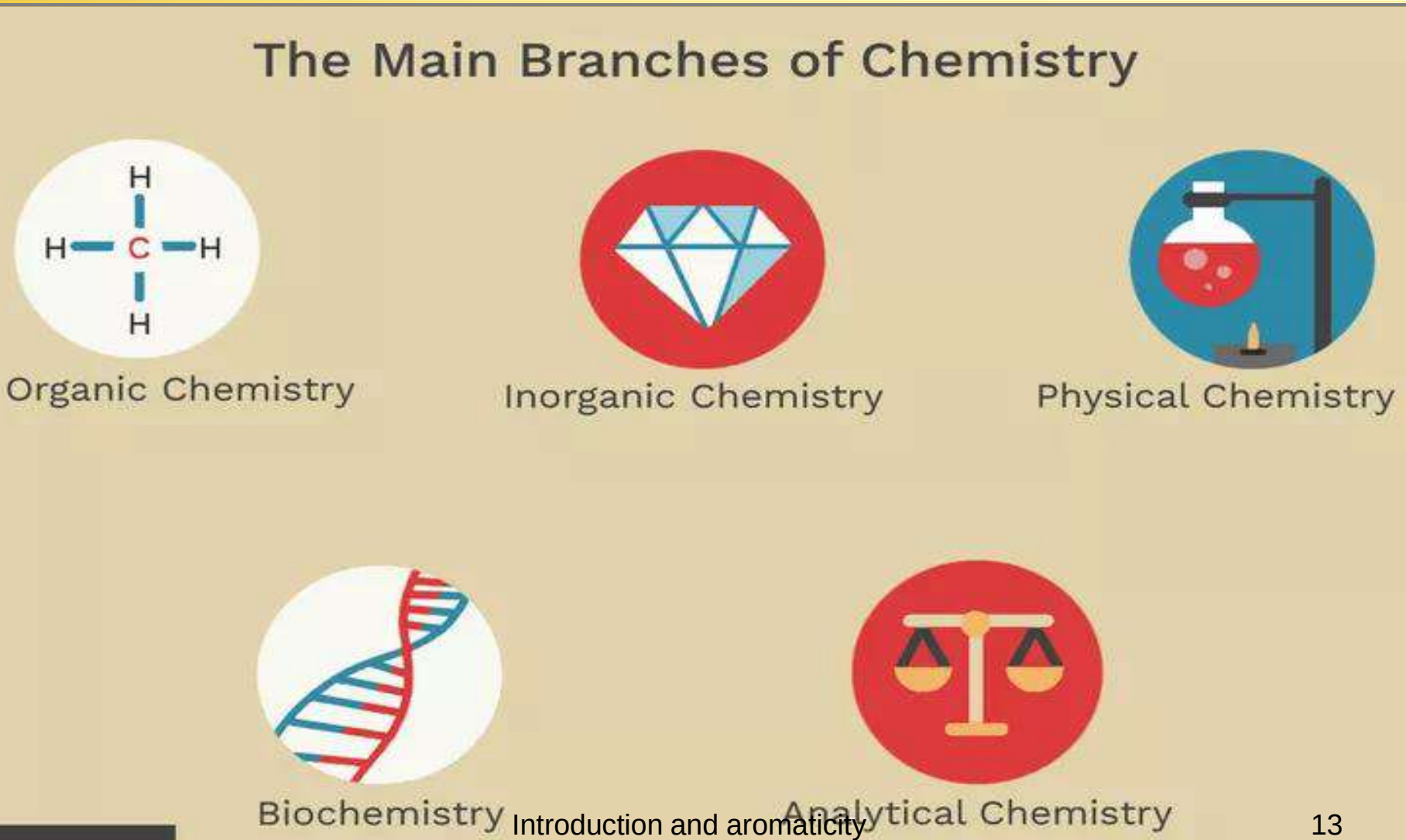


After graduation; What about work or job opportunities? Are you a drug seller ?



What Skills Do You Need to Study Pharmacy?

Chemistry and Science



Chemistry courses in pharmacy plan

1.	General Chemistry	[1 Course]
2.	Pharmaceutical Organic Chemistry	[2 Courses]
3.	Pharmaceutical physical Chemistry	[2 Courses]
4.	Pharmaceutical analytical Chemistry	[2 Courses]
5.	Pharmaceutical PhytoChemistry	[2 Courses]
6.	Pharmaceutical Chemistry	[4 Courses]
7.	Pharmaceutical Biochemistry	[3 Courses]
8.	Clinical Chemistry	[1 Course]
9.	Practical chemistry Labs	[12 labs]

What is the relationship between chemistry in general and organic chemistry in particular ?

As pharmacy student you have to know;

- **Drugs are chemical compounds; whatever the origin of these drugs; plant , animal or synthetic one. (ex aspirin tree**

- **Each pharmaceutical compound " Drug" is classified as chemical compound; while not each chemical compound is classified as pharmaceutical compound "Drug".**

- **you have to know that there is a strong relation between pharmacy and organic chemistry , since the organic chemistry is being involved strongly in all pharmaceutical sciences "Drugs" in particular and in the bio-system in general.**

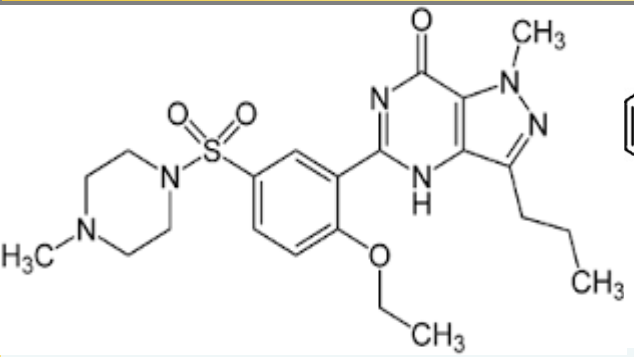
What is organic chemistry?

A branch of chemistry that is concerned with studying compounds that contain both carbon and hydrogen.

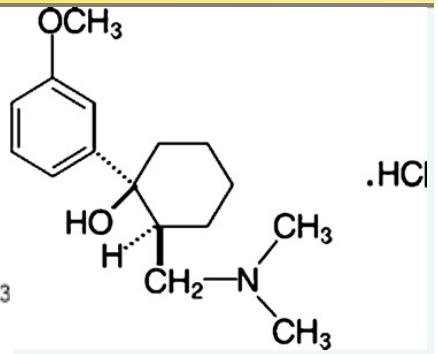
The old definition was; chemistry of carbon. After Graphite and Diamond as inorganic compounds which have only carbon.

So the organic compound must have the C-H bond; otherwise the compound is an inorganic one

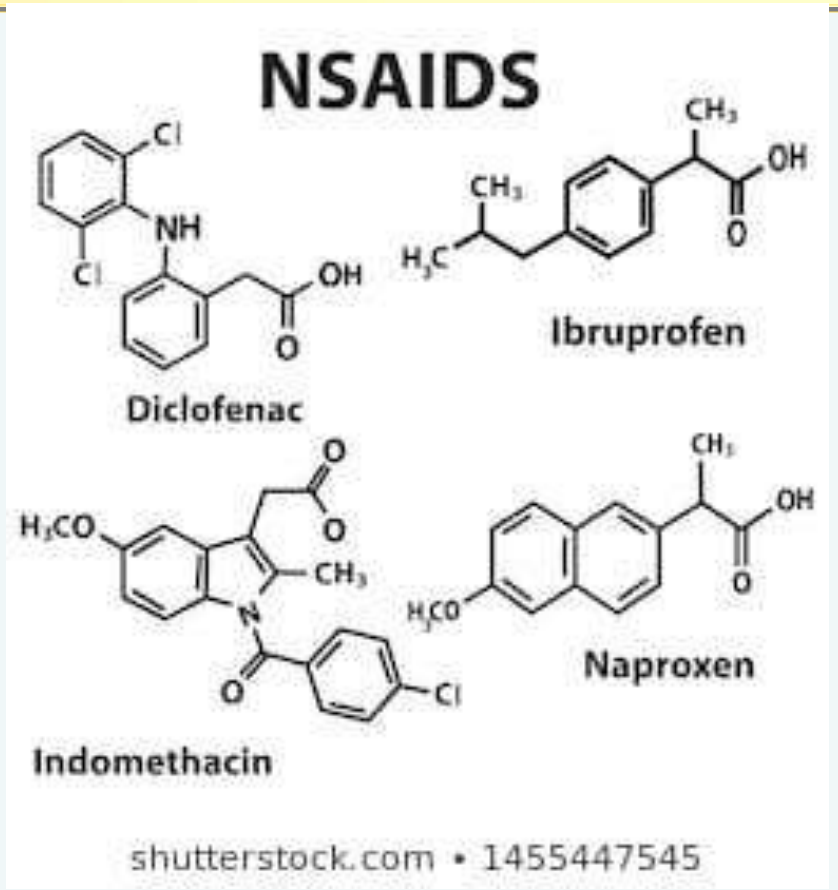
Some examples about well-known Drugs as organic compounds.

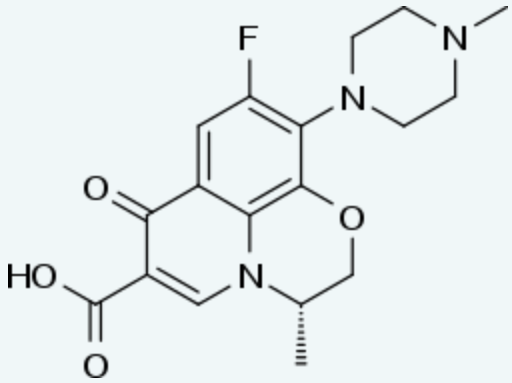


Sildenafil

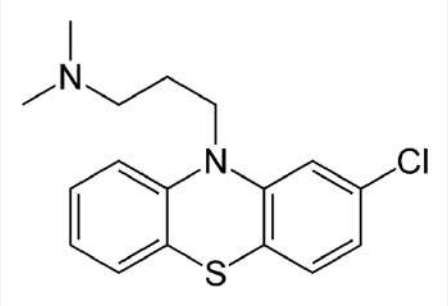


Tramadol





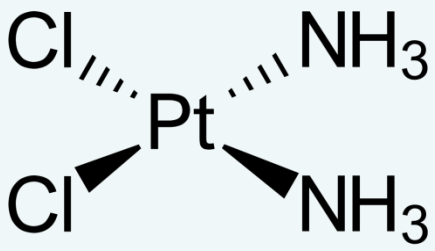
Levox



Chlorpromazine

Not all drugs are organic compounds !!!

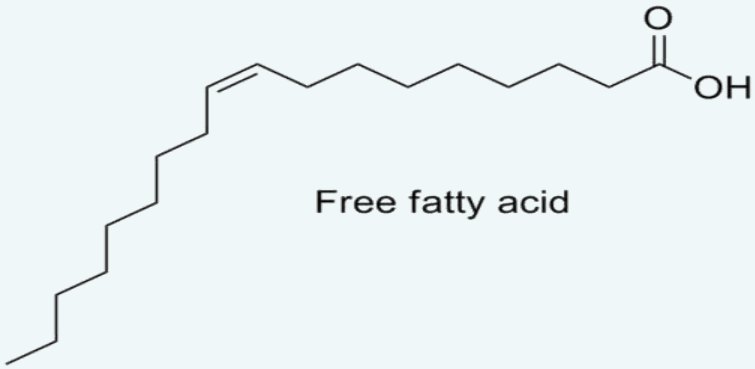
- **The majority of drugs are organic with few cases are inorganic such as; Cisplatin**



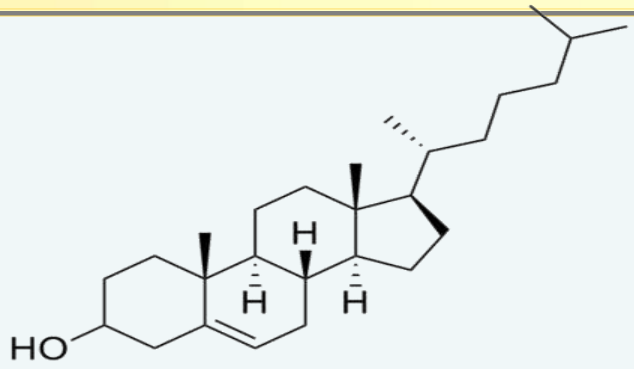
Cisplatin

- **Anti-acid such as these that contain $Al(OH)_3$ $Mg(OH)_2$, $NaHCO_3$ and $CaCO_3$ are classified as inorganic**

Some well-known Lipids as organic compds

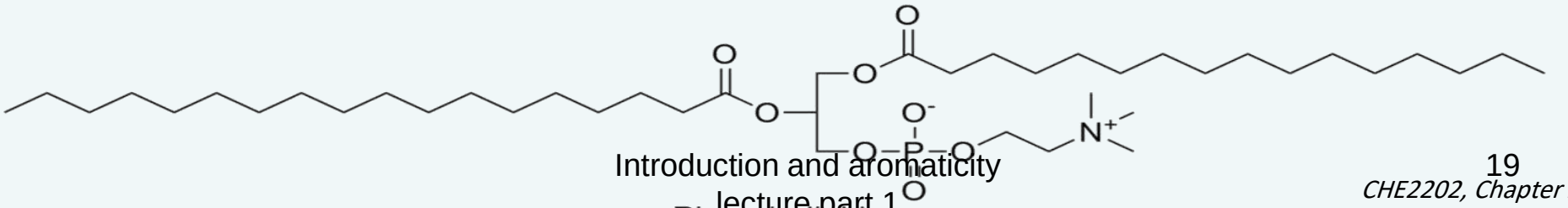


Free fatty acid



Cholesterol

Triglyceride



Phospholipid

Vitamins as organic compounds

THE CHEMICAL STRUCTURES OF VITAMINS

Vitamins are the essential nutrients that our body needs in small amounts. More specifically, an organic compound is defined as a vitamin when it is required by an organism, but not synthesised by that organism in the required amounts (or at all). There are thirteen recognised vitamins.

VITAMIN A

RETINOL
active form in mammalian tissues

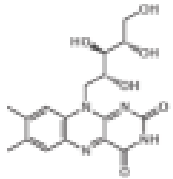
Important for eyesight. Also strengthens immune system and keeps skin and linings of parts of the body healthy.

VITAMIN B1

THIAMIN
can also occur in pyrophosphate ester form

Used to keep nerves & muscle tissue healthy. Also important for processing of carbohydrates and some proteins.

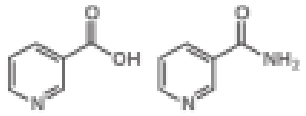
VITAMIN B2



RIBOFLAVIN
excess turns urine bright yellow

Important for body growth, red blood cell production, and keeping the eyes healthy. Also helps processing of carbohydrates.

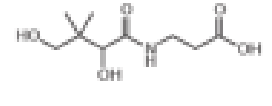
VITAMIN B3



NICOTINIC ACID — NICOTINAMIDE
niacin is collective name for these compounds

Helps with digestion and digestive system health. Also helps with the processing of carbohydrates.

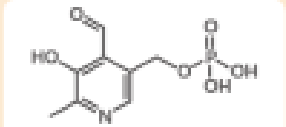
VITAMIN B5



PANTOTHENIC ACID
also occurs in pyrophosphate ester form

Important for manufacturing red blood cells and maintaining a healthy digestive system. Also helps process carbohydrates.

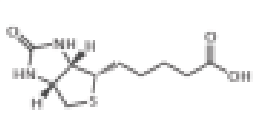
VITAMIN B6



PYRIDOXAL PHOSPHATE
active form in mammalian tissues

Helps make some brain chemicals; needed for normal brain function. Also helps make red blood cells and immune system cells.

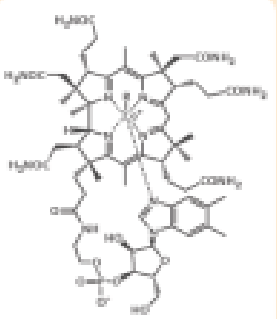
VITAMIN B7



BIOTIN
produced by intestinal bacteria

Needed for metabolism of various compounds. Often recommended for strengthening hair, but evidence is variable.

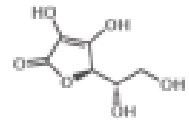
VITAMIN B12



COBALAMIN
usually contains CN on the R group

Important for the nervous system, for making red blood cells, and helps in the production of DNA and RNA.

VITAMIN C



ASCORBIC ACID
deficiency can cause scurvy

Important for a healthy immune system, helps produce collagen, used to make skin and other tissues. Also helps wound healing.

VITAMIN D

CHOLECALCIFEROL
natural form, different form used in supplements

Important for bone health and maintaining the immune system function. May also have a preventative role in cancers.

VITAMIN E

ALPHA-TOCOPHEROL
group includes tocopherols & tocotrienols

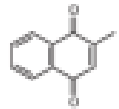
An antioxidant that helps prevent damage to cells and may have a preventative role in cancer. Also helps make red blood cells.

VITAMIN B9

FOLIC ACID
found as tetrahydrofolate in food

Important for brain function & mental health. Aids production of DNA & RNA. Important when tissues are growing quickly.

VITAMIN K



MENADIONE
all K vitamins are menadione or derivatives

Helps blood clot properly, & plays a key role in bone health. Newborns receive vitamin K injections to prevent bleeding.

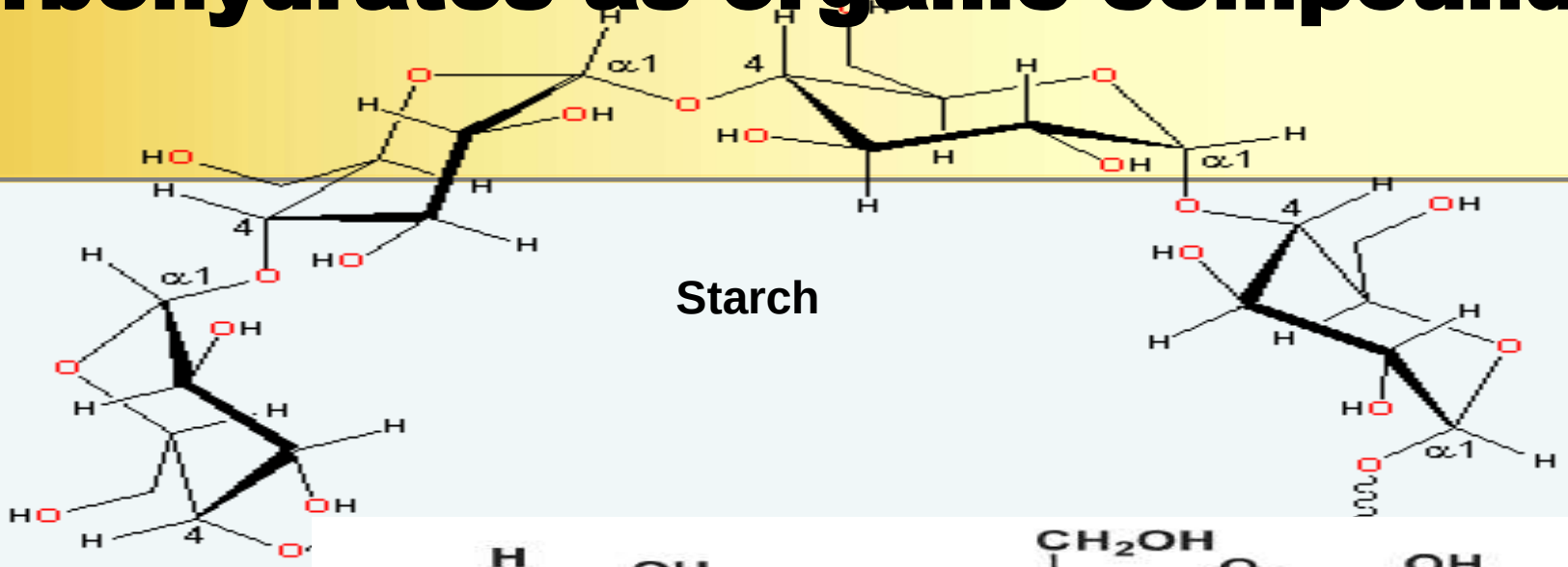
Key

Vitamins can be divided broadly into two classes.

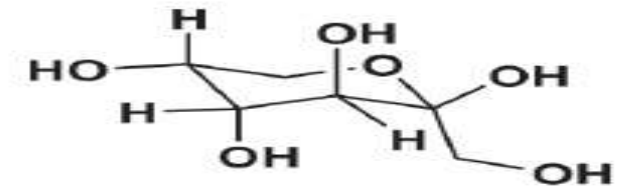
WATER-SOLUBLE VITAMINS
These vitamins are not stored in the body. As such, generally, they are required more frequently than the fat-soluble vitamins.

FAT-SOLUBLE VITAMINS
These vitamins are stored in the liver and fatty tissues until required. As such, they can be harmful if too much is taken in.

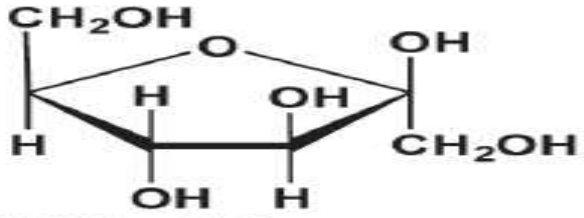
Carbohydrates as organic compounds



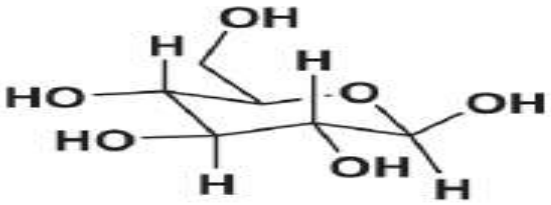
Starch



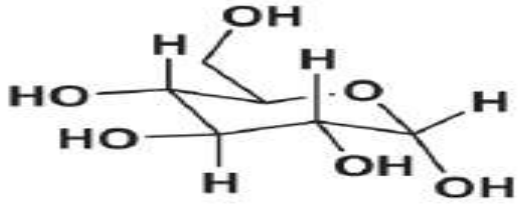
β-D-fructopyranose



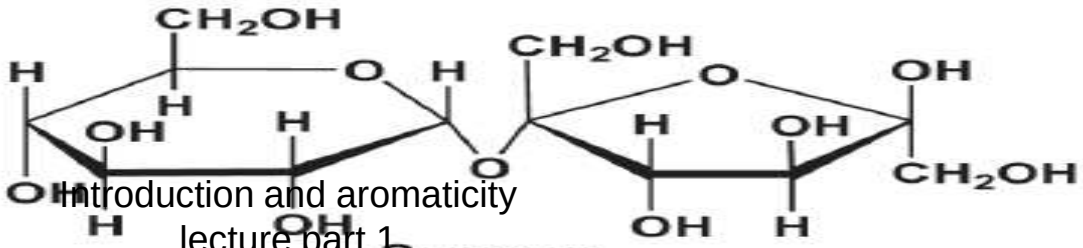
β-D-fructofuranose



β-D-glucopyranose

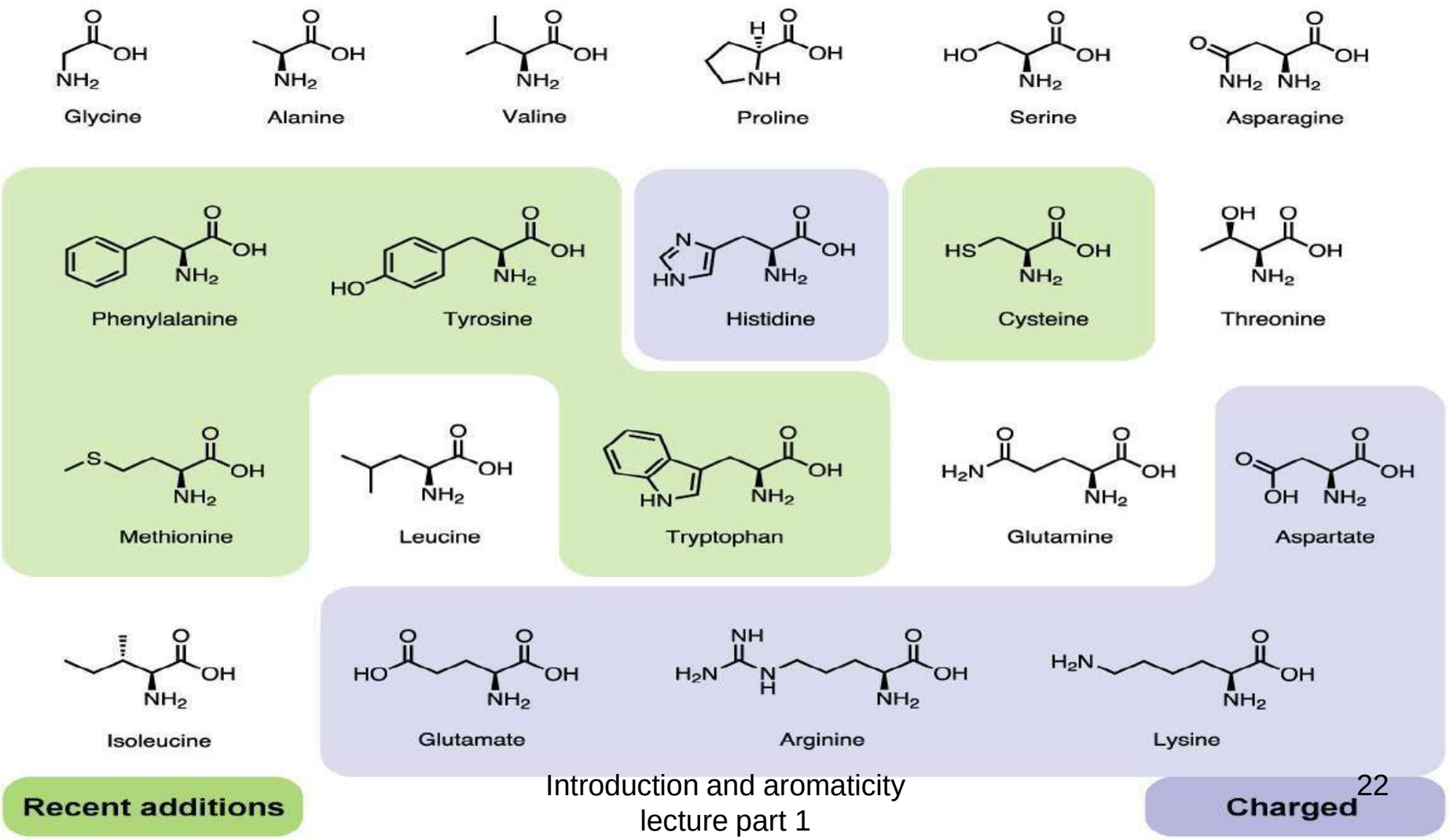


α-D-glucopyranose

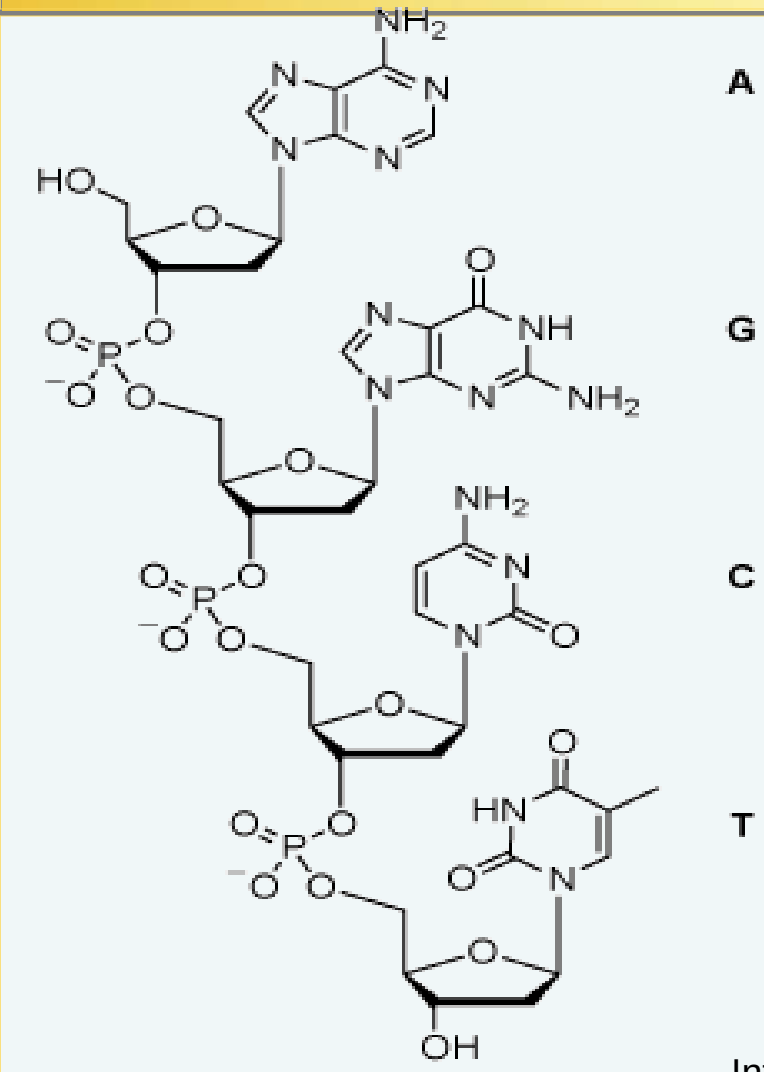


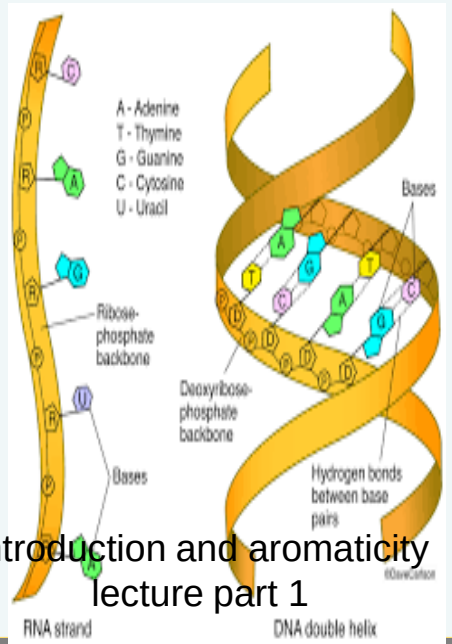
Sucrose

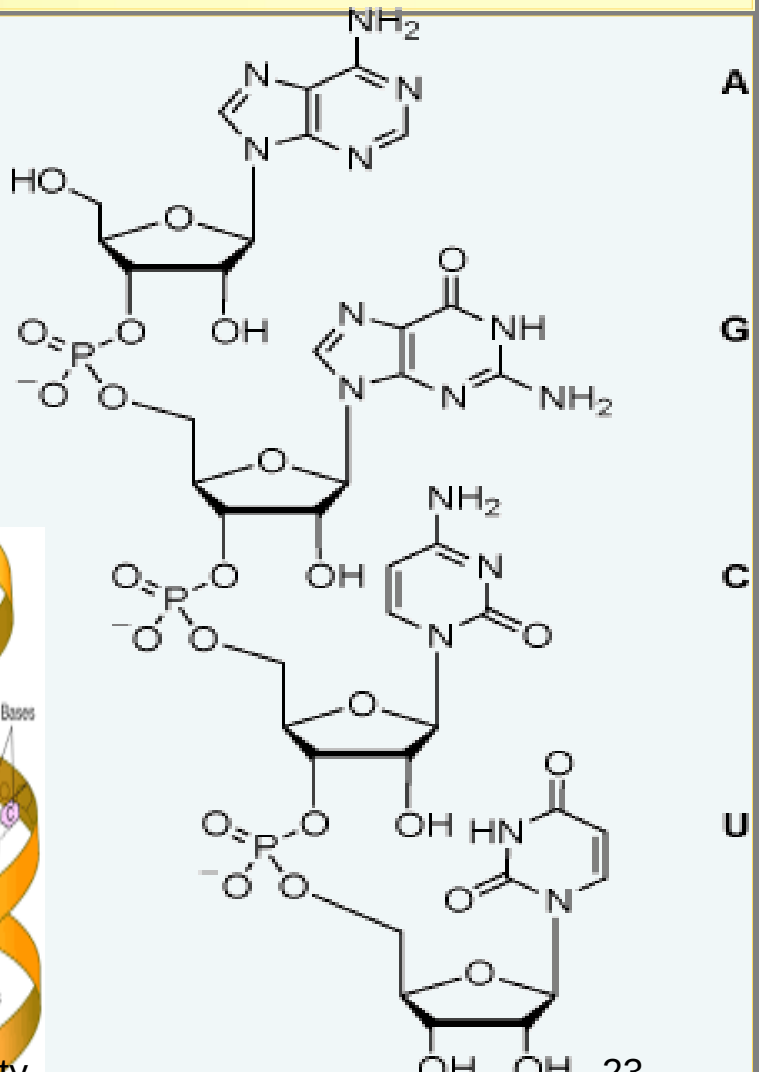
Amino acids as organic compounds
“ precursor of proteins”



Nucleic acids "RNA and DNA" as organic compounds







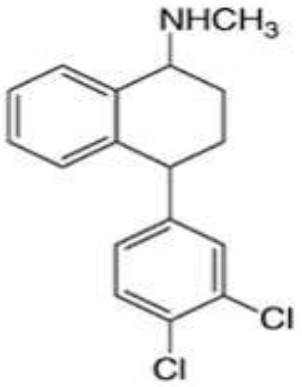
What student is expected to gain after completing this course?

At the end of this course you will be able to:- Deal with all types of related topics that include any organic compound (nomenclature, synthesis, physicochemical properties, drug receptor interaction, pharmacology,…..etc).

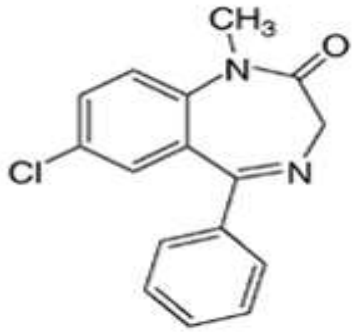
Lecture no. 2

Benzene and Aromatic Compounds

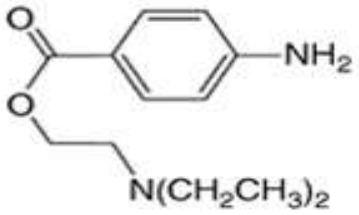
Selected drugs that contain benzene ring



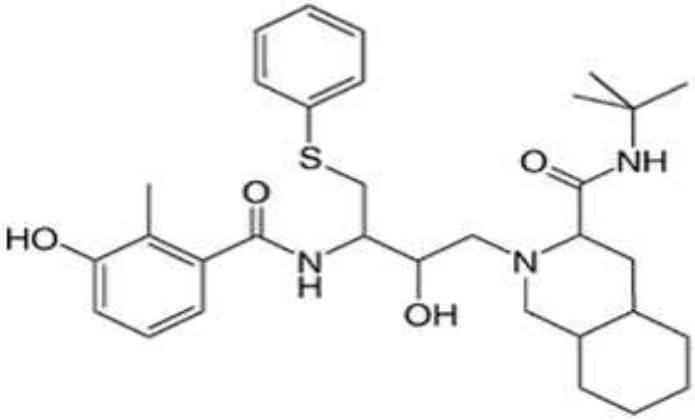
- Trade name: **Zoloft**
- Generic name: **sertraline**
- Use: a psychotherapeutic drug for depression and panic disorders



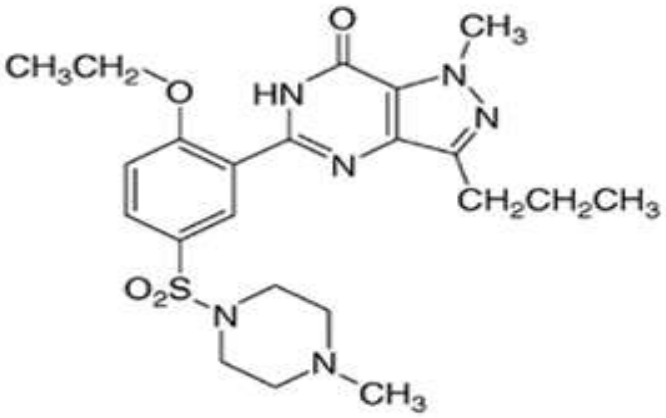
- Trade name: **Valium**
- Generic name: **diazepam**
- Use: a sedative



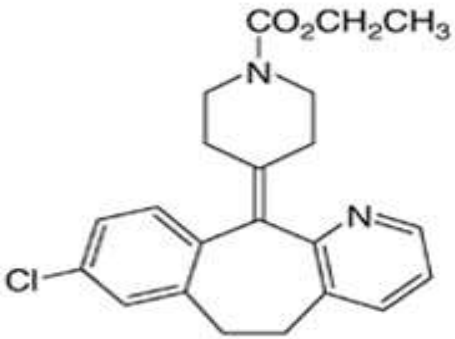
- Trade name: **Novocain**
- Generic name: **procaine**
- Use: a local anesthetic



- Trade name: **Viracept**
- Generic name: **nelfinavir**
- Use: an antiviral drug used to treat HIV



- Trade name: **Viagra**
- Generic name: **sildenafil**
- Use: a drug used to treat erectile dysfunction



- Trade name: **Claritin**
- Generic name: **loratadine**
- Use: an antihistamine for seasonal allergies

Aromaticity

- **A property of some unusually stable organic molecules such as benzene.**
- **The term "aromaticity" actually has nothing to do with smell. We saw that aromatic molecules:**
  a] Have an extremely high resonance
  b] have delocalized pi-electrons
  c] Energy (36 kcal/mol for benzene).
  d] undergo substitution rather than addition reactions.

N.B:-

a- Benzene is not the only aromatic compounds

b- Smell has nothing to do with aromaticity.

c- Aromatic compounds might be organic or inorganic

d- Aromatic feature might be inclusive in neutral, anionic or cationic species.

What are conditions that are responsible for aromaticity?!!!

There turn out to be 3 conditions a molecule must meet in order for it to be aromatic.
It's all or nothing. If any of these conditions are violated, no aromaticity is possible.

1- It must be cyclic.

2- The molecule must have [4n+2] pi electrons we'll

3- Every atom in the ring must be conjugated(Every atom in the ring must be able to participate in resonance).
Flat molecule

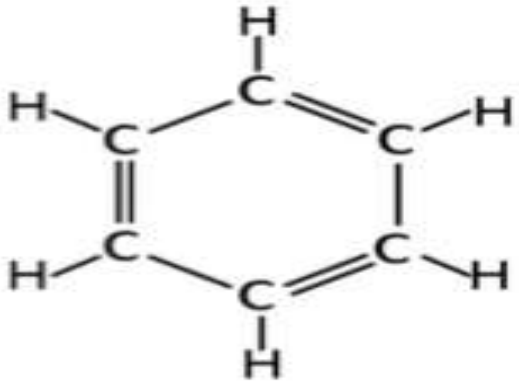
..

Benzene and Aromatic Compounds

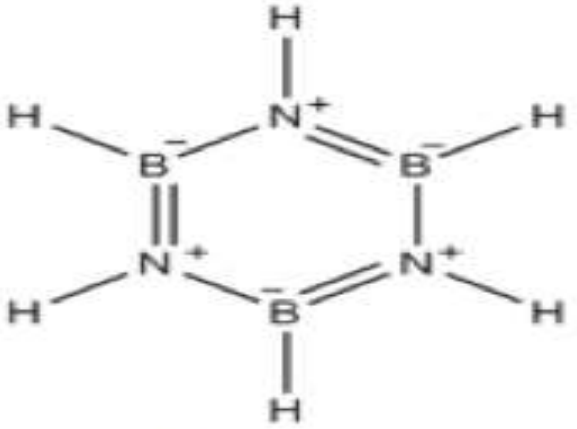
The Criteria for Aromaticity—Hückel's Rule

Considering aromaticity, a compound can be classified in one of three ways:

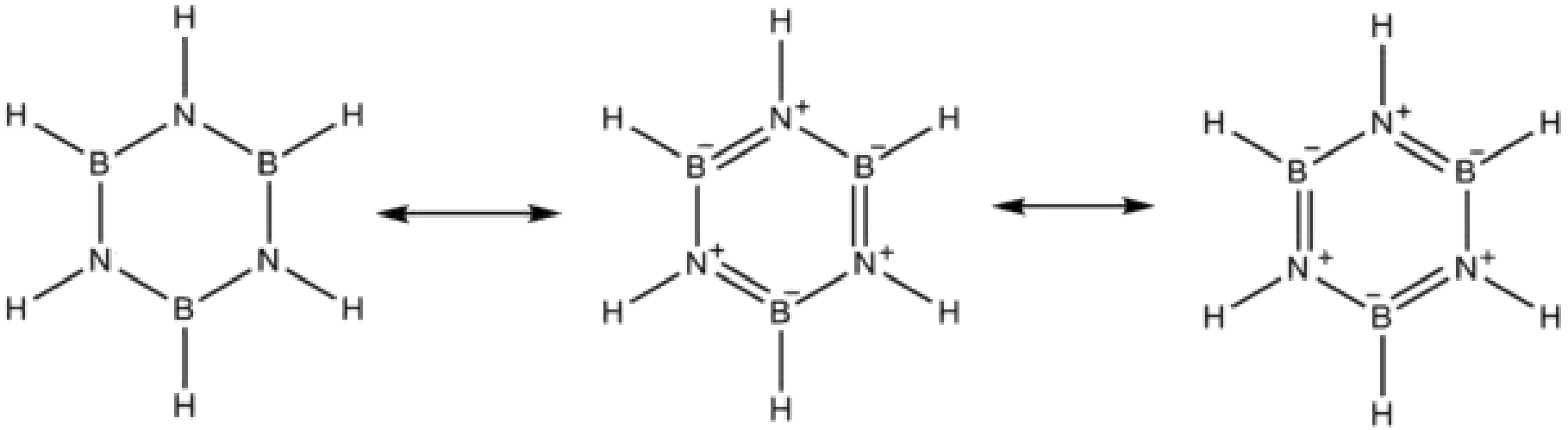
1. **<u>Aromatic</u>:- A cyclic, planar, completely conjugated compound with $4n + 2$ π electrons.**
2. **<u>Antiaromatic</u>:- A cyclic, planar, completely conjugated compound with $4n$ π electrons.**
3. **<u>Nonaromatic</u>:- A compound that lacks one (or more) of the following requirements for aromaticity:"cyclic, planar, and completely conjugated".**



Benzene

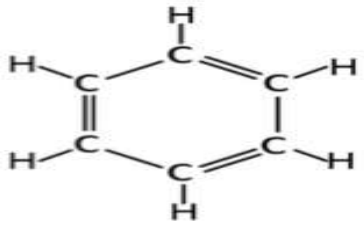


Borazine
Inorganic Benzene

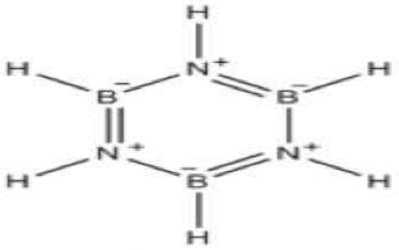


Aromatic compounds may be organic or inorganic

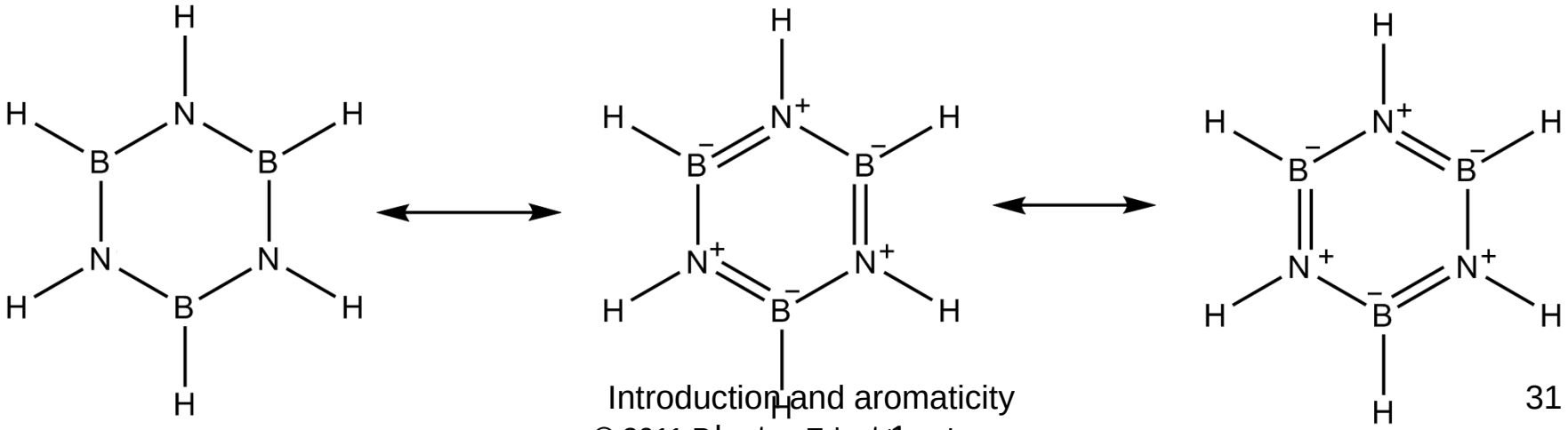
Borazine is aromatic as there are 3 nitrogen atoms in the structure of borazine that donate two electrons each. Boron doesn't donate any, but it has an empty p-orbital available through which the electrons can delocalize. Hence, in total it has 6 π-electrons. Though the delocalisation is lesser than that in benzene, it still is aromatic.



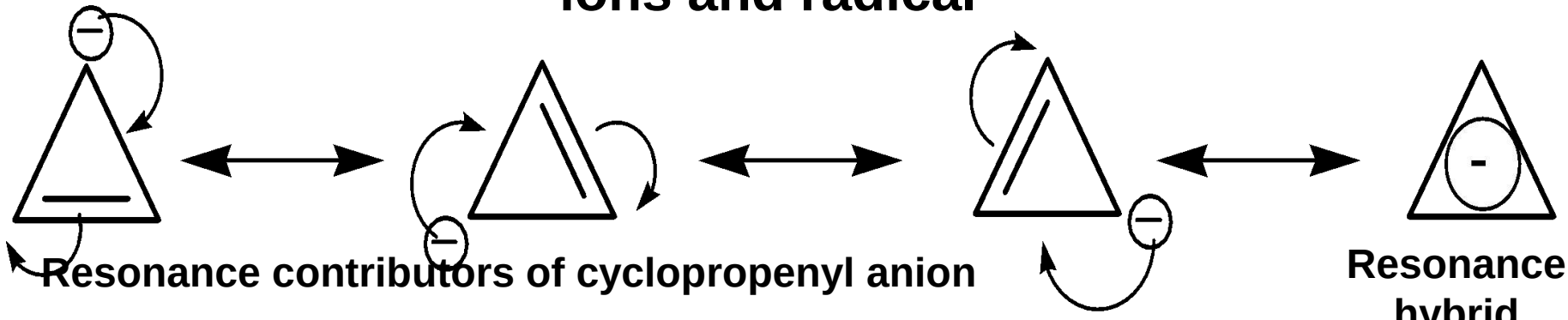
Benzene



Borazine
Inorganic Benzene

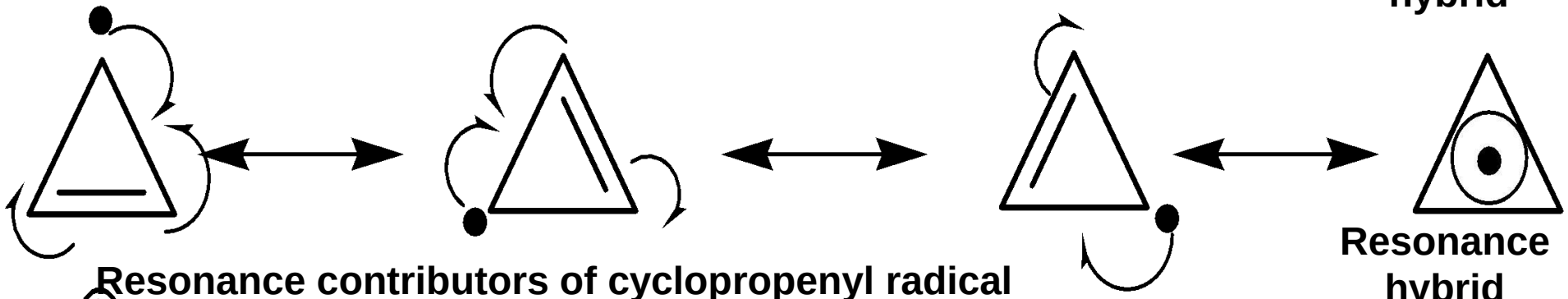


Aromaticity and resonance contributors of cyclopreopenyl ions and radical



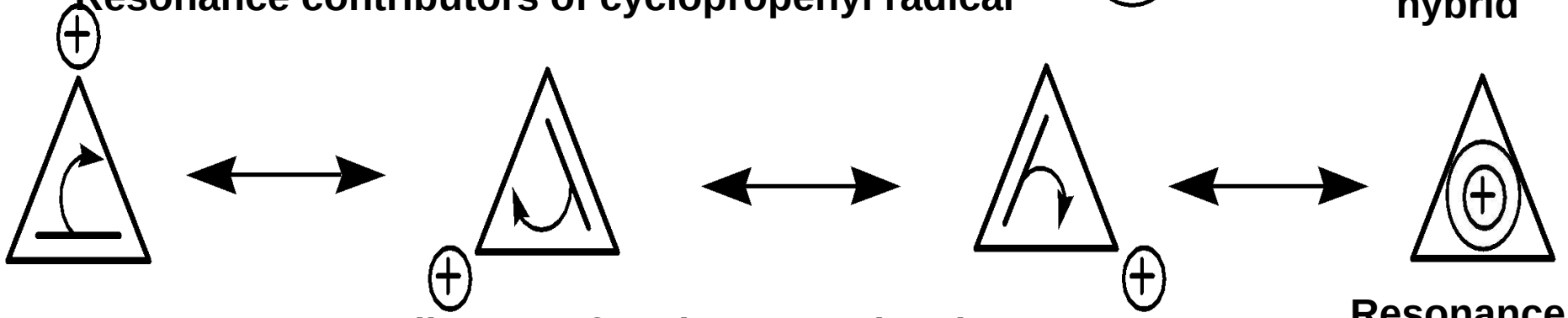
Resonance contributors of cyclopropenyl anion

Resonance hybrid



Resonance contributors of cyclopropenyl radical

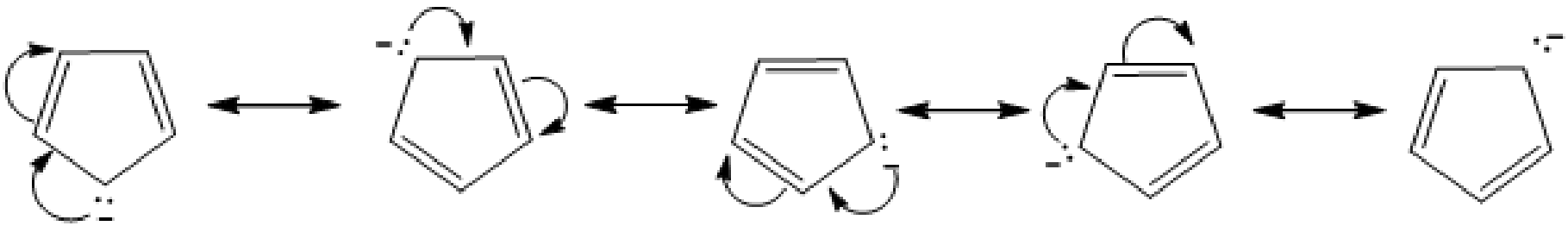
Resonance hybrid

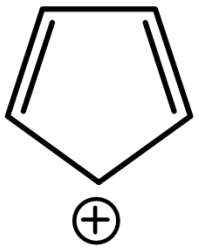


Resonance contributors of cyclopropenyl cation

Resonance hybrid

Aromaticity and resonance contributors of cyclopentadienyl and its ions and radical





cyclopentadienyl anion
- 6 π electrons
- contains $4n + 2$ π electrons

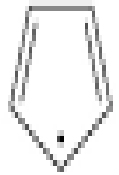
aromatic

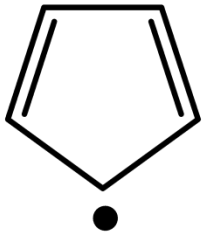
cyclopentadienyl cation
- 4 π electrons
- contains $4n$ π electrons

antiaromatic

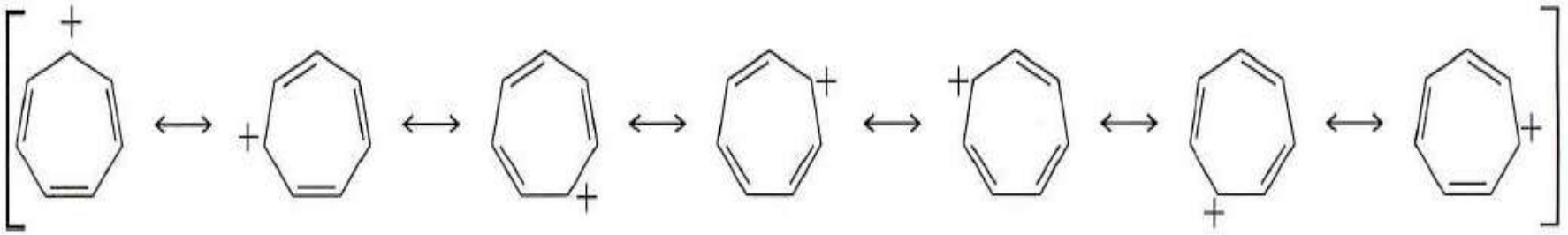
cyclopentadienyl radical
- 5 π electrons
- does not contain either $4n$ or $4n + 2$ π electrons

nonaromatic

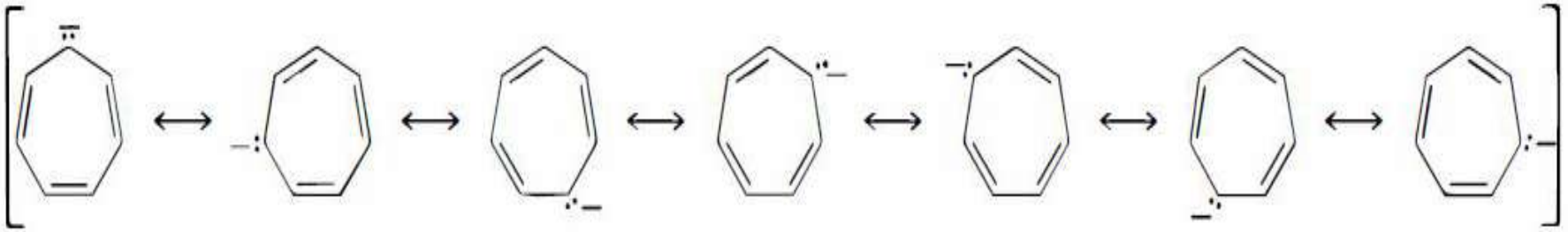




Aromaticity and resonance contributors of cycloheptatrienyl cation and the not aromatic cycloheptrienyl anion



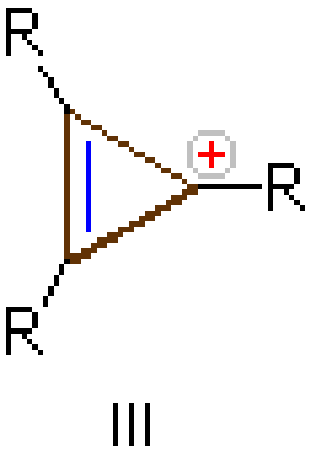
cycloheptatrienyl cation (tropylium ion): six pi electrons, aromatic



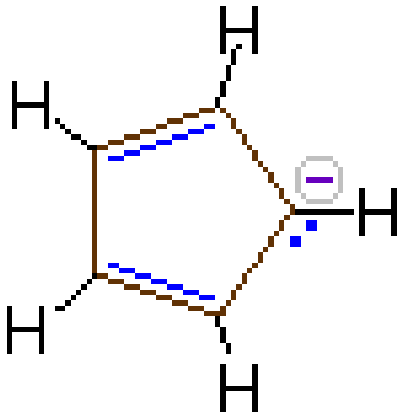
cycloheptatrienyl anion: eight pi electrons, antiaromatic (if planar)

The resonance picture gives a misleading suggestion of stability.

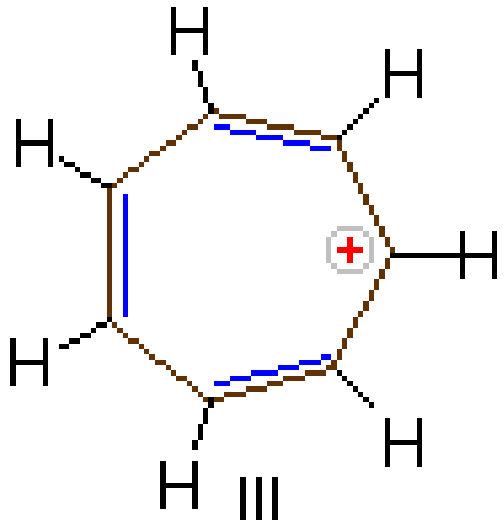
The most common cationic and anionic aromatic compounds



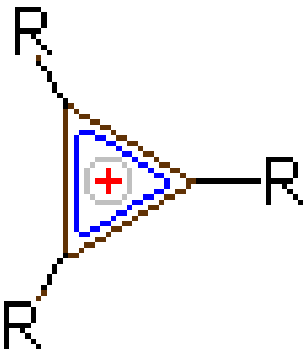
III

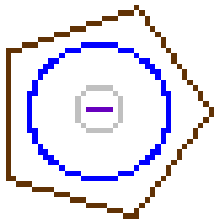


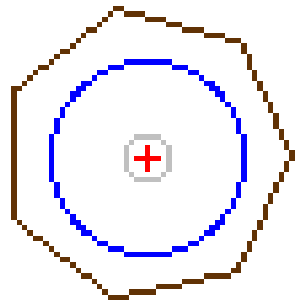
III

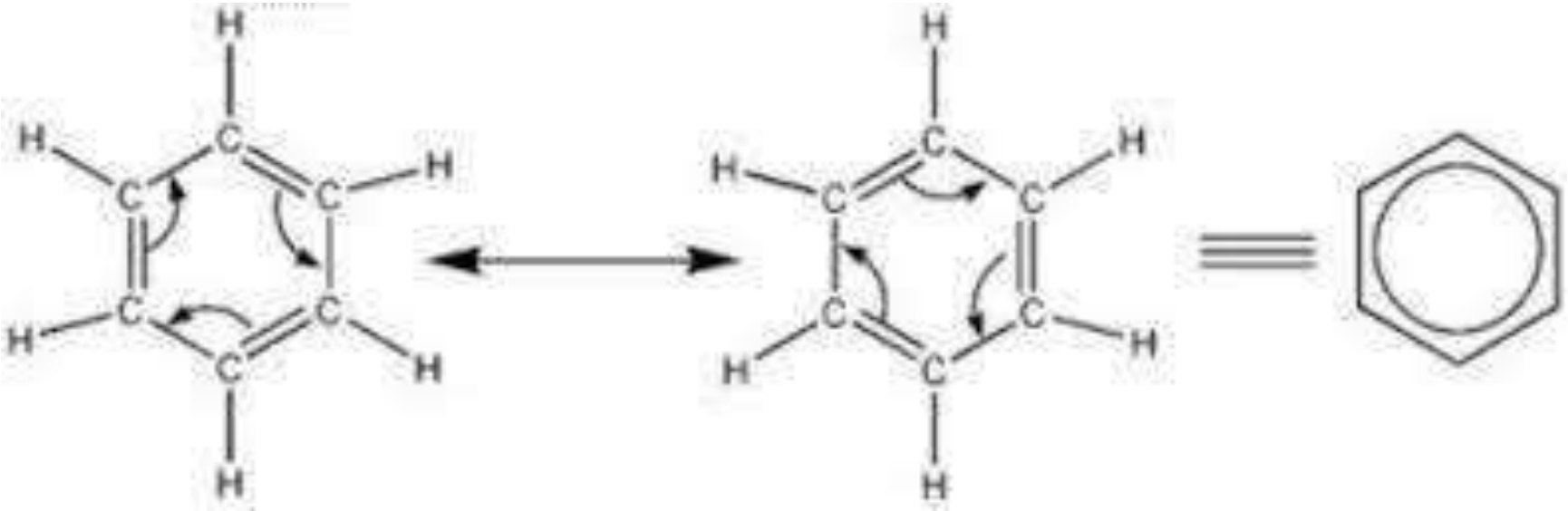


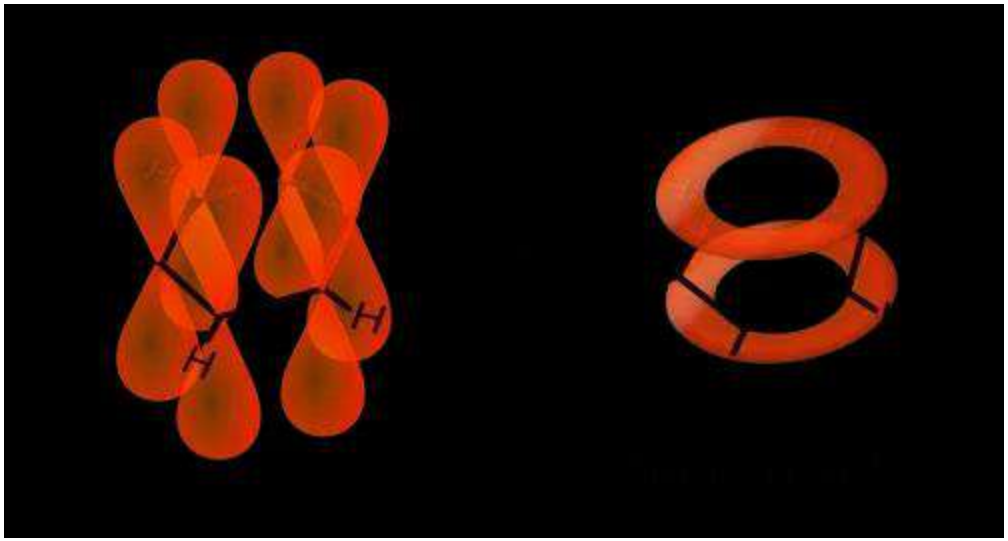
III

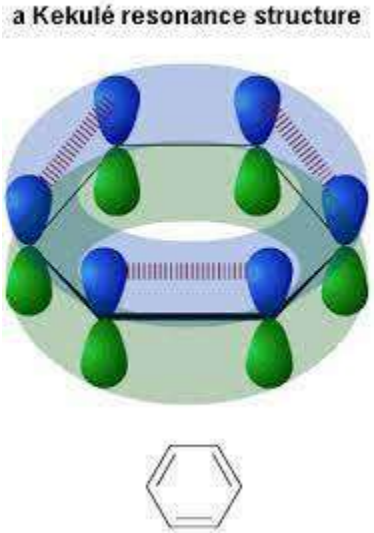




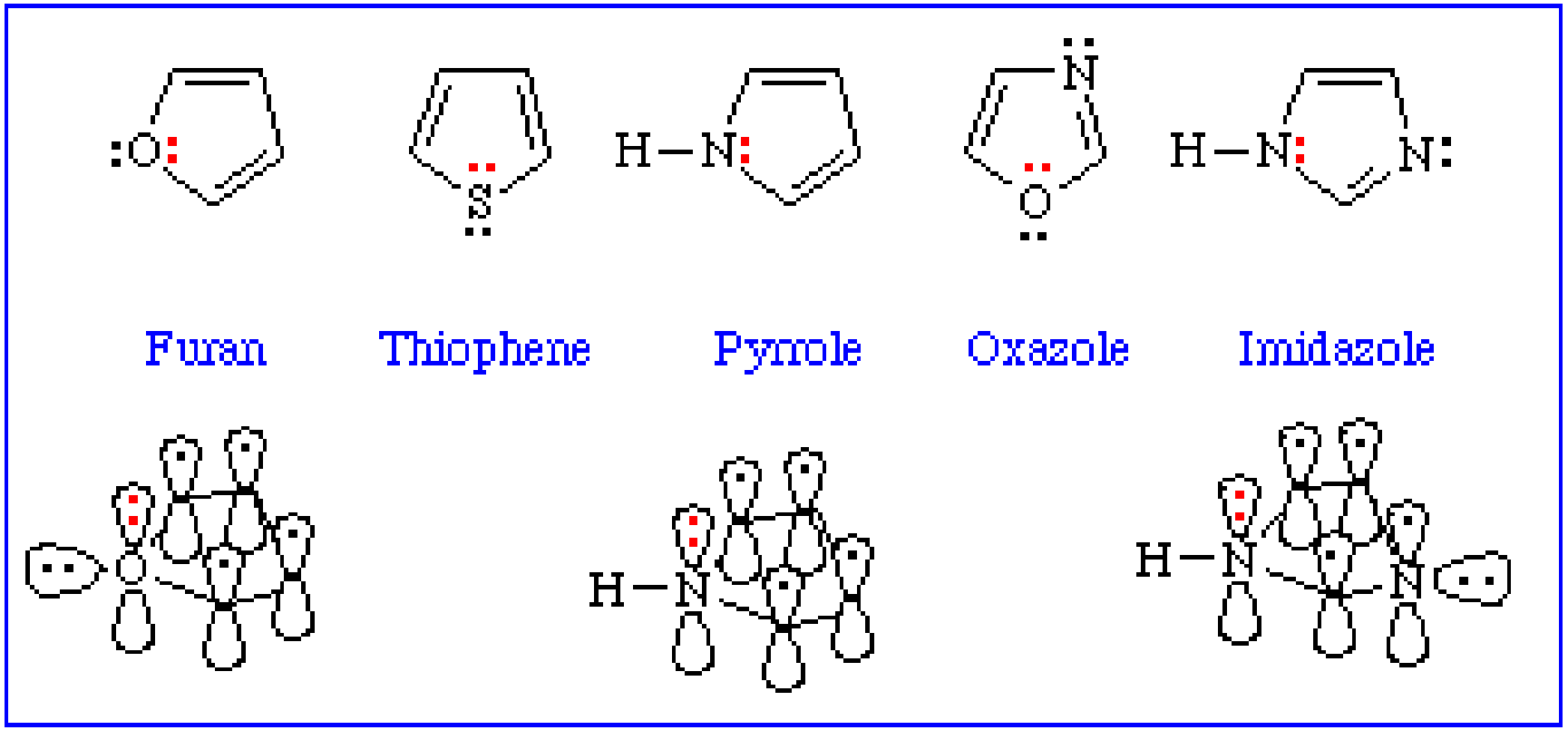






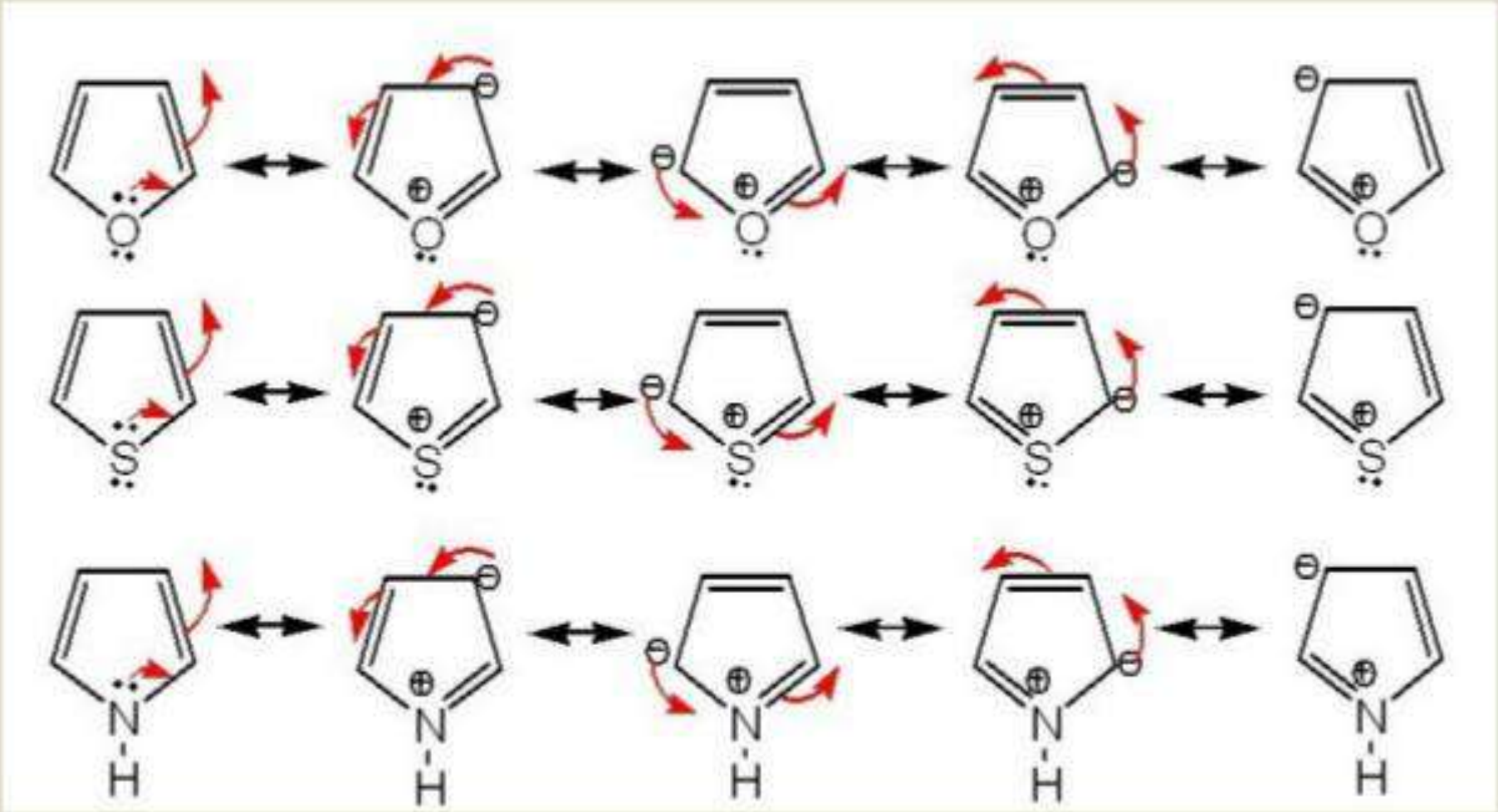


Some well-known Hetero-aromatic compounds

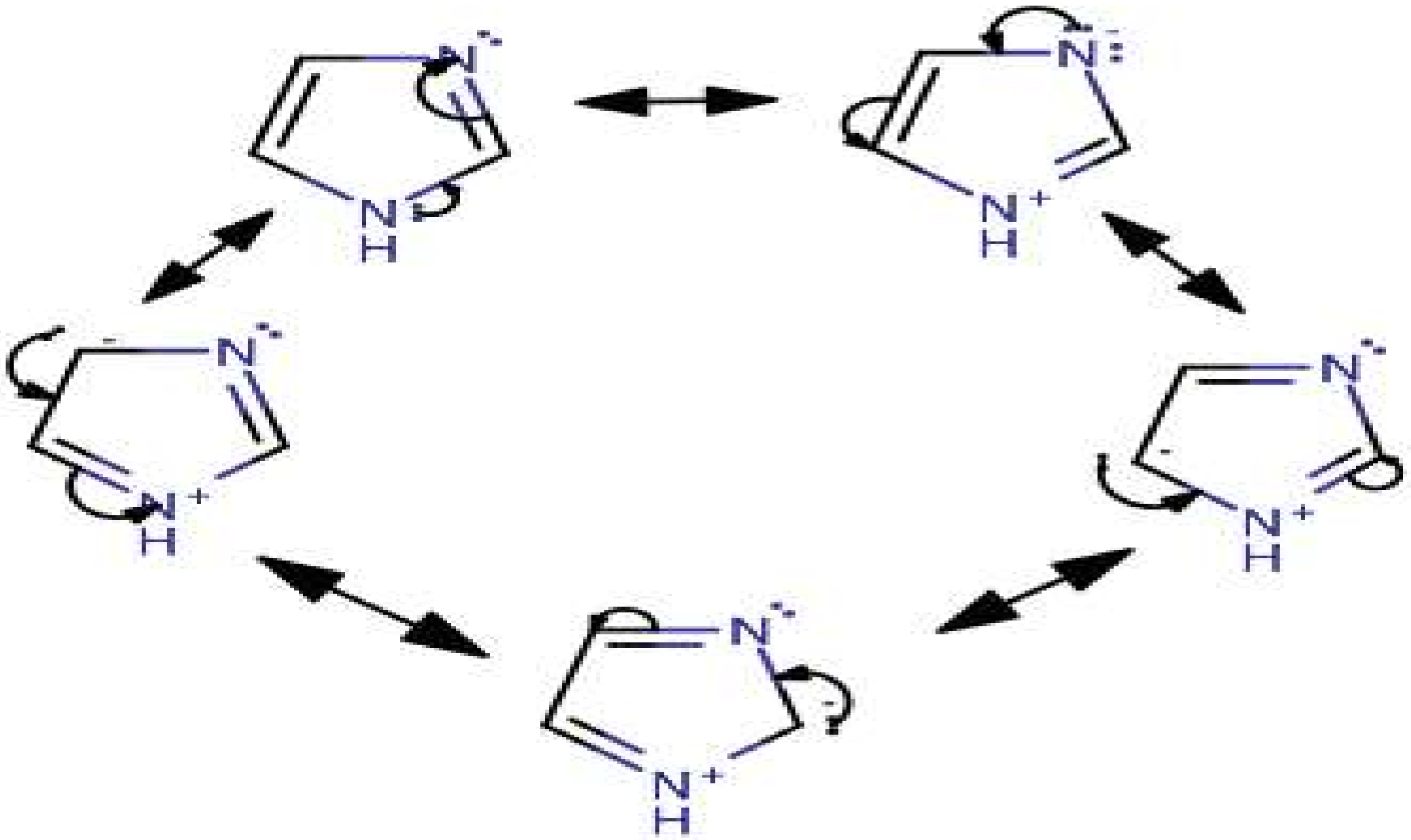


There is a sort of similarity between the above 5 compounds and cyclopentadienyl anion

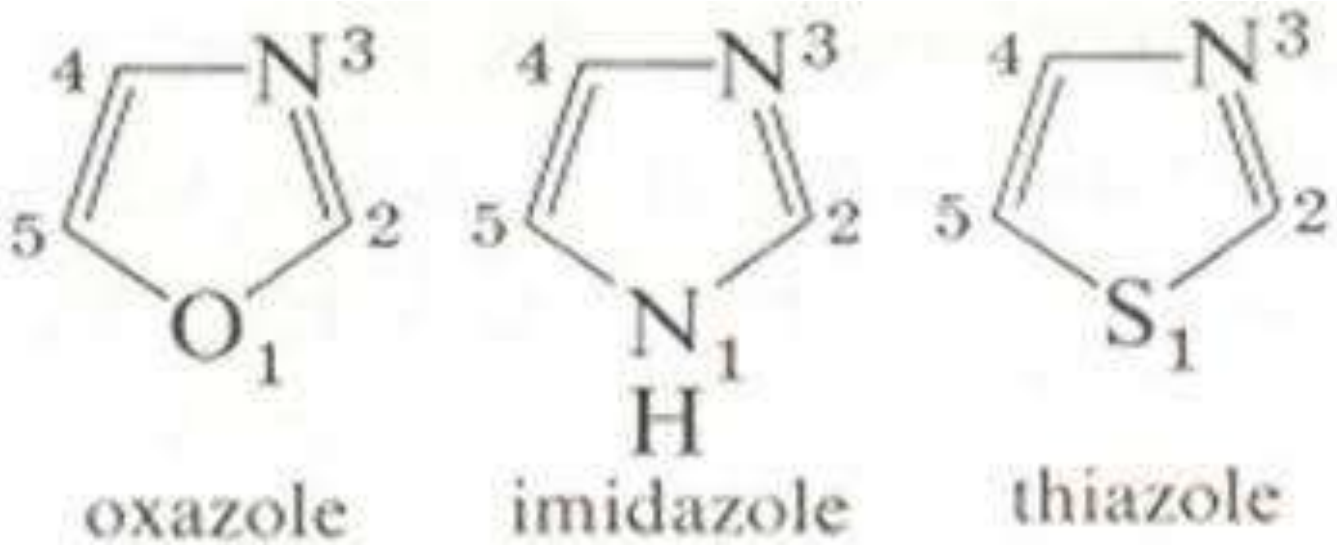
Resonance structures of furan Thiphene and Pyrrole



Imidazole ring and aromaticity



Imidazole, thiazole and oxazole have the same situation of aromaticity interpritation



The above three heterocycic compounds are aromatic; because the three requirements are available

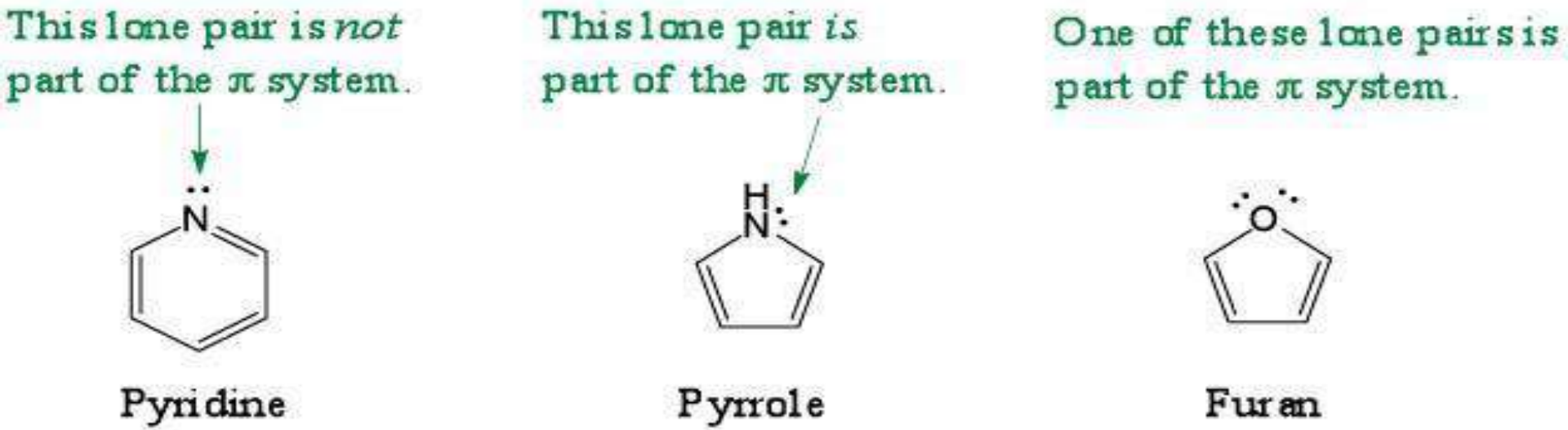
1- cyclic

2- 4n+2= 6

3- The six electrons resonate over the whole ring and each atom participate in this resonance

Lecture no. 3

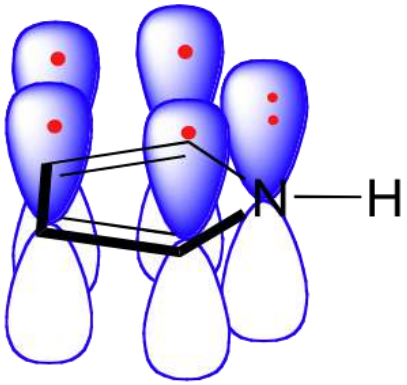
Effect of aromaticity on basicity

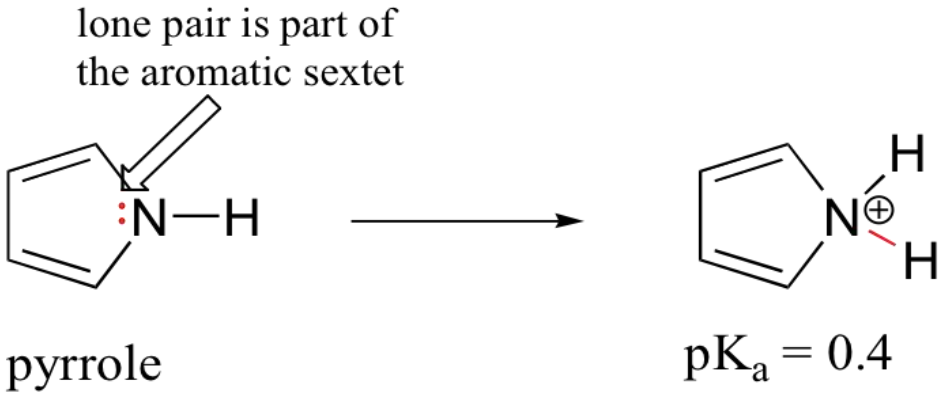


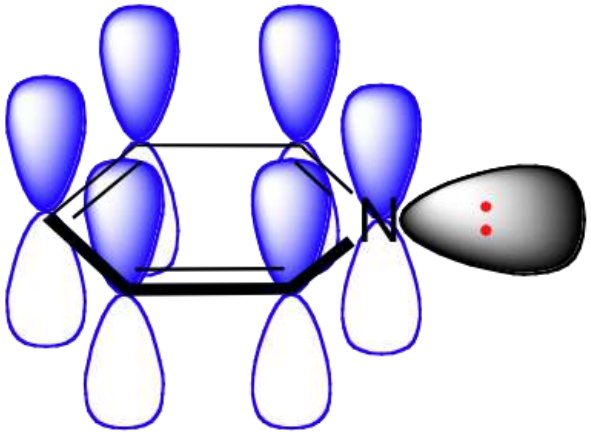
The Rule :- if the lone pair on nitrogen is a part of the Huckle electrons that are required to get aromaticity achieved; this case indicates that aromaticity is at the Expense of basicity .

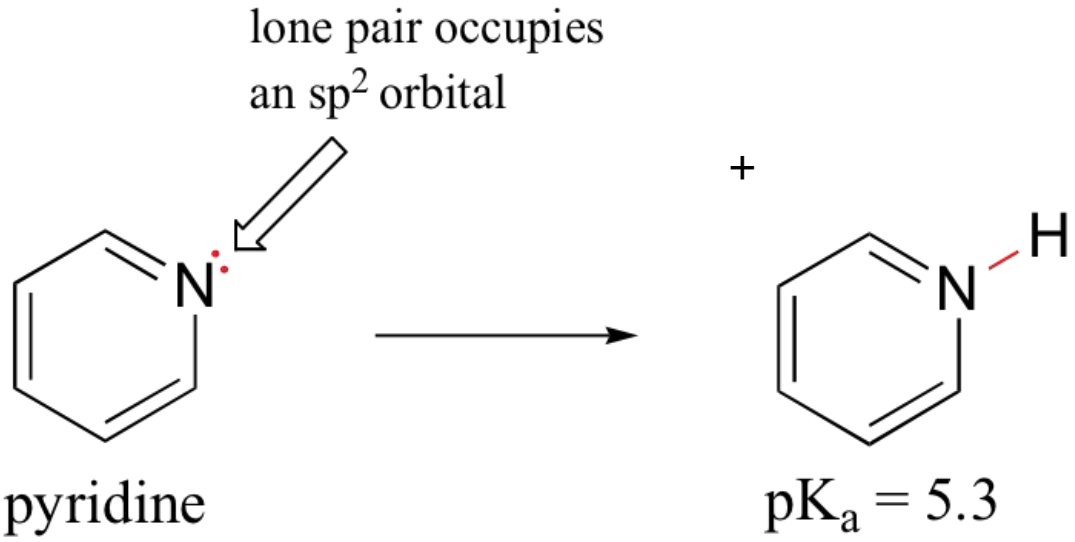
For example; in Pyrrole ; aromaticity affects negatively on nitrogen basicity due to the participation of nitrogen lone pair in creating aromaticity (this is called sixtet system). While in pyridine; the lone pair of nitrogen is localized on nitrogen atom; no need to enter the ring to create aromaticity since it is already aromatic having the sixtet system and no need otherwise electrons number becomes 8 which means destroying aromaticity is expected; while having aromaticity means stability.

How to make sure that your interpretation is correct? Or what is the proof of Pyrrole to be less basic than pyridine? What is reason responsible for different pKa values?

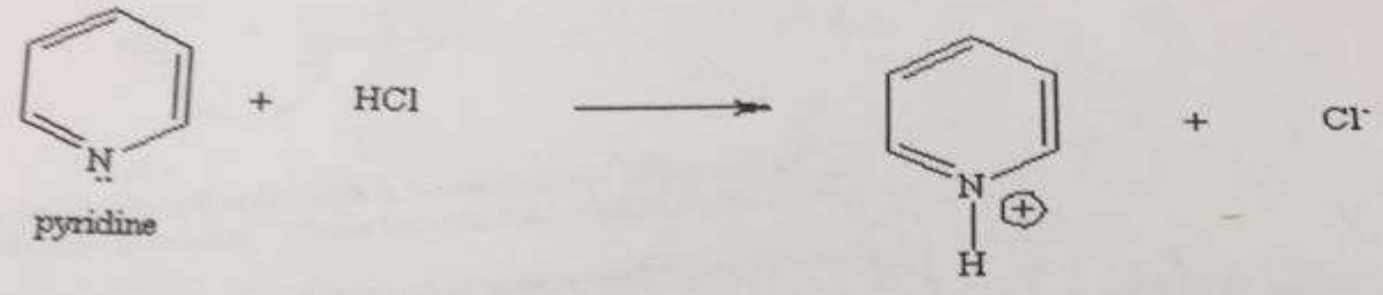








Explain why pyrrole is a much weaker base than pyridine.



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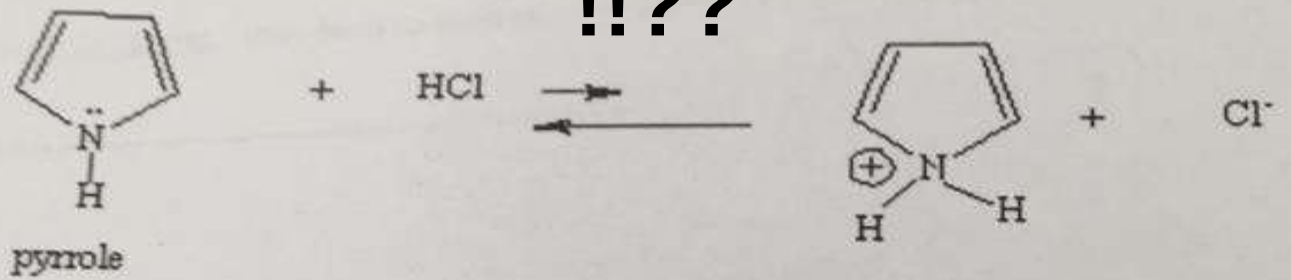
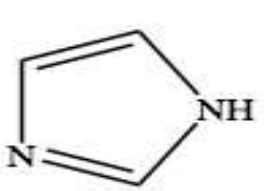
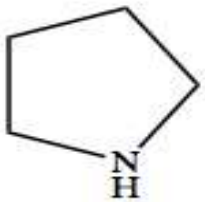


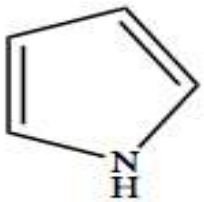
Which is the weakest base?



A



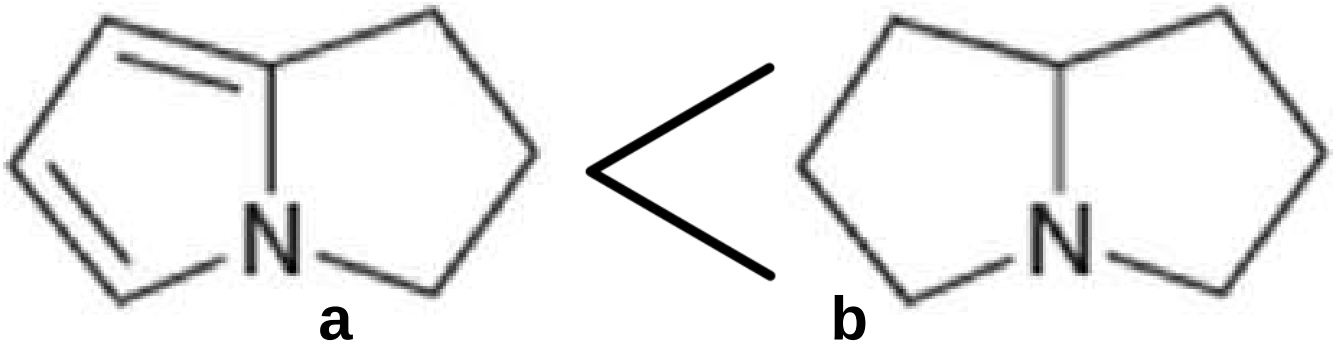
B



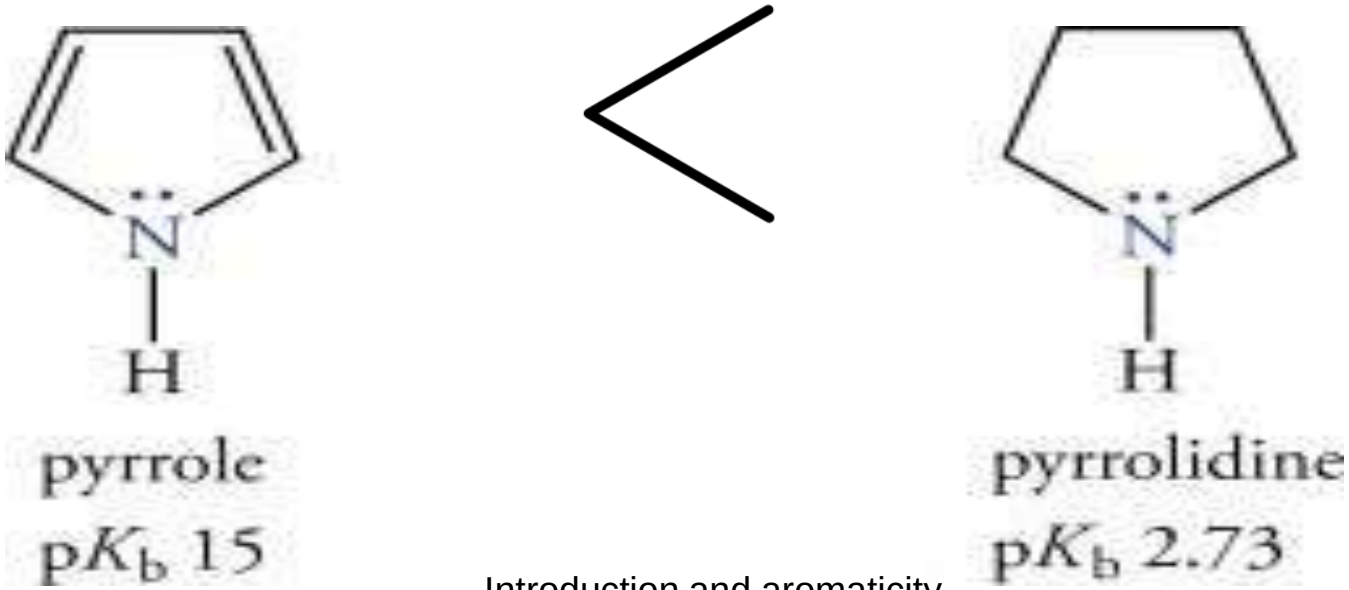
C

D

Identify which of the following compounds is expected to be a stronger base.



a b

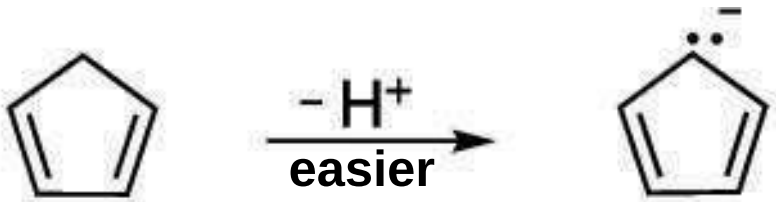


pyrrole
pK_b 15

pyrrolidine
pK_b 2.73

45

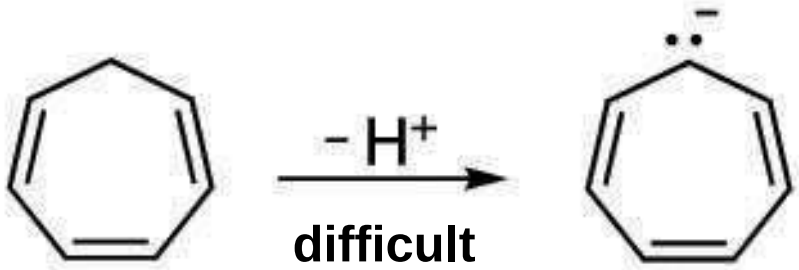
Effect of aromaticity on acidity



pKa = 16

6π electrons; aromatic

Easier ; because it creates an aromatic ion; Notice the value of pKa = 16

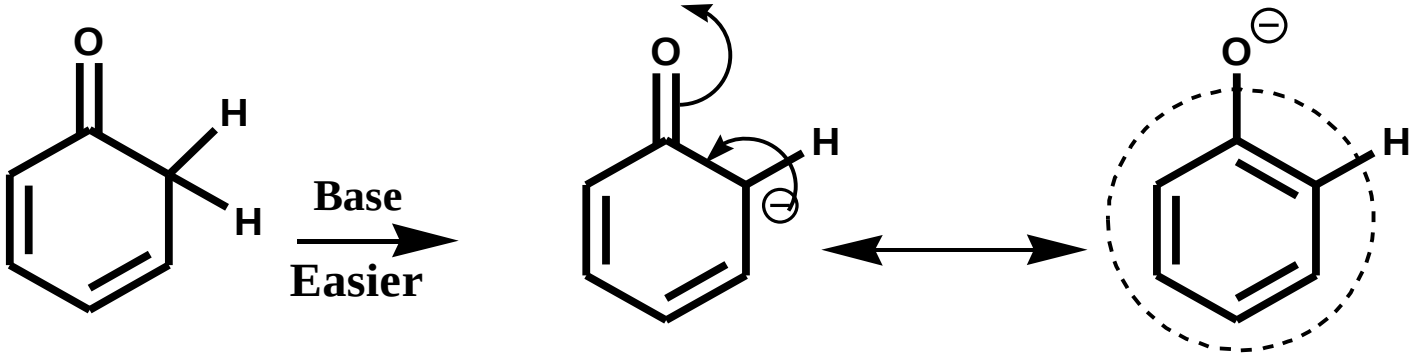


8π electrons; not aromatic

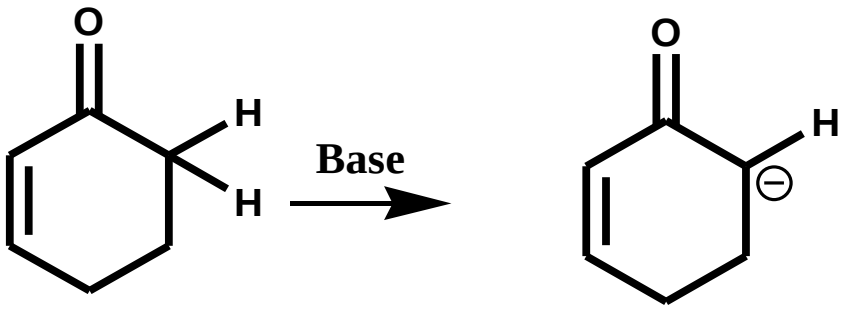
pKa = 36

Difficult ; because it doesnt create an aromatic ion; notice the value of pKa = 36

All compounds try to be aromatic; they all seek for aromaticity

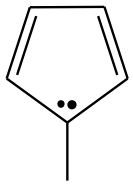


Loosing the acidic proton create a structure in which upon resonace; an aromatic ring is formed

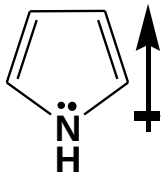


This resonance form is not aromatic

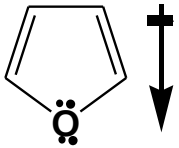
Effect of aromaticity on polarity



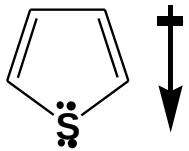
H
Cyclopentadienyl anion



1.81 D
Pyrrole

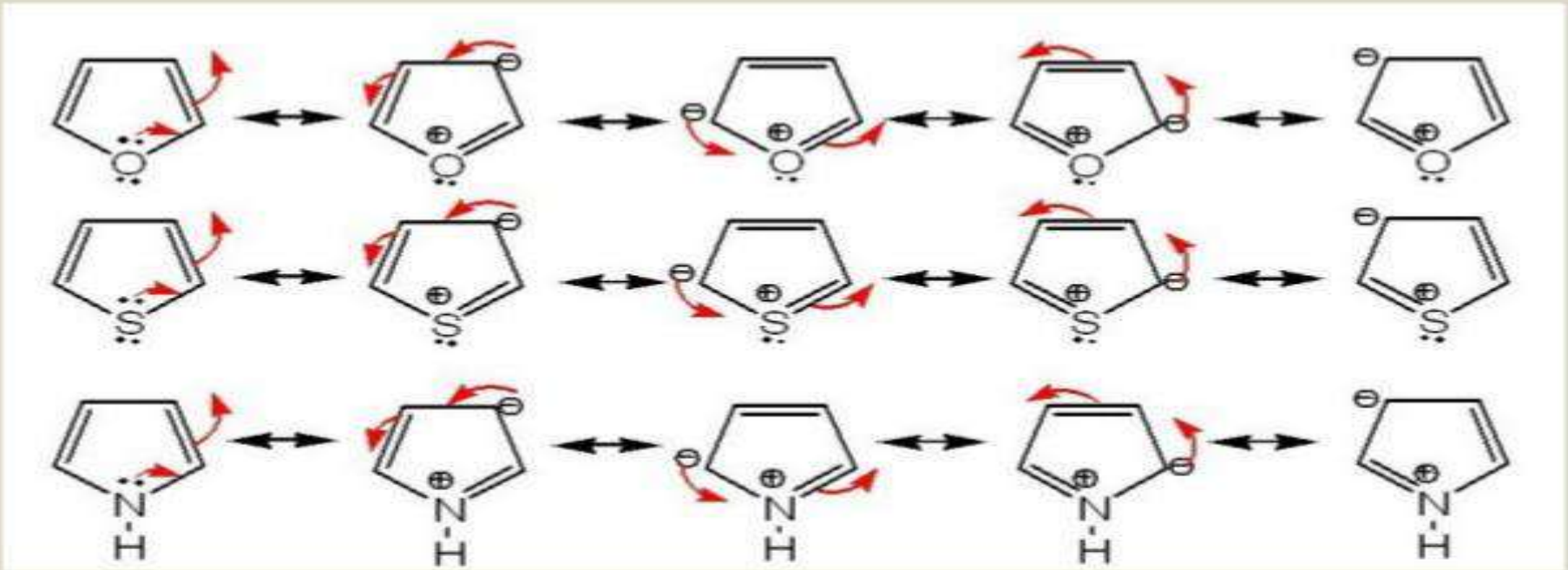


0.70 D
Furan

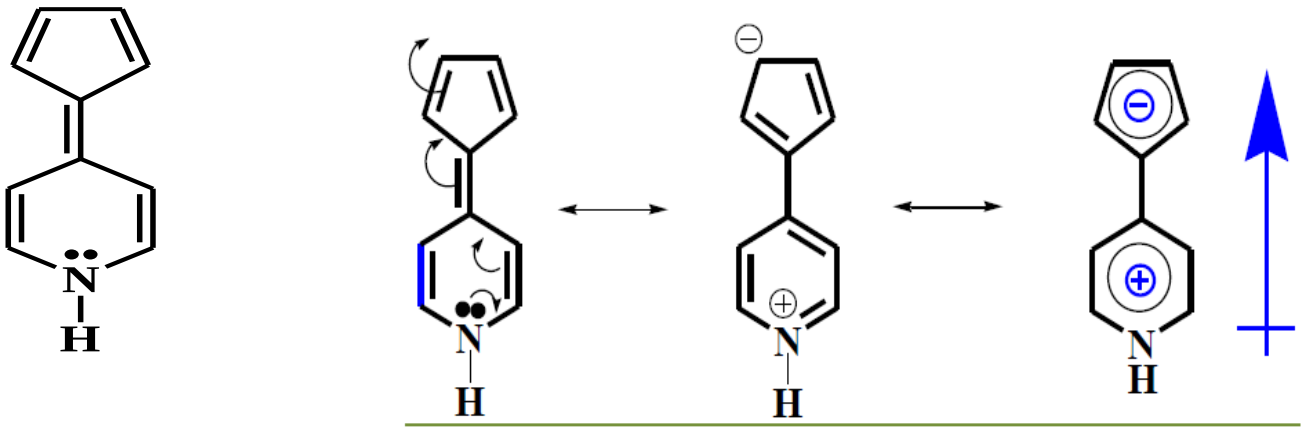


0.51D
Thiophene

Resonance structures of furan Thiphene and Pyrrole

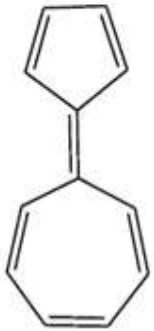


Indicate the polarity direction in the following compound



Yes, the compound is aromatic due to the availability of all requirements of aromaticity (cyclic, 4n+2= 6 in the 5 and in the six memeberd rings, all these electrons are resonated over the whole ring "planarity")

[redacted] Is the below compound an aromatic? Use resonance drawing to indicate its polarity direction. [redacted]

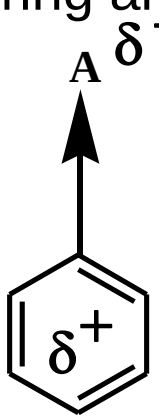


Lecture no . 4

Inductive and mesomeric effects in benzene ring

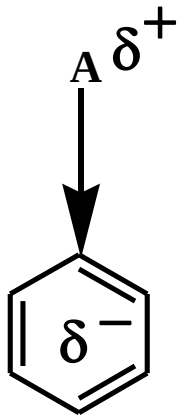
1-Inductive effect:-

In the organic compound molecule, due to the influence of different electronegativity substituents (atoms or atomic groups), the density of the bonding electron cloud in the whole molecule is shifted in a certain direction, and the effect of polarization of the molecule is called an Induction effect. If it is away from the ring it leads to minimize electron density in the ring and called (-I effect) or leads to maximize the electron density inside the ring and then it is called + I effect.



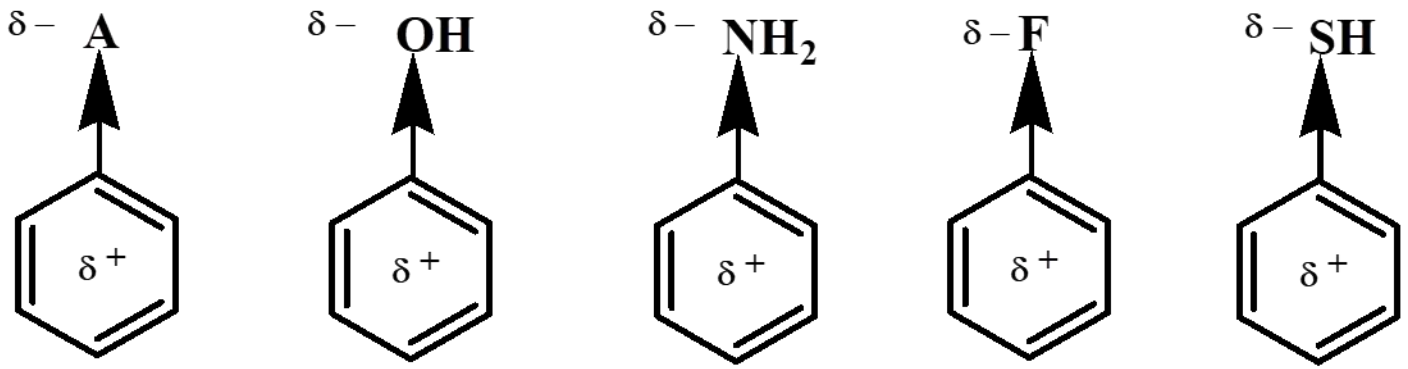
- I effect

atoms group 5,6 and 7 (N,P,O,S,F,Cl ...etc)

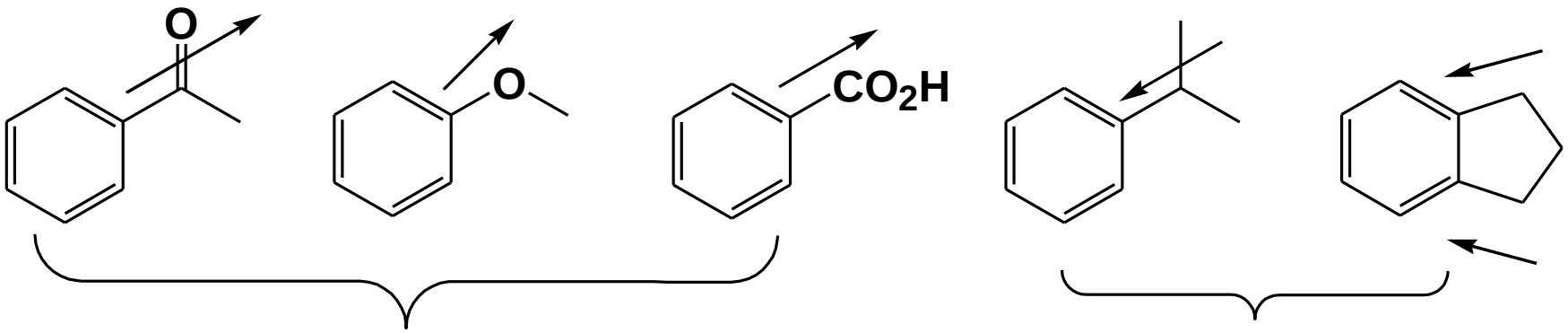


+I effect

Mainly, alkyl group



A = Atom or group in which ; its electronegativity is more than carbon such as:- O, N, S, F,Cl, S, ...etc.



- I effect **+I effect**

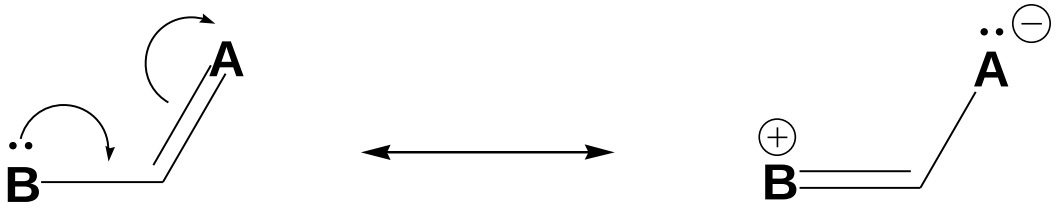
2- Mesomeric “resonance” effect

M Effect

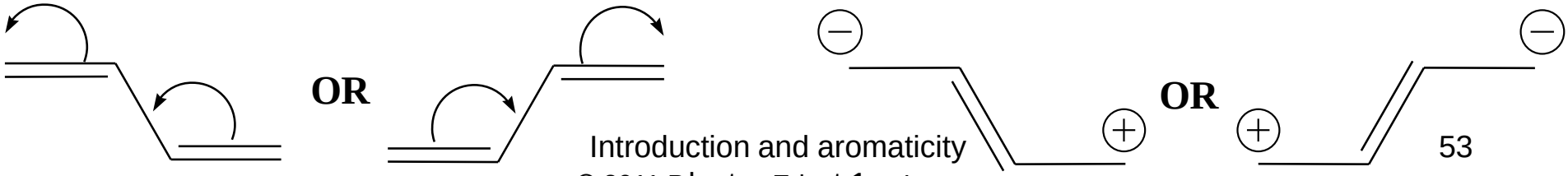
It involves the delocalization of the π or n electrons in a conjugated orbital system.

We will focus only on two types of resonance cases:-

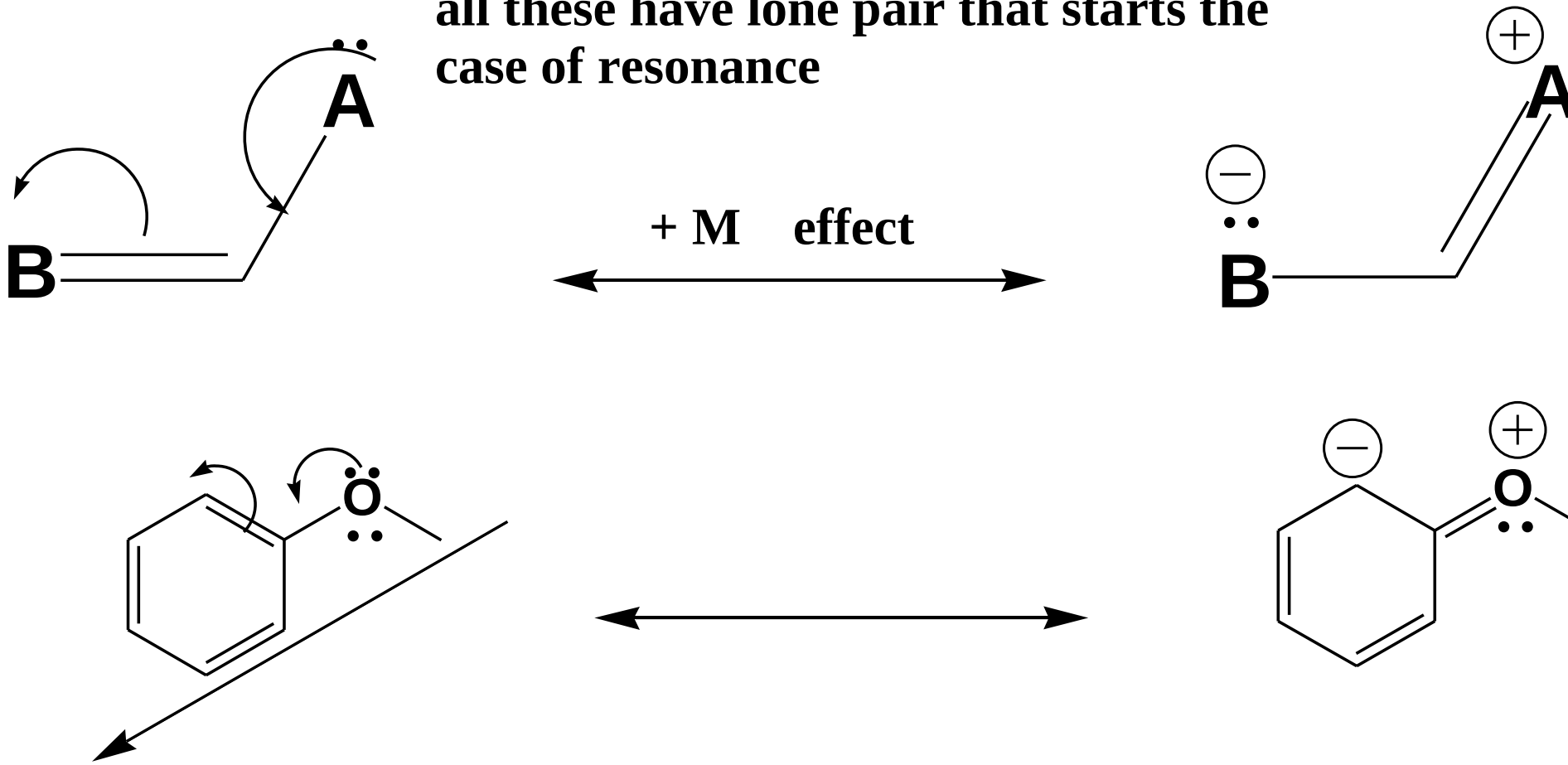
a] Case 1 “n-π”:- (lone pair, single bond and π bond are delocalized to double bond, single bond and lone pair with two opposite charges on each terminal.



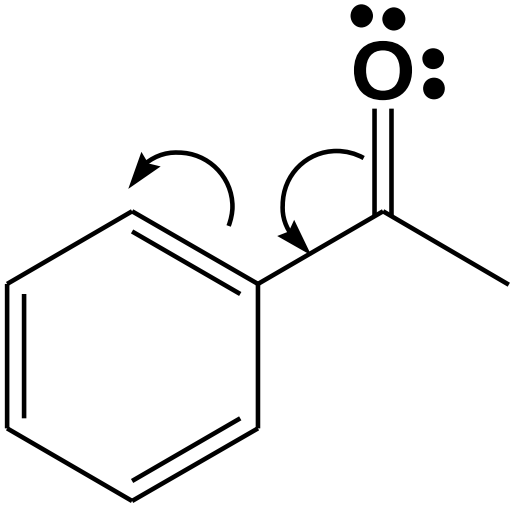
b] Case 2 “π-π”:- (π bond, single bond and π bond “conjugated system” are delocalized to a π bond in between with two opposite charges on each terminal



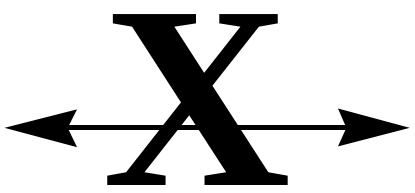
A is an atom from the group 5,6 or 7 all these have lone pair that starts the case of resonance

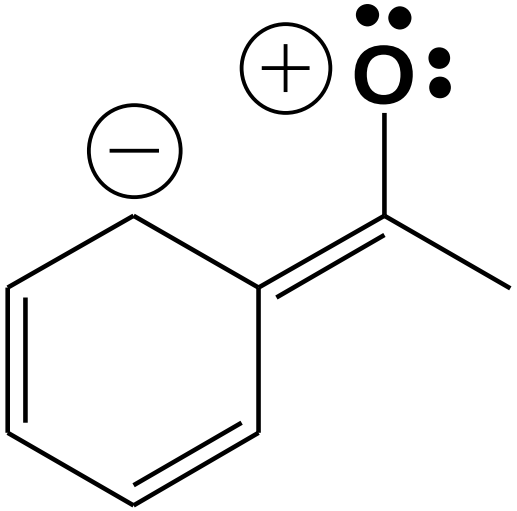


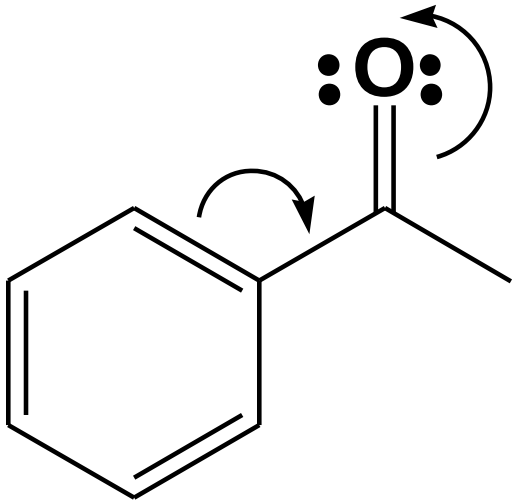
Free electrons (lone pair) move towards the ring; thus the amount of elecrons increases inside the ring at the expenss of the part outside the ring that push electrons; as a result it is a + M effect

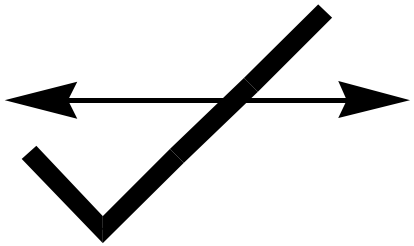


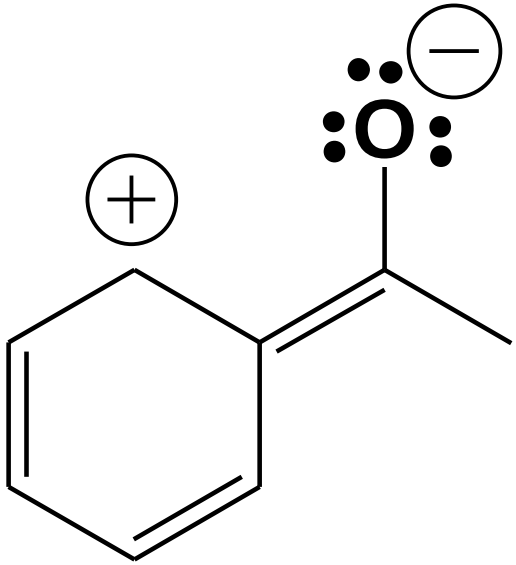
resonance does not occur in this way



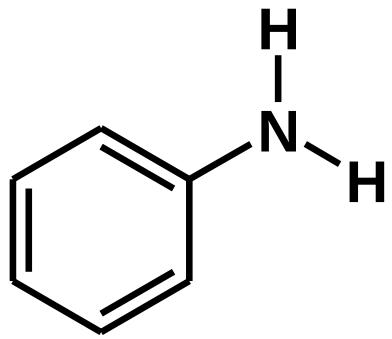


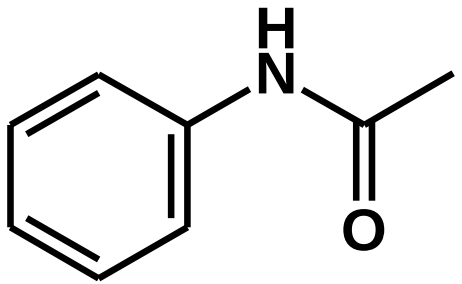


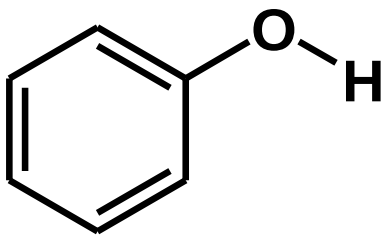


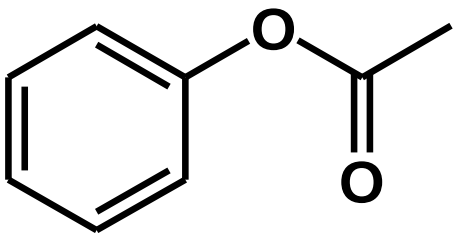


- **The M-effect is more effective than the I effect. Why ?**
- **Discuss both I and m effect for each of the following.**

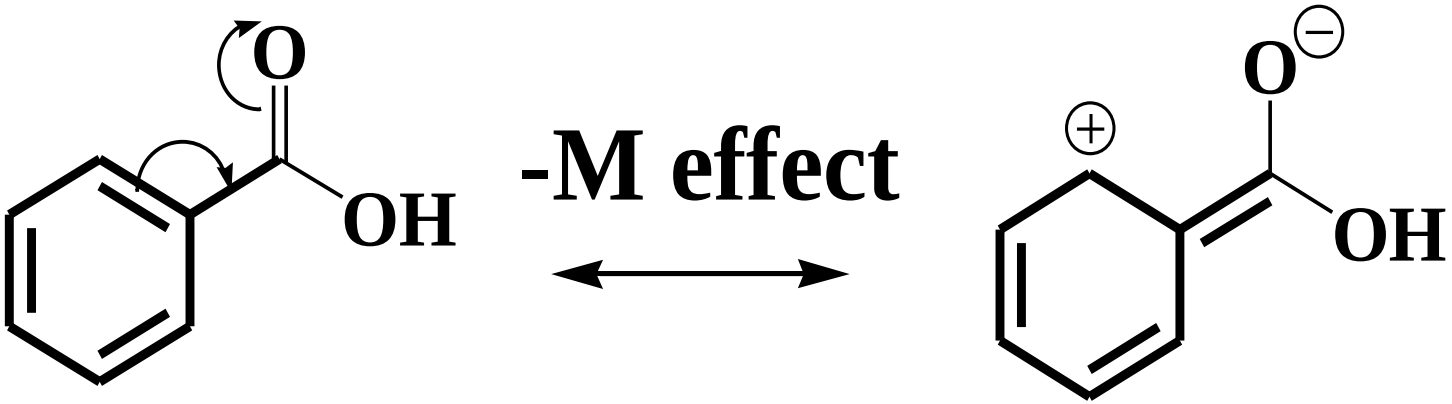


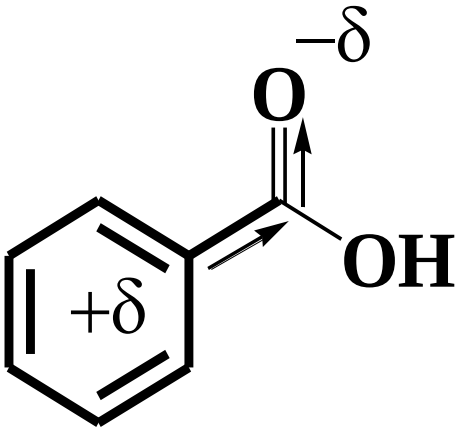






Benzoic acid



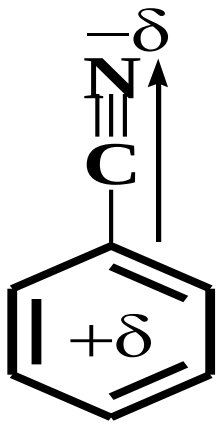


O is more EN than C

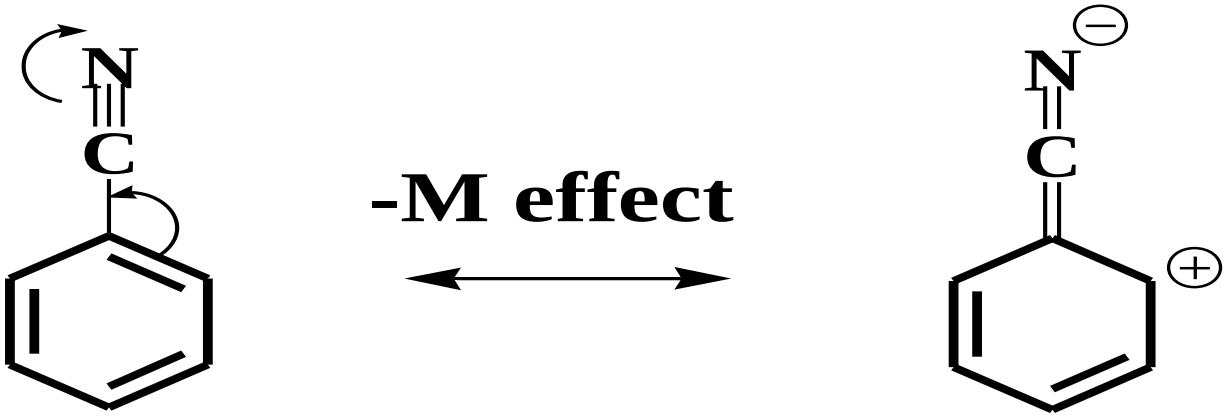
electrons flow out the ring

hence; it is -I effect

Benzonitrile



N is more EN than C electrons flow out the ring hence; it is –I effect

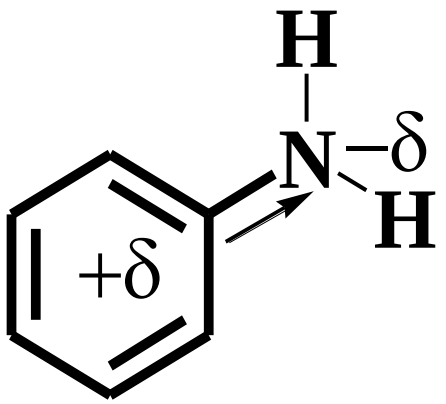


Discussion

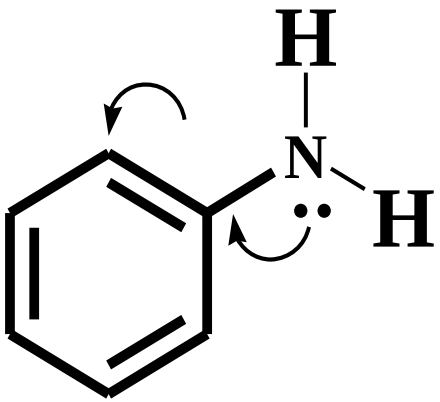
Indicate both I and M-effect for each of the following;

1- Benzoic acid (- I & - M)
2- Phenol (- I & + M)
3- Acetophenone (- I & - M)
4- Benzaldehyde (- I & - M)
5- Nitrobenzene (- I & - M)
6- Acetanilide (- I & + M)
7- Benzonitrile (- I & - M)
8- Aniline (- I & + M)
9- Anisol (- I & + M)
10- Benzene sulphonic acid (- I & - M)
11- Toluene (+ I & M effect is N A)

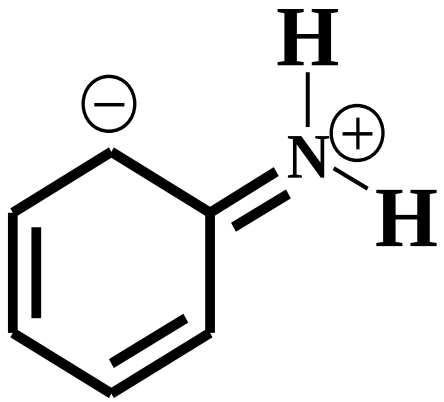
Aniline



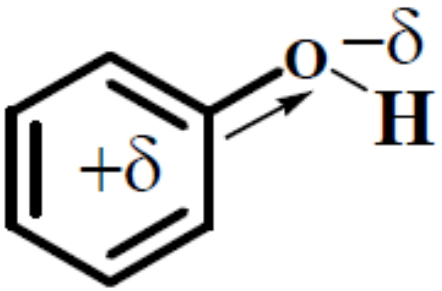
N is more EN than C electrons flow out the ring hence; it is -I effect



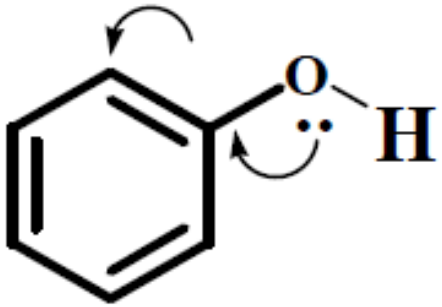
+M effect



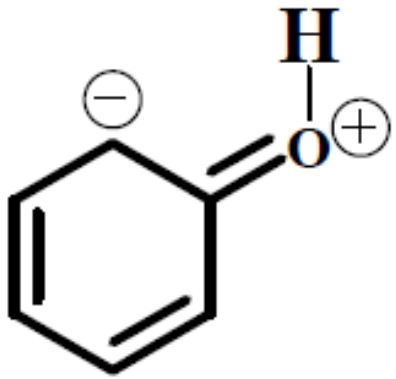
Phenol



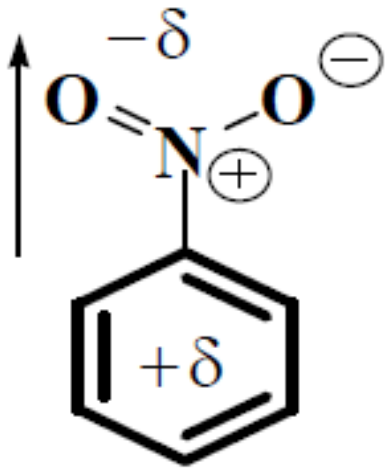
O is more EN than C
electrons flow out the ring
hence; it is -I effect



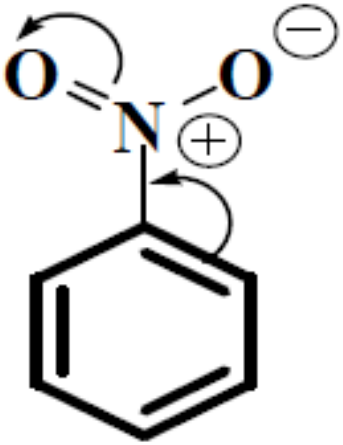
+M effect



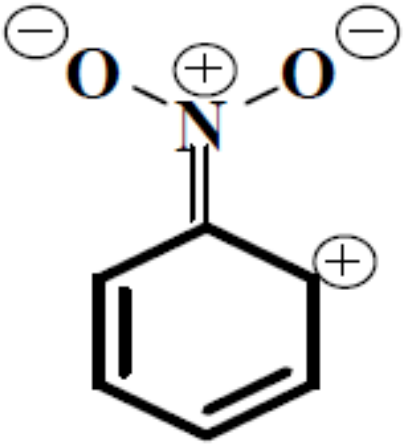
Nitrobenzene



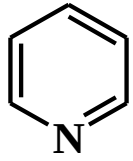
N and O more EN than C electrons flow out the ring hence; it is -I effect

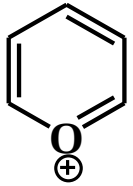


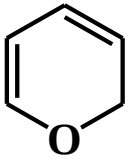
-M effect



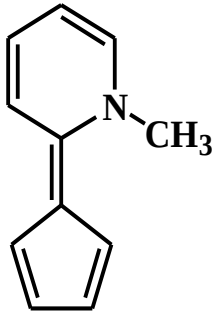
Q1] Discuss aromaticity feature for the following compounds



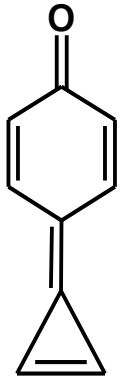




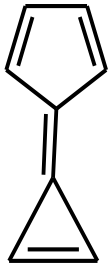
Q2] Indicate the polarity direction for the following compound



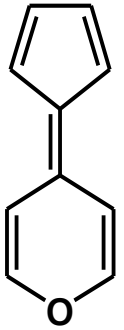
X



Y

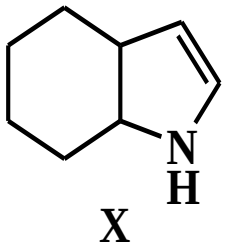


Z

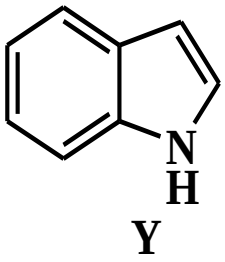


A

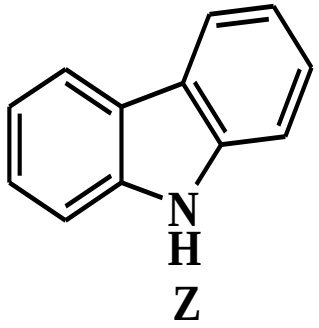
Q3] Arrange the following compounds according to the increase in their basicity



X

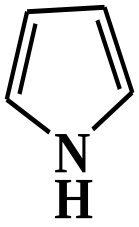


Y

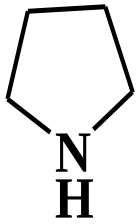


Z

Q4] Arrange the following according to the increase in their basicity



1



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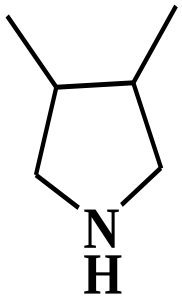
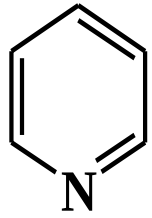
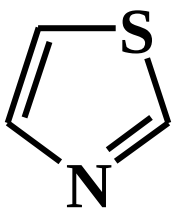


3

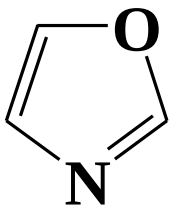


4

Q5] Which is more basic; Thiazole or Oxazole? Explain

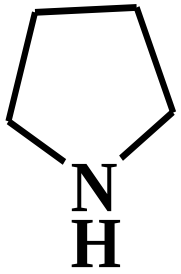


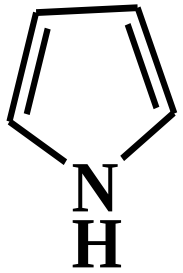
Thiazole



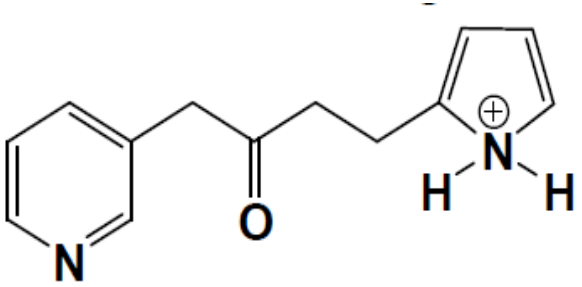
Oxazole

Q6] Discuss the acidity for the following

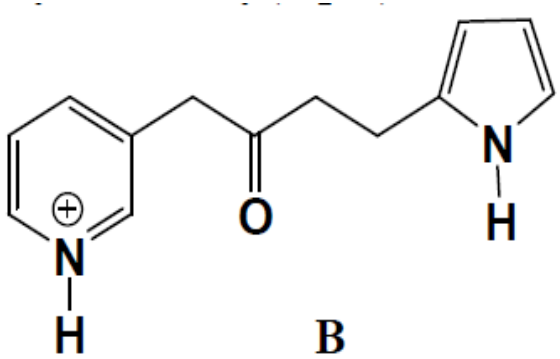




Q7] Which of the following two salts is drawn in a wrong way. Tell why

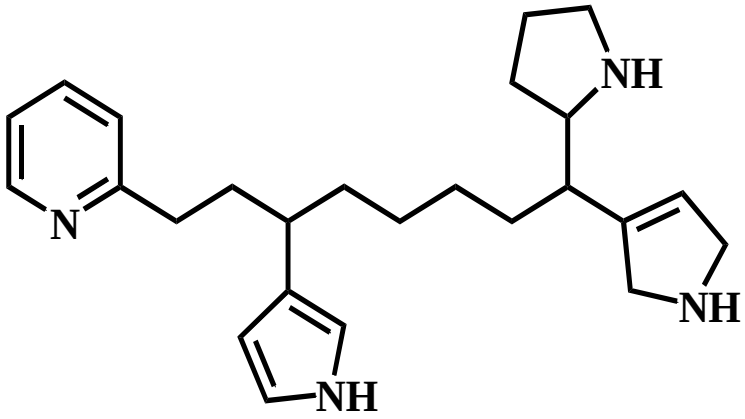


A

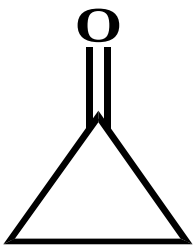


B

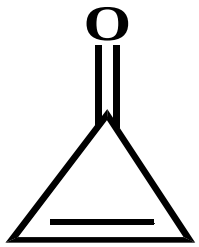
Q8] What is expected salt structure of mono, di, tri and tetra salt



Q9] Discuss Oxygen nucleophilicity in the following two compounds



1



2

Q10] Which is the most Nucleophilic center in the following compound