South Valley University

Faculty of Education

Chemistry Department

Chemistry of Cyclic Compounds

4th year students – Faculty of Education

Chemistry group

Second Term 2022/2023

Dr/ Ibrahim Abdul-Motaleb Mousa

Heterocyclic Chemistry

4th year students Chemistry group Faculty of Education

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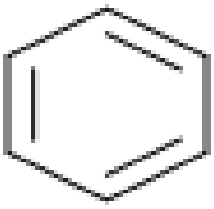
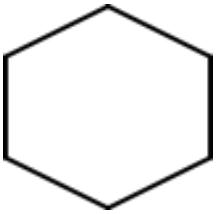
Contents

WHAT IS HETEROCYCLIC CHEMISTRY?

What are carbocyclic compounds?



benzene



cyclohexane

Carbocyclic Compound

Carboxylic Compound

Cyclic Compound





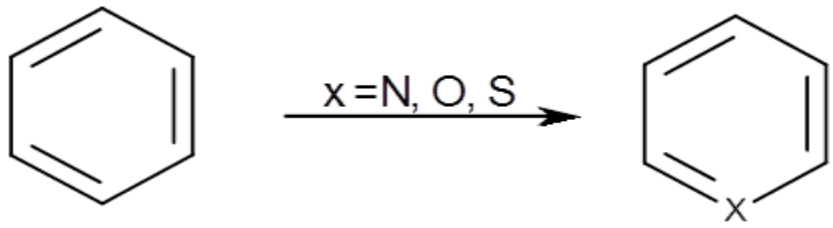



Aromatic Compound

What's aheterocyclic compound

If the ring system is made up of carbon atoms and at least one other element, the compound can be classified as hetero cyclic.

The elements that are found most commonly together with carbon in a ring system are Nitrogen (N), Oxygen(O), and Sulfur(S).

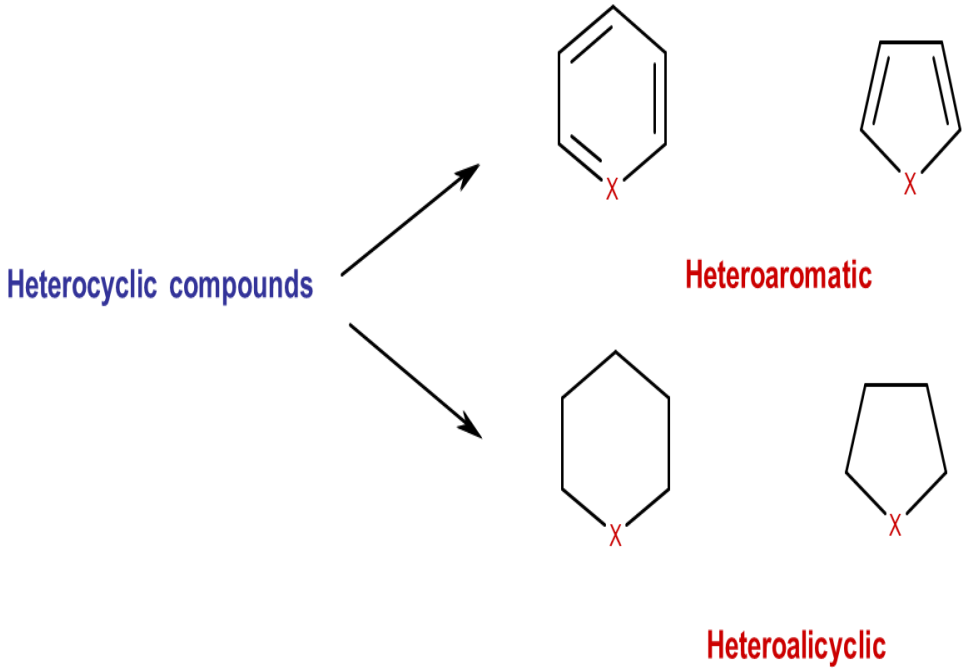


Heterocyclic compounds

are organic compounds that contain a ring structure containing atoms in addition to carbon, such as sulfur, oxygen or nitrogen, as the heteroatom.

Heterocyclic classification

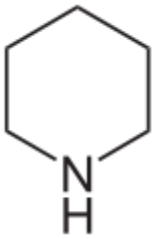
It can be classified into



Heterocyclic classification

1- Aliphatic heterocycles :-

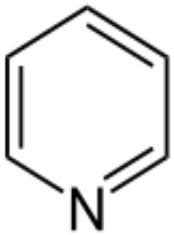
Oxirane



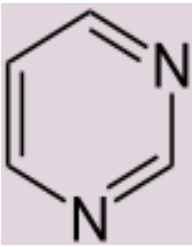
Piperidine

2- Aromatic heterocycles :-

a- six-membered aromatic hetrocycles

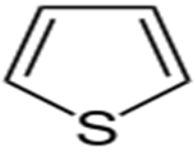


Pyridine

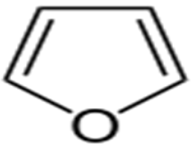


Pyrimidine

b- five-membered aromatic hetrocycles

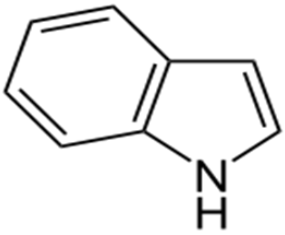


Thiophen

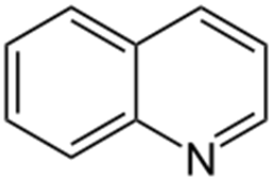


Furan

c- bicyclic heteroaromatic compounds



Indol



Quinoline

Importantce and uses of Heterocyclic compounds:-

- ***Biosynthesized***
- ***Essential for life (haem, chlorophyll)***
- ***Their metabolitis used as***

- toxin towords off predators

- colouring agents to attact mates

In general various important compounds such as:-

alkaloids, vitamins, antibiotics, essential amino acids, hormones, drugs and dyes contain heterocyclic structure.

• in general: nucleic acids, amino acids (proteins),

• feeding: proteins, carbohydrates, vitamins

• alkaloids: nicotine, caffeine

Application:

• antibiotics (penicillins, sulfonamides)

• insecticides (triazoles)

• herbicides (triazines, pyridines)

HETEROCYCLIC NOMENCLAUTURE

Nomenclature of heterocyclic compounds

- **There are three systems for naming heterocylic compounds:**

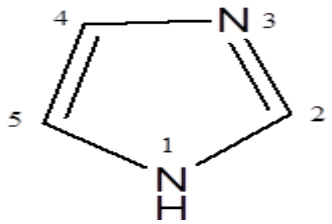
1) **The common nomenclature: which convey little or no structural information but it still widely used.**

2) **The Hantzsch-Widman (IUPAC or Systematic) method which in contrast is designed so that one may deduce from it the structure of the compound.**

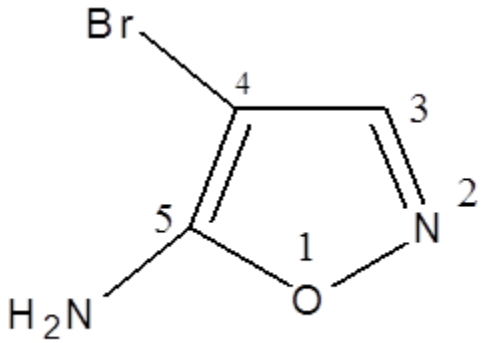
I- Common Nomenclature

1) Each compound is given the corresponding trivial name (which should be memorized, see the following slides). This usually originates from the compounds occurrence, its first preparation or its special properties.

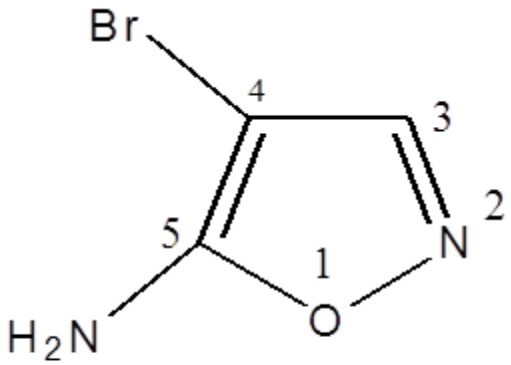
2) If there is more than one hetroatom of the same type numbering starts at the saturated one, e.g. imidazole.



3) If there is more than one type of the heteroatoms, the ring is numbered starting at the hetroatom of the higher priority (O>S>N) and it continues in the direction to give the other hetroatoms the lower numbers as possible.

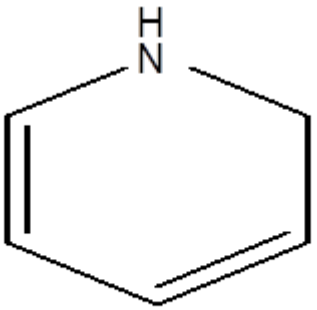


4) If substituents are present, their position should be identified by the number of the atoms bearing them and then they should be listed in alphabetical order.



5-Amino-4-bromoisoxazole

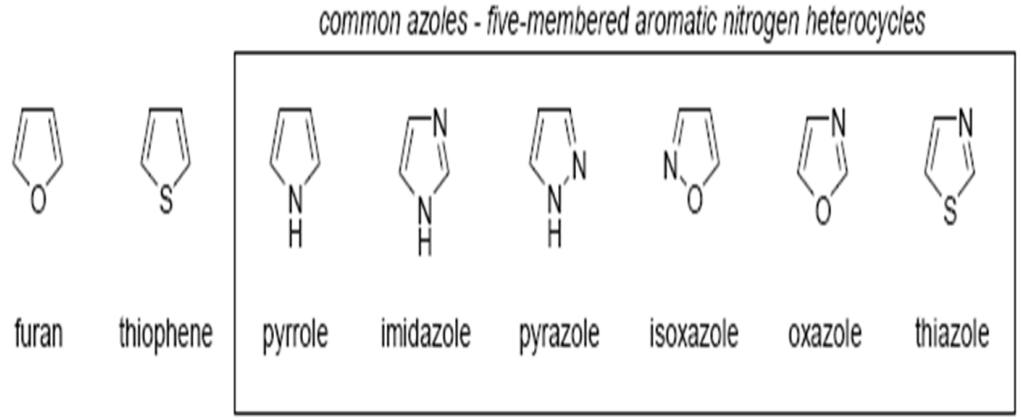
5) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated trivial name.



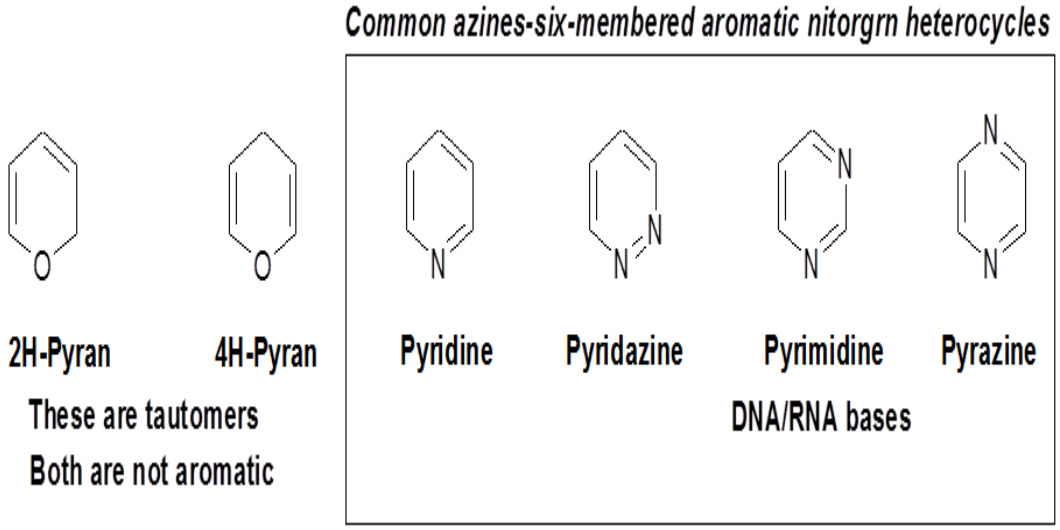
1,2-Dihydro-pyridine

Trivial names:

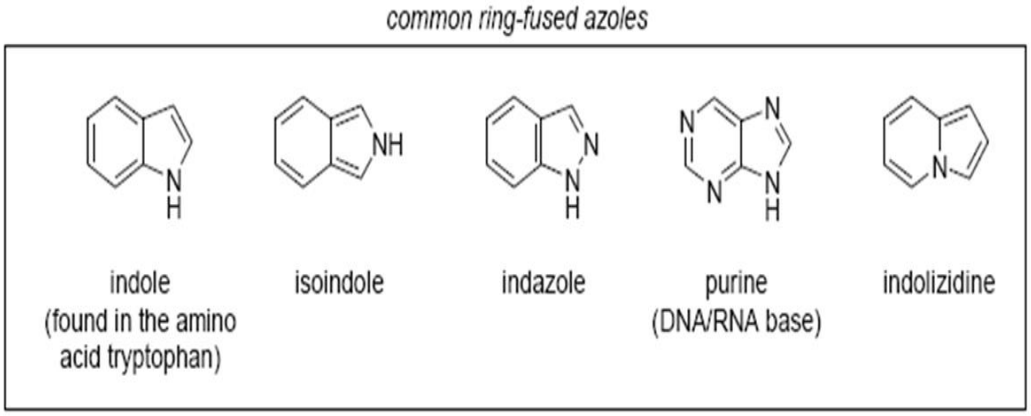
1) 5-membered heterocycles with one or two heteroatoms

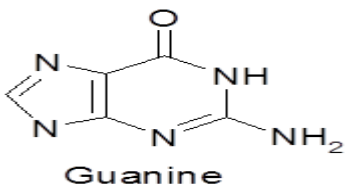


2) 6-membered heterocycles with one or two heteroatoms

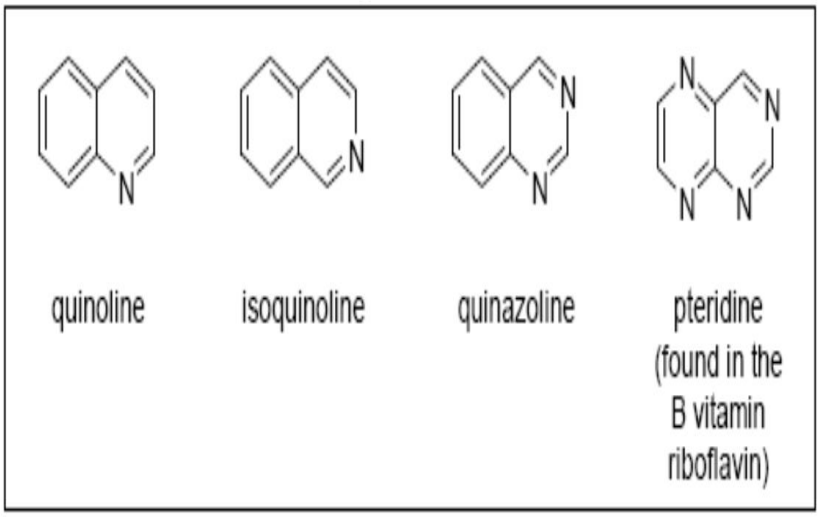


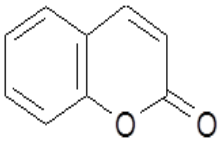
3) Fused heterocycles



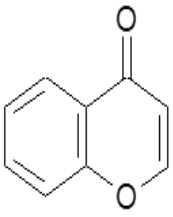


common ring-fused azines

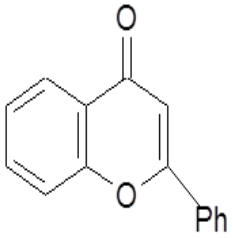




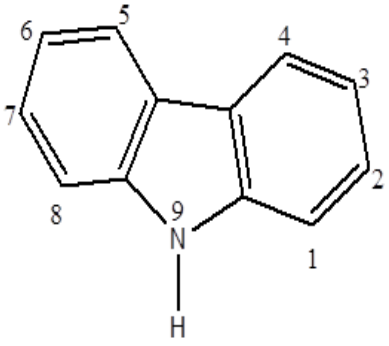
Coumarine
Chromen-2-one



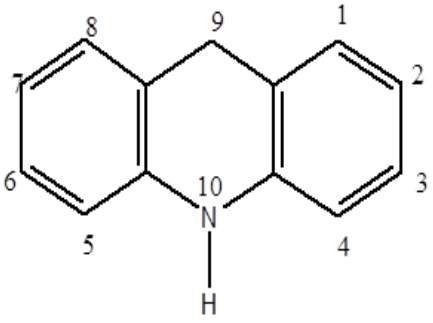
Chromen-4-one



Flavone

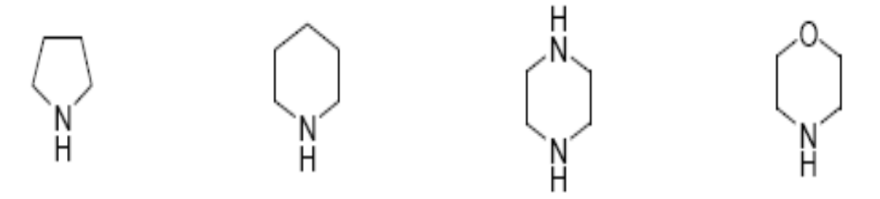


9H-Carbazole



9,10-Dihydro-acridine

4) Saturated heterocycles



II-Hantzsch-Widman nomenclature (IUPAC)

- **Hantzsch-Widman nomenclature is named after the German chemists Arthur Hantzsch and Oskar Widman, who proposed similar methods for the systematic naming of heterocyclic compounds in 1887 and 1888 respectively.**

- **According to this system three to ten-membered rings are named by combining the appropriate prefix (or prefixes) that denotes the type and position of the heteroatom present in the ring with suffix that determines both the ring size (depending on the total number of atoms in the ring) and the degree of unsaturation (note that fully saturated and fully unsaturated have certain rules for nomenclature while partially unsaturation**

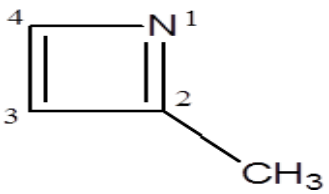
will be indicated in certain ways). In addition, the suffixes distinguish between nitrogen-containing heterocycles and heterocycles that do not contain nitrogen

- **IUPAC name = locants +Prefix + suffix**

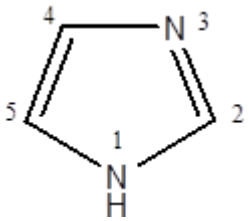
Hantzsch-Widman rules for fully saturated and fully unsaturated heterocycles

1) **Identify the hetroatom present in the ring and choose from (table 1 on slide 11) the corresponding prefix (e.g. thia for sulfur, aza for nitrogen and oxa for oxygen).**

2) **The position of a single heteroatom control the numbering in a monocyclic compound. The heteroatom is always assigned position 1 and if substituents present are then counted around the ring in a manner so as to take the lowest possible numbers. <u>For example:</u>**



3) **A multiplicative prefix (di, tri, ect.) and locants are used when two or more similar heteroatoms contained in the ring(two nitrogen indicated by diaza) and the numbering preferably commenced at a saturated rather than an unsaturated atom, as depicted in the following example: 1,3-diaza….**

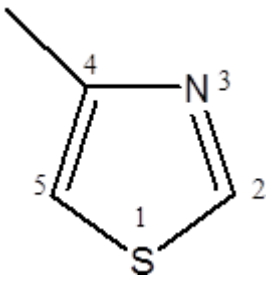


4- **If more than one type of hetroatoms present in the ring the name will include more than one prefix with locants to indicate the relative position of the heteroatoms.**

5- **Atom prefixes have a strict order of priority (preference) in which they are to be listed. For example,''Oxa''(for oxygen) always comes before ''aza'' (for nitrogen) in a name (see table 1).**

6- **When combining the prefixes (e.g. oxa and aza) two vowels may end up together, therefore the vowel on the end of the first part should be omitted (oxaza).**

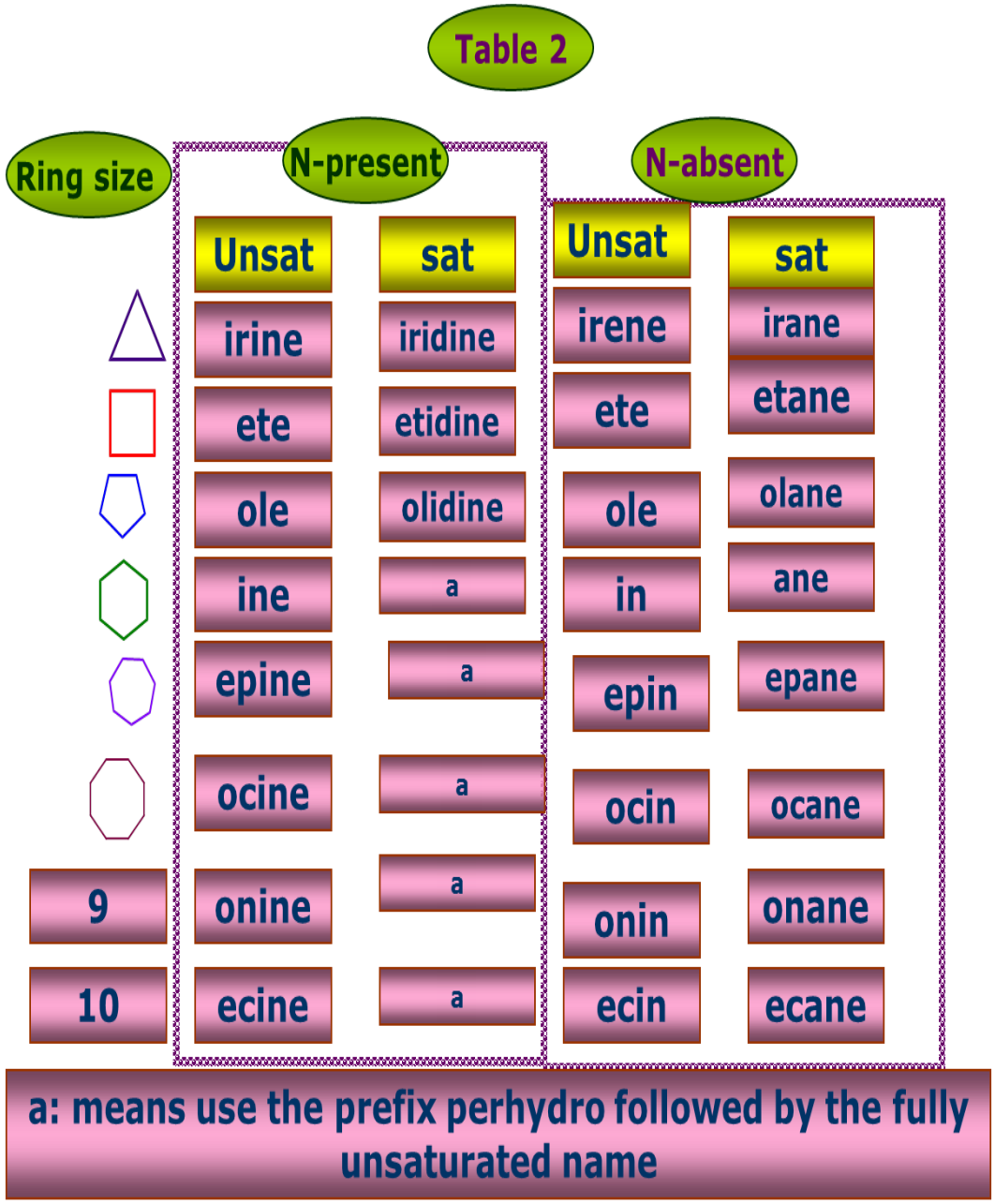
7- The numbering is started from the heteroatom of the highest priority in such a way so as to give the smallest possible numbers to the other heteroatoms in the ring (the substituents are irrelevant). For example the prefix corresponding to the following compound is 4-Methyl-1,3-Thiaza….



5) Choose the appropriate suffix from (table 2) depending on whether or not nitrogen atom is present in the ring, the size of the ring and presence or absence of any double bonds

6) Combine the prefix(s) and suffix together and drop the first vowel if two vowels came together.

Hantzsch-Widman rules



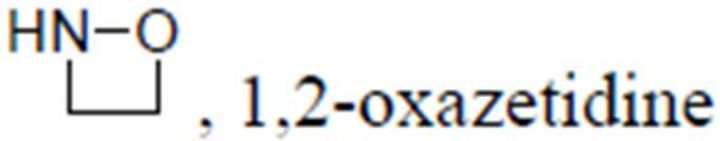
❖ **Examples**

- **This ring contains (N) Prefix is aza**
- **The ring is 3-membered and fully saturated**

  suffix is iridine
- **By combining the prefix and suffix, two vowels**

  ended up together (azairidine), therefore the vowel on the end of the first part should be dropped. This gives the correct name: Aziridine

❖ **Example 2:**

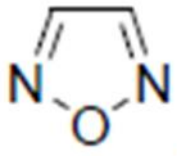


❖ **This ring contains nitrogen = aza-**

❖ **And oxygen = oxa-**

❖ **And is a fully saturated four-membered**

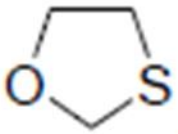
- **ring = -etidine**
- **Drop the vowels in oxa & aza**
- **The name = 1,2-Oxazetidine**
- **Example 3:**



, 1,2,5-oxadiazole

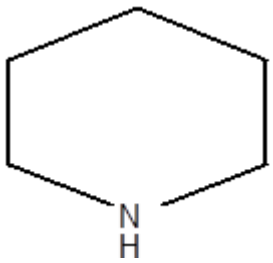
- **This ring contains nitrogen = aza-**
- **And oxygen = oxa-**
- **And Unsaturated five-membered rings with nitrogen = –ole**
- **Oxygen is higher priority than nitrogen, so it is in position 1.**
- **The two nitrogens are therefore at positions 2 and 5**
- **The name = 1,2,5-Oxadiazole**

- **Example 4:**



, 1,3-oxathiolane

- **This ring contains sulpher= thia-**
- **And oxygen = oxa-**
- **And saturated five-membered rings without nitrogen = –olane**
- **Oxygen is higher priority than sulpher, so it is in position 1.**
- **Drop the vowel in thia**
- **The name = 1,3-Oxathiolane**



- **The ring is 6-memberd, fully saturated with N**

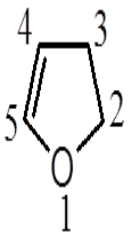
Prefix perhydro followed by the name of fully unsaturated 6-memberd ring with nitrogen azine

- **Thus the full name is perhydroazine**

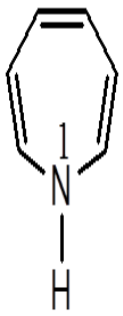
Hantzsch-Widman rules for partially unsaturated heterocycles

- **Partial unsaturation in heterocyclic compounds can be indicated by one of the following methods:**

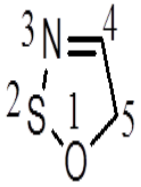
a) **The position of nitrogen or carbon atoms which bear extra hydrogen atoms must be indicated by numbers and italic capital H (e.g. 1*H*, 2*H*, etc.) followed by the name of maximally unsaturated ring.**



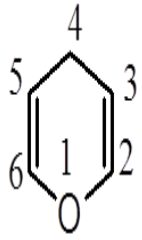
2*H*, 3*H*-Oxole



1*H*-Azepine



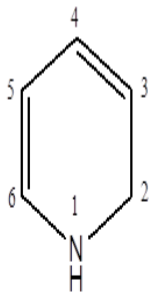
5*H*-1,2,3-Oxathiazole



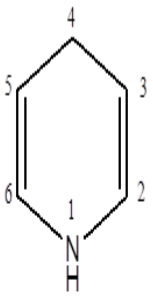
4*H*-Oxin

Hantzsch-Widman rules for partially unsaturated heterocycles

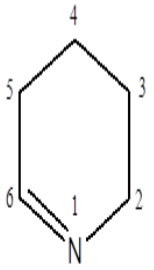
b) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated Hantzsch-Widman name.



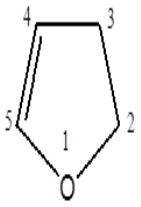
1,2-Dihydroazine



1,4-Dihydroazine



2,3,4,5-Tetrahydroazine



2,3-Dihydrooxole

Isomers have the same M.F. but differ in the position of the double bond

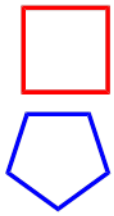
c) Alternatively, the partially unsaturated 4 and 5 rings (i.e. rings contain one double bond) are given special Hantzsch-Widman suffixes as in table 3 and

the double bond is specified as Δ^1, Δ^2, Δ^3, etc.. Which indicates 1 and ; 2 and 3; 3 and 4 atoms respectively have a double bond

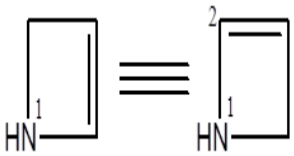
(i.e. Name : Δ^x + Prefix + special suffix)

(x= locant of the double bond)

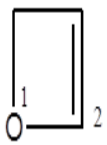
Table 3

Ring size	With N	Without N
	-etine	-etene
	-oline	-olene

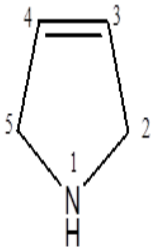
❖ **Examples**



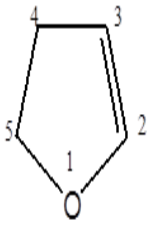
Δ^2 -Azetine



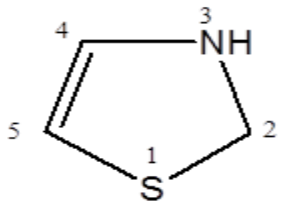
Δ^2 -Oxetene



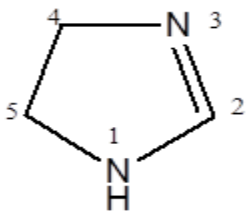
Δ^3 -Azoline



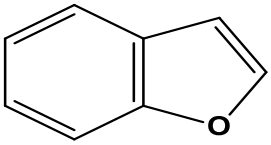
Δ^2 -Oxolene



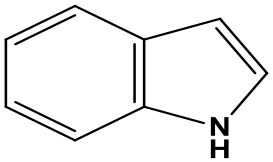
Δ^4 -1,3-Thiazoline



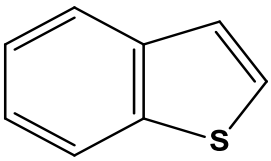
Δ^2 -1,3-Diazoline



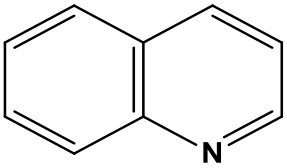
Benzo[b]furan



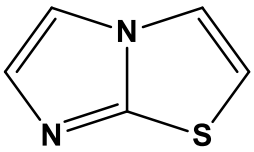
benzo[b]pyrrole



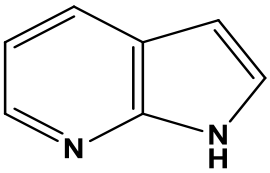
Benzo[b]thiophene



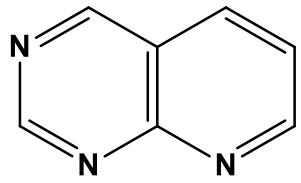
benzo[b]pyridine



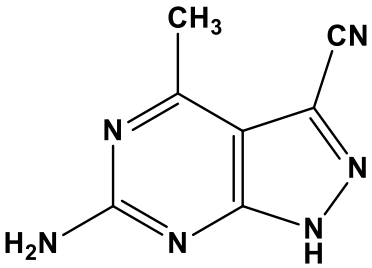
imidazo[2,1-*b*]thiazole



(pyrrolo[2,3-*b*]pyridine)

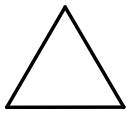


(pyrido[2,3-*d*]pyrimidine)



6-amino-4-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-3-carbonitrile

Three membered ring



Cyclopropane **cyclopropane**

Three membered ring compounds are unstable because the strain in the ring, the hybridization is sp^3 and the angle should be 109,28, but it is 60 degree only.

The organic heterocyclic compounds can be prepared from intermolecular reaction to form cycle and we will study some of these compounds.

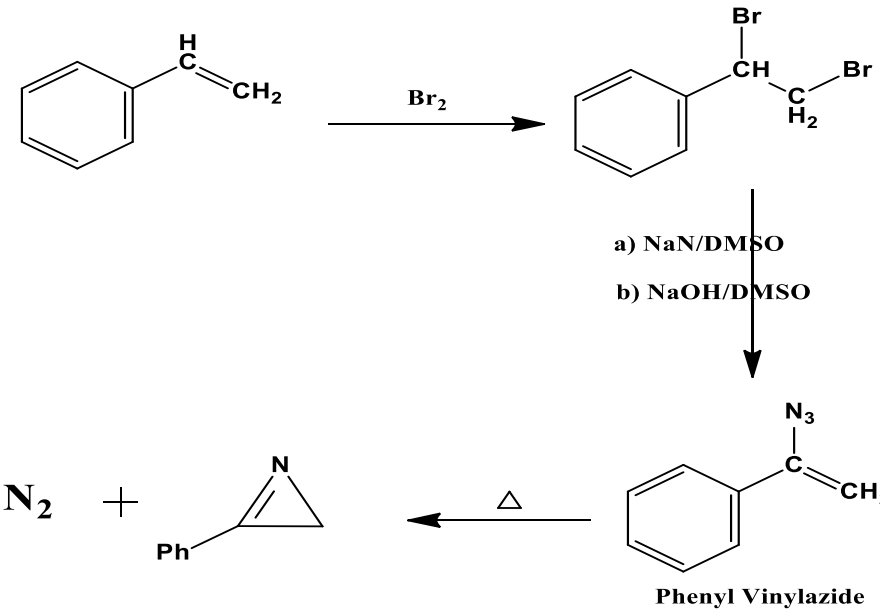
Azirine

Azirine contains nitogen atom and double bond in the ring, numbering started from the heteroatom.

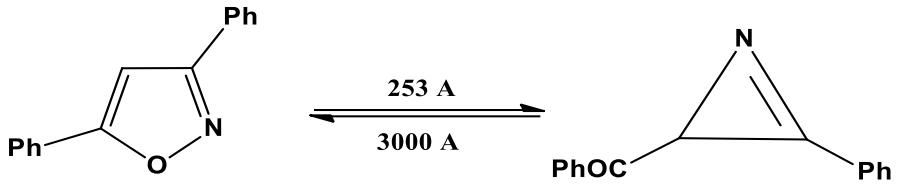
Preparation of azirine:

1- **From azide:**

By thermal analysis or photochemical reaction of phenyl vinyl azide to give 2-phenyl azirine.



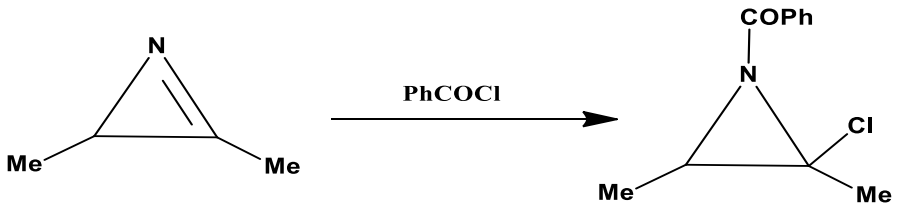
From isooxazole:



Reactions of azirine:

Because the ring has strain so, the reactions lead to open the ring.

1- With benzoyl chloride:



Oxirane

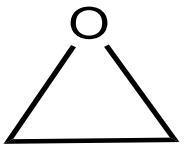
oxirane

Ethylene oxide

epoxyethane

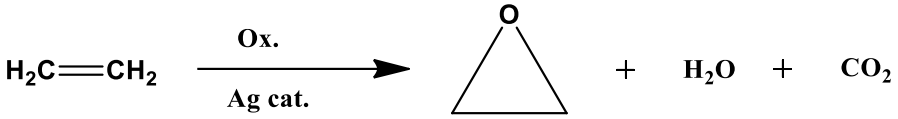
oxacyclopropane

1,2- or beta oxidoethane

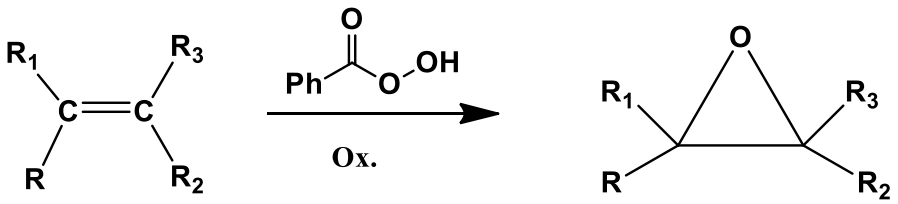


Preparation of oxirane:

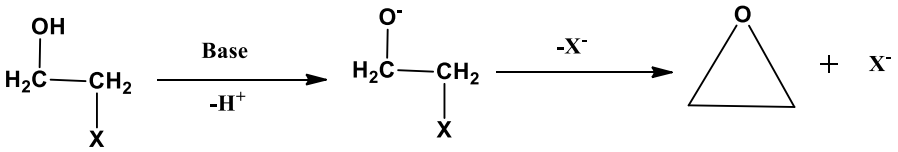
1- By oxidation of ethylene:



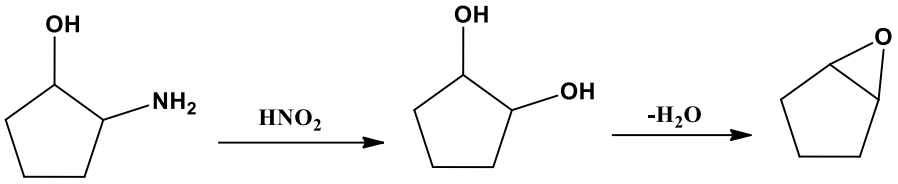
2- Oxidation of oliefins by perbenzoic acid:



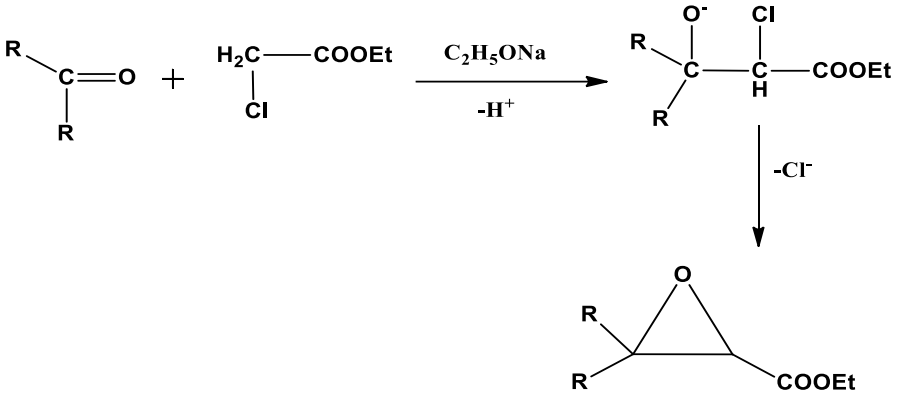
3- By elimination of HX from halohydrine:



4- Effect of nitrous acid on alcoholic amine:

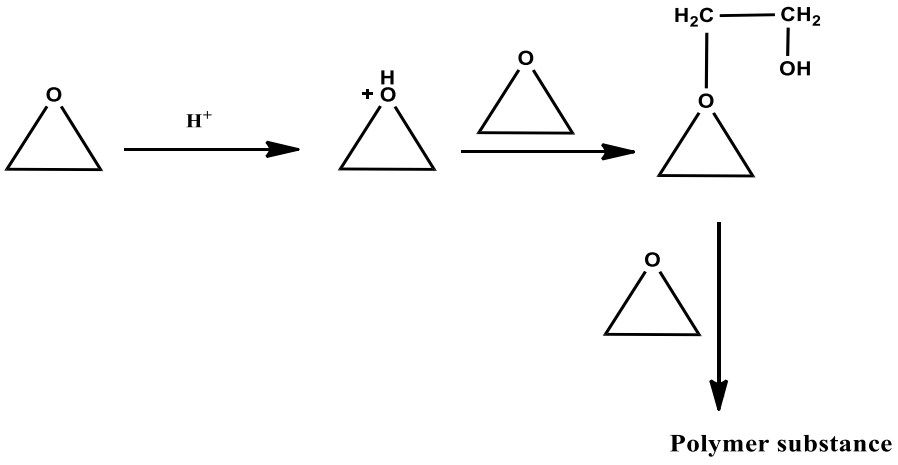


5- Darzins reaction:



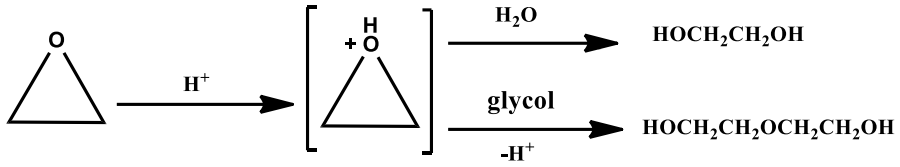
Reactions of oxirane:

1- Polymerization:

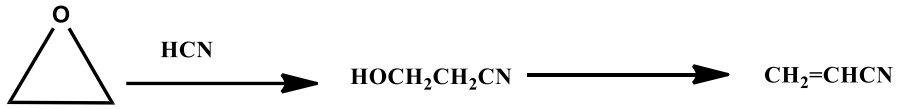


2- Reaction with water:

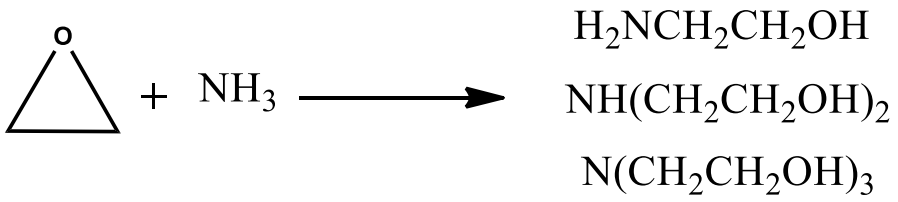
Which give ethylene glycol then give diethyl glycol.



With HCN:



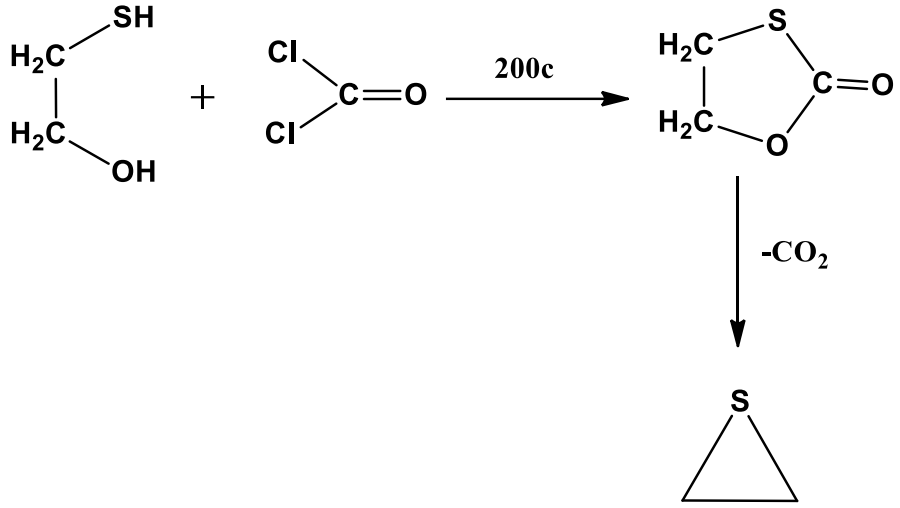
3- With ammonia:



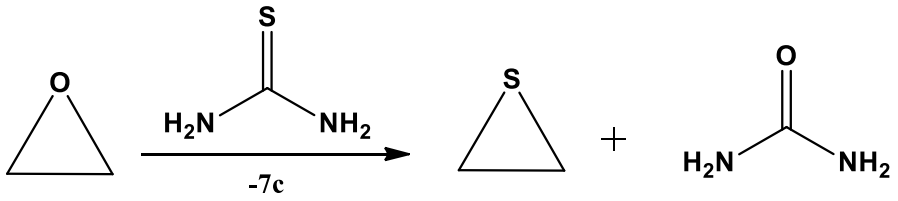
Thiarane

Preparation of thiarane:

1- From phosogine with 2-mercaptoethanol in the presence of amm.acetate and pyridine to give monothioethylene carbonate which lose carboxlic group to give thiarane in 88%.



2- From oxirane with thiourea:



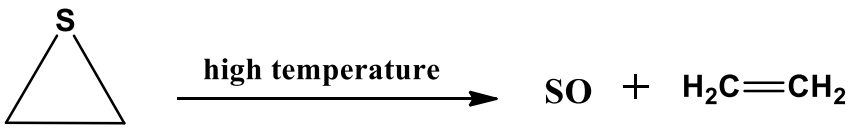
Reactions of thiarane:

Thiarane is less stable than oxirane.

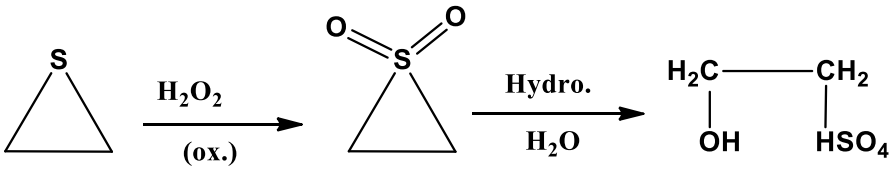
1- Polymerization:

Polymerization of thiarane is more easily than oirane in dark or by catalysts as mineral acids or bases or by free radicals.

2- Thermal analysis:

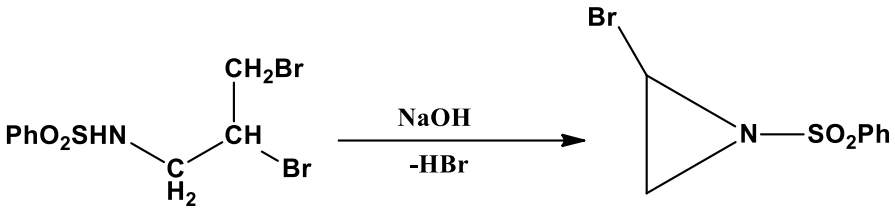


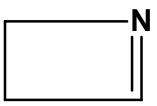
3- Open the ring:



Four membered ring

Preparation of four membered rings is more difficult than three membered rings as follow:

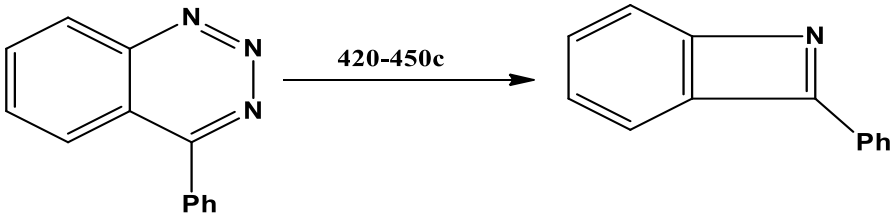




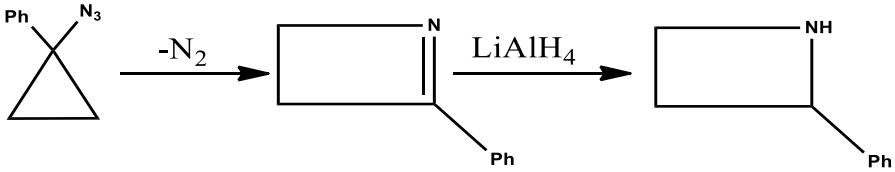
Azitene

Azitene does not prepared yet but we can prepare azitene derivatives:

Example 1:



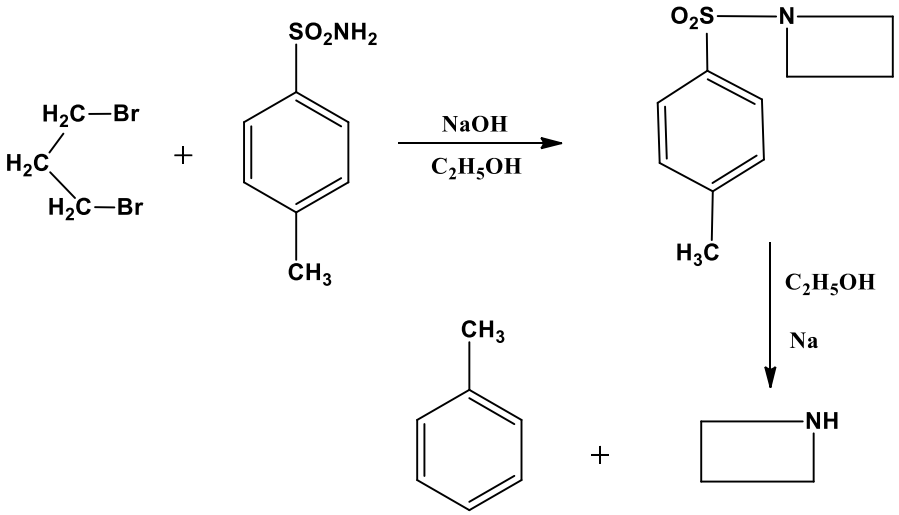
Example 2:



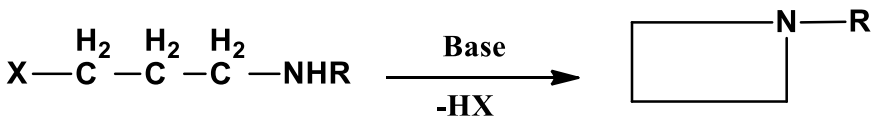
Azitidine

Preparation of azitidine:

1- From 1,2-dibromopropane:



2- from 2-aminopropane halide or sulfonate:



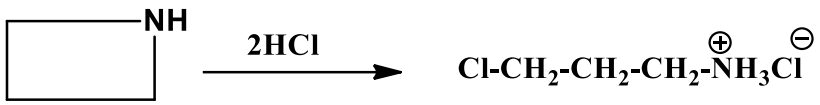
Physical properties:

Azitidine is colorless liquid, boil at 61c has an odor as ammonia, form clouds when touch air, miscible with water and ethanol, more basic than aziridine.

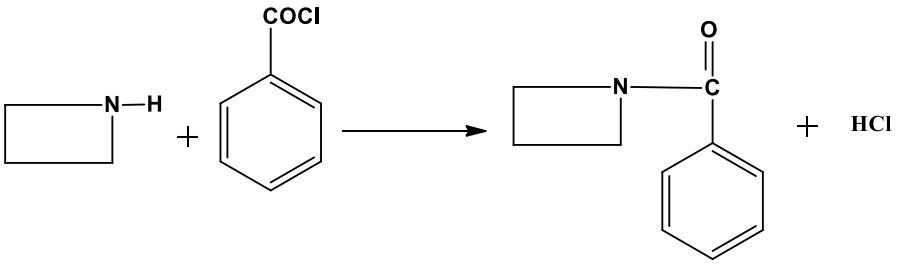
Chemical properties:

1- **Azitidine is stable compound, azitidine is less reactive than aziridine.**

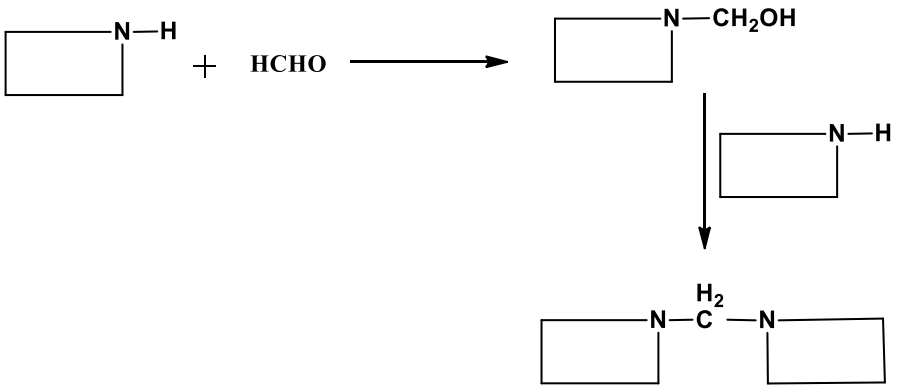
2- **Effect of hydrochloric acid:**



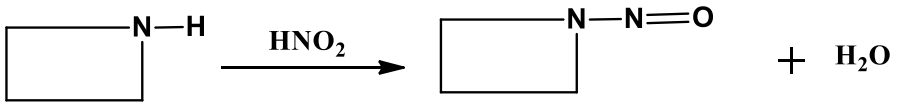
3- **With benzoyl chloride;**



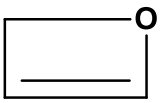
4- **Effect of formaldehyde:**



5- effect of nitrous acid:



N-nitroso azitidine compouond is a yellow oil, boil at 197c.



Oxetine

Oxetine is four membered ring compound contains an oxygen atom and has double bond, and has strain less than three membered ring.

Preparation:

1- **From hexafluro acetone:**

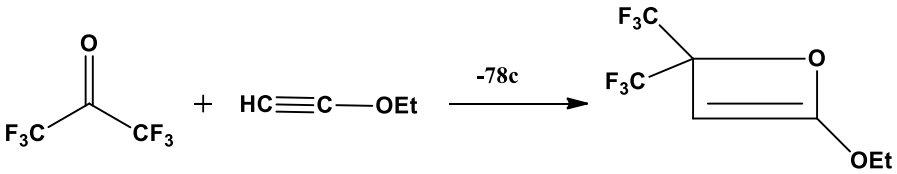
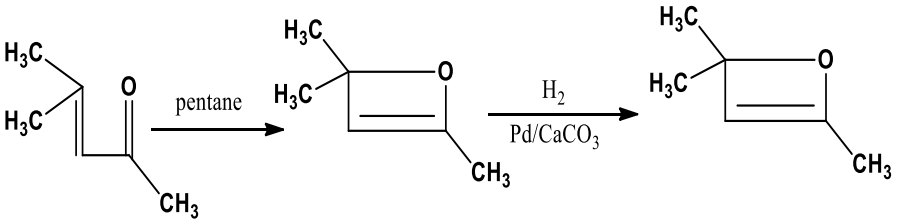
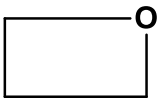


Photo reaction of mesetyl oxide:



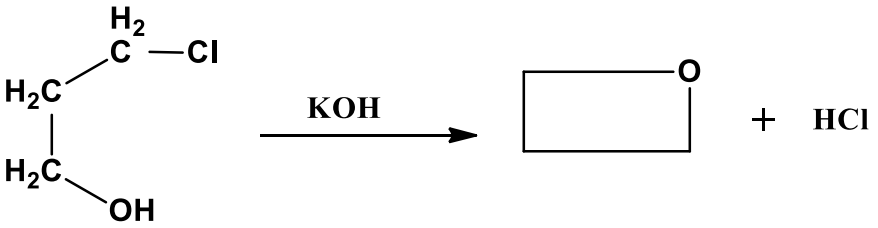


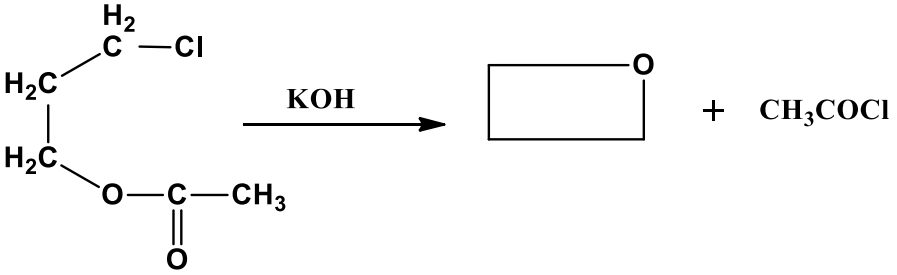
Oxetane

Oxitane can be also called trimethylene oxide, it is colorless liquid, boil at 48c.

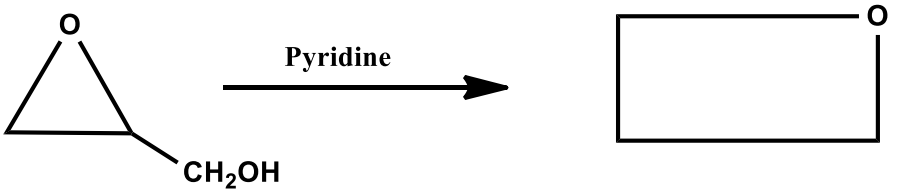
Preparation:

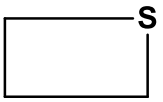
1- From 3-chloro propanol:





2- by rearrangement of oxirane ring:

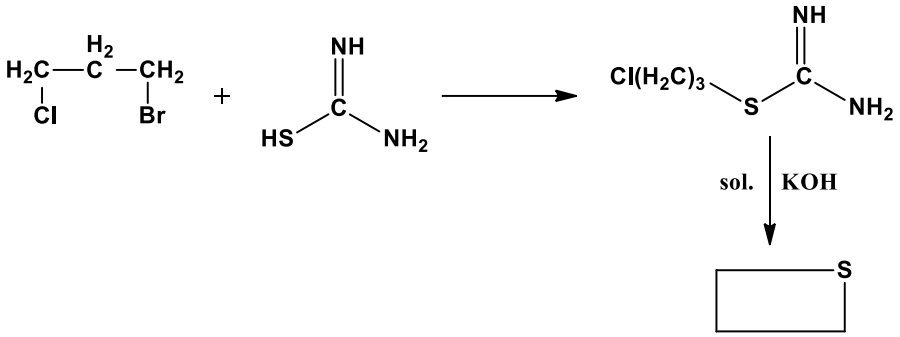




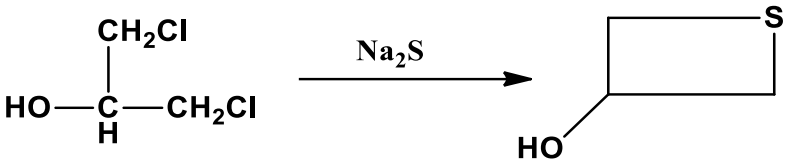
Thiatane

Thiatane can be also called trimethylene sulfide or 1,3-propylene sulfide.

Preparation: 1- From 3-bromopropylchloride:

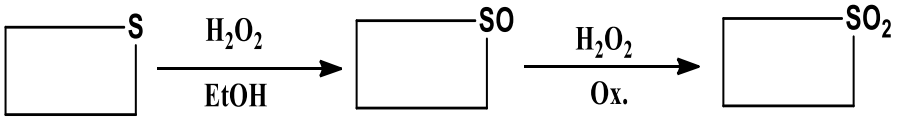


2- by 1,3-dibromopropane or 1,3-dichlorobropane or its derivatives with sodium sulfide:

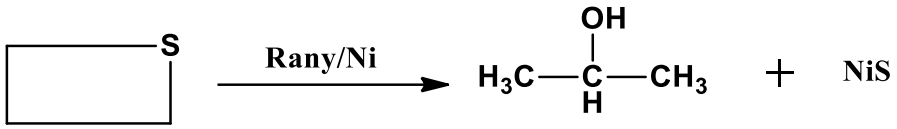


Properties:

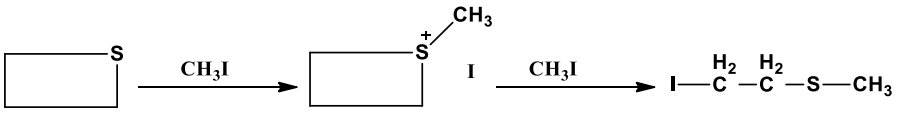
1- **Oxidation: thiatane oxidized by hydrogen peroxide to give stable oxide then give sulfone:**



2- Remove of sulfur:



3- Open the ring by methyl iodide:

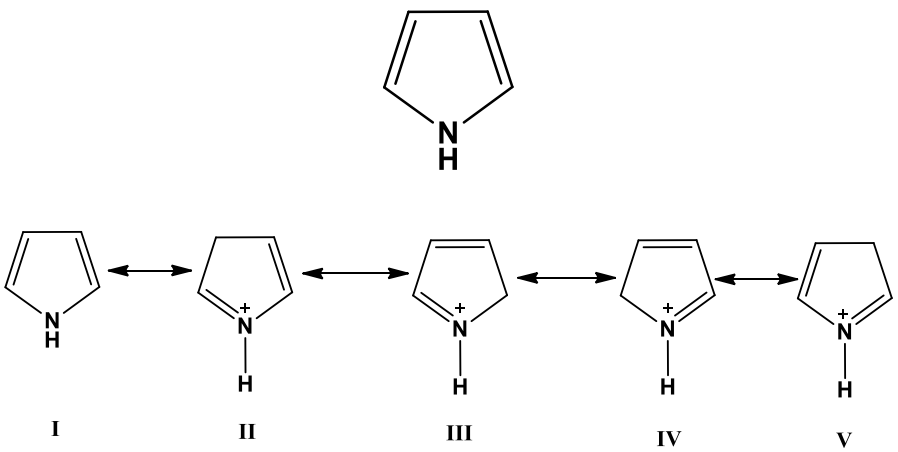


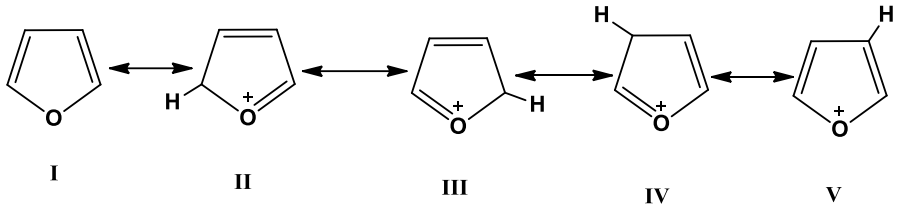
Five membered ring

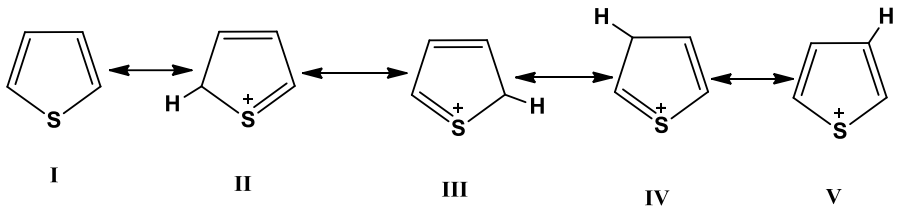
Five membered ring compounds are the most known heterocyclic compounds which contain one heteroatom as furan, pyrrole and thiophene.

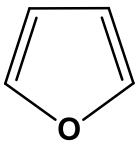
Properties of these compounds as aromatic compounds which have resonance structure because the lone pair of electrons on heteroatom contribute in aromaticity, so these compounds have electrophilic substitution reactions as:

1- **Nitration.**
2- **sulphonation**
3- **halogenation**
4- **Friedel-Crafts reaction**
5- **Coupling with diazonium salts.**







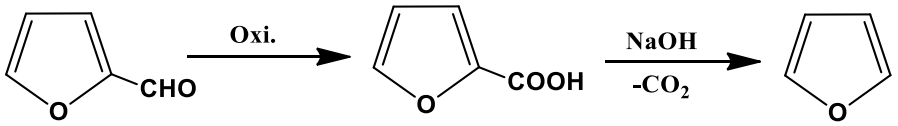


Furan

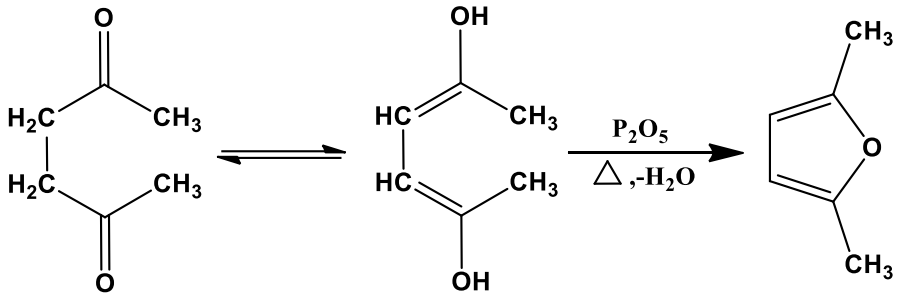
Furan is colorless liquid, with low boiling point at 31c.

Preparation:

1- **From oxidation of furfural to furic acid then elimination of carboxylic group:**



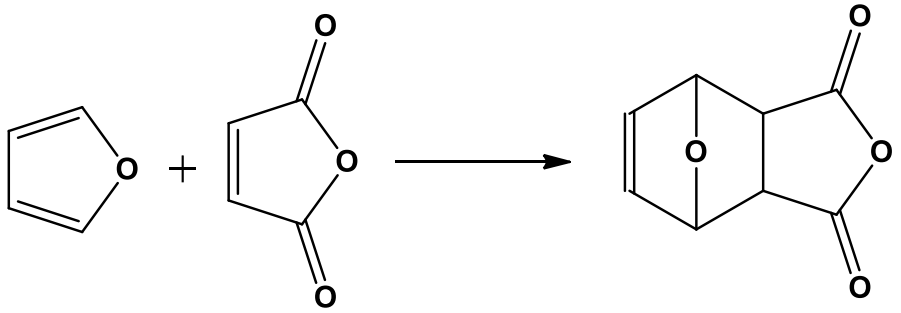
2- **2,5-dimethylfuran can be prepared from acetonylacetone;**



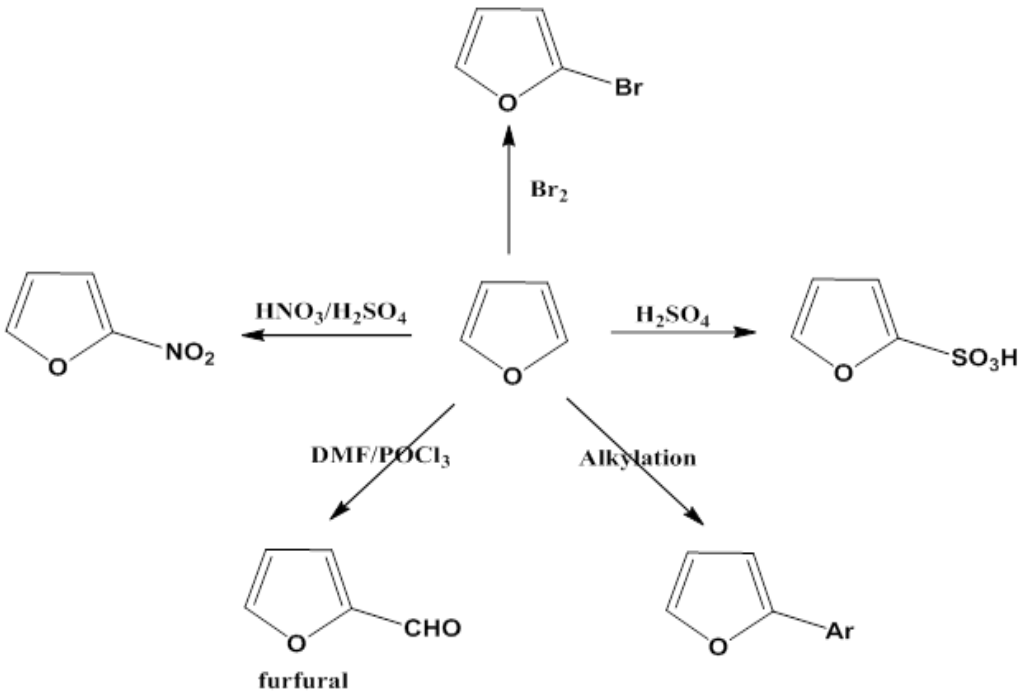
Chemical properties:

Furan is more reactive than benzene (resonance energy of furan is less than benzene)

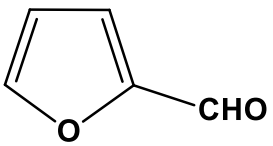
1- Diel's-Alder reaction:



2- electrophilic substitution:



Furfural

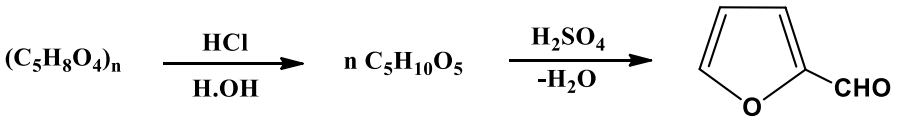


Furfural is colorless liquid, turn to brown color when to air, boil at 96c.

Test for furfural by exposure the vapor of furfural to a paper wetted with aniline acetate the paper become red color.

Preparation of furfural:

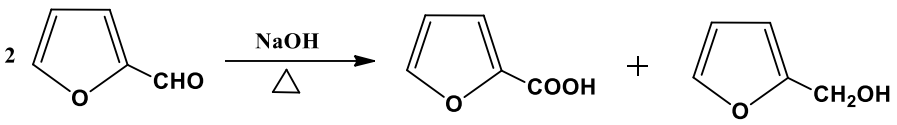
1- From pentoses;



Chemical properties:

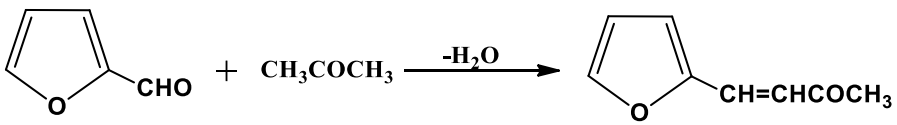
Furfural react as benzaldehyde as:

1- Cannizaro reaction:

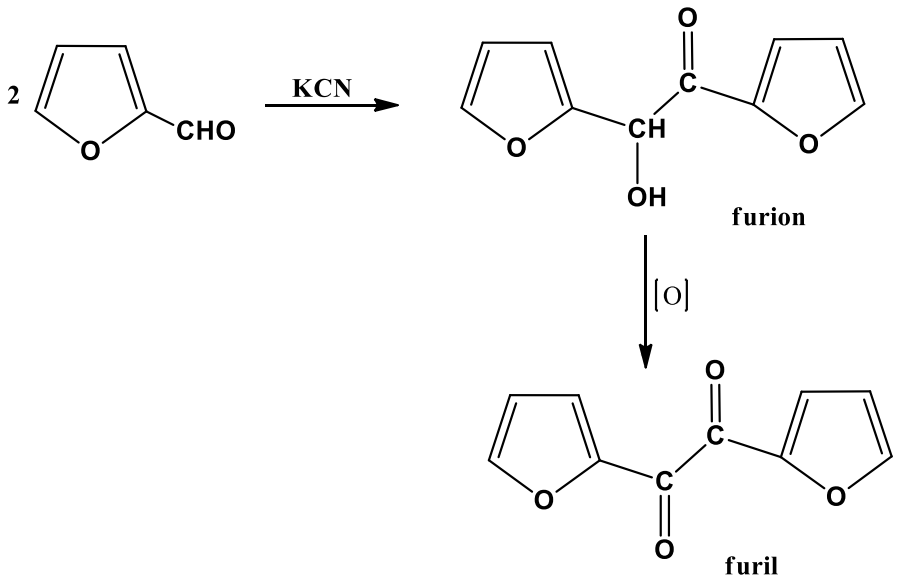


2- Condensation reactions:

a- With acetone:

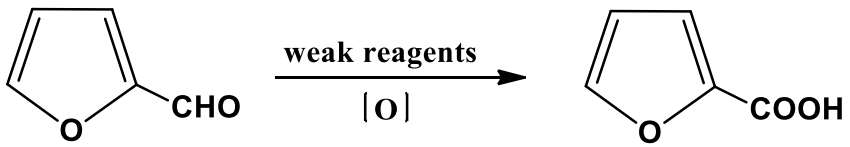


b- With KCN (as benzoin condensation):

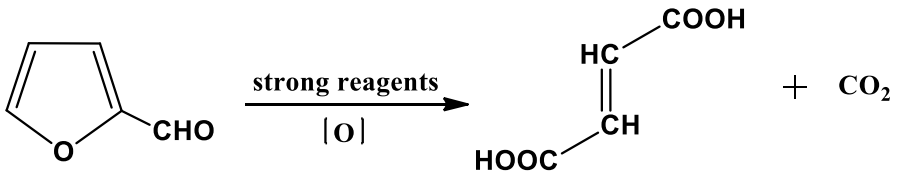


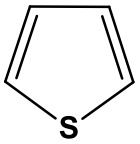
3- Oxidation:

a- By weak oxidizing agents:



b- By strong oxidizing agents:



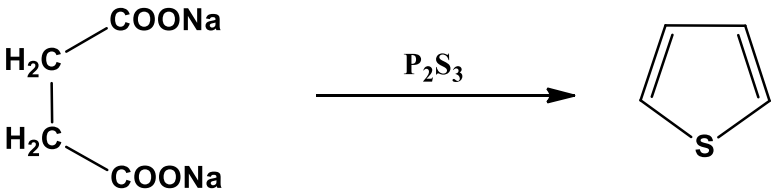


Thiophene

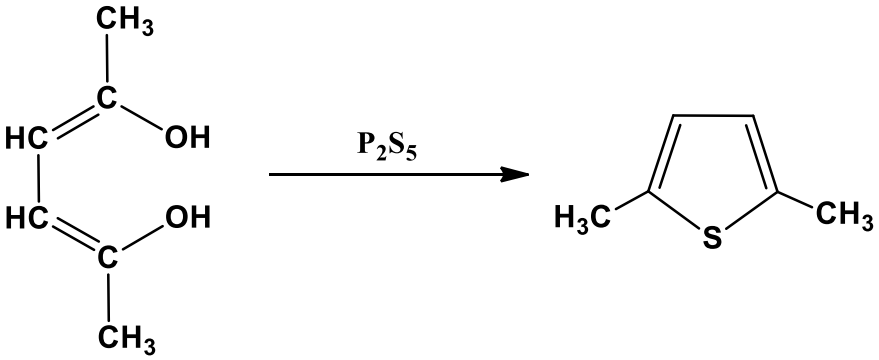
Thiophene is colorless liquid boil at 84c present with benzene in coal-tar and separated by chemical methods.

Preparation:

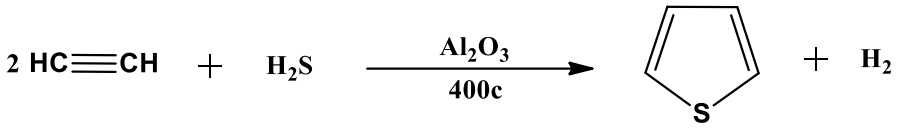
1- **From distillation of sodium succinate with phosphorus trisulfide:**



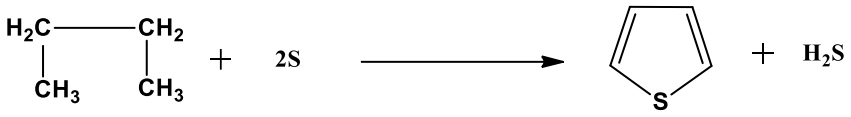
2- **From enol form of acetonylacetone with phosphorus pentasulfide:**



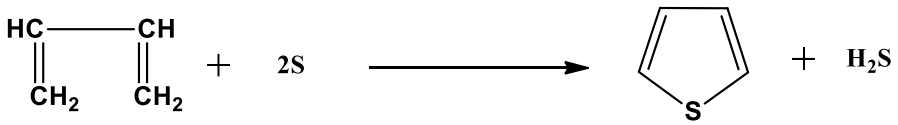
3- By heating a mixture of acetylene with H_2S:



4- By heating a mixture of butane gas with Sulphur:

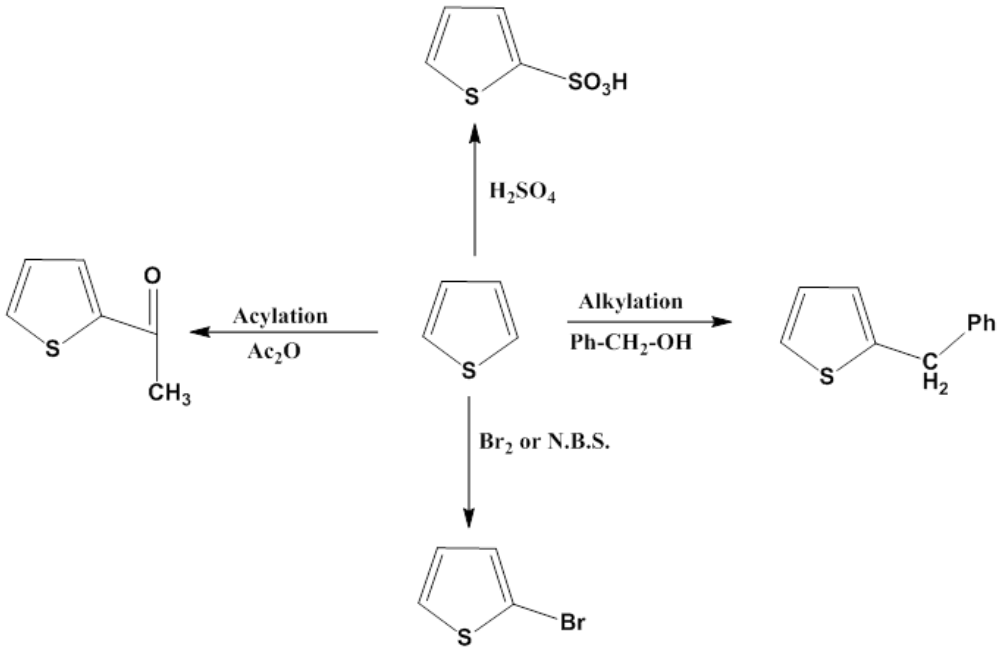


5- By heating of butadiene with Sulphur:



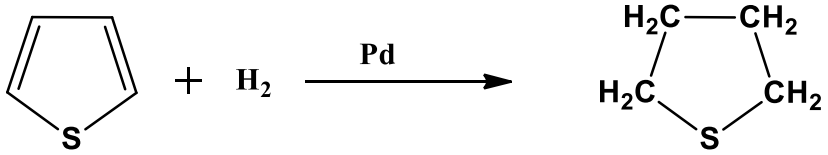
Chemical properties of thiophene:

1- Electrophilic substitution of thiophene:

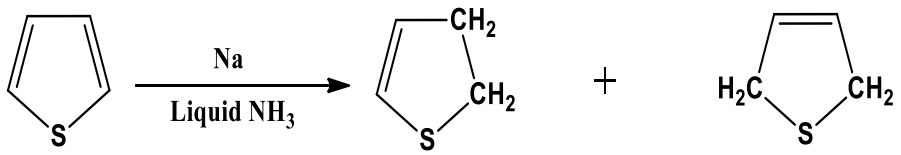


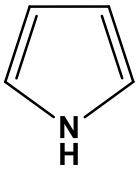
2- Hydrogenation (reduction):

a- Fully hydrogenation:



b- partial hydrogenation:



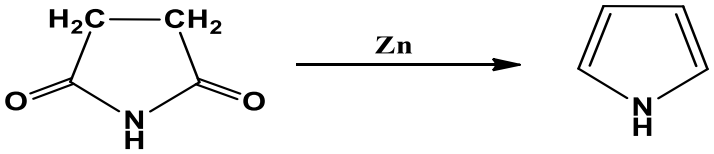


Pyrrole

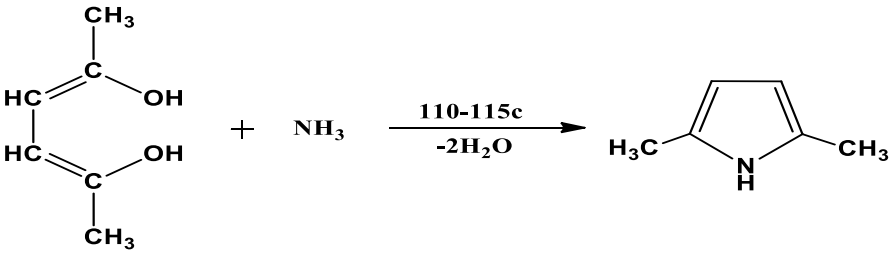
Pyrrole is colorless liquid has odor as chloroform, boil at 129c, partially soluble in water and organic solvents.

Preparation of pyrrole:

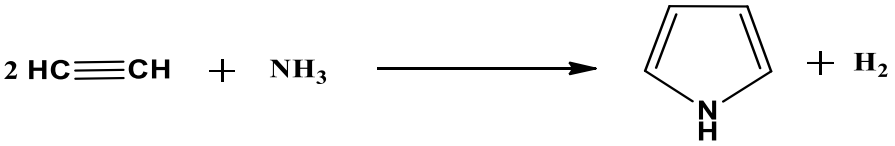
1- from distillation of succinimide with Zn dust:



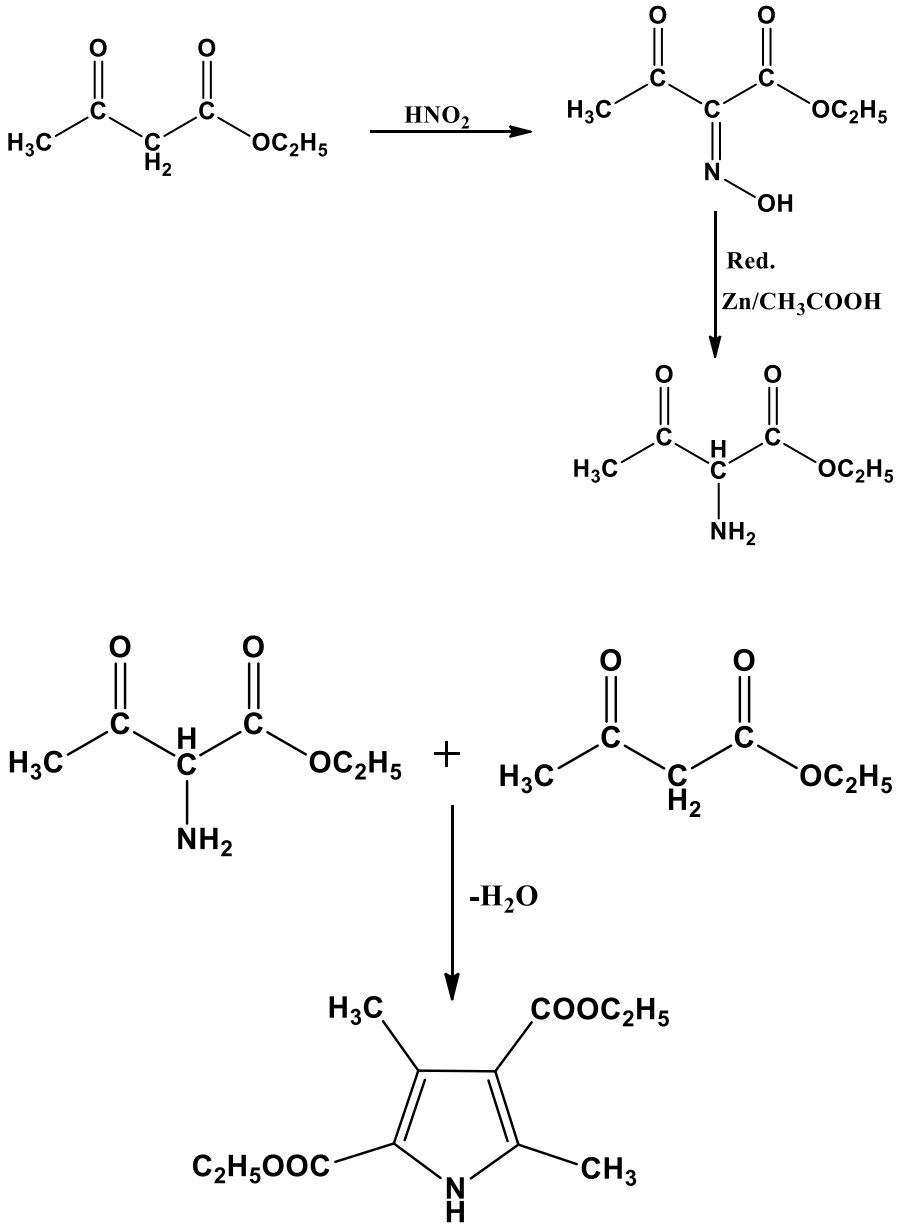
2- from enol form of acetonylacetone with ammonia:



3- from passing a mixture of acetylene with ammonia:

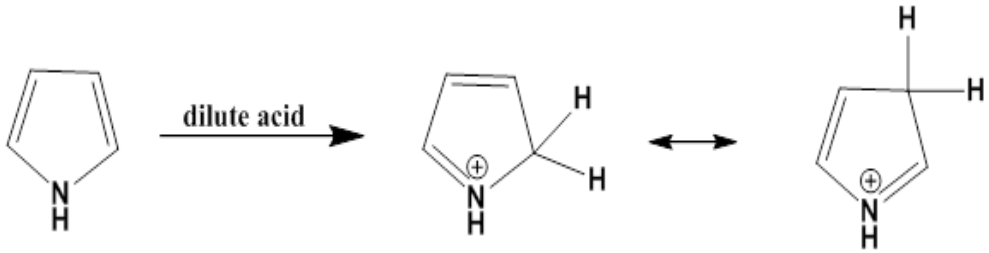


4- Knorr synthesis:

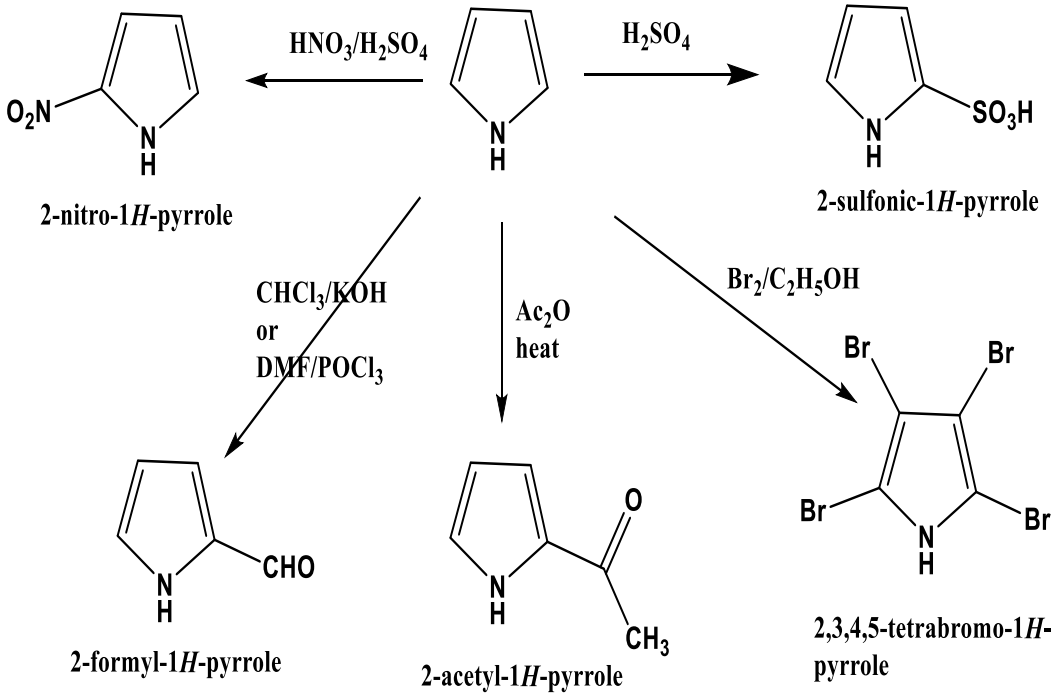


Chemical reactions of pyrrole:

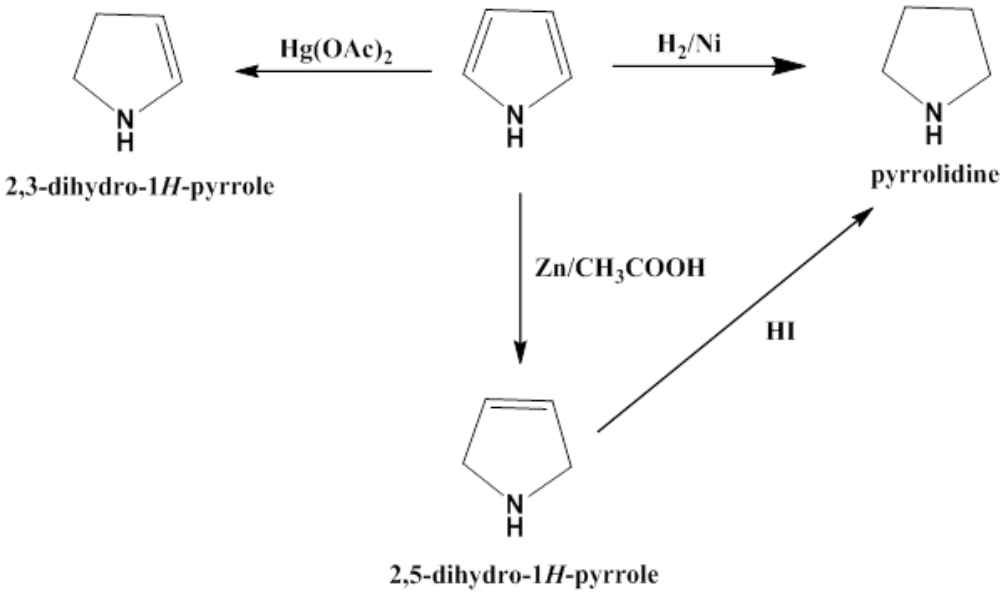
Pyrrole has aromatic character from the lone pair of electrons on nitrogen atom contribute in resonance, so the basic properties of pyrrole is low (pyrrole is less basic than pyridine).



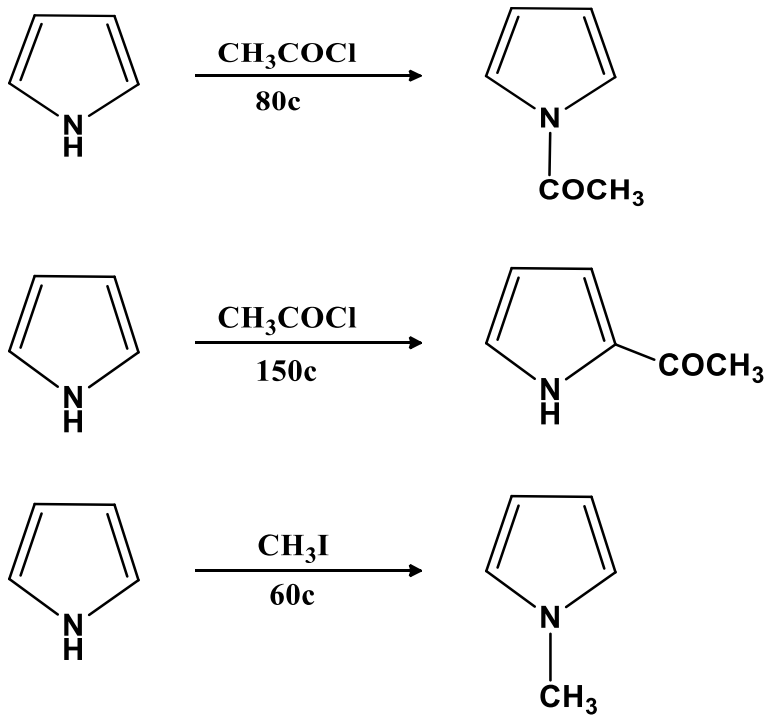
1- Electrophilic substitution:

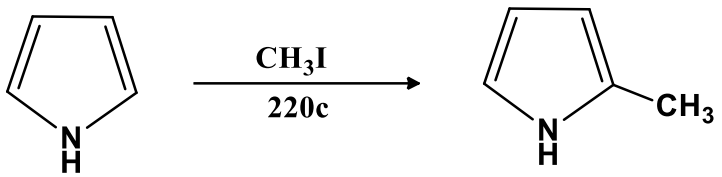


2- Reduction of pyrrole:

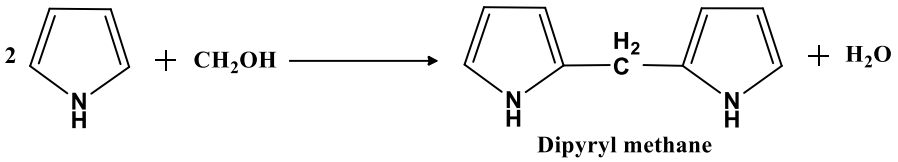


3- Alkylation and acylation:





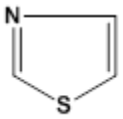
4- With formaldehyde:



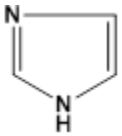
Dipyryl methane

Five membered ring with two heteroatoms

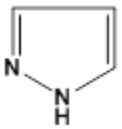
The most important compounds of this class are:



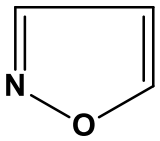
Thiazole



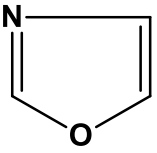
imidazole



pyrazole



Isooxazole

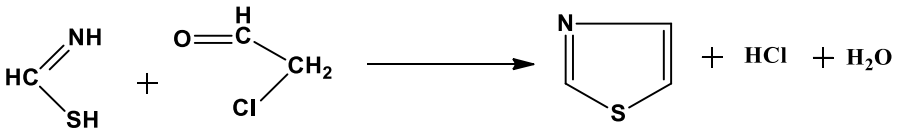


oxazole

Thiazoles

These are stable compounds have basic properties, inter in vitamin E and penicillin.

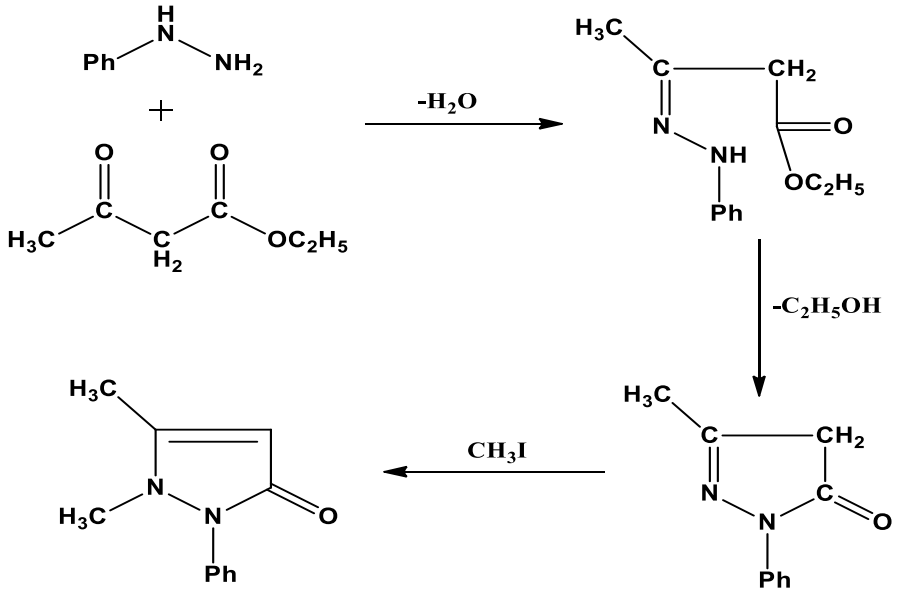
Thiazole derivative can be prepared as follow:



thioformamide **α-chloroacetaldehyde**

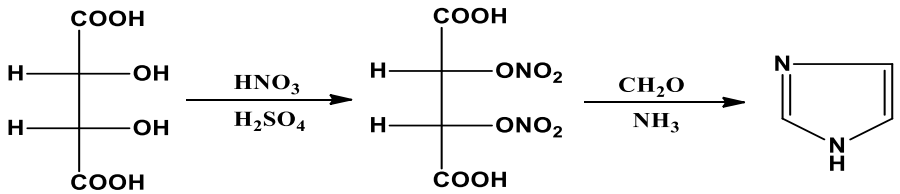
Pyrazole

Pyrazole has aromatic properties, it is solid, its melting point is 70c, the most important derivative of pyrazole is 1-phenyl-2,3-dimethyl-pyrazolin-5-one (antipyrine), that used in medicine as antipyretic, which prepared from the reaction of phenylhydrazine with ethylacetoacetate.



Imidazole

Imidazole has amphoteric properties and can be prepared as follow:



Six membered ring

Six membered ring contains one heteroatom, the most important compounds in this class are 1,2-pyran, 1,4-pyran, 1,2-thiopyran, 1,4-thiopyran and pyridine. Pyran is present in vitamin H.

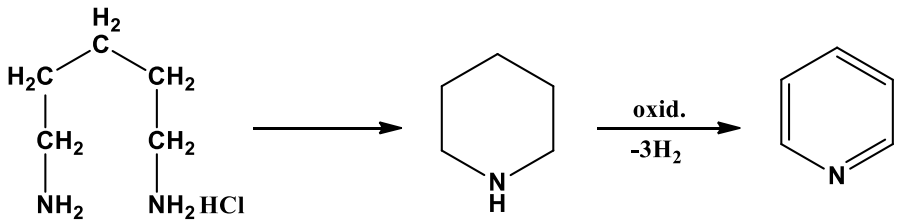
Pyridine

Pyridine is colorless liquid has brown color when exposure to air, boil at 115c, soluble in water and organic solvents, it has basic properties, it used in industry as catalyst and as a solvent.

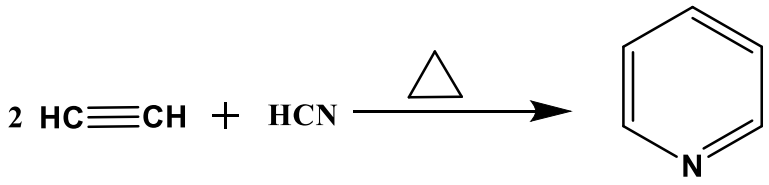
Pyridine present in nicotinamide adenine dinucleotide phosphate, and vitain B6.

Preparation of pyridine:

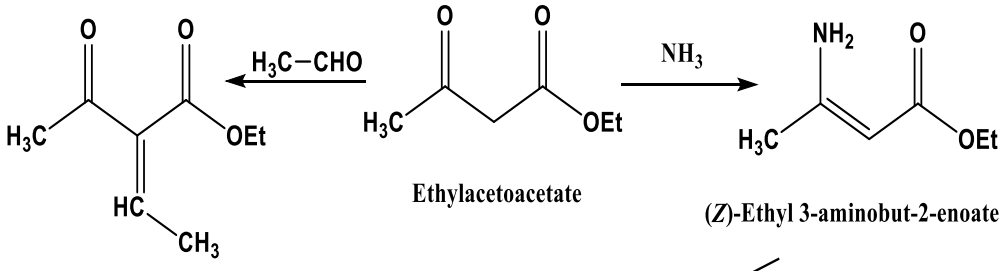
1- **By heating pentamethylene diamine hydrochloride to give pipridine which by oxidation give pyridine.**

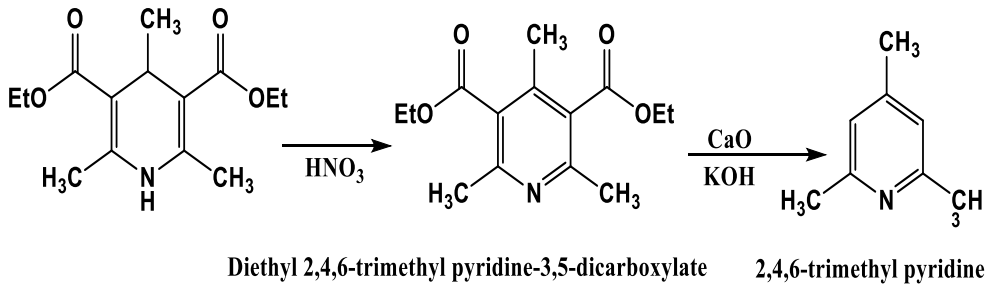


2- Reaction of acetylene with HCN:



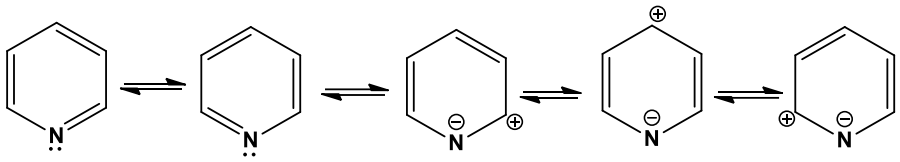
3- Hantzch synthesis:





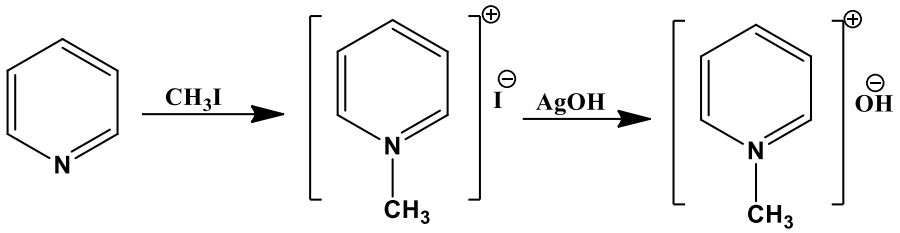
Chemical reaction of pyridine:

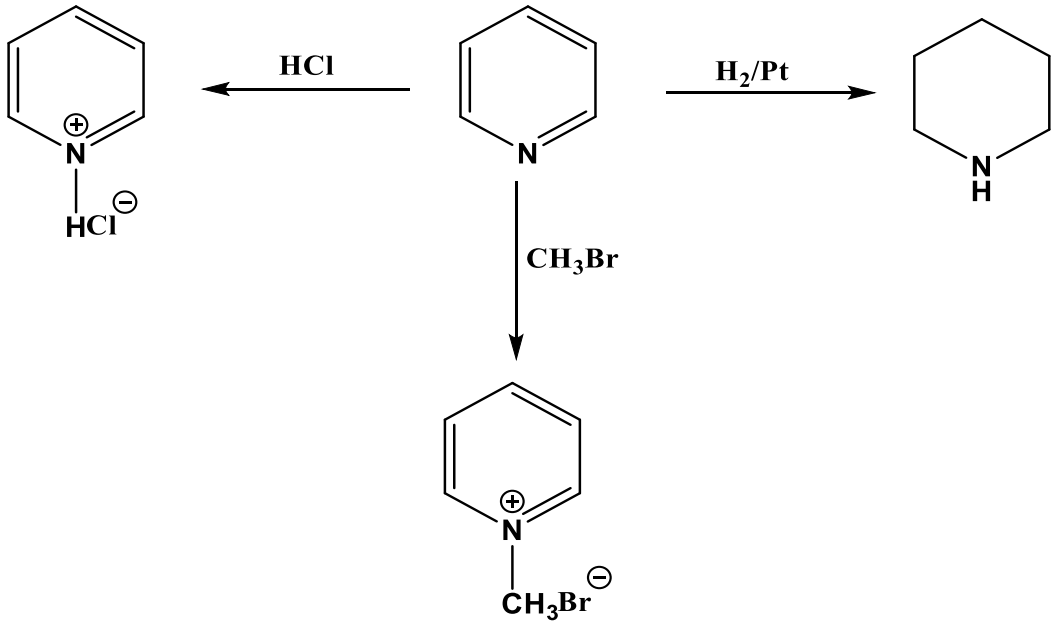
1- Aromaticity:



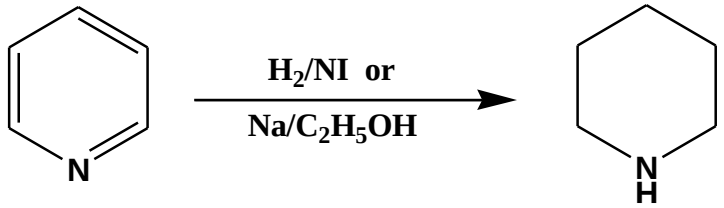
2- Formation of salts:

Pyridine act as a base, so it can form salts easily:

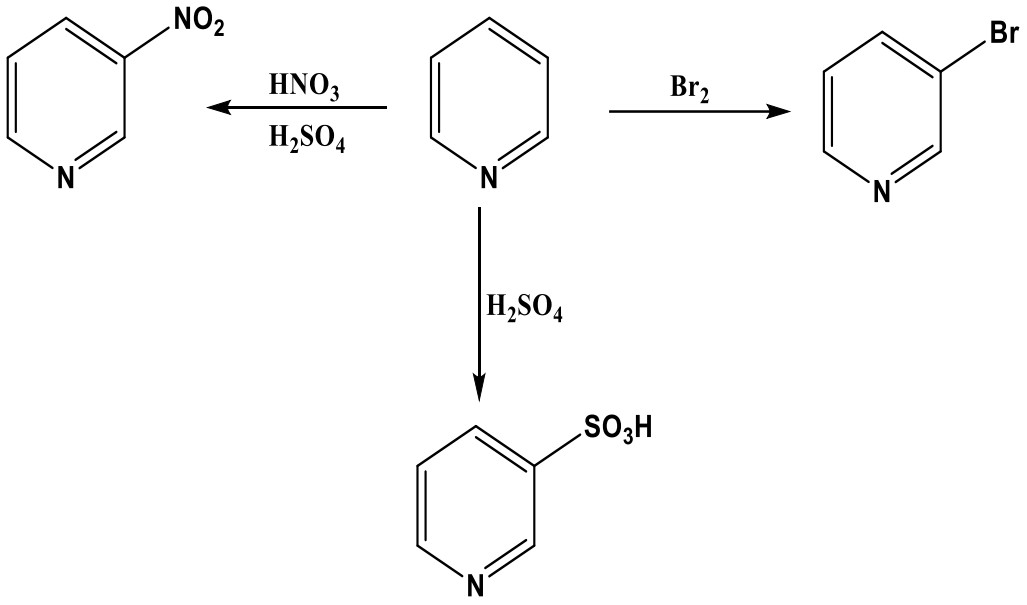




3- Reduction:

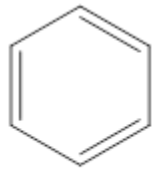


4- Electrophilic substitution:

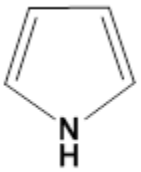


Fused heterocyclic compounds

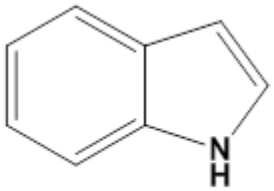
Indole



Benzene



Pyrrole

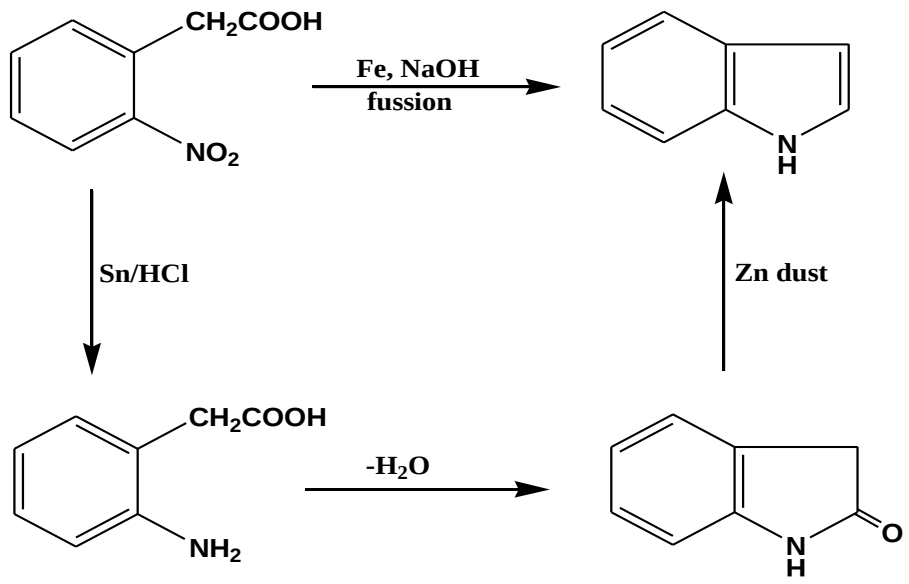


Indole

Physical properties:

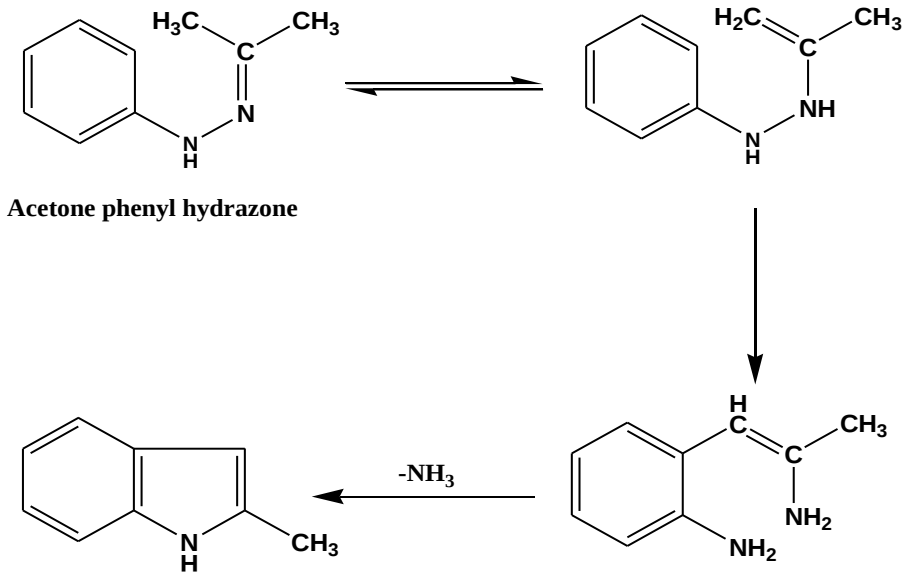
- **Indole is a solid compound has melting point at 52c.**
- **More stable than pyrrole because of its molecular weight.**
- **Electrophilic substitution preferred position 3 than position 2.**
- **It is present in dyes and proteins.**

Basir confirm the molecular formula of indole from this preparation method:



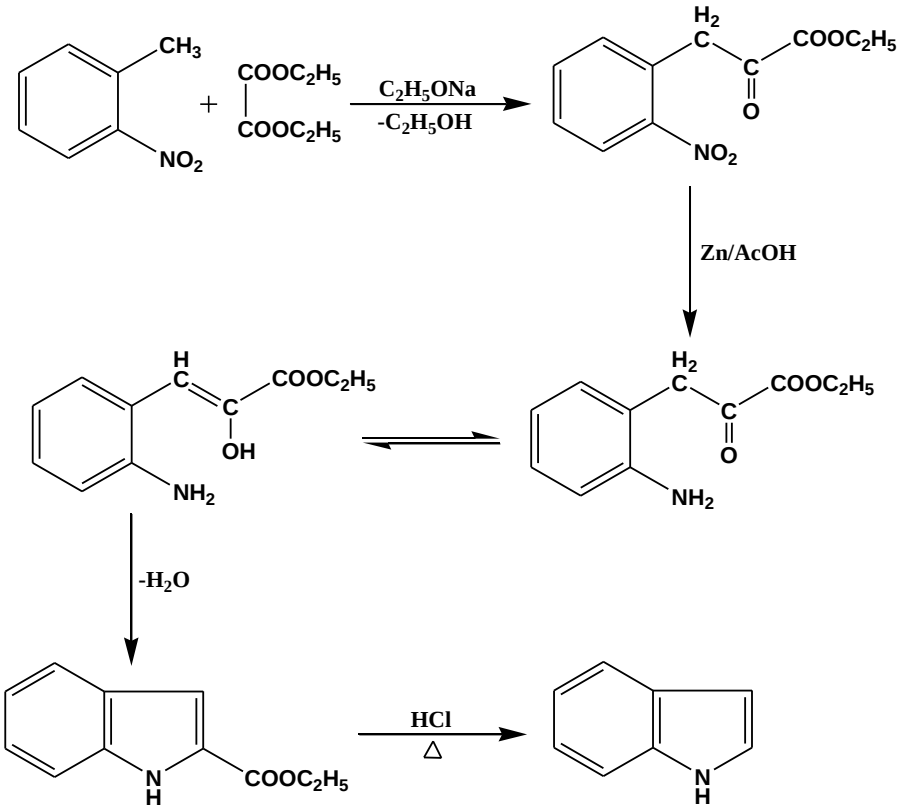
Preparation of indole:

1- Fiescher method;



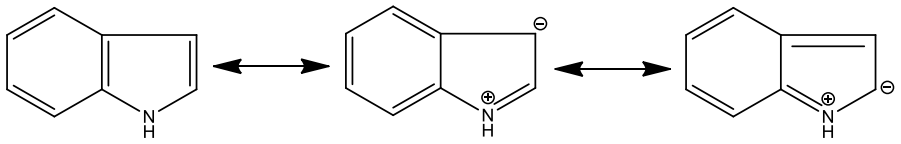
Acetone phenyl hydrazone

2- Resiert synthesis:

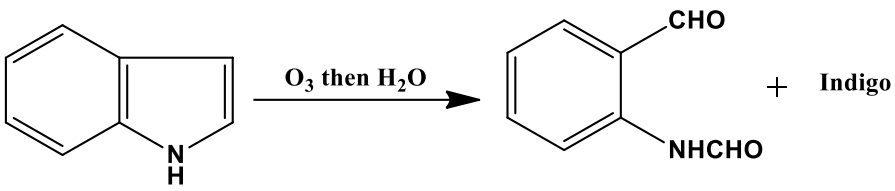


Chemical properties of indole:

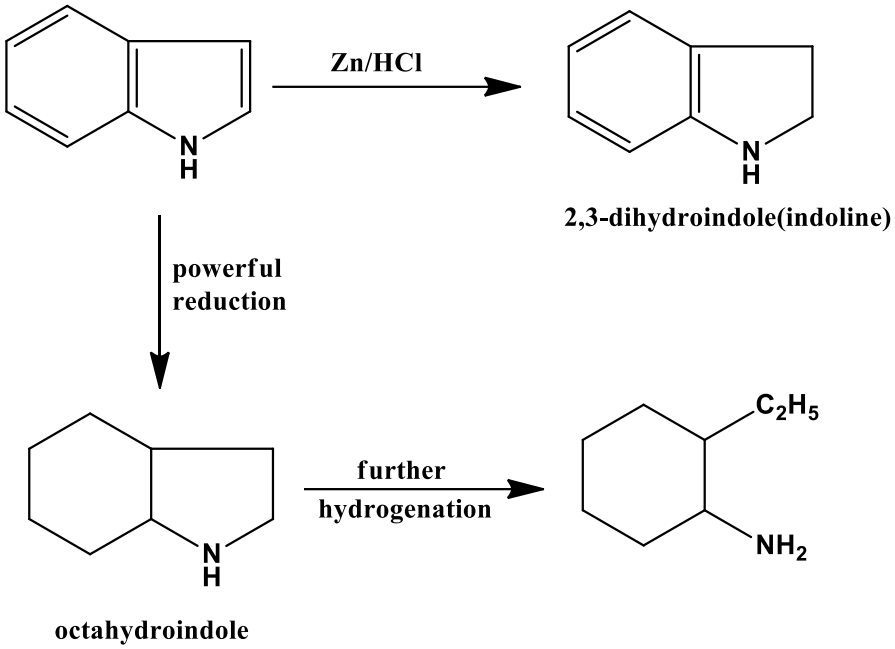
1- Resonance structure:



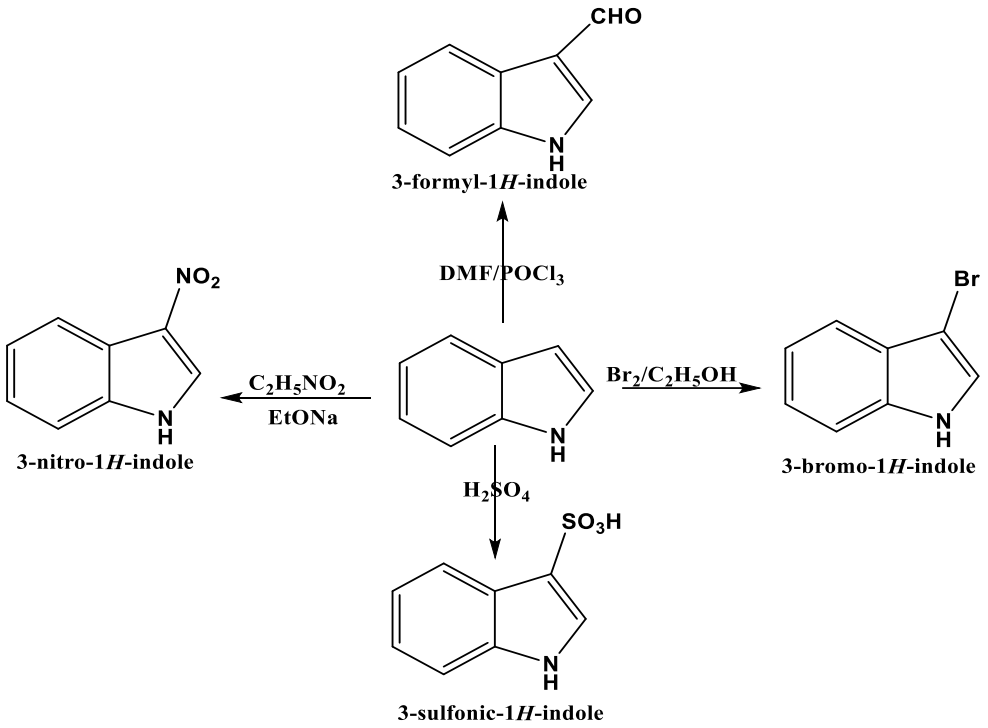
2- Oxidation:



3- Reduction:

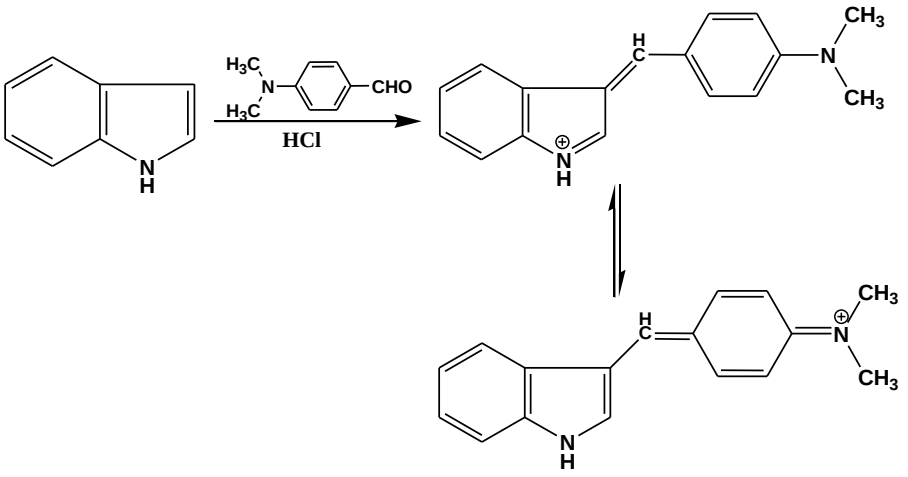


4- Electrophilic substitution:



5- Test for indole (Arac method):

Treatment of indole by HCl and dimethyl amino benzaldehyde give red violet color.



References

- **1- Handbook of Heterocyclic chemistry (3rd Edition) 2014.**
- **2- Comprehensive Heterocyclic Chemistry III: Alan Katritzky, Christopher Ramsden, Eric Scriven, Richard Taylor (2008).**
- **3- Heterocyclic Chemistry I, Mahndra Kumar, Fandana Jupta, Radha Ar. Jupta (2011).**
- **4- Heterocyclic Chemistry II, Mahndra Kumar, Fandana Jupta, Radha Ar. Jupta (1998).**
- **5- Advances in Heterocyclic Chemistry, Eric F. V. Scriven, (2016).**
- **6- Modern Heterocyclic Chemistry, Julio Alvarez-Builla, Juan J. Vaquero, and Jose Barluenga, (2011).**
- **7- The Chemistry of Heterocyclic compounds, R. Ian Fryer, (1991).**

Chemistry OF Dyes

4th Year Students Faculty of Education South Valley University

second term 2022/2023

Dr/ Ibrahim Abdul-Motaleb Mousa

Dyes

General characters of the dye molecule:

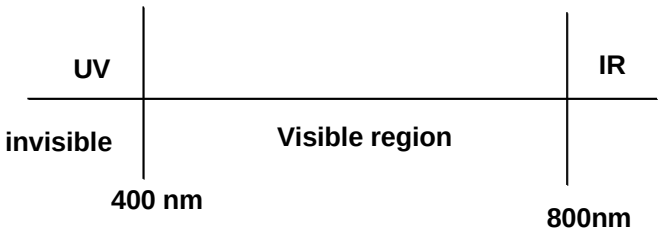
1- **It must have a suitable color.**

2- **It must be fixed to the fabric.**

3- **Dye must have fastness properties to light, washing acids, alkalis, and perspiration, rubbing.**

Introduction on dyes

- **The spectra are mainly classified into main three region as shown**



- **When light fall on substance, part is absorbed and other reflected, and we see the reflected part**
- **Black substance absorb all light**
- **White substance reflect all the incident light**

The absorption of radiation by molecules

- **According to quantum theory $\Delta E = h\upsilon = hc/\lambda$**
- **For any substance to be colored its molecules must contains mobile electrons (present in chrmophores) which can raised from ground state to excited state at values of ΔE**
- **At higher ΔE, so higher υ and hence shorter λ (blue shift)**
- **At lower ΔE, so lower υ and hence longer λ (red shift)**

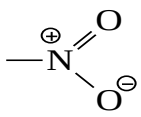
<u>Relation between color and chemical constitution:</u>

The organic compound to be colored it must have

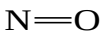
a) **Chromophores.**
b) **Auxochromes.**
c) **Quinoid structure.**

<u>A) Chromophores:</u>

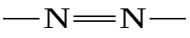
- Chromophores are these groups with multiple bonds examples of chromophores



nitro

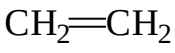


nitroso

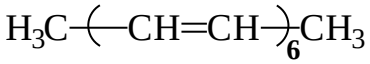


azo

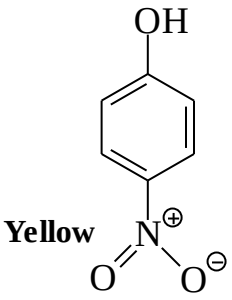
- **The compound contain the chromophores is called chromogen.**
- **Single chromophore is not sufficient to produce color but a number of chromophores must be attached in conjugation to produce color and as number of chromophores increase degree of color increase.**

e.g. 

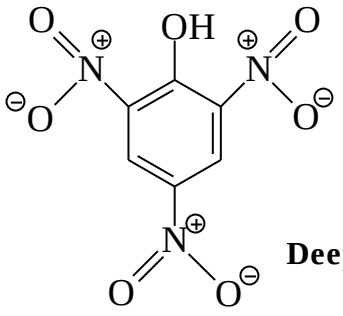
Colourless



Yellow



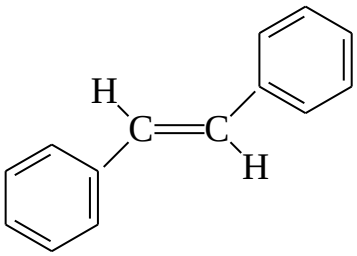
Yellow



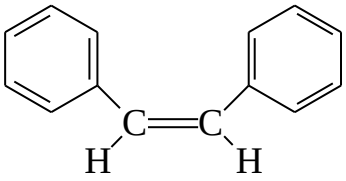
Deep Yellow

The position of groups in space can affect on color

e.g. stillbene



Trans
(Coloured)



Cis
(Colourless)

- **In case of trans (colored) the molecule is planner so conjugation involves two benzene rings and one double bond.**
- **In case of cis (colorless) the molecule not planner due to sterice hindrance of two benzene rings so conjugation is extended only on one benzene ring and double bond.**

B) Auxochromes:

- **Auxochromes are groups, which deepen the color.**
- **It classified into acidic (phenolic) e.g. OH or basic e.g. NH_2, NHR, NR_2**
- **Auxochromes are known as bathochromic groups, which makes shift from violet to red *(red shift)*.**

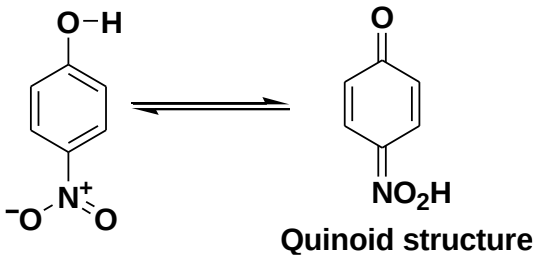
- **Groups which decrease the depth of color are known as hypochomic groups e.g $NHCOCH_3$ such groups shift the color from red to violet *(blue shift).***
- **Presence of auxochromes with chromogen make chromogen dye because it:**

1- Deepen the color.

2- Fix the dye with fabric by formation of salts.

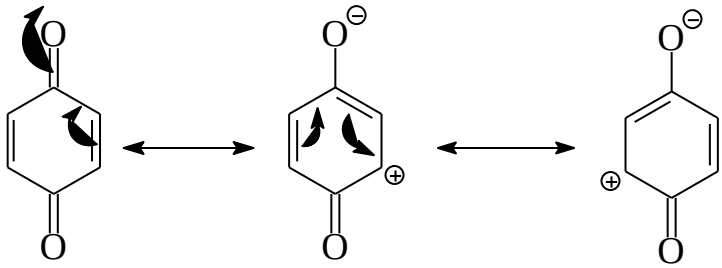
C) Quinonoid structure:

- **Presence of quinoid structure is essential for the production of color in compound containing benzene ring.**



Quinoid structure

- **The color of quinoid structure can be explained via resonance.**



Classification of dyes according to application:

Dye class	Description	Fiber application
1- Acidic (anionic)	Contain SO_3Na or-COONa	Wool, silk
2- Basic(cationic)	Contain NR_2, NHR, NH_2, as salt	Cotton, silk
3- Direct dye	Water soluble dye of azoic dye contain -COONa or SO_3Na	Vegetable fiber
4- Mordant	Has no affinity to fiber so must be pretreated with metal oxide	Vegetable and protein fiber
5- Azoic dye	Contain N=N, water insoluble pigments formed	Cotton

	within the fiber	
6- Vat dye	**applied in reduced (leuco) form (soluble) and oxidized on fiber (insoluble)**	**Cotton**
7- Reactive dye	**Forms covalent bond with fiber**	**Cotton, wool**
8- sulphur e.g thioindigo	**Contain S, applied in reduced form and oxidized on fiber**	**Cotton**

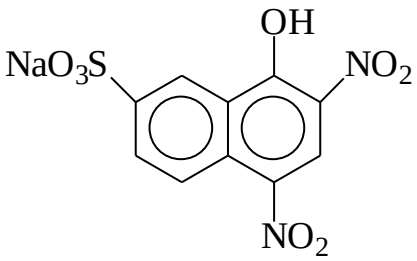
Chemical classification of dyes:

- **It is classified according to the groups present or main nucleus**

Examples: Nitro dyes - Nitroso dyes - Azo dyes - triphenyl methane dyes,

<u>1) Nitro dyes:</u>

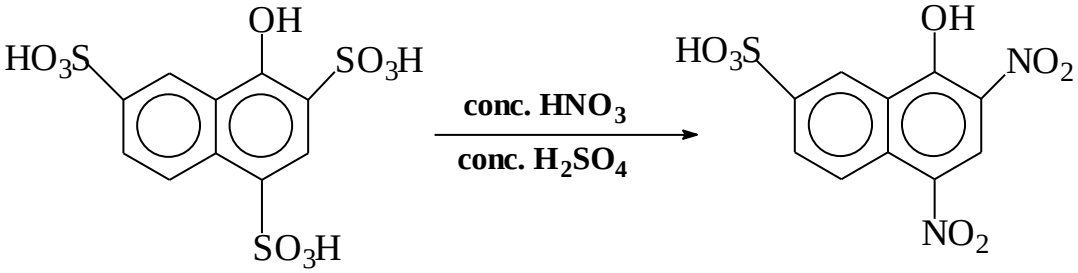
Dyes contain -NO_2 as chromophore and OH as auxochrome e.g.



Naphthol Yellow S

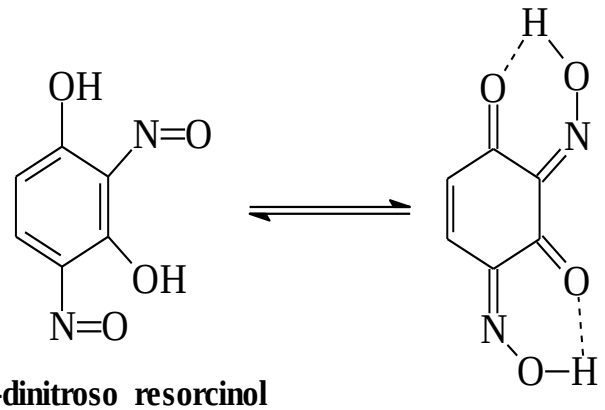
2,4-dinitro Naphthol-7-sulphonic acid sod. salt

Preparation:



2) Nitroso dyes:

Dyes contain N=O as chromophore and OH as auxochrome e.g. fast green O.



2,4-dinitroso resorcinol

3) Azo dyes:

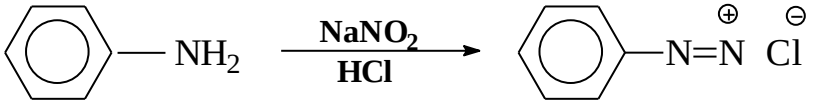
- **Azo dyes which contain N=N as chromophre and NH_2 or OH as auxochromes and both chromophore (-N=N-) and auxochrome attach with one more aromatic system.**
- **The dye is called monoazo if contain one N=N and is called diazo if it contain two N=N and so on.**
- **Azo dye is prepared through two steps:**

1- Diazotization.

2- Coupling.

1- Diazotization:

- **Diazotization is conversion of 1ry aromatic amine to diazonium salt.**



benzene diazonium chloride

<u>Mechanism of diazotization:</u>

It occur by the following steps:

1- Nitrosation of amines and this occur by nitrosating agent e.g.

$$\overset{\oplus}{N}O\ ,\quad NOCl\ ,\quad H_2\overset{\oplus}{O}-N=O\ ,\quad N_2O_3$$

2- Conversion of N-nitroso to diazonism salt.

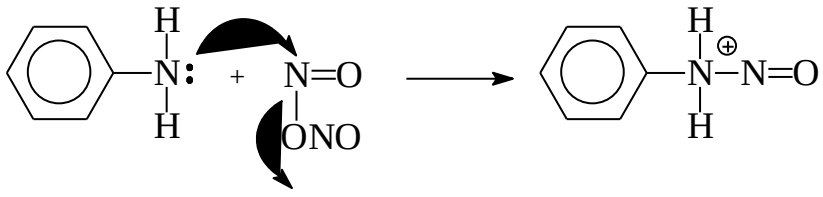
A) Mechanism of diazotization of 1ry aromatic amine:

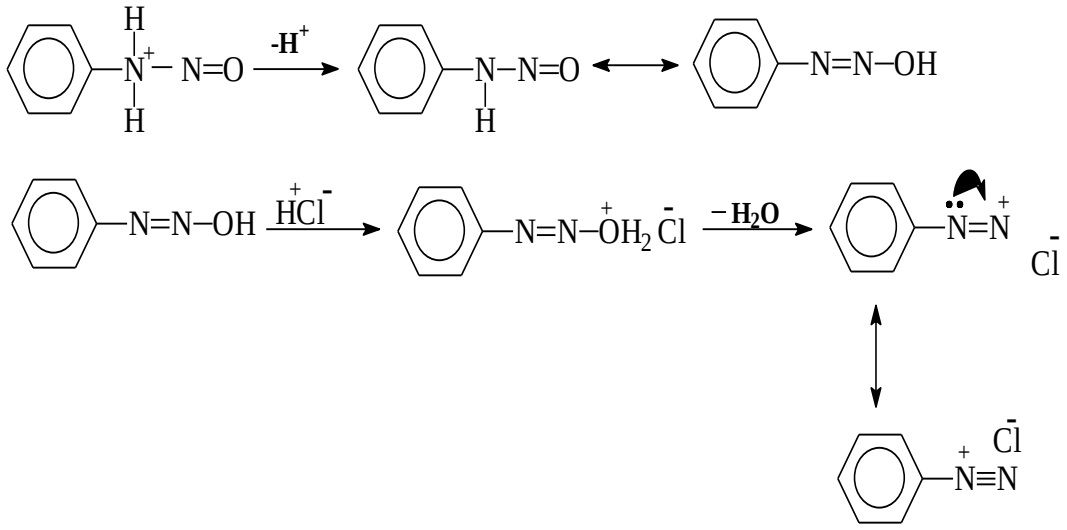
$$NaNO_2 + HCl \longrightarrow NaCl + HO-N=O$$

Nitrous acid

$$2\,HO-N=O \longrightarrow H_2O + N_2O_3$$

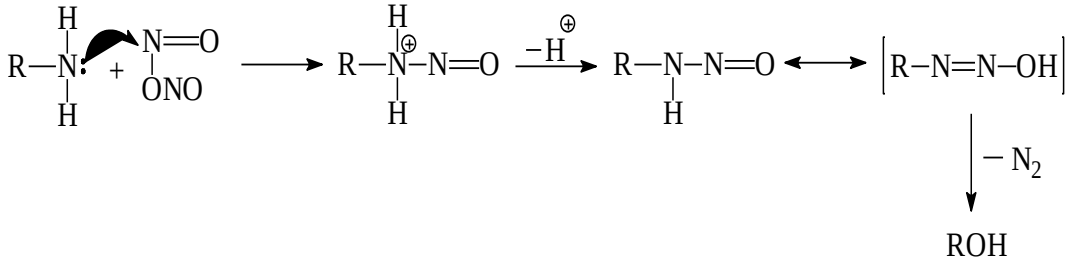
Dinitrogen trioxide





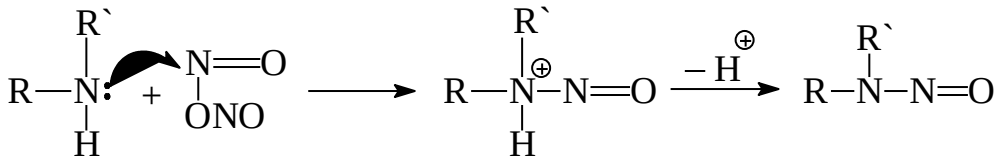
benzene diazonium chloride

B) 1ry aliphatic amines:



i.e. No diazotization of aliphatic amines.

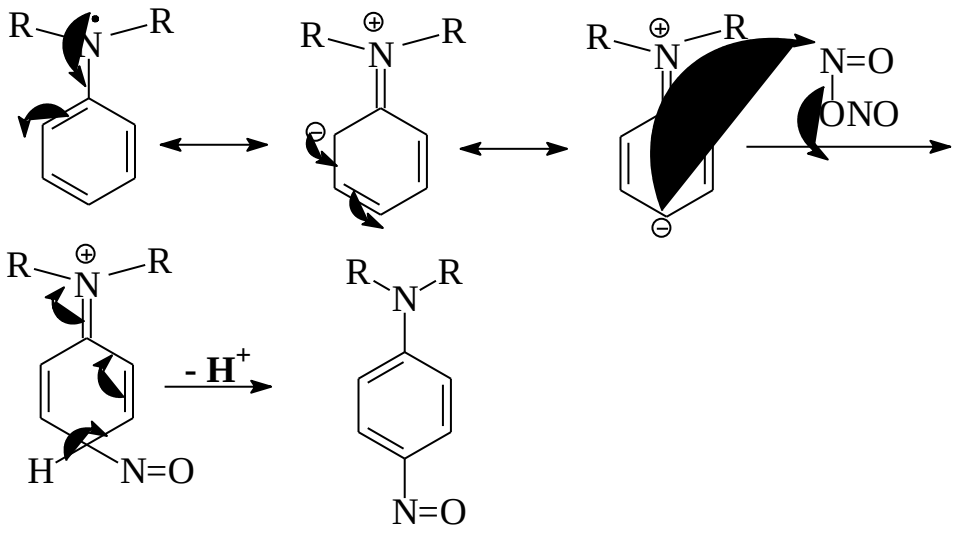
C) 2nd aromatic and aliphatic amines:



R may be aliphatic or Aromatic

N Nitroso compound

a) t- aromatic amines



P-Nitroso-N,N-dialkylaniline

- **For t-aliphatic amine, it does not react.**

  From the above only 1ry aromatic amines can be diazotized.

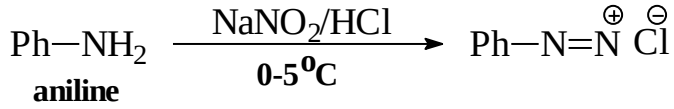
Effect of substituents on diazotization:

Diazotization of 1ry aromatic amines depends on nature and position of substituent groups.

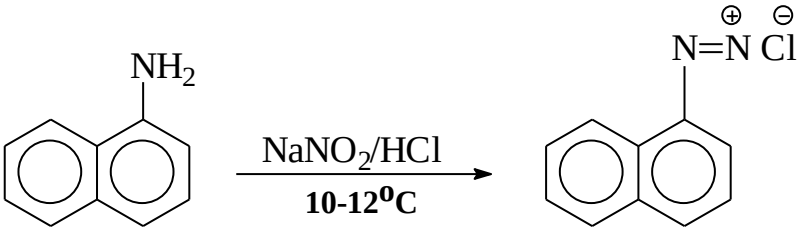
1- for unsubstituted 1ry aromatic amine:

It need equimolar of $NaNO_3$ and 3 equivalent of HCl

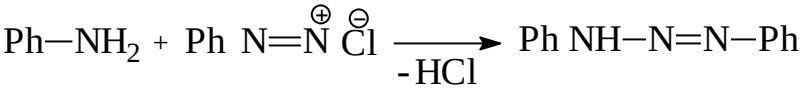
e.g.



For amino naphthalene



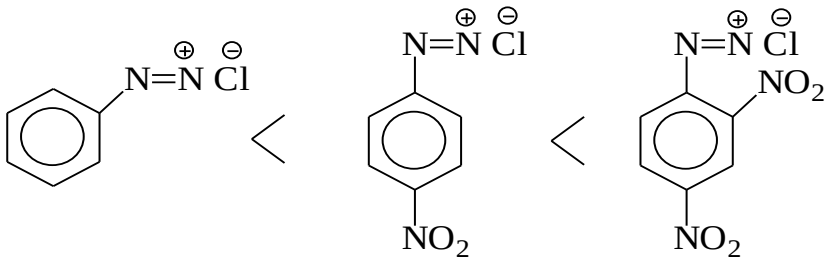
Secondary reaction can occur if some aniline is unreacted.



2- for nitro anilines:

- NO_2 group decreases the basicity of amines so it needs 7-equivalnt HCl.

- NO_2 group decrease the besicity because it act as electron withdrawing group but it increase the activity of diazonium salt so:



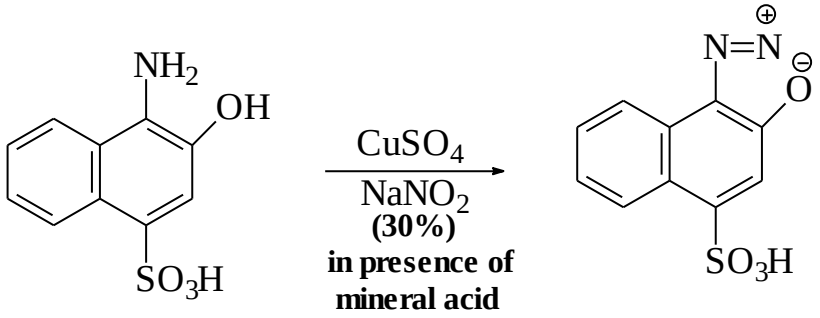
3- In case of acidic substituent:

The presence of acidic group e.g. SO_3H make diazotization occur after dissolving amino sulphonic acid in $NaHCO_3$ solution and $NaNO_2$ is added to aqueous solution of aminosulphonic acid then diluted acid is added to make diazotization (this method is called reversed diazotization).

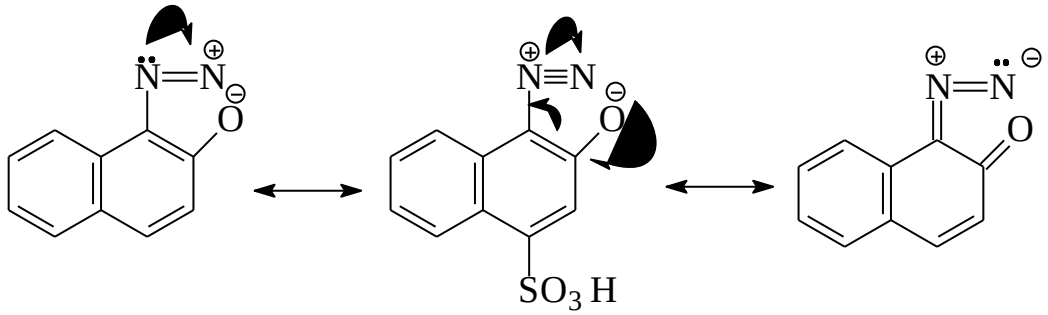
4- In case of aminophenol and aminonaphthol:

- **Amino phenol and amino naphthol in which NH_2 and OH are in position 1,2 or 1,4 for each other forming diazoxides.**
- **1,3-aminophenols don not form diazo-oxides**

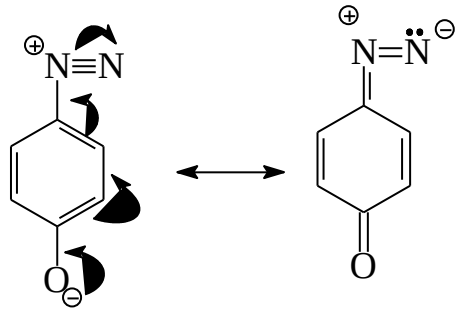
e.g.



- **Diazo–oxide is more stable than diazonium salt due to resonance e.g.**



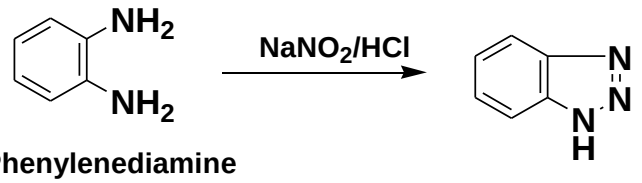
Also 1,4 aminophenol



1,2 aminohydroxyl compounds are used in manufacture of metal azo complex

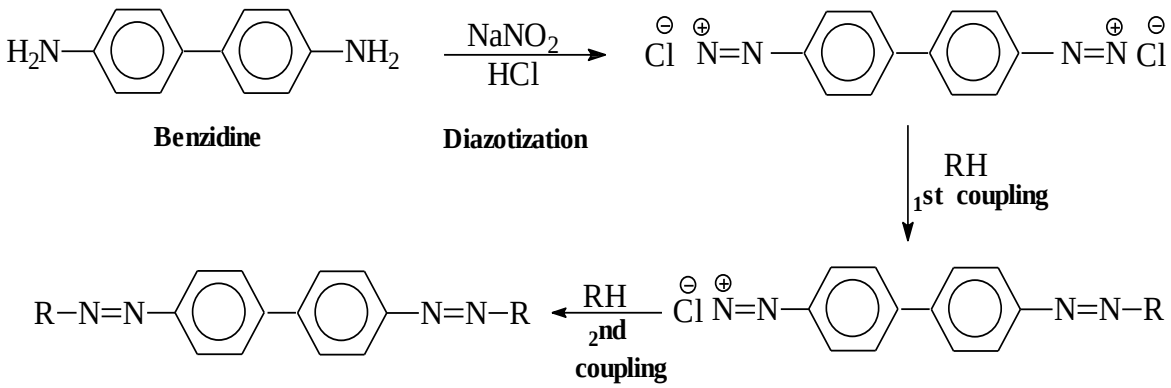
5- for diamines:

A) If two amino in o- position, no coupling occur due to ring closure.



O-Phenylenediamine **1*H*-Benzotriazole**

B) if two NH_2 are not in *o*- position diazatization occur.

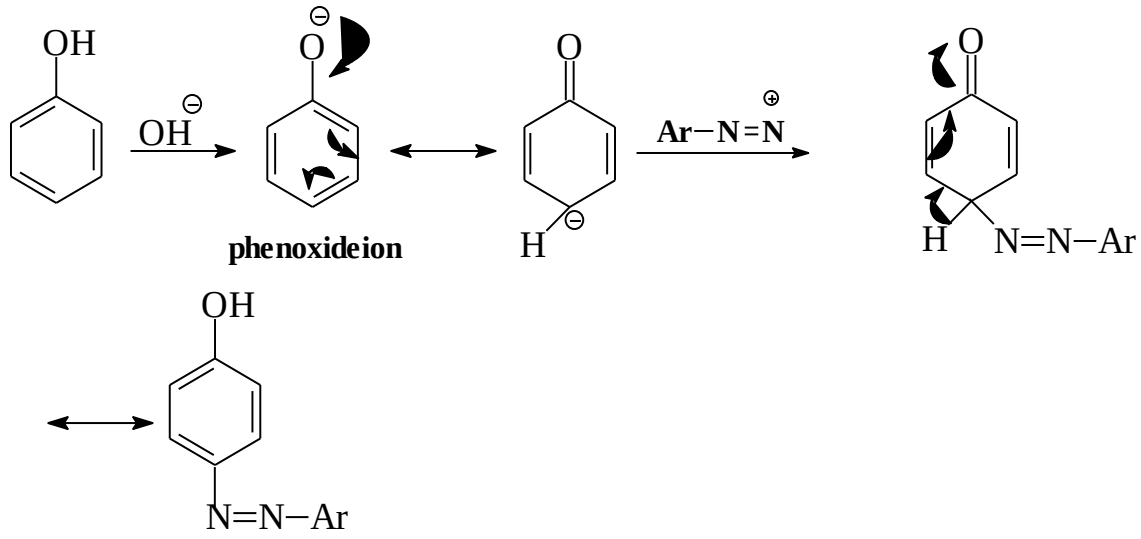


The 2nd coupling occurs slower than 1st.

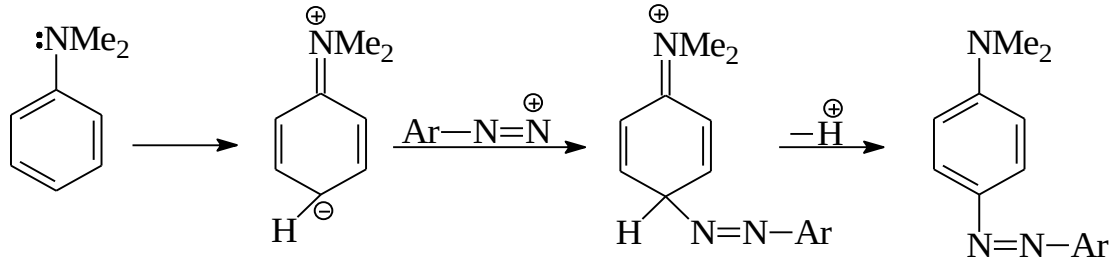
Diazo coupling

- **Diazo coupling is electrophilic substitution by diazonium cation.**
- **It occurs often in para-position.**
- **Coupling occurs for phenols in alkaline medium and for amines in slightly acidic medium.**

Mechanism of Diazo coupling of phenols:



Mechanism of Diazo-coupling of aromatic amines:



Coupling component:

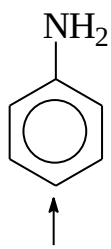
1) Benzene derivative:

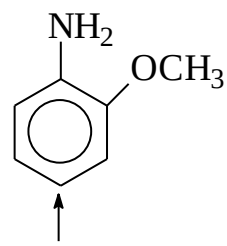
A) Amines:

- **Medium of coupling: acidic medium**

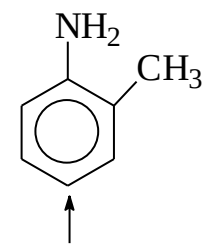
- **Position of coupling: para-position of amino group.**

i- Primary amines:

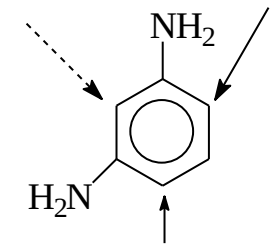




o-Ansidine



o-Toludine

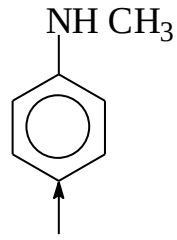


m–phenylenediamine

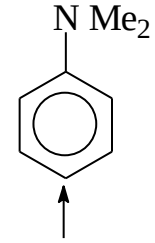
The arrow indicates the coupling position.

The arrow ⇢ indicate the less reactive position

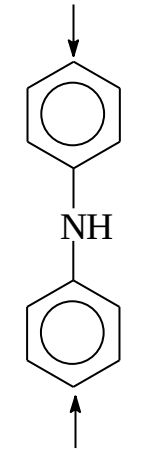
ii- Secondary and t–amines:



N–methyl aniline



N,N dimethyl aniline

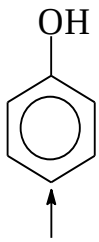


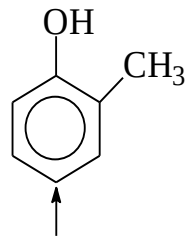
diphenyl amine

B) Hydroxy derivatives:

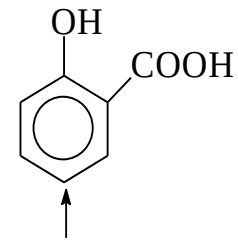
Medium of coupling: alkaline medium.

Position of coupling: para-position of –OH

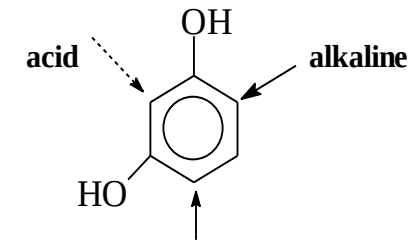




o- Cresol



Salicylic acid



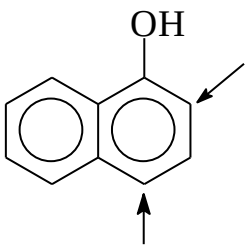
alkaline resoricnol

2) Naphthalene derivatives:

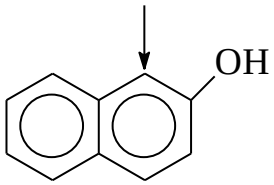
A) Naphthols:

Medium of coupling: alkaline

Position of coupling: usually p-position of 1-Naphthol and position 1 for β-Naphthols



1 Naphthol or α–Naphthol

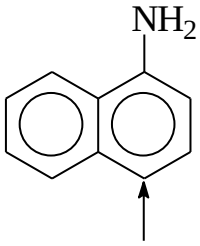


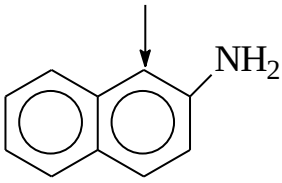
2-Naphthol or β-Naphthol

B) Naphthyl amines:

Medium: acidic

Position: position 4- for 1- Naphthylamine and position 1- for 2-naphthylamine.

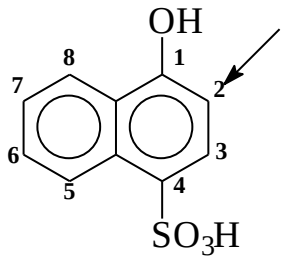




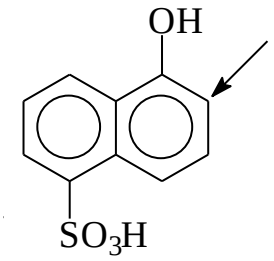
C) Naphthol sulphonic acid:

Medium: alkaline.

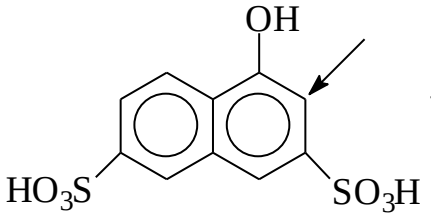
Position of coupling: ortho-position of OH.



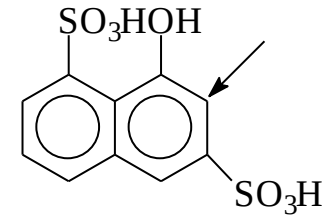
1-Naphthol-4-Sulphonic acid



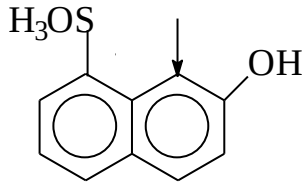
1-Naphthol-5-Sulphonic acid



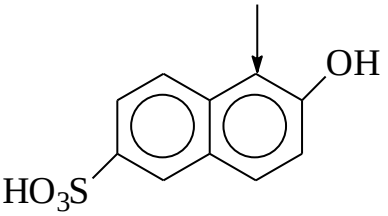
1-Naphthol-3,6-diSulphonic acid

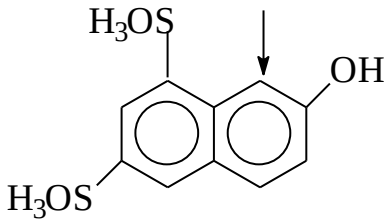


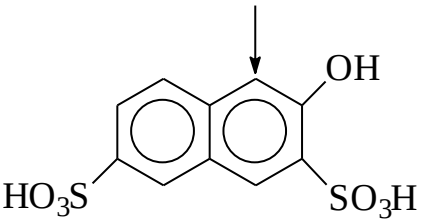
1-Naphthol-3,8-diSulphonic acid



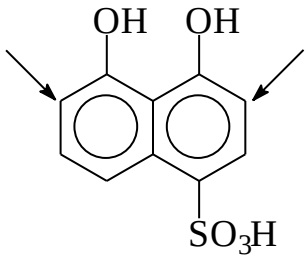
2-Naphthol-8-sulphonic acid

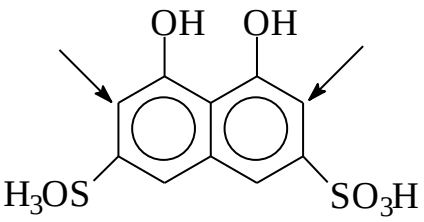






For dihydroxy naphthalene sulphonic acids





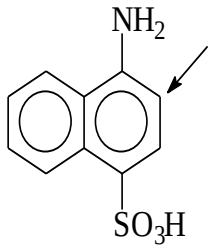
4,5 dihydroxy Naphthalene
1- sulphonic acid

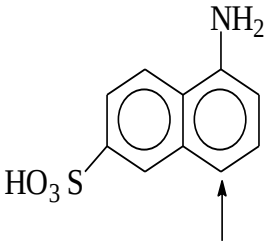
D) Naphthyl amine sulphonic acids:

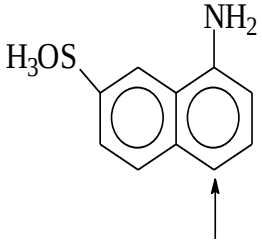
Medium: acidic

Position of coupling: position 4- for 1-Naphthylamine

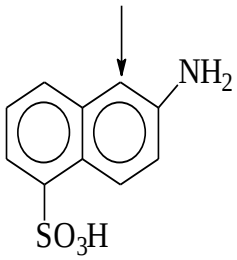
Position 1- for 2-Naphthylamine



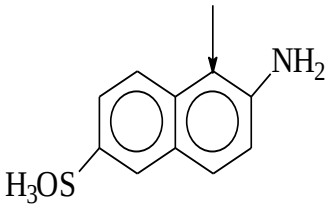




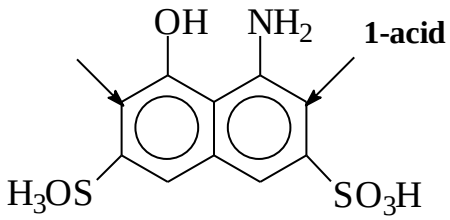
1-amino-7-Naphthalensulphonic acid acid



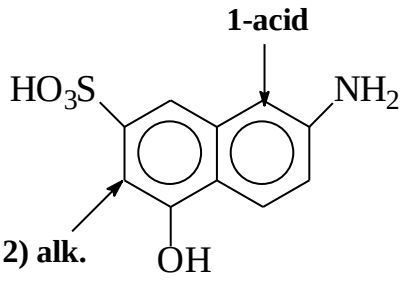
2-amino 5-Naphthene
sulphonic acid



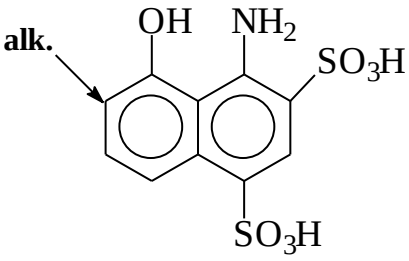
E) Amino naphthol sulphonic acids:

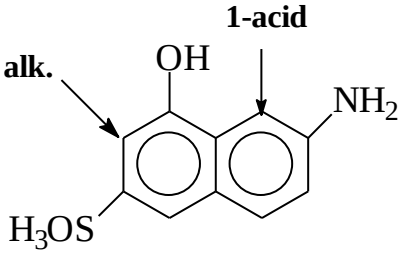


1- amino- 8-Naphthol 3,6 disulphonic acid



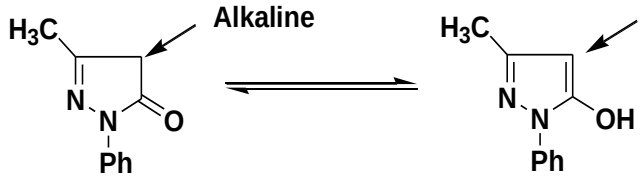
2-Amino-5-hydroxy-7-Naphthlene Sulphonic acid



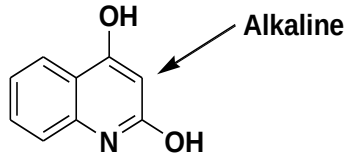


Active methylene component

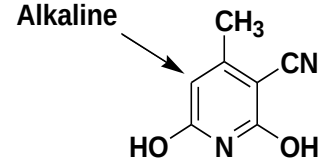
A) Hetero cyclic



3-Methyl-1-phenyl-2-pyrazoline-3-one

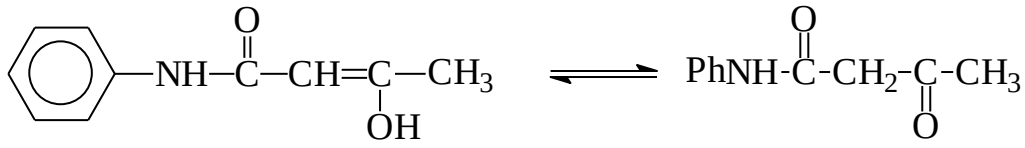


2,4-Dihydroxy-quinoline



2,6-Dihydroxy-4-methyl-nicotinonitrile
Or 3-Cyano-2,6-Dihydroxy-4-methyl-pyridine

Other example of active methylene acetoacetanilide



e.g of direct and acid dye

Questions

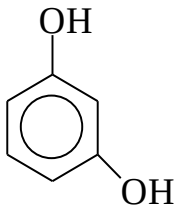
1- Give structure of Azo dyes prepared from aryl diazonium cation (ArN_2^+) and the following coupling agent.

a- Acetoacetanilide.

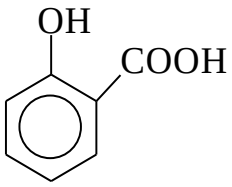
b- 1- amino–8-naphthol-3, 6-disuphonic acid.

c- 3- methyl-1-phenyl-2-pyrazolin-5-one.

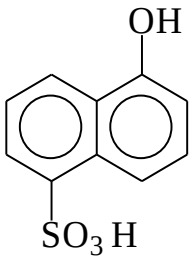
2- Give the structure of the following azo dyes which could be obtained from the interaction of diazonium cation (ArN_2^+) with the following coupling component



(1)



(2)



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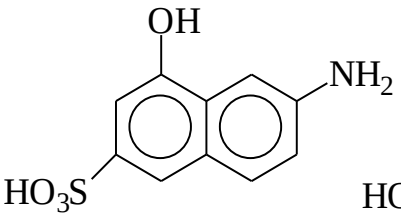

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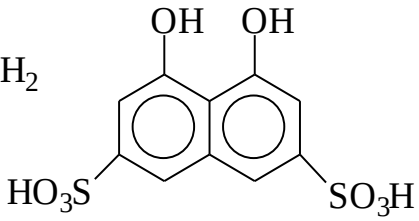

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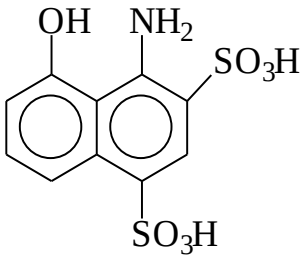

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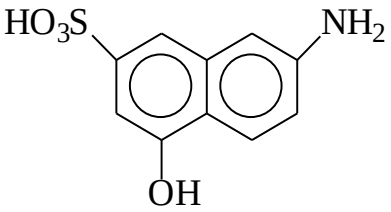
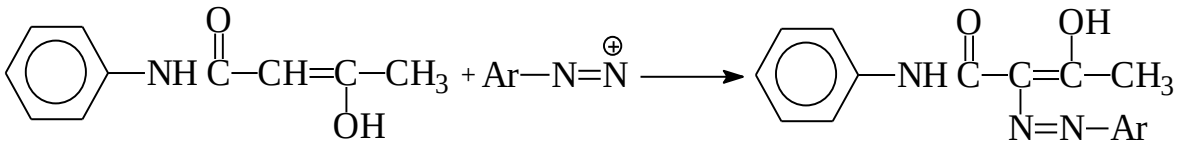


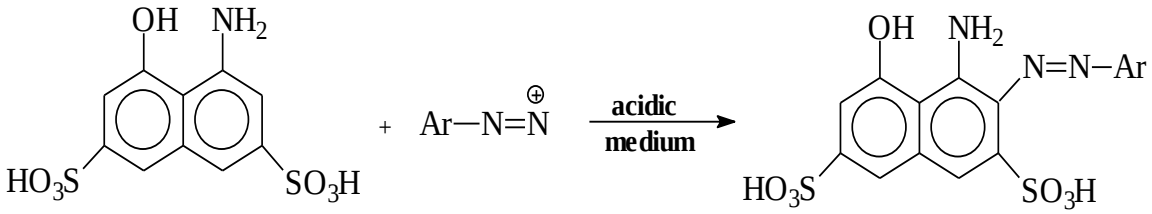
(7)

ـ بالنسبة لإجابة السؤال الأول

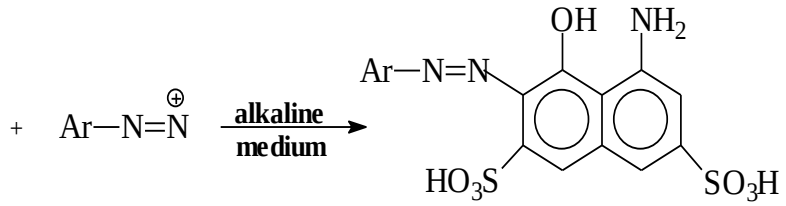
1) Acetoacetalide:



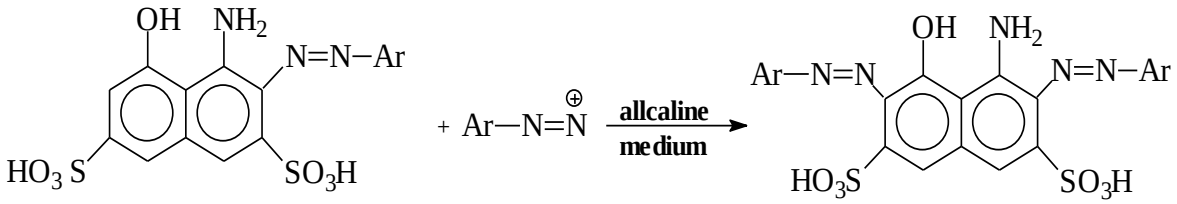
2) 1-amino–8-naphthol–3,6-disulphonic acid:



2-Arylazo-1- amino
8- naphthol-3,6 disulphonic acid

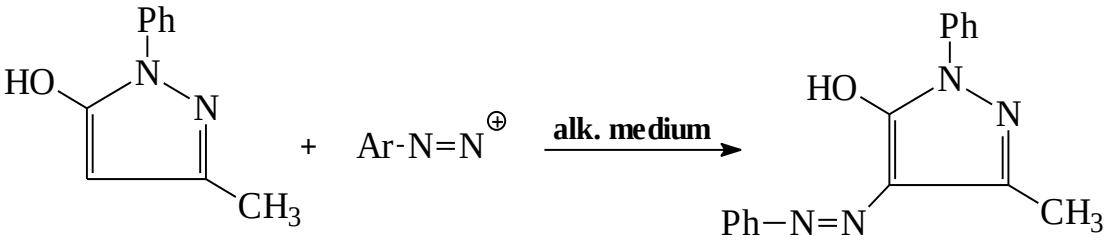


7-Arylazo-1- amio
-8-naphthol- 3,6 disulphonic acid



2,7 diarylazo-1- amino
-8-Naphthol-3,6 disulphonic acid

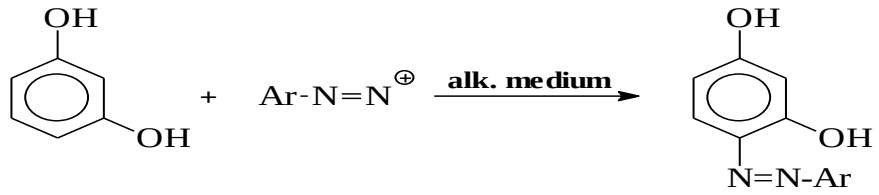
3) 3-methyl-1-phenyl-2-pyrazolin-5-one:



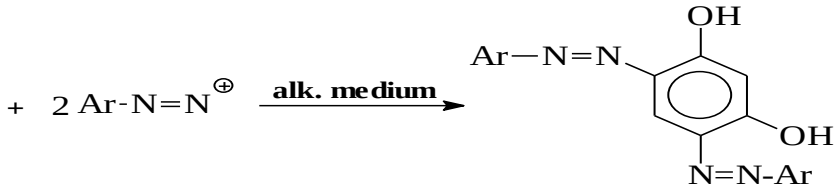
4-arylazo-3-methyl-1-phenyl-2- pyrazolin-5-one

- إجابـــــــــــــــــة الســـــــــــــــــؤال الثـــــــــــــــــاني

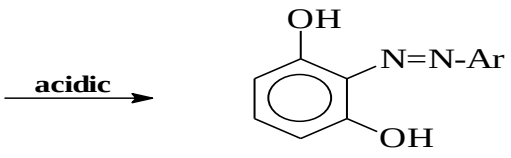
(1)



Resorcinol **4-arylazo resorcinol**

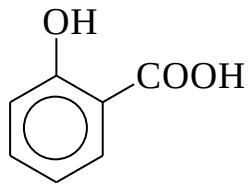


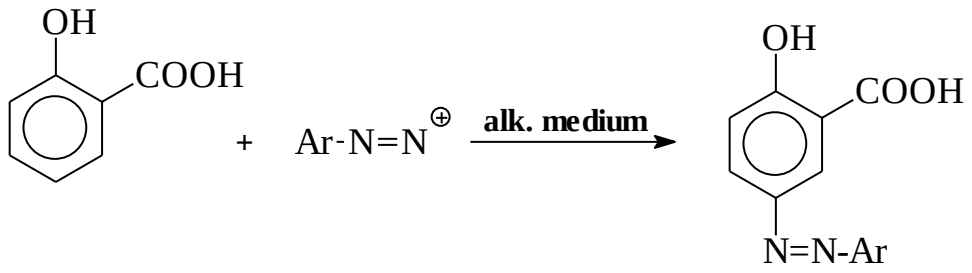
4,6-arylazo resorcinol



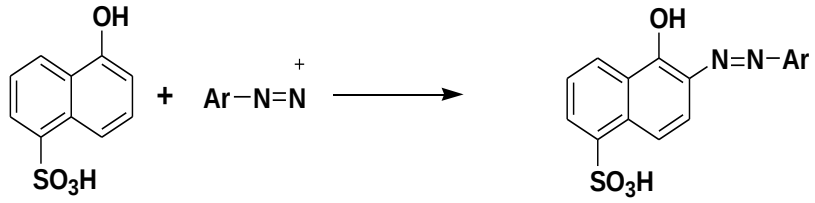
2-arylazo resorcinol

(2)





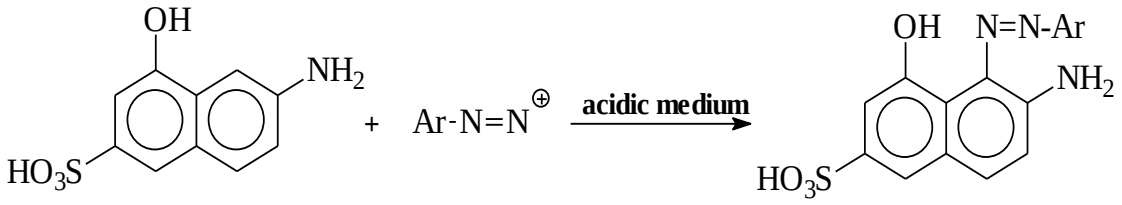
4-arylazo salicylic acid



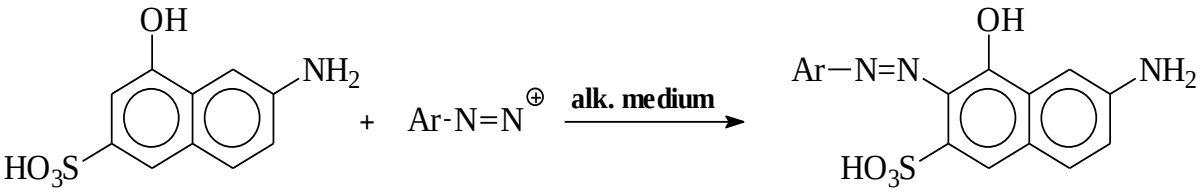
5-Hydroxy-naphthalene-1-sulfonic acid

2-Aryazo-5-Hydroxy-naphthalene-1-sulfonic acid

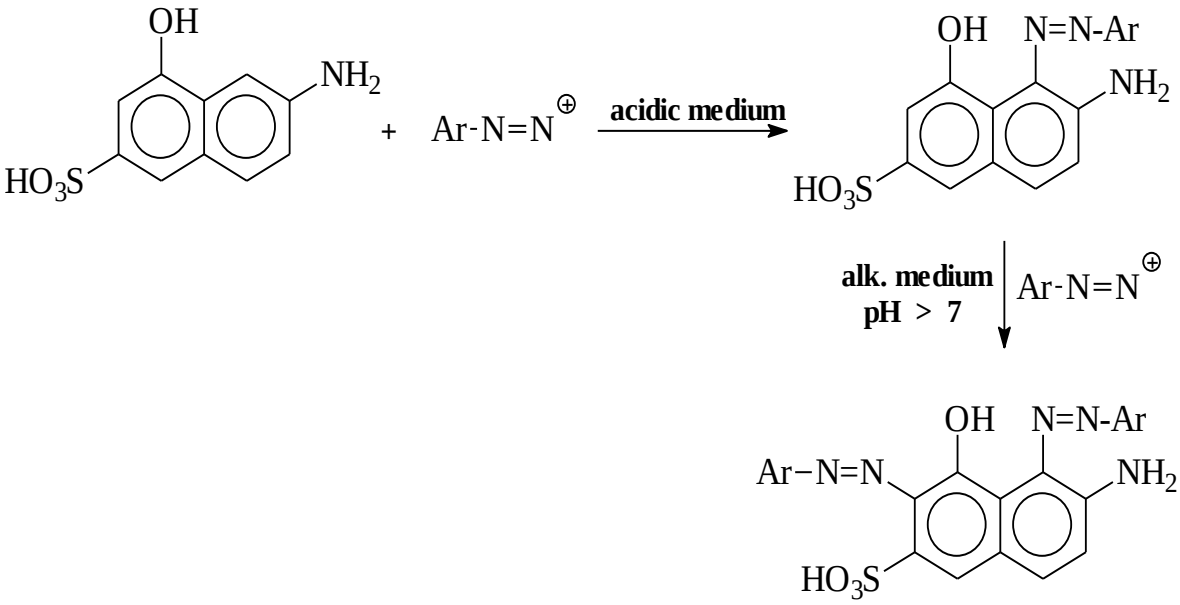
(a)

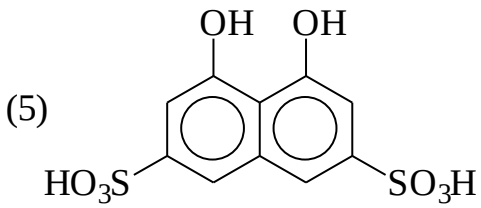


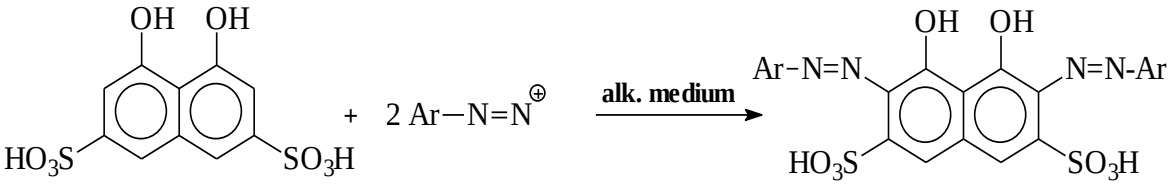
1-arylazo-2-amino-8-hydroxy naphthlene-6-sulphonic acid



7-arylazo-2-amino-8-hydroxy naphthlene-6-sulphonic acid

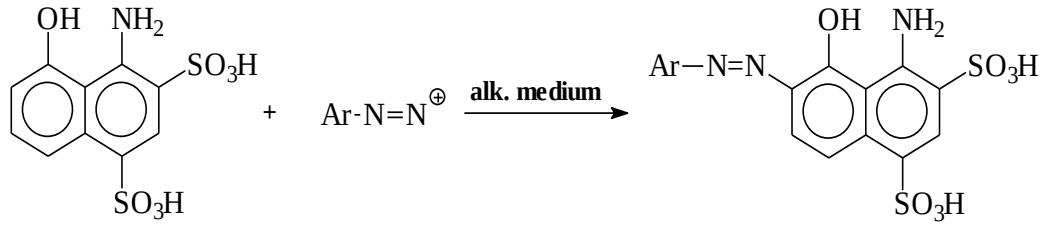






2,7-diarylazo-1,8-dihydroxy naphthalnene 3,6-disulphoric acid

(6)



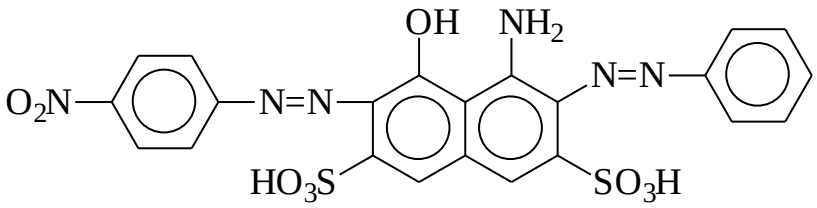
7-arylazo-1-amino-8-hydroxy naphthalnene 2,4-disulphoric acid

(7) Like (4).

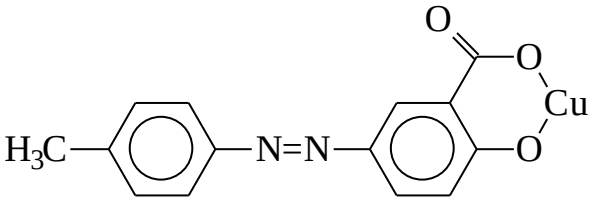
Question:

Synthesis of the following dyes:

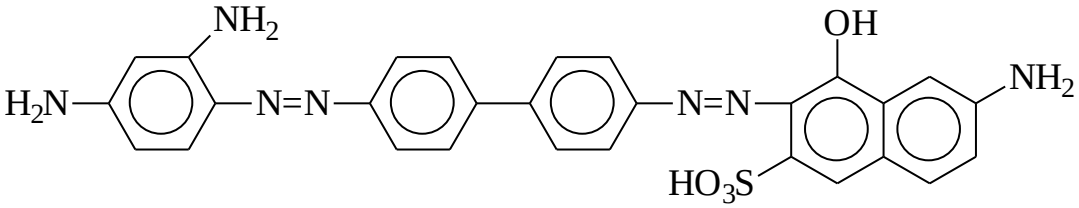
(1)



(2)

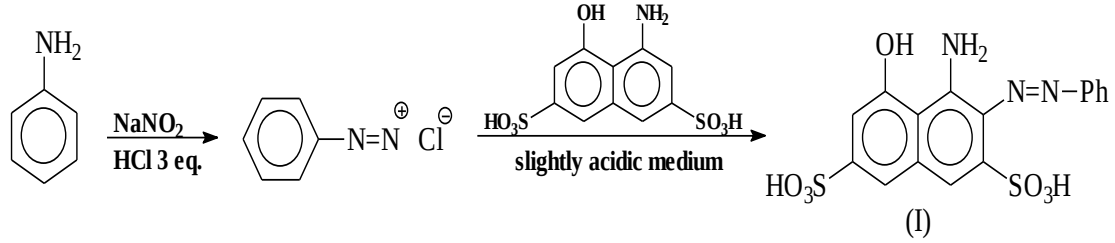


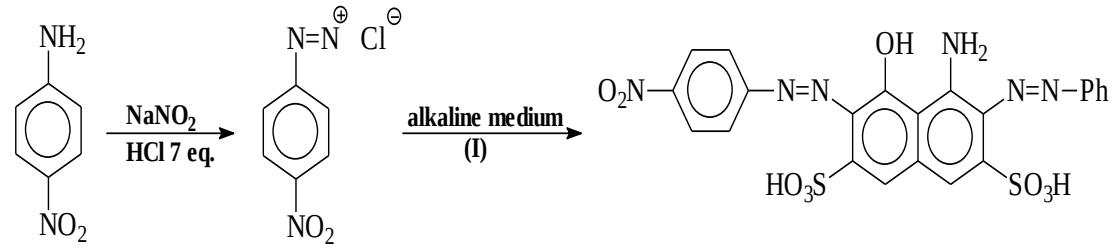
(3)



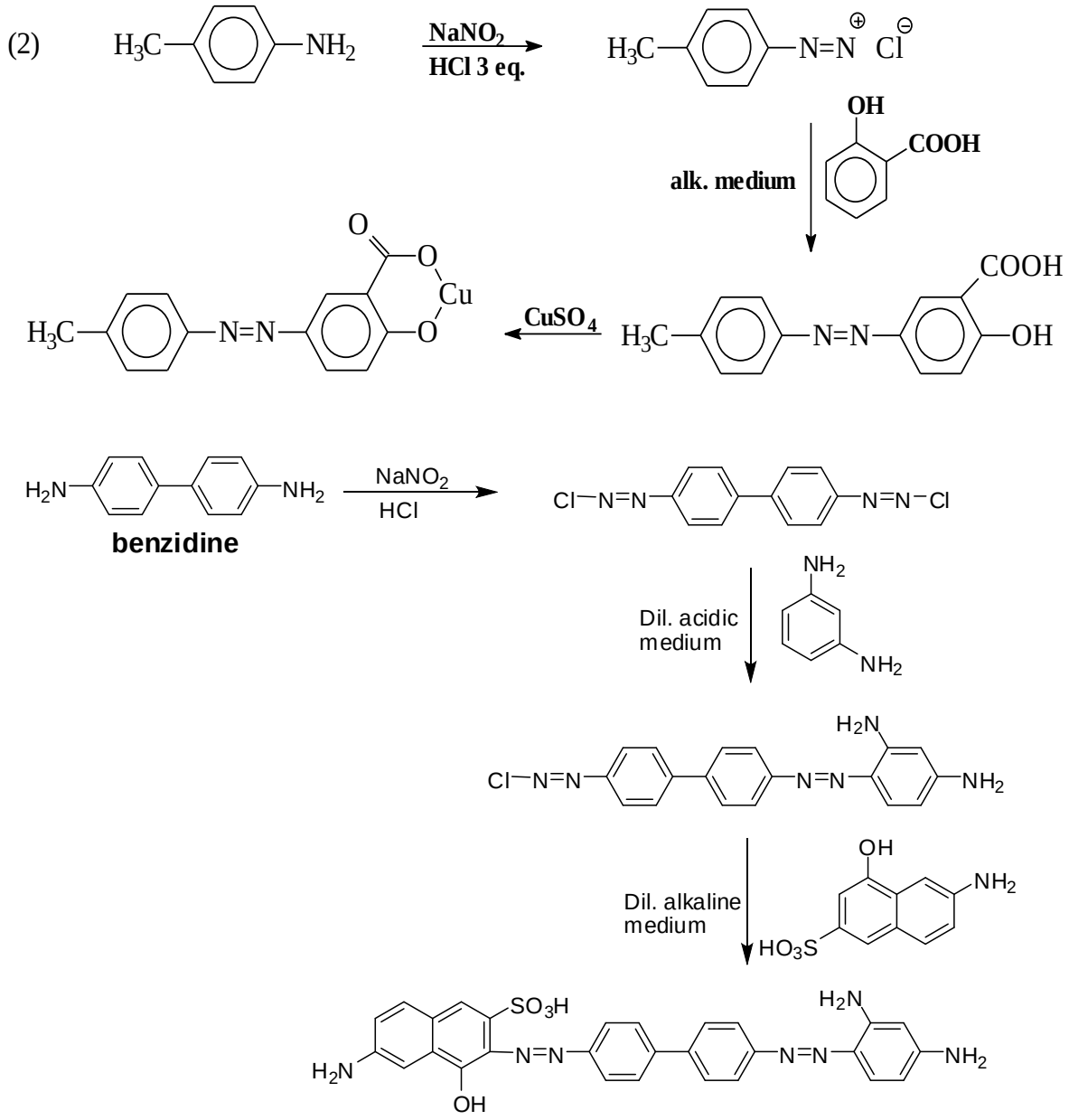
Solution:

(1)



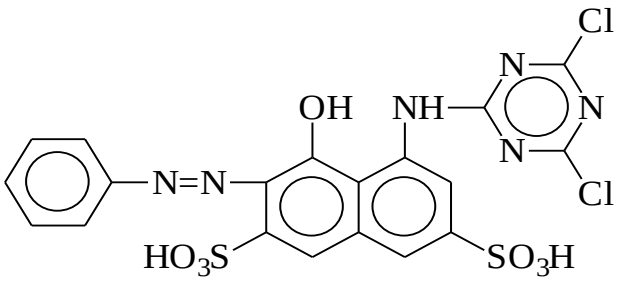


(2)

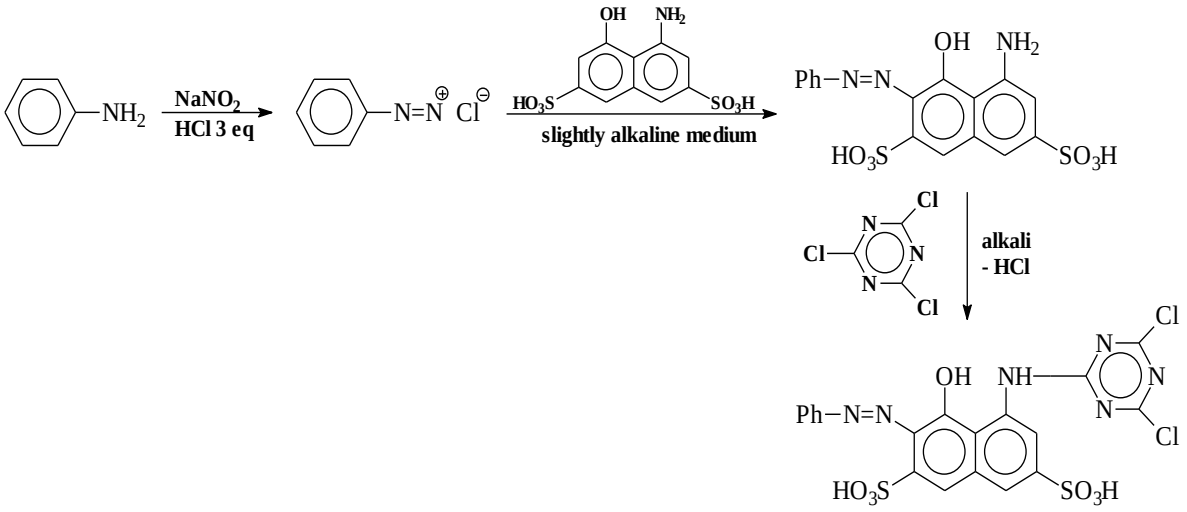

H3C
NH2
NaNO2
HCl 3 eq.
N=N
Cl
OH
COOH
alk. medium
CuSO4
Cu
O
H2N
benzidine
Cl—N=N
Dil. acidic medium
Dil. alkaline medium
HO3S
SO3H

Question:

Synthesis



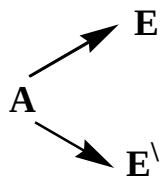
Solution:



Types of Disazo dyes

- **There are four types of Disazo dyes**

  1. **A→ E→ E\ or A→ M→ E**

2. 

3. **A→ E← A**

4. **A→ E.X.E ← A**

   Where A is diazo component (amine)

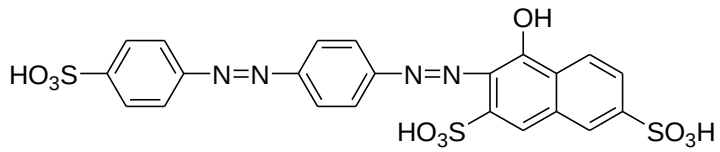
   E is coupling component

   X is agent used for binding two amines

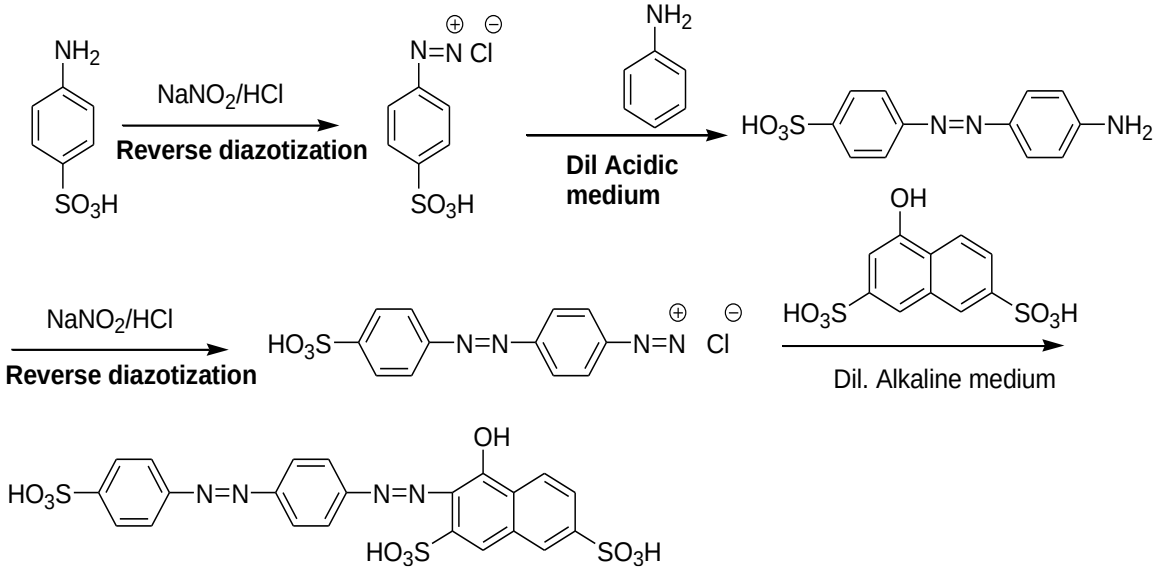
5. **<u>Type 1</u> A→ E→ E\ or A→ M→ E**

- **In this type we use diazonum salt to couple with amine, the resulted dye is used as amine for second coupling**

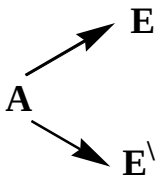
  <u>e.g.</u>



  <u>Synthesis</u>

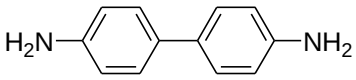


Type 2

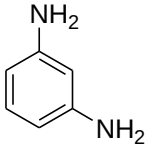


- **In this type we use Diamine as benzidine and couple it with two coupling component**

A as

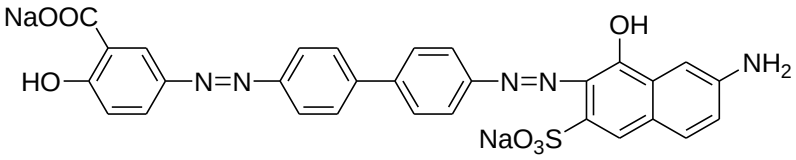


Benzidine

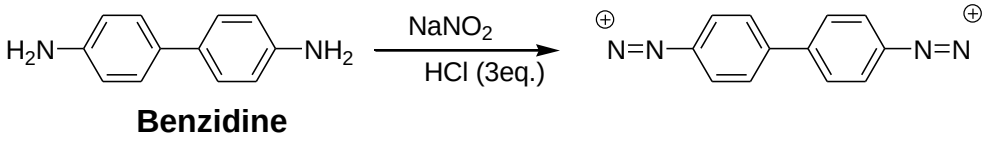


m-phenylenediamine

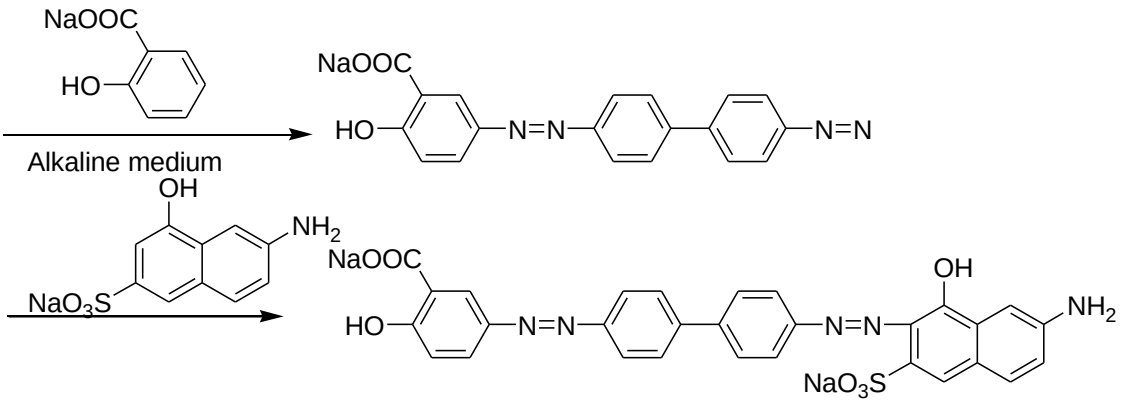
e.g.



Synthesis

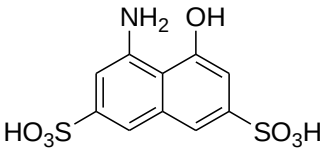


Benzidine



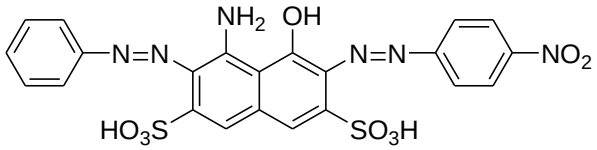
Type 3 A→ E← A

- **In this type, we use coupling component of more than one position of coupling and couple it with two amines**
  - **The best example of E in this case is**



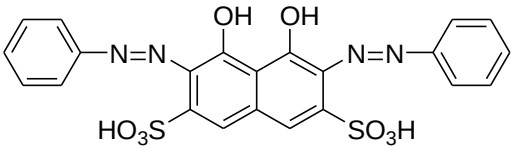
4-amino-5-hydroxynaphthalene-2,7-disulfonic acid

e.g.



See synthesis page 20

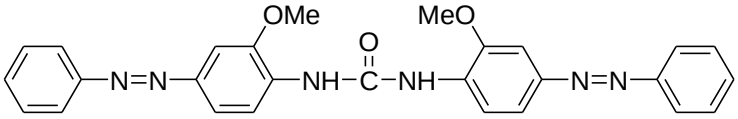
Example of A→ E← A



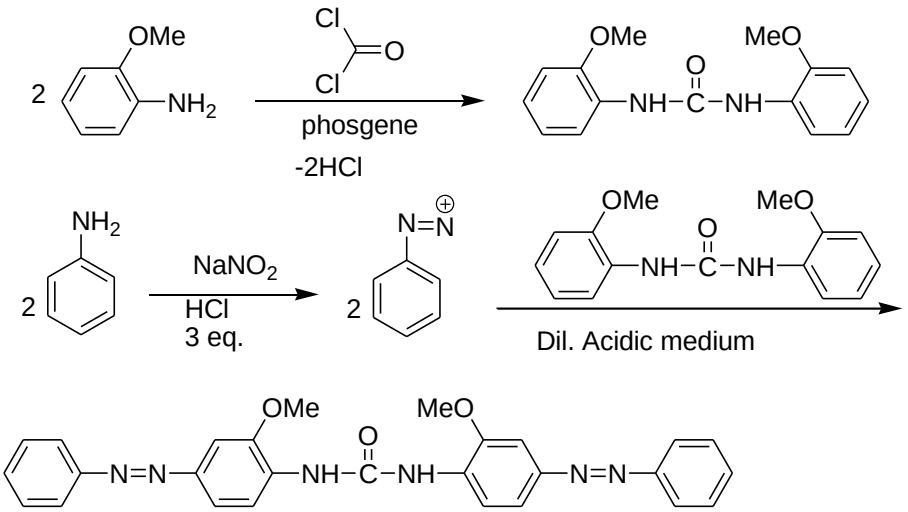
Type 4

- **In this type, we link two amines by using phosogene and then couple the products with two diazonium salts**

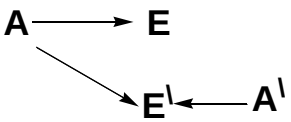
E.g.



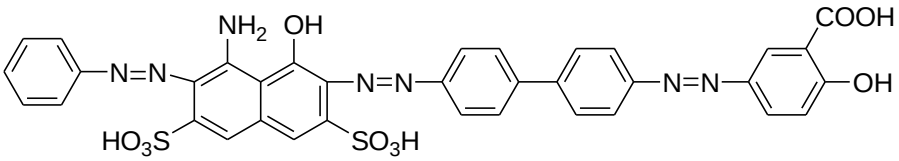
Synthesis



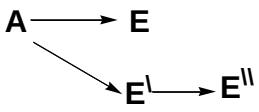
1. **Triazodyes**



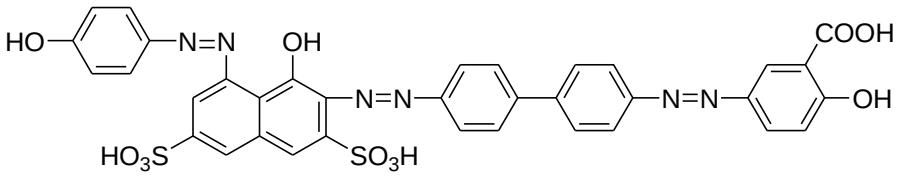
- **Like 3 but we introduce other coupling component on E**



2.

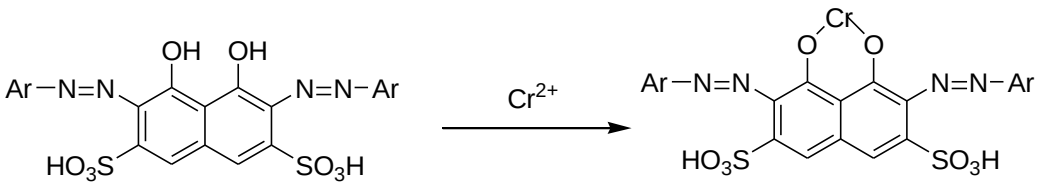


- **$E^{\backslash}$ must contain NH_2 which can be converted into diazonium salt can couple other coupling component**



<u>Metalazo compounds</u>

- **This dyes are azodyes usually contain OH groups ortho to azo group so can form stable complexes with metals. e.g.**



Some notes

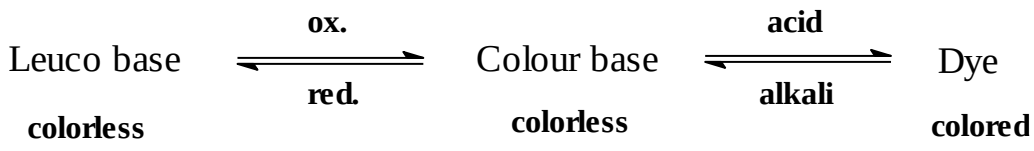
- **The diazonium salt produced from diamines such as benzidine are called tetrazonium salt and the dye produced is called bisazo dye**

The bis azo dyes can be prepared by many methods as explained in

Triphenyl methane dyes

- **Triphenyl methane dyes are obtained by introduction of NH_2, NHR, NR_2 or OH groups in para-position of two rings at least of three phenyl groups.**

- **The compounds obtained are colorless (leuco-base) on oxidation converted into t-alcohol (color-base), which forms quinoniud structure in the presence of acid.**



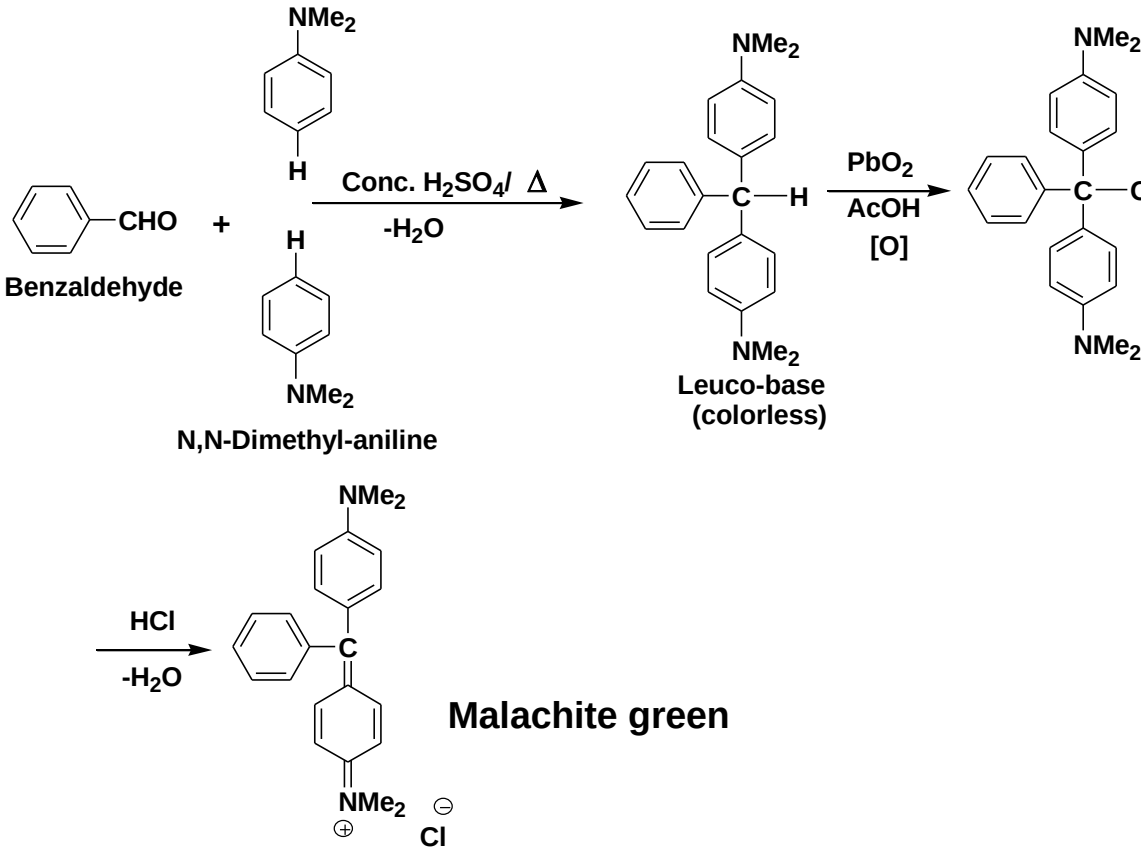
- Triphenyl methane dyes are classified into:

1- Base Dyes or cationic dyes.

2- Acid Dyes or anionic dyes.

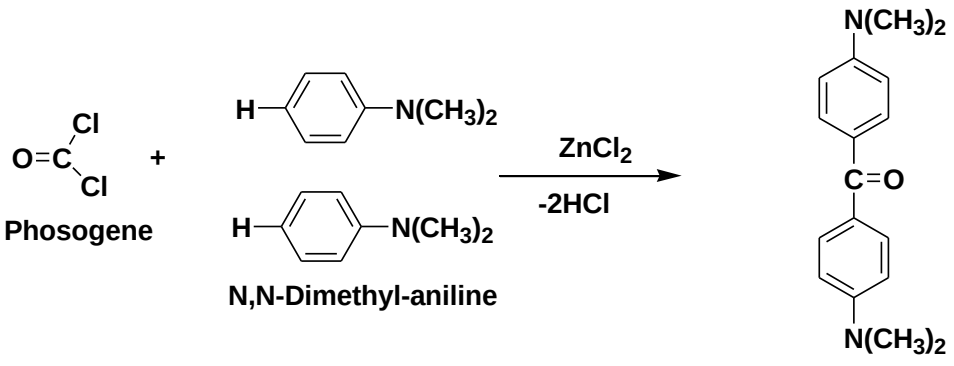
1) Base Dyes or cationic dyes

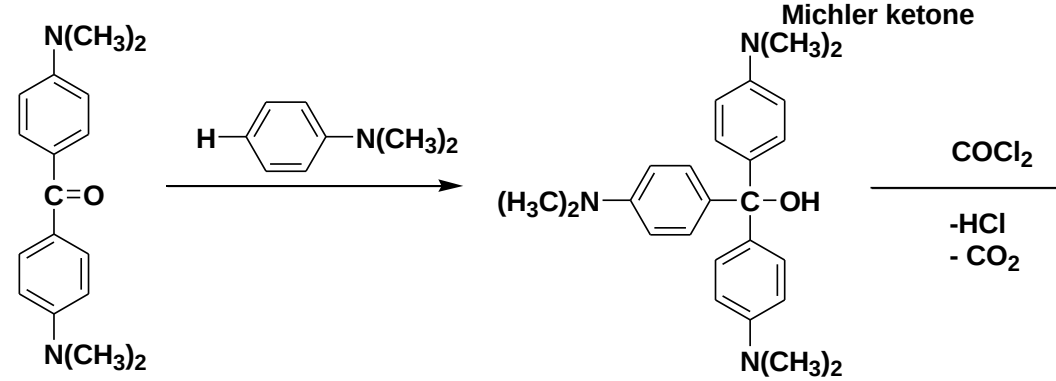
A) Malachite green

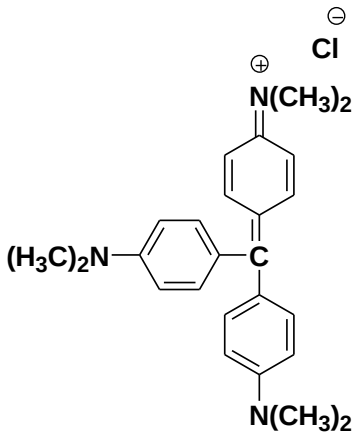


- ***Malachite green is used for dying cotton and polyacrylonitrile***

B) Crystal violet

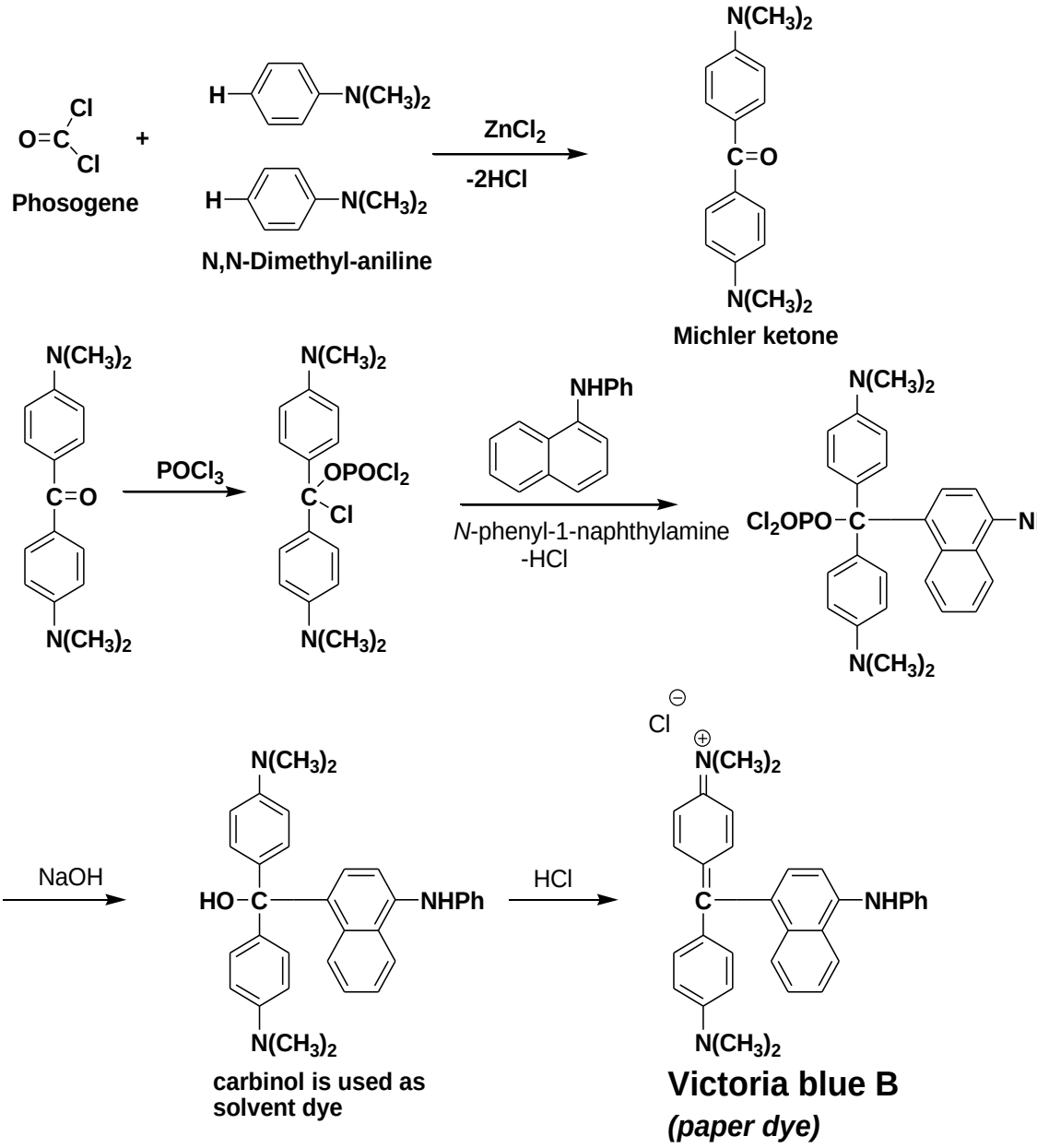






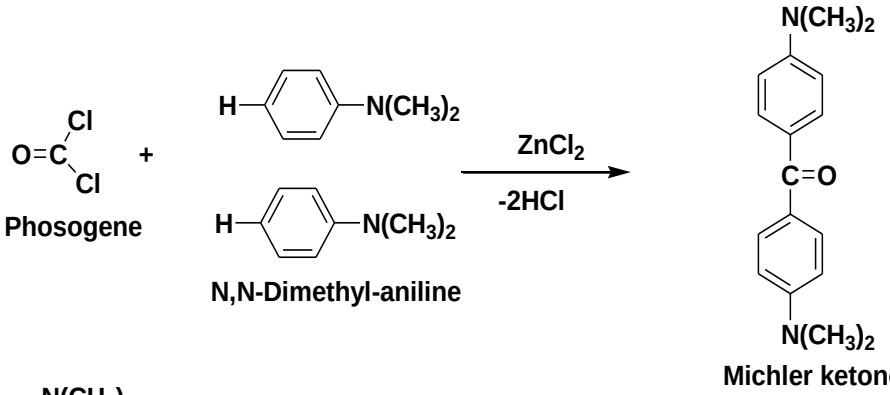
Crystal violet

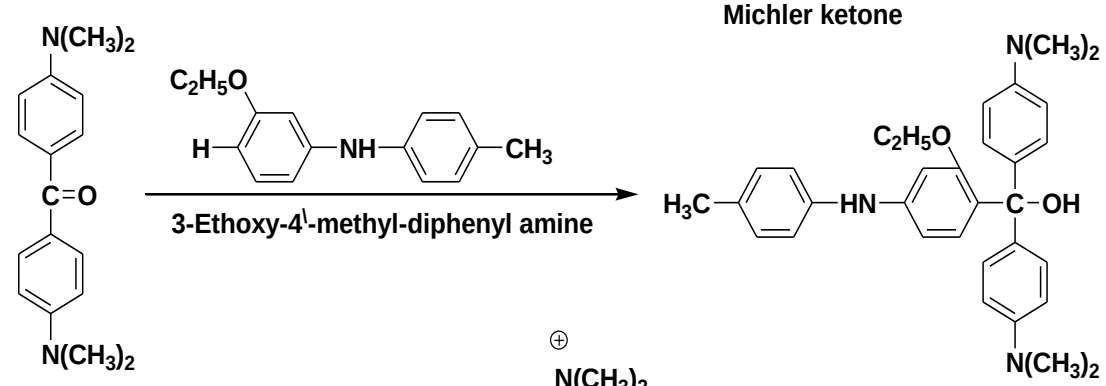
C) Victoria blue B (paper dye)

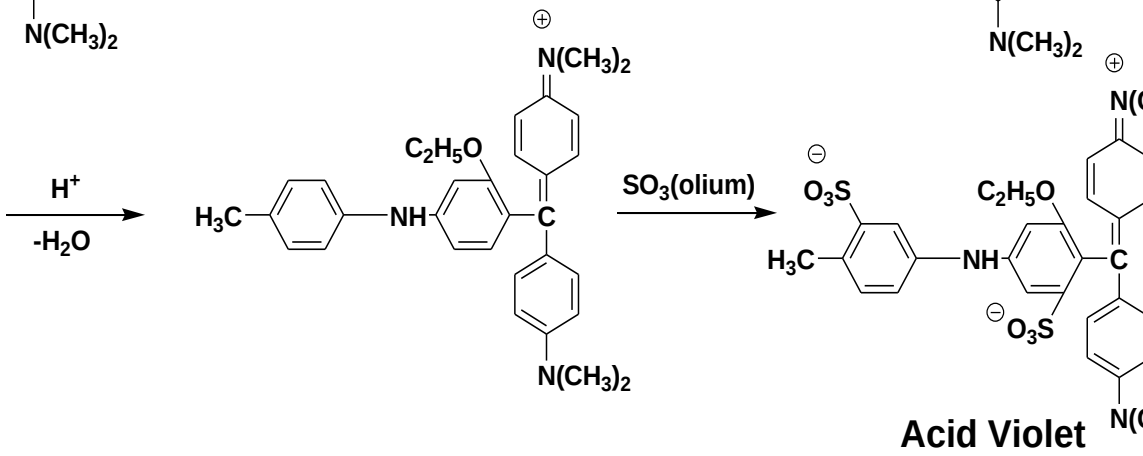


Acid dyes

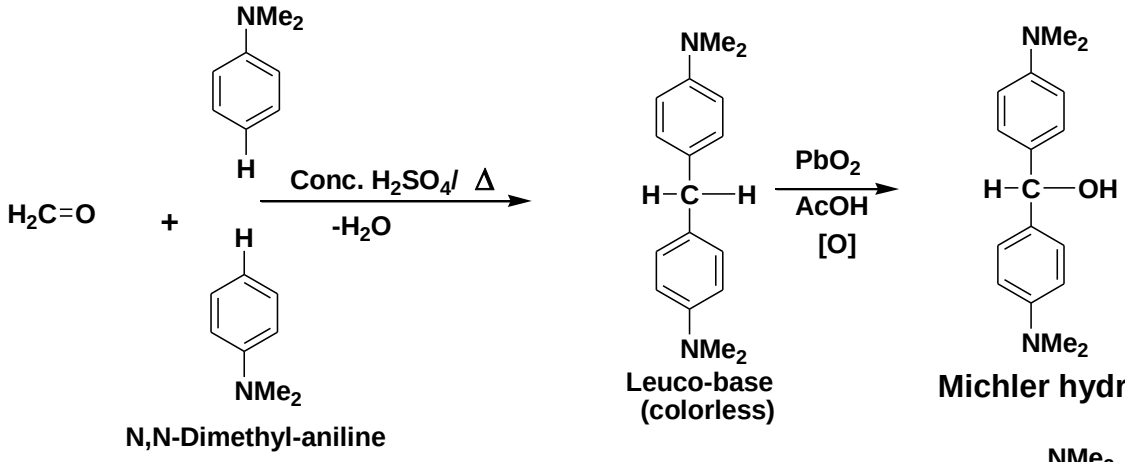
1) Acid violet

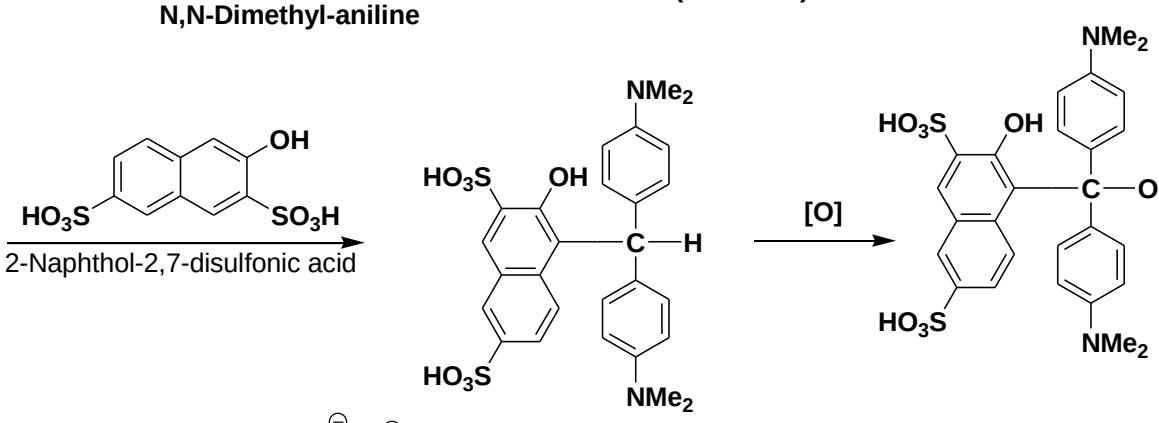


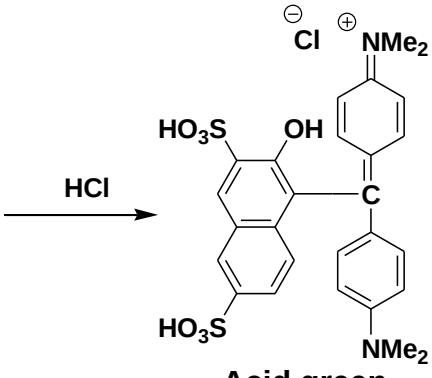




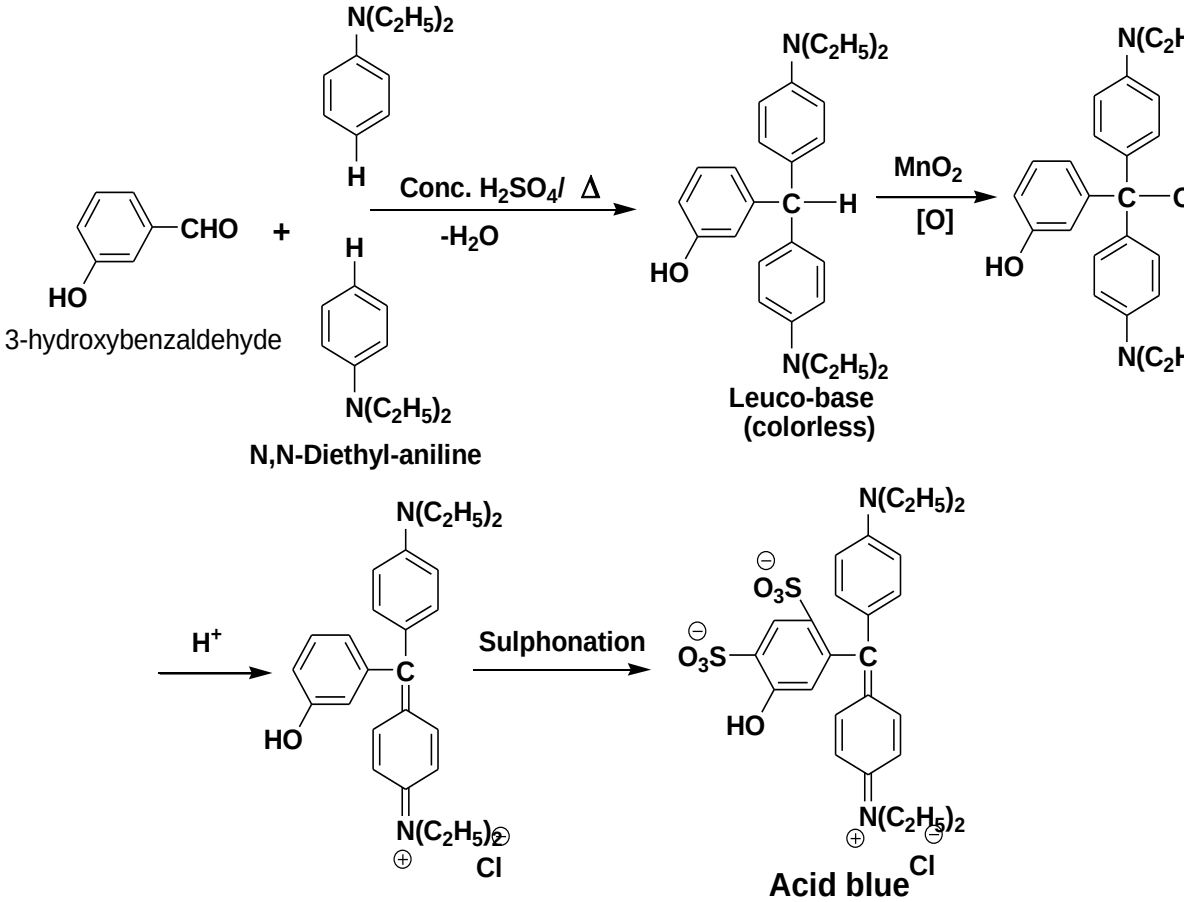
2) Acid green (wool green):





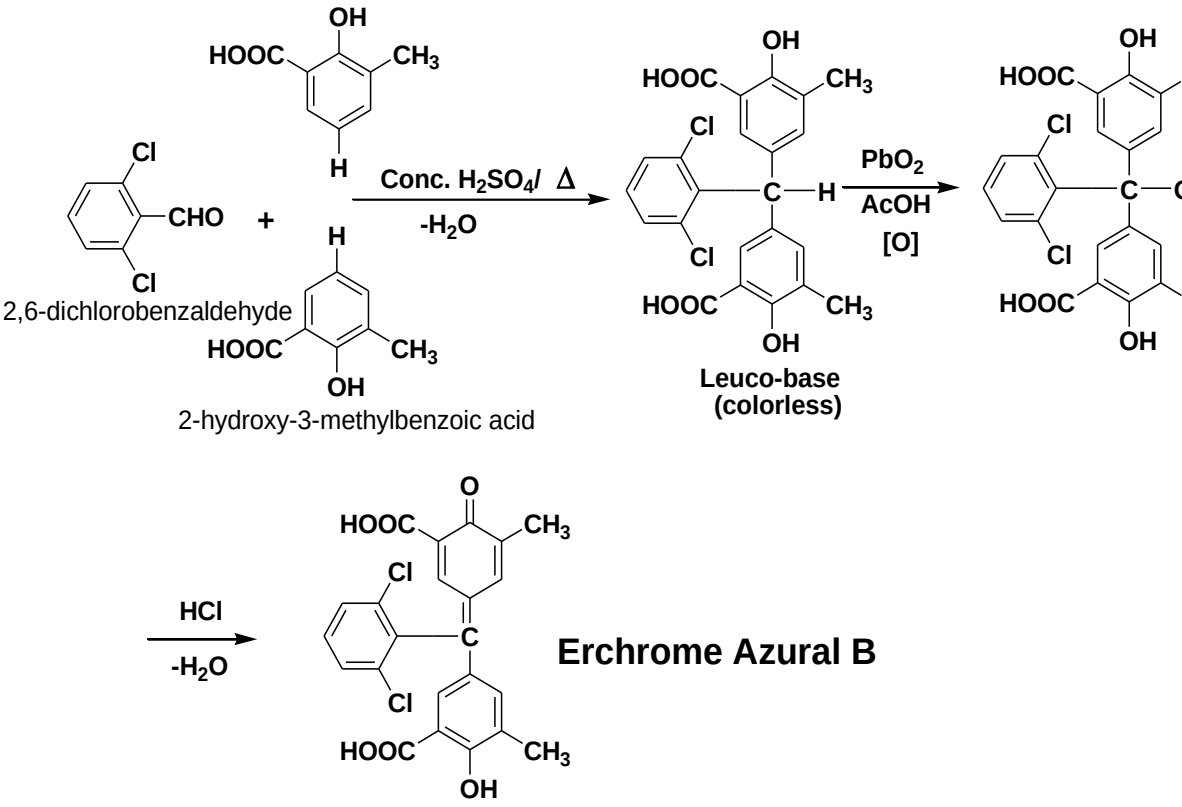


3) Acid blue (patent blue):

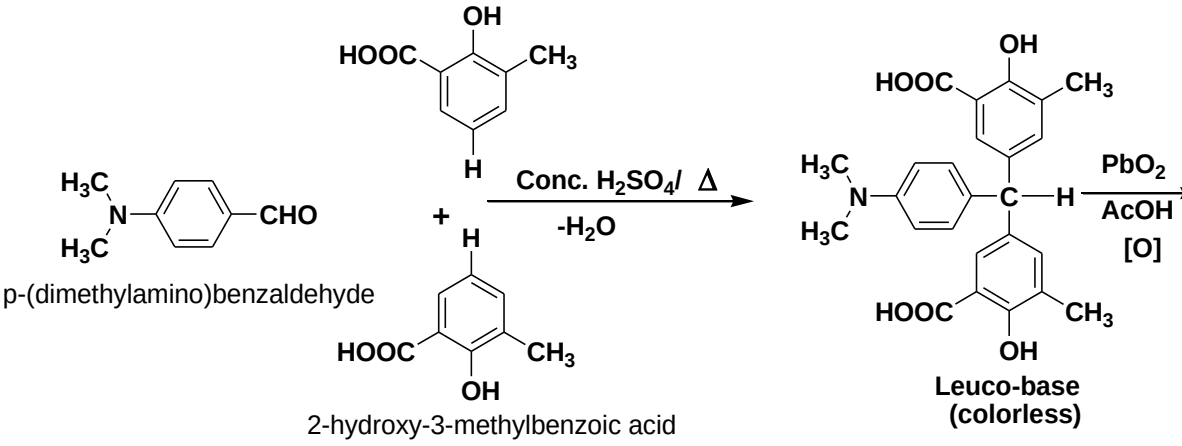


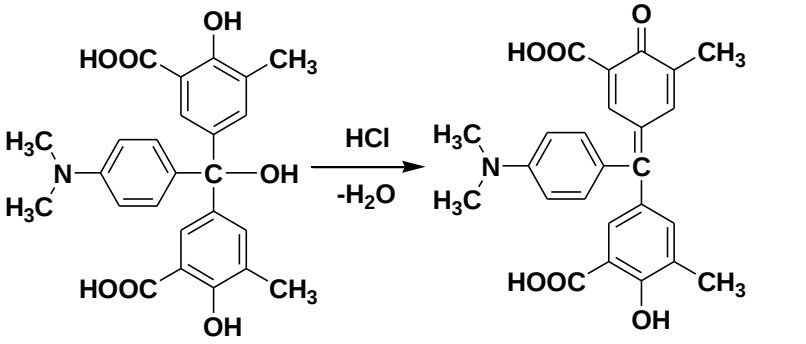
Hydroxy triaryl methane dye

1-Erichrome azurol B:

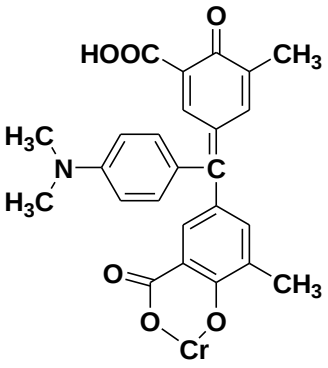

OH
HOOC
CH3
H
Cl
CHO
Cl
+
Conc. H2SO4/ Δ
-H2O
2,6-dichlorobenzaldehyde
2-hydroxy-3-methylbenzoic acid
Cl
C
H
PbO2
AcOH
[O]
Leuco-base
(colorless)
HCl
-H2O
O
Erchrome Azural B

2-C.I Mordant violet Dye





- **This dye is used for dying wool after treatment by Cr with bright blue shade.**


O
HOOC
CH3
H3C
N
H3C
C
O
CH3
O
O
Cr

Xanthene dyes

- The general skeleton:

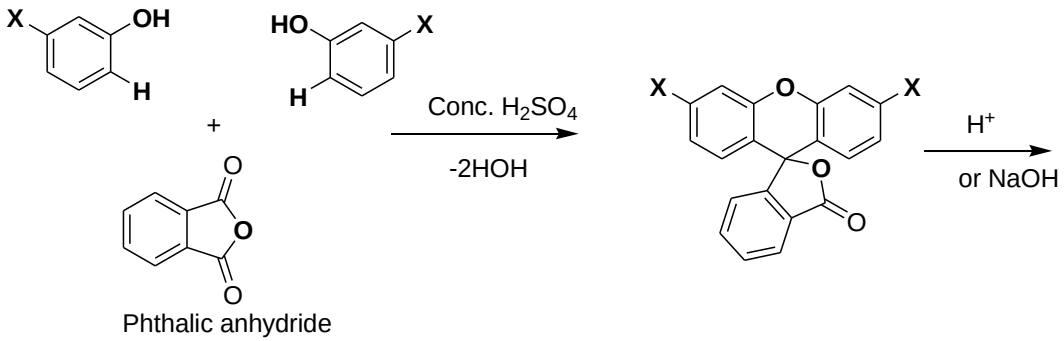
X = auxochromes (NH_2, NHR, NR_2, OH).

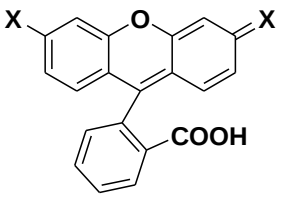
X must be in para-position to CR_2

- The color is due to formation of quinoid structure.

Xanthene dyes

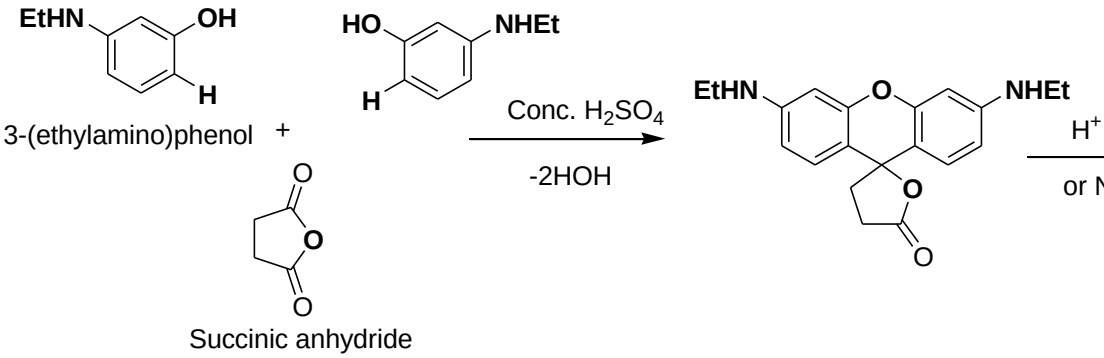
General procedures

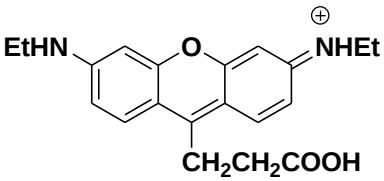




Where X = NH_2 or NHR or NR_2 the dye is called rhodamine

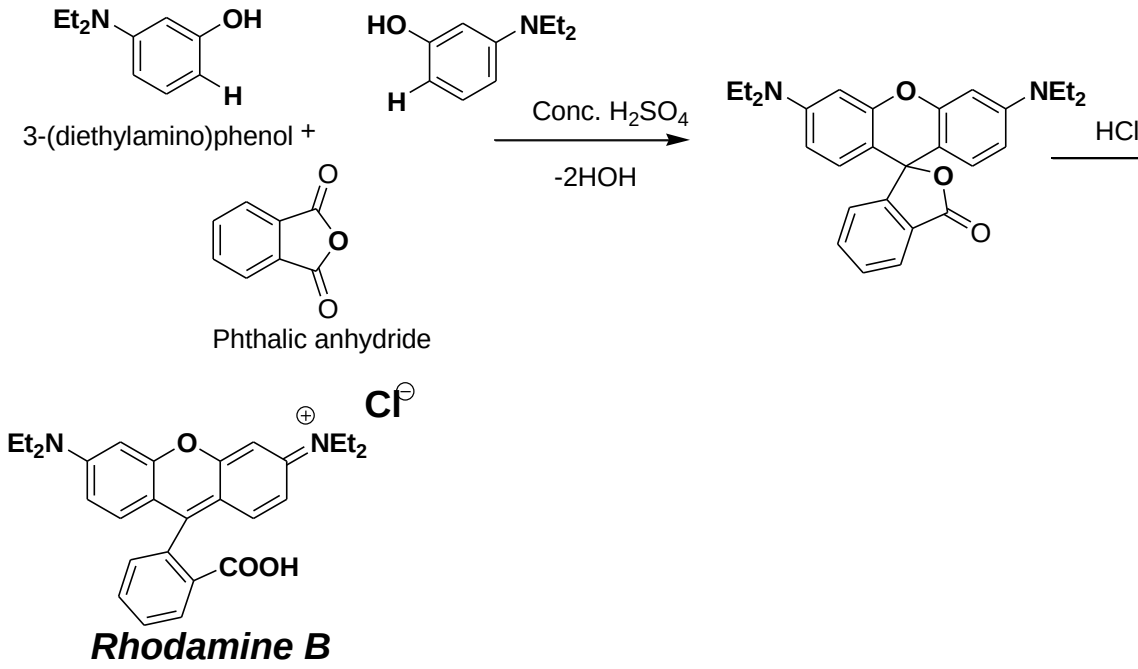
1- C.I. Basic red



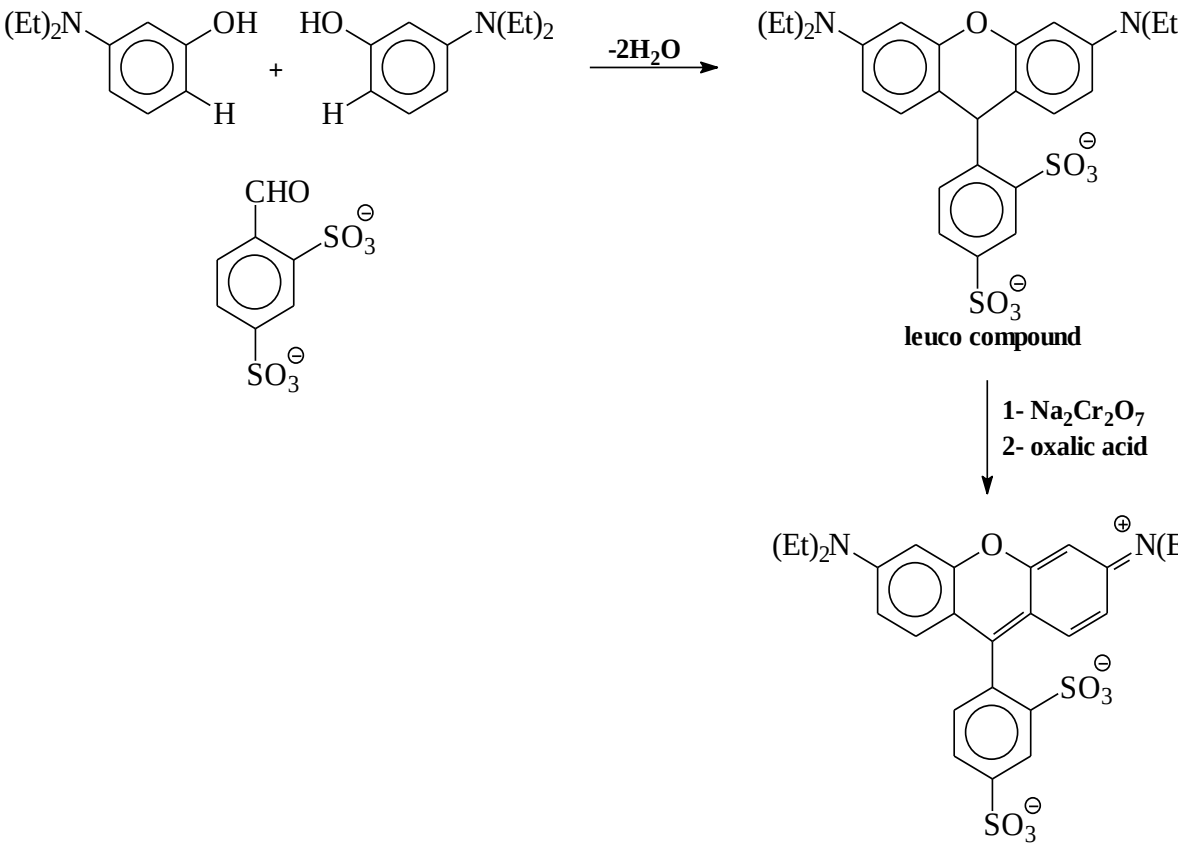


C. I. Basic red

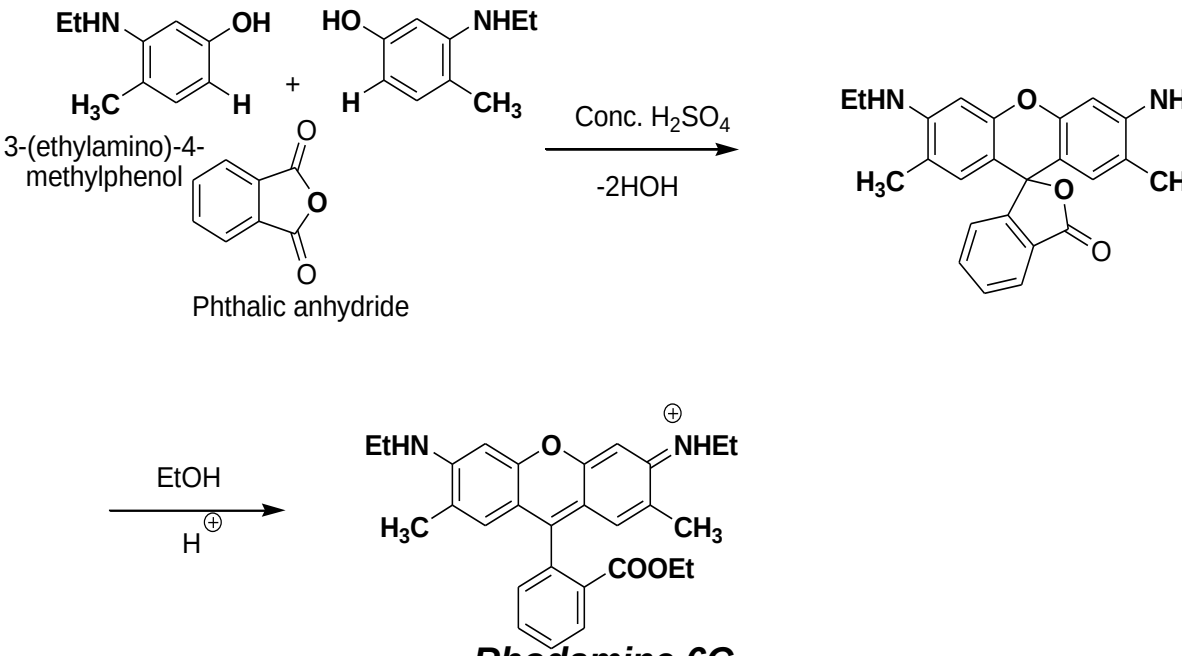
2) Rhodamine B



3) Sulphorhodamine (Rosamine dye)

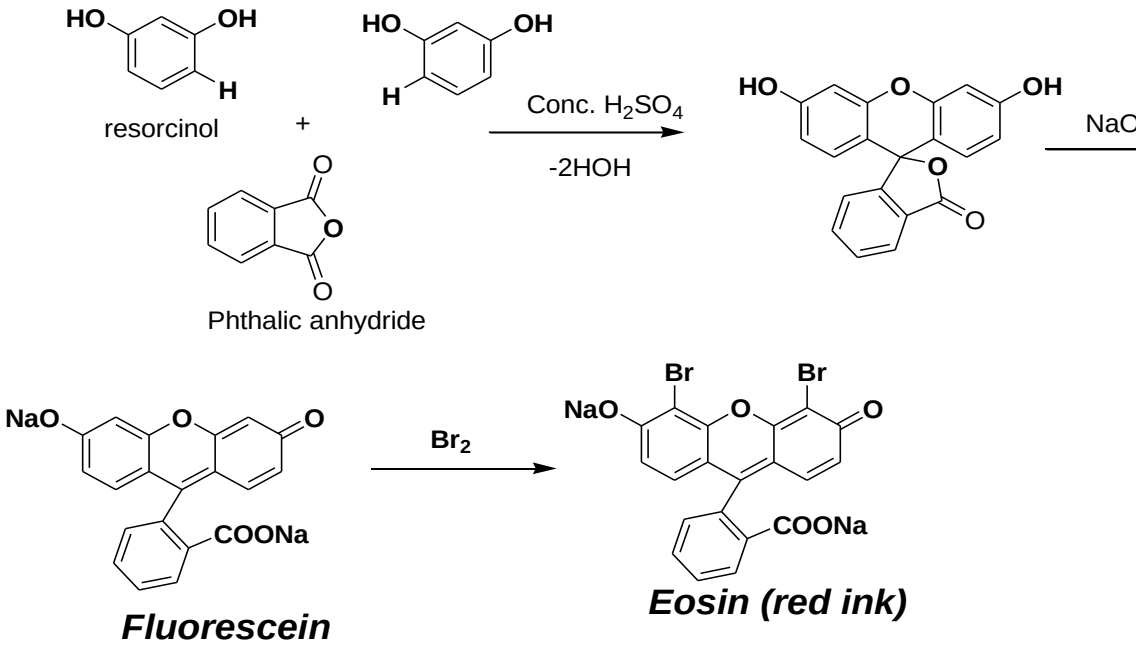

(Et)2N
OH
H
+
HO
N(Et)2
H
CHO
SO3
SO3
-2H2O
(Et)2N
O
N(Et
SO3
SO3
leuco compound
1- Na2Cr2O7
2- oxalic acid
(Et)2N
O
N(E
SO3
SO3

4) Rhodamine 6G



Rhodamine 6G

5) Fluorescein dye and its derivative (Eosin)



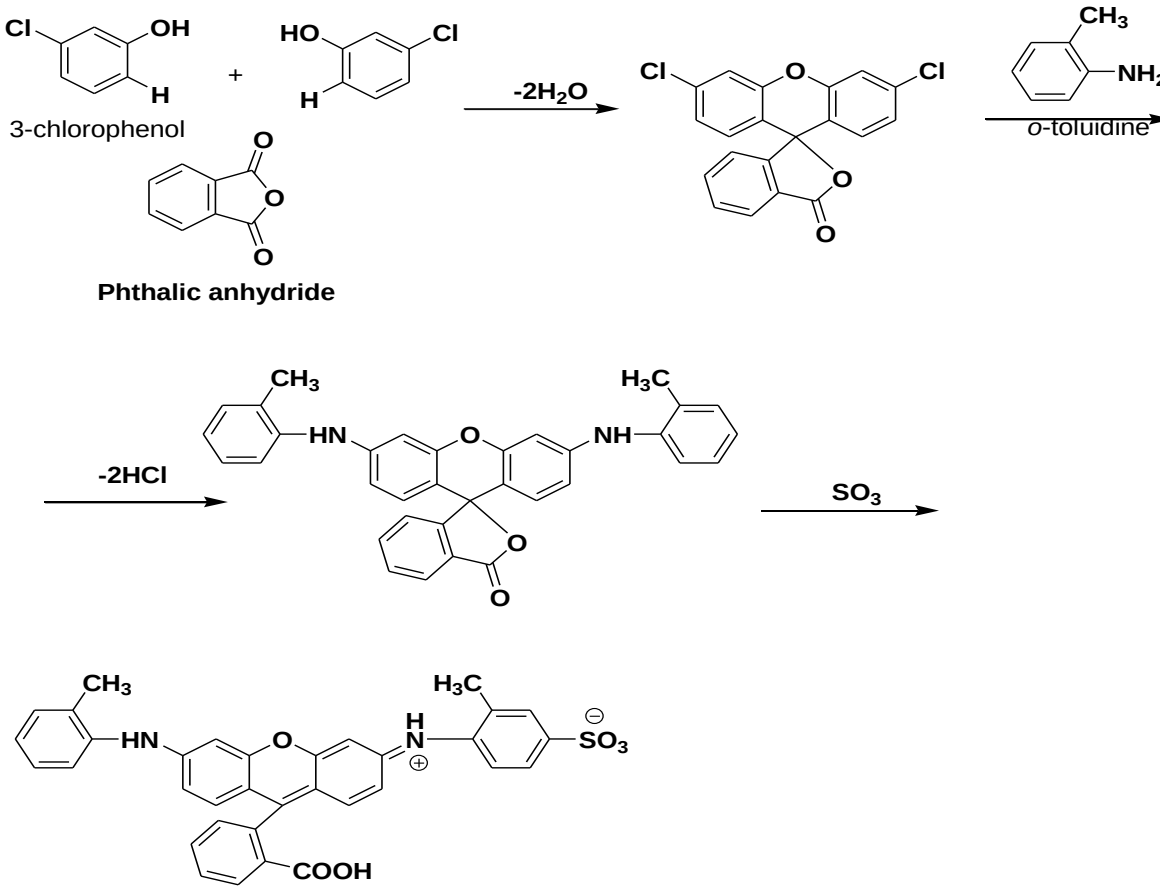
3-Kiton fuchine A_2R:

It is wool dye.

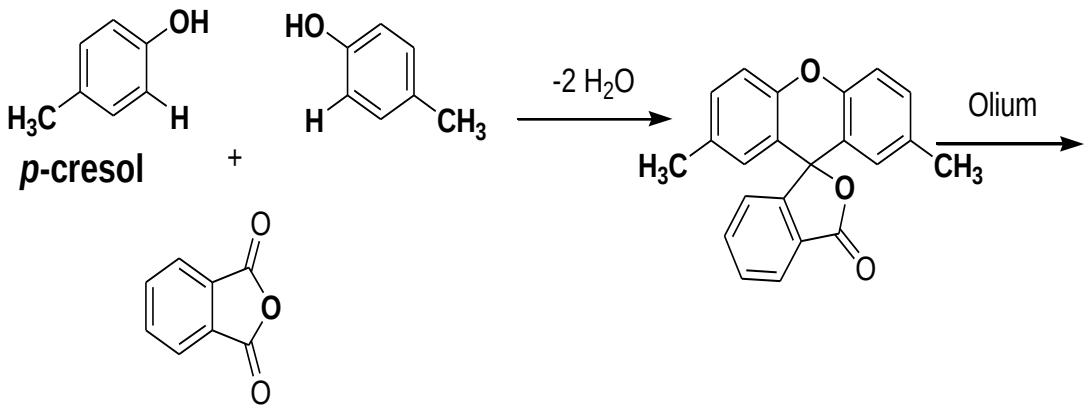
It is reddish violet dye with good fastness.

It can be used for paper coloration.

It can be prepared as follow.



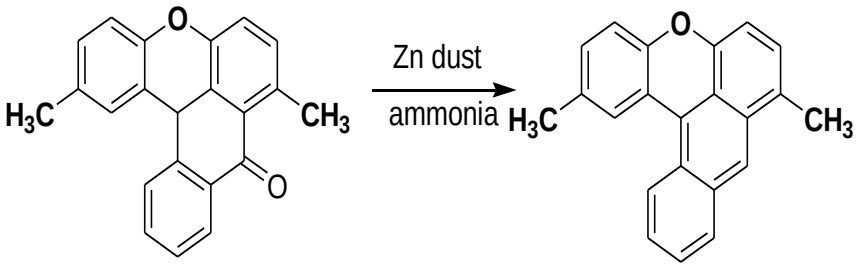
4-Fluorol 5-G: (Coloring mineral oil)



***p*-cresol**

+

Phthalic anhydride



Fluorol 5G
Coloring mineral oil)

Vat dyes

It classified into two types:

1- **Indigo dyes.**

2- **Anthraquinone dyes.**

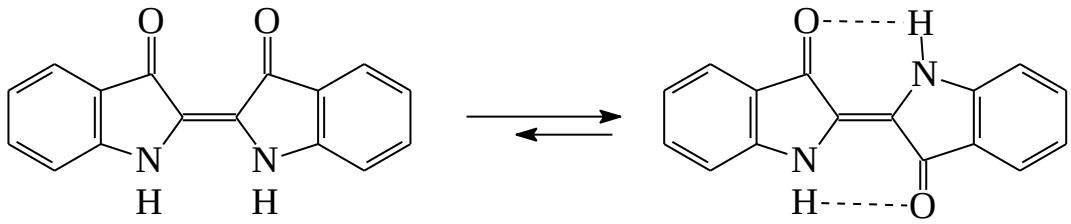
Vat dye (insol. dye) $\xrightarrow{\text{Reduction}}$ Leuco compound (soulble colorless)

$\downarrow$ [O]

Colored insoluble dye

Structure of indigotin:

Indigotin can exist in both cis and trans form.

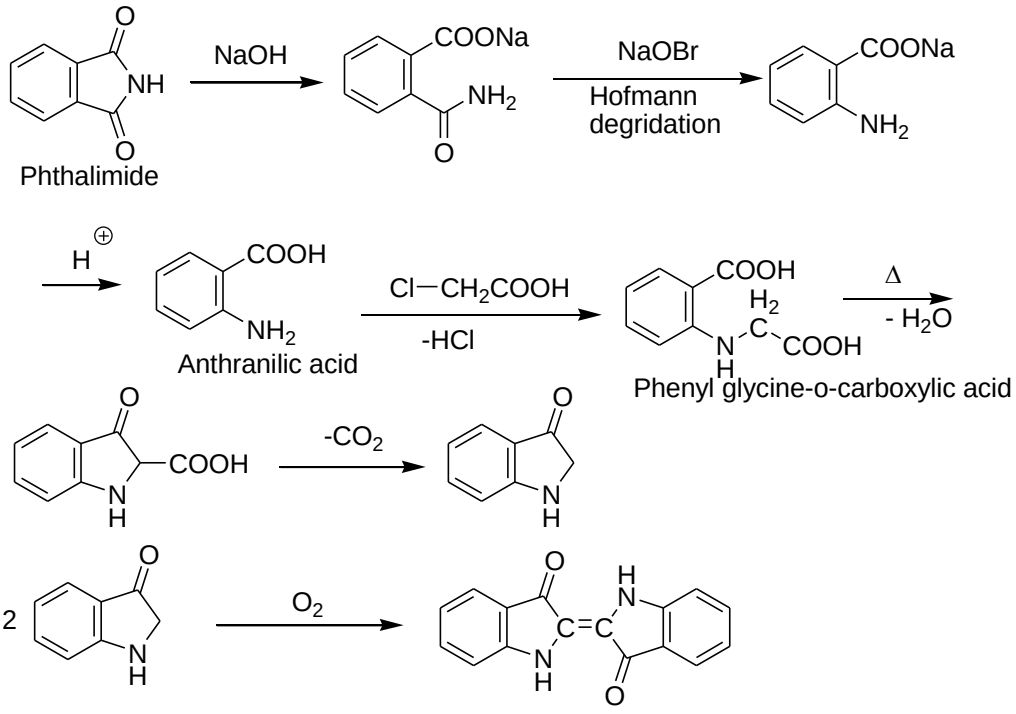


cis form
less stable

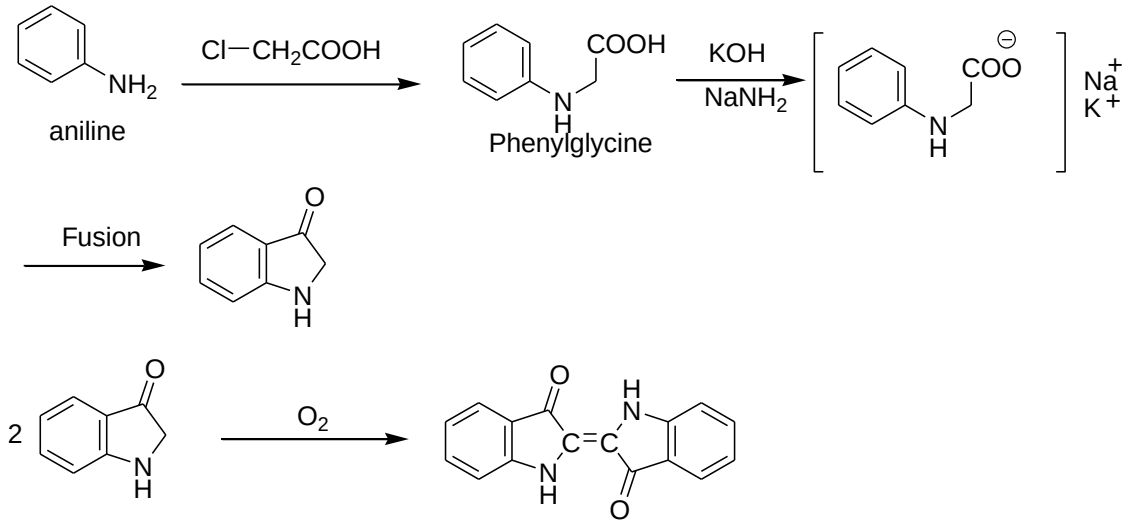
trans form
more stable due to formation of H.b.

<u>Synthesis of Indigo</u>

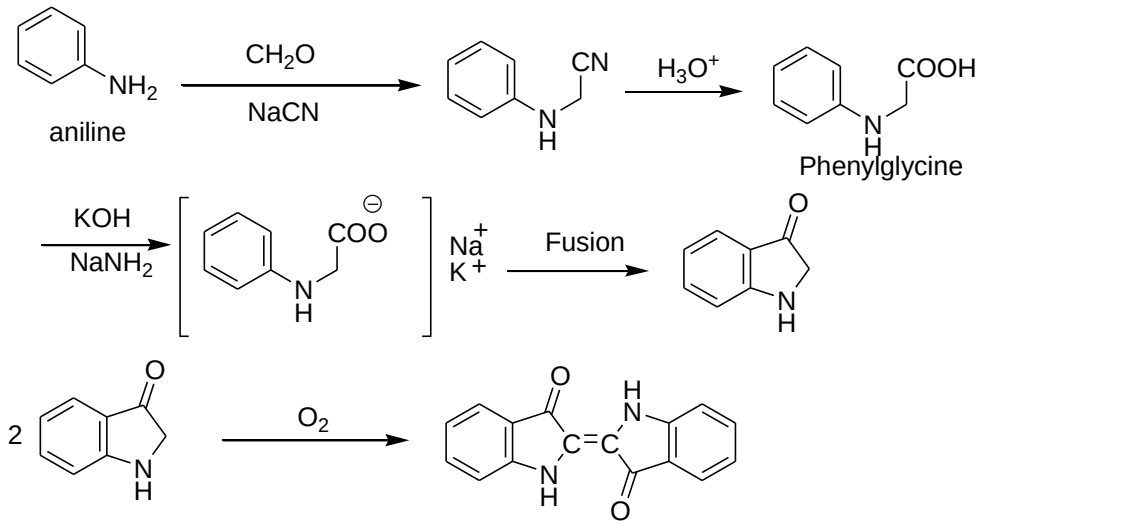
1. Heumann process



2. Sodamide process

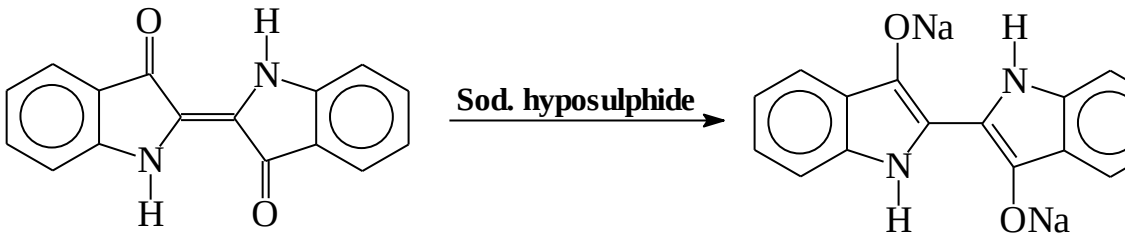


3. From aniline and sodium cyanide



Application of indigotin (vat dye) on cotton:

- **When indigotin paste is agitated with alkali in large amount, the indogotin is reduced to soluble leuco compound (colorless).**



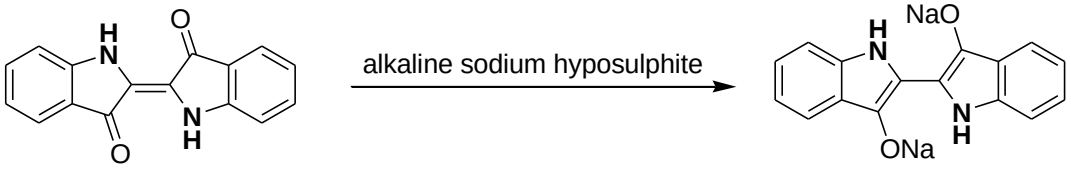
indigotin blue oxidized form water insol.

indigotin colorless redu form water soluble

- **When cotton is to be dyed is soaked in the alkaline medium and then exposed to air, where upon the original blue dye is regenerated in cloth.**

Indigotin derivatives

1) Indigotin white

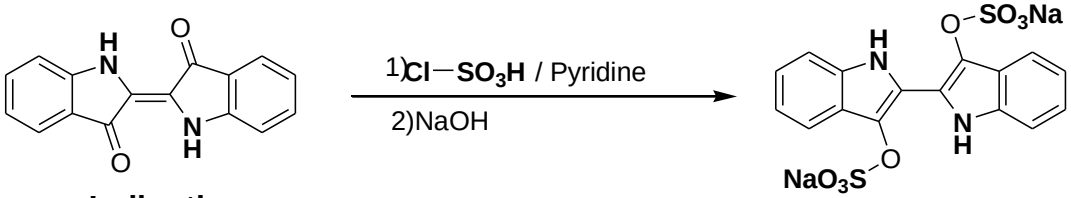


Indigotin
dark blue
water insoluble

White Indigotin
colorless
water soluble

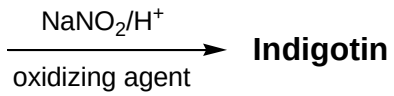
2) Indigosol O

- **It is used for dying wool**



Indigotin

Indgosol O
Water soluble



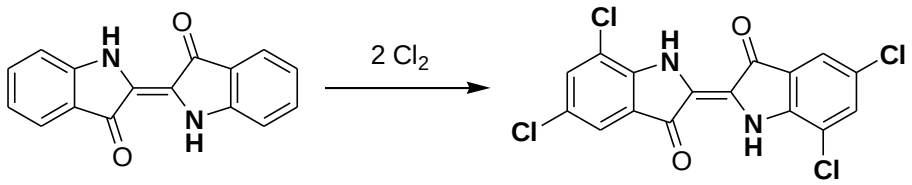
Indigotin

Application of Indigosol on fibres

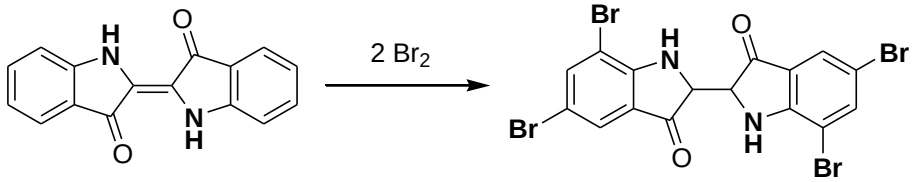
- **Indigosol O is applied on both animal and vegetable fibres by soaking نقع the fabic in the**

solution, and then oxidizing the indigosol O in acid solution (with $NaNO_2$) to the original insoluble vat dye.

3) Brilliant indigo B and Brilliant indigo 2B



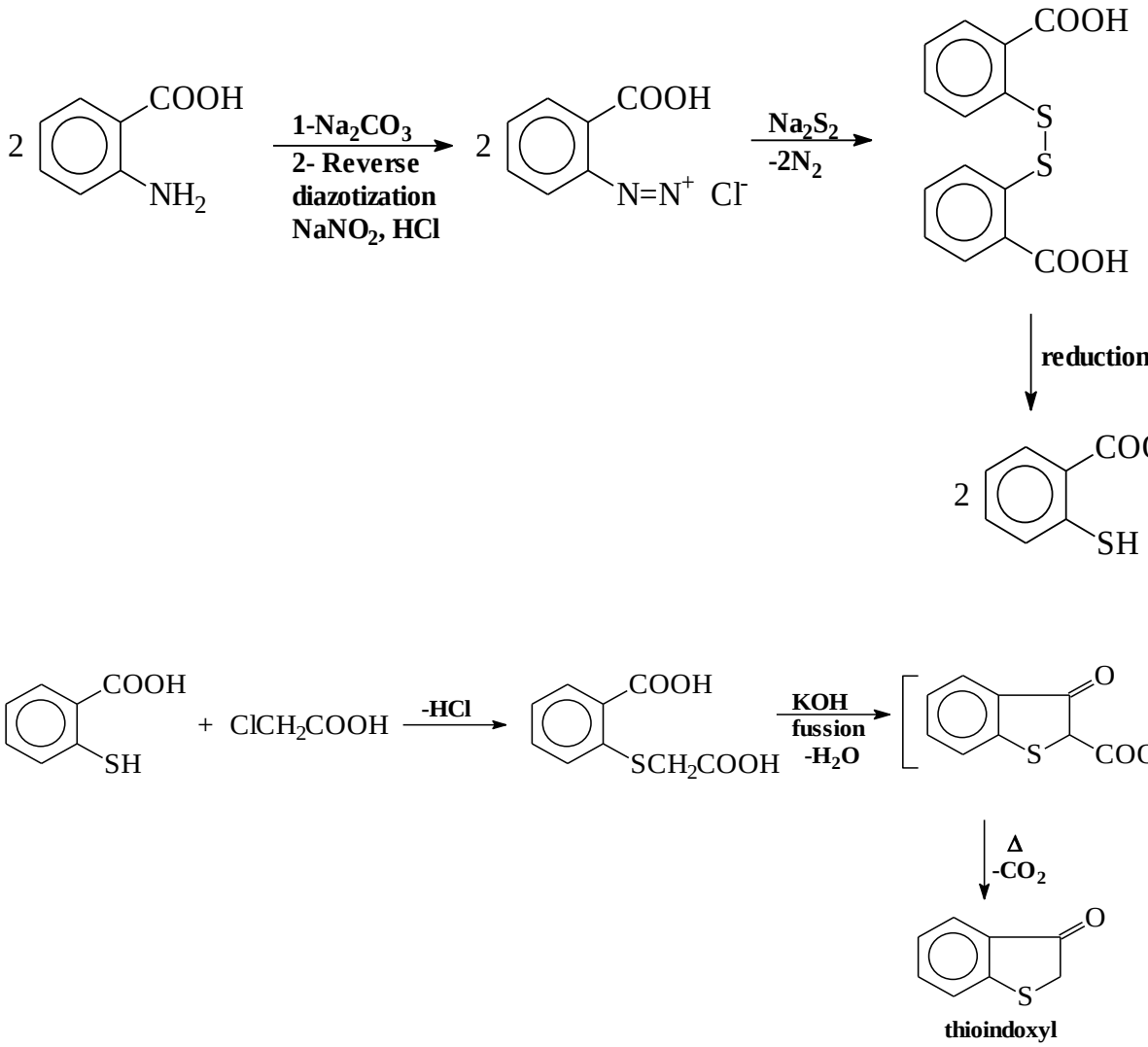
Indigotin **Brilliant Indigo B**

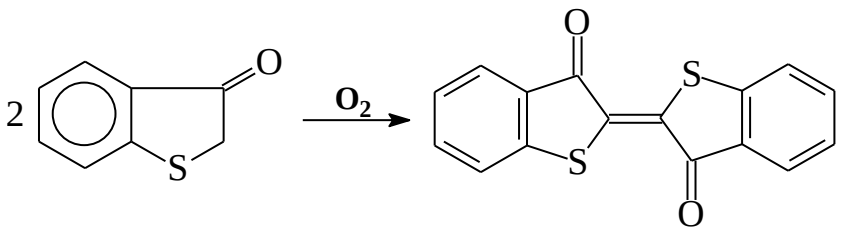


Indigotin **Brilliant Indigo 2B**

5,5',7,7'-tetrabromo Brilliant Indigo 2B

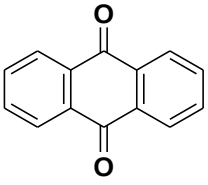
Preparation of thio-indigo:





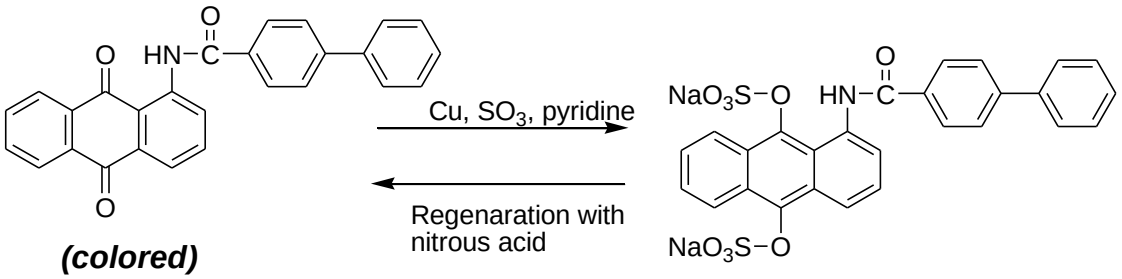
Thioindig red

Anthraquinone vat dyes:



Anthraquinone

- **The application of anthraquinone dye, where it is used as leuco form and the color regenerated on fibre by nitrous acid as shown**

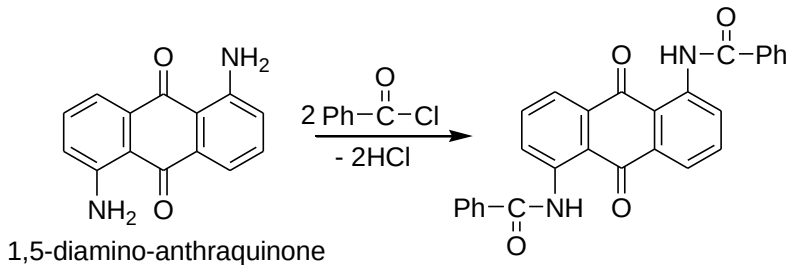


(colored)

Leuco form (colorless)

1) Indanthrone dyes:

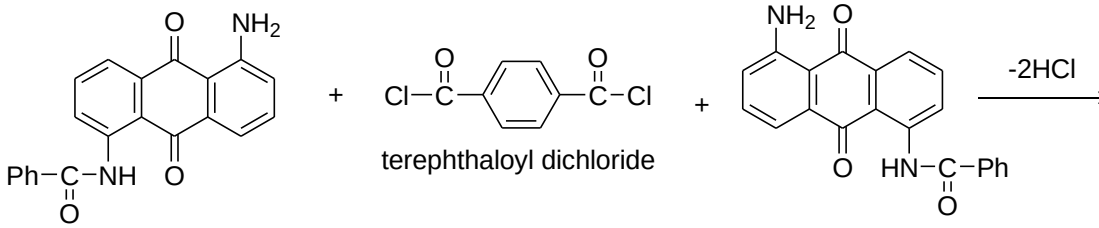
Synthesis of C.I vat yellow(cibanone yellow FGK), (Indanthrene yellow GK)



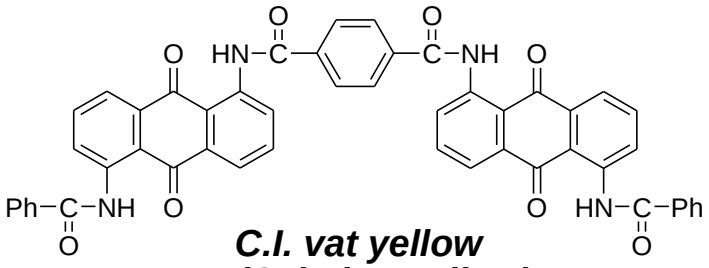
1,5-diamino-anthraquinone

C.I vat yellow(cibanone yellow FGK), (Indanthrene yellow GK)

Synthesis of C.I vat yellow (Caledon yellow)



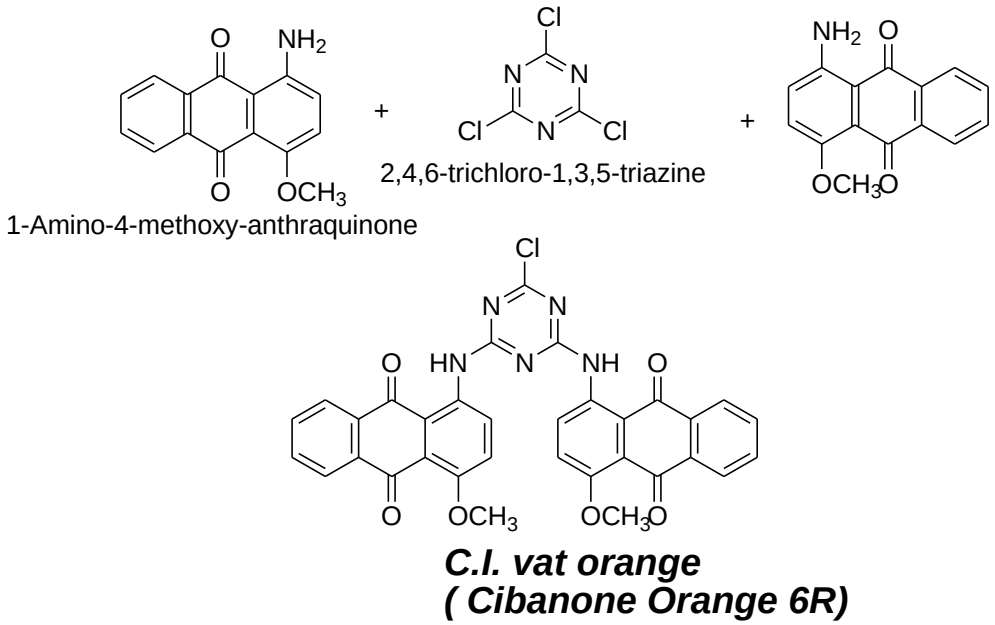
1-Amino-5-benzoylamino-anthraquinone



C.I. vat yellow (Caledon yellow)

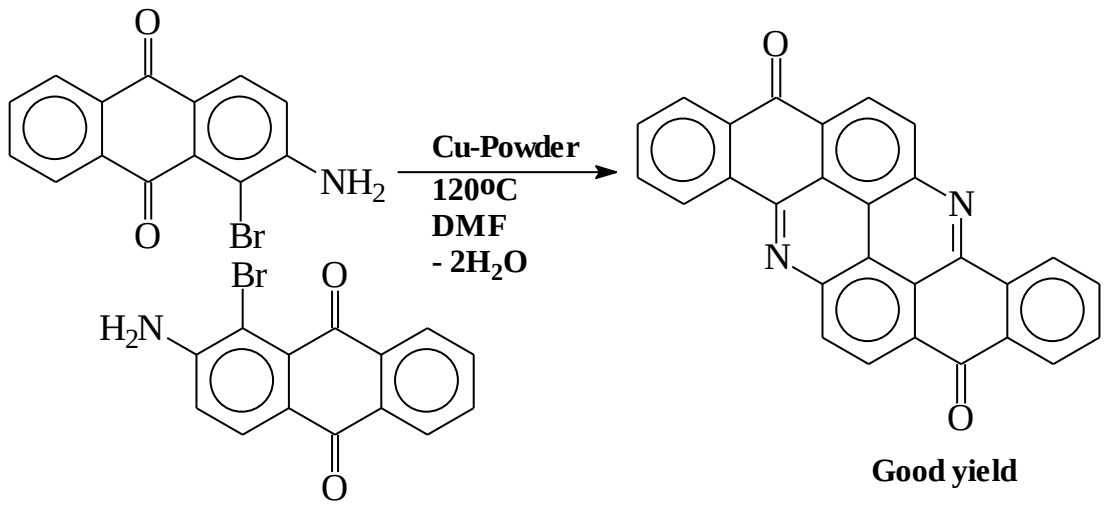
Synthesis of C.I. vat orange (Cibanone Orange 6R)

- **Cibanone Orange 6R is an example of reactive dye which is used for dying cellulosic fibres**
- **It is type of reactive dye**



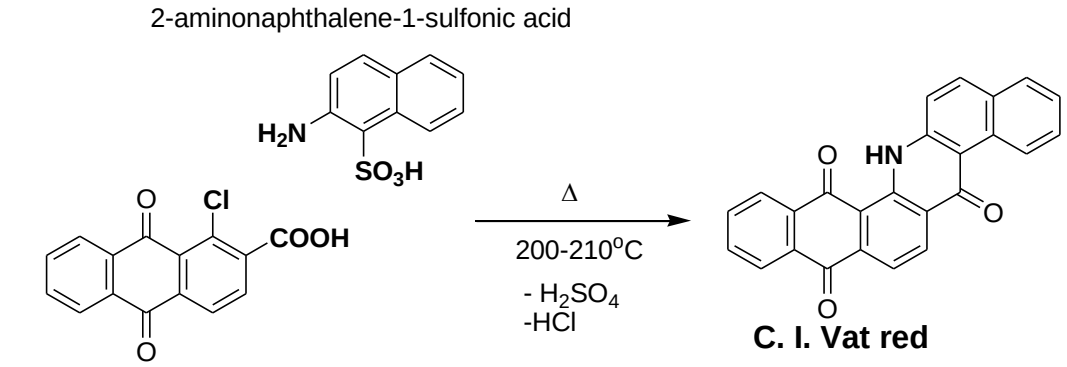
C.I. vat orange
(Cibanone Orange 6R)

C) Flavanthrone (Indanthrone yellow G):

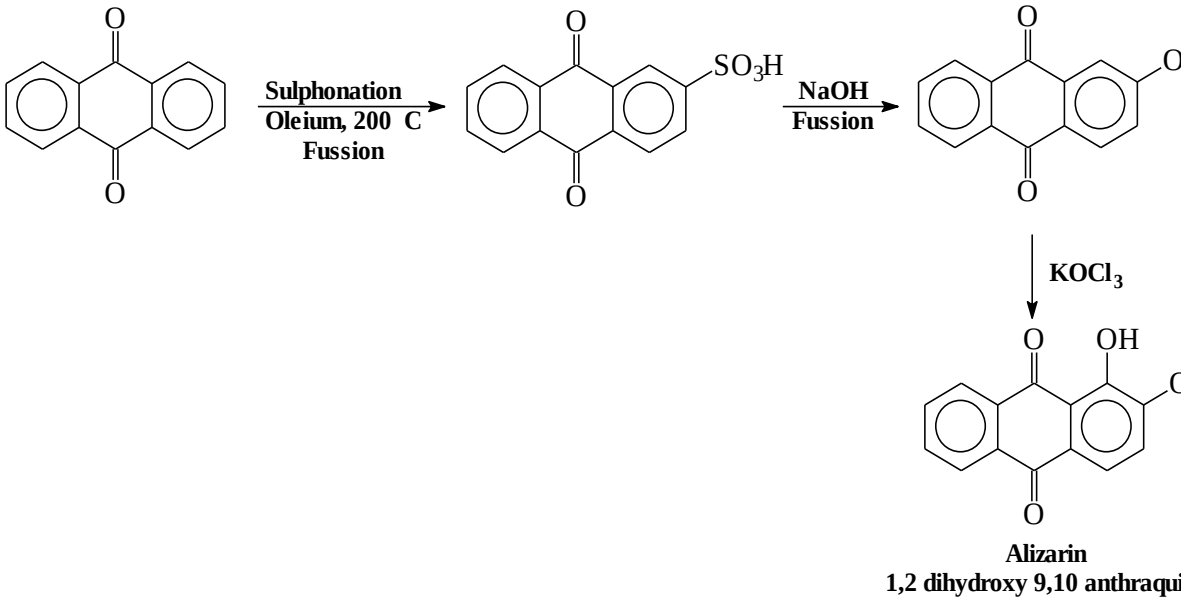


Anthraquinonacridine

Synthesis of C.I Vat red



Alizarine



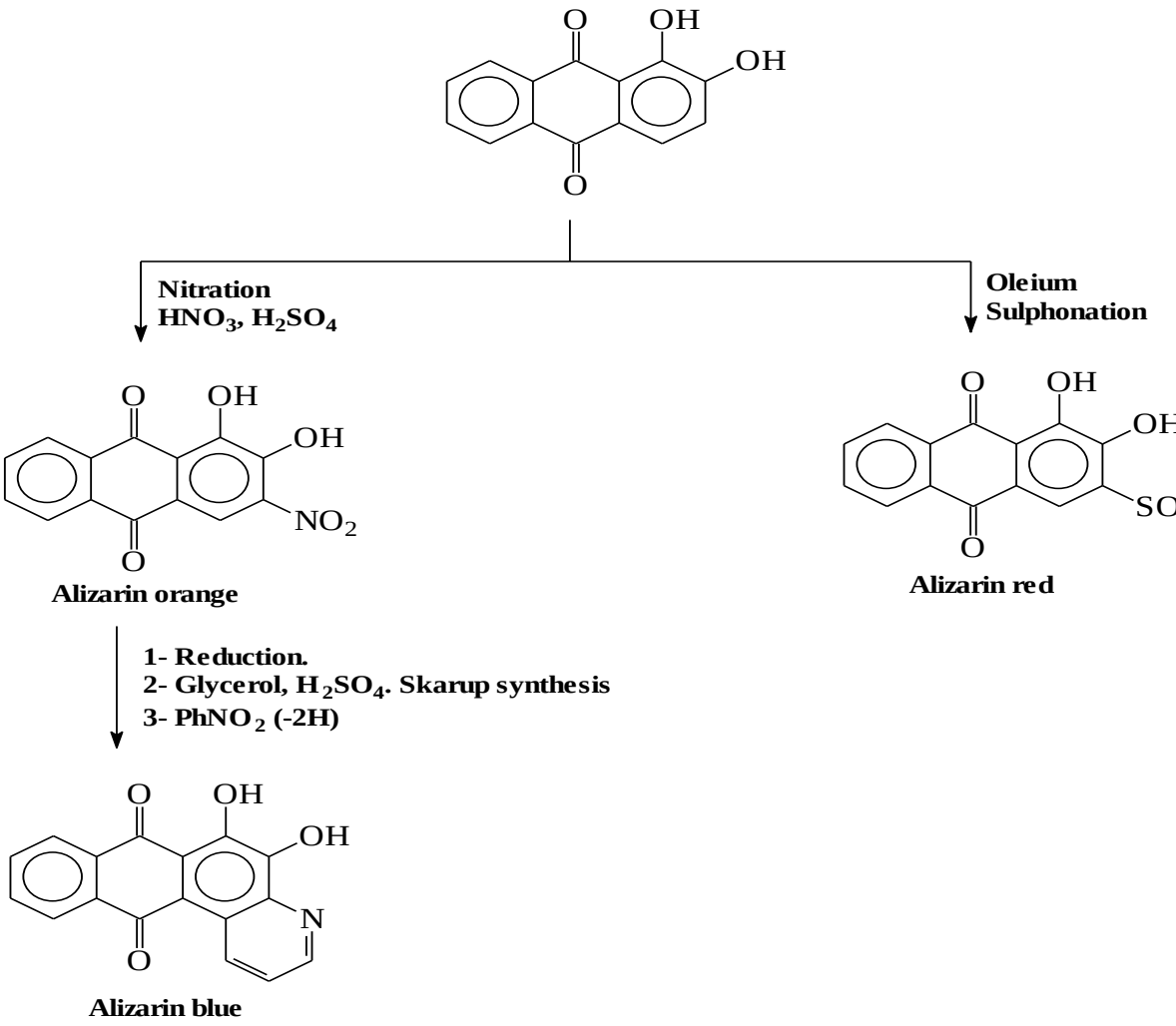
Alizarin is used to prepare:

a- Alizarin orange.

b- Alizarin red.

c- Alizarin blue.

As the following:



Cyanine dyes:

- **Cyanine dyes have no value as dyes, but it is very important as photographic sanitizers.**

- **Cyanine consists of two heterocyclic nuclei linked by odd number of conjugated double bond.**

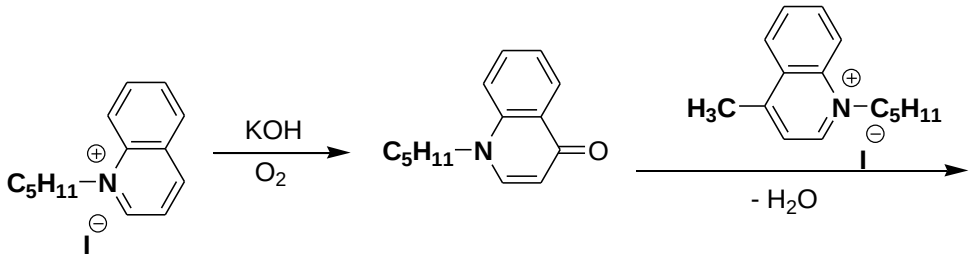
- **Photographic plates of AgCl are sensitive to light from (350-450 nm),AgBr (350-530). By using cyanine dyes, the sensitivity becomes from (350-600 nm) and some of cyanines make sensitive to (350-700 nm) i.e. cover all colors in the visible region.**

- **Cyanine dyes are two quinoline attached to each other by =CH from 4, 4` position.**

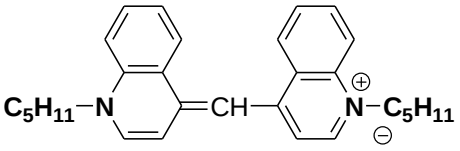
- **Isocyanines attachment from 4,2` by =CH-.**

- **Carbocyanines attachment from 2,2` by =CH-CH=CH- (e.g. sensitol red).**

1) Synthesis of cyanine dyes:

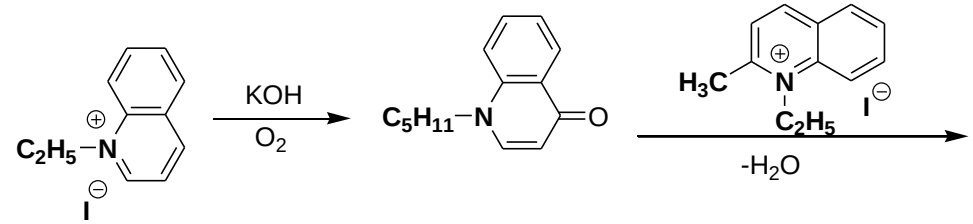


Amyl quinolinium iodide

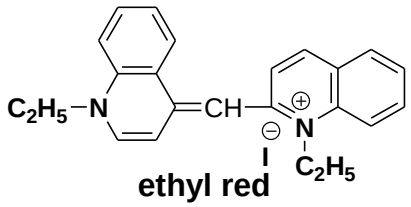


Cyanine

2)Synthesis of isocyanine: e.g. ethyl red



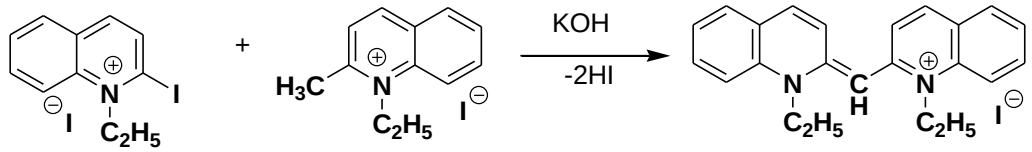
ethyl quinolinium iodide



ethyl red

- **Ethyl red is sensitive from orange to UV**

3) Synthesis of Pesudocyanine

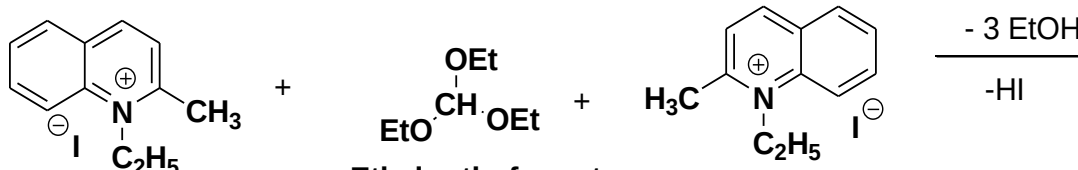


2-Iodo ethyl quinolinium iodie

Pesudocyanine dy

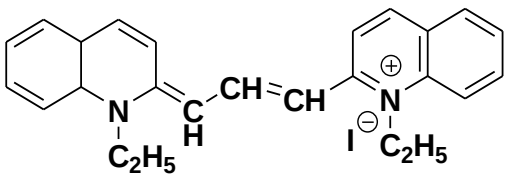
- **This dye has sensitivity from blue to green color**

4) Synthesis of carbocyanine



2methyl ethyl quinolinium iodie

Ethyl orthoformate



Sensitol red

- **This dye has sensitivity from red to orange color**

SOUTH VALLY UNIVERSITY

FACULTY OF SCIENCE
AT QENA

Chemotherapy

اعداد
د. امنية سيد زكي
كلية العلوم – قسم الكيمياء
العام الجامعي
٢٠٢٣

بيانات الكتاب

الكلية :- كلية التربية

الفرقة :- الرابعة كيمياء

المحتوي :-

Introduction of chemothereapy
Sulpha drug
Antipyretic and analgesic
Anti-inflammatory
Antihistamines
Diuretic
Local anesthesia
Antidiabetics
Antifungal
antibiotics

Chemotherapy

Paul ehrlich (1907 s) is the first scientist who introduced the term " chemotherapy “ . The higher plants made the earliest druge discovered , herbal remedies have been important throughout human history , crude plant product such as opium and belladonna have been valuable for centuries.

This field has changed when the antibiotics were discovered and change into drug biosynthesis.

In recent year the introduction of new synthesis pharmaceuticals has outpaced that of natural product . furthermore ,the isolated and purified active material superseded preparation of the parent crud drug.

These factors led to de-emphasis on chemotherapy in the pharmacy curriculum and often to its combination with medicinal chemistry.

Classification of drug on the basis of their origin

1-Drug from natural origin: Herbal or plant or mineral origin, some drug substances are of marine origin.

2-Drug from chemical as well as natural origin: Derived from partial herbal and partial chemical synthesis Chemical, example steroidal drugs

3-Drug derived from **chemical synthesis**.

4-Drug derived from animal origin: For example, hormones, and enzymes.

5-Drug derived from microbial origin: **Antibiotics**

6-Drug derived by biotechnology genetic-engineering, hybridoma technique for example

7-Drug derived from radioactive substances

A sampling of classes of medicine includes

1-Antipyretics: reducing fever (pyrexia/pyresis)

2-Analgesics: reducing pain (pain killers)

3-Antimalarial drugs: treating malaria

4-Antibiotics: inhibiting germ growth

5-Antiseptics : prevention of germ growth near burns, cuts

Definition of medicinal chemistry

Medicinal chemistry is the science which deals with the synthesis, chemistry of mode of action, chemical assay of drug substance.

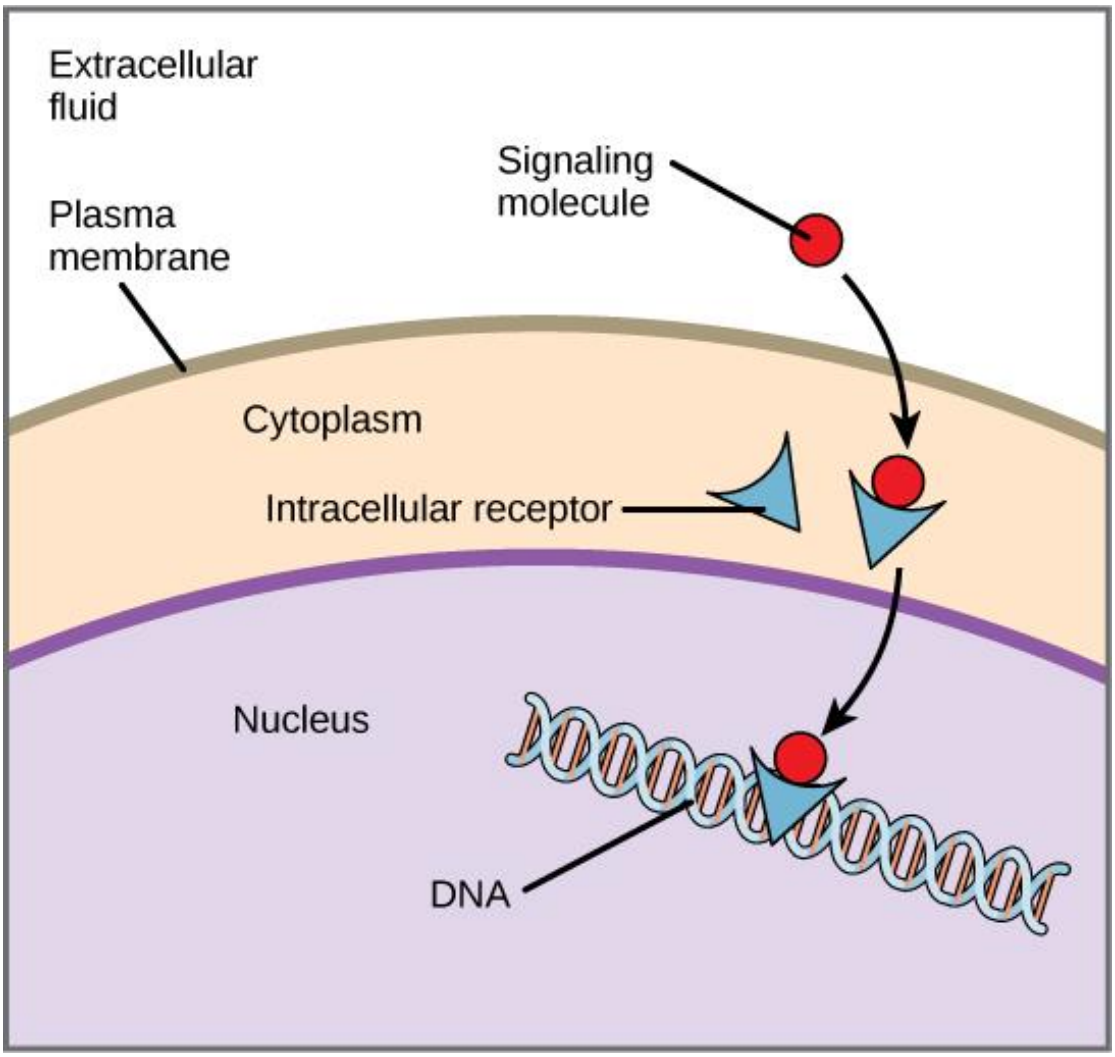
Definition of drug

Drug is any substance presented for treating, curing or preventing disease in human beings or in animals. It may also be used for making a medical diagnosis or for restoring, correcting, or modifying physiological functions.

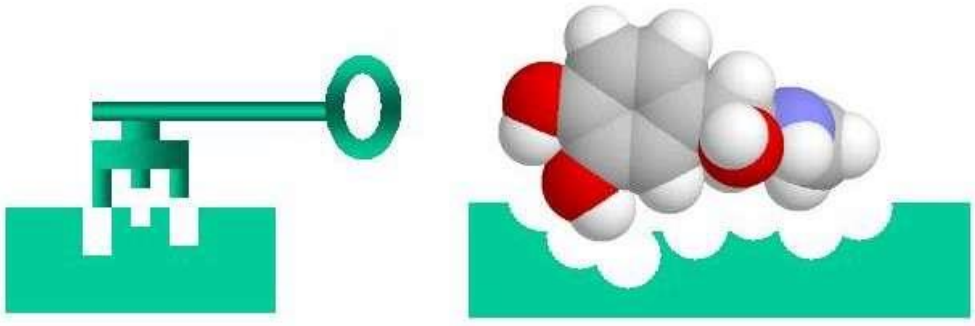



Definition of receptor

Receptor: It is a membrane bound or intracellular macromolecular protein which is capable of binding the specific functional groups of the drug with body.



LOCK & KEY" model of RECEPTORS



Four types of binding takes place between the receptor and the drug molecule

1. Van der Waals forces
2. Hydrogen bonding
3. Ionic interaction
4. Dipole- dipole bonding
5. Covalent bonding

1. Van der Waals Attraction

■weakest intermolecular force (0.5-1.0 kcal/mole)

■electrostatic

■occurs between nonpolar groups (e.g. hydrocarbons)

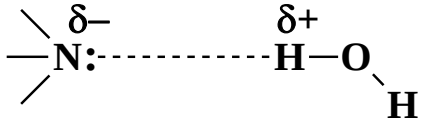
■highly distance and temperature dependent

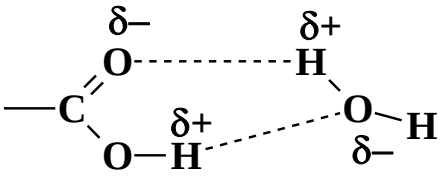
2. Dipole-Dipole Bonding

■stronger (1.0 to 10 kcal/mole)

■occurs electrostatically between electron deficient and electron excessive /ric atoms (dipoles)

■hydrogen bonding is a specific example of this bonding and serves as a prime contributor to hydrophilicity



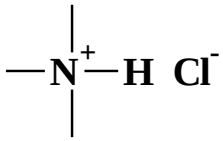


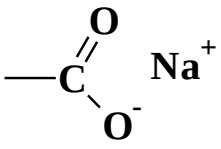
3.Ionic Bonding

■electrostatic attraction between cations and anions

■common in inorganic compounds and salts of organic molecules

■relatively strong (5 kcal/mole)





4.Ion-Dipole Bonding

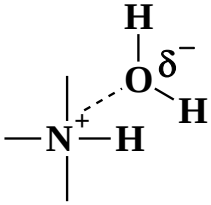
■electrostatic between a cation/anion and a dipole

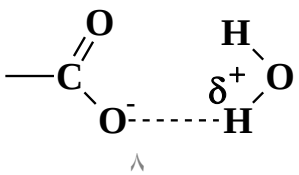
■relatively strong (1-5 kcal/mole)

■low temperature and distance dependence

■important attraction between OMAs**(organic medicinal agents**) and H2O

- **hydrophilic.....water loving**
- **lipophobic.....lipid hating**
- **lipophilic.....lipid loving**
- **hydrophobic.....water hating**

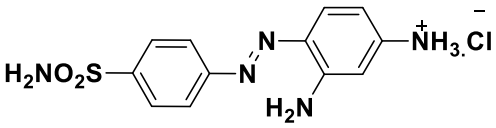




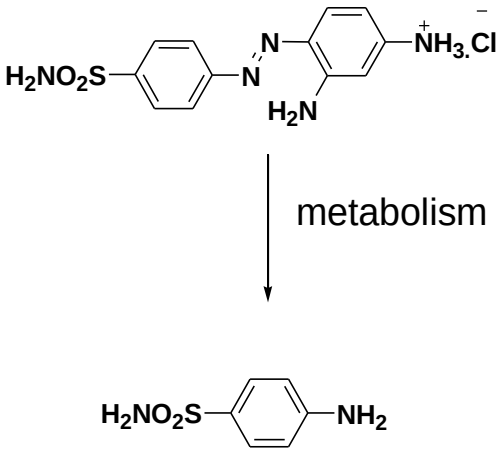
Sulpha drugs

Sulfonamides:-

The sulfonamide are synthetic ,not of natural origin which called " antimicrobials " and not antibiotics. They were the first antibacterial drugs that were not overtly toxic to human.

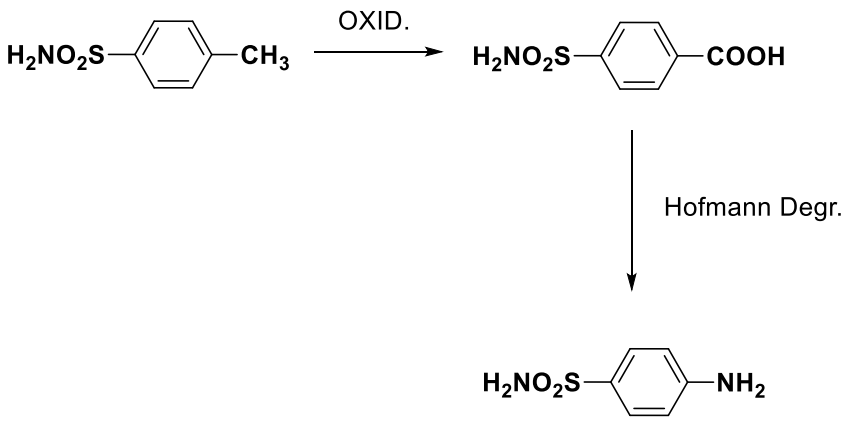


Prontosil which is 2,4-diamino-4-sulphamyl azobenzen hydrochloride was the first sulpha drug to be used in medicine ,it is red dye and metabolized in the body to p-aminobenzene sulphonamide.



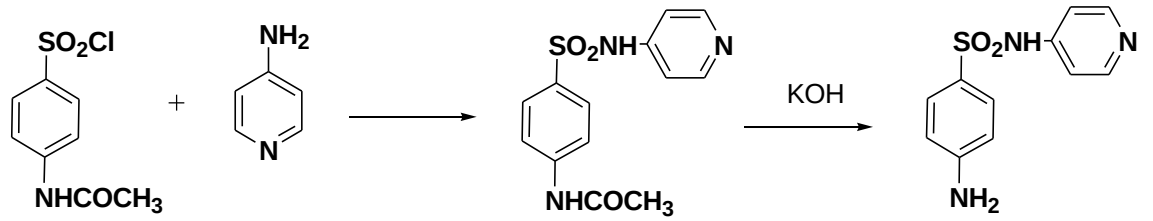
Synthesis of sulphanilamides derivative :-

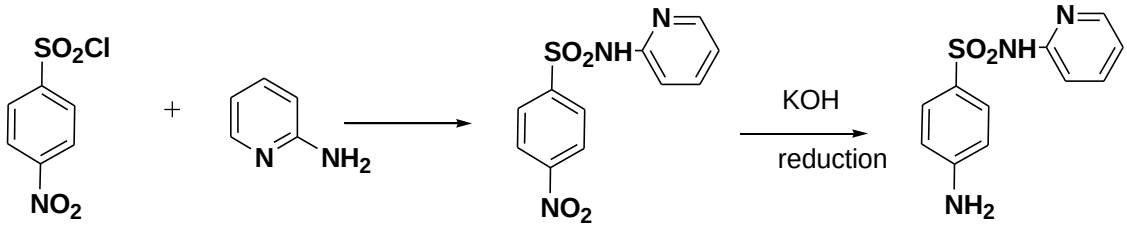
Oxidation of p-toluenesulphonamide to p-sulphamidobenzoic acid fallowed by Hoffmann degradation.



Sulpha pyridine

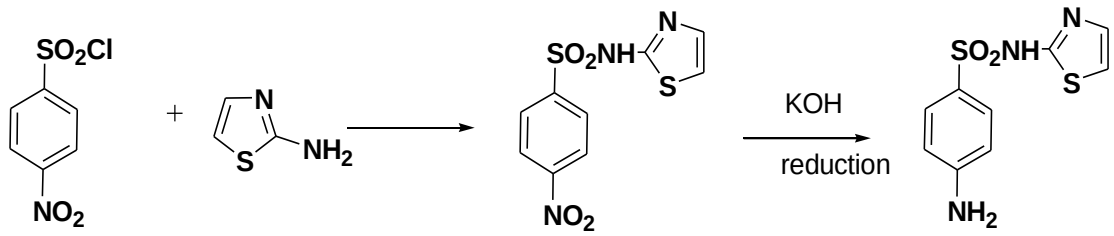
Used to treatment the cocci pneumonia ,but it high toxicity in men ,it is rarely used any longer.





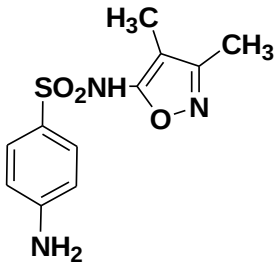
Sulpha thiazole

2-thiazolyl sulponilamide is more patent than sulphapyridine and less toxic ,it most highly bacteriostatic drug which has a permanent place in the pharma.



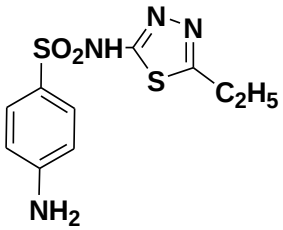
Sulphaisoxazole

Is soluble over a wide pH range ,which have highest bacteriostatic activity and rapid excretion through the kidney.



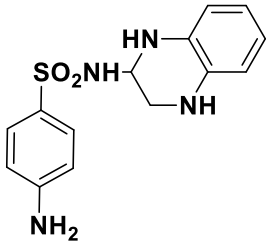
Sulphathiadiazole :-

2-sulphanilamide-5-ethyl-1,3,4-thiadizole is highly soluble and rapidly excretion from the kidney in urine so it consider the most suitable for urinary tract infection.



Sulphaquinoxaline :-

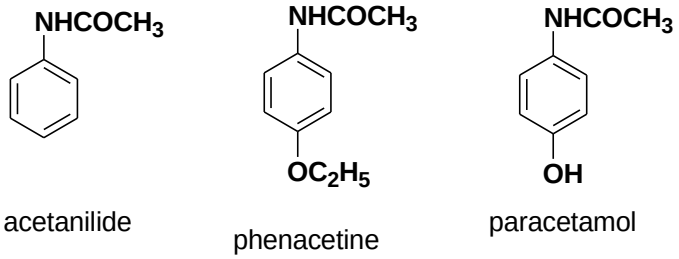
It is widely used in the treatment of coccidiasis infection caused by Eimeria tenella in chickens pheasants.



Antipyretic and analgesics

Aniline and p-aminophenol derivative :-

They have analgesic activity comparable to that of aspirin but don't have anti-inflammatory activity e.g. acetanilide , paracetamol and phenacetin .



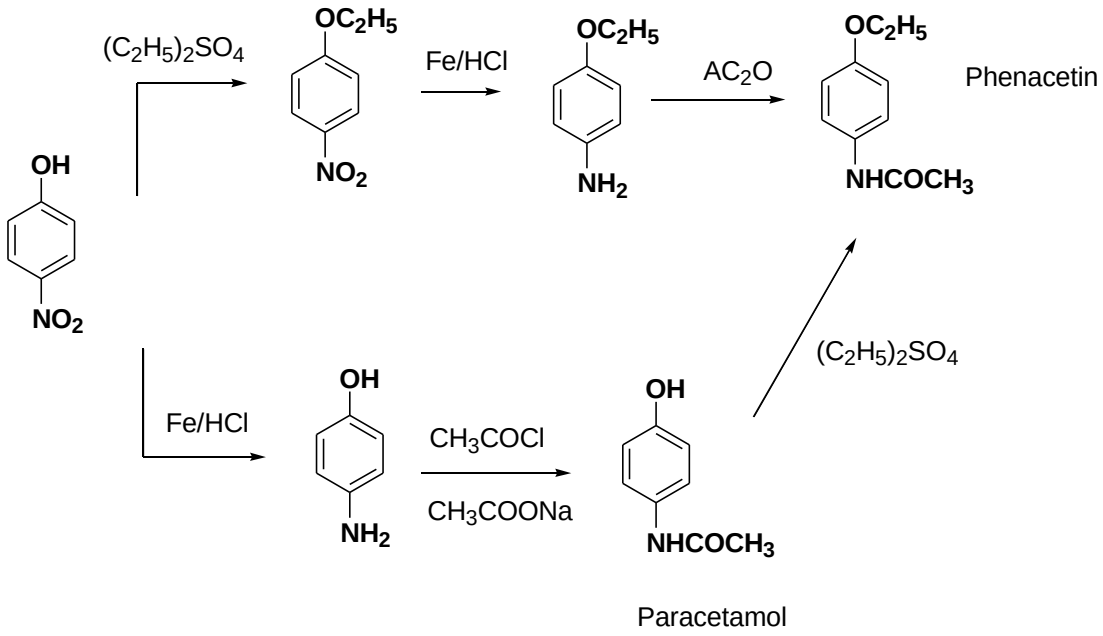
acetanilide phenacetine paracetamol

Acetanilide was introduced into therapy in 1886 as antipyretic-analgesic but it found later too toxic.

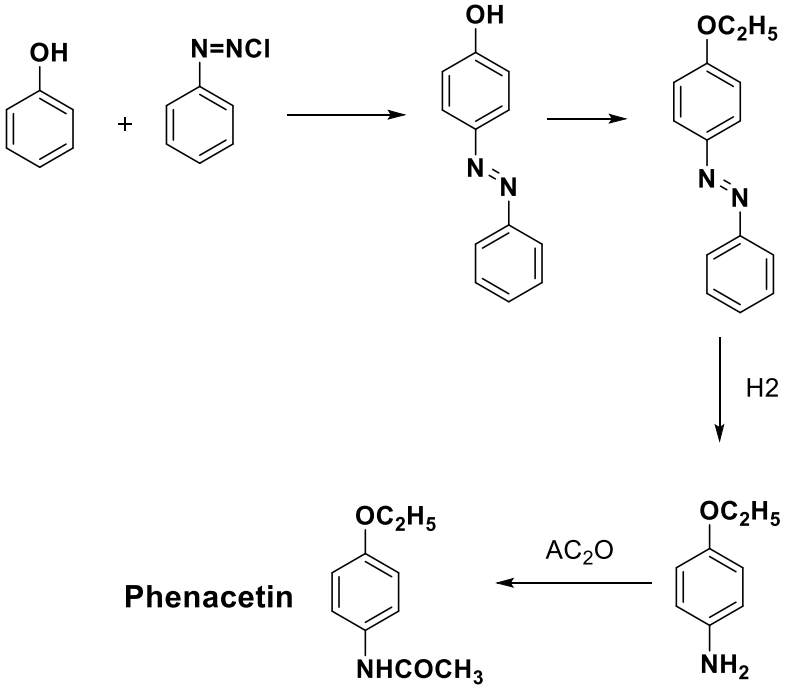
Phenacetin was introduced in the following year and it was widely used but recently it found nephrotoxicity.

Paracetamol is subseguently introduced in 1893 and it remains the only popular agent for this group.

Synthesis of paracetamol

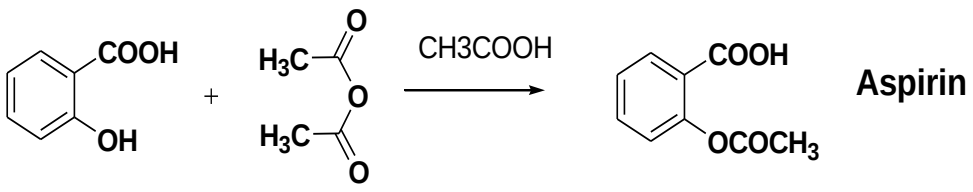


Industrial method for phenacetine



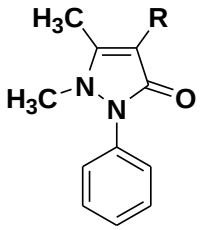
Salicylic acid derivatives

The major chemical classes of salicylates used in medicine are the ester ,the most common one is aspirin .

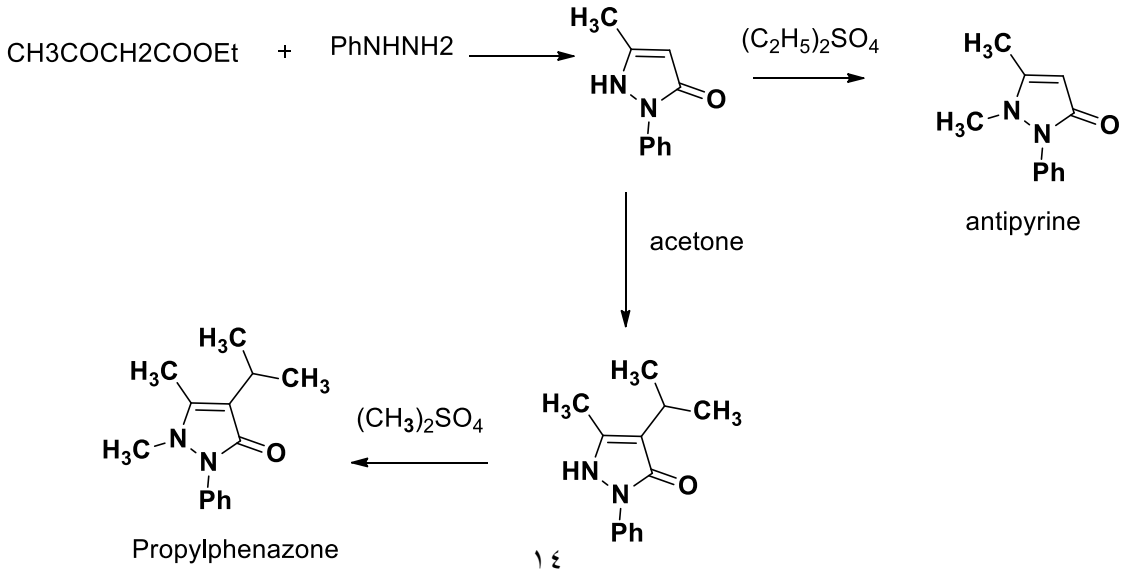


3-pyrazolone derivatives

Antipyrine(phenazone) and propylphenazone have analgesic, antipyretic and antirhumatic activities similar to those of aspirine and used for the same purpose.



Synthesis of antipyrine



Aryl and hetroarylacetic acid derivative

(aryl alkanoic acid derivative)

This class of compounds represents the largest group of NSAIDS (Nonsteroidal anti-inflammatory drugs). They have the following general chemical structure .

Ar-CH(R)-COOH

(R = H,CH3,alkyl ….)

(Ar = Aryl or heteroaryl)

- The main type of NSAID include
- ibuprofen.
- naproxen.
- diclofenac.

Ketoprofene (Propionic acid derivatives)

- mefenamic acid.
- etoricoxib.
- indomethacin.
- high-dose aspirin (low-dose aspirin is not normally considered to be an NSAID)

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are medicines that are widely used to relieve pain, reduce inflammation, and bring down a high temperature.

They're often used to relieve symptoms of headaches, painful periods, sprains and strains, colds and flu, arthritis, and other causes of long-term pain.

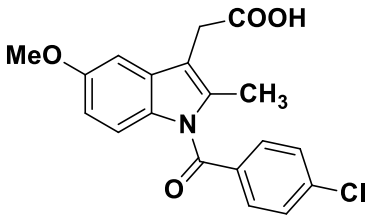
Although NSAIDs are commonly used, they're not suitable for everyone and can sometimes cause troublesome side effects.

Indoleacetic acid derivative

1- indomethacin

Indemethacin is one of the most potent non-steroidal anti-inflammatory agents.

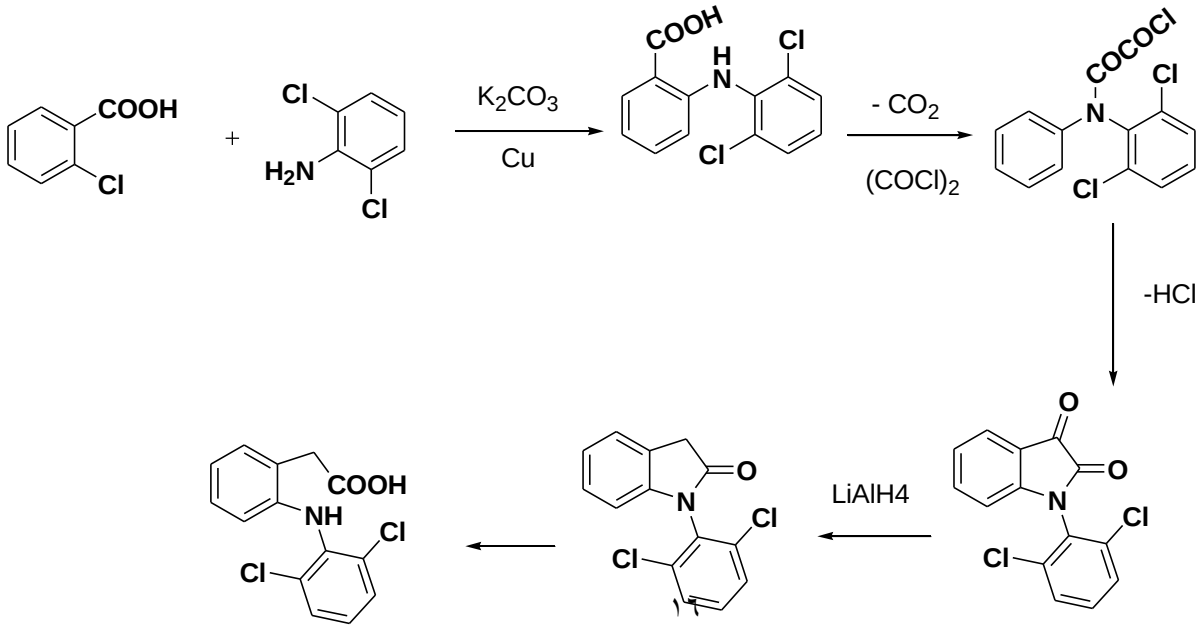
Substitution of a methyl group on the carbon atom separating the acid center from the aromatic ring tends to increase anti-inflammatory activity groups .



Phenylacetic acid derivatives (diclofenac sodium)

Diclofenac is available in 120 different countries and the most widely used NSAIDA in the world It is 6 time more potent than indomethacin and 40 time more potent than aspirin as antipyretic.

Synthesis of diclofenac

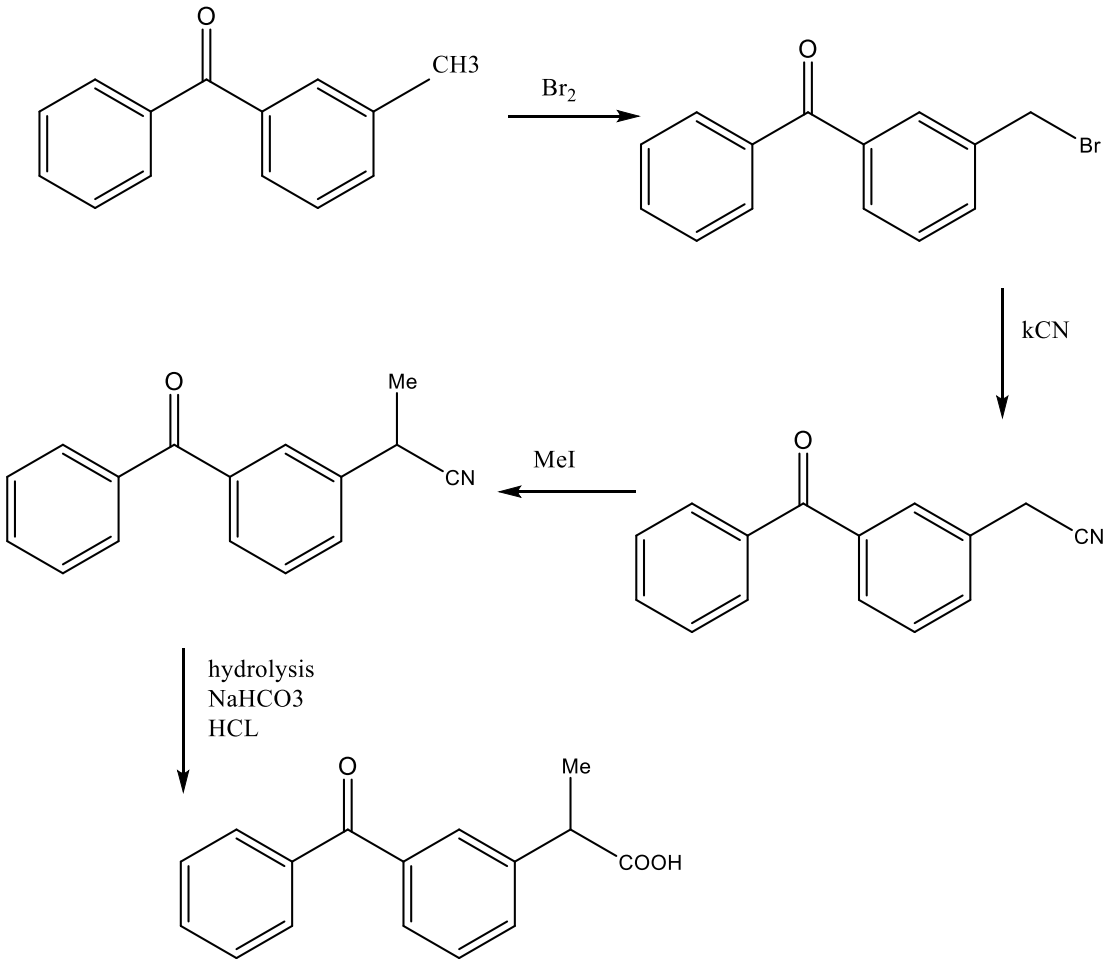


Ketoprofen

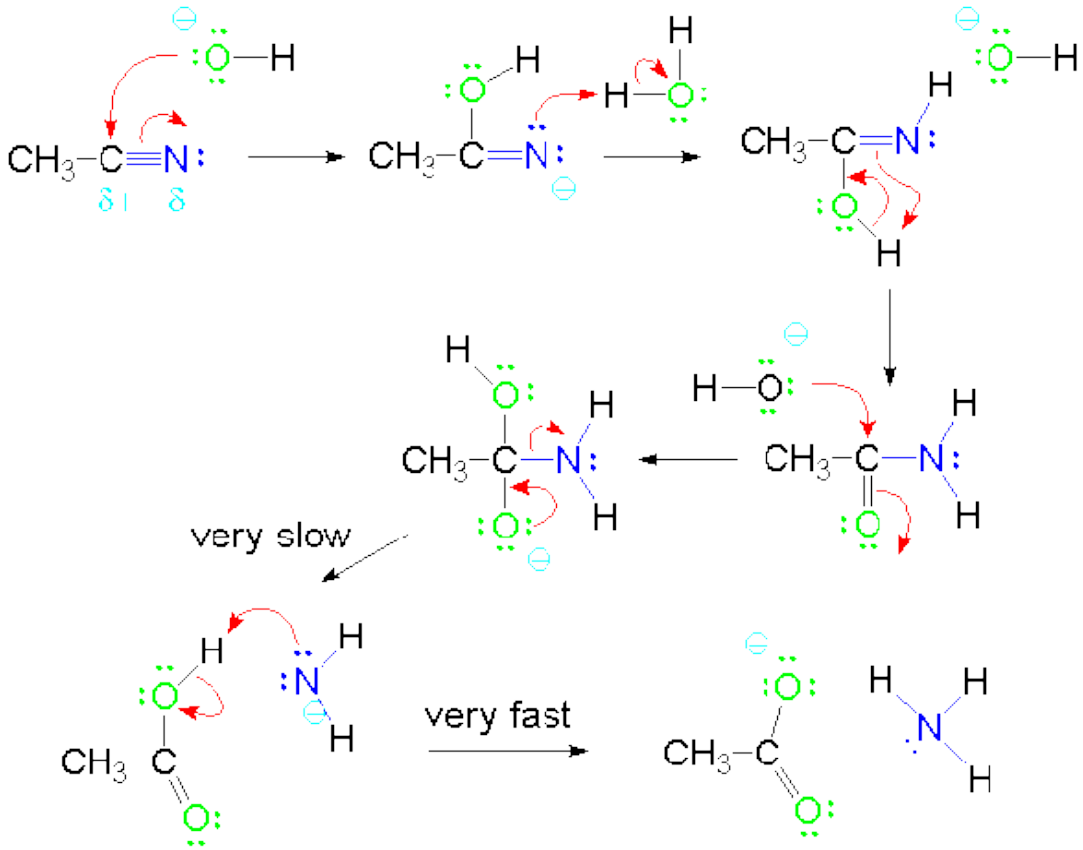
is one of the propionic acid class of nonsteroidal anti-inflammatory drugs (NSAID)with analgesic and antipyretic effects It acts by inhibiting the body's production of prostaglandin.

(The prostaglandins are **a group of lipids made at sites of tissue damage or infection that are involved in dealing with injury and illness**. They control processes such as inflammation, blood flow, the formation of blood clots and the induction of labour)

Synthesis of ketoprofen

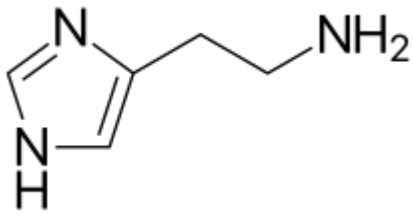

O
CH3
Br2
O
Br
kCN
O
CN
MeI
O
Me
CN
hydrolysis
NaHCO3
HCL
O
Me
COOH

Hydrolysis of cyanide group to carboxylic group



Antihistamine

Histamine



Histamine is an organic nitrogenous compound involved in local immune responses, histamine is produced by basophils and by mast cells found in nearby connective tissues. Histamine increases the permeability of the capillaries to white blood cells and some proteins, to allow them to engage pathogens in the infected tissues.

The discovery of the H1and H2 antagonist burimamide in the early 1970 opened a new ear in the history of the attempt to explane histamine related physiologic processes

Antihistamine

Antihistamines are drugs which treat allergic rhinitis, common cold, influenza, and other allergies. Typically, people take antihistamines as an inexpensive, not patented (generic), drug that can be bought without a prescription and relieves from nasal congestion, sneezing, or hives caused by pollen, dust mites, or animal allergy with few side effects. Antihistamines are usually for short-term treatment.

Mechanism of action

1-Antihistamines are reversible blockers of histamine H1 receptor (**H_1 antagonists**, also called **H_1 blockers**, are a class of medications that block the action of histamine at the H_1 receptor, helping to relieve allergic reactions.) on tissues, such as skin ,bronchi ,eye….etc.

2- Antihistamines are reversible blockers of histamine H2 receptor on tissues, such as stomach ,intestine….etc.

3-Many of antihistamines also possess adrenaline-antagonism which act as anesthetic

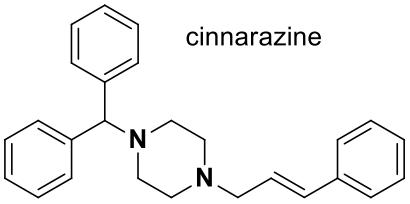
(The adrenal (suprarenal) glands are located at the top of both kidneys. The produce hormones that regulate the immune system, blood pressure, metabolism, and the stress response. In addition, also helps your body do the following:

- Promoting proper cardiovascular function
- Helps in how we respond to stress
- Properly utilizing carbohydrates and fats
- Helps distribute stored fat
- Gives you body odor and pubic hair
- Promotes healthy gastrointestinal functions

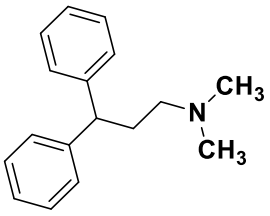
4- many of the traditional antihistamines (first generation) possess some sedative and antimuscarinic effects

5-Now developed antihistamines (second generation) free from these side effect which known as " non-sedating antihistamines "

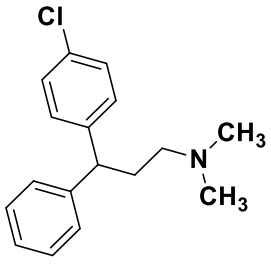
6-some like cinnarazine (second generation) act by inhibiting calcium ions transfer from the outside to inside of the cell so it is value in motion sickness and in vascular disorders



7- Substituents in one of the aryls influence the antihistaminic potency



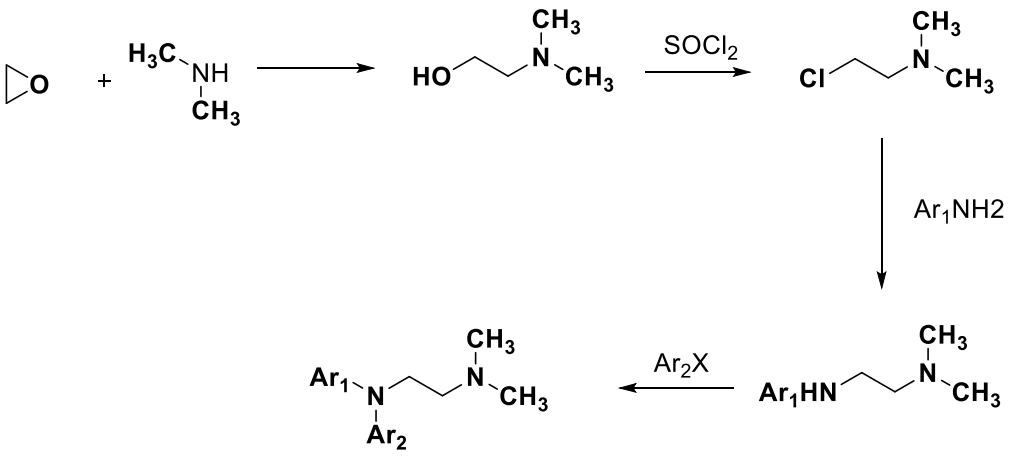
Pheniramine
Usual dose is 20-40mg
Three times daily

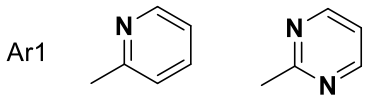


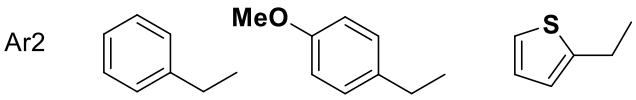
chlorpheniramine
Usual dose is 2-4mg
Three times daily

8- antazoline is a weak antihistamine but potent local anesthetic which used in the eye allergic condition.

General Synthesis of Antazoline derivatives



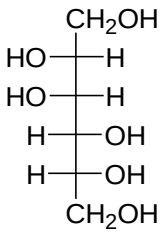


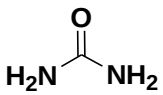


Diuretic

A diuretic is any substance that promotes the production of urine.

In medicine, diuretics are used to treat heart failure, liver cirrhosis, influenza, water poisoning, and certain kidney diseases.

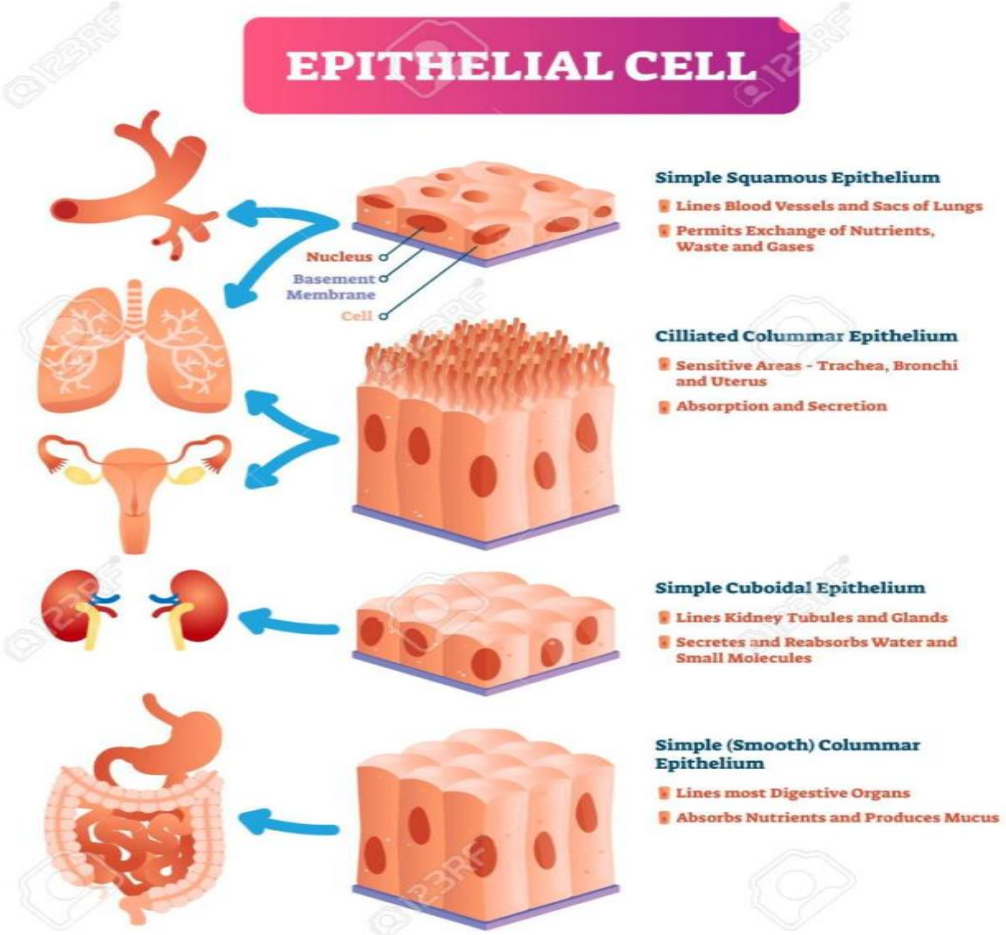




Osmotic diuretics

Osmotic diuretics (e.g. mannitol and urea) are substances that increase osmotlality but have limited tubular **epithelial cell** permeability.

They work primarily by expanding extracellular fluid and plasma volume, therefore increasing blood flow to the kidney.



Mechanism of action

1-Diuretics they effectively reduce blood pressure

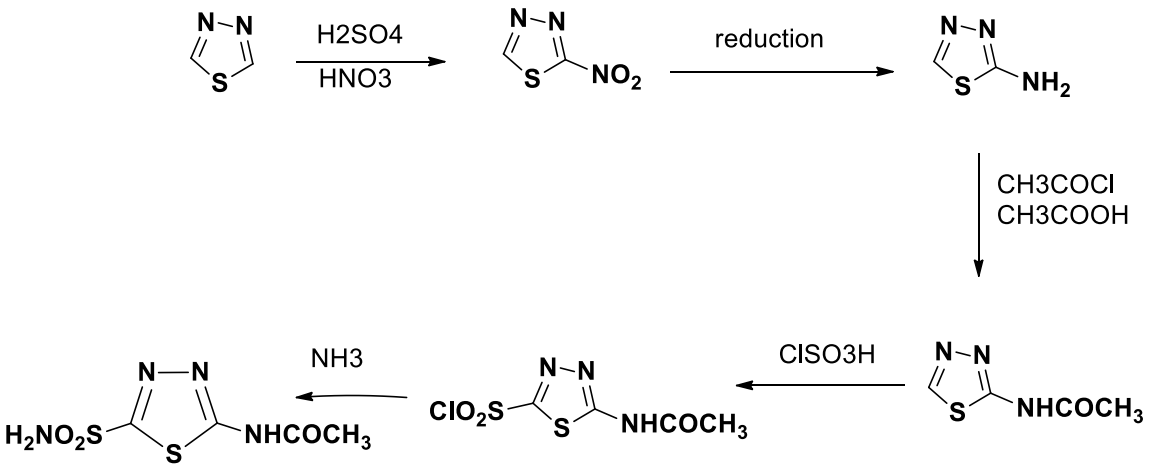
2- Diuretics are a diverse group of compounds that either stimulate or inhibit various hormones that naturally occur in the body to regulate urine production by the kidneys .

Carbonic anhydrase inhibitors: They increase the excretion of sodium, potassium, bicarbonate, and water. Some types of carbonic anhydrase inhibitors include:

Methazolamide .

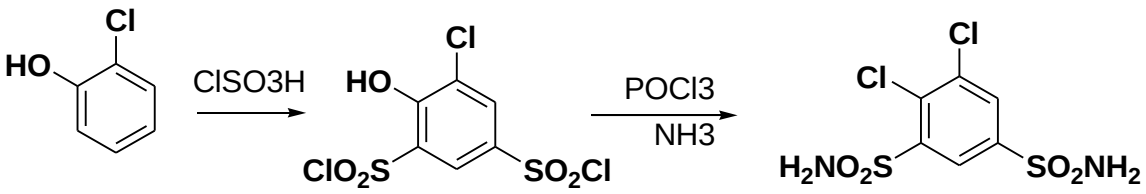
acetazolamide

carbonic anhydride inhibitors (acetazolamide)



2-acetylamino-1,3,4-thiadiazole-5-sulfonamide

dichlorphenamide (Daranide)

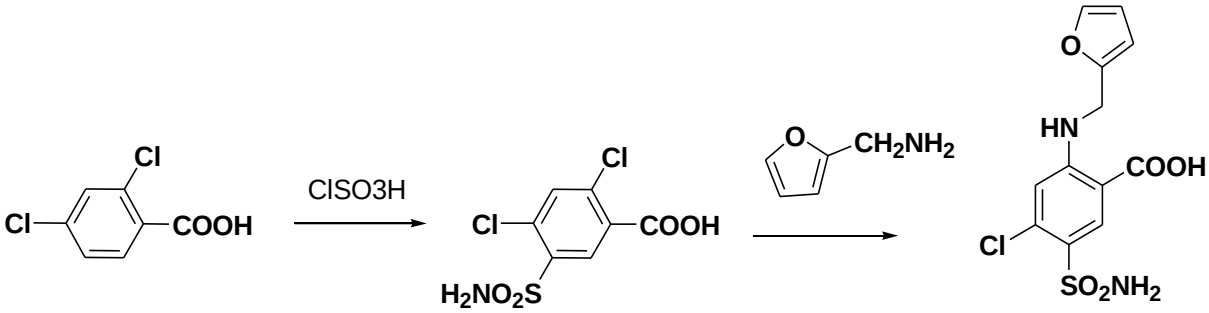


4,5-Dichloro-benzene-1,3-disulfonic acid diamide

Lasix

is a drug choice for urine secretion

(it reduce the body water content and the undesirable salts.)



Local anesthesia

is any technique to induce the absence of sensation in a specific part of the body by block the generation and the conduction of impulses analog a nerve fiber .

It uses :-

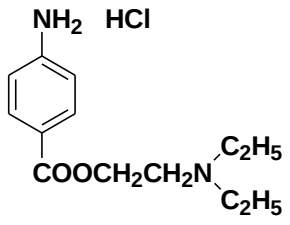
It allows patients to undergo surgical , spinal cord anesthesia and dental procedures with reduced pain and distress Reduced pain caused by minor burns, insect bites, allergic response .

Chemistry

1- ester derivatives e.g cocaine which dose not penetrate the skin ,but absorbed from mucous membranes

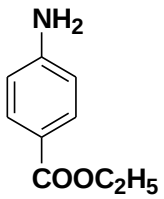
2- amino benzoic acid derivative

a- procaine.HCl



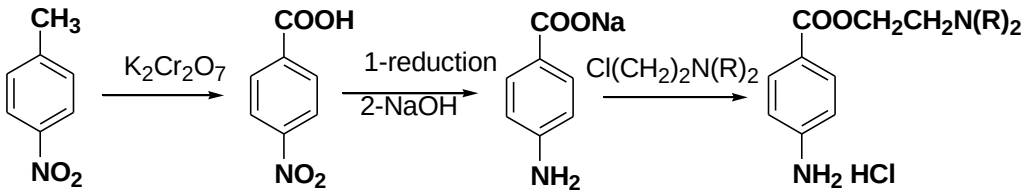
Effective in contact skin or mucous membrane

b- Ethyl p-aminobenzoate



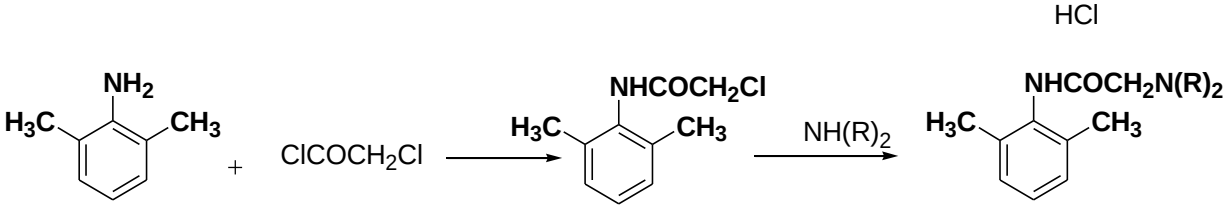
It used in the form of ointment and cream

synthesis of procaine and it's derivative



3-amide derivatives

lidocaine which used in injection, ointment, eye drop .



R= C_2H_5

Diabetes

Diabetes is a disease that occurs when your blood glucose, is too high. Blood glucose is your main source of energy and comes from the food you eat.

Insulin, a hormone made by the pancreas, helps glucose from food get into your cells to be used for energy.

Sometimes your body doesn't make enough—or any—insulin or doesn't use insulin well. Glucose then stays in your blood and doesn't reach your cells.

Antidiabetics

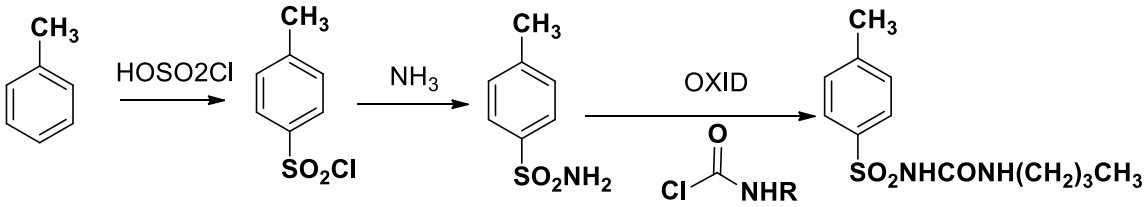
Drugs used in diabetes treat diabetes mellitus by lowering glucose levels in the blood for example :-

1- Type 1 diabetes is a condition in which your immune system destroys insulin-making cells in your pancreas. These are called beta cells. The condition is usually diagnosed in children and young people which treatment with insulin.

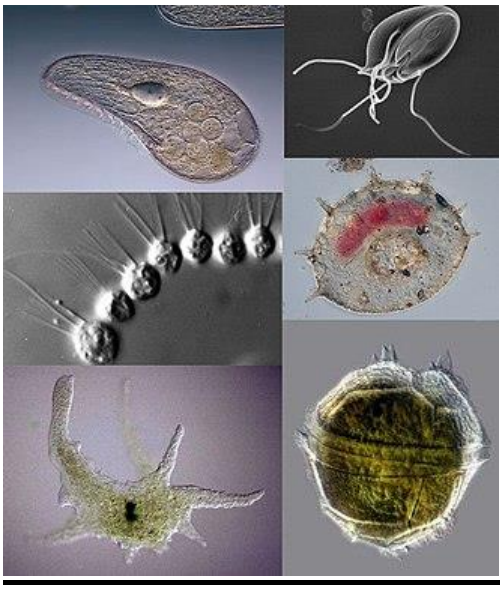
2- type 2 diabetes, in which your body doesn't respond to insulin which treatment with different kind of drug like

sulfonylurea (tolbutamide)

Synthesis of tolbutamide



Anti protozoa drugs

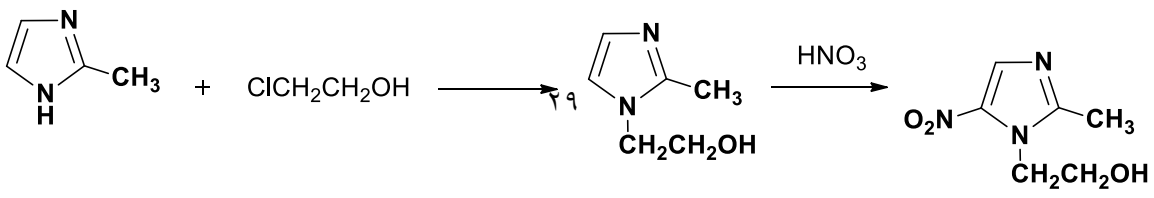


Protozoa Historically, the protozoa were regarded as "one-celled animals", either free-living or parasitic, which feed on organic matter such as other microorganisms or organic tissues

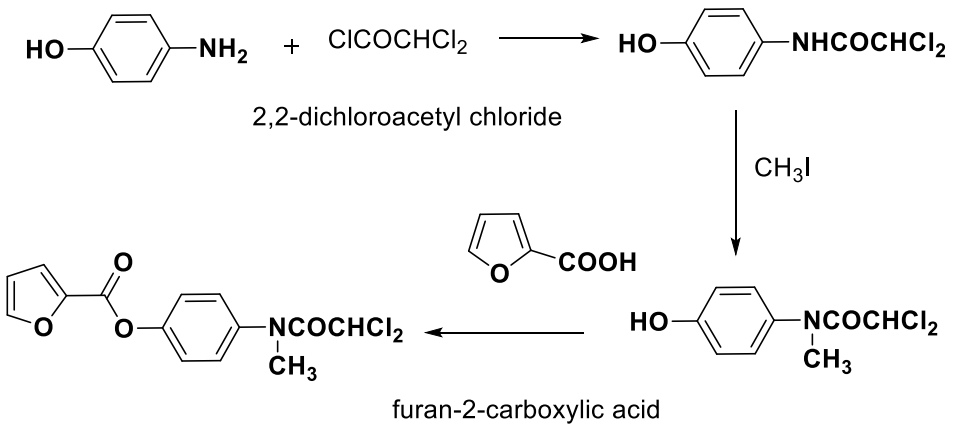
which considered a tropical disease

Treatment:-

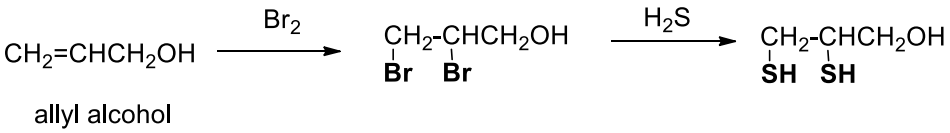
1-Metronidazole (M)



Diloxanide furoate



Dimercaptal



Antifungal agent

Fungi infect skin and lungs and cause diseases

Fungi treatment include:-

1- polyenes :- is a molecule with multiple conjugated double bonds

2- thiazole

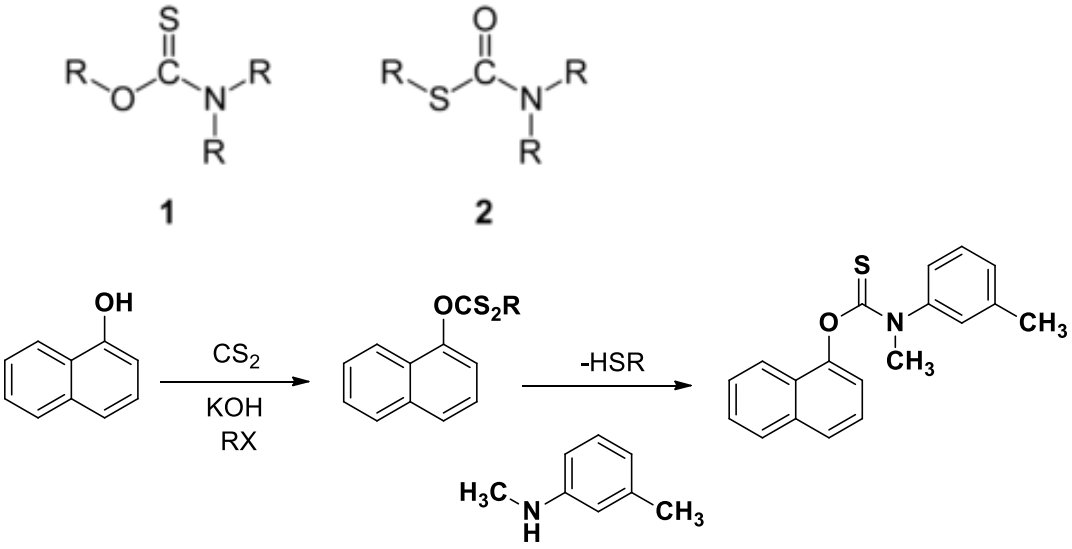
3- unsaturated fatty acid derived from natural castor oil

4-Imidazoles

5- tolnaftate – a thiocarbamate antifungal

synthesis of tolnaftate

Tolnaftate is a synthetic thiocarbamate



Antibiotics

Antibiotics or antibacterials are a type of antimicrobial used in the treatment and prevention of bacterial infection. They may either kill or inhibit the growth of bacteria. Several antibiotics are also effective against fungi and protozoans, and some are

toxic to humans and animals, even when given in therapeutic dosage. Antibiotics are not effective against viruses such as the common cold or influenza, and may be harmful when taken inappropriately

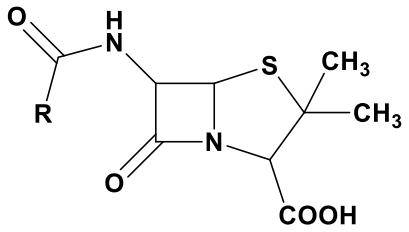
Penicillin (PCN or pen) is a group of antibiotics which include penicillin G (intravenous use), penicillin V (oral use), and benzathine penicillin (intramuscular use). They are derived from Penicillium fungi.

Penicillin antibiotics were among the first medications to be effective against many bacterial infections caused by staphylococci and streptococci.

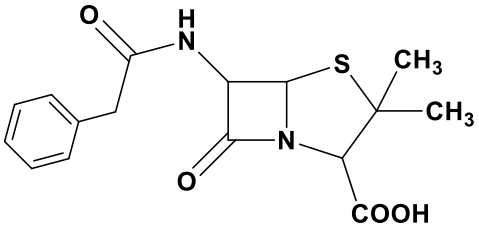
Penicillins are still widely used today, though many types of bacteria have developed resistance following extensive use. All penicillins are β-lactam antibiotics.

About 10% of people report that they are allergic to penicillin

Pencilline derivative

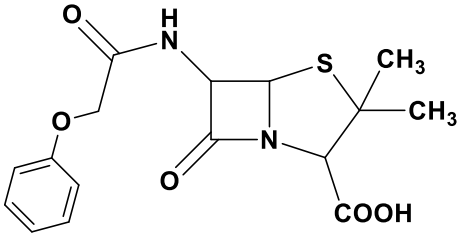


Pencilline G
Benzylpenicillin



As an antibiotic, Penicillin G is noted to possess effectiveness mainly against Gram-positive organisms. Some Gram-negative organisms

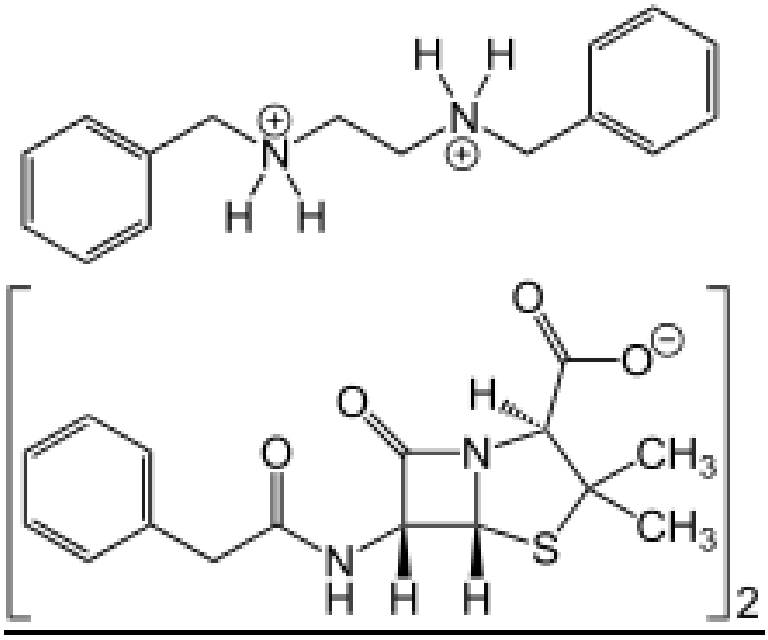
Pencilline v
Phenoxymethylpenicillin



penicillin V, is an antibiotic useful for the treatment of a number of bacterial infections. It is a penicillin that is orally

active. It is less active than benzylpenicillin (penicillin G) against Gram-negative bacteria.

benzathine penicillin
Benzathine benzylpenicillin



It is slowly absorbed into the circulation, after intramuscular injection, and hydrolysed to benzylpenicillin in vivo. It is the drug-of-choice when prolonged low concentrations of benzylpenicillin are required and appropriate, allowing prolonged antibiotic action over 2–4 weeks after a single IM dose

Medical uses for benzathine penicillin include: prevention of rheumatic fever