class - B.Sc. IIIrd yr (Vth - sem)

sec - A.

Organic chemistry

Heterocyclic compounds

unit - I :

1) Introduction :⇒

Hetero is the Greek word and meaning is other / different.

Heterocyclic compounds are those, which contains at least one hetero atom other than carbons as hetero atom in their cyclic structure such compounds are known as heterocyclic compounds.

All the known heterocyclic compounds involve an element from group IV-B, V-B & VI-B of periodic table but mostly N, O, S atoms are present as hetero atom. The element like P, B, Si, Sn, Al, As, Cu are also occasionally incorporated in the ring.

Those heterocyclic compounds are relatively stable compounds hence they are referred as heterocyclic aromatic compounds. Ethylene oxide, succinic anhydride, lactones & cyclic carbohydrates. These compounds are readily formed from open chain substance and are easily converted into open-chain derivatives & generally excluded from heterocyclic compounds due to the relative instability of their ring system.

* Nomenclature

The following rules are used for the IUPAC Nomenclature of heterocyclic compounds.

1. The following prefixes are used for the various hetero atoms.

Atom	prefixes used
oxygen	— oxa
sulphur	— Thia
nitrogen	— Aza
phosphorus	— phospha
silicon	— sila

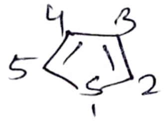
2. The size of heterocyclic ring is indicated by it's suffix. i.e. the last vowel of prefixes are replaced by the respective name ending words that indicate the size of ring

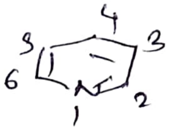
No. of atom in ring	Ending name or Suffix
3	- irine
4	- ete
5	- ole
6	- ine
7	- epine

examples

Structure					
Trival Name →	Furan	Thiophene	Pyrrole	Pyridine	-
IUPAC →	Oxole	Thiole	1H-Azole	Azine	1H-Azepine.

In monocyclic compounds if only one hetero atom is present then numbering is given in such way that the hetero atom gets the lowest number and proceeds in anticlockwise around the ring.





4. when two or more of the same hetero atoms present in the ring, then the prefixes, di, tri-tetra; etc. are used.

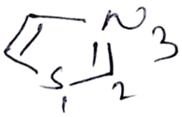
Pyrimidine Pyrazine

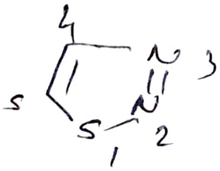
Common Name → 1H-Pyrazole

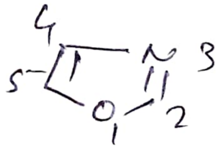
IUPAC → 1H,-1,2-Diazole 1,3-diazine 1,4-Diazine 1,2,4-Triazine

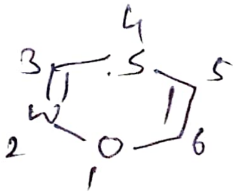
5. when the ring containing more than one, different hetero atom in their ring, then the numbering starts from that hetero atom which is in the highest group in the periodic table.

If the two different hetero atoms belong to same group, then the numbering starts from those, which is having low atomic no. & numbering to the hetero atoms around the ring should be minimum.









1,3-Thiazole 1,2,3-Thiadiazole 1,3-oxazole 1,2 4

Classification :→

Heterocyclic aromatic compounds are clas

on the basis of size of heterocyclic ring contain

one or more hetero atom, as well as condensed

system (two. or more fused ring).

Classification :-

1) Five member heterocyclic compounds containing one hetero atom.

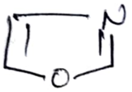
e.g.

oxole

Thiole

Azole.

(2) Five membered heterocyclic compounds contai two hetero atoms.



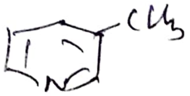
IUPAC 1,3-oxazole 1,3-Thiazole 1,3-Diazole 1,2-Diazole

common Name - oxazole Thiazole (Imidazole) (pyrazole)

3.) six member heterocyclic compounds containing one hetero atom.

e.g.

Azine



3-methyl Azine

β-methyl pyridine

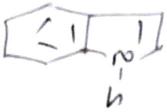
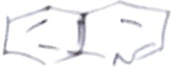
4) Six member heterocyclic compounds containg two hetero atoms.

e.g.

				
IUPAC	1,2-Diazine	1,3-Diazine	1,4-Diazine	1,3,5-Triazine
Trival Name	Pyridazine	Pyrimidine	Pyrazine	

(5) Bicyclic compounds containing one hetero atom.

e.g.

			
common	Indole	Quinoline	Isoquinoline
	1H-Benzopyrrole	α,β-Benzopyridine	4,5 Benzo Pyridine

6) Bicyclic compounds containing two hetero atom

e.g

Benzothiazole

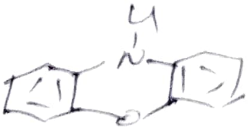
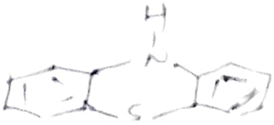
1,3-Benzothiazole

Benzooxazole

1,3-Benzooxazole

7) polycyclic compounds containing more than two rings.

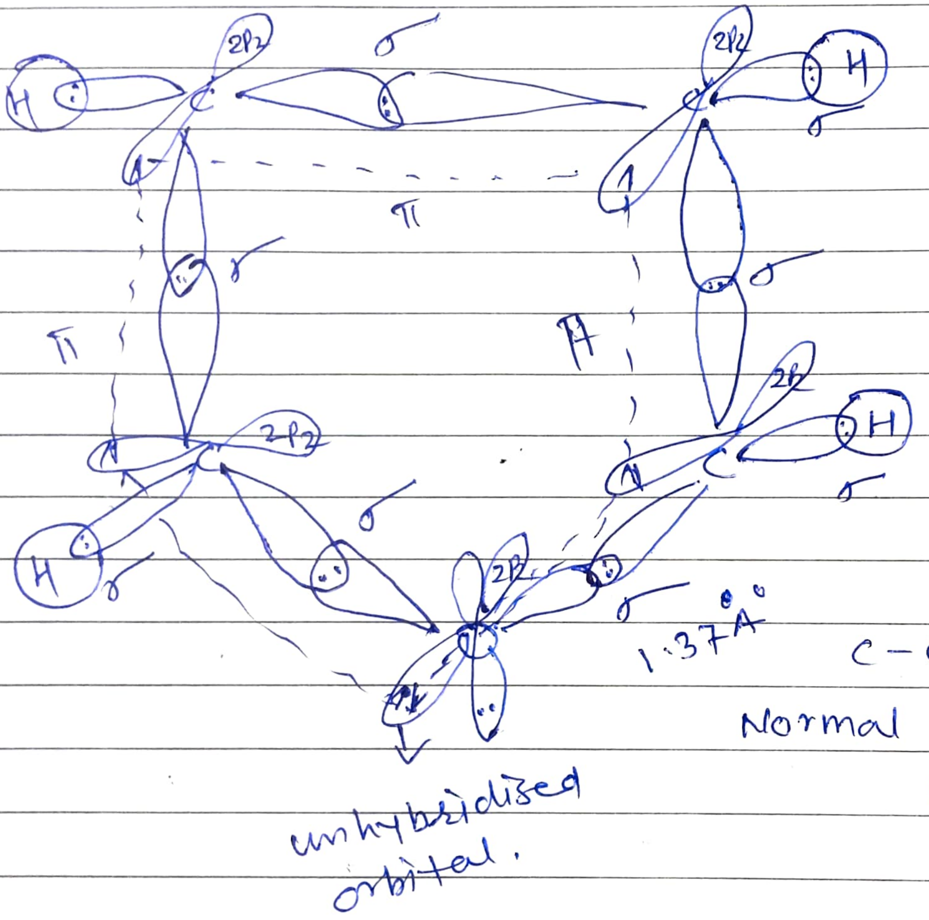
e.g.

		
common Name -	phenoxazine	phenthiazine
IUPAC Name -	10,10-α-dihydro 4a-phenoxazine	10,10 α-dihydro-4αH-Phenothiazine

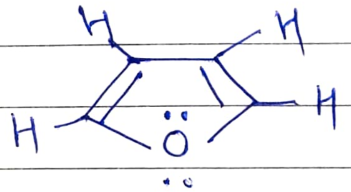
(ii) Molecular orbital structure, resonance structure and reactions of Furan, pyrrole, thiophene & pyridine.

Molecular orbital structure:-

1) Furan.



M.F.
C_4H_4O



C-O in furan 1.37 A°

Normal C-O bond length is 1.43 A°.

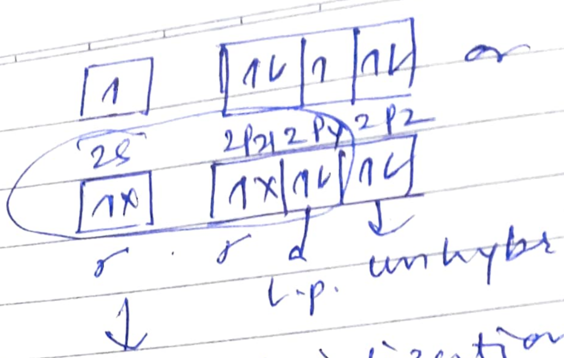
Ato. No - O is - 8

O - electronic configuration is.

$1s^2, 2s^2, 2p^4$

outer electronic ~~trasi~~ configuration in G.S. — [↑↓] [↑↓ | ↑ | ↑]

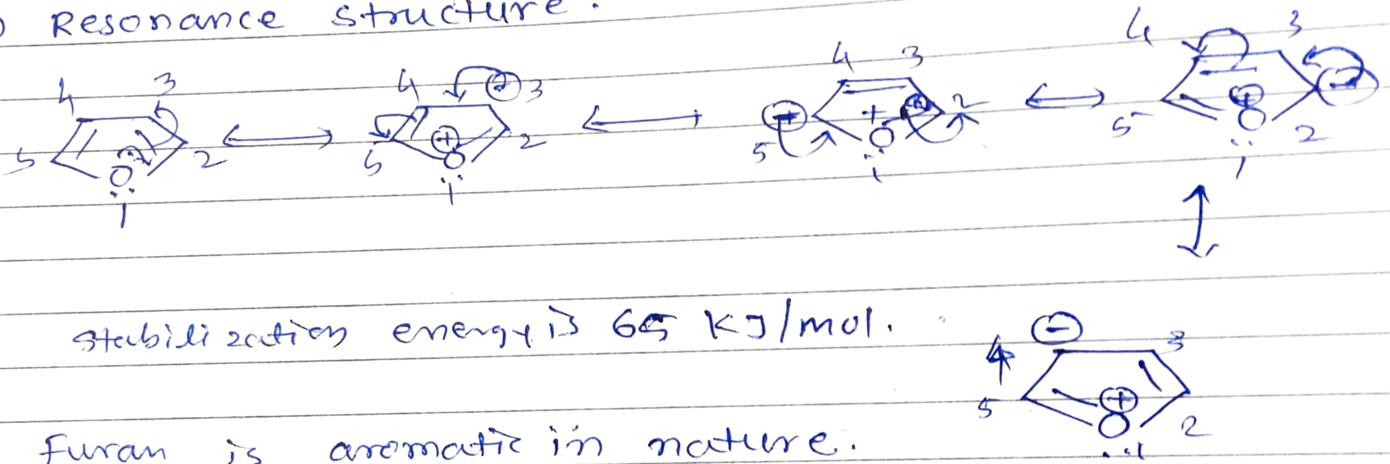
in excited states.



sp²-hybridization of O atom

in furan

2) Resonance structure.



Stabilization energy is 65 KJ/mol.

Furan is aromatic in nature.

It show the Huckel Rule $(4n+2)\pi$. & plannar.

$n = 1$

$4 \times 1 + 2 = 6 \pi e^-$

Furan contain $4 \pi e^-$ & 2 nonbonding electron.

total is $6 e^-$.

2). Thiophene :- (C_4H_4S)

1) Molecular formula is C_4H_4S.

2) Structure is

Atomic No. of S is 16.

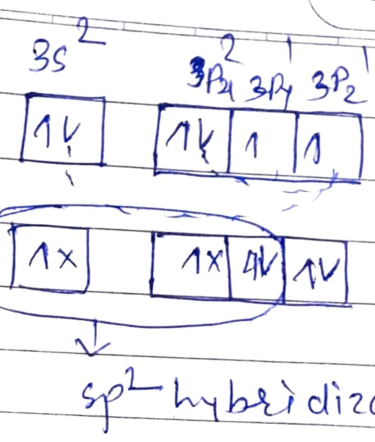
S_{16} - $1s^2, 2s^2, 2p^6, 3s^2, 3p^4$

S-

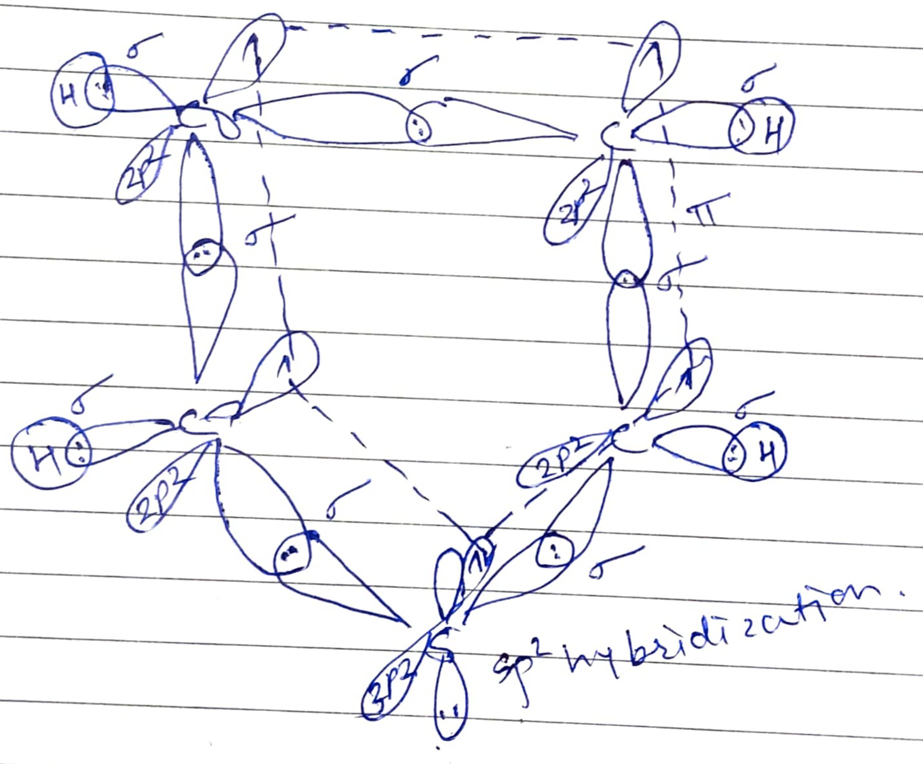
outer electronic configuration ~~transition~~ in $3s^2$ $3P_x^2$ $3P_y^1$ $3P_z^1$

Ground state —

Electr configurn in excited



In thiophene ~~in~~ S-atom show the sp^2 hybridization. & all carbon shows sp^2-hybridization.



Molecular ~~Mo~~ orbital picture Diagram of thiophene.

Thiophene is more aromatic character than furan.

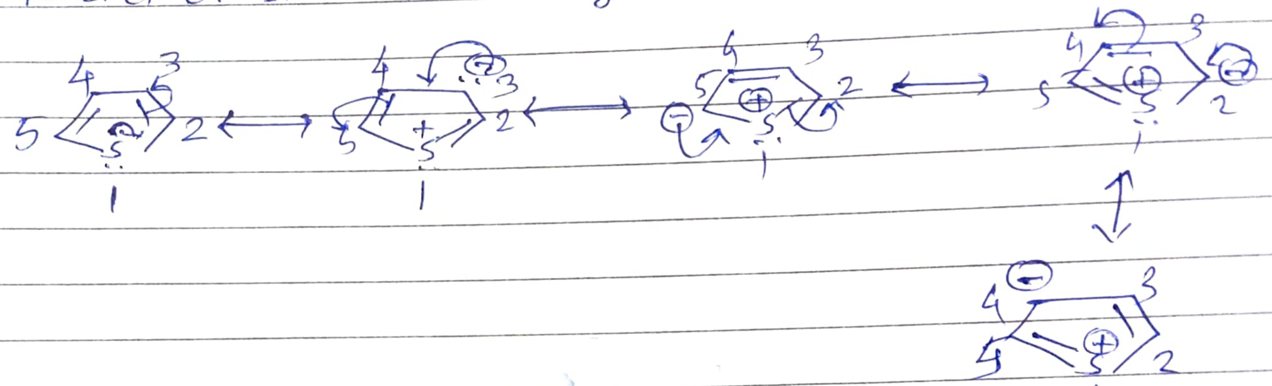
$$(4n+2)\pi$$

$n=1$ $(4\times1+2)\ \pi e$

$$\underline{\underline{6\pi e^-}}$$

Resonance structure

In the light of 125 KJ mol^{-1} as stabilisation energy, thiophene was considered as resonance hybrid of the following resonating structures.



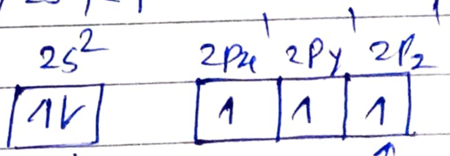
It is confirmed from measurement of bond lengths and dipole moments.

3) Pyrrole

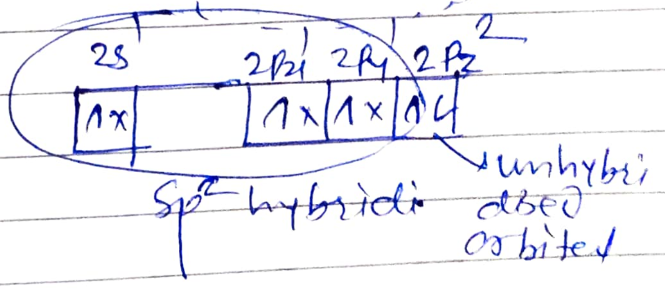
1) M.f. C_4H_5N. & structure is

N_7 electronic configuration
4 N — $1s^2, 2s^2, 2p^3$.

outer electronic configuration in ground state -



outer electronic configur. In excited state



3-acet

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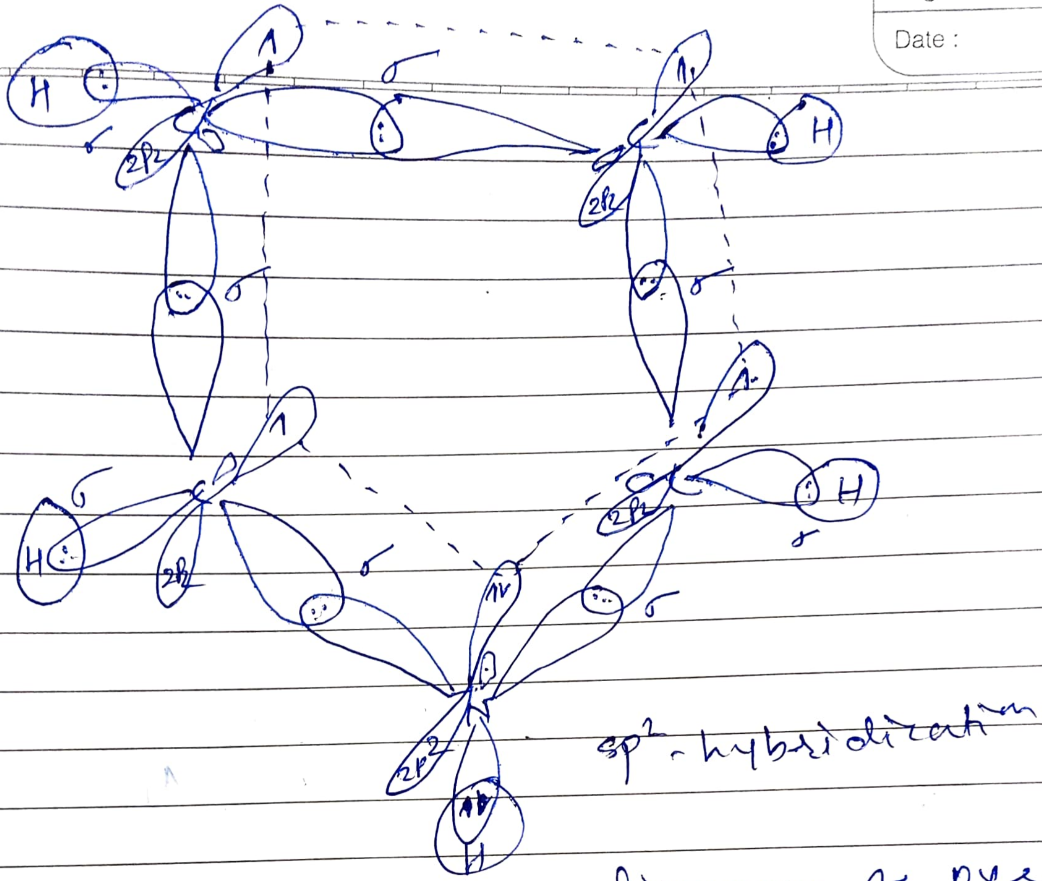
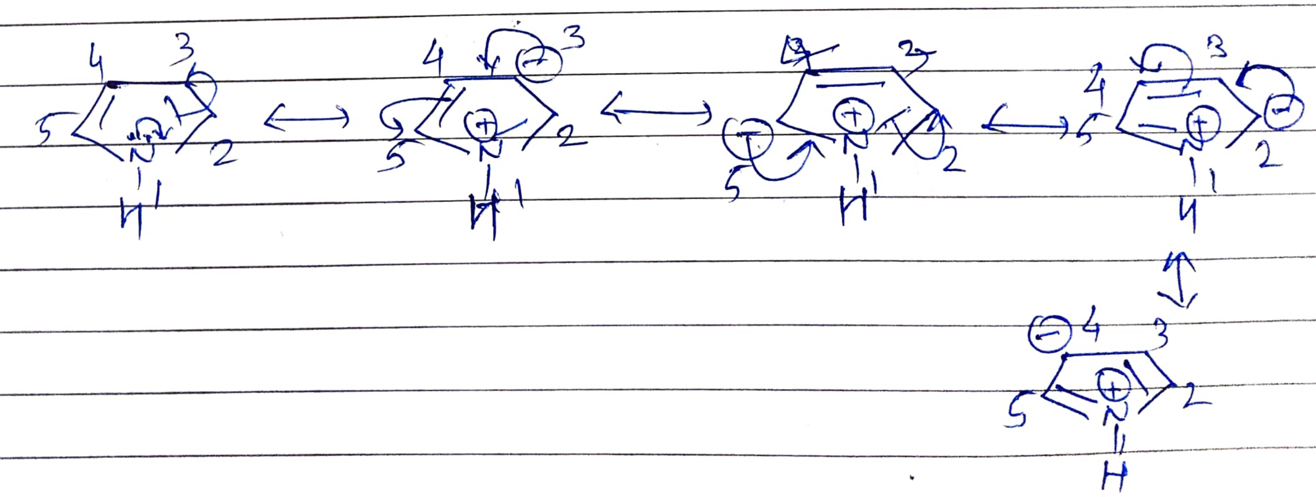


orbital picture diagram of pyrrole.

Resonance structure of Pyrrole.

:.

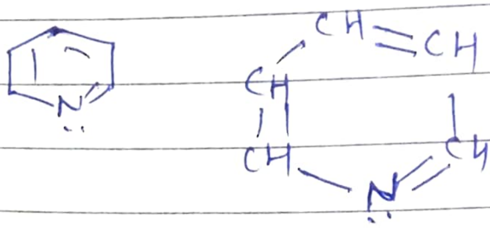
Heat of combustion studies revel that it is resonance stabilized to the extent of 100 KJ/mol



Pyridine

M.f. C_5H_5N.

Structure !.



①. Electronic configuration

N- in pyridine — $1s^2, 2s^2, 2p^3$

outer electronic configuration in G.S. — $2s^2$ $\boxed{\uparrow\downarrow}$ $2p_x^1\ 2p_y^1\ 2p_z^1$ $\boxed{\uparrow}\boxed{\uparrow}\boxed{\uparrow}$

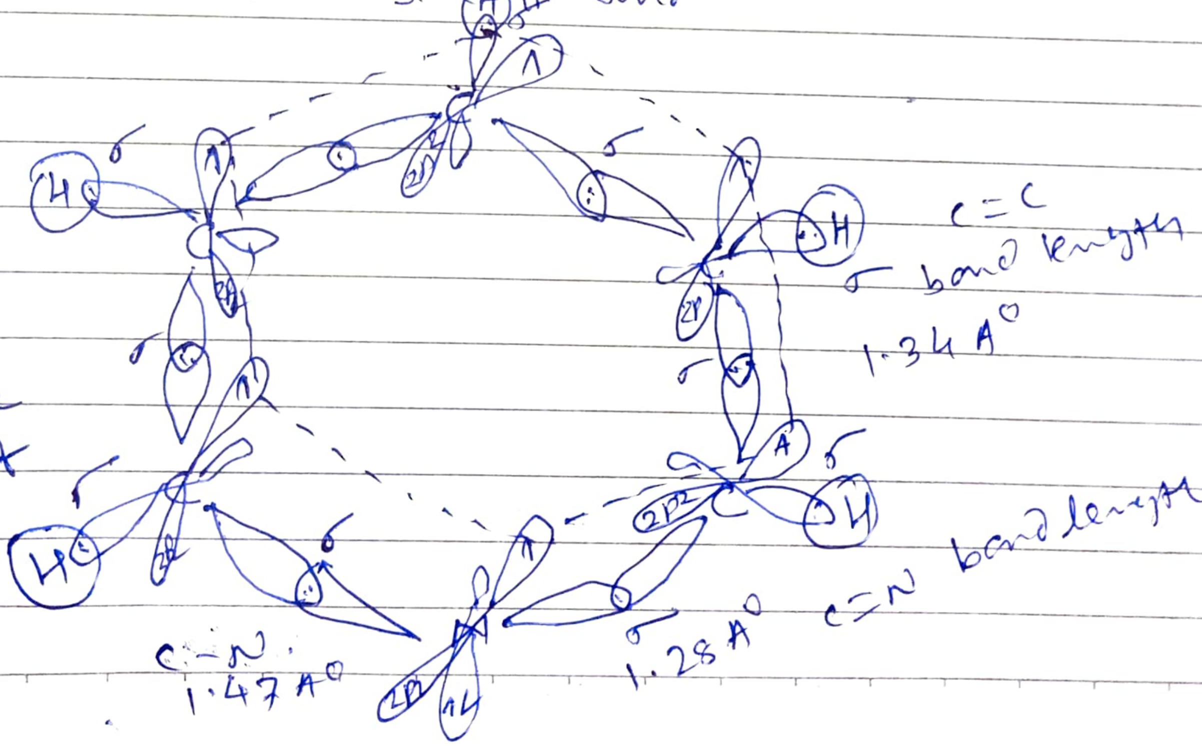
In excited state $\boxed{\uparrow\times}$ $\boxed{\uparrow\times}\boxed{\uparrow\vee}\boxed{\uparrow\cdot}$

L.P. → unhybridised orbital.

sp2 hybridization.

In pyridine $2p^z$ orbital is unhybridised due to it shows the π- band.

molecular orbital picture diagram of pyridine.



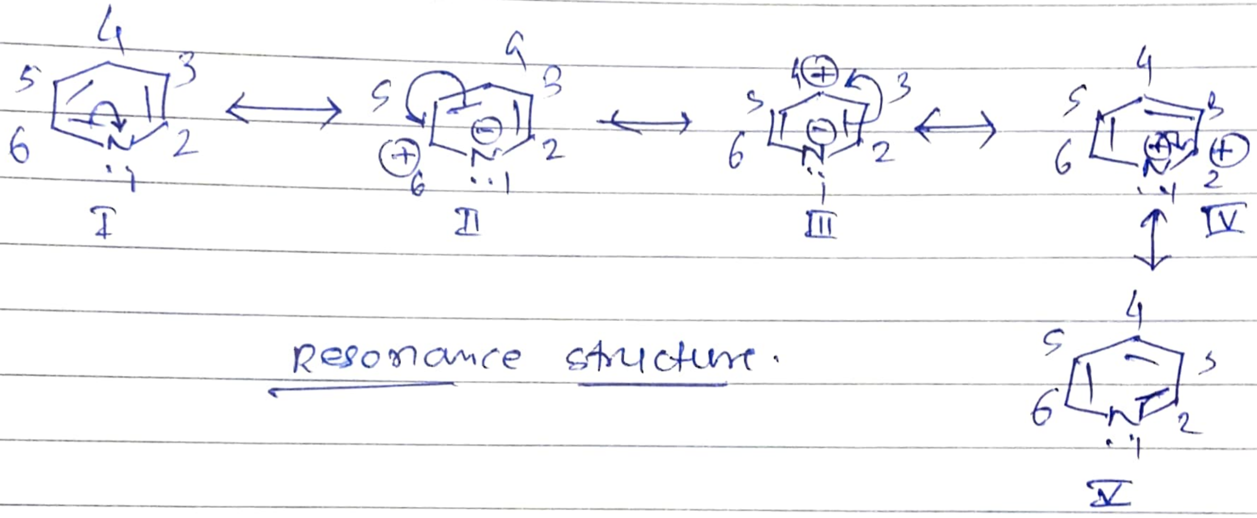
C=C σ band length 1.34 A°

C=N band length 1.28 A°

C–N. 1.47 A°

Resonance structure of pyridine.

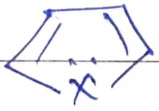
1) Its resonance energy is $96\ kJ\ mol^{-1}$.



Resonance structure.

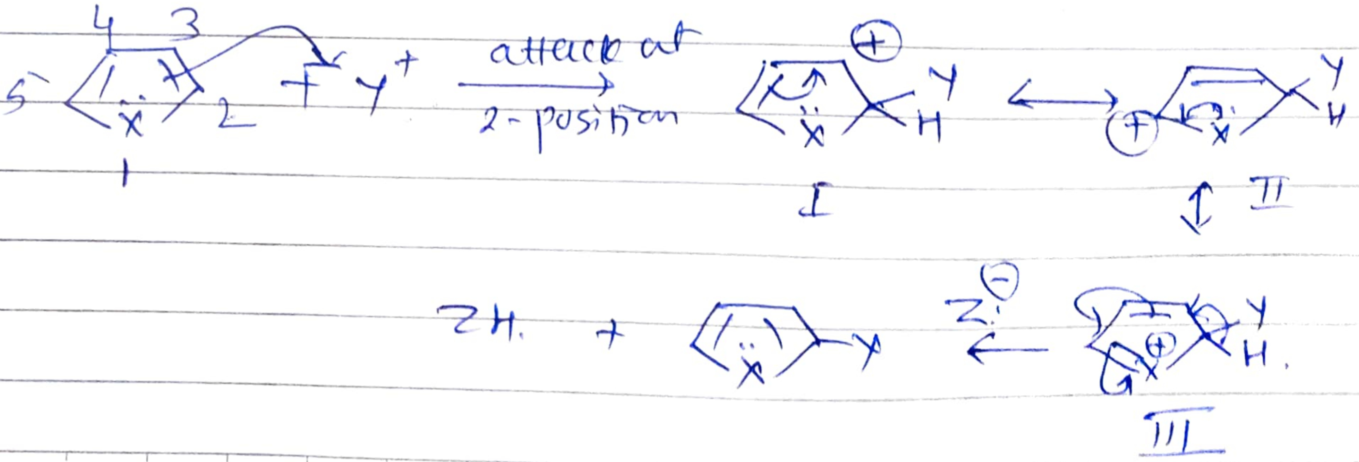
Reaction of Furan, pyrrole & Thiophene.

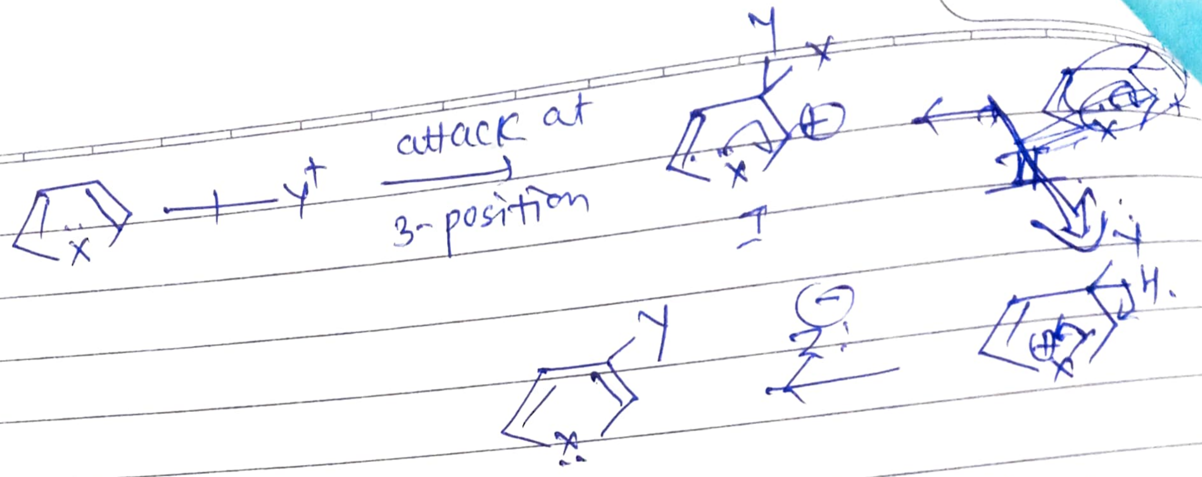
The mechanism of electrophilic substitution in furan, thiophene and pyrrole which occurs preferentially at α-position. ~~or~~ (2 or 5 position)



X = O, S or NH

$Y:Z \longrightarrow Y^{+} + Z^{\ominus}:$



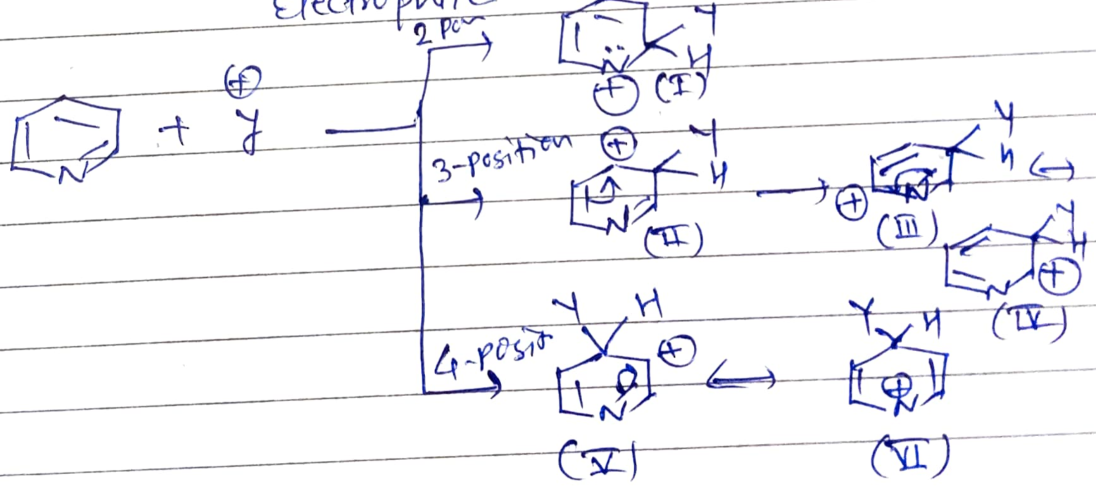


Electrophile attack at 2- position it gives. Three resonating structure & at 3- position Two resonating structure. Hence ~~subs~~ electeeophilic substitution at 2- position.

Pyridine

$Y:2 \longrightarrow Y^{\oplus} + :Z^{\ominus}$

Electrophile



Structure I & VI are highly unstable due to the +ve charge on Nitrogen atom i.e. Electrophilic substitution reaction at 3-position or 5- position.

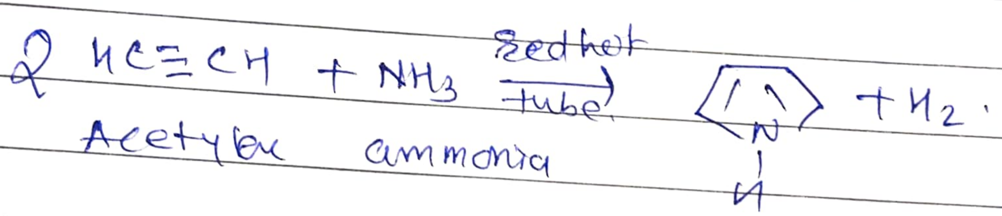
Nucleophilic substitution reaction at 2,4&6 position

(B) Pyrrole : (Azole) (C_4H_5N)

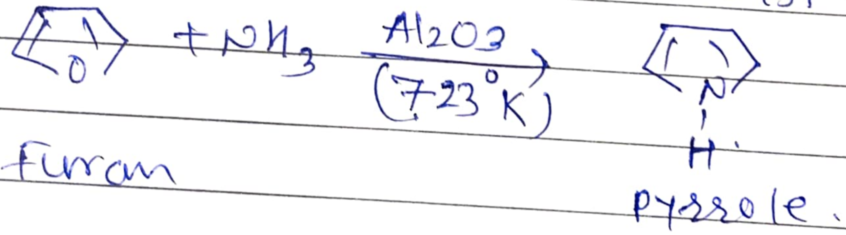
1.2.1 Synthesis From:.

(a) Acetylene :

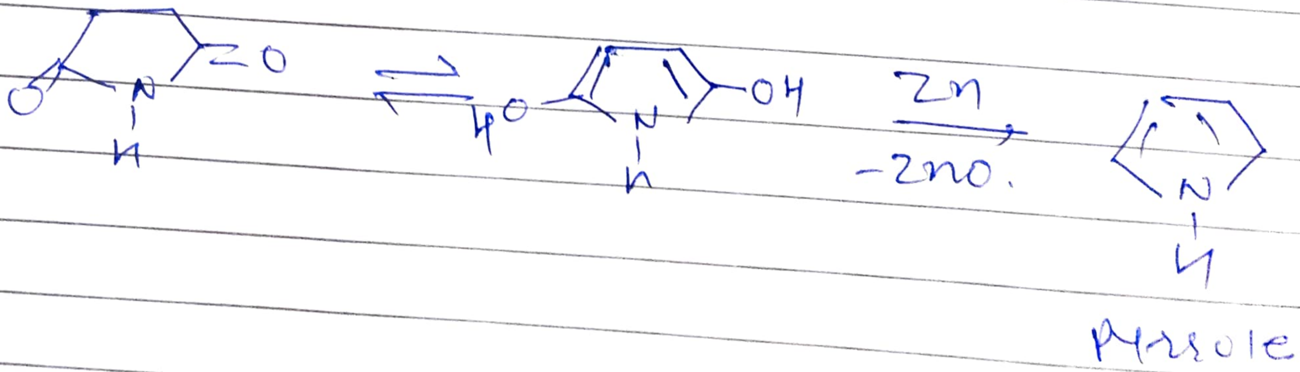
By passing a mixture of acetylene and NH_3 through red hot tube.



(b) Furan:- Pyrrole can be manufactured by passing mixture of furan, ammonia and steam over heated alumina at catalyst.



(c) succinimide:-



1.2.2 physical properties:-

1) The boiling point of pyrrole is 402-404 °K
2) It is soluble in organic solvent & insoluble in water.
3) It is colourless volitile liquid.

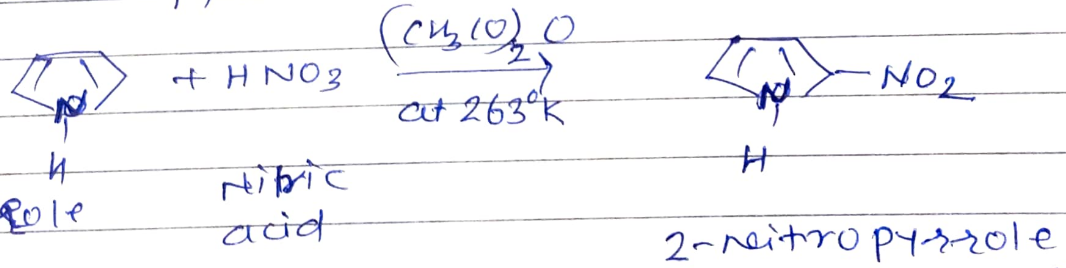
chemical properties:-

1. Electrophilic substitution Reaction:-

1. Electrophilic substitution Reaction:-

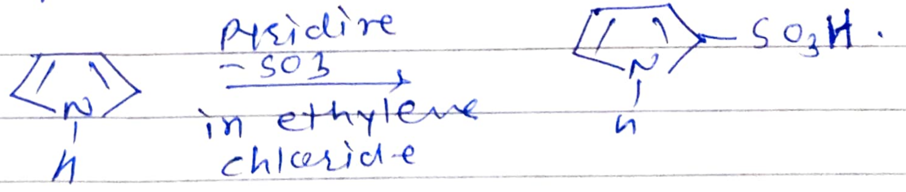
(i) Nitration :⇒

with HNO_3 in acetic anhydride, pyrrole gives 2-nitropyrrole.

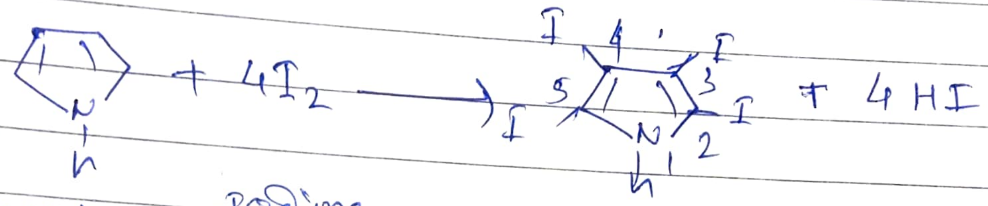


(ii) sulphonation:-

with pyridine - SO_3 mixture in ethylene chloride, pyrrole is sulphonated to give 2-pyrrole sulphonic acid.

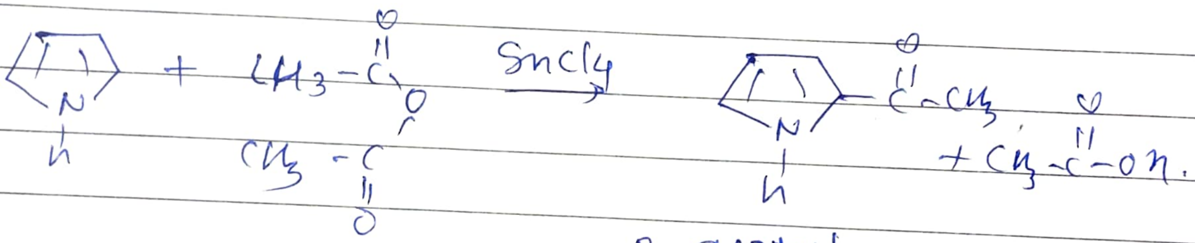


(iii) Halogenation:-



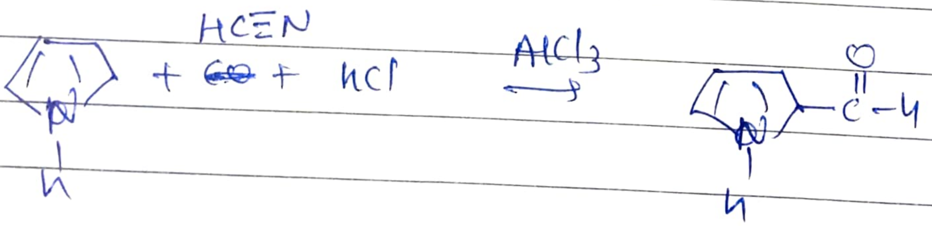
Pyrrole   Iodine   2,3,4,5-Tetra Iodo pyrrole

(iv) Friedel-craft acylation!-



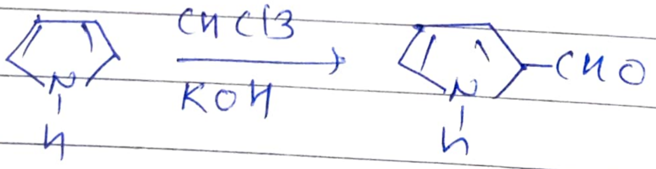
2-acetyl pyrrole

(v) Gattermann reaction.



Pyrrole   pyrrole-2-aldehyde

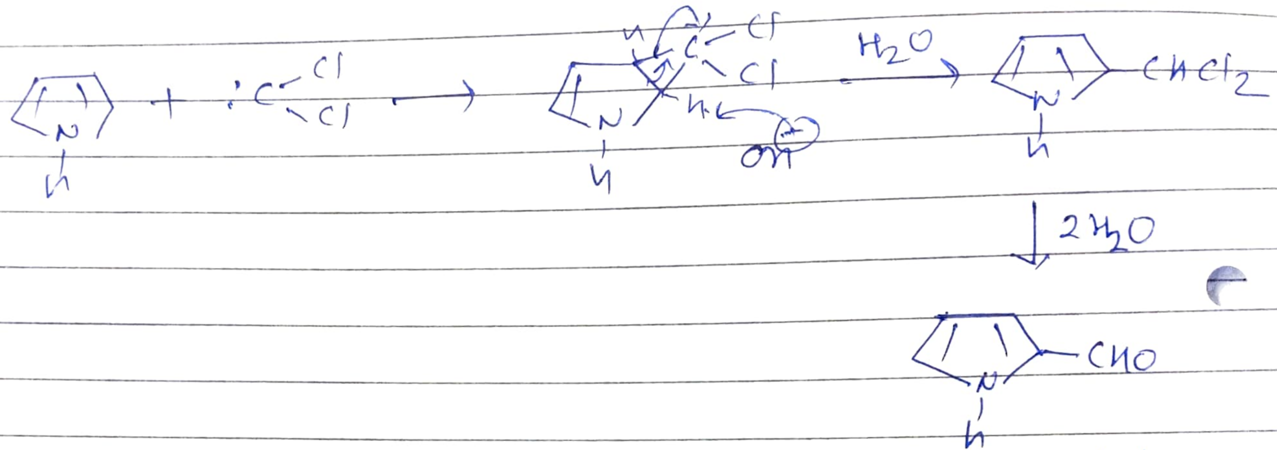
(vi) Reimer-Tiemann reaction!-



pyrrole-2-aldehyde.

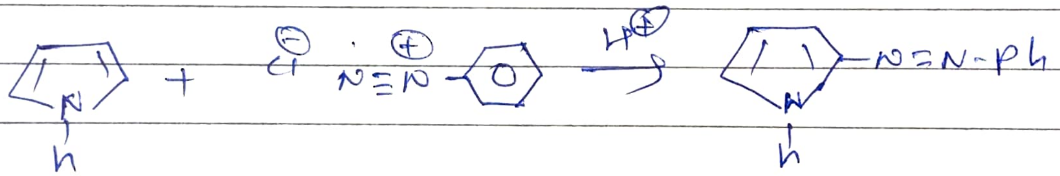
Mechanism :-

$CHCl_3 + KOH \rightarrow :CCl_2 + KCl + H_2O.$



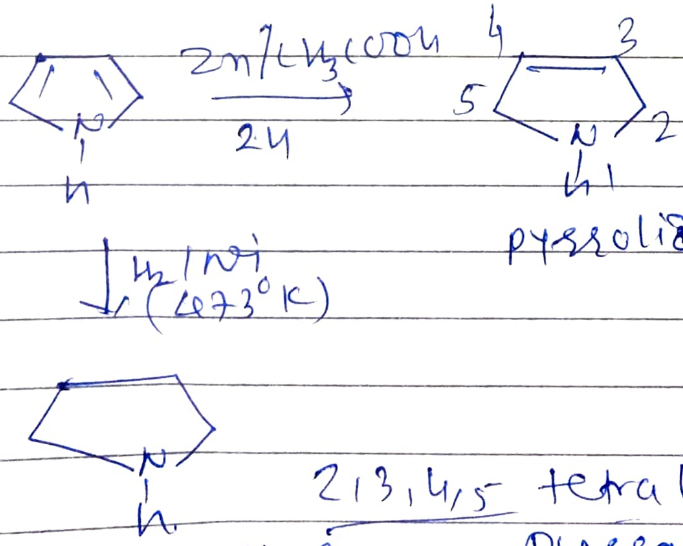
pyrrole-2-aldehyde.

(vii) coupling reaction :-



2- phenyldiazo - pyrrole

Reduction:



2,5 dihydro pyrrole

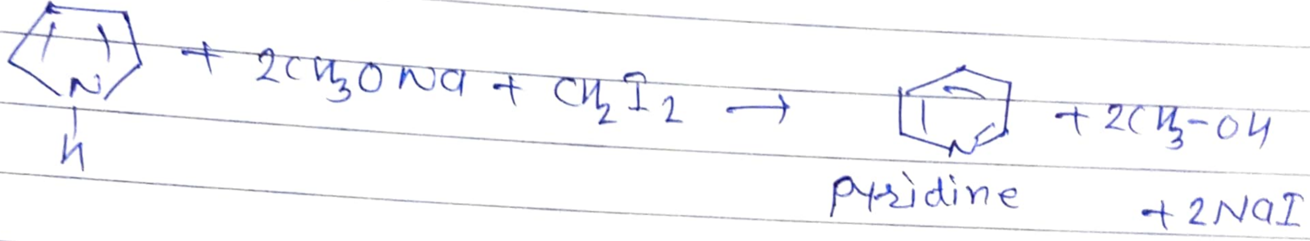
pyrrolidine

2,3,4,5 tetrahydro pyrrole

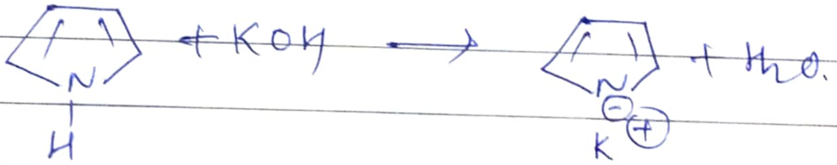
pyrrolidine.

(1,2 diazines)

Ring expansion reaction:-



Acid character:-

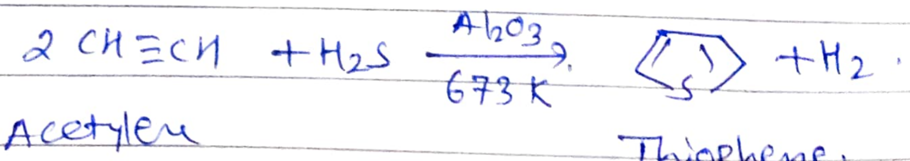


(3) Thiophene:- (C_4H_4S)
(Thiole)

1.3.1 Synthesis from.

(a) Acetylene

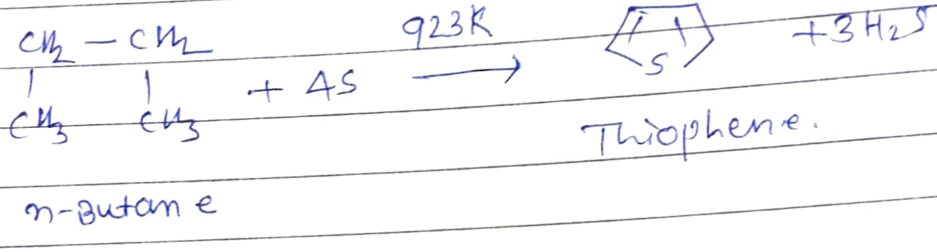
Thiophene is manufactured by passing a mixt. of acetylene and hydrogen sulphide through a tube containing Al_2O_3 at 673 K



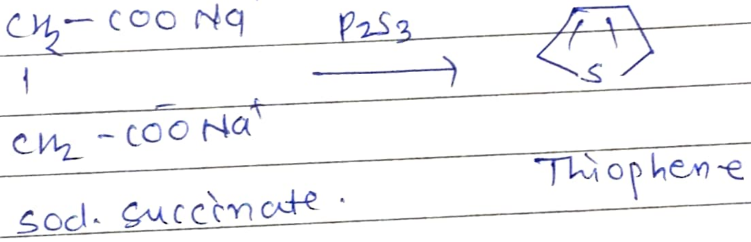
Date :

(b) n-Butane :-

on heating n-butane with sulphur at 923 K thiophene is formed.



(c) Sodium. succinate :-



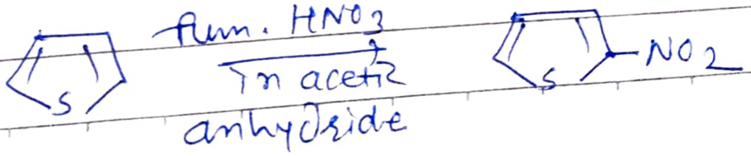
physical properties :-

1) Thiophene is a colourless liquid boiling at 375 °K
2. It smell like benzene.
3. It is soluble in alcohol & ether but insoluble in water.

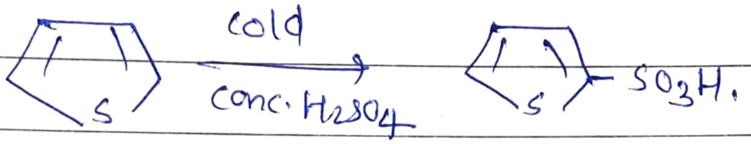
chemical properties

1) Electrophilic Substitution Reaction :-

a) Nitration :- Thiophene when nitrated with fuming HNO_3 in acetic anhydride gives 2-nitro thiophene.



(ii) Sulphonation:-

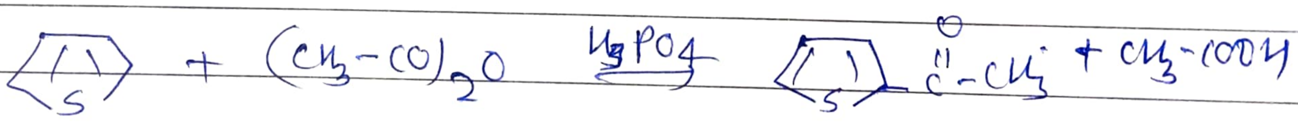


2-Thiophene Sulphonic acid.

(iii) Halogenation.

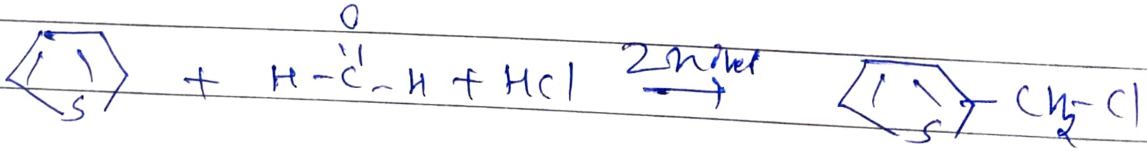
2,5-dibromo thiophene.

(iv) fridel craft acylation:-



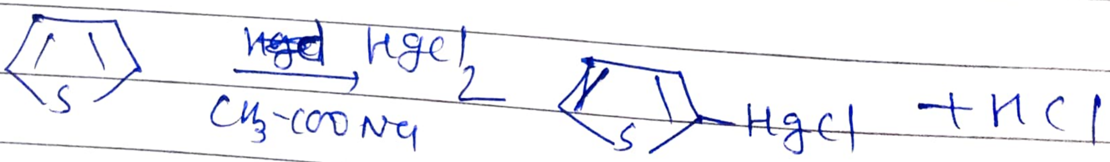
~~methyl~~ 2-acetyl Thiophene

(v) chloro methylation:-



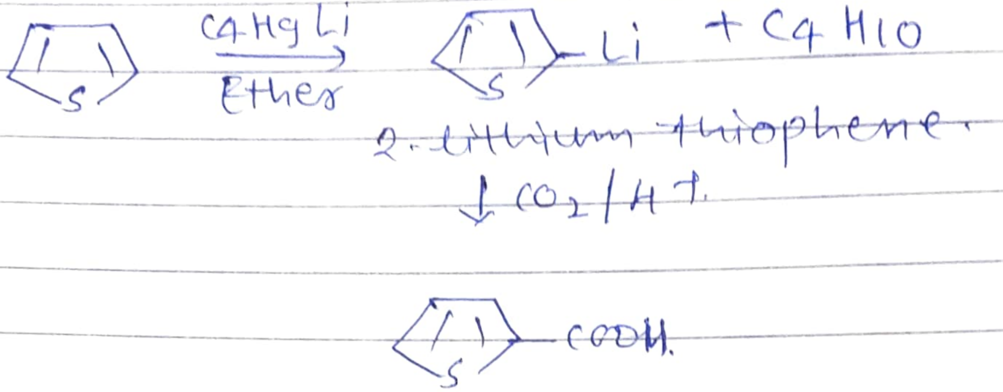
2-chloromethyl thiophene

(vi) mercuration:-

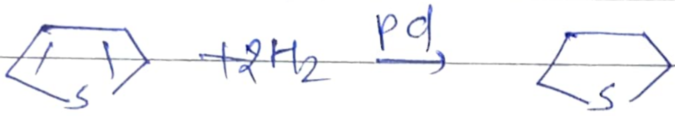


Reaction

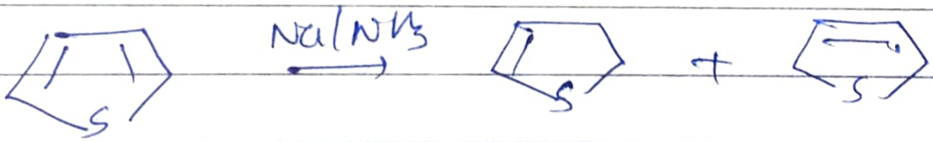
vii) n-Butyl lithium:-



Reduction:-

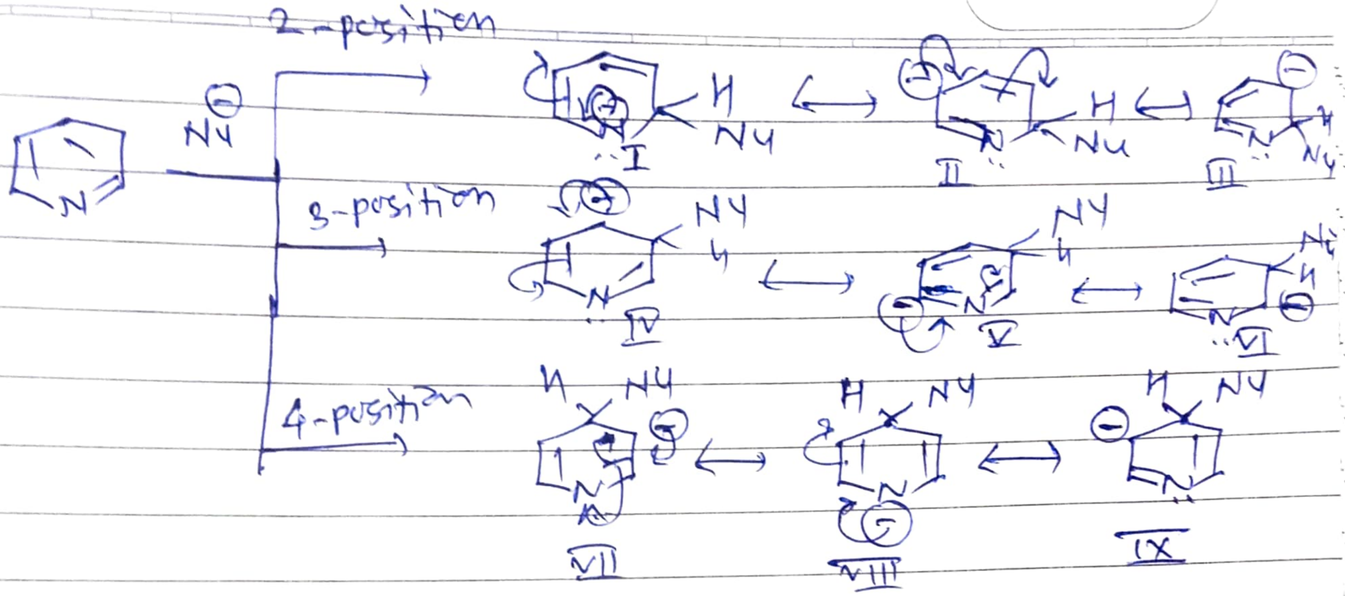


Tetrahydrothiophene



2,3 Dihydro thiophene

2,5-dihydro thiophene.



structure I & VIII are more stable than other. i.e. Nucleophilic substitution reaction at 2, 4 or 6 position only than 3^{rd} position.

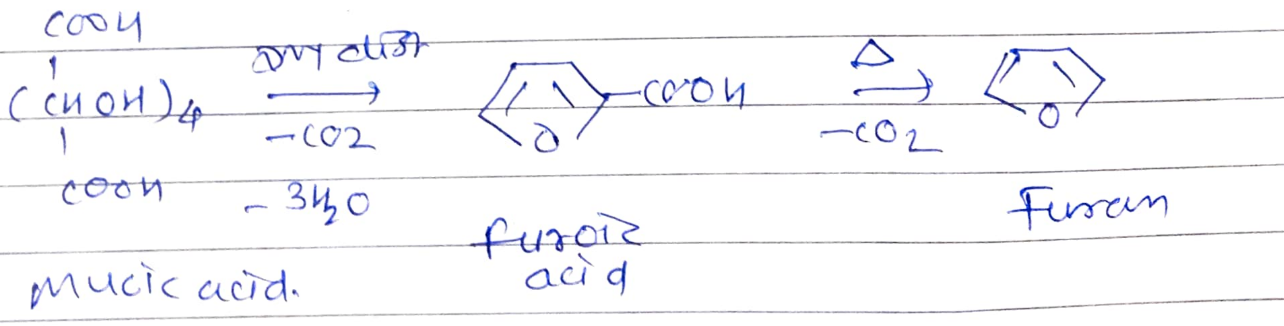
(A) Five-membered heterocycles.

(1) Furan (oxole) (C_4H_4O)

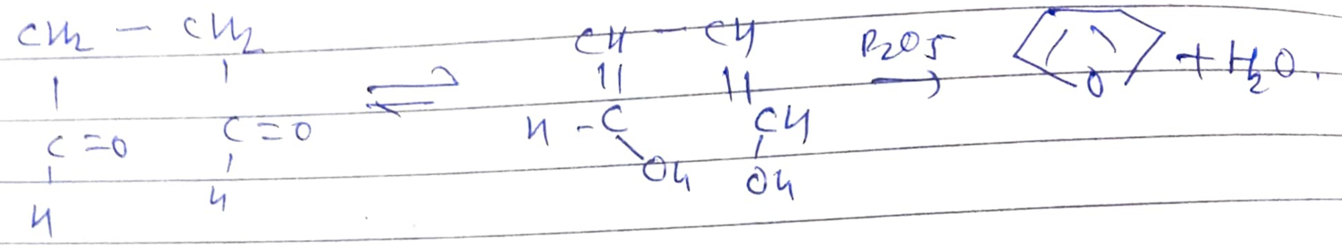
1.1.1 Synthesis from :

(a) mucic acid. :

Dry distillation of mucic acid gives furan



(b) from succinaldehyde:-

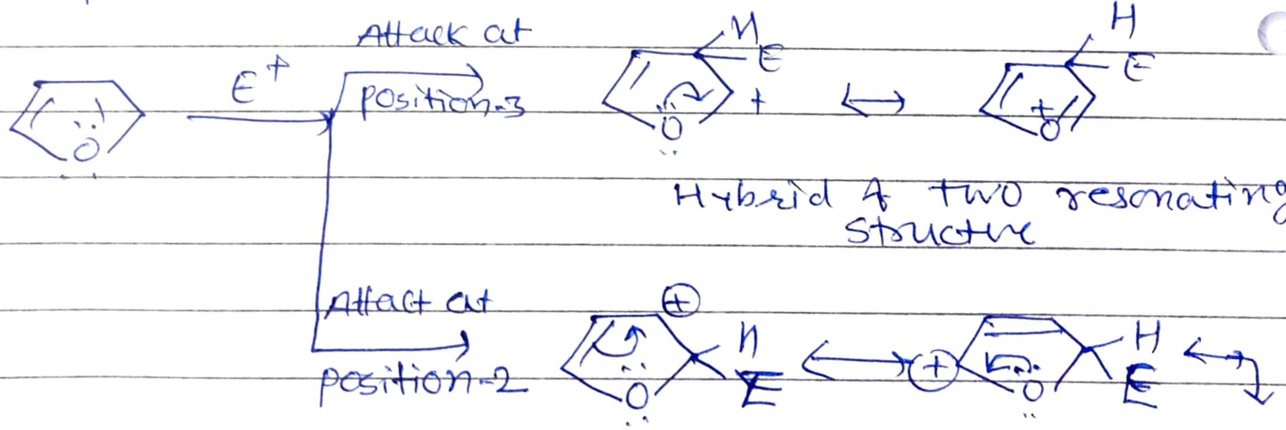


Succinaldehyde is react with P_2O_5 to give furan.

physical properties:-

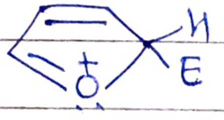
1. It is a coloured liquid boiling at 305 K.
2. It is smell like chloroform.
3. It is soluble in alcohol & ether but insoluble in water.

chemical properties:-
Electrophilic substitution reactions:



Hybrid of two resonating structure

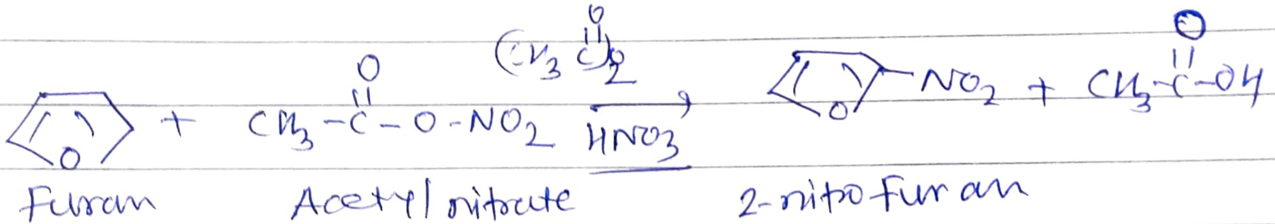
Hybrid of three resonating structures.



Electrophilic substitutions of furan occurs preferentially at the -2 or -5 position. The intermediate carbonium ion in the case of -2 or -5 substitution is resonance stabilised to a greater extent than in the case of 3 or 4 substitution.

Nitration :-

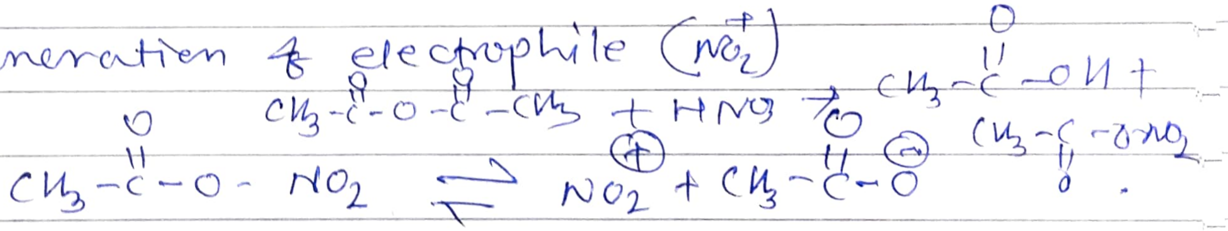
when furan is treated with acetyl nitrate 2- nitrofuran is obtained



Mechanism

Step-I

(i) Generation of electrophile ($\overset{+}{NO_2}$)

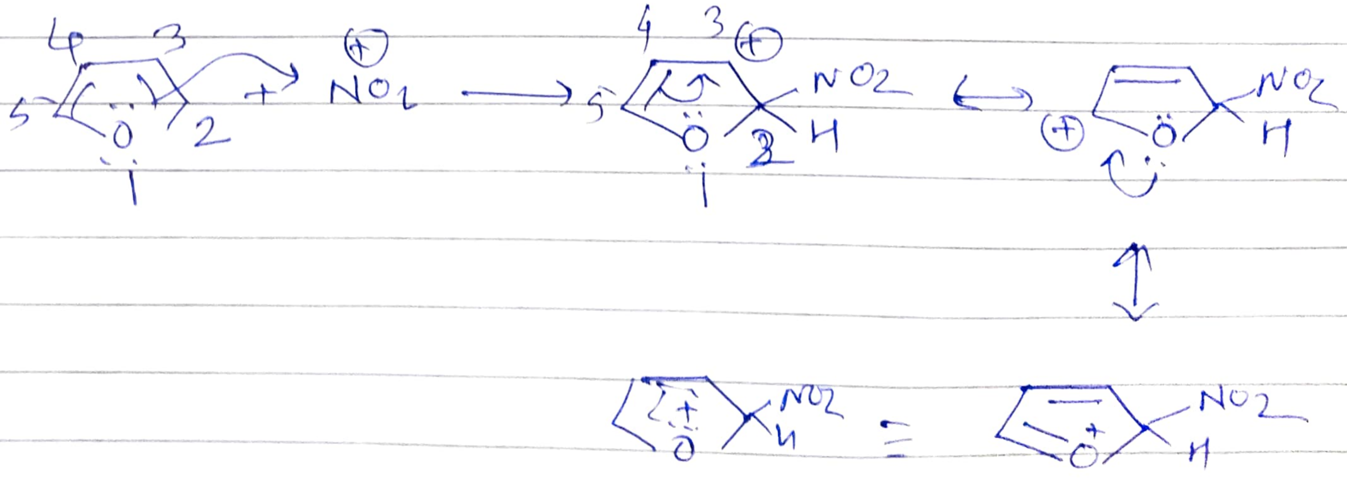


$$CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 + HNO_3 \rightarrow CH_3-\overset{O}{\overset{\|}{C}}-OH + CH_3-\underset{O}{\underset{\|}{C}}-O-NO_2$$

$$CH_3-\overset{O}{\overset{\|}{C}}-O-NO_2 \rightleftharpoons \overset{\oplus}{NO_2} + CH_3-\overset{O}{\overset{\|}{C}}-\overset{\ominus}{O}$$

Step-II

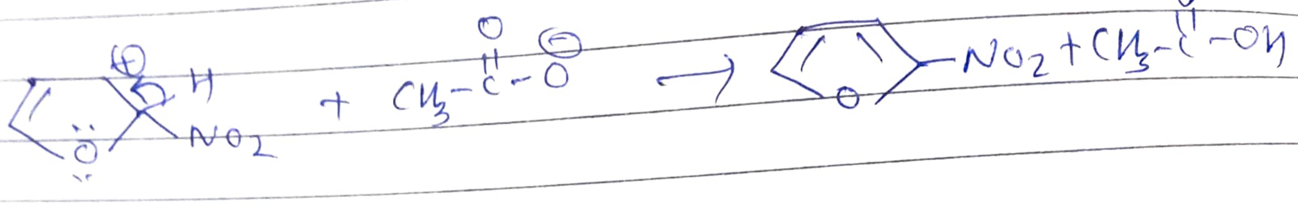
(ii) electrophile is attact on 2 or 5 position of furan.



σ-complex.

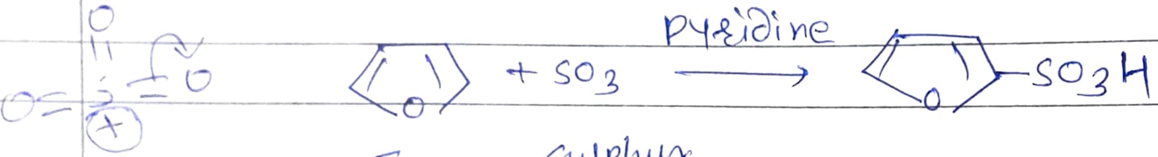
Step III

Deprotonation or removal of proton from σ-complex.



2) sulphonation :-

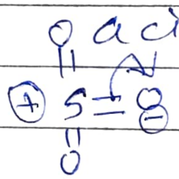
Furan reacts with sulphurtrioxe in presence of pyridine to give furan 2-sulphonic acid.

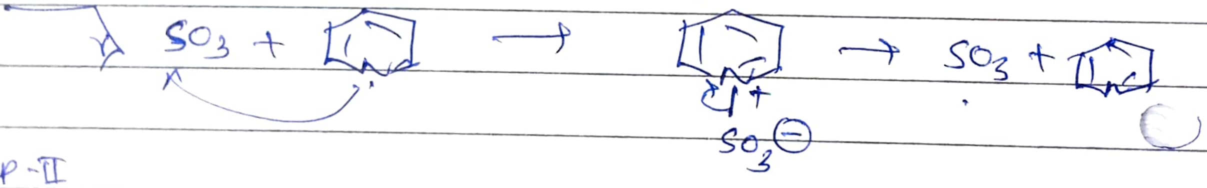


Furan Sulphur trioxide furan 2-Sulphonic acid

Mechanism :-

1) Generation of electrophile





Step-II

2) SO₃ electrophile is attack on furan 2-position