Heterocyclic Chemistry

* Carbocyclic system that has an hetero atom in the ring system.

Nomenclature:

A. Hantszch and O. Widman 1886.

Prefixes for heteroatoms

O –	Oxa	I –	ioda
S –	Thia	Se –	Selena
N –	Aza	Te –	Tellura
F –	Flaura	P –	Phospha
Cl –	chlora	As –	Arsa
Br –	Broma		

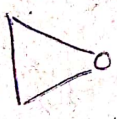
Ring size	Unsaturated	Saturated
3A	~~-iridine~~	- iridine
	- irine	
	- irene	- irane
3B	- ete	- etidine
4A	- ete	- itane
4B	- ole	- olidine
5A	- ole	- olane
5B	- ine	- ane
6A	- ine	- inane
6B	- inine	inane
6C	- epine	
7		

Ring Size	Saturated	Unsaturated	Saturated with N
3	irane	irine	iridine
4	etane	ete	etidine
5	olane	ole	olidine
6	inane	ine	
7	epane	epine	
8	ocane	ocine	
9	onane	onine	
10	ecane	ecine	

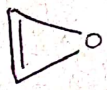
Combination & prefix

Eg:-

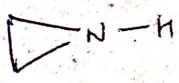
3 ⇒



oxiorane



oxiorine

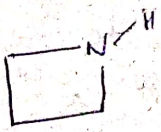


Aziridine

4 ⇒

oxitane

oxete



Azetidine

5 ⇒

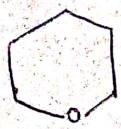
Oxolane

Oxole (Furan)

Azolidine

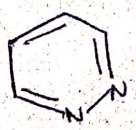
Azole

6 ⇒

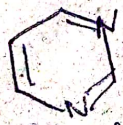


oxinane

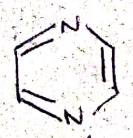
Oxine



1,2-diazine (Pyrazine)

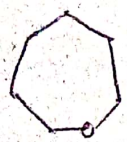


1,3-diazine (Pyrimidine)



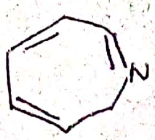
Pyridazine

7 =>



oxipane

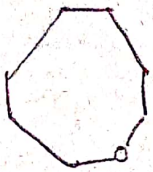
oxipine



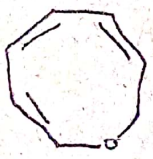
Azepine

Azepane

8 =>

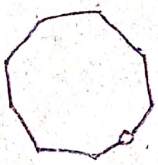


Oxocane

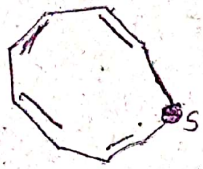


Oxocine

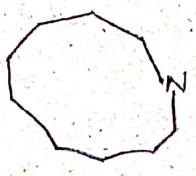
9 =>



Oxonane



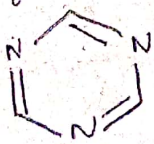
Thiazine



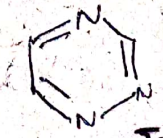
Azonane

* When two or more heteroatom of the same type are present, then the prefixes di, tri, tri. etc are used and placed before prefix used for the heteroatom. Numbering is starts from heteroatom and have lower number for other hetero atom

1, 3, -Dioxalone



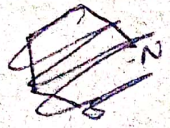
1, 3, 5- ~~Tria~~ Triazine

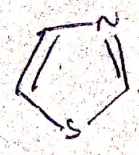


1, 2, 4, Triazine

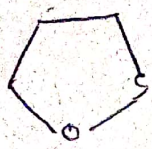
* When two or more different heteroatoms are present in the same ring the prefixes of heteroatoms are combined in the order of preference.

Oxa - Thia - Aza

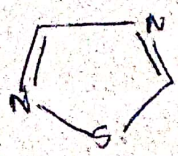




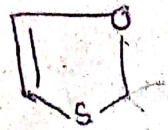
1, 3 - Thiazole



1, 2 - oxathiolane



1, 2, 4 - Thiadiazole



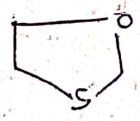

1, 3 - oxathiole

At the 2 position, there was one hydrogen present when there was two double bonds. Now, it is saturated at 2- position, i.e., one more hydrogen is added. So, one hydrogen should be represented while naming. So the name of the above compound is,

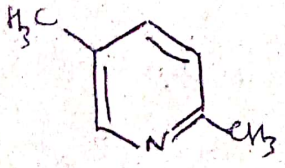
2 [H] - 1, 3- oxathiole

Such naming should be written when the molecule is partially saturated.

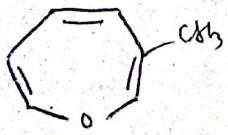
i.e. the naming if above compound is saturated completely is,



1, 3 -oxathiolane



2, 5 - Dimethylpyridine



3-methyloxepine

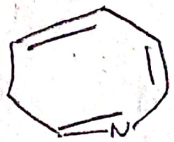
~~when heterocy~~

Presence of Saturated atom:

When heterocyclic ring with maximum number of non-cumulative double bonds contains a saturated atom, its position is given in the lowest possible locant and is numerically indicated by an italic capital H before the name of the heteroaplic ring system.

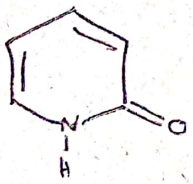
2H- pyrrole

2H-1,3-Thiazine

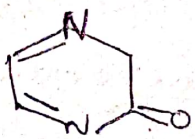


3H-Azepine

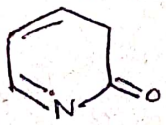
* However, the heterocyclic system in which a carbon atom of the ring is involved in the carbonyl group, the indicated hydrogen is normally cited as an italic capital H in parenthesis after the locant of the additional structural features



Pyridin-2(1H)-one
1H-Pyridin-2-one



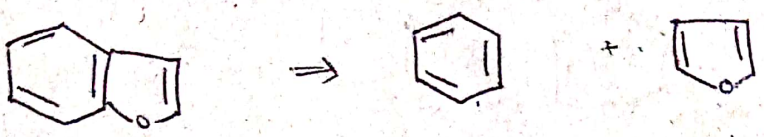
Pyrazin-2(3H)-one



Pyridin-2(3H)-one

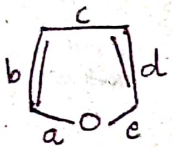
Saturation of the nitrogen in the ring also should be considered:

Naming of Fused Heterocycles



minor ring Major ring (Base component)

* Aways, the heterocyclic compound taken as major ring.
* Minor ring is written as prefix like substituents (chloro, bromo etc---)
* The sites of heterocyclic compound named as

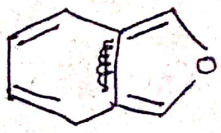


The site of fusion should get minimum denomination

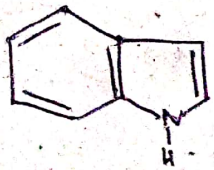
* The site of fusion is written in between the names of prefix & name of heterocycle in squar bracket
* So, name of above compound is

Benzo [b] furan (Common name : Benzofuran)

Eg :

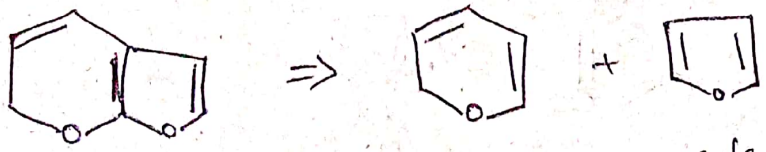


Benzo [c] furan
[Isobenzofuran]



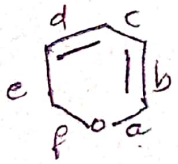
1H-Benzo [b] azole [1H-Benzo [b] pyrole]
[Indole]

Two fused heterocycles

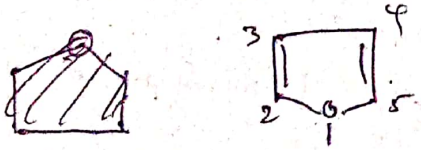


2H- oxine [Pyran] + oxole

* When two heterocycles of same heteso atom is fused, then the ring size is considered for naming.
* The heterocycle with ~~more numbers~~ higher ring size is taken as major ring.. other ~~el~~ hetero atom is taken as substituent an written in prefix.
* Fusion sites [a, b, c, d etc..] are named for major ring



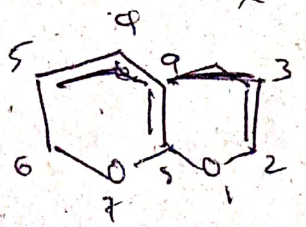
* Minor ring is numbered in numericals



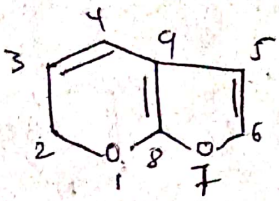
* the carbon atom 2 & 3 of Furan is bonding to b site of pyran
* So the name is

Furo [2,3-b] pyran or Furano [2,3-b] Pyran

* The numbering in fused ring ~~is~~ ~~two~~ can be of two ways



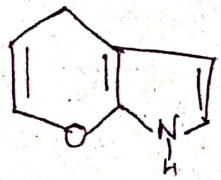
or

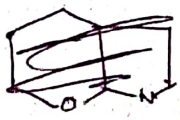


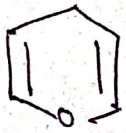
Here, the saturated carbon should be at lower numbered position. So, name becomes

2H - Furo [2,3-b] Pyran.

The quaternary carbon ~~sto~~ [i.e., carbon at fusion point] should be numbered at the end.







Pyran

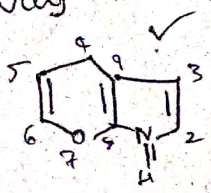
Pyrrole

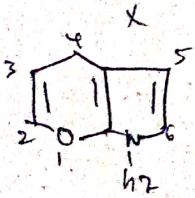
In the fused heterocycles, in which both heterocycles have different heteroatom, then the heterocycle having nitrogen as heteroatom is taken as major ring irrespective of ring size.

So, the name of the above compound is

Pyrano [2,3-b] pyrrole

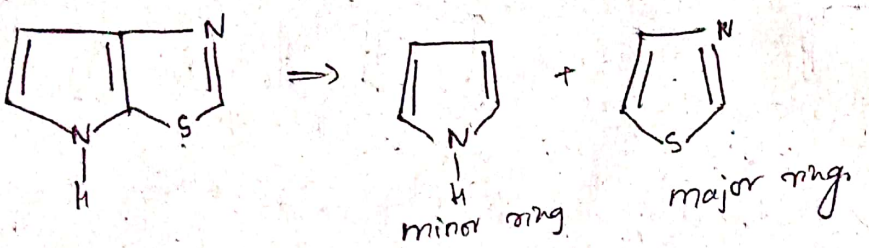
Here, nitrogen & 4th carbon of pyran also saturated. So numbering is should be such a way that, both get minimum number





⇒ Name is

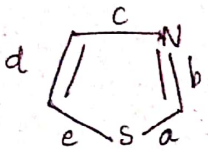
1H, 4H - Pyrano [2,3-b] Pyrrole

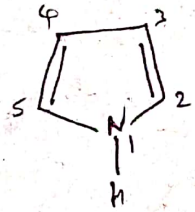


minor ring major ring

The heterocycle having variety of heteroatom is taken as major ring in the above cases.

Here Thiazole is taken as major ring and pyrrole is taken as minor ring.

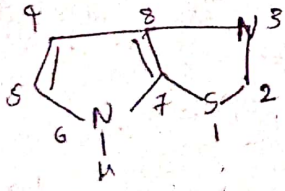




a, b, c ... is in the order of numbering way.

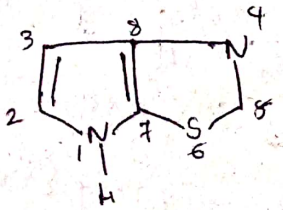
Pyrrolo[2,3-~~d~~]1,3thiazole

X



✓

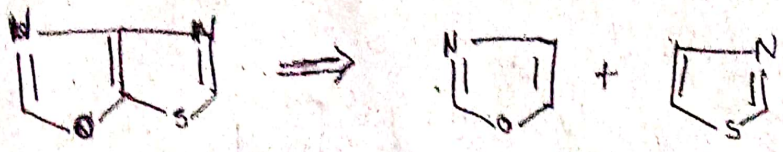
or



Numbering should be in such a way that the saturated ~~hydrogen~~ nitrogen get minimum number

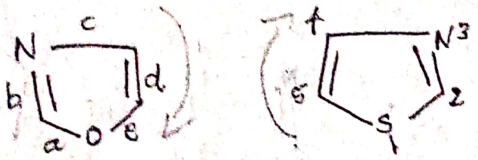
So, it is 1H- Pyrrolo[2,3-d]1,3thiazole

Eg:-

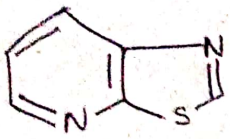


1,3-oxazole 1,3-thiazole

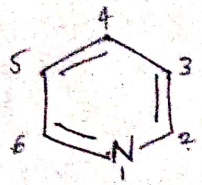
While ~~con~~ considering such rings, the Oxa> Thia> aza order is maintained. So 1,3-oxazole becomes the major ring and 1,3 thiazole is minor ring.



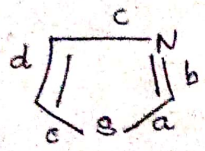
Name: 1,3-Thiazolo [5,4-d]-1,3-oxazole



In a fused ring, having a less numbered ~~of~~ hetero atom but more membered ring and another heterocycle with ~~be~~ more number of heteroatom but less membered ring, then the ring with more number of heteroatom is considered as major ring.



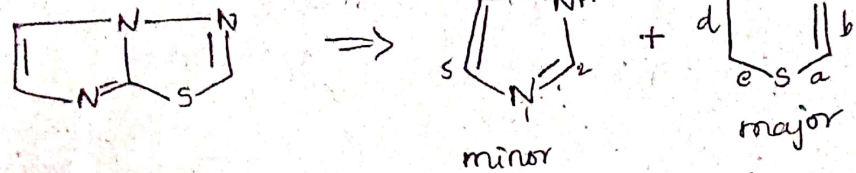
minor
pyridine



1,3-Thiazole
major

So - name is Pyrido [2,3-d] 1,3 -thiazole

Eg:

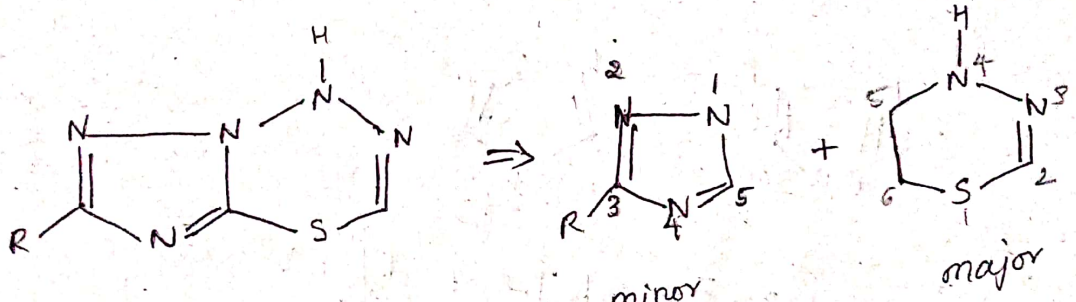


minor

major
(more heteroatom)

Imidazo [2,3-d] 1,3- thiazole

Eg:

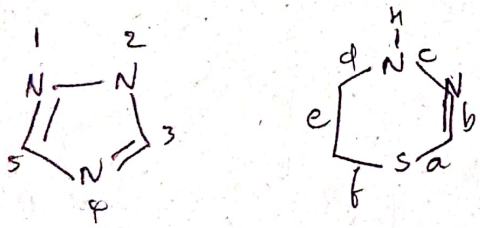


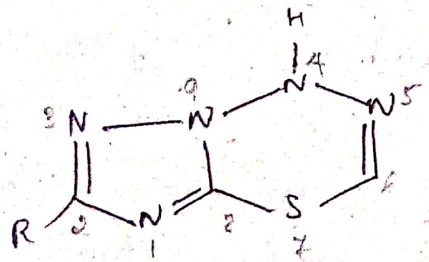
minor

major

1,3,4 -Thiadiazine

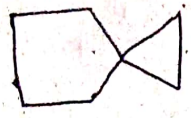
3-substituted -1,2,4 triazole





2 - Substituted - 4H - 1,2,4-triazolo [3,2-e] -1,3,4- Thidia zine

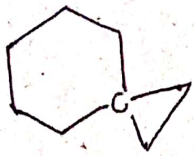
Naming of Spiroheterocycles



Spiroalkane

A spiro compound is the compound in which the quaternary carbon is fused between two rings.

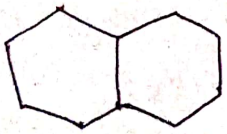
Eg:



Spiro-octane

Octane
(not spiro compound)

This is different from 2 carbon fusion



– 2 carbon bond fusion

– 1 carbon bond – spiro

The connecting atom called spiro atom, most often it is a quaternary carbon.

→ Name starts from a prefix called spiro

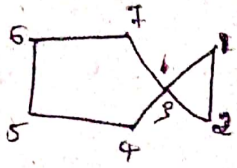
→ Naming is always clockwise

→ The carbon next to spiro atom ~~named as~~ number as 1.

→ Number of carbon or any hetero atom at RHS ring excluding spiro atom is calculated, similarly for ring at LHS

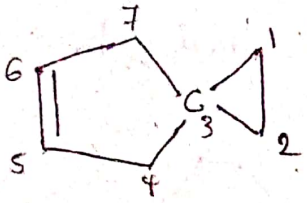
these two are written in square bracket, seperated by a dot

Eg:-



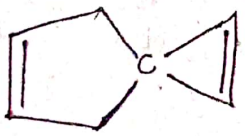
Spiro [2.4] heptane

Eg:-



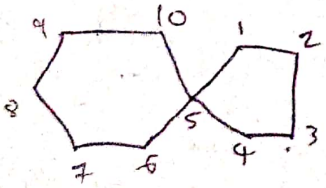
Spiro [2.4] hept-2-ene

Eg:-



Spiro [2:4] hept-1,5-diene

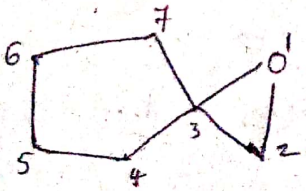
Eg:-



Spiro [4.5] decane

In case of hetero atom,

Eg:



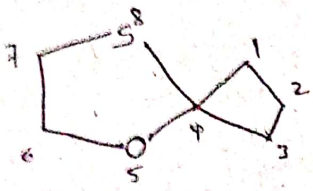
1-Oxa-spiro [2.4] heptane

Eg:-

~~1-oxa-5-aza[2.4]heptane~~

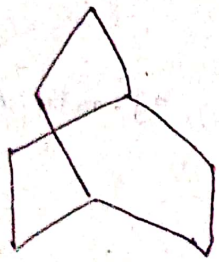
5-aza-1-oxa-spiro[2.4]heptane

Eg:-

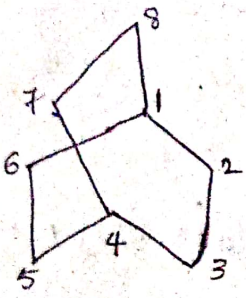


5-oxa-8-thia-spiro[3.4]octane

Bicyclic system



* There will be two quaternary carbon forming bridge
* Numbering starts from one of the quaternary carbon



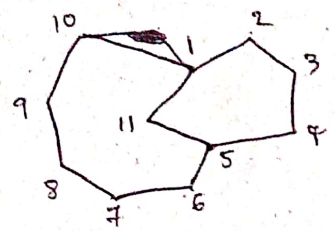
* Numbering is clockwise, bridge is numbered later
* Prefix is bicyclo.

* The C carbon at LHS, RHS & bridge are mentioned seperately

The name of above example is

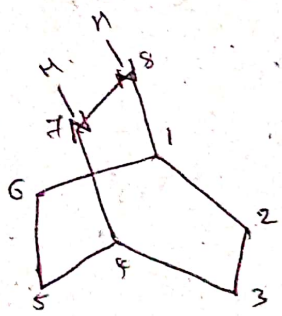
Bicyclo[2.2.2] octane

Eg:-



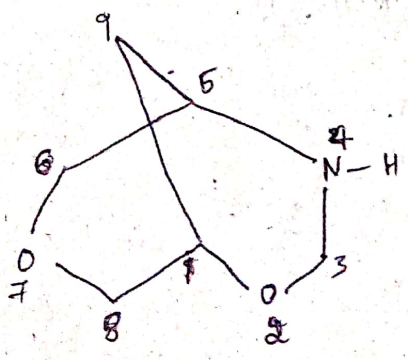
Bicyclo[3.5.1] undecane

Eg:-



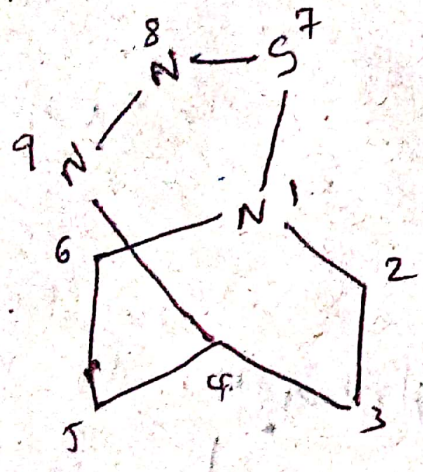
7,8-diaza-Bicyclo[2.2.2]octane

Eg:-



4-Aza-2,7-dioxo-Bicyclo[3.3.1] nonane

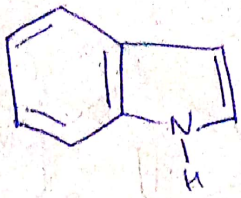
Eg:-



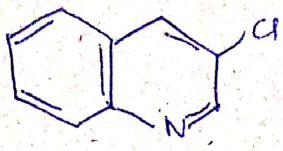
7-Thia-1,8,9-triaza-Bicyclo [2.2.3] nonane

Conversions in heterocyclic Chemistry

Indole to Quinoline

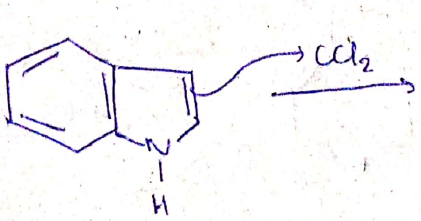


$CHCl_3$ / NaOH

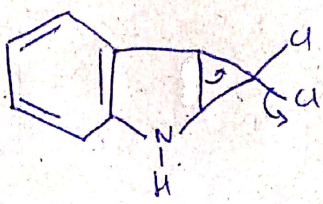


3-chloro quinoline

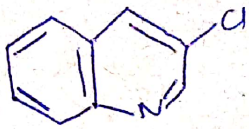
Mechanism:



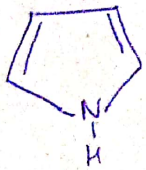
CCl_2



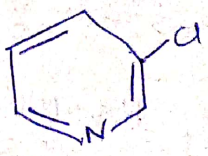
$-HCl$



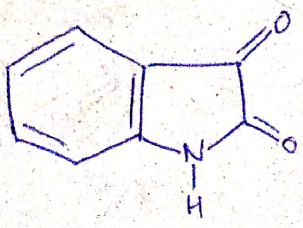
Pyrrole to pyridine



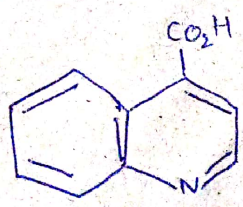
$CHCl_3$ / NaOH



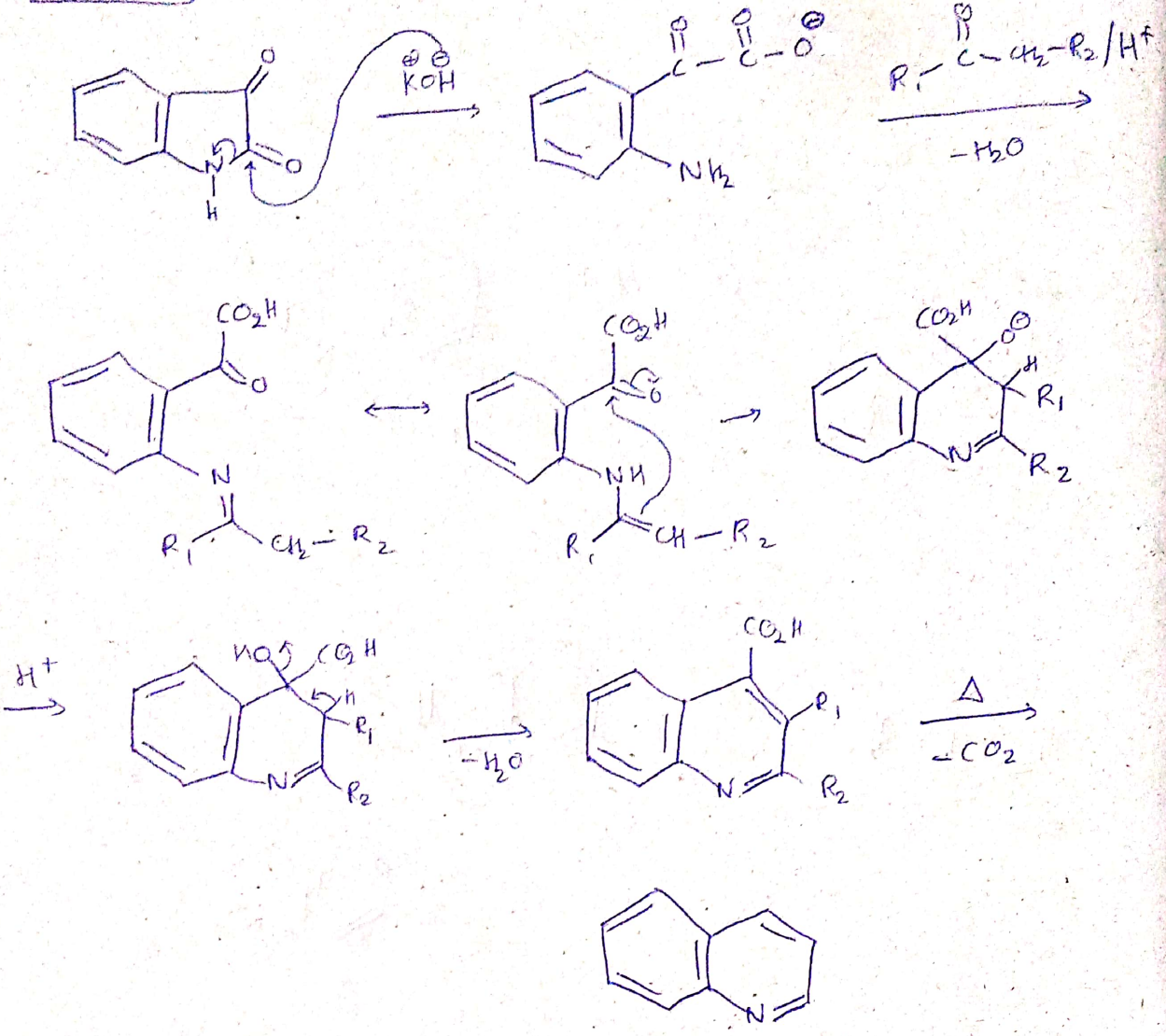
Isatin to Quinoline



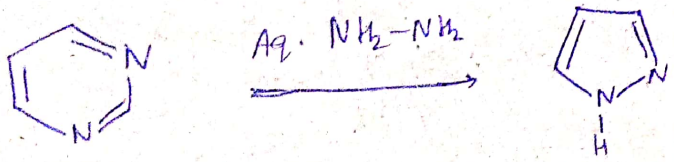
KOH



Mechanism:



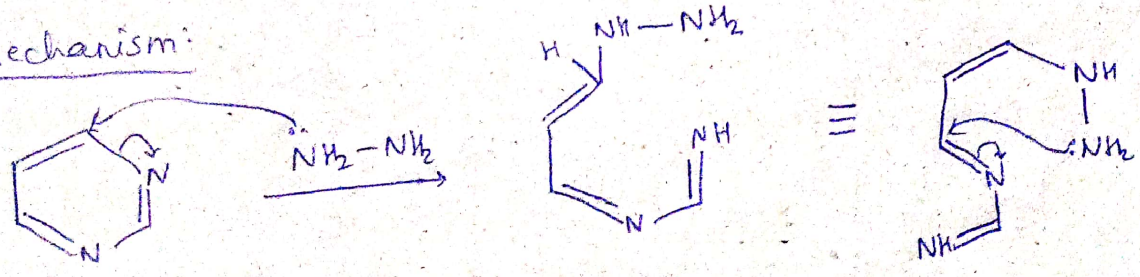
Pyrimidine to Pyrazole

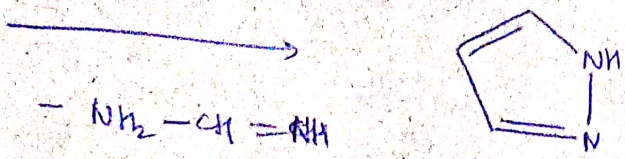


1, 3 - diazine
(Pyrimidine)

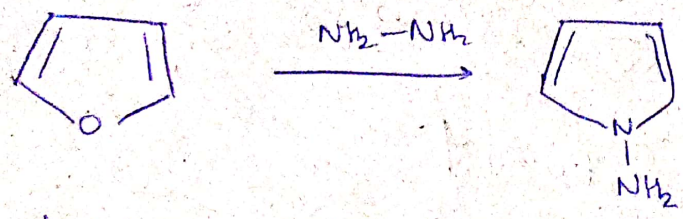
1, 2 - diazole
(Pyrazole)

Mechanism:

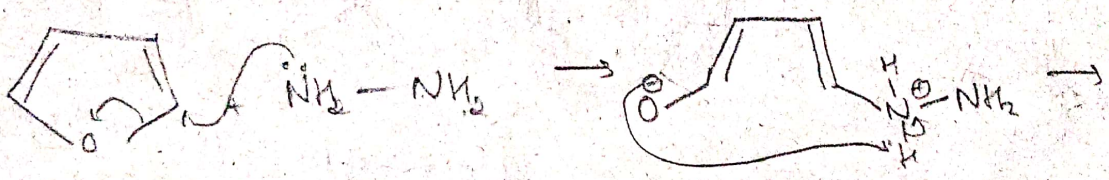


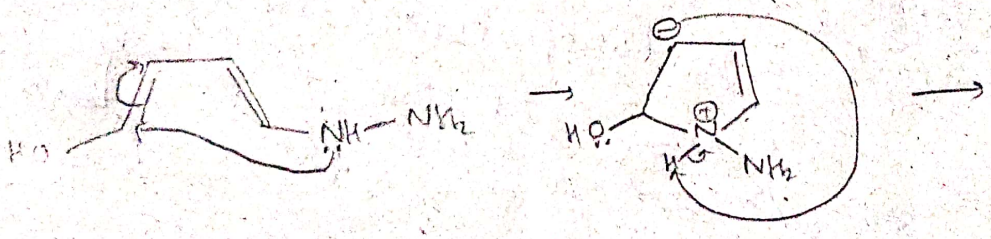


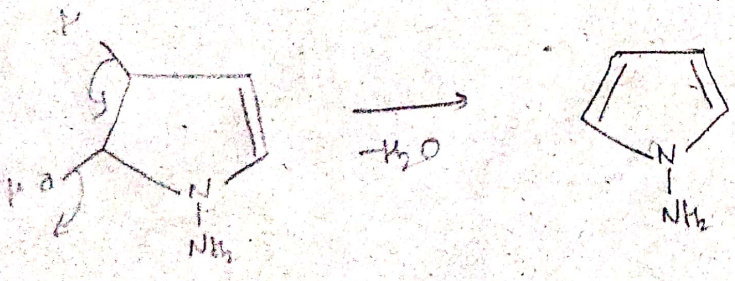
Furan to Pyrrole



Mechanism:

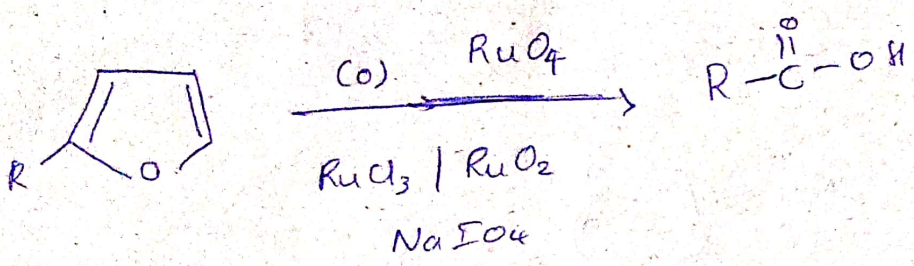




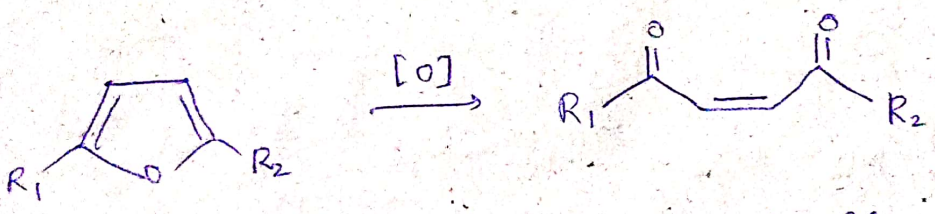


Use of Heterocycles in the synthesis of Non-heterocycles

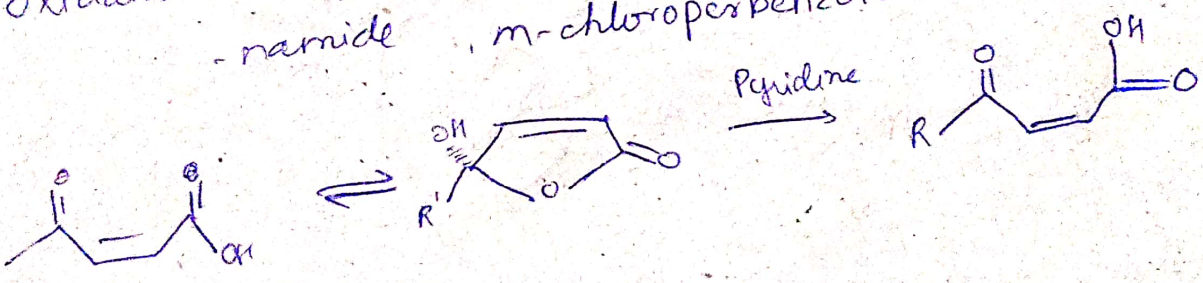
From Furan:



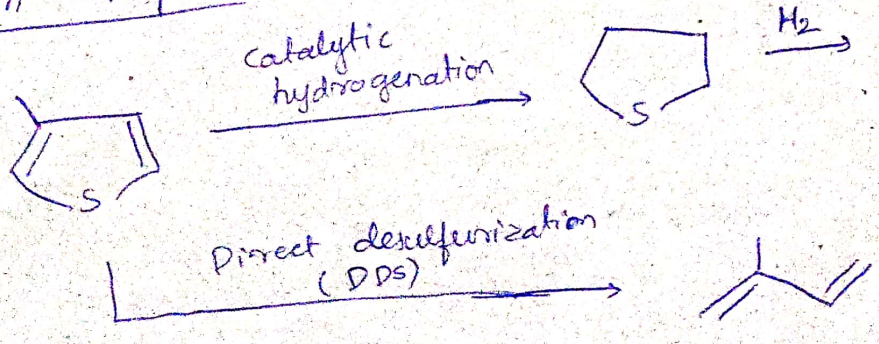
[$RuCl_3 + RuO_2 \xrightarrow{NaIO_4} RuO_4$]

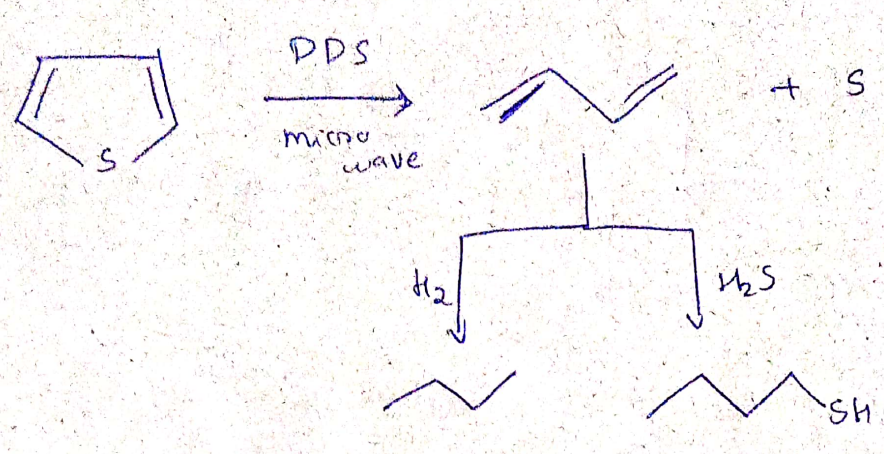


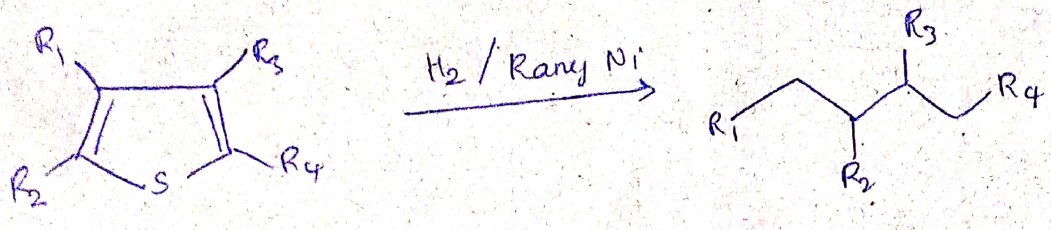
Oxidants : Singlet oxygen, dioxirane, N-bromosuccinamide, m-chloroperbenzoic acid



From thiophenes:





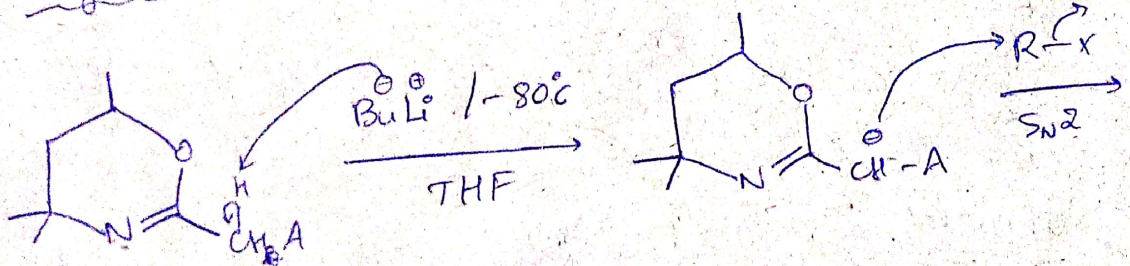


From oxazine & oxazole

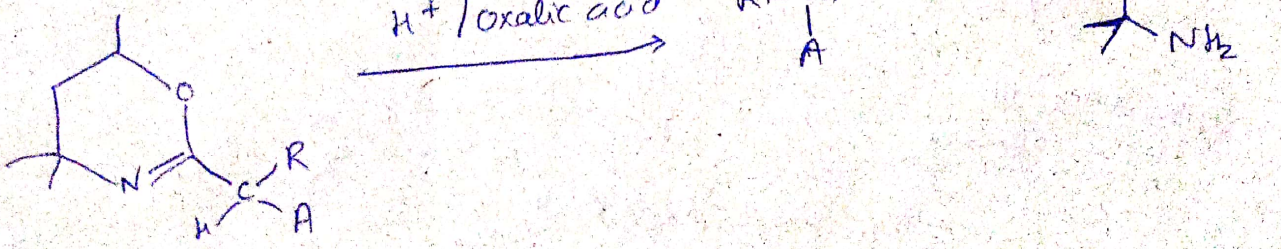
Mayer's Synthesis of aldhydes, Ketones & Carboxylic acid

Alkylation of Dihydro-1, 3-Oxazine

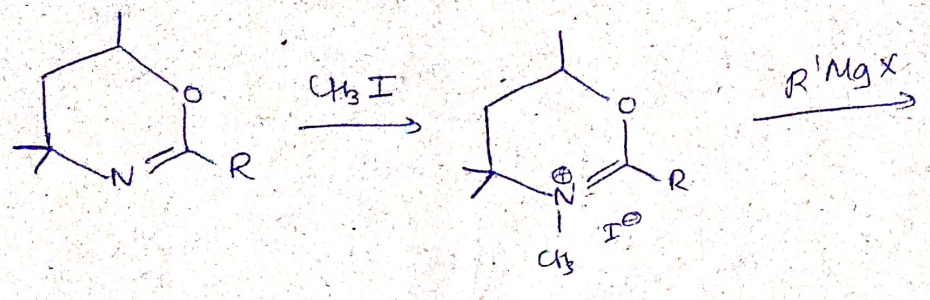
1.

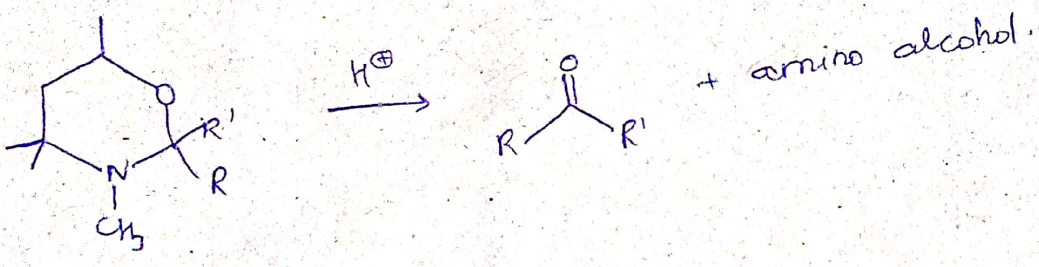


A = H, Ph, CO_2Et



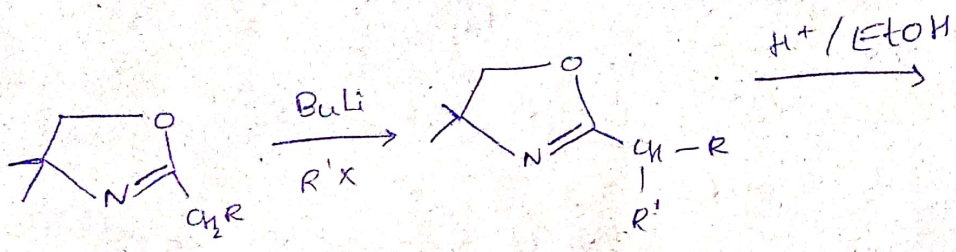
2.

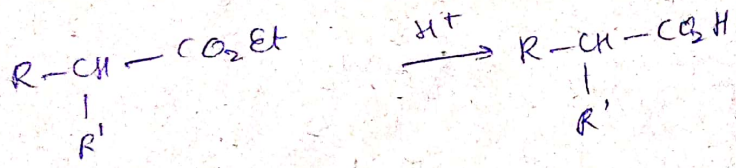




+ amino alcohol.

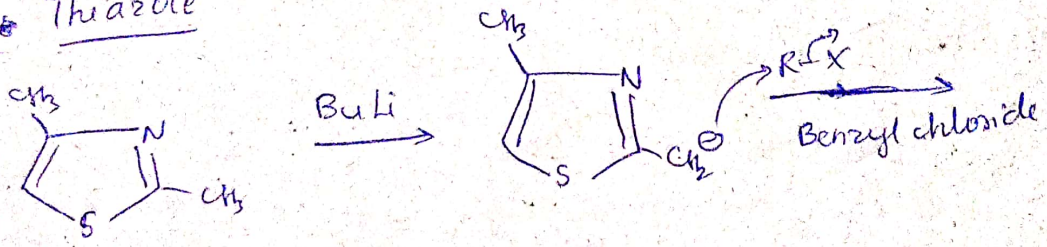
3.





ester

From Thiazole



Benzyl chloride

2, 4 - dimethyl
1, 3 - thiazole