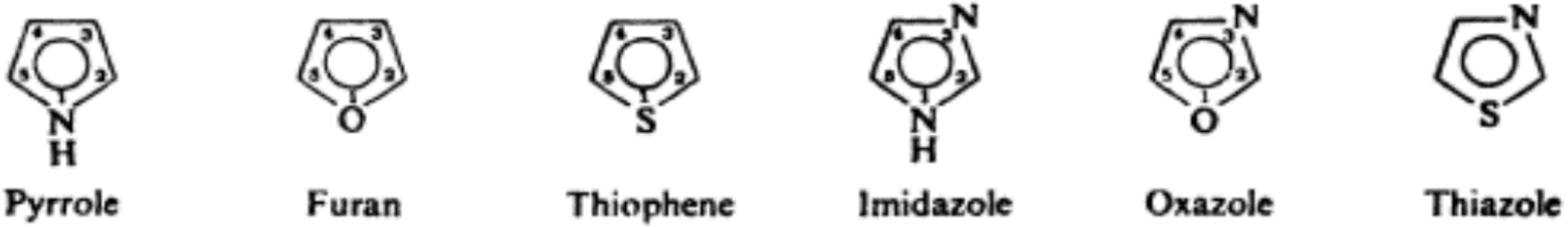
# Heterocyclic Compounds

## Six-membered ring system

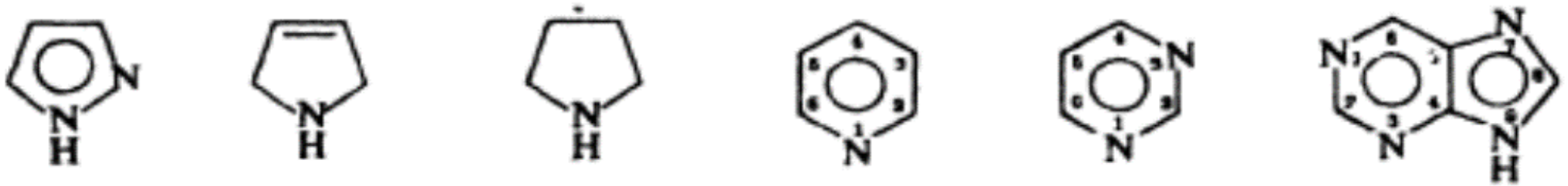
# Heterocyclic Compounds

- Heterocyclic systems
- A heterocyclic compound is one that contains a ring made up of more than one kind of atom.
- In most of the cyclic compounds that we have studied so far benzene, naphthalene, cyclohexanol, cyclopentadiene the rings are made up only of carbon atoms; such compounds are called homocyclic or alicyclic compounds. But there are also rings containing, in addition to carbon, other kinds of atoms, most commonly nitrogen, oxygen, or sulfur. For example:

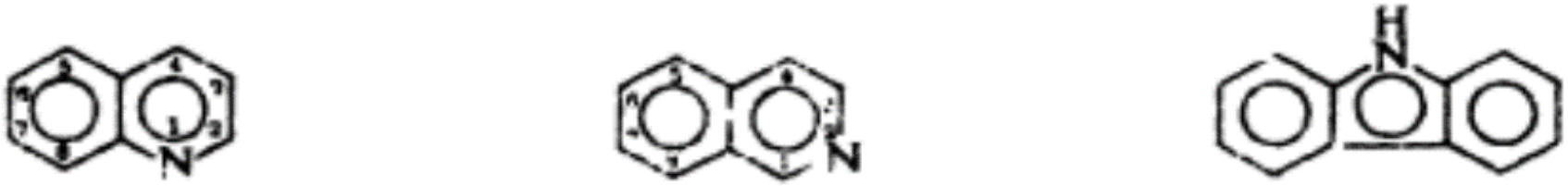
We notice that in numbering the ring position, heteroatoms are generally given the lowest possible numbers



Pyrrole Furan Thiophene Imidazole Oxazole Thiazole



Pyrazole 3-Pyrroline Pyrrolidine Pyridine Pyrimidine Purine



Quinoline Isoquinoline Carbazole

# Heterocyclic Compounds

| Name | M.p., °C | B.p., °C | Name | M.p., °C | B.p., °C |
|---|---|---|---|---|---|
| Furan | − 30 | 32 | Pyridine | − 42 | 115 |
| Tetrahydrofuran | −108 | 66 | α-Picoline | − 64 | 128 |
| Furfuryl alcohol | | 171 | β-Picoline | | 143 |
| Furfural | − 36 | 162 | γ-Picoline | | 144 |
| Furoic acid | 134 | | Piperidine | − 9 | 106 |
| Pyrrole | | 130 | Picolinic acid | 137 | |
| Pyrrolidine | | 88 | Nicotinic acid | 237 | |
| Thiophene | − 40 | 84 | Isonicotinic acid | 317 | |
| | | | Indole | 53 | 254 |
| | | | Quinoline | − 19 | 238 |
| | | | Isoquinoline | 23 | 243 |

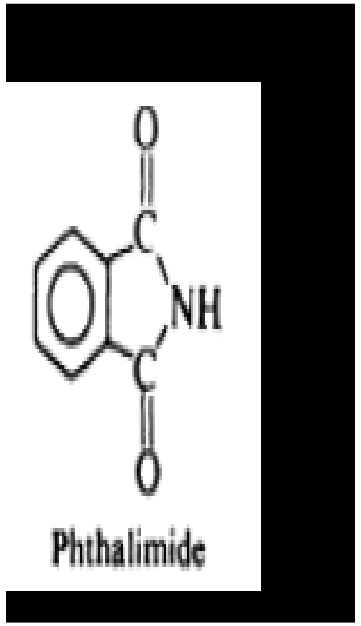
# Heterocyclic Compounds

- Numerous heterocyclic compounds have been encountered for example:

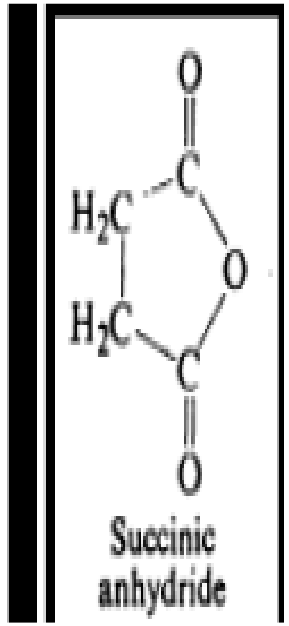
- Cyclic anhydrides and cyclic imides like:

--- Succinic anhydride and phthalimide

Note: In all these, the chemistry is essentially that of their open-chain analogs.



Phthalimide

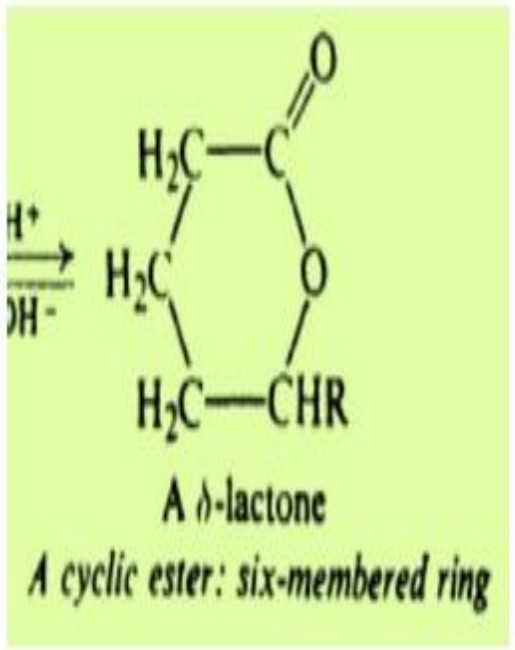


Succinic anhydride

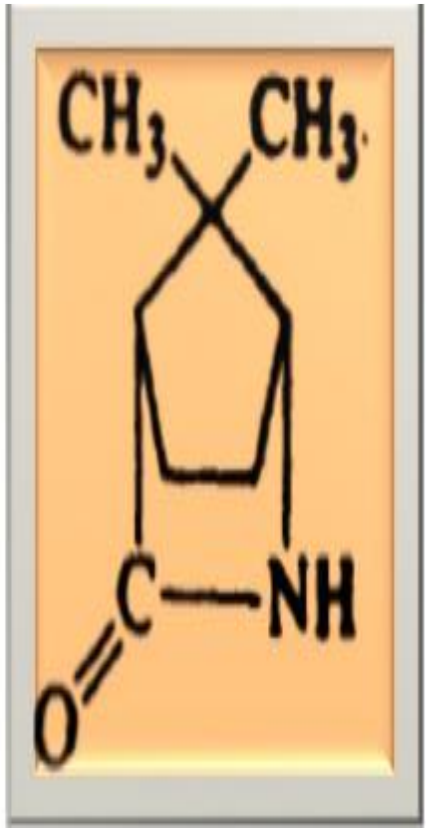
# Heterocyclic Compounds

- Cyclic esters and cyclic amides:

--- Lactones




--- Lactams

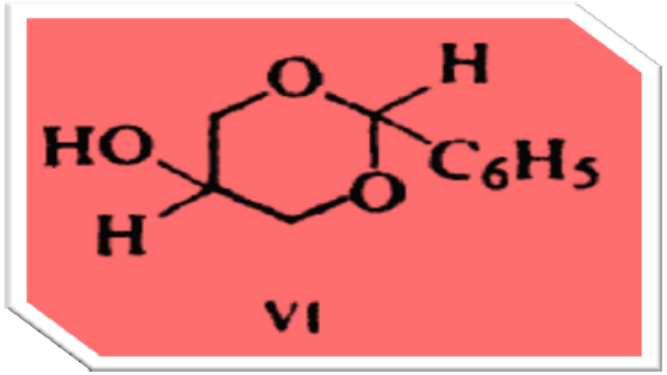


# Heterocyclic Compounds

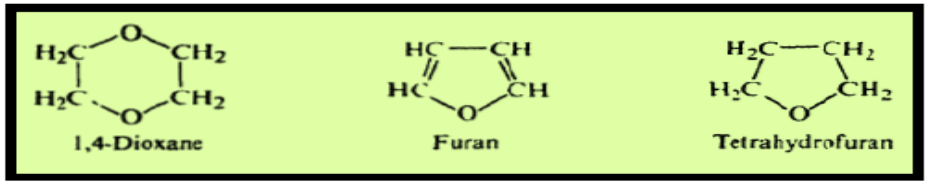
- Cyclic acetals of dihydroxy alcohols like:

--- The solvents dioxane and tetrahydrofuran.

Note: In all these, the chemistry is essentially that of their open-chain analogs.



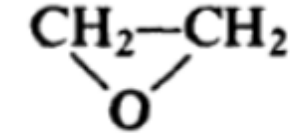
VI



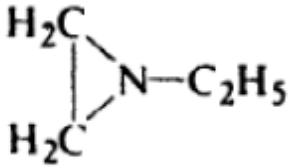
# Heterocyclic Compounds

- Three-membered heterocyclic rings which, because of ring strain, are highly reactive like:

--- Epoxides and aziridines.

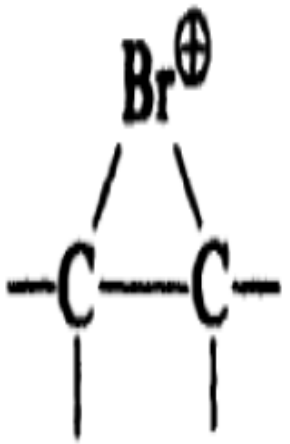



Ethylene oxide

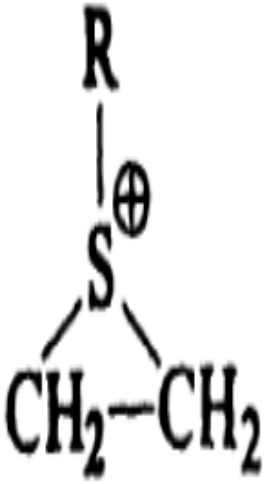


# Heterocyclic Compounds

--- The fleeting but important intermediates like cyclic halonium ions and cyclic sulfonium ions.




A bromonium ion

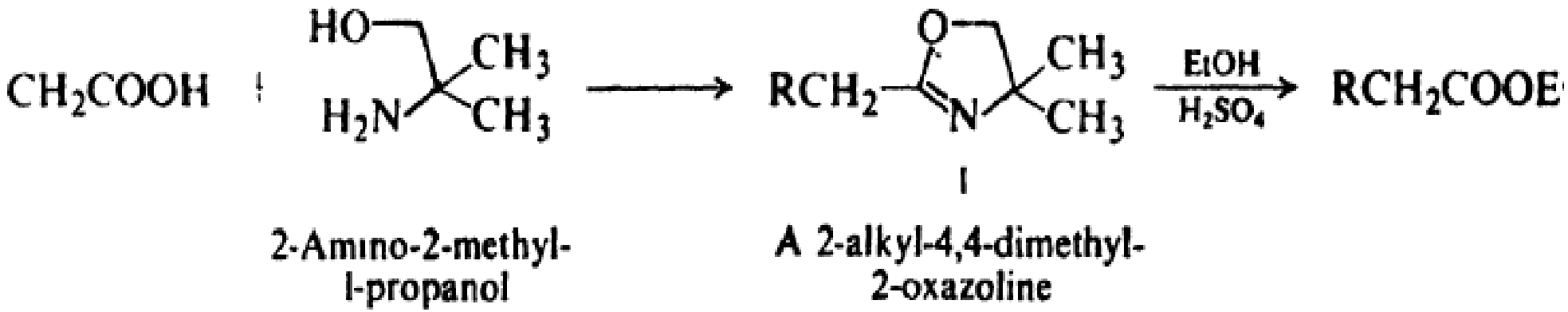



A sulfonium ion

# Heterocyclic Compounds

- Heterocyclic intermediates are being used more and more in synthesis as protecting groups, readily generated and, when their job is done, readily removed. We have seen two examples of this:

--- The temporary incorporation of the carboxyl group into a 2-oxazoline ring and then regeneration of acid ester by ethanolysis.



# Heterocyclic Compounds

--- and the temporary formation of tetrahydropyranyl (THP) esters, resistant toward alkali but extremely easily cleaved by acid. Carboxyl groups are often masked by reaction with dihydropyran, which yields esters that are stable toward base but easily hydrolyzed by dilute aqueous acids.

# Heterocyclic Compounds

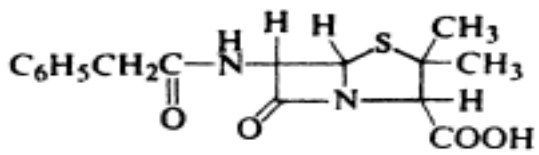
- In the biological world, the heterocyclic compounds are everywhere:
--- Carbohydrates are heterocyclic.

--- So are chlorophyll and hemin which make leaves green and blood red and bring life to plants and animals.

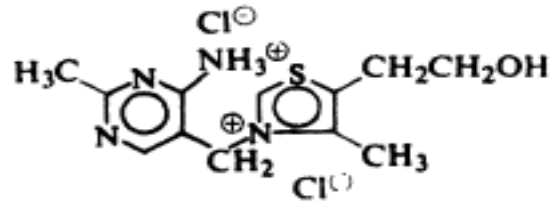
--- Heterocycles form the sites of reaction in many enzymes and coenzymes.

--- Heredity comes down, ultimately, to the particular sequence of attachment of a half-dozen heterocyclic rings to the long chains of nucleic acids.

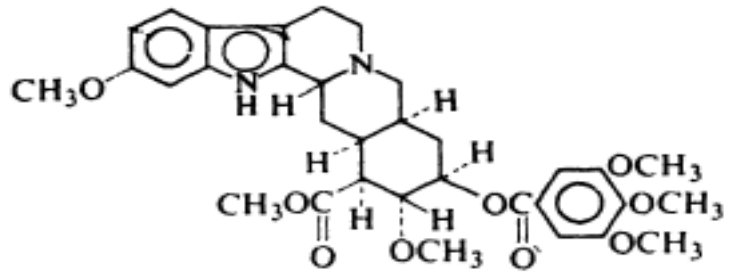
# Heterocyclic Compounds



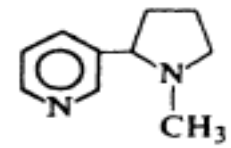
Penicillin G
*Antibiotic*



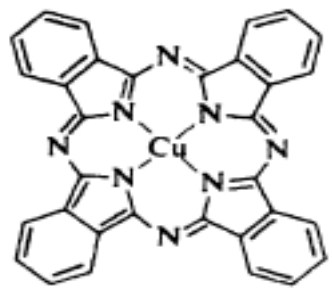
Thiamine
Vitamin $B_1$
*Anti-beriberi factor*



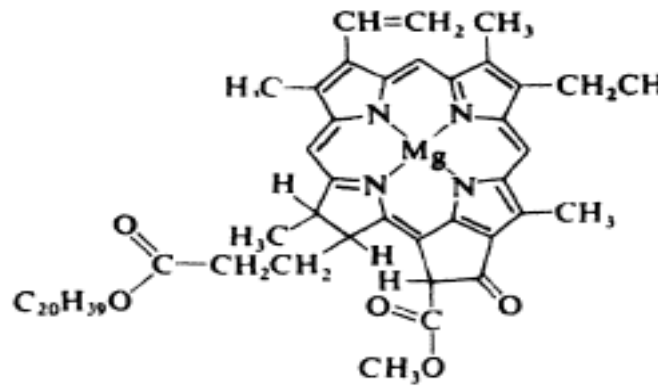
Reserpine
*A tranquilizing drug*



Nicotine
*A tobacco alkaloid*



Copper phthalocyanine
*A blue pigment*



Chlorophyll a
*Green plant pigment:*
*catalyst for photosynthesis*

# Heterocyclic Compounds

Only a very few of the many different heterocyclic systems can be taken up and looked briefly. Among the most important and most interesting heterocycles are the ones that ***possess aromatic properties*** to be focused in our attention.

# Heterocyclic Compounds

Some idea of the importance as well as complexity of heterocyclic systems can be gotten from the following examples:

-- Hemin

-- Nicotinamide

-- Adenine dinucleotide and oxytocin

# Heterocyclic Compounds