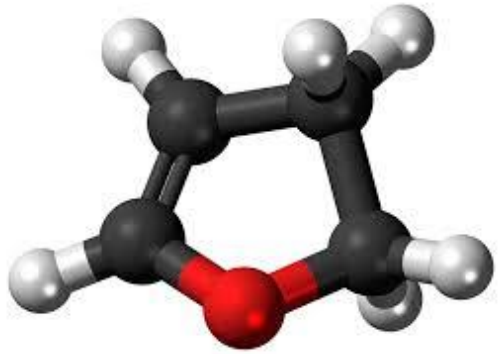
2302687 – Heterocyclic Compounds – Part I

Lecture 1-1

Introduction to Heterocyclic Compounds



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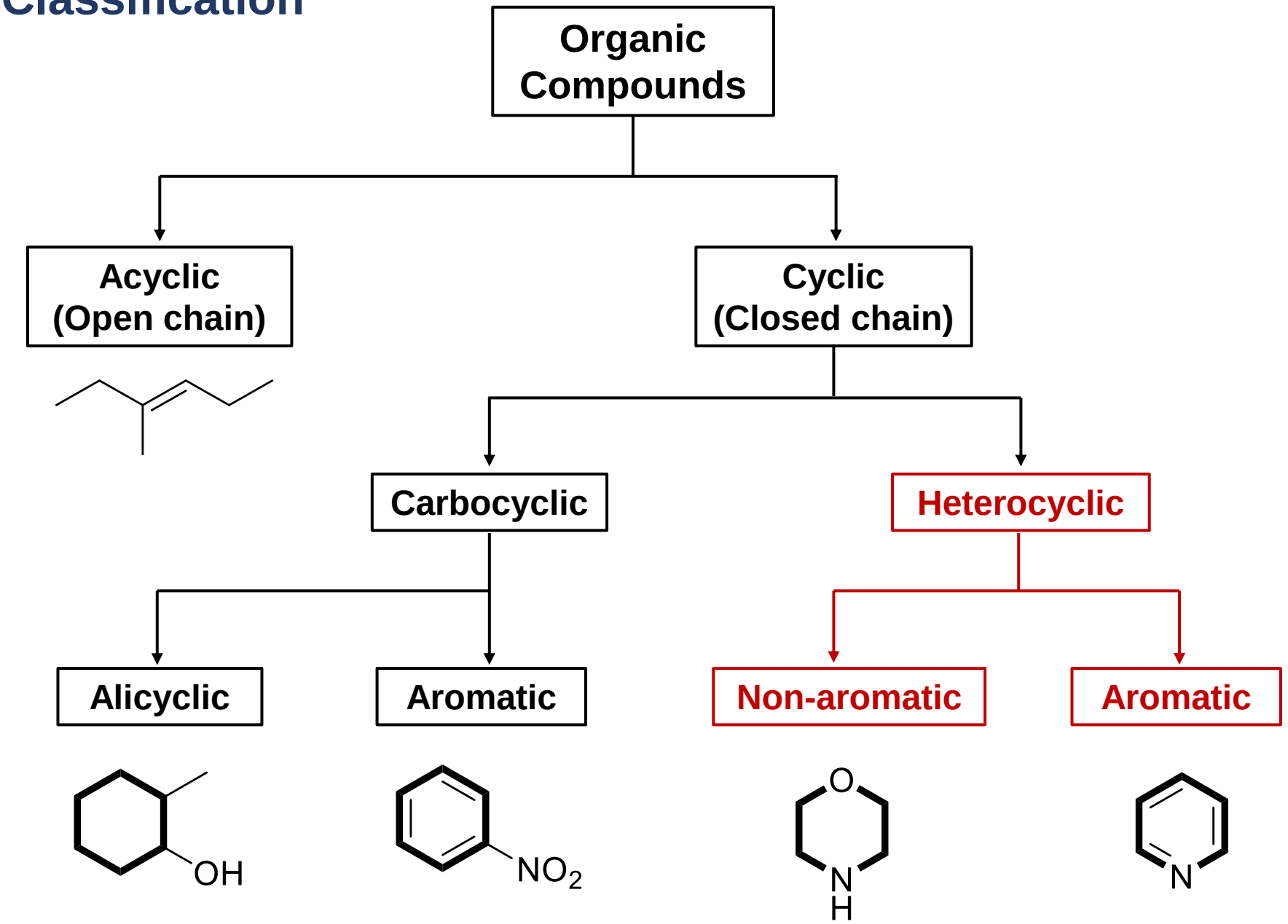
Recommended Textbook:

Heterocyclic Chemistry, 5th Edition, J. A. Joule, K. Mills, **2010**, Wiley

Classification



Heterocyclic Compounds

- Heterosubstituted rings are those in which one or more carbon atoms in a purely carbon-containing ring (known as a carbocyclic ring) is **replaced by some other atom** (referred to as a heteroatom).

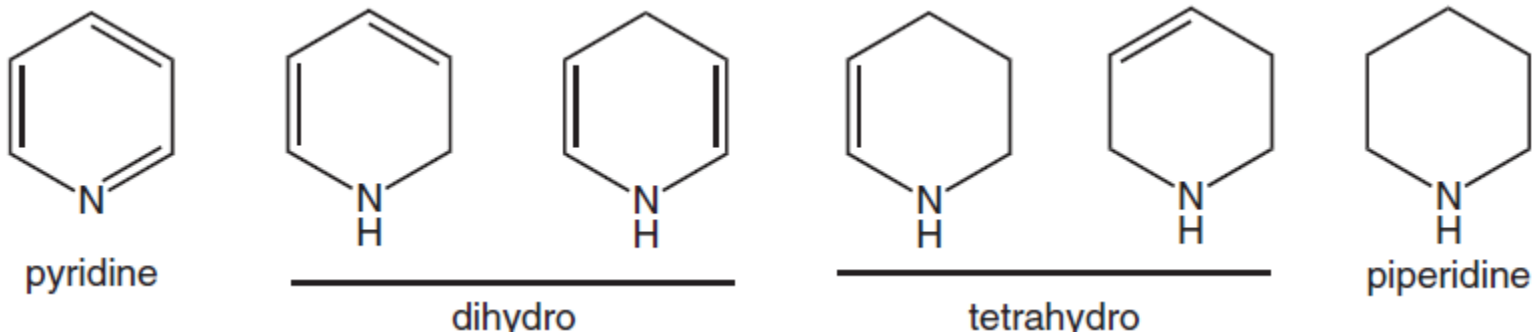
carbocycle heterocycles – X, Y, Z are usually O, N or S

- In practice, the most commonly found heteroatom is **nitrogen**, followed by **oxygen** and **sulphur**

- However, many other atoms can form the stable covalent bonds; of note are **phosphorus**, **arsenic**, **antimony**, **silicon**, **selenium**, **tellurium**, **boron**, and **germanium**

Heterocyclic Compounds

- **Pyridine** is an excellent example of a simple heterocycle. Here, one carbon of **benzene** is replaced by **nitrogen**, without interrupting the classic unsaturation and aromaticity

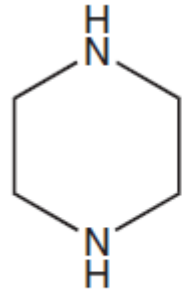


- Similarly, replacement of a carbon in **cyclohexane** by **nitrogen** produces the saturated heterocycle **piperidine**

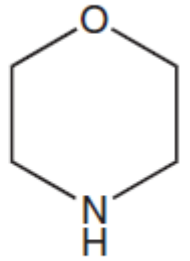
- Between these extremes of saturation come several structures with one or two double bonds

Heterocyclic Compounds

- Rings may have **more than one heteroatom**, which may be the same or different, as in the examples that follow

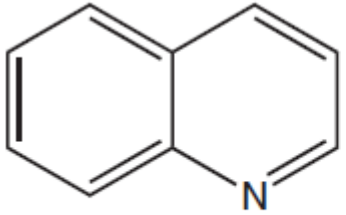


piperazine

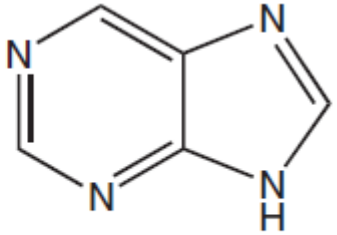


morpholine

- To broaden the field, other rings may be **fused** onto a parent heterocycle



quinoline



purine

- 133,326 different heterocyclic ring systems had been reported by 1984, and many more have been reported since then

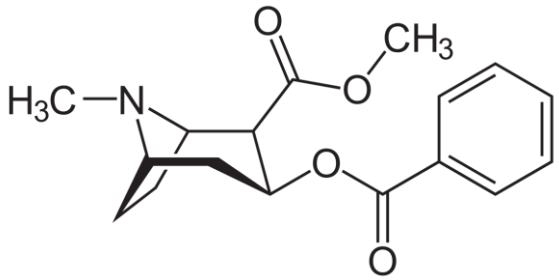
- Moreover, hydrogens on these rings can be replaced by a multitude of **substituents**. As a result, millions of heterocyclic compounds are known! (24,282,284 compounds in 2007 !)

Heterocyclic Compounds in Nature

- Nature abounds in heterocyclic compounds, many of profound importance in biological processes

- We find heterocyclic rings in **vitamins**, **coenzymes**, **porphyrins** (like hemoglobin), **DNA**, **RNA**, and so on

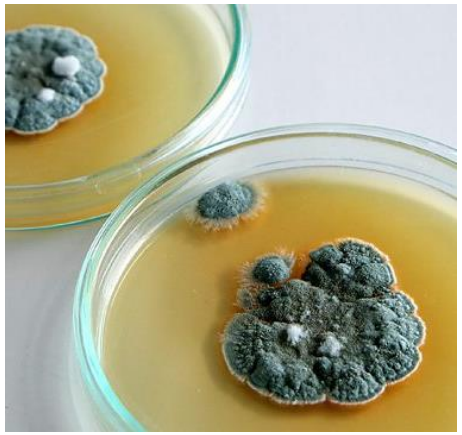
- The **plant** kingdom contains thousands of nitrogen heterocyclic compounds, most of which are weakly basic and called **alkaloids**

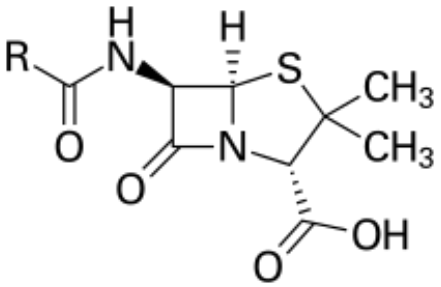


Cocaine
(Psychoactive)

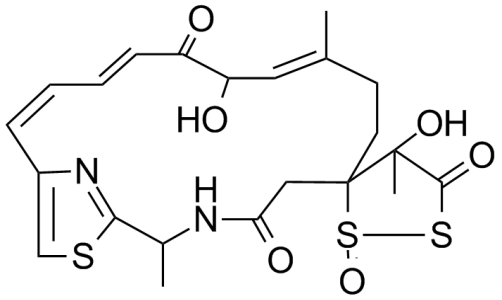
Heterocyclic Compounds in Nature

- **Complex heterocyclic** compounds are elaborated by **microorganisms** and are useful as antibiotics in medicine



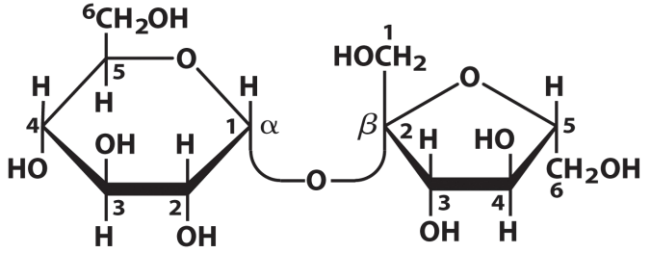


Penicillin
(Antibacterial)



Leinamycin
(Antitumor)

- The huge field of **carbohydrate** chemistry depends on heterocyclic frameworks; all disaccharides and polysaccharides have rings usually of **five** (called **furanose**) or **six** (called **pyranose**) members that contain an oxygen atom



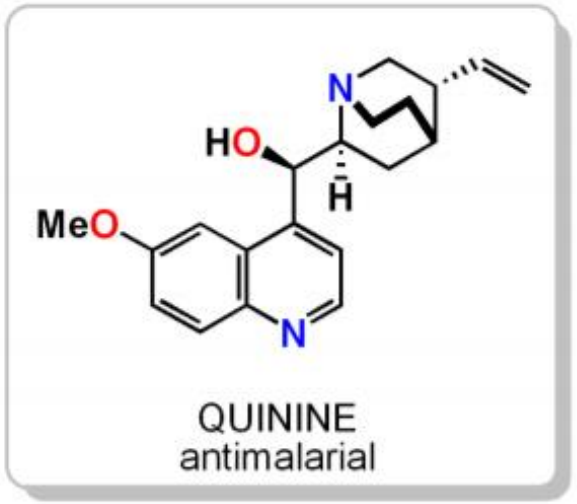
Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

Applications of Heterocyclic Compounds

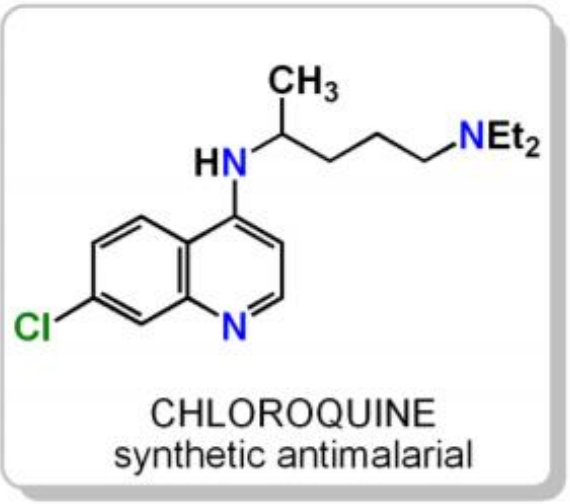
- Heterocyclic compounds can be synthesized in many ways
- Many synthetic (as well as natural) heterocyclic compounds are of extreme value as **medicinals**, **agrochemicals**, **plastics precursors**, **dyes**, **photographic chemicals**, and so on, and new structures are constantly being sought in research in these areas

Applications of Heterocyclic Compounds

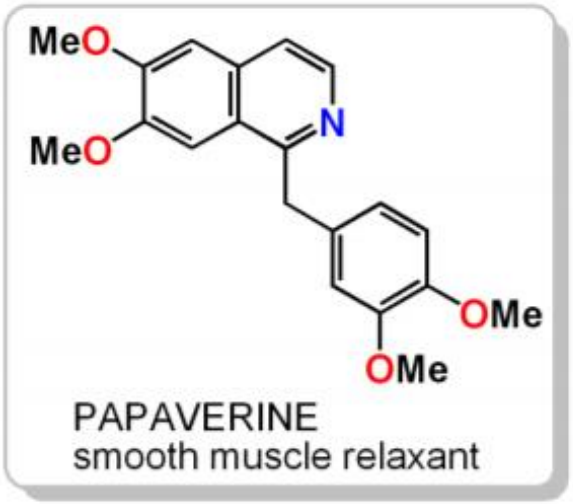
Medicinal chemistry especially is associated intimately with heterocyclic compounds; most of all chemicals used in medicine are based on heterocyclic frameworks



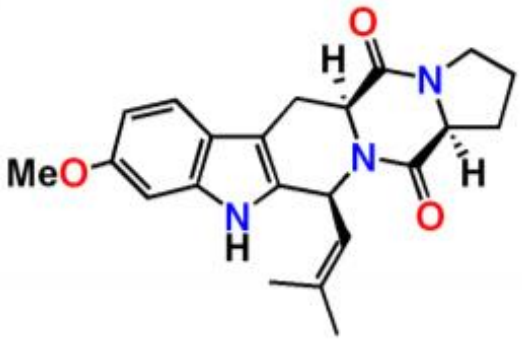
QUININE
antimalarial



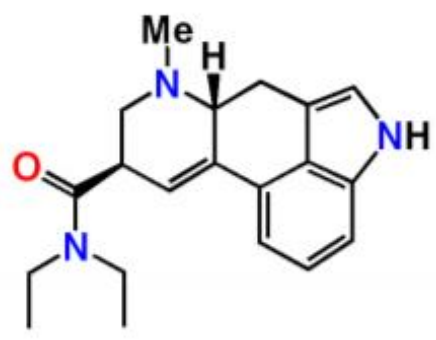
CHLOROQUINE
synthetic antimalarial



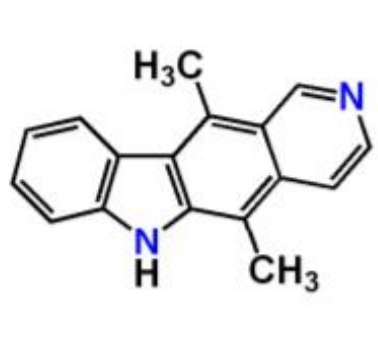
PAPAVERINE
smooth muscle relaxant



FUMITREMORGIN-C



LYSERGIC ACID
DIETHYLAMIDE

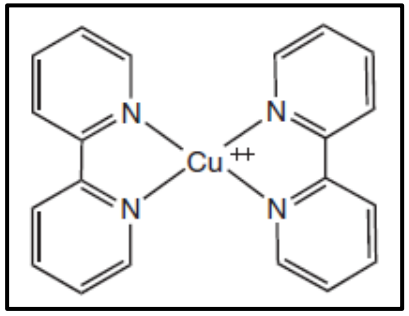


ELLIPTICINE
anti-tumour agent

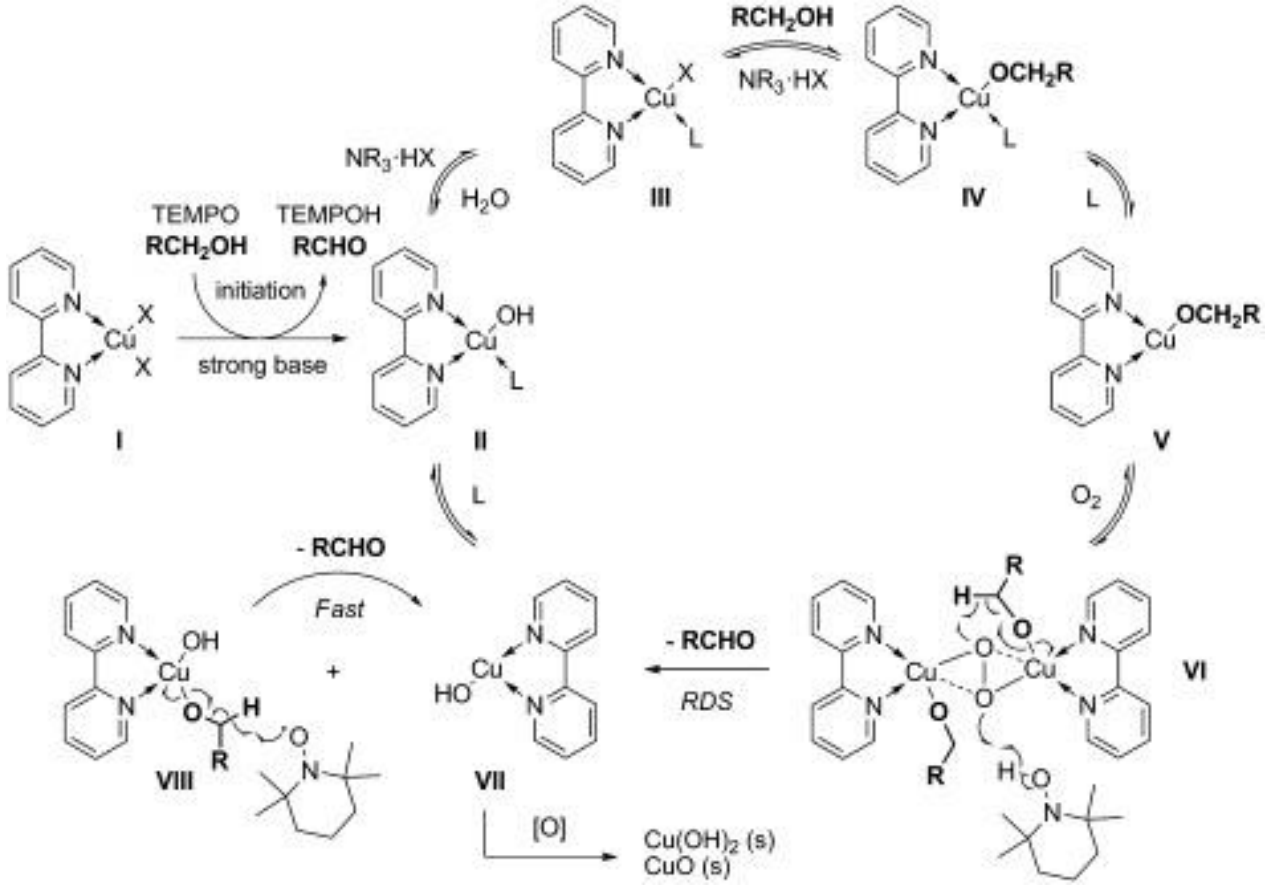
Applications of Heterocyclic Compounds

- Heterocyclic compounds can be useful **ligands** (through their lone pair electrons or pi-systems) in the construction of coordination complexes

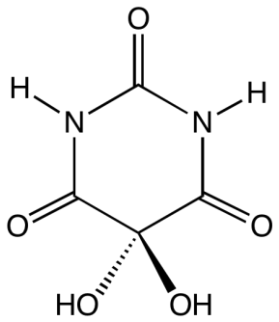
- An example of a heterocycle frequently used for this purpose is 2,2-bipyridyl, which is shown here as complexed to cupric ion



- These complexes can be used as a catalyst for various organic transformations

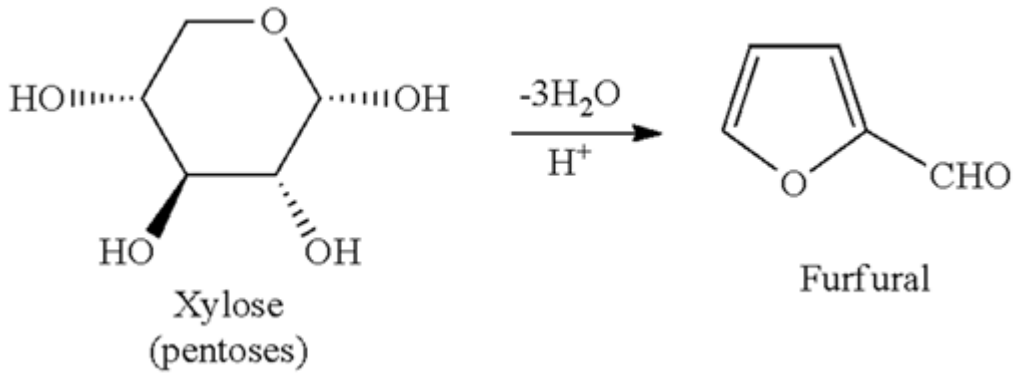


History of Heterocyclic Compounds



alloxan

- **1818**: Brugnatelli isolates **alloxan** from uric acid

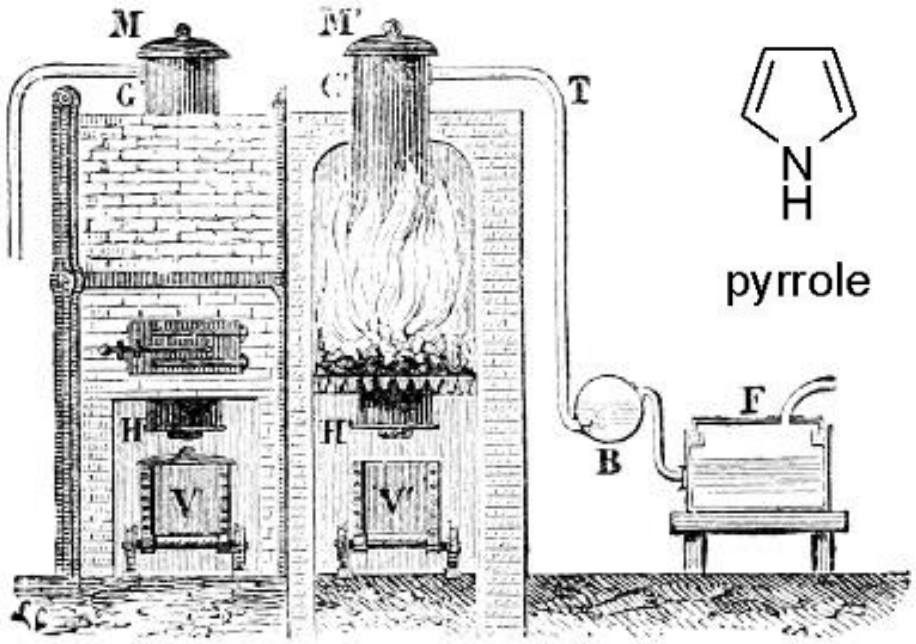


Xylose (pentoses)

Furfural

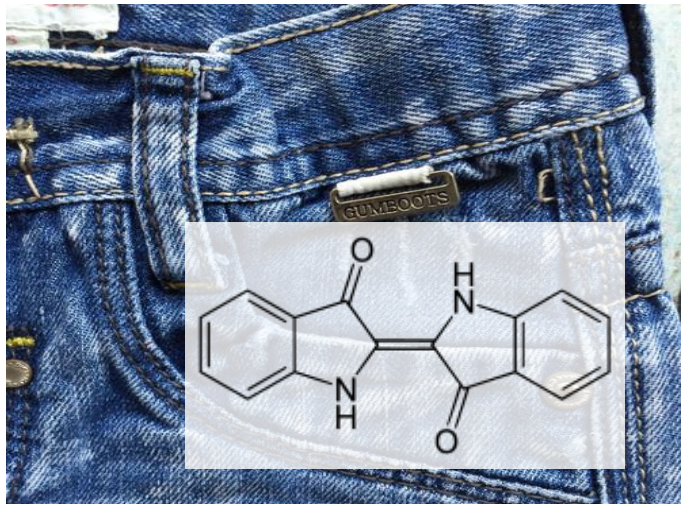
- **1832**: Dobereiner produces **furfural** by treating starch with sulfuric acid

- **1834**: Runge obtains pyrrole ("fiery oil") by dry distillation of bones

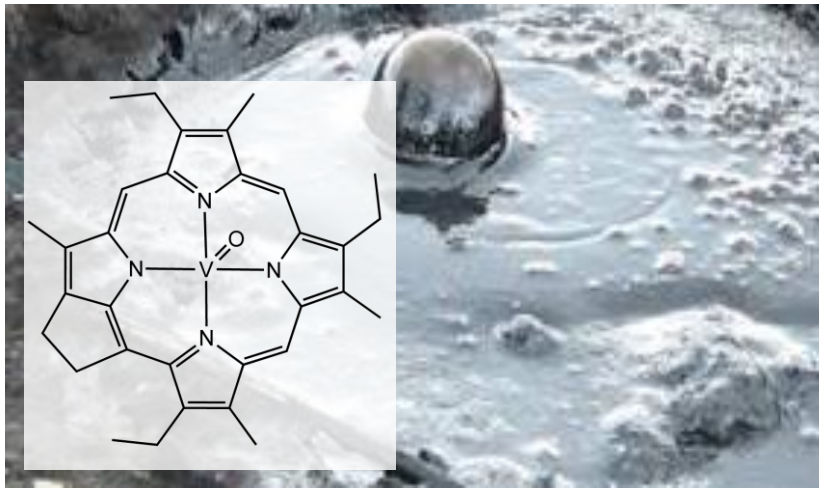


pyrrole

History of Heterocyclic Compounds



- **1906**: Friedlander synthesizes **indigo dye**, allowing synthetic chemistry to displace a large agricultural industry



- **1936**: Treibs isolates **chlorophyl** derivatives from crude oil, explaining the biological origin of petroleum

- **1951**: Chargaff's rules are described, highlighting the role of heterocyclic compounds in the genetic code (**purines** and **pyrimidines**)