



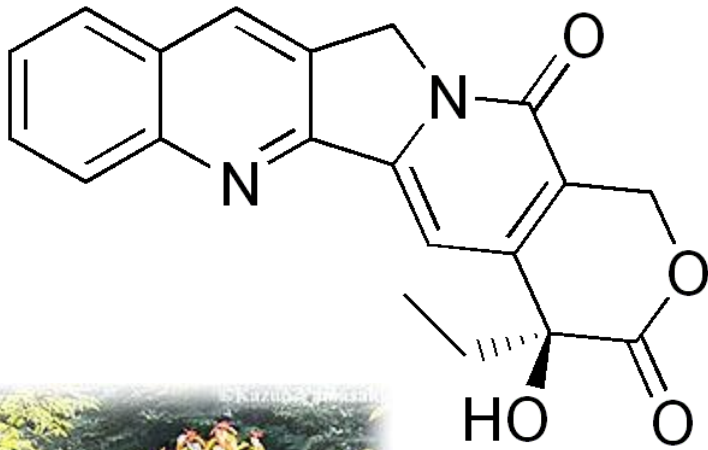
Heterocyclic Chemistry



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Camptothecin



Camptotheca acuminata

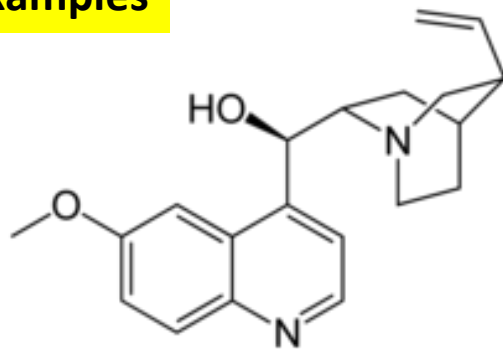
Happy Tree
(China)

(Also known as cancer tree)

Definition: **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. The ring may be aromatic or non-aromatic

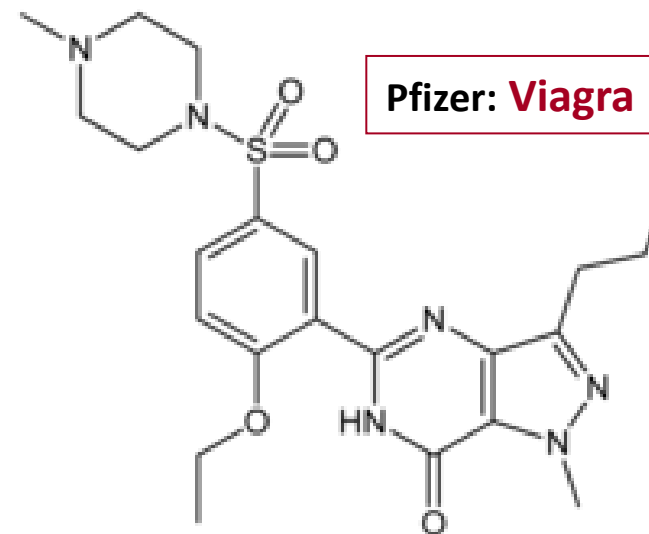
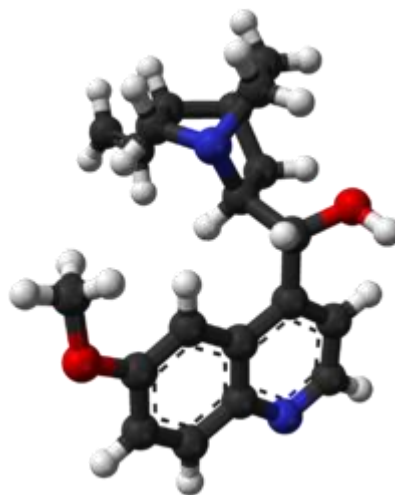
Significance – Two thirds of all organic compounds are aromatic heterocycles. Most pharmaceuticals are heterocycles.

Examples



Quinine

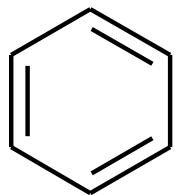
Treatment of malaria for 400 years (Peru)



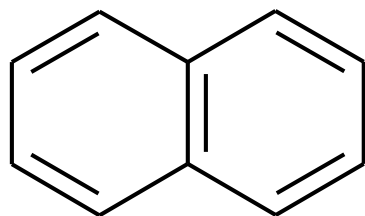
Erectile dysfunction

When Is A Molecule Aromatic?

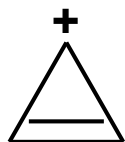
- For a molecule to be aromatic it must:
 - Be cyclic
 - Have a p -orbital on every atom in ring
 - Be planar
 - Posses $4n+2$ p electrons ($n = \text{any integer}$)



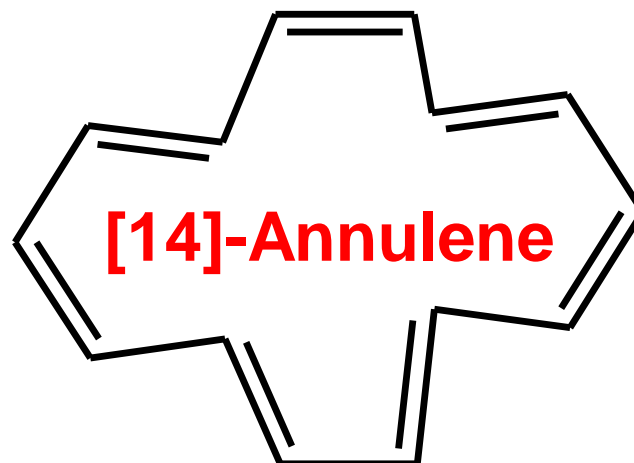
benzene



naphthalene



cyclopropenyl cation

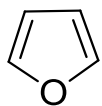


Erich Hückel

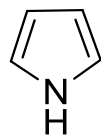
Heterocyclic compound: *Any cyclic organic compound in which there is at least one heteroatom (e.g. N, O or S).* These are widely distributed in nature.

Some common heterocyclic compounds are given below.

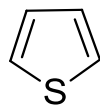
5-membered heterocyclic compounds:



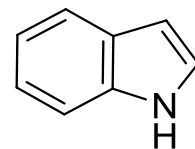
Furan



Pyrrole

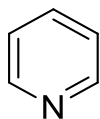


Thiophene

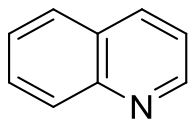


Indole

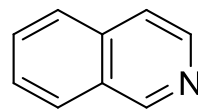
6-membered heterocyclic compounds:



Pyridine

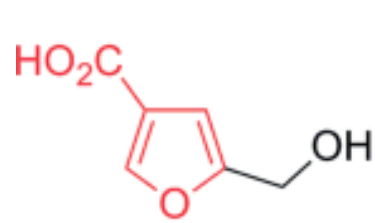


Quinoline

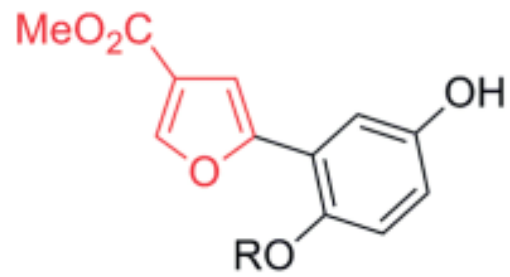


Isoquinoline

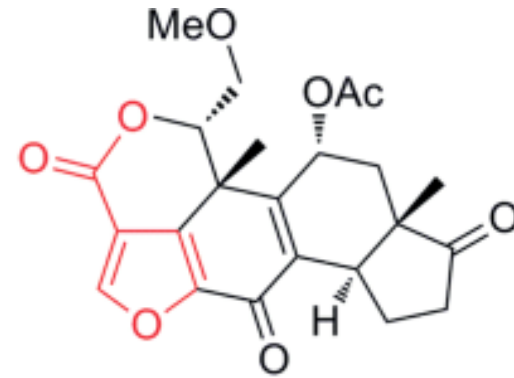
Furan containing natural products



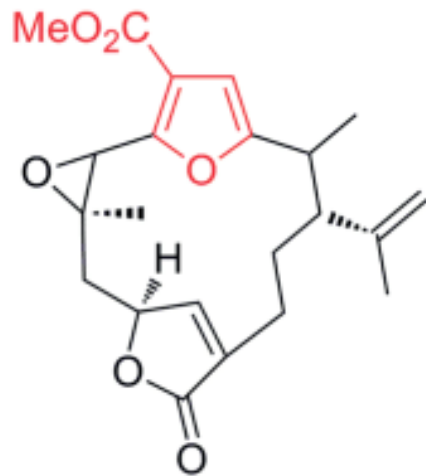
flufuran



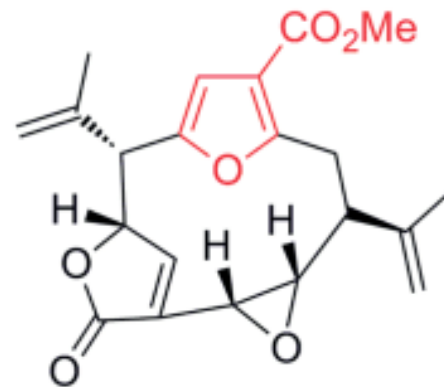
R=Me, tournefolin B
R=H, tournefolin C



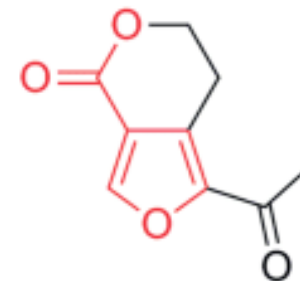
wortmannin



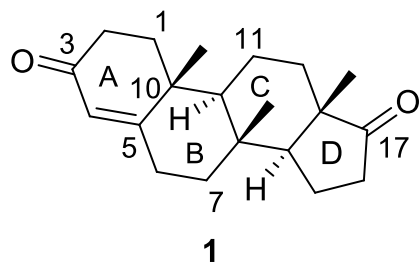
pukalide



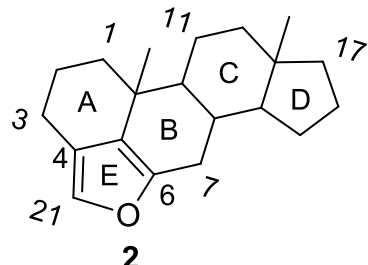
pseudopteroide



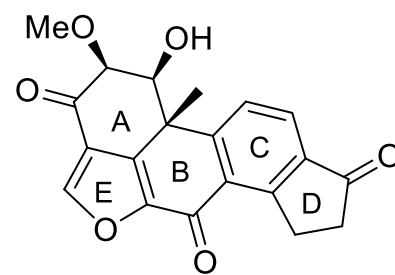
angelone



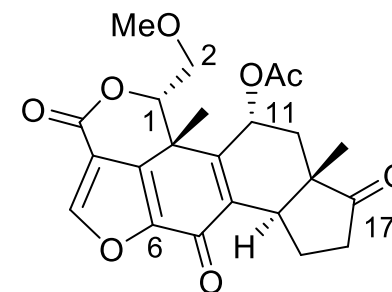
Typical steroid molecule



Furanosteroid skeleton



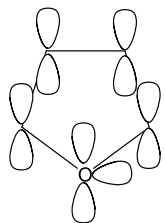
Viridin (**3**)



Wortmannin (**4**)

FURAN:

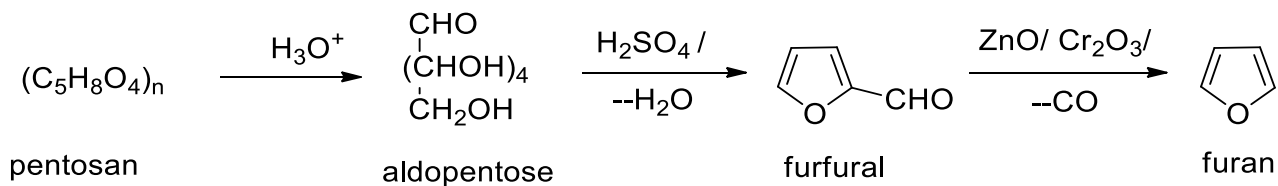
All the ring atoms in furan are Sp^2 hybridized and overlap with each other. All these σ -bonds lie in the same plane. Furan shows aromatic properties or aromaticity because the resulting π -system satisfies the Huckel rule ($n = 1$ in $4n+2$)



Resonance energy = 98 kJ/mole (~ 20 kcal/mole); b.p. 32 °C

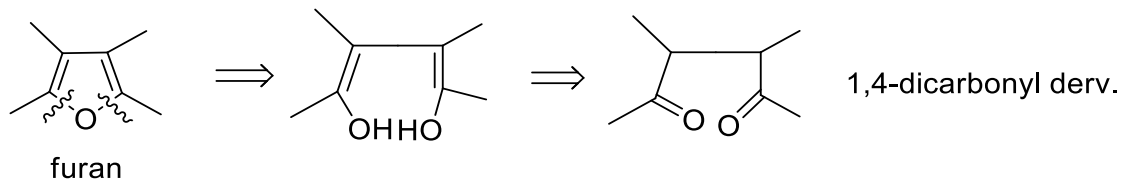
Preparation: Furan is synthesized from furfural (oat and rice hulls and corncobs)

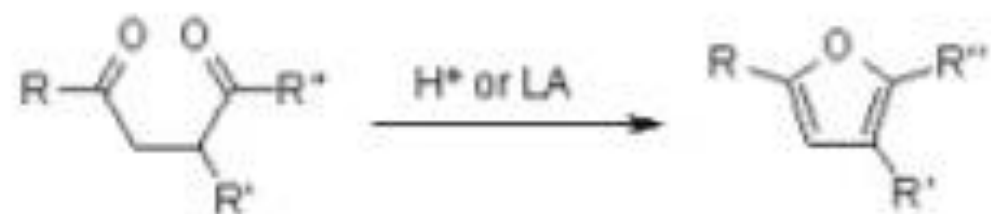
obtained by acid-hydrolysis of pentosan



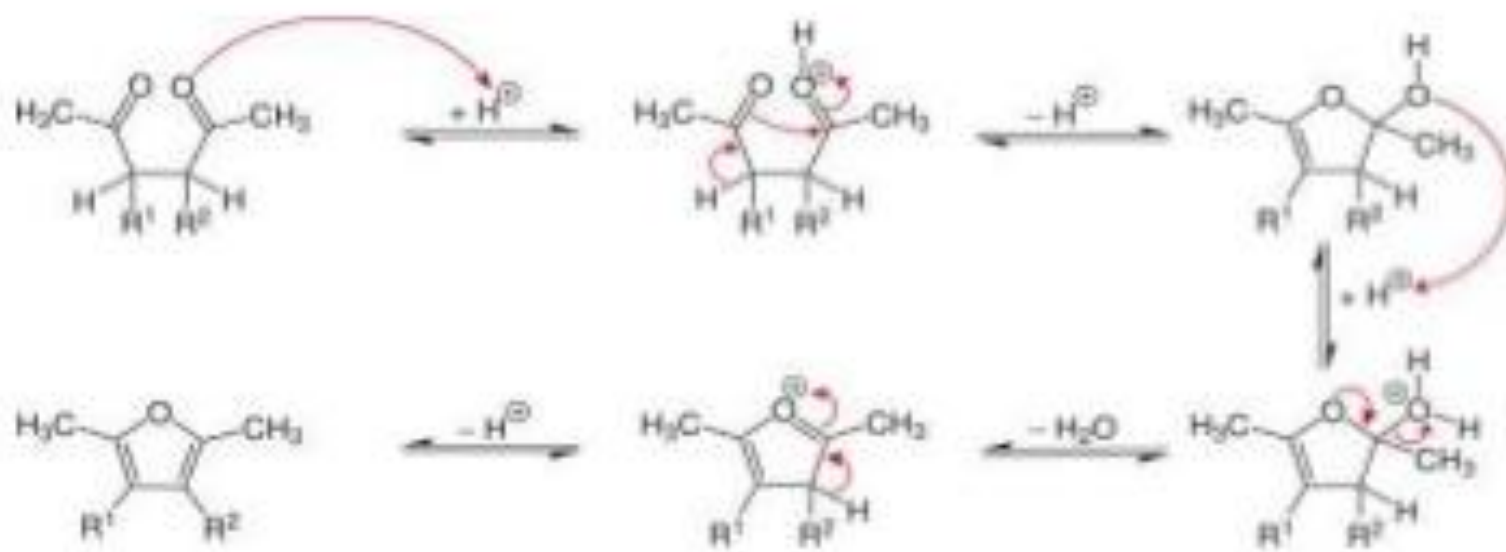
Chemical synthesis:

1. Paal-Knorr methods:

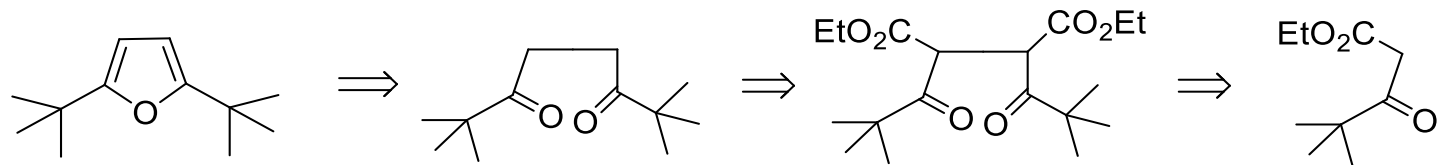




Mechanism:

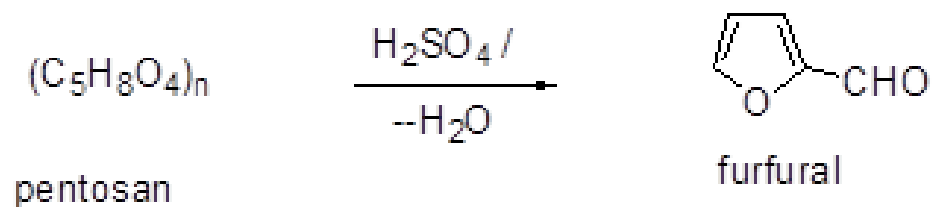


Example 3.



Furfural:

It is manufactured from agricultural waste material such as corncobs, oat hulls, rice hulls which are richer in pentosan, a C5-polysaccharide. The pentosans on acid-hydrolysis (mainly xylose) give aldopentoses that dehydrates to yield furfural (purified by distillation).

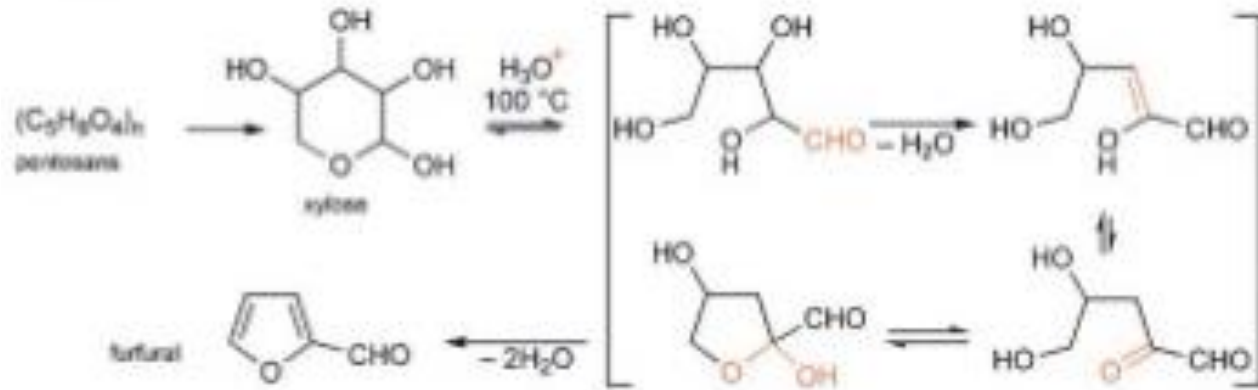


Furfural is industrially important compound as various furan derivatives are prepared from it.

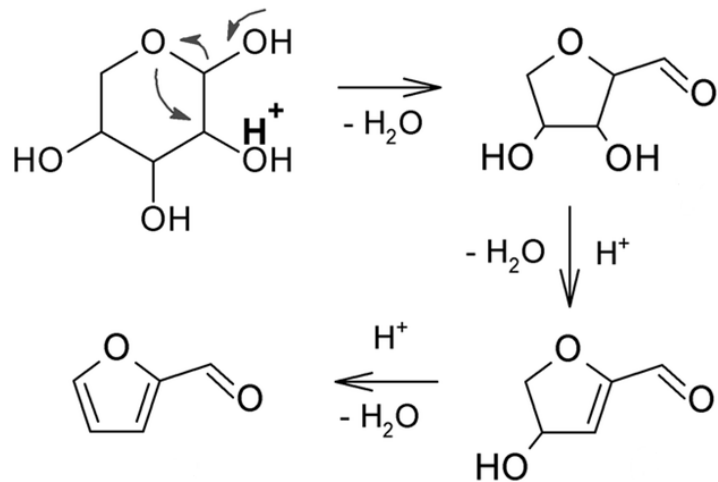
Furfural is an almond-scented, oily, colorless liquid that turns yellow to dark brown when exposed to air. It is used as a solvent for refining lubricating oils, as a fungicide and weed killer and in the production of tetrahydrofuran, an **important industrial** solvent.

Mechanism:

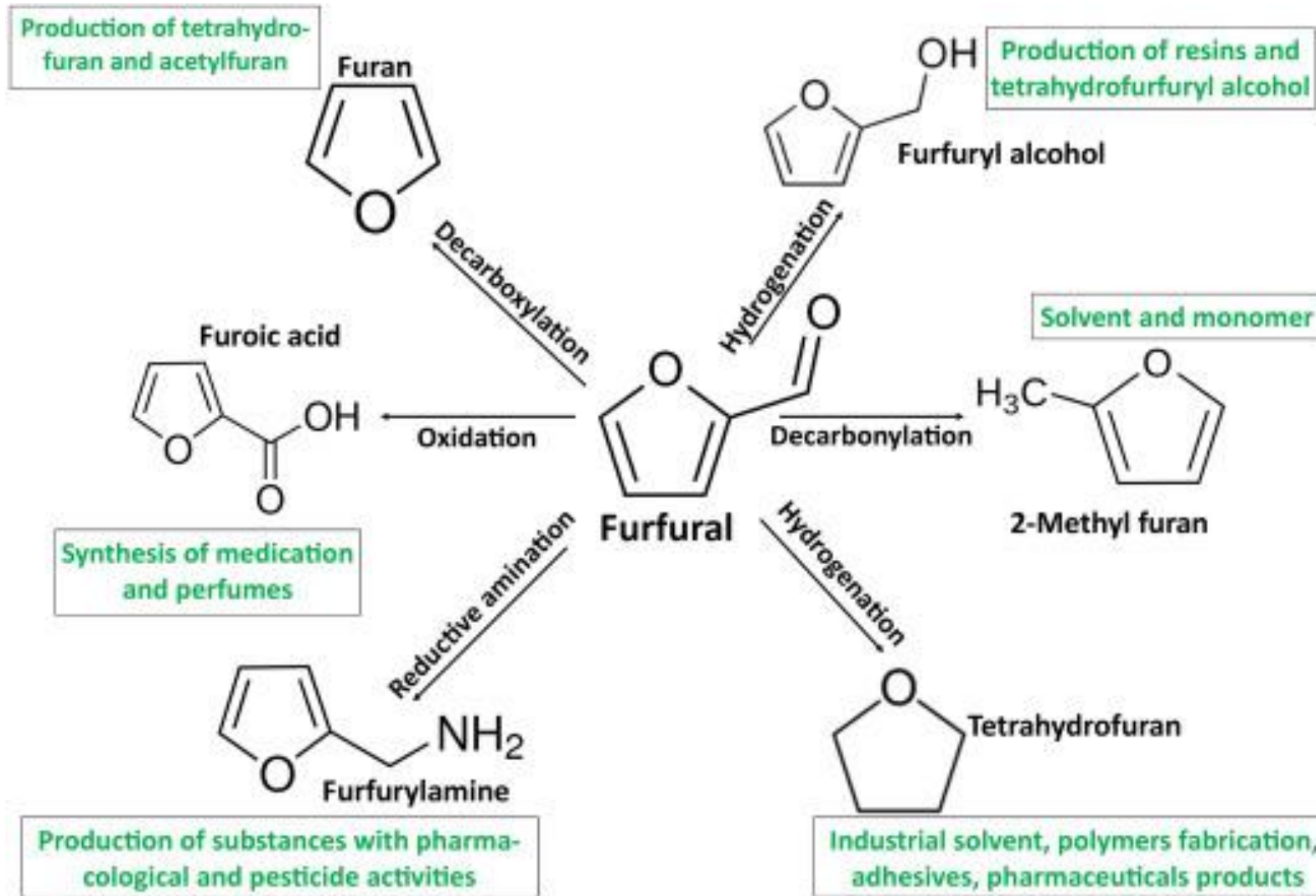
Pentosans are hydrolyzed to Xylose followed by dehydration and cyclization to give furfural

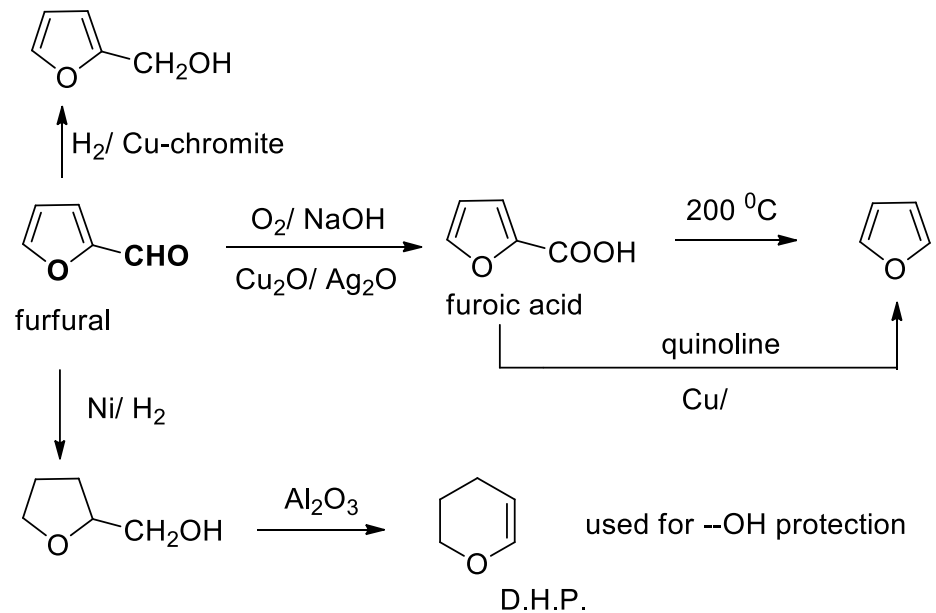


D-Xylopyranose



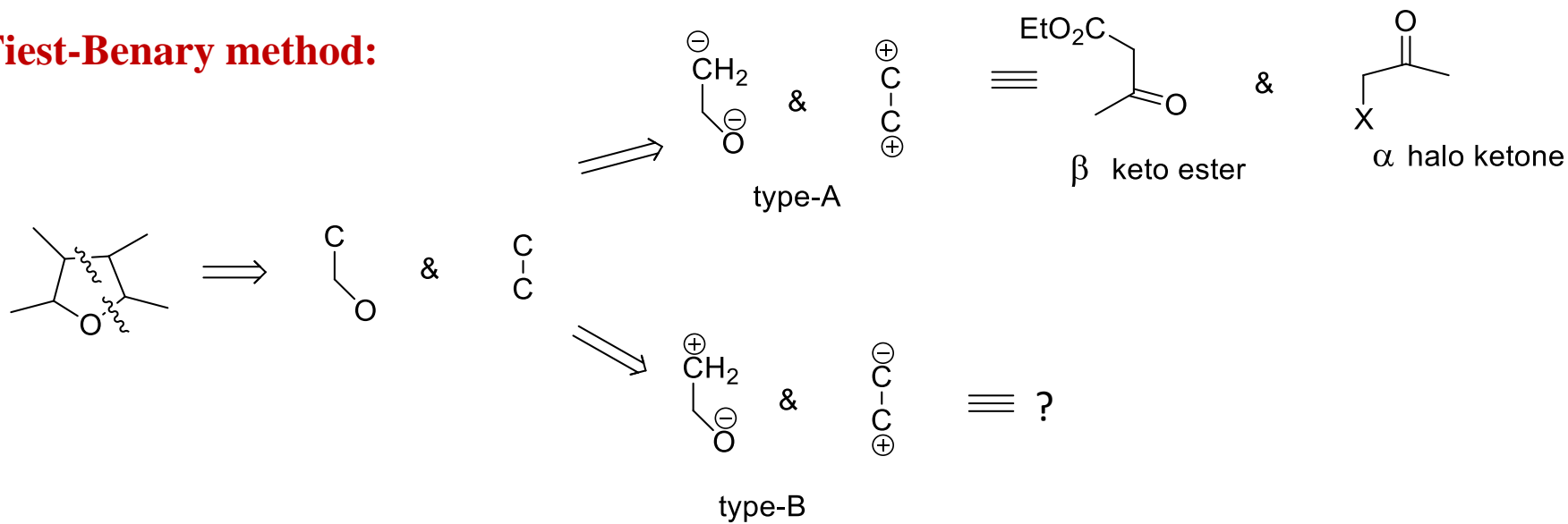
Importance of furfural



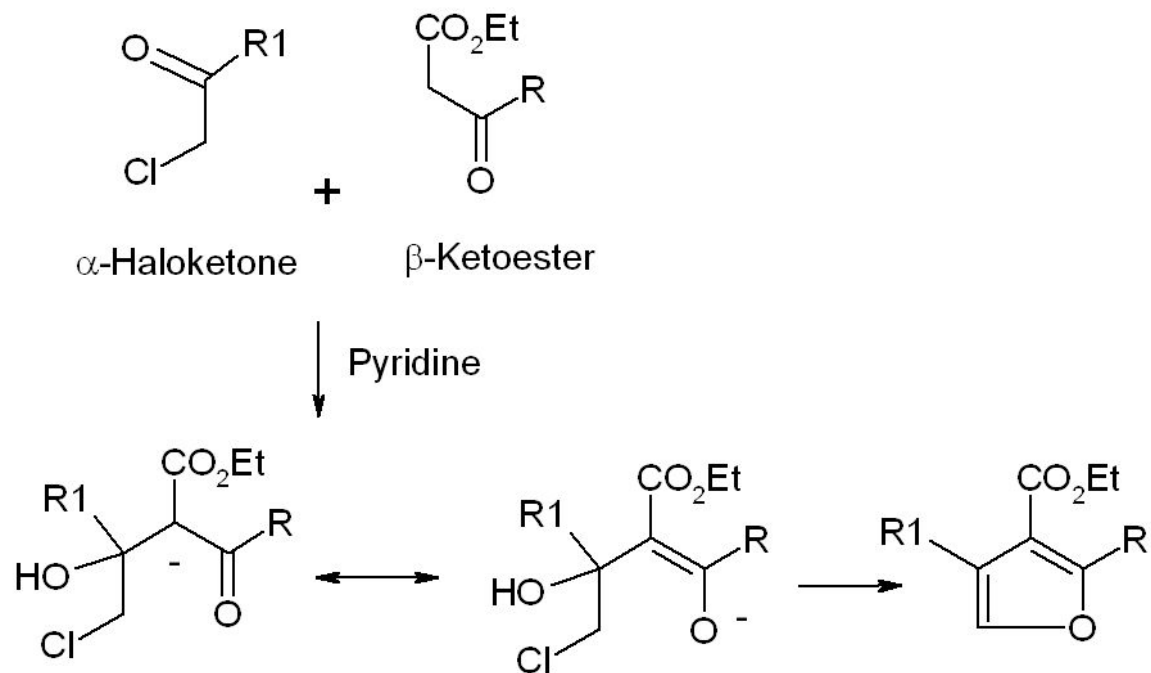


Furan Synthesis Continued:

2. Fiest-Benary method:



Feist-Benary Furane Synthesis



Example:

