Organic Chemistry II

PHA284

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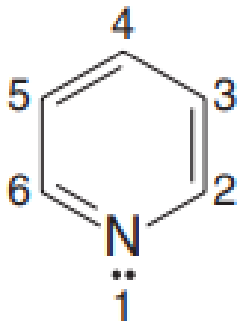
Heterocyclic Aromatic Compounds

Heterocyclic Aromatic Compounds

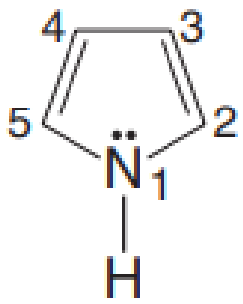
- The criteria for Hückel's rule require a ring of atoms, all with unhybridized *p* orbitals overlapping in a continuous ring. In discussing aromaticity, we have considered only compounds composed of rings of sp^2 -hybrid carbon atoms. Heterocyclic compounds, with rings containing sp^2 -hybridized atoms of other elements, can also be aromatic.

Heterocyclic Aromatic Compounds

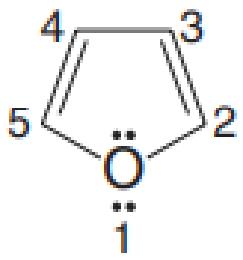
- Nitrogen, oxygen, and sulfur are the most common heteroatoms in heterocyclic aromatic compounds.



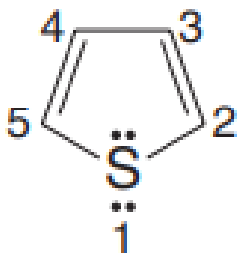
Pyridine



Pyrrole

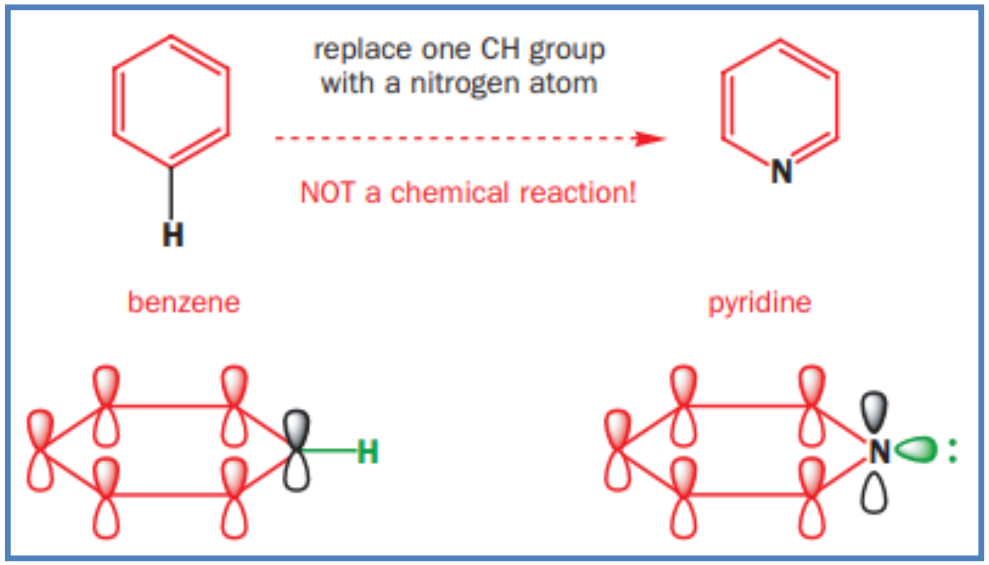


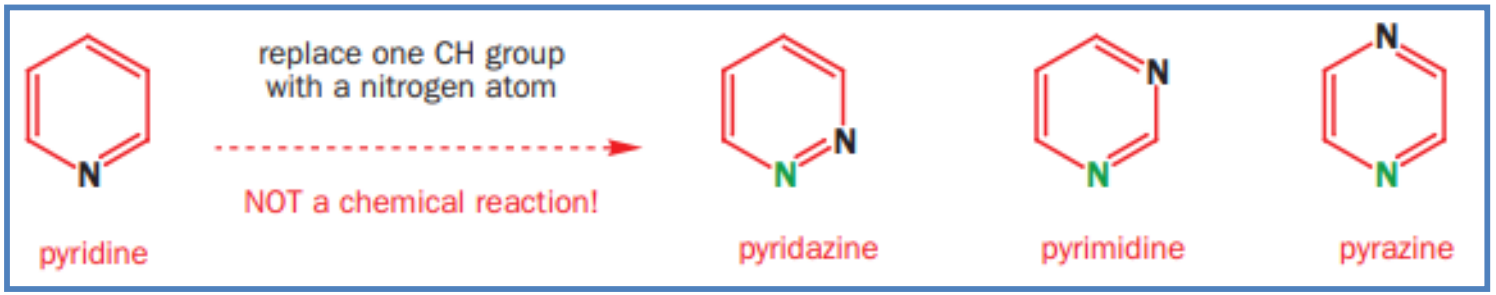
Furan



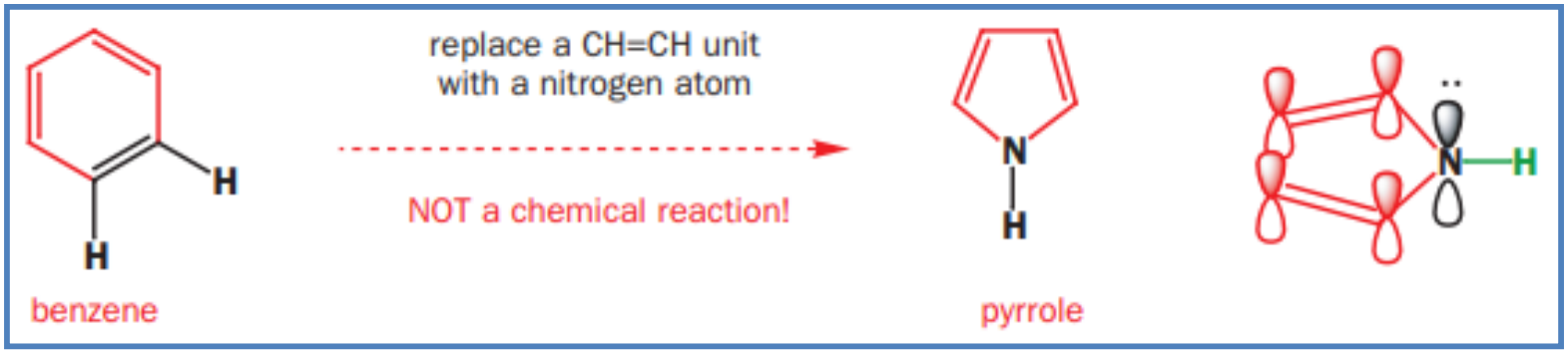
Thiophene

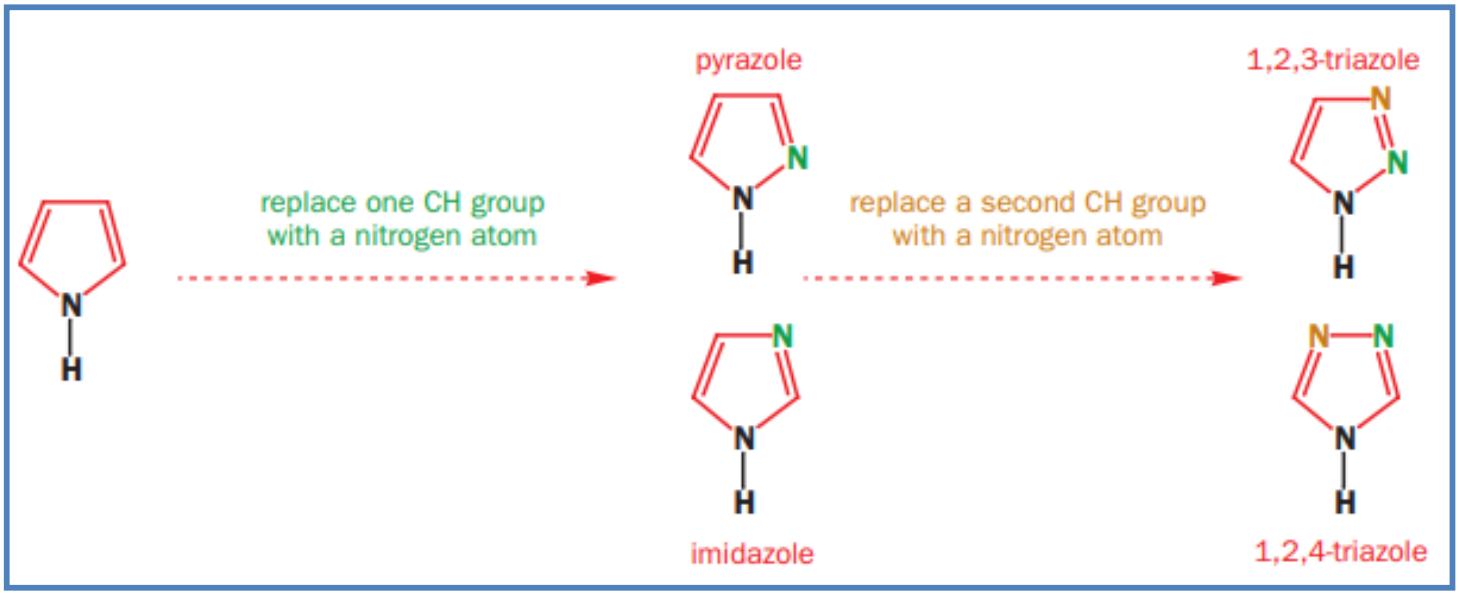
Aromatic nitrogen analogues of benzene





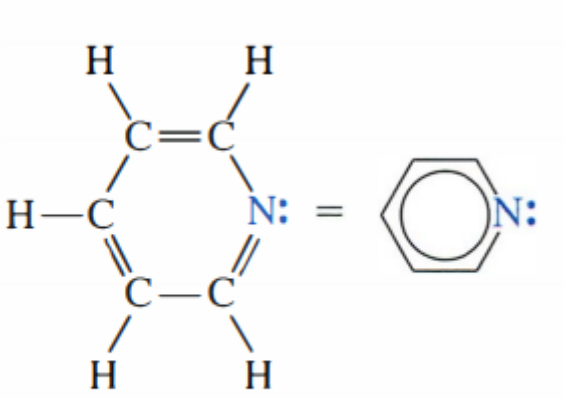
Aromatic nitrogen analogues of benzene





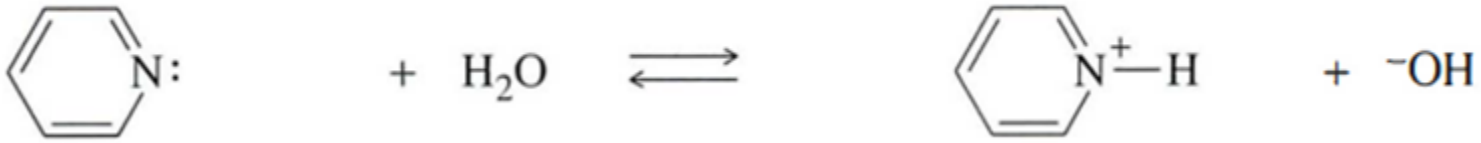
Pyridine

Pyridine is an aromatic nitrogen analogue of benzene. It has a six-membered heterocyclic ring with six pi electrons. Pyridine has a nitrogen atom in place of one of the six C - H units of benzene, and the nonbonding pair of electrons on nitrogen replaces the bond to a hydrogen atom. These nonbonding electrons are in an sp^2 -hybrid orbital in the plane of the ring. They are perpendicular to the pi system and do not overlap with it.



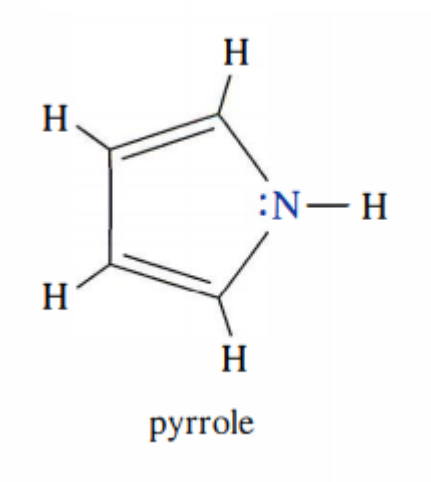
pyridine

- Pyridine shows all the characteristics of aromatic compounds. It has a resonance energy of 113 kJ/mol and it usually undergoes substitution rather than addition. Because it has an available pair of non bonding electrons, pyridine is basic.
- In an acidic solution, pyridine protonates to give the pyridinium ion. The pyridinium ion is still aromatic because the additional proton has no effect on the electrons of the aromatic sextet: It simply bonds to pyridine's nonbonding pair of electrons.



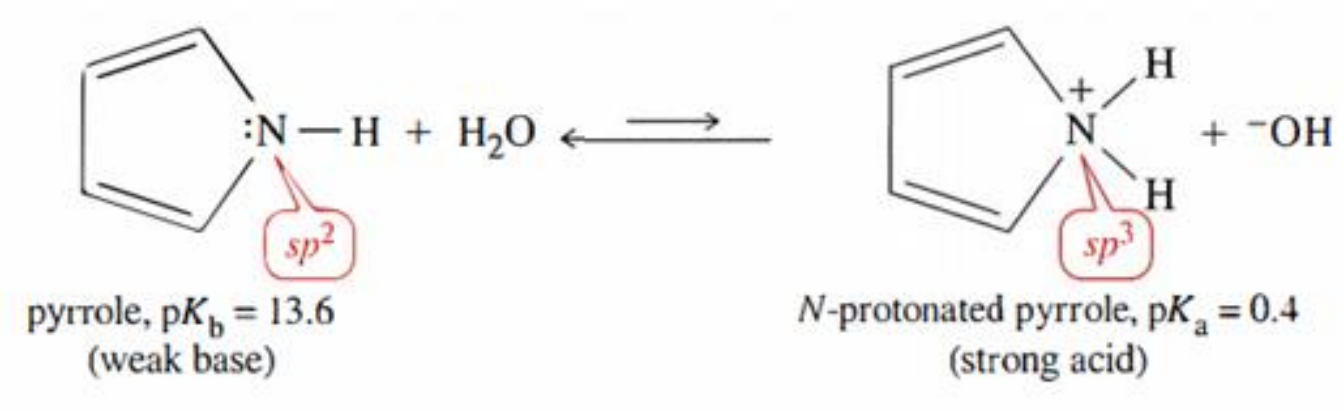
Pyrrole

Pyrrole is an aromatic five-membered heterocycle, with one nitrogen atom and two double bonds. Although it may seem that pyrrole has only four pi electrons, the nitrogen atom has a lone pair of electrons. The pyrrole nitrogen atom is sp^2. hybridized, and its unhybridized p orbital overlaps with the *p* orbitals of the carbon atoms to form a continuous ring. The lone pair on nitrogen occupies the *p* orbital, and (unlike the lone pair of pyridine) these electrons take part in the pi bonding system. These two electrons, added to the four pi electrons of the two double bonds, complete an aromatic sextet.



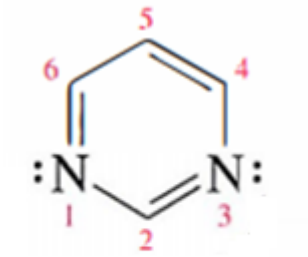
pyrrole

Pyrrole (pK_b = 13.6) is a much weaker base than pyridine (pK_b = 8.8). This difference is due to the structure of the protonated pyrrole. To form a bond to a proton requires the use of one of the electron pairs in the aromatic sextet. In the protonated pyrrole, the nitrogen atom is bonded to four different atoms (two carbon atoms and two hydrogen atoms), requiring sp^3 hybridization and leaving no unhybridized *p* orbital. The protonated pyrrole is nonaromatic. In fact, a sufficiently strong acid actually protonates pyrrole at the 2-position, on one of the carbon atoms of the ring, rather than on nitrogen.



Pyrimidine and Imidazole

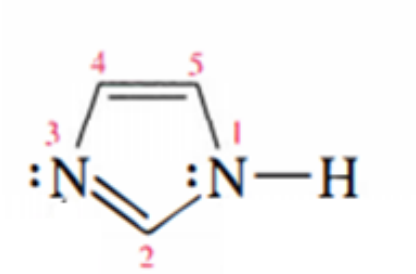
Pyrimidine is a six-membered heterocycle with two nitrogen atoms situated in a 1,3 arrangement. Both nitrogen atoms are like the pyridine nitrogen. Each has its lone pair of electrons in the sp^2 -hybrid orbital in the plane of the aromatic ring. These lone pairs are not needed for the aromatic sextet, and they are basic, like the lone pair of pyridine.



pyrimidine

Pyrimidine and Imidazole

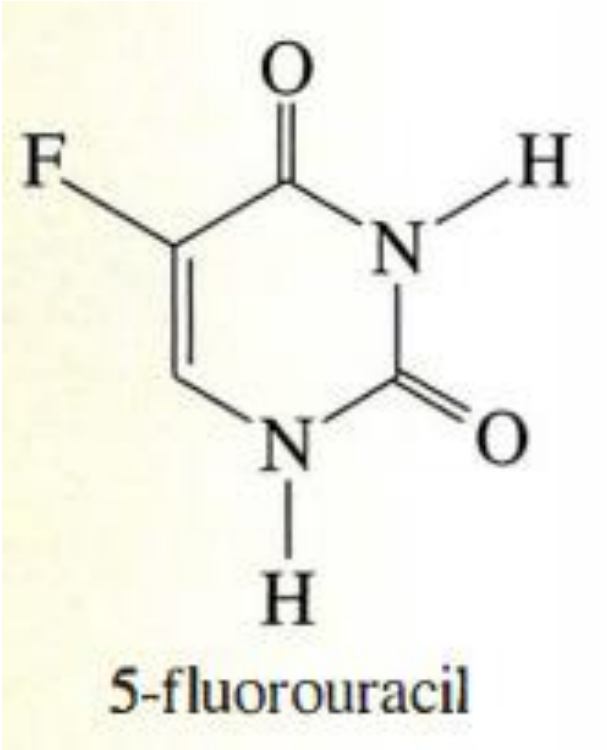
Imidazole is an aromatic five-membered heterocycle with two nitrogen atoms. The lone pair of one of the nitrogen atoms (the one not bonded to a hydrogen) is in an sp^2 orbital that is not involved in the aromatic system; this lone pair is basic. The other nitrogen uses its third sp^2 orbital to bond to hydrogen, and its lone pair is part of the aromatic sextet. Like the pyrrole nitrogen atom, this imidazole N -H nitrogen is not very basic. Once imidazole is protonated, the two nitrogen become chemically equivalent. Either nitrogen can lose a proton and return to an imidazole molecule.



imidazole

Note that;

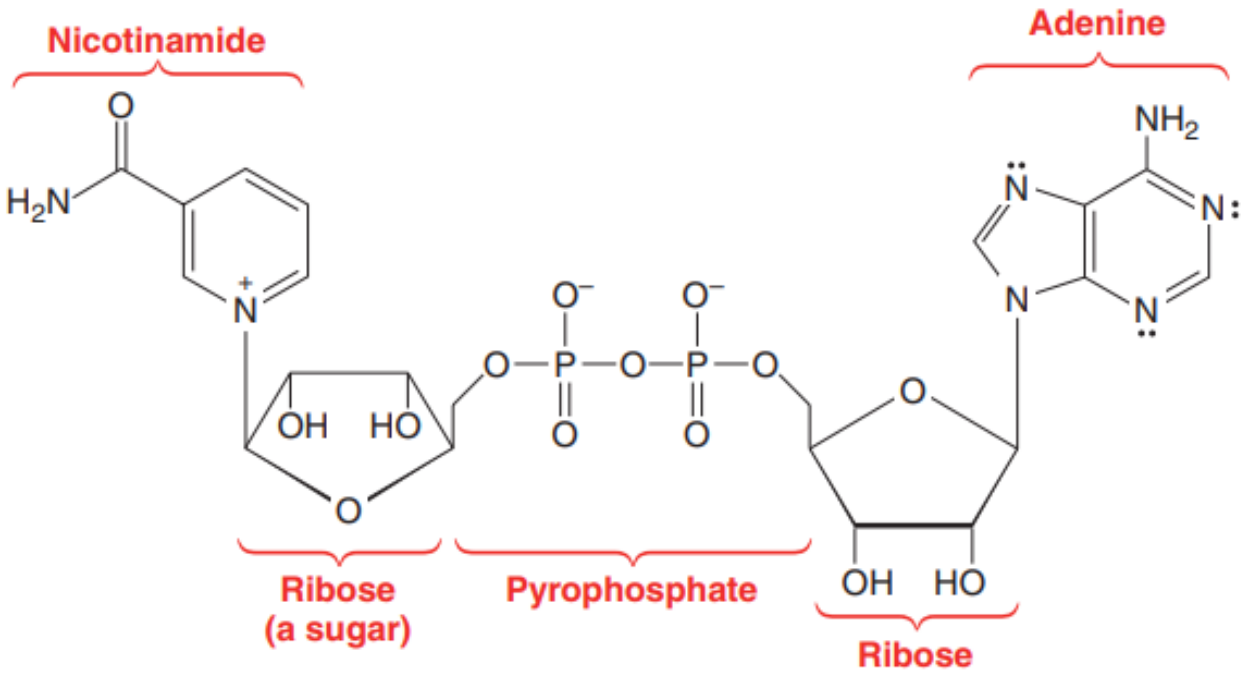
- A number of purine and pyrimidine analogs are used as anti-cancer drugs. For example, 5-fluorouracil blocks the enzyme that produces thymidine, a key base in DNA, and results in the death of many cancerous as well as some healthy cells.



5-fluorouracil

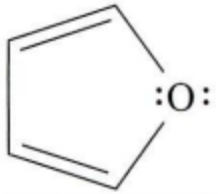
Note that;

Nicotinamide adenine dinucleotide, one of the most important coenzymes in biological oxidations and reductions, includes both a pyridine derivative (nicotinamide) and a purine derivative (adenine) in its structure.



Furan and Thiophene

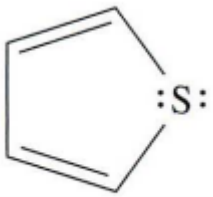
- **Furan** is an aromatic five-membered heterocycle-like pyrrole, but the heteroatom is oxygen instead of nitrogen. The classical structure for furan shows that the oxygen atom has two lone pairs of electrons. The oxygen atom is sp^2 hybridized, and one of the lone pairs occupies an sp^2-hybrid orbital. The other lone pair occupies the unhybridized *p* orbital, combining with the four electrons in the double bonds to give an aromatic sextet.



furan

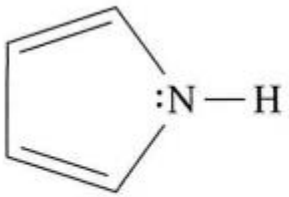
Furan and Thiophene

- **Thiophene** is similar to furan, with a sulfur atom in place of the furan oxygen. The bonding in thiophene is similar to that in furan, except that the sulfur atom uses an unhybridized 3*p* orbital to overlap with the 2*p* orbitals on the carbon atoms.

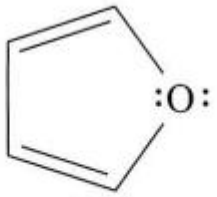


thiophene

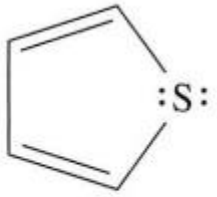
- Pyrrole, furan, and thiophene are isoelectronic. In furan and thiophene, the pyrrole N - H bond is replaced by a nonbonding pair of electrons in the sp^2-hybrid orbital.



pyrrole



furan



thiophene

References

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