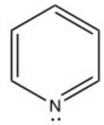
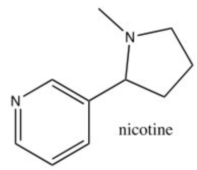
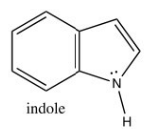
8.8: Heterocyclic Aromatic Compounds



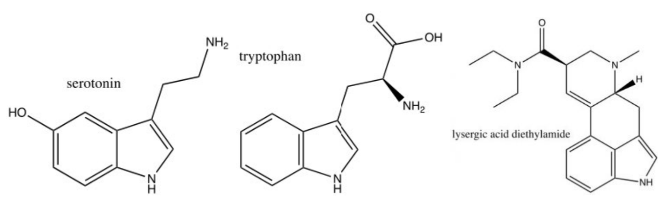
While the aromatic ions are interesting curiosities, there is a class of aromatic compounds that are of practical importance from a biological perspective: the heterocyclic aromatic compounds. These compounds typically have one or more carbons replaced by N, O, or S. For example, pyridine can be considered as the nitrogen analog of benzene. The nitrogen is sp^2 hybridized and contributes an electron to the aromatic system. Pyridine is an important component of many biological molecules; for example, nicotine, a component of the NAD and NADH oxidation/reduction system discussed earlier. The lone pair on the pyridine nitrogen sits in an sp^2 hybrid orbital at right angles to the pi system (like the $\mathrm{C-H}$ bonds) and, therefore, pyridine is basic because the lone pair is accessible. In fact, pyridine is often used as a base to react with any by-product acid such as HCl that might be produced in a reaction.





Indole is another heterocyclic aromatic system, but, in contrast to pyridine, indole uses the nitrogen lone pair to contribute the aromatic pi system. Indole has 10π electrons ($n = 2$), of which two are from the nitrogen lone pair.

Consequently, indole is not basic. The ring system of indole also appears in many biologically important molecules, including the neurotransmitter serotonin, amino acid tryptophan, and hallucinogen lysergic acid diethylamide (LSD).



There are many biologically important nitrogenous aromatic heterocycles, for example the bases in DNA and RNA all contain heterocyclic aromatic rings. For example, cytosine, which is usually written in the keto form (structure A) – which may not at first sight seem to be aromatic. However, all the atoms in the ring are planar sp^2 hybridized and there are six electrons in the ring. The result is that cytosine can exist in its tautomeric enol form (B), but the keto form is actually more stable (because of the $\mathrm{C=O}$). Both enol and keto forms are aromatic.