Heterocyclic compounds are compounds with rings that contain more than one element. The heterocyclic compounds of greatest interest to organic chemists have rings containing carbon and one or more heteroatoms—atoms other than carbon. Although the chemistry of many saturated heterocyclic compounds is analogous to that of their noncyclic counterparts, a significant number of unsaturated heterocyclic compounds exhibit aromatic behavior. The remainder of this chapter focuses primarily on the unique chemistry of a few of these aromatic heterocycles. The principles that emerge should enable you to understand the chemistry and properties of other heterocyclic compounds that you may encounter.

### 25.1 NOMENCLATURE AND STRUCTURE OF THE AROMATIC HETEROCYCLES

#### A. Nomenclature

The names and structures of some important aromatic heterocyclic compounds are given in Fig. 25.1. This figure also shows how the rings are numbered in substitutive nomenclature. In all but a few cases, a heteroatom is given the number 1. (Isoquinoline is an exception.) As illustrated by thiazole and oxazole, the convention is that oxygen and sulfur are given a lower number than nitrogen. Substituent groups are given the lowest number consistent with the ring numbering. (These are the same rules used in numbering and naming saturated heterocyclic compounds; see Secs. 8.1C and 23.1B.)

![Diagram of heterocyclic compounds]

- 3-ethylpyrrole
- 5-methoxyindole
- 2-nitrofuran
- 3-thiophenecarboxylic acid
25.1 NOMENCLATURE AND STRUCTURE OF THE AROMATIC HETEROCYCLES

PROBLEMS

25.1 Draw the structure of
(a) 4-(dimethylamino)pyridine  (b) 4-ethyl-2-nitroimidazole

25.2 Name the following compounds.
(a) (b) (c) (d)

B. Structure and Aromaticity

The aromatic heterocyclic compounds furan, thiophene, and pyrrole can be written as resonance hybrids, illustrated here for furan.

![Resonance structures of furan](image)

Because separation of charge is present in all but the first structure, the first structure is considerably more important than the others. Nevertheless, the importance of the other structures is evident in a comparison of the dipole moments of furan and tetrahydrofuran, a saturated heterocyclic ether.
The dipole moment of tetrahydrofuran is attributable mostly to the bond dipoles of its polar C—O single bonds. That is, electrons in the $\sigma$ bonds are pulled toward the oxygen because of its electronegativity. This same effect is present in furan, but in addition there is a second effect: the resonance delocalization of the oxygen unshared electrons into the ring shown in Eq. 25.1. This tends to push electrons away from oxygen into the $\pi$-electron system of the ring.

Because these two effects in furan nearly cancel, furan has a very small dipole moment. The relative boiling points of tetrahydrofuran and furan reflect the difference in their dipole moments.

Pyridine, like benzene, can be represented by two equivalent neutral resonance structures. Three additional pyridine structures of less importance reflect the relative electronegativities of nitrogen and carbon.

The aromaticity of some heterocyclic compounds was considered in the discussion of the Hückel $4n + 2$ rule (Sec. 15.7D). It is important to understand which unshared electron pairs in a heterocyclic compound are part of the $4n + 2$ aromatic $\pi$-electron system, and which are not (Fig. 25.2). Vinylic heteroatoms, such as the nitrogen of pyridine, contribute one $\pi$ electron to the six $\pi$-electron aromatic system, just like each of the carbon atoms in the $\pi$ system. The orbital containing the unshared electron pair of the pyridine nitrogen is perpendicular to the $2p$ orbitals of the ring and is therefore not involved in $\pi$ bonding. In contrast, allylic heteroatoms, such as the nitrogen of pyrrole, contribute two electrons (an unshared pair) to the
NOMENCLATURE AND STRUCTURE OF THE AROMATIC HETEROCYCLES

This nitrogen adopts \( sp^2 \) hybridization and trigonal planar geometry so that its unshared electron pair can occupy a \( 2p \) orbital, which has the optimum shape and orientation to overlap with the carbon \( 2p \) orbitals and thus to be part of the aromatic \( \pi \)-electron system. Consequently, the hydrogen of pyrrole lies in the plane of the ring. The oxygen of furan contributes one unshared electron pair to the aromatic \( \pi \)-electron system, and the other unshared electron pair occupies a position analogous to the carbon–hydrogen bond of pyrrole—in the ring plane, perpendicular to the \( 2p \) orbitals of the ring.

The empirical resonance energy can be used to estimate the additional stability of a heterocyclic compound due to its aromaticity. (This concept was introduced in the discussion of the aromaticity of benzene in Sec. 15.7C.) The empirical resonance energies of benzene and some heterocyclic compounds are given in Table 25.1. To the extent that resonance energy is a measure of aromatic character, furan has the least aromatic character of the heterocyclic compounds in the table. The modest resonance energy of furan has significant consequences for its reactivity, as we’ll learn in Sec. 25.3B.

**Table 25.1** Empirical Resonance Energies of Some Aromatic Compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>Resonance energy</th>
<th>Resonance energy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \text{kJ mol}^{-1} )</td>
<td>( \text{kcal mol}^{-1} )</td>
</tr>
<tr>
<td>benzene</td>
<td>138–151</td>
<td>33–36</td>
</tr>
<tr>
<td>pyridine</td>
<td>96–117</td>
<td>23–28</td>
</tr>
<tr>
<td>furan</td>
<td>67</td>
<td>16</td>
</tr>
</tbody>
</table>
25.3 Draw the important resonance structures for pyrrole.

25.4 (a) The dipole moments of pyrrole and pyrrolidine are similar in magnitude but have opposite directions. Explain, indicating the direction of the dipole moment in each compound. 
(Hint: Use the result in Problem 25.3.)

\[
\begin{align*}
\text{Pyrrole} & : & \mu = 1.80 \text{ D} \\
\text{Pyrrolidine} & : & \mu = 1.57 \text{ D}
\end{align*}
\]

(b) Explain why the dipole moments of furan and pyrrole have opposite directions.

(c) Should the dipole moment of 3,4-dichloropyrrole be greater than or less than that of pyrrole? Explain.

25.5 Each of the following NMR chemical shifts goes with a proton at carbon-2 of either pyridine, pyrrolidine, or pyrrole. Match each chemical shift with the appropriate heterocyclic compound, and explain your answer: \(\delta 8.51; \delta 6.41; \) and \(\delta 2.82.\)

25.2 BASICITY AND ACIDITY OF THE NITROGEN HETEROCYCLES

A. Basicity of the Nitrogen Heterocycles

Pyridine and quinoline act as ordinary amine bases.

\[
\text{Pyridine} + \text{H}_3\text{O}^+ \rightleftharpoons \text{Pyridinium} + \text{H}_2\text{O} \quad \text{pK}_a = 5.2
\]

\[
\text{Quinoline} + \text{H}_3\text{O}^+ \rightleftharpoons \text{Quinolinium} + \text{H}_2\text{O} \quad \text{pK}_a = 4.9
\]

Pyridine and quinoline are much less basic than aliphatic tertiary amines (Sec. 23.5A) because of the \(sp^2\) hybridization of their nitrogen unshared electron pairs. (Recall from Sec. 14.7A that the basicity of an unshared electron pair decreases with increasing \(s\) character.

Because pyrrole and indole look like amines, it may come as a surprise that neither of these two heterocycles has appreciable basicity. These compounds are protonated only in strong acid, and protonation occurs on carbon, not nitrogen.