CHAPTER 1

THE SCOPE OF THE FIELD OF HETEROCYCLIC CHEMISTRY

We must start out by examining what is meant by a heterocyclic ring system. To do this, we must use as examples some structures and their names, but we defer discussion of the naming systems for heterocyclic compounds to Chapter 2.

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). In practice, the most commonly found heteroatom is nitrogen, followed by oxygen and sulfur. However, many other atoms can form the stable covalent bonds necessary for ring construction and can lead to structures of considerable importance in contemporary heterocyclic chemistry. Of note are phosphorus, arsenic, antimony, silicon, selenium, tellurium, boron, and germanium. In rare cases, even elements generally considered to be metallic, such as tin and lead, can be incorporated in ring systems. In a 1983 report, the International Union of Pure and Applied Chemistry (IUPAC) recognized 15 elements coming from Groups II to IV of the Periodic System capable of forming cyclic structures with carbon atoms.

The compound 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 of benzene. 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.

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

To broaden the field, other rings may be fused onto a parent heterocycle. This gives rise to many new ring systems.

By such bonding arrangements, 133,326 different heterocyclic ring systems had been reported by 1984, and many more have been reported since then. But that is not the whole story; hydrogens on these rings can be replaced by a multitude of substituents, including all the functional groups (and others) common to aliphatic and aromatic compounds. As a result, millions of heterocyclic compounds are known, with more being synthesized every day in search of some with special properties, which we will consider in later chapters. A recent analysis of the organic compounds registered in Chemical Abstracts revealed that as of June 2007, there were 24,282,284 compounds containing cyclic structures, with heterocyclic systems making up many of these compounds.

Heterocyclic compounds are far from being just the result of some synthetic research effort. 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 (alkali like). Complex heterocyclic compounds are elaborated by microorganisms and are useful as antibiotics in medicine. Marine animals and plants are also a source of complex heterocyclic compounds and are receiving much attention in current research efforts. We should even consider that 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. Similar oxygen-containing ring structures also are important in monosaccharides, where they can be in equilibrium with ring-opened structures, as observed in the case of D-glucose.

![Chemical structures](image)

However, in this book we will not give additional attention to carbohydrates, which constitute a field all to themselves.

A low concentration of nitrogen and sulfur heterocycles also can be found in various petroleums. Coal was for years the major source of pyridine-based heterocycles, obtained by pyrolysis in the absence of oxygen (destructive distillation). An intriguing new detection of heterocycles in nature has occurred in the field of chemistry of the solar system. Pyridine carboxylic acids have been detected in a meteorite that landed in Canada (near Tagish Lake). Nicotinic acid and its two isomers were isolated along with 12 methylated and other derivatives.
Here, great caution had to be exerted to ensure that contamination by terrestrial compounds had not occurred. One wonders what other heterocycles can be detected (and confirmed) in the current intensive research activity in astrochemistry. In this connection, molecules known as porphyrins that contain the porphin nucleus have been tentatively identified spectroscopically on the moon.

As we shall find in later chapters, heterocyclic compounds can be synthesized in many ways. Although some of this work is performed to study fundamental properties or establish new synthetic routes, much more is concerned with the practical aspects of heterocyclic chemistry. Thus, many synthetic (as well as natural) 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. These applications are discussed in Chapter 11. Medicinal chemistry especially is associated intimately with heterocyclic compounds, and most of all known chemicals used in medicine are based on heterocyclic frameworks. We shall observe many of the prominent biologically active heterocyclic compounds as this book proceeds to develop the field of heterocyclic chemistry.

Is heterocyclic chemistry somehow different from the much more familiar aliphatic and aromatic chemistry studied in basic organic chemistry courses? Certainly, many reactions used to close rings and to modify ring substituents are common to these fields, and as they are encountered, the reader should review them in a basic organic chemistry textbook. However, some reactions can be found only in heterocyclic chemistry. An excellent example is the cycloaddition of 1,3-dipolar compounds with unsaturated groups, as in the example that follows, which has no counterpart in purely carbon chemistry.
Heterocyclic compounds find use in other synthetic processes. In some cases, heterocyclic ring systems can be opened to give valuable non-cyclic compounds useful in synthetic work. Acting through their lone electron pairs or pi-systems, they can be useful ligands 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.

A large amount of literature is available on the subject of heterocyclic chemistry. There are advanced textbooks to help expand the knowledge imparted in this book, and there are expansive collections that cover almost all types of heterocycles and are exhaustive in providing methods of synthesis and treatment of their properties. Information on these books is given in the Appendix of this chapter. Particularly valuable is the series *Comprehensive Heterocyclic Chemistry*, and this is often the first place to go for detailed information on a particular heterocyclic family. The third edition (2008) consists of 15 volumes. Other series cover physical properties or provide detailed reviews of topics or compound families in heterocyclic chemistry. There are also many books on specific topics or types of heterocycles, but these are not listed in the Appendix.

**REFERENCES**


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APPENDIX

1. Some textbooks published since 1980 include the following:

2. Reference works

