CHAPTER 1

Localized Chemical Bonding

Localized chemical bonding may be defined as bonding in which the electrons are shared by two and only two nuclei. In Chapter 2, we will consider *delocalized bonding*, in which electrons are shared by more than two nuclei.

COVALENT BONDING[1]

Wave mechanics is based on the fundamental principle that electrons behave as waves (e.g., they can be diffracted) and that consequently a wave equation can be written for them, in the same sense that light waves, sound waves, and so on can be described by wave equations. The equation that serves as a mathematical model for electrons is known as the *Schrödinger equation*, which for a one-electron system is

$$\frac{\delta^2\psi}{\delta x^2}+\frac{\delta^2\psi}{\delta y^2}+\frac{\delta^2\psi}{\delta z^2}+\frac{8\pi^2 m}{h^2}(E-V)\psi=0$$

where m is the mass of the electron, E is its total energy, V is its potential energy, and h is Planck's constant. In physical terms, the function Ψ expresses the square root of the probability of finding the electron at any position defined by the coordinates x, y, and z, where the origin is at the nucleus. For systems containing more than one electron, the equation is similar, but more complicated.

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[1] The treatment of orbitals given here is necessarily simplified. For much fuller treatments of orbital theory as applied to organic chemistry, see Matthews, P.S.C. *Quantum Chemistry of Atoms and Molecules*, Cambridge University Press, Cambridge, ***1986***; Clark, T. *A Handbook of Computational Chemistry*, Wiley, NY, ***1985***; Albright, T.A.; Burdett, J.K.; Whangbo, M. *Orbital Interactions in Chemistry*, Wiley, NY, ***1985***; MacWeeny, R.M. *Coulson's Valence*, Oxford University Press, Oxford, ***1980***; Murrell, J.N.; Kettle, S.F.A; Tedder, J.M. *The Chemical Bond*, Wiley, NY, ***1978***; Dewar, M.J.S.; Dougherty. R.C. *The PMO Theory of Organic Chemistry*, Plenum, NY, ***1975***; Zimmerman, H.E. *Quantum Mechanics for Organic Chemists*, Academic Press, NY, ***1975***; Borden, W.T. *Modern Molecular Orbital Theory for Organic Chemists*, Prentice-Hall, Englewood Cliffs, NJ, ***1975***; Dewar, M.J.S. *The Molecular Orbital Theory of Organic Chemistry*, McGraw-Hill, NY, ***1969***; Liberles, A. *Introduction to Molecular Orbital Theory*, Holt, Rinehart, and Winston, NY, ***1966***.

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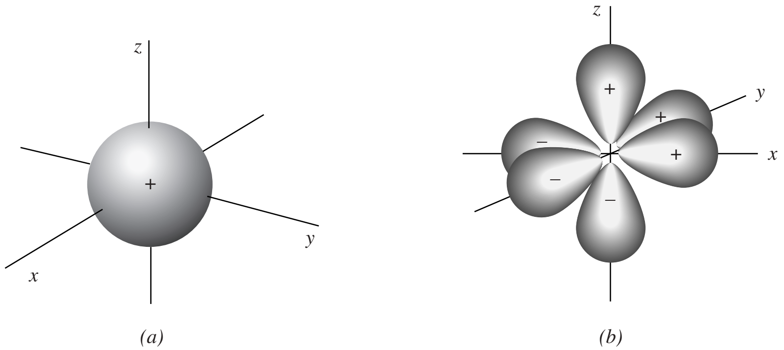

Fig. 1.1. (*a*) The 1*s* orbital. (*b*) The three 2*p* orbitals.

The Schrödinger equation is a differential equation, which means that solutions of it are themselves equations, but the solutions are not differential equations. They are simple equations for which graphs can be drawn. Such graphs, which are three-dimensional (3D) pictures that show the electron density, are called *orbitals* or electron clouds. Most students are familiar with the shapes of the *s* and *p* atomic orbitals (Fig. 1.1). Note that each *p* orbital has a *node*: A region in space where the probability of finding the electron is extremely small.[2] Also note that in Fig. 1.1 some lobes of the orbitals are labeled + and others −. These signs do not refer to positive or negative *charges*, since both lobes of an electron cloud must be negatively charged. They are the signs of the wave function Ψ. When two parts of an orbital are separated by a node, Ψ always has opposite signs on the two sides of the node. According to the Pauli exclusion principle, no more than two electrons can be present in any orbital, and they must have opposite spins.

Unfortunately, the Schrödinger equation can be solved exactly only for one-electron systems, such as the hydrogen atom. If it could be solved exactly for molecules containing two or more electrons,[3] we would have a precise picture of the shape of the orbitals available to each electron (especially for the important ground state) and the energy for each orbital. Since exact solutions are not available, drastic approximations must be made. There are two chief general methods of approximation: the molecular-orbital method and the valence-bond method.

In the molecular-orbital method, bonding is considered to arise from the overlap of atomic orbitals. When any number of atomic orbitals overlap, they combine to

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[2] When wave-mechanical calculations are made according to the Schrödinger equation, the probability of finding the electron in a node is zero, but this treatment ignores relativistic considerations. When such considerations are applied, Dirac has shown that nodes do have a very small electron density: Powell, R.E. *J. Chem. Educ.* ***1968***, *45*, 558. See also, Ellison, F.O. and Hollingsworth, C.A. *J. Chem. Educ.* ***1976***, *53*, 767; McKelvey, D.R. *J. Chem. Educ.* ***1983***, *60*, 112; Nelson, P.G. *J. Chem. Educ.* ***1990***, *67*, 643. For a review of relativistic effects on chemical structures in general, see Pyykkö, P. *Chem. Rev.* ***1988***, *88*, 563.

[3] For a number of simple systems containing two or more electrons, such as the H_2 molecule or the He atom, approximate solutions are available that are so accurate that for practical purposes they are as good as exact solutions. See, for example, Roothaan, C.C.J.; Weiss, A.W. *Rev. Mod. Phys.* ***1960***, *32*, 194; Kolos, W.; Roothaan, C.C.J. *Rev. Mod. Phys.* ***1960***, *32*, 219. For a review, see Clark, R.G.; Stewart, E.T. *Q. Rev. Chem. Soc.* ***1970***, *24*, 95.

form an equal number of new orbitals, called *molecular orbitals*. Molecular orbitals differ from atomic orbitals in that they are clouds that surround the nuclei of two or more atoms, rather than just one atom. In localized bonding the number of atomic orbitals that overlap is two (each containing one electron), so that two molecular orbitals are generated. One of these, called a *bonding orbital*, has a lower energy than the original atomic orbitals (otherwise a bond would not form), and the other, called an *antibonding orbital*, has a higher energy. Orbitals of lower energy fill first. Since the two original atomic orbitals each held one electron, both of these electrons can now go into the new molecular *bonding* orbital, since any orbital can hold two electrons. The antibonding orbital remains empty in the ground state. The greater the overlap, the stronger the bond, although total overlap is prevented by repulsion between the nuclei. Figure 1.2 shows the bonding and antibonding orbitals that arise by the overlap of two 1*s* electrons. Note that since the antibonding orbital has a node between the nuclei, there is practically no electron density in that area, so that this orbital cannot be expected to bond very well. Molecular orbitals formed by the overlap of two atomic orbitals when the centers of electron density are on the axis common to the two nuclei are called σ (*sigma*) orbitals, and the bonds are called σ bonds. Corresponding antibonding orbitals are designated σ^*. Sigma orbitals are formed not only by the overlap of two *s* orbitals, but also by the overlap of any of the kinds of atomic orbital (*s, p, d*, or *f*) whether the same or different, but the two lobes that overlap must have the same sign: a positive *s* orbital can form a bond only by overlapping with another positive *s* orbital or with a positive lobe of a *p, d*, or *f* orbital. Any *s* orbital, no matter what kind of atomic orbitals it has arisen from, may be represented as approximately ellipsoidal in shape.

Orbitals are frequently designated by their symmetry properties. The σ orbital of hydrogen is often written ψ_g. The *g* stands for *gerade*. A gerade orbital is one in which the sign on the orbital does not change when it is inverted through its center of symmetry. The σ^* orbital is *ungerade* (designated ψ_u). An ungerade orbital changes sign when inverted through its center of symmetry.

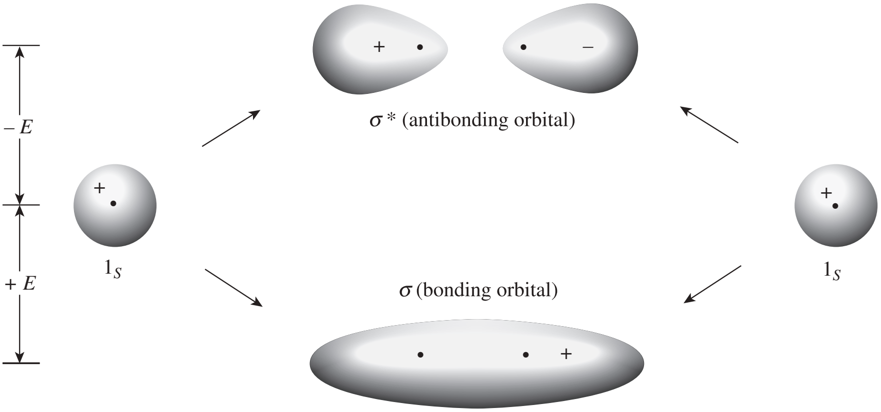

Fig. 1.2. Overlap of two 1*s* orbitals gives rise to a σ and a σ^* orbital.

In molecular-orbital calculations, a wave function is formulated that is a linear combination of the atomic orbitals that have overlapped (this method is often called the *linear combination of atomic orbitals*, or LCAO). Addition of the atomic orbitals gives the bonding molecular orbital:

$$\psi = c_A\psi_A + c_B\psi_B \tag{1-1}$$

The functions ψ_A and ψ_B are the functions for the atomic orbitals of atoms A and B, respectively, and c_A and c_B represent weighting factors. Subtraction is also a linear combination:

$$\psi = c_A\psi_A - c_B\psi_B \tag{1-2}$$

This gives rise to the antibonding molecular orbital.

In the valence-bond method, a wave equation is written for each of various possible electronic structures that a molecule may have (each of these is called a *canonical form*), and the total ψ is obtained by summation of as many of these as seem plausible, each with its weighting factor:

$$\psi = c_1\psi_1 + c_2\psi_2 + \cdots \tag{1-3}$$

This resembles Eq. (1), but here each ψ represents a wave equation for an imaginary canonical form and each c is the amount contributed to the total picture by that form. For example, a wave function can be written for each of the following canonical forms of the hydrogen molecule:[4]

$$\text{H–H} \qquad \text{H:}^- \quad \text{H}^+ \qquad {}^+\text{H} \quad \text{H:}^-$$

Values for c in each method are obtained by solving the equation for various values of each c and choosing the solution of lowest energy. In practice, both methods give similar solutions for molecules that contain only localized electrons, and these are in agreement with the Lewis structures long familiar to the organic chemist. Delocalized systems are considered in Chapter 2.

MULTIPLE VALENCE

A univalent atom has only one orbital available for bonding. But atoms with a valence of 2 or more must form bonds by using at least two orbitals. An oxygen atom has two half-filled orbitals, giving it a valence of 2. It forms single bonds by the overlap of these with the orbitals of two other atoms. According to the principle of maximum overlap, the other two nuclei should form an angle of 90° with the oxygen nucleus, since the two available orbitals on oxygen are *p* orbitals, which are perpendicular. Similarly, we should expect that nitrogen, which has three mutually perpendicular *p* orbitals, would have bond angles of 90° when it forms three single bonds. However, these are not the observed bond angles. The bond

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[4] In this book, a pair of electrons, whether in a bond or unshared, is represented by a straight line.

angles are,[5] in water, 104°27′, and in ammonia, 106°46′. For alcohols and ethers the angles are even larger (see p. 25). A discussion of this will be deferred to p. 25, but it is important to note that covalent compounds do have definite bond angles. Although the atoms are continuously vibrating, the mean position is the same for each molecule of a given compound.

HYBRIDIZATION

Consider the case of mercury. Its electronic structure is

$$[\mathbf{Xe}\ \text{core}]4f^{14}5d^{10}6s^{2}$$

Although it has no half-filled orbitals, it has a valence of 2 and forms two covalent bonds. We can explain this by imagining that one of the 6*s* electrons is promoted to a vacant 6*p* orbital to give the excited configuration

$$[\mathbf{Xe}\ \text{core}]4f^{14}5d^{10}6s^{1}6p^{1}$$

In this state, the atom has two half-filled orbitals, but they are not equivalent. If bonding were to occur by the overlap of these orbitals with the orbitals of external atoms, the two bonds would not be equivalent. The bond formed from the 6*p* orbital would be more stable than the one formed from the 6*s* orbital, since a larger amount of overlap is possible with the former. A more stable situation is achieved when, in the course of bond formation, the 6*s* and 6*p* orbitals combine to form two new orbitals that *are* equivalent; these are shown in Fig. 1.3.

Since these new orbitals are a mixture of the two original orbitals, they are called *hybrid orbitals*. Each is called an *sp* orbital, since a merger of an *s* and a *p* orbital was required to form it. The *sp* orbitals, each of which consists of a large lobe and a very small one, are atomic orbitals, although they arise only in the bonding process and do not represent a possible structure for the free atom. A mercury atom forms

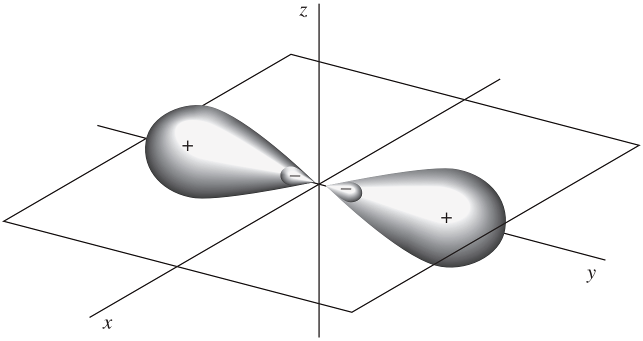

Fig. 1.3. The two *sp* orbitals formed by mercury.

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[5] Bent, H.A. *Chem. Rev.* ***1961***, *61*, 275, p. 277.

its two bonds by overlapping each of the large lobes shown in Fig. 1.3 with an orbital from an external atom. This external orbital may be any of the atomic orbitals previously considered (*s, p, d*, or *f*) or it may be another hybrid orbital, although only lobes of the same sign can overlap. In any of these cases, the molecular orbital that arises is called a σ orbital since it fits our previous definition of a σ orbital.

In general, because of mutual repulsion, equivalent orbitals lie as far away from each other as possible, so the two *sp* orbitals form an angle of 180°. This means that $HgCl_2$, for example, should be a linear molecule (in contrast to H_2O), and it is. This kind of hybridization is called *digonal hybridization*. An *sp* hybrid orbital forms a stronger covalent bond than either an *s* or a *p* orbital because it extends out in space in the direction of the other atom's orbital farther than the *s* or the *p* and permits greater overlap. Although it would require energy to promote a 6*s* electron to the 6*p* state, the extra bond energy more than makes up the difference.

Many other kinds of hybridization are possible. Consider boron, which has the electronic configuration

$$1s^2 2s^2 2p^1$$

yet has a valence of 3. Once again we may imagine promotion and hybridization:

$$1s^2 2s^2 2p^1 \xrightarrow{\text{promotion}} 1s^2 2s^1 2p_x^1 2p_y^1 \xrightarrow{\text{hybridization}} 1s^2 (sp^2)^3$$

In this case, there are three equivalent hybrid orbitals, each called sp^2 (*trigonal hybridization)*. This method of designating hybrid orbitals is perhaps unfortunate since nonhybrid orbitals are designated by single letters, but it must be kept in mind that *each* of the three orbitals is called sp^2. These orbitals are shown in Fig. 1.4. The three axes are all in one plane and point to the corners of an equilateral triangle. This accords with the known structure of BF_3, a planar molecule with angles of 120°.

The case of carbon (in forming four single bonds) may be represented as

$$1s^2 2s^2 2p_x^1 2p_y^1 \xrightarrow{\text{promotion}} 1s^2 2s^1 2p_x^1 2p_y^1 2p_z^1 \xrightarrow{\text{hybridization}} 1s^2 (sp^3)^4$$

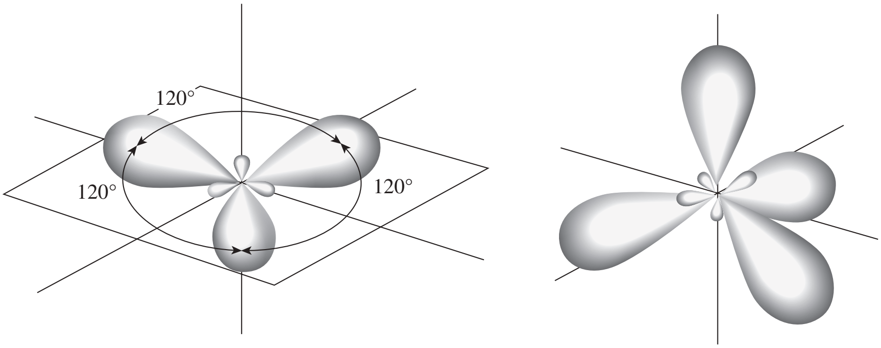

Fig. 1.4. The three sp^2 and the four sp^3 orbitals.

There are four equivalent orbitals, each called sp^3, which point to the corners of a regular tetrahedron (Fig. 1.4). The bond angles of methane would thus be expected to be 109°28′, which is the angle for a regular tetrahedron.

Although the hybrid orbitals discussed in this section satisfactorily account for most of the physical and chemical properties of the molecules involved, it is necessary to point out that the sp^3 orbitals, for example, stem from only one possible approximate solution of the Schrödinger equation. The *s* and the three *p* atomic orbitals can also be combined in many other equally valid ways. As we shall see on p. 13, the four C—H bonds of methane do not always behave as if they are equivalent.

MULTIPLE BONDS

If we consider the ethylene molecule in terms of the molecular-orbital concepts discussed so far, we have each carbon using sp^2 orbitals to form bonds with the three atoms to which it is connected. These sp^2 orbitals arise from hybridization of the $2s^1$, $2p_x^1$, and $2p_y^1$ electrons of the promoted state shown on p. 8. We may consider that any carbon atom that is bonded to only three different atoms uses sp^2 orbitals for this bonding. Each carbon of ethylene is thus bonded by three σ bonds: one to each hydrogen and one to the other carbon. Each carbon therefore has another electron in the $2p_z$ orbital that is perpendicular to the plane of the sp^2 orbitals. The two parallel $2p_z$ orbitals can overlap sideways to generate two new orbitals, a bonding and an antibonding orbital (Fig. 1.5). Of course, in the ground state, both electrons go into the bonding orbital and the antibonding orbital remains vacant. Molecular orbitals formed by the overlap of atomic orbitals whose axes are parallel are called π orbitals if they are bonding and π^* if they are antibonding.

In this picture of ethylene, the two orbitals that make up the double bond are not equivalent.[6] The σ orbital is ellipsoidal and symmetrical about the C—C axis. The π orbital is in the shape of two ellipsoids, one above the plane and one below. The plane itself represents a node for the π orbital. In order for the *p* orbitals to maintain maximum overlap, they must be parallel. This means that free rotation is not possible about the double bond, since the two *p* orbitals would have to reduce their overlap to allow one H—C—H plane to rotate with respect to the other. The six atoms of a double bond are therefore in a plane with angles that should be $\sim$120°. Double bonds are shorter than the corresponding single bonds because maximum stability is obtained when the *p* orbitals overlap as much as possible. Double bonds between carbon and oxygen or nitrogen are similarly represented: they consist of one σ and one π orbital.

In triple-bond compounds, carbon is connected to only two other atoms and hence uses *sp* hybridization, which means that the four atoms are in a straight

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[6] The double bond can also be pictured as consisting of two equivalent orbitals, where the centers of electron density point away from the C—C axis. This is the bent-bond or banana-bond picture. Support for this view is found in Pauling. L. *Theoretical Organic Chemistry, The Kekulé Symposium*, Butterworth, London, ***1959***, pp. 2–5; Palke, W.E. *J. Am. Chem. Soc.* ***1986***, *108*, 6543. However, most of the literature of organic chemistry is written in terms of the σ–π picture, and we will use it in this book.

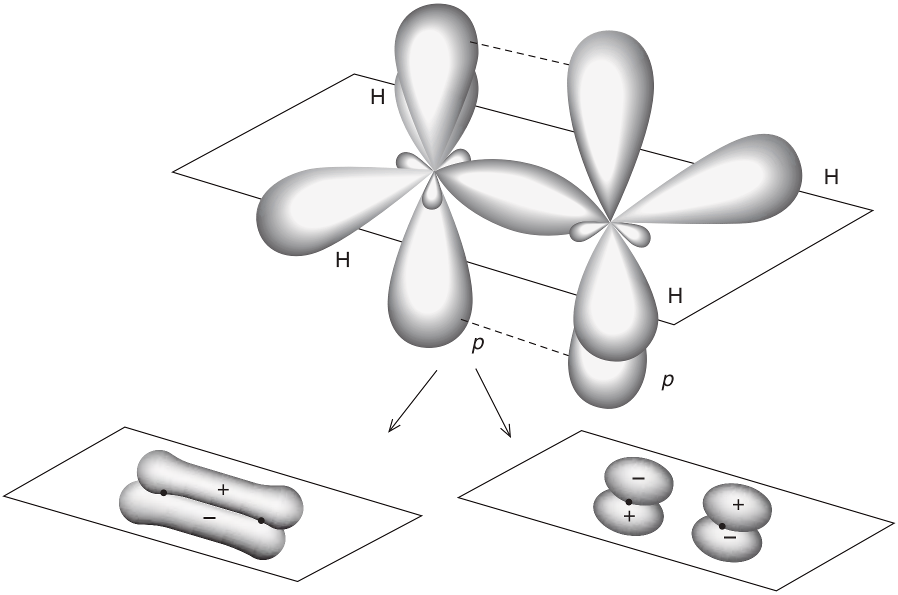

Fig. 1.5. Overlapping *p* orbitals form a π and a π* orbital. The σ orbitals are shown in the upper figure. They are still there in the states represented by the diagrams below, but have been removed from the picture for clarity.

line (Fig. 1.6).[7] Each carbon has two *p* orbitals remaining, with one electron in each. These orbitals are perpendicular to each other and to the C—C axis. They overlap in the manner shown in Fig. 1.7 to form two π orbitals. A triple bond is thus composed of one σ and two π orbitals. Triple bonds between carbon and nitrogen can be represented in a similar manner.

Double and triple bonds are important only for the first-row elements carbon, nitrogen, and oxygen.[8] For second-row elements multiple bonds are rare and

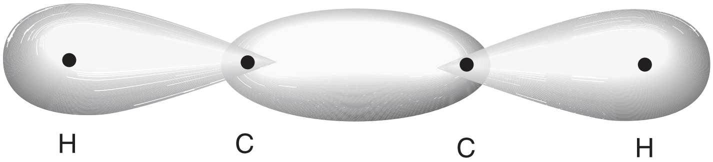

Fig. 1.6. The σ electrons of acetylene.

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[7] For reviews of triple bonds, see Simonetta, M.; Gavezzotti, A., in Patai, S. *The Chemistry of the Carbon-Carbon Triple Bond*, Wiley, NY, ***1978***, pp. 1–56; Dale, J., in Viehe, H. G. *Acetylenes*, Marcel Dekker, NY, ***1969***, pp. 3–96.

[8] This statement applies to the representative elements. Multiple bonding is also important for some transition elements. For a review of metal–metal multiple bonds, see Cotton, F.A. *J. Chem. Educ.* ***1983***, *60*, 713.

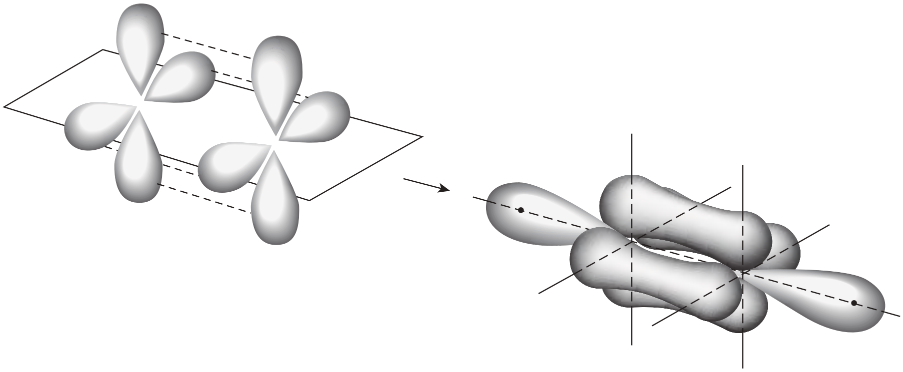

Fig. 1.7. Overlap of p orbitals in a triple bond for clarity, the σ orbitals have been removed from the drawing on the left, although they are shown on the right.

compounds containing them are generally less stable[9] because these elements tend to form weaker π bonds than do the first-row elements.[10] The only ones of any importance at all are C=S bonds, and C=S compounds are generally much less stable than the corresponding C=O compounds (however, see *p*π–*d*π bonding, p. $$$). Stable compounds with Si=C and Si=Si bonds are rare, but examples have been reported,[11] including a pair of cis and trans Si=Si isomers.[12]

[9] For a review of double bonds between carbon and elements other than C, N, S, or O, see Jutzi, P. *Angew. Chem. Int. Ed.* ***1975***, *14*, 232. For reviews of multiple bonds involving silicon and germanium, see Barrau, J.; Escudié, J.; Satgé, J. *Chem. Rev.* ***1990***, *90*, 283 (Ge only); Raabe, G.; Michl, J., in Patai, S. and Rappoport, Z. *The Chemistry of Organic Silicon Compounds, part 2*, Wiley: NY, ***1989***, pp. 1015–1142; *Chem. Rev.* ***1985***, *85*, 419 (Si only); Wiberg, N. *J. Organomet. Chem.* ***1984***, *273*, 141 (Si only); Gusel'nikov, L.E.; Nametkin, N.S. *Chem. Rev.* ***1979***, *79*, 529 (Si only). For reviews of C=P and C+P bonds, see Regitz, M. *Chem. Rev.* ***1990***, *90*, 191; Appel, R.; Knoll, F. *Adv. Inorg. Chem.* ***1989***, *33*, 259; Markovski, L.N.; Romanenko, V.D. *Tetrahedron* ***1989***, *45*, 6019. For reviews of other second-row double bonds, see West, R. *Angew. Chem. Int. Ed.* ***1987***, *26*, 1201 (Si=Si bonds); Brook, A.G.; Baines, K.M. *Adv. Organometal. Chem.* ***1986***, *25*, 1 (Si=C bonds); Kutney, G.W.; Turnbull, K. *Chem. Rev.* ***1982***, *82*, 333 (S=S bonds). For reviews of multiple bonds between heavier elements, see Cowley, A.H.; Norman, N.C. *Prog. Inorg. Chem.* ***1986***, *34*, 1; Cowley, A.H. *Polyhedron* ***1984***, *3*, 389; *Acc. Chem. Res.* ***1984***, *17*, 386. For a theoretical study of multiple bonds to silicon, see Gordon, M.S. *Mol. Struct. Energ.* ***1986***, *1*, 101.

[10] For discussions, see Schmidt, M.W.; Truong, P.N.; Gordon, M.S. *J. Am. Chem. Soc.* ***1987***, *109*, 5217; Schleyer, P. von R.; Kost, D. *J. Am. Chem. Soc.* ***1988***, *110*, 2105.

[11] For Si=C bonds, see Brook, A.G.; Nyburg, S.C.; Abdesaken, F.; Gutekunst, B.; Gutekunst, G.; Kallury, R.K.M.R.; Poon, Y.C.; Chang, Y.; Wong-Ng, W. *J. Am. Chem. Soc.* ***1982***, *104*, 5667; Schaefer III, H.F. *Acc. Chem. Res.* ***1982***, *15*, 283; Wiberg, N.; Wagner, G.; Riede, J.; Müller, G. *Organometallics* ***1987***, *6*, 32. For Si=Si bonds, see West, R.; Fink, M.J.; Michl, J. *Science* ***1981***, *214*, 1343; Boudjouk, P.; Han, B.; Anderson, K.R. *J. Am. Chem. Soc.* ***1982***, *104*, 4992; Fink, M.J.; DeYoung, D.J.; West, R.; Michl, J. *J. Am. Chem. Soc.* ***1983***, *105*, 1070; Fink, M.J.; Michalczyk, M.J.; Haller, K.J.; West, R.; Michl, J. *Organometallics* ***1984***, *3*, 793; West, R. *Pure Appl. Chem.* ***1984***, *56*, 163; Masamune, S.; Eriyama, Y.; Kawase, T. *Angew. Chem. Int. Ed.* ***1987***, *26*, 584; Shepherd, B.D.; Campana, C.F.; West, R. *Heteroat. Chem.* ***1990***, *1*, 1. For an Si=N bond, see Wiberg, N.; Schurz, K.; Reber, G.; Müller, G. *J. Chem. Soc. Chem. Commun.* ***1986***, 591.

[12] Michalczyk, M.J.; West, R.; Michl, J. *J. Am. Chem. Soc.* ***1984***, *106*, 821, *Organometallics* ***1985***, *4*, 826.

PHOTOELECTRON SPECTROSCOPY

Although the four bonds of methane are equivalent according to most physical and chemical methods of detection (e.g., neither the nuclear magnetic resonances (NMR) nor the infrared (IR) spectrum of methane contains peaks that can be attributed to different kinds of C—H bonds), there is one physical technique that shows that the eight valence electrons of methane can be differentiated. In this technique, called *photoelectron spectroscopy*,[13] a molecule or free atom is bombarded with vacuum ultraviolet (UV) radiation, causing an electron to be ejected. The energy of the ejected electron can be measured, and the difference between the energy of the radiation used and that of the ejected electron is the *ionization potential* of that electron. A molecule that contains several electrons of differing energies can lose any one of them as long as its ionization potential is less than the energy of the radiation used (a single molecule loses only one electron; the loss of two electrons by any individual molecule almost never occurs). A photoelectron spectrum therefore consists of a series of bands, each corresponding to an orbital of a different energy. The spectrum gives a direct experimental picture of all the orbitals present, in order of their energies, provided that radiation of sufficiently high energy is used.[14] Broad

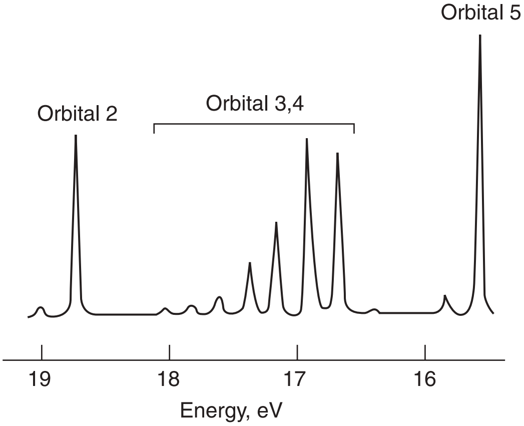

Fig. 1.8. Photoelectron spectrum of N_2.[15]

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[13] Only the briefest description of this subject is given here. For monographs, see Ballard, R.E. *Photoelectron Spectroscopy and Molecular Orbital Theory*, Wiley, NY, ***1978***; Rabalais, J.W., *Principles of Ultraviolet Photoelectron Spectroscopy*, Wiley, NY, ***1977***; Baker, A.D.; Betteridge, D. *Photoelectron Spectroscopy*, Pergamon, Elmsford, NY, ***1972***; Turner, D.W.; Baker, A.D..; Baker, C.; Brundle, C.R. *High Resolution Molecular Photoelectron Spectroscopy*, Wiley, NY, ***1970***. For reviews, see Westwood, N.P.C. *Chem. Soc. Rev.* ***1989***, *18*, 317; Carlson, T.A. *Annu. Rev. Phys. Chem.* ***1975***, *26*, 211; Baker, C.; Brundle, C.R.; Thompson, M. *Chem. Soc. Rev.* ***1972***, *1*, 355; Bock, H.; Mollère, P.D. *J. Chem. Educ.* ***1974***, *51*, 506; Bock, H.; Ramsey, B.G. *Angew. Chem. Int. Ed.* ***1973***, *12*, 734; Turner, D.W. *Adv. Phys. Org. Chem.* ***1966***, *4*, 31. For the IUPAC descriptive classification of the electron spectroscopies, see Porter, H.Q.; Turner, D.W. *Pure Appl. Chem.* ***1987***, *59*, 1343.

[14] The correlation is not perfect, but the limitations do not seriously detract from the usefulness of the method. The technique is not limited to vacuum UV radiation. Higher energy radiation can also be used.

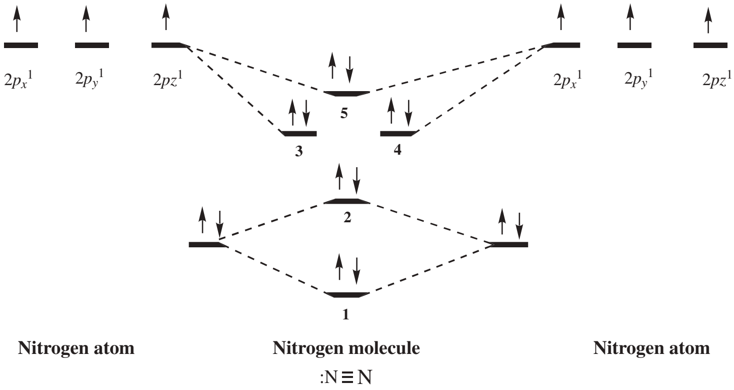

Fig. 1.9. Electronic structure of N_2 (inner-shell electrons omitted).

bands usually correspond to strongly bonding electrons and narrow bands to weakly bonding or nonbonding electrons. A typical spectrum is that of N_2, shown in Fig. 1.8.[15] The N_2 molecule has the electronic structure shown in Fig. 1.9. The two 2*s* orbitals of the nitrogen atoms combine to give the two orbitals marked 1 (bonding) and 2 (antibonding), while the six 2*p* orbitals combine to give six orbitals, three of which (marked 3, 4, and 5) are bonding. The three antibonding orbitals (not indicated in Fig. 1.9) are unoccupied. Electrons ejected from orbital 1 are not found in Fig. 1.8 because the ionization potential of these electrons is greater than the energy of the light used (they can be seen when higher energy light is used). The broad band in Fig. 1.8 (the individual peaks within this band are caused by different vibrational levels; see Chapter 7) corresponds to the four electrons in the degenerate orbitals 3 and 4. The triple bond of N_2 is therefore composed of these two orbitals and orbital 1. The bands corresponding to orbitals 2 and 5 are narrow; hence these orbitals contribute little to the bonding and may be regarded as the two unshared pairs of $\ddot{N}{\equiv}\ddot{N}$. Note that this result is contrary to that expected from a naive consideration of orbital roverlaps, where it would be expected that the two unshared pairs would be those of orbitals 1 and 2, resulting from the overlap of the filled 2*s* orbitals, and that the triple bond would be composed of orbitals 3, 4, and 5, resulting from overlap of the *p* orbitals. This example is one illustration of the value of photoelectron spectroscopy.

The photoelectron spectrum of methane[16] shows two bands,[17] at ~23 and 14 eV, and not the single band we would expect from the equivalency of the four C—H

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[15] From Brundle, C.R.; Robin, M.B., in Nachod, F.C.; Zuckerman, J.J. *Determination of Organic Structures by Physical Methods, Vol. 3*, Academic Press, NY, ***1971***, p. 18.

[16] Brundle, C.R.; Robin, M.B.; Basch, H. *J. Chem. Phys.* ***1970***, *53*, 2196; Baker, A.D.; Betteridge, D.; Kemp, N.R.; Kirby, R.E. *J. Mol. Struct.* ***1971***, *8*, 75; Potts, A.W.; Price, W.C. *Proc. R. Soc. London, Ser A* ***1972***, *326*, 165.

[17] A third band, at 290 eV, caused by the 1*s* electrons of carbon, can also found if radiation of sufficiently high energy is used.

bonds. The reason is that ordinary sp^3 hybridization is not adequate to explain phenomena involving ionized molecules (e.g., the CH_4^+ radical ion, which is left behind when an electron is ejected from methane). For these phenomena it is necessary to use other combinations of atomic orbitals (see p. 9). The band at 23 eV comes from two electrons in a low-energy level (called the a_1 level), which can be regarded as arising from a combination of the 2*s* orbital of carbon with an appropriate combination of hydrogen 1*s* orbitals. The band at 14 eV comes from six electrons in a triply degenerate level (the t_2 level), arising from a combination of the three 2*p* orbitals of carbon with other combinations of 1*s* hydrogen orbitals. As was mentioned above, most physical and chemical processes cannot distinguish these levels, but photoelectron spectroscopy can. The photoelectron spectra of many other organic molecules are known as well,[18] including monocyclic alkenes, in which bands <10 eV are due to π-orbital ionization and those >10 eV originate from ionization of s-orbitals only.[19]

ELECTRONIC STRUCTURES OF MOLECULES

For each molecule, ion, or free radical that has only localized electrons, it is possible to draw an electronic formula, called a *Lewis structure*, that shows the location of these electrons. Only the valence electrons are shown. Valence electrons may be found in covalent bonds connecting two atoms or they may be unshared.[20] The student must be able to draw these structures correctly, since the position of electrons changes in the course of a reaction, and it is necessary to know where the electrons are initially before one can follow where they are going. To this end, the following rules operate:

1. The total number of valence electrons in the molecule (or ion or free radical) must be the sum of all outer-shell electrons "contributed" to the molecule by each atom plus the negative charge or minus the positive charge, for the case of ions. Thus, for H_2SO_4, there are 2 (one for each hydrogen) + 6 (for the sulfur) + 24 (6 for each oxygen) = 32; while for SO_4^{2-}, the number is also 32, since each atom "contributes" 6 plus 2 for the negative charge.
2. Once the number of valence electrons has been ascertained, it is necessary to determine which of them are found in covalent bonds and which are unshared. Unshared electrons (either a single electron or a pair) form part of the outer shell of just one atom, but electrons in a covalent bond are part of the outer shell of both atoms of the bond. *First-row atoms* (B, C, N, O, F) *can have a maximum of eight valence electrons*, and usually have this number, although some cases are known where a first-row atom has only six or seven.

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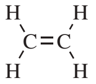
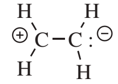
[18] See Robinson, J.W., *Practical Handbook of Spectroscopy*, CRC Press, Boca Raton, FL, ***1991***, p. 178.

[19] Novak, I.; Potts, A.W. *Tetrahedron* ***1997***, *53*, 14713.

[20] It has been argued that although the Lewis picture of two electrons making up a covalent bond may work well for organic compounds, it cannot be successfully applied to the majority of inorganic compounds: Jørgensen, C.K. *Top. Curr. Chem.* ***1984***, *124*, 1.

Where there is a choice between a structure that has six or seven electrons around a first-row atom and one in which all such atoms have an octet, it is the latter that generally has the lower energy and that consequently exists. For example, ethylene is


and not

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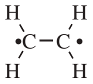
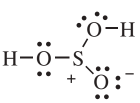
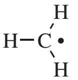


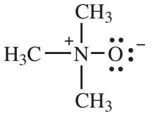
There are a few exceptions. In the case of the molecule O_2, the structure $:\dot{O}-\dot{O}:$ has a lower energy than $:\ddot{O}=\ddot{O}:$. Although first-row atoms are limited to 8 valence electrons, this is not so for second-row atoms, which can accommodate 10 or even 12 because they can use their empty *d* orbitals for this purpose.[21] For example, PCl_5 and SF_6 are stable compounds. In SF_6, one *s* and one *p* electron from the ground state $3s^23p^4$ of the sulfur are promoted to empty *d* orbitals, and the six orbitals hybridize to give six sp^3d^2 orbitals, which point to the corners of a regular octahedron.

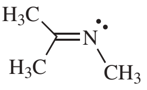
3. It is customary to show the formal charge on each atom. For this purpose, an atom is considered to "own" all unshared electrons, but only *one-half of the electrons in covalent bonds*. The sum of electrons that thus "belong" to an atom is compared with the number "contributed" by the atom. An excess belonging to the atom results in a negative charge, and a deficiency results in a positive charge. The total of the formal charges on all atoms equals the charge on the whole molecule or ion. Note that the counting procedure is not the same for determining formal charge as for determining the number of valence electrons. For both purposes, an atom "owns" all unshared electrons, but for outer-shell purposes it "owns" both the electrons of the covalent bond, while for formal-charge purposes it "owns" only one-half of these electrons.

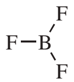
Examples of electronic structures are (as mentioned in Ref. 4, an electron pair, whether unshared or in a bond, is represented by a straight line):



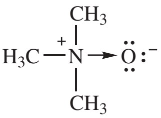








A coordinate-covalent bond, represented by an arrow, is one in which both electrons come from the same atom; that is, the bond can be regarded as being formed by the overlap of an orbital containing two electrons with an empty one. Thus trimethylamine oxide would be represented



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[21] For a review concerning sulfur compounds with a valence shell larger than eight, see Salmond, W.G. *Q. Rev. Chem. Soc.* ***1968***, *22*, 235.

For a coordinate-covalent bond the rule concerning formal charge is amended, so that both electrons count for the donor and neither for the recipient. Thus the nitrogen and oxygen atoms of trimethylamine oxide bear no formal charges. However, it is apparent that the electronic picture is exactly the same as the picture of trimethylamine oxide given just above, and we have our choice of drawing an arrowhead or a charge separation. Some compounds, for example, amine oxides, must be drawn one way or the other. It seems simpler to use charge separation, since this spares us from having to consider as a "different" method of bonding a way that is really the same as ordinary covalent bonding once the bond has formed.

ELECTRONEGATIVITY

The electron cloud that bonds two atoms is not symmetrical (with respect to the plane that is the perpendicular bisector of the bond) except when the two atoms are the same and have the same substituents. The cloud is necessarily distorted toward one side of the bond or the other, depending on which atom (nucleus plus electrons) maintains the greater attraction for the cloud. This attraction is called *electronegativity*;[22] and it is greatest for atoms in the upper-right corner of the periodic table and lowest for atoms in the lower-left corner. Thus a bond between fluorine and chlorine is distorted so that there is a higher probability of finding the electrons near the fluorine than near the chlorine. This gives the fluorine a partial negative charge and the chlorine a partial positive charge.

A number of attempts have been made to set up quantitative tables of electronegativity that indicate the direction and extent of electron-cloud distortion for a bond between any pair of atoms. The most popular of these scales, devised by Pauling, is based on bond energies (see p. 27) of diatomic molecules. It is rationalized that if the electron distribution were symmetrical in a molecule A—B, the bond energy would be the mean of the energies of A—A and B—B, since in these cases the cloud must be undistorted. If the actual bond energy of A—B is higher than this (and it usually is), it is the result of the partial charges, since the charges attract each other and make a stronger bond, which requires more energy to break. It is necessary to assign a value to one element arbitrarily ($F = 4.0$). Then the electronegativity of another is obtained from the difference between the actual energy of A—B and the mean of A—A and B—B (this difference is called Δ) by the formula

$$x_A - x_B = \sqrt{\frac{\Delta}{23.06}}$$

where x_A and x_B are the electronegativities of the known and unknown atoms and 23.06 is an arbitrary constant. Part of the scale derived from this treatment is shown in Table 1.1.

[22] For a collection of articles on this topic, see Sen, K.D.; Jørgensen, C.K. *Electronegativity* (Vol. 6 of *Structure and Bonding*); Springer: NY, ***1987***. For a review, see Batsanov, S.S. *Russ. Chem. Rev.* ***1968***, *37*, 332.

TABLE 1.1. Electronegativities of Some Atoms on the Pauling[23] and Sanderson[24] Scales

Element	Pauling	Sanderson	Element	Pauling	Sanderson
F	4.0	4.000	H	2.1	2.592
O	3.5	3.654	P	2.1	2.515
Cl	3.0	3.475	B	2.0	2.275
N	3.0	3.194	Si	1.8	2.138
Br	2.8	3.219	Mg	1.2	1.318
S	2.5	2.957	Na	0.9	0.835
I	2.5	2.778	Cs	0.7	0.220
C	2.5	2.746			

Other treatments[25] have led to scales that are based on different principles, for example, the average of the ionization potential and the electron affinity,[26] the average one-electron energy of valence-shell electrons in ground-state free atoms,[27] or the "compactness" of an atom's electron cloud.[24] In some of these treatments electronegativities can be calculated for different valence states, for different hybridizations (e.g., *sp* carbon atoms are more electronegative than sp^2, which are still more electronegative than sp^3),[28]and even differently for primary, secondary, and tertiary carbon atoms. Also, electronegativities can be calculated for groups rather than atoms (Table 1.2).[29]

Electronegativity information can be obtained from NMR spectra. In the absence of a magnetically anisotropic group[30]the chemical shift of a ^{1}H or a ^{13}C nucleus is approximately proportional to the electron density around it and hence to the electronegativity of the atom or group to which it is attached. The greater the electronegativity of the atom or group, the lower the electron density around the proton, and the further downfield the chemical shift. An example of the use of this correlation is found in the variation of chemical shift of the *ring* protons in the series

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[23] Taken from Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, p. 93, except for the value for Na, which is from Sanderson, R.T. *J. Am. Chem. Soc.* ***1983***, *105*, 2259; *J. Chem. Educ.* ***1988***, *65*, 112, 223.

[24] See Sanderson, R.T. *J. Am. Chem. Soc.* ***1983***, *105*, 2259; *J. Chem. Educ.* ***1988***, *65*, 112, 223.

[25] For several sets of electronegativity values, see Huheey, J.E. *Inorganic Chemistry*, 3rd ed., Harper and Row: NY, ***1983***, pp. 146–148; Mullay, J., in Sen, K.D.; Jørgensen, C.K. *Electronegativity* (Vol. 6 of *Structure and Bonding*), Springer, NY, ***1987***, p. 9.

[26] Mulliken, R.S. *J. Chem. Phys.* ***1934***, *2*, 782; Iczkowski, R.P.; Margrave, J.L. *J. Am. Chem. Soc.* ***1961***, *83*, 3547; Hinze, J.; Jaffé, H.H. *J. Am. Chem. Soc.* ***1962***, *84*, 540; Rienstra-Kiracofe, J.C.; Tschumper, G.S.; Schaefer III, H.F.; Nandi, S.; Ellison, G.B. *Chem. Rev.* ***2002***, *102*, 231.

[27] Allen, L.C. *J. Am. Chem. Soc.* ***1989***, *111*, 9003.

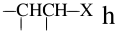
[28] Walsh, A.D. *Discuss. Faraday Soc.* ***1947***, *2*, 18; Bergmann, D.; Hinze, J., in Sen, K.D.; Jørgensen, C.K. *Electronegativity* (Vol. 6 of *Structure and Bonding*), Springer, NY, ***1987***, pp. 146–190.

[29] Inamoto, N.; Masuda, S. *Chem. Lett.* ***1982***, 1003. For a review of group electronegativities, see Wells, P.R. *Prog. Phys. Org. Chem.* ***1968***, *6*, 111. See also Bratsch, S.G. *J. Chem. Educ.*, ***1988***, *65*, 223; Mullay, J. *J. Am. Chem. Soc.* ***1985***, *107*, 7271; Zefirov, N.S.; Kirpichenok, M.A.; Izmailov, F.F.; Trofimov, M.I. *Dokl. Chem.* ***1987***, *296*, 440; Boyd, R.J.; Edgecombe, K.E. *J. Am. Chem. Soc.* ***1988***, *110*, 4182.

[30] A magnetically anisotropic group is one that is not equally magnetized along all three axes. The most common such groups are benzene rings (see p. 55) and triple bonds.

TABLE 1.2. Some Group Electronegativites Relative to H = 2.176.[29]

CH_3	2.472	**CCl_3**	2.666
CH_3CH_2	2.482	**C_6H_5**	2.717
CH_2Cl	2.538	**CF_3**	2.985
CBr_3	2.561	**$C{\equiv}N$**	3.208
$CHCl_2$	2.602	**NO_2**	3.421

toluene, ethylbenzene, isopropylbenzene, *tert*-butylbenzene (there is a magnetically anisotropic group here, but its effect should be constant throughout the series). It is found that the electron density surrounding the ring protons decreases[31] in the order given.[32] However, this type of correlation is by no means perfect, since all the measurements are being made in a powerful field, which itself may affect the electron density distribution. Coupling constants between the two protons of a system  $-\underset{|}{C}H\underset{|}{C}H-X$ have also been found to depend on the electronegativity of X.[33]

When the difference in electronegativities is great, the orbital may be so far over to one side that it barely covers the other nucleus. This is an *ionic bond*, which is seen to arise naturally out of the previous discussion, leaving us with basically only one type of bond in organic molecules. Most bonds can be considered intermediate between ionic and covalent. We speak of percent ionic character of a bond, which indicates the extent of electron-cloud distortion. There is a continuous gradation from ionic to covalent bonds.

DIPOLE MOMENT

The *dipole moment* is a property of the molecule that results from charge separations like those discussed above. However, it is not possible to measure the dipole moment of an individual bond within a molecule; we can measure only the total moment of the molecule, which is the vectorial sum of the individual bond moments.[34] These individual moments are roughly the same from molecule to molecule,[35] but this constancy is by no means universal. Thus, from the dipole moments of toluene and nitrobenzene (Fig. 1.10)[36] we should expect the moment of *p*-nitrotoluene to be ~4.36 D.

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[31] This order is opposite to that expected from the field effect (p. 19). It is an example of the Baker–Nathan order (p. 96).

[32] Moodie, R.B.; Connor, T.M.; Stewart, R. *Can. J. Chem.* ***1960***, *38*, 626.

[33] Williamson, K.L. *J. Am. Chem. Soc.* ***1963***, *85*, 516; Laszlo, P.; Schleyer, P.v.R. *J. Am. Chem. Soc.* ***1963***, *85*, 2709; Niwa, J. *Bull. Chem. Soc. Jpn.* ***1967***, *40*, 2192.

[34] For methods of determining dipole moments and discussions of their applications, see Exner, O. *Dipole Moments in Organic Chemistry*; Georg Thieme Publishers: Stuttgart, ***1975***. For tables of dipole moments, see McClellan, A.L. *Tables of Experimental Dipole Moments*, Vol. 1; W.H. Freeman: San Francisco, ***1963***; Vol. 2, Rahara Enterprises: El Cerrito, CA, ***1974***.

[35] For example, see Koudelka, J.; Exner, O. *Collect. Czech. Chem. Commun.* ***1985***, *50*, 188, 200.

[36] The values for toluene, nitrobenzene, and *p*-nitrotoluene are from MacClellan, A.L., *Tables of Experimental Dipole Moments*, Vol. 1, W.H. Freeman, San Francisco, ***1963***; Vol. 2, Rahara Enterprises, El Cerrito, CA, ***1974***. The values for phenol and *p*-cresol were determined by Goode, E.V.; Ibbitson, D.A. *J. Chem. Soc.* ***1960***, 4265.

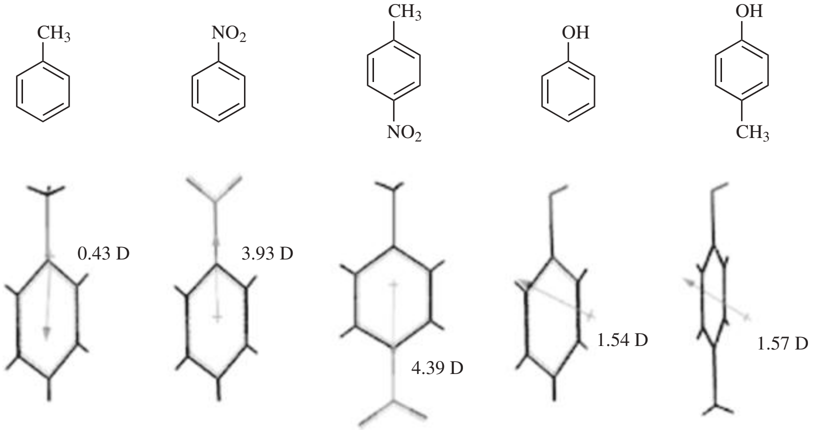


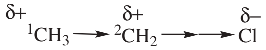
Fig. 1.10. Some dipole moments, in debye units, measured in benzene. In the 3D model, the arrow indicates the direction of the dipole moment for the molecule, pointing to the negative part of the molecule.[36]

The actual value 4.39 D is reasonable. However, the moment of *p*-cresol (1.57 D) is quite far from the predicted value of 1.11 D. In some cases, molecules may have substantial individual bond moments but no total moments at all because the individual moments are canceled out by the overall symmetry of the molecule. Some examples are CCl_4, *trans*-1,2-dibromoethene, and *p*-dinitrobenzene.

Because of the small difference between the electronegativities of carbon and hydrogen, alkanes have very small dipole moments, so small that they are difficult to measure. For example, the dipole moment of isobutane is 0.132 D[37] and that of propane is 0.085 D.[38] Of course, methane and ethane, because of their symmetry, have no dipole moments.[39] Few organic molecules have dipole moments >7 D.

INDUCTIVE AND FIELD EFFECTS

The C—C bond in ethane has no polarity because it connects two equivalent atoms. However, the C—C bond in chloroethane is polarized by the presence of the electronegative chlorine atom. This polarization is actually the sum of two effects. In the first of these, the C-1 atom, having been deprived of some of its electron density by the


$$\overset{\delta+}{{}^{1}CH_3} \longrightarrow \overset{\delta+}{{}^{2}CH_2} \longrightarrow\!\!\longrightarrow \overset{\delta-}{Cl}$$

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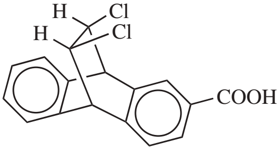
[37] Maryott, A.A.; Birnbaum, G. *J. Chem. Phys.* **1956**, *24*, 1022; Lide Jr., D.R.; Mann, D.E. *J. Chem. Phys.* ***1958***, *29*, 914.

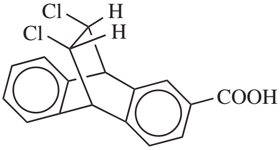
[38] Muenter, J.S.; Laurie, V.W. *J. Chem. Phys.* ***1966***, *45*, 855.

[39] Actually, symmetrical tetrahedral molecules like methane do have extremely small dipole moments, caused by centrifugal distortion effects; these moments are so small that they can be ignored for all practical purposes. For CH_4 μ is $\sim 5.4 \times 10^{-6}$ *D*: Ozier, I. *Phys. Rev. Lett.* ***1971***, *27*, 1329; Rosenberg, A.; Ozier, I.; Kudian, A.K. *J. Chem. Phys.* ***1972***, *57*, 568.

greater electronegativity of Cl, is partially compensated by drawing the C—C electrons closer to itself, resulting in a polarization of this bond and a slightly positive charge on the C-2 atom. This polarization of one bond caused by the polarization of an adjacent bond is called the *inductive effect*. The effect is greatest for adjacent bonds but may also be felt farther away; thus the polarization of the C—C bond causes a (slight) polarization of the three methyl C—H bonds. The other effect operates not through bonds, but directly through space or solvent molecules, and is called the *field effect*.[40] It is often very difficult to separate the two kinds of effect, but it has been done in a number of cases, generally by taking advantage of the fact that the field effect depends on the geometry of the molecule but the inductive effect depends only on the nature of the bonds. For example, in isomers **1** and **2**[41] the inductive effect of the chlorine atoms on the position of the electrons in the COOH group (and hence on the acidity, see Chapter 8) should be the same since the same bonds intervene; but the field effect is different because the chlorines are closer in space to the COOH in **1** than they are in **2**. Thus a comparison of the acidity of **1** and **2** should reveal whether a field effect is truly operating. The evidence obtained from such experiments is overwhelming that field effects are much more important than inductive effects.[42] In most cases, the two types of effect are considered together; in this book, we will not attempt to separate them, but will use the name *field effect* to refer to their combined action.[43]



1
pK_a = 6.07



2
pK_a = 5.67

Functional groups can be classified as electron-withdrawing $(-I)$ or electron-donating $(+I)$ groups relative to hydrogen. This means, for example, that NO_2, a $-I$ group, will draw electrons to itself more than a hydrogen atom would if it

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[40] Roberts, J.D.; Moreland, Jr., W.T. *J. Am. Chem. Soc.* ***1953***, *75*, 2167.

[41] This example is from Grubbs, E.J.; Fitzgerald, R.; Phillips, R.E.; Petty, R. *Tetrahedron* ***1971***, *27*, 935.

[42] For example, see Dewar, M.J.S.; Grisdale, P.J. *J. Am. Chem. Soc.* ***1962***, *84*, 3548; Stock, L.M. *J. Chem. Educ.*, ***1972***, *49*, 400; Golden, R.; Stock, L.M. *J. Am. Chem. Soc.* ***1972***, *94*, 3080; Liotta, C.; Fisher, W.F.; Greene Jr., G.H.; Joyner, B.L. *J. Am. Chem. Soc.* ***1972***, *94*, 4891; Wilcox, C.F.; Leung, C. *J. Am. Chem. Soc.* ***1968***, *90*, 336; Butler, A.R. *J. Chem. Soc. B* ***1970***, 867; Rees, J.H.; Ridd, J.H.; Ricci, A. *J. Chem. Soc. Perkin Trans. 2* ***1976***, 294; Topsom, R.D. *J. Am. Chem. Soc.* ***1981***, *103*, 39; Grob, C.A.; Kaiser, A.; Schweizer, T. *Helv. Chim. Acta* ***1977***, *60*, 391; Reynolds, W.F. *J. Chem. Soc. Perkin Trans. 2* ***1980*****,** 985, *Prog. Phys. Org. Chem.* ***1983***, *14*, 165-203; Adcock, W.; Butt, G.; Kok, G.B.; Marriott, S.; Topsom, R.D. *J. Org. Chem.* ***1985***, *50*, 2551; Schneider, H.; Becker, N. *J. Phys. Org. Chem.* ***1989***, *2*, 214; Bowden, K.; Ghadir, K.D.F. *J. Chem. Soc. Perkin Trans. 2* ***1990***, 1333. Inductive effects may be important in certain systems. See, for example, Exner, O.; Fiedler, P. *Collect. Czech. Chem. Commun.* ***1980***, *45*, 1251; Li, Y.; Schuster, G.B. *J. Org. Chem.* ***1987***, *52*, 3975.

[43] There has been some question as to whether it is even meaningful to maintain the distinction between the two types of effect: see Grob, C.A. *Helv. Chim. Acta* ***1985***, *68*, 882; Lenoir, D.; Frank, R.M. *Chem. Ber.* ***1985***, *118*, 753; Sacher, E. *Tetrahedron Lett.* ***1986***, *27*, 4683.

TABLE 1.3. Field Effects of Various Groups Relative to Hydrogen[a]

$+I$		$-I$	
O^-	NR_3^+	COOH	OR
COO^-	SR_2^+	F	COR
CR_3	NH_3^+	Cl	SH
CHR_2	NO_2	Br	SR
CH_2R	SO_2R	I	OH
CH_3	CN	OAr	$C{\equiv}CR$
D	SO_2Ar	COOR	Ar
			$C{\equiv}CR_2$

[a]The groups are listed approximately in order of decreasing strength for both $-I$ and $+I$ groups.

occupied the same position in the molecule.

$$O_2N \leftarrow\!\!\leftarrow\!\!\!-\!\!-\, CH_2 \leftarrow\!\!\!-\!\!-\, Ph$$
$$H \text{———} CH_2 \text{———} Ph$$

Thus, in α-nitrotoluene, the electrons in the N—C bond are farther away from the carbon atom than the electrons in the H—C bond of toluene. Similarly, the electrons of the C—Ph bond are farther away from the ring in α-nitrotoluene than they are in toluene. Field effects are always comparison effects. We compare the $-I$ or +I effect of one group with another (usually hydrogen). It is commonly said that, compared with hydrogen, the NO_2 group is electron-withdrawing and the O^- group electron-donating or electron releasing. However, there is no actual donation or withdrawal of electrons, though these terms are convenient to use; there is merely a difference in the position of electrons due to the difference in electronegativity between H and NO_2 or between H and O^-.

Table 1.3 lists a number of the most common $-I$ and $+I$ groups.[44] It can be seen that compared with hydrogen, most groups are electron withdrawing. The only electrondonating groups are groups with a formal negative charge (but not even all these), atoms of low electronegativity (Si,[45] Mg, etc., and perhaps alkyl groups). Alkyl groups[46] were formerly regarded as electron donating, but many examples of behavior have been found that can be interpreted only by the conclusion that alkyl groups are electron withdrawing compared with hydrogen.[47] In accord with this is the value of 2.472 for the group electronegativity of CH_3 (Table 1.2) compared with 2.176 for H. We will see that when an alkyl group is attached to an unsaturated or trivalent carbon (or other atom), its behavior is best explained by assuming it is $+I$ (see, e.g., pp. 239, 251, 388, 669), but when it is connected to a saturated atom, the results are not as clear,

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[44] See also Ceppi, E.; Eckhardt, W.; Grob, C.A. *Tetrahedron Lett.* ***1973***, 3627.

[45] For a review of field and other effects of silicon-containing groups, see Bassindale, A.R.; Taylor. P.G., in Patai, S.; Rappoport, Z. *The Chemistry of Organic Silicon Compounds*, pt. 2, Wiley, NY, ***1989***, pp. 893–963.

[46] For a review of the field effects of alkyl groups, see Levitt, L.S.; Widing, H.F. *Prog. Phys. Org. Chem.* ***1976***, *12*, 119.

[47] See Sebastian, J.F. *J. Chem. Educ.* ***1971***, *48*, 97.

and alkyl groups seem to be $+I$ in some cases and $-I$ in others[48] (see also p. 391). Similarly, it is clear that the field-effect order of alkyl groups attached to unsaturated systems is tertiary > secondary > primary > CH_3, but this order is not always maintained when the groups are attached to saturated systems. Deuterium is electron-donating with respect to hydrogen.[49] Other things being equal, atoms with *sp* bonding generally have a greater electron-withdrawing power than those with sp^2 bonding, which in turn have more electron-withdrawing power than those with sp^3 bonding.[50] This accounts for the fact that aryl, vinylic, and alkynyl groups are $-I$. Field effects always decrease with increasing distance, and in most cases (except when a very powerful $+I$ or $-I$ group is involved), cause very little difference in a bond four bonds away or more. There is evidence that field effects can be affected by the solvent.[51]

For discussions of field effects on acid and base strength and on reactivity, see Chapters 8 and 9, respectively.

BOND DISTANCES[52]

The distances between atoms in a molecule are characteristic properties of the molecule and can give us information if we compare the same bond in different molecules. The chief methods of determining bond distances and angles are X-ray diffraction (only for solids), electron diffraction (only for gases), and spectroscopic methods, especially microwave spectroscopy. The distance between the atoms of a bond is not constant, since the molecule is always vibrating; the measurements obtained are therefore average values, so that different methods give different results.[53] However, this must be taken into account only when fine distinctions are made.

Measurements vary in accuracy, but indications are that similar bonds have fairly constant lengths from one molecule to the next, though exceptions are known.[54] The variation is generally less than 1%. Table 1.4 shows

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[48] See, for example, Schleyer, P. von.R.; Woodworth, C.W. *J. Am. Chem. Soc.* ***1968***, *90*, 6528; Wahl Jr., G.H.; Peterson Jr., M.R. *J. Am. Chem. Soc.* ***1970***, *92*, 7238. The situation may be even more complicated. See, for example, Minot, C.; Eisenstein, O.; Hiberty, P.C.; Anh, N.T. *Bull. Soc. Chim. Fr.* ***1980***, II-119.

[49] Streitwieser Jr., A.; Klein, H.S. *J. Am. Chem. Soc.* ***1963***, *85*, 2759.

[50] Bent, H.A. *Chem. Rev.* ***1961***, *61*, 275, p. 281.

[51] See Laurence, C.; Berthelot, M.; Lucon, M.; Helbert, M.; Morris, D.G.; Gal, J. *J. Chem. Soc. Perkin Trans. 2* ***1984***, 705.

[52] For tables of bond distances and angles, see Allen, F.H.; Kennard, O.; Watson, D.G.; Brammer, L.; Orpen, A.G.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* ***1987***, S1–S19 (follows p. 1914); Tables of Interatomic Distances and Configurations in Molecules and Ions *Chem. Soc. Spec. Publ.* No. 11, ***1958***; Interatomic Distances Supplement *Chem. Soc. Spec. Publ.* No. 18, ***1965***; Harmony, M.D. Laurie, V.W.; Kuczkowski, R.L.; Schwendeman, R.H.; Ramsay, D.A.; Lovas, F.J.; Lafferty, W.J.; Maki, A.G. *J. Phys. Chem. Ref. Data* ***1979***, *8*, 619–721. For a review of molecular shapes and energies for many small organic molecules, radicals, and cations calculated by molecular-orbital methods, see Lathan, W.A.; Curtiss, L.A.; Hehre, W.J.; Lisle, J.B.; Pople, J.A. *Prog. Phys. Org. Chem.* ***1974***, *11*, 175. For a discussion of substituent effects on bond distances, see Topsom, R.D. *Prog. Phys. Org. Chem.* ***1987***, *16*, 85.

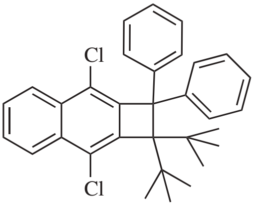
[53] Burkert, U.; Allinger, N.L. *Molecular Mechanics*; ACS Monograph 177, American Chemical Society, Washington, ***1982***, pp. 6–9; Whiffen, D.H. *Chem. Ber.* ***1971***, *7*, 57–61; Stals, J. *Rev. Pure Appl. Chem.* ***1970***, *20*, 1, pp. 2–5.

[54] Schleyer, P.v.R.; Bremer, M. *Angew. Chem. Int. Ed.* ***1989***, *28*, 1226.

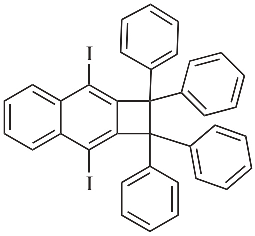
TABLE 1.4. **Bond Lengths between sp^3 Carbons in Some Compounds**

C—C bond in	Reference	Bond length, Å
Diamond	55	1.544
C_2H_6	56	1.5324 ± 0.0011
C_2H_5Cl	57	1.5495 ± 0.0005
C_3H_8	58	1.532 ± 0.003
Cyclohexane	59	1.540 ± 0.015
tert-Butyl chloride	60	1.532
n-Butane to *n*-heptane	61	1.531 – 1.534
Isobutane	62	1.535 ± 0.001

distances for single bonds between two sp^3 carbons. However, an analysis of C—OR bond distances in >2000 ethers and carboxylic esters (all with sp^3 carbon) shows that this distance increases with increasing electron withdrawal in the R group and as the C changes from primary to secondary to tertiary.[63] For these compounds, mean bond lengths of the various types ranged from 1.418 to 1.475 Å. Certain substituents can also influence bond length. The presence of a silyl substituent β- to a C—O (ester) linkage can lengthen the C—O, thereby weakening it.[64] This is believed to result from σ-σ* interactions in which the C—Si σ-bonding orbital acts as the donor and the C—O σ* orbitals acts as the receptor.



3



4

Although a typical carbon—carbon single bond has a bond length of ~1.54 Å, certain molecules are known that have significantly longer bond lengths.[65] Calculations

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[55] Lonsdale, K. *Phil. Trans. R. Soc. London* ***1947***, *A240*, 219.

[56] Bartell, L.S.; Higginbotham, H.K. *J. Chem. Phys.* ***1965***, *42*, 851.

[57] Wagner, R.S.; Dailey, B.P. *J. Chem. Phys.* ***1957***, *26*, 1588.

[58] Iijima, T. *Bull. Chem. Soc. Jpn.* ***1972***, *45*, 1291.

[59] Tables of Interatomic Distances, Ref. 52.

[60] Momany, F.A.; Bonham, R.A.; Druelinger, M.L. *J. Am. Chem. Soc.* ***1963***, *85*, 3075; also see, Lide, Jr., D.R.; Jen, M. *J. Chem. Phys.* ***1963***, *38*, 1504.

[61] Bonham, R.A.; Bartell, L.S.; Kohl, D.A. *J. Am. Chem. Soc.* ***1959***, *81*, 4765.

[62] Hilderbrandt, R.L.; Wieser, J.D. *J. Mol. Struct.* ***1973***, *15*, 27.

[63] Allen, F.H.; Kirby, A.J. *J. Am. Chem. Soc.* ***1984***, *106*, 6197; Jones, P.G.; Kirby, A.J. *J. Am. Chem. Soc.* ***1984***, *106*, 6207.

[64] White, J.M.; Robertson, G.B. *J. Org. Chem.* ***1992***, *57*, 4638.

[65] Kaupp, G.; Boy, J *Angew. Chem. Int. Ed.* ***1997***, *36*, 48.

have been done for unstable molecules that showed them to have long bond lengths, and an analysis of the X-ray structure for the photoisomer of [2.2]-tetrabenzoparacyclophane (see Chapter 2) showed a C—C bond length of 1.77 Å.[66,65] Long bond lengths have been observed in stable molecules such as benzocyclobutane derivatives.[67] A bond length of 1.729 Å was reliably measured in 1,1-di-*tert*-butyl-2, 2-diphenyl-3,8-dichlorocyclobutan[*b*]naphthalene, **3**.[68] X-ray analysis of several of these derivations confirmed the presence of long C—C bonds, with **4** having a confirmed bond length of 1.734 Å.[69]

Bond distances for some important bond types are given in Table 1.5.[70] As can be seen in this table, carbon bonds are shortened by increasing *s* character.

TABLE 1.5. Bond distances[a]

Bond Type	Length, Å	Typical Compounds
C—C		
sp^3–sp^3	1.53	
sp^3–sp^2	1.51	Acetaldehyde, toluene, propene
sp^3–sp	1.47	Acetonitrile, propyne
sp^2–sp^2	1.48	Butadiene, glyoxal, biphenyl
sp^2–sp	1.43	Acrylonitrile, vinylacetylene
sp–*sp*	1.38	Cyanoacetylene, butadiyne
C=C		
sp^2–sp^2	1.32	Ethylene
sp^2–*sp*	1.31	Ketene, allenes
sp–*sp*[71]	1.28	Butatriene, carbon suboxide
C≡C[72]		
sp–*sp*	1.18	Acetylene
C—H[73]		
sp^3–**H**	1.09	Methane
sp^2–**H**	1.08	Benzene, ethylene
sp–**H**[74]	1.08	**HCN**, acetylene

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[66] Ehrenberg, M. *Acta Crystallogr.* ***1966***, *20*, 182.

[67] Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I *Acta Crystallogr., Sect. C* ***1996***, *52*, 177.

[68] Toda, F.; Tanaka, K.; Watanabe, M.; Taura, K.; Miyahara, I.; Nakai, T.; Hirotsu, K. *J. Org. Chem.* ***1999***, *64*, 3102.

[69] Tanaka, K.; Takamoto, N.; Tezuka, Y.; Kato, M.; Toda, F. *Tetrahedron* ***2001***, *57*, 3761.

[70] Except where noted, values are from Allen, F.H.; Kennard, O.; Watson, D.G.; Brammer, L.; Orpen, A.G.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* ***1987***, S1-S19 (follows p. 1914). In this source, values are given to three significant figures.

[71] Costain, C.C.; Stoicheff, B.P. *J. Chem. Phys.* ***1959***, *30*, 777.

[72] For a full discussion of alkyne bond distances, see Simonetta, M.; Gavezzotti, A, in Patai, S. *The Chemistry of the Carbon–Carbon Triple Bond,* Wiley, NY, ***1978***.

[73] For an accurate method of C—H bond distance determination, see Henry, B.R. *Acc. Chem. Res.* ***1987***, *20*, 429.

[74] Bartell, L.S.; Roth, E.A.; Hollowell, C.D.; Kuchitsu, K.; Young, Jr., J.E. *J. Chem. Phys.* ***1965***, *42*, 2683.

TABLE 1.5. (*continued*)

Bond Type	Length, Å	Typical Compounds
C–O		
sp^3–**O**	1.43	Dimethyl ether, ethanol
sp^2–**O**	1.34	Formic acid
C=O		
sp^2–**O**	1.21	Formaldehyde, formic acid
sp–**O**[59]	1.16	**CO_2**
C–N		
sp^3–**N**	1.47	Methylamine
sp^2–**N**	1.38	Formamide
C=N		
sp^2–**N**	1.28	Oximes, imines
C≡N		
sp–**N**	1.14	**HCN**
C–S		
sp^3–**S**	1.82	Methanethiol
sp^2–**S**	1.75	Diphenyl sulfide
sp–**S**	1.68	CH_3SCN
C=S		
sp–**S**	1.67	**CS_2**

C–halogen[75]	**F**	**Cl**	**Br**	**I**
sp^3–halogen	1.40	1.79	1.97	2.16
sp^2–halogen	1.34	1.73	1.88	2.10
sp–halogen	1.27[76]	1.63	1.79[77]	1.99[77]

[a]The values given are average lengths and do not necessarily apply exactly to the compounds mentioned.[70]

This is most often explained by the fact that, as the percentage of *s* character in a hybrid orbital increases, the orbital becomes more like an *s* orbital and hence is held more tightly by the nucleus than an orbital with less *s* character. However, other explanations have also been offered (see p. 39), and the matter is not completely settled.

Indications are that a C—D bond is slightly shorter than a corresponding C—H bond. Thus, electron-diffraction measurements of C_2H_6 and C_2D_6 showed a C—H bond distance of 1.1122 ± O.0012 Å and a C—D distance of 1.1071 ± 0.0012 Å.[56]

BOND ANGLES

It might be expected that the bond angles of sp^3 carbon would always be the tetrahedral angle 109°28′, but this is so only where the four groups are identical, as in

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[75] For reviews of carbon-halogen bonds, see Trotter, J., in Patai, S. *The Chemistry of the Carbon–Halogen Bond*, pt. 1, Wiley, NY, ***1973***, pp. 49–62; Mikhailov, B.M. *Russ. Chem. Rev.* ***1971***, *40*, 983.

[76] Lide, Jr., D.R. *Tetrahedron* ***1962***, *17*, 125.

[77] Rajput, A.S.; Chandra, S. *Bull. Chem. Soc. Jpn.* ***1966***, *39*, 1854.

methane, neopentane, or carbon tetrachloride. In most cases, the angles deviate a little from the pure tetrahedral value. For example, the C—C—Br angle in 2-bromopropane is 114.2°.[78] Similarly, slight variations are generally found from the ideal values of 120 and 180° for sp^2 and sp carbon, respectively. These deviations occur because of slightly different hybridizations, that is, a carbon bonded to four other atoms hybridizes one s and three p orbitals, but the four hybrid orbitals thus formed are generally not exactly equivalent, nor does each contain exactly 25% s and 75% p character. Because the four atoms have (in the most general case) different electronegativities, each makes its own demand for electrons from the carbon atom.[79] The carbon atom supplies more p character when it is bonded to more electronegative atoms, so that in chloromethane, for example, the bond to chlorine has somewhat more than 75% p character, which of course requires that the other three bonds have somewhat less, since there are only three p orbitals (and one s) to be divided among the four hybrid orbitals.[80] Of course, in strained molecules, the bond angles may be greatly distorted from the ideal values (see p. 216).

For oxygen and nitrogen, angles of 90° are predicted from p^2 bonding. However, as we have seen (p. 6), the angles of water and ammonia are much larger than this, as are the angles of other oxygen and nitrogen compounds (Table 1.6); in fact, they are much closer to the tetrahedral angle of 109°28′ than to 90°. These facts have

TABLE 1.6. Oxygen, Sulfur, and Nitrogen Bond Angles in Some Compounds

Angle	Value	Compound	Reference
H—O—H	104°27′	Water	5
C—O—H	107–109°	Methanol	59
C—O—C	111°43′	Dimethyl ether	81
C—O—C	124° ± 5°	Diphenyl ether	82
H—S—H	92.1°	H_2S	82
C—S—H	99.4°	Methanethiol	82
C—S—C	99.1°	Dimethyl sulfide	83
H—N—H	106°46′	Ammonia	5
H—N—H	106°	Methylamine	84
C—N—H	112°	Methylamine	83
C—N—C	108.7°	Trimethylamine	85

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[78] Schwendeman, R.H.; Tobiason, F.L. *J. Chem. Phys.* ***1965***, *43*, 201.

[79] For a review of this concept, see Bingel, W.A.; Lüttke, W. *Angew. Chem. Int. Ed.* ***1981***, *20*, 899.

[80] This assumption has been challenged: see Pomerantz, M.; Liebman, J.F. *Tetrahedron Lett.* ***1975***, 2385.

[81] Blukis, V.; Kasai, P.H.; Myers, R.J. *J. Chem. Phys.* ***1963***, *38*, 2753.

[82] Abrahams, S.C. *Q. Rev. Chem. Soc.* ***1956***, *10*, 407.

[83] Iijima, T.; Tsuchiya, S.; Kimura, M. *Bull. Chem. Soc. Jpn.* ***1977***, *50*, 2564.

[84] Lide, Jr., D.R. *J. Chem. Phys.* ***1957***, *27*, 343.

[85] Lide, Jr., D.R.; Mann, D.E. *J. Chem. Phys.* ***1958***, *28*, 572.

led to the suggestion that in these compounds oxygen and nitrogen use sp^3 bonding, that is, instead of forming bonds by the overlap of two (or three) *p* orbitals with 1*s* orbitals of the hydrogen atoms, they hybridize their 2*s* and 2*p* orbitals to form four sp^3 orbitals and then use only two (or three) of these for bonding with hydrogen, the others remaining occupied by unshared pairs (also called *lone pairs*). If this description is valid, and it is generally accepted by most chemists today,[86] it becomes necessary to explain why the angles of these two compounds are in fact not $109°28'$ but a few degrees smaller. One explanation that has been offered is that the unshared pair actually has a greater steric requirement than a pair in a bond, since there is no second nucleus to draw away some of the electron density and the bonds are thus crowded together. However, most evidence is that unshared pairs have smaller steric requirements than bonds[87] and the explanation most commonly accepted is that the hybridization is not pure sp^3. As we have seen above, an atom supplies more *p* character when it is bonded to more electronegative atoms. An unshared pair may be considered to be an "atom" of the lowest possible electronegativity, since there is no attracting power at all. Consequently, the unshared pairs have more *s* and the bonds more *p* character than pure sp^3 orbitals, making the bonds somewhat more like p^2 bonds and reducing the angle. As seen in Table 1.6, oxygen, nitrogen, and sulfur angles generally increase with decreasing electronegativity of the substituents. Note that the explanation given above cannot explain why some of these angles are *greater* than the tetrahedral angle.

BOND ENERGIES[88,89]

There are two kinds of bond energy. The energy necessary to cleave a bond to give the constituent radicals is called the *dissociation energy D*. For example, *D* for $H_2O \rightarrow HO + H$ is $118\,\text{kcal mol}^{-1}$ (494/mol). However, this is not taken as the energy of the O—H bond in water, since *D* for $H\text{—}O \rightarrow H + O$ is $100\,\text{kcal mol}^{-1}$ ($418\,\text{kJ mol}^{-1}$). The average of these two values, $109\,\text{kcal mol}^{-1}$ ($456\,\text{kJ mol}^{-1}$), is taken as the *bond energy E*. In diatomic molecules, of course, $D = E$.

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[86] An older theory holds that the bonding is indeed p^2, and that the increased angles come from repulsion of the hydrogen or carbon atoms. See Laing, M., *J. Chem. Educ.* ***1987***, *64*, 124.

[87] See, for example, Pumphrey, N.W.J.; Robinson, M.J.T. *Chem. Ind. (London)* ***1963***, 1903; Allinger, N.L.; Carpenter, J.G.D.; Karkowski, F.M. *Tetrahedron Lett.* ***1964***, 3345; Jones, R.A.Y.; Katritzky, A.R.; Richards, A.C.; Wyatt, R.J.; Bishop, R.J.; Sutton, L.E. *J. Chem. Soc. B* ***1970***, 127; Blackburne, I.D.; Katritzky, A.R.; Takeuchi, Y. *J. Am. Chem. Soc.* ***1974***, *96*, 682; *Acc. Chem. Res.* ***1975***, *8*, 300; Aaron, H.S.; Ferguson, C.P. *J. Am. Chem. Soc.* ***1976***, *98*, 7013; Anet, F.A.L.; Yavari, I. *J. Am. Chem. Soc.* ***1977***, *99*, 2794; Vierhapper, F.W.; Eliel, E.L. *J. Org. Chem.* ***1979***, *44*, 1081; Gust, D.; Fagan, M.W. *J. Org. Chem.* ***1980***, *45*, 2511. For other views, see Lambert, J.B.; Featherman, S.I. *Chem. Rev.* ***1975***, *75*, 611; Crowley, P.J.; Morris, G.A.; Robinson, M.J.T. *Tetrahedron Lett.* ***1976***, 3575; Breuker, K.; Kos, N.J.; van der Plas, H.C.; van Veldhuizen, B. *J. Org. Chem.* ***1982***, *47*, 963.

[88] Blanksby, S.J.; Ellison, G.B. *Acc. Chem. Res.* ***2003***, *36*, 255.

[89] For reviews including methods of determination, see Wayner, D.D.M.; Griller, D. *Adv. Free Radical Chem. (Greenwich, Conn.)* ***1990***, *1*, 159; Kerr, J.A. *Chem. Rev.* ***1966***, *66*, 465; Benson, S.W. *J. Chem. Educ.* ***1965***, *42*, 520; Wiberg, K.B., in Nachod, F.C.; Zuckerman, J.J. *Determination of Organic Structures by Physical Methods*, Vol. 3, Academic Press, NY, ***1971***, pp. 207–245.

				kcal	kJ
$C_2H_{6\,(gas)}$	$+ 3.5\ O_2$	$= 2\ CO_{2\,(gas)}$	$+ 3\ H_2O_{(liq)}$	+372.9	+1560
	$2\ CO_{2\,(gas)}$	$= 2\ C_{(graphite)}$	$+ 2\ O_{2\,(gas)}$	–188.2	–787
	$3\ H_2O_{(liq)}$	$= 3\ H_{2\,(gas)}$	$+ 1.5\ O_{2\,(gas)}$	–204.9	–857
	$3\ H_{2\,(gas)}$	$= 6\ H_{(gas)}$		–312/5	–1308
	$2\ C_{(graphite)}$	$= 2\ C_{(gas)}$		–343.4	–1437
	$C_2H_{6\,(gas)}$	$= 6\ H_{(gas)}$	$+ 2\ C_{(gas)}$	–676.1 kcal	–2829 kJ

Fig. 1.11. Calculation of the heat of atomization of ethane at 25°C.

The D values may be easy or difficult to measure, and they can be estimated by various techniques.[90] When properly applied, "Pauling's original electronegativity equation accurately describes homolytic bond dissociation enthalpies of common covalent bonds, including highly polar ones, with an average deviation of (1.5 kcal mol^{-1} [≈6.3 kJ mol^{-1}] from literature values)."[91] Whether measured or calculated, there is no question as to what D values mean. With E values the matter is not so simple. For methane, the total energy of conversion from CH_4 to $C + 4H$ (at 0 K) is 393 kcal mol^{-1} (1644 kJ mol^{-1}).[92] Consequently, E for the C—H bond in methane is 98 kcal mol^{-1} (411 kJ mol^{-1}) at 0 K. The more usual practice, though, is not to measure the heat of atomization (i.e., the energy necessary to convert a compound to its atoms) directly but to calculate it from the heat of combustion. Such a calculation is shown in Figure 1.11.

Heats of combustion are very accurately known for hydrocarbons.[93] For methane the value at 25°C is 212.8 kcal mol^{-1} (890.4 kJ mol^{-1}), which leads to a heat of atomization of 398.0 kcal mol^{-1} (1665 kJ mol^{-1}) or a value of E for the C—H bond at 25°C of 99.5 kcal mol^{-1} (416 kJ mol^{-1}). This method is fine for molecules like methane in which all the bonds are equivalent, but for more complicated molecules assumptions must be made. Thus for ethane, the heat of atomization at 25°C is 676.1 kcal mol^{-1} or 2829 kJ mol^{-1} (Fig. 1.11), and we must decide how much of this energy is due to the C—C bond and how much to the six C—H bonds. Any assumption must be artificial, since there is no way of actually obtaining this information, and indeed the question has no real meaning. If we make the assumption that E for each of the C—H bonds is the same as E for the C—H bond in methane (99.5 kcal mol^{-1} or 416 kJ mol^{-1}), then 6×99.5 (or 416) $= 597.0$ (or 2498), leaving 79.1 kcal mol^{-1} (331 kJ mol^{-1}) for the C—C bond. However, a similar calculation for propane gives a value of 80.3 (or 336) for the

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[90] Cohen, N.; Benson, S.W. *Chem. Rev.* ***1993***, *93*, 2419; Korth, H.-G.; Sicking, W. *J. Chem. Soc. Perkin Trans. 2* ***1997***, 715.

[91] Matsunaga, N.; Rogers, D.W.; Zavitsas, A.A. *J. Org. Chem*, ***2003***, *68*, 3158.

[92] For the four steps, D values are 101 to 102, 88, 124, and 80 kcal mol^{-1} (423–427, 368, 519, and 335 kJ mol^{-1}), respectively, though the middle values are much less reliable than the other two: Knox, B.E.; Palmer, H.B. *Chem. Rev.* ***1961***, *61*, 247; Brewer, R.G.; Kester, F.L. *J. Chem. Phys.* ***1964***, *40*, 812; Linevsky, M.J. *J. Chem. Phys.* ***1967***, *47*, 3485.

[93] For values of heats of combustion of large numbers of organic compounds: hydrocarbons and others, see Cox, J.D.; Pilcher, G., *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, NY, ***1970***; Domalski, E.S. *J. Phys. Chem. Ref. Data* ***1972***, *1*, 221–277. For large numbers of heats-of-formation values (from which heats of combustion are easily calculated) see Stull, D.R.; Westrum, Jr., E.F.; Sinke, G.C. *The Chemical Thermodynamics of Organic Compounds*, Wiley, NY, ***1969***.

C—C bond, and for isobutane, the value is 81.6 (or 341). A consideration of heats of atomization of isomers also illustrates the difficulty. *E* values for the C—C bonds in pentane, isopentane, and neopentane, calculated from heats of atomization in the same way, are (at 25°C) 81.1, 81.8, and 82.4 kcal mol^{-1} (339, 342, 345 kJ mol^{-1}), respectively, even though all of them have twelve C—H bonds and four C—C bonds.

These differences have been attributed to various factors caused by the introduction of new structural features. Thus isopentane has a tertiary carbon whose C—H bond does not have exactly the same amount of *s* character as the C—H bond in pentane, which for that matter contains secondary carbons not possessed by methane. It is known that *D* values, which *can* be measured, are not the same for primary, secondary, and tertiary C—H bonds (see Table 5.3). There is also the steric factor. Hence, it is certainly not correct to use the value of 99.5 kcal mol^{-1} (416 kJ mol^{-1}) from methane as the *E* value for all C—H bonds. Several empirical equations have been devised that account for these factors; the total energy can be computed[94] if the proper set of parameters (one for each structural feature) is inserted. Of course, these parameters are originally calculated from the known total energies of some molecules which contain the structural feature.

Table 1.7 gives *E* values for various bonds. The values given are averaged over a large series of compounds. The literature contains charts that take account of

TABLE 1.7. Bond Energy *E* Values at 25°C for Some Important Bond Types[95a]

Bond	kcal mol^{-1}	kJ mol^{-1}	Bond	kcal mol^{-1}	kJ mol^{-1}
O—H	110–111	460–464	C—S[96]	61	255
C—H	96–99	400–415	C—I	52	220
N—H	93	390			
S—H	82	340	C≡C	199–200	835
			C=C	146–151	610–630
C—F	—	—	C—C	83–85	345–355
C—H	96–99	400–415			
C—O	85–91	355–380	C≡N	204	854
C—C	83–85	345–355	C=O	173–81	724–757
C—Cl	79	330			
C—N[97]	69–75	290–315	C=N[97]	143	598
C—Br	66	275	O—O[98]	42.9	179.6 ± 4.5

[a] The *E* values are arranged within each group in order of decreasing strength. The values are averaged over a large series of compounds.

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[94] For a review, see Cox, J.D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, NY, ***1970***, pp. 531–597. See also, Gasteiger, J.; Jacob, P.; Strauss, U. *Tetrahedron* ***1979***, *35*, 139.

[95] These values, except where noted, are from Lovering, E.G.; Laidler, K.J. *Can. J. Chem.* ***1960***, *38*, 2367; Levi, G.I.; Balandin, A.A. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* ***1960***, 149.

[96] Grelbig, T.; Pötter, B.; Seppelt, K. *Chem. Ber.* ***1987***, *120*, 815.

[97] Bedford, A.F.; Edmondson, P.B.; Mortimer, C.T. *J. Chem. Soc.* ***1962***, 2927.

[98] The average of the values obtained was *DH*°(O—O). dos Santos, R.M.B.; Muralha, V.S.F.; Correia, C.F.; Simões, J.A.M. *J. Am. Chem. Soc.* ***2001***, *123*, 12670.

hybridization (thus an sp^3 C—H bond does not have the same energy as an sp^2 C—H bond).[99] Bond dissociation energies, both calculated and experientially determined, are constantly being refined. Improved values are available for the O—O bond of peroxides,[100] the C—H bond in alkyl amines,[101] the N—H bond in aniline derivatives,[102] the N—H bond in protonated amines,[103] the O—H bond in phenols,[104] the C—H bond in alkenes,[105] amides and ketones,[106] and in CH_2X_2 and CH_3X derivatives ($X = COOR$, C=O, SR, NO_2, etc.),[107] the O—H and S—H bonds of alcohols and thiols,[108] and the C—Si bond of aromatic silanes.[109] Solvent plays a role in the E values. When phenols bearing electron-releasing groups are in aqueous media, calculations show that the bond dissociation energies of decrease due to hydrogen-bonding interactions with water molecules, while electron-withdrawing substituents on the phenol increase the bond dissociation energies.[110]

Certain generalizations can be derived from the data in Table 1.7.

1. There is a correlation of bond strengths with bond distances. A comparison of Tables 1.5 and 1.7 shows that, in general, *shorter bonds are stronger bonds*. Since we have already seen that increasing *s* character shortens bonds (p. 24), it follows that bond strengths increase with increasing *s* character. Calculations show that ring strain has a significant effect on bond dissociation energy, particularly the C—H bond of hydrocarbons, because it forces the compound to adopt an undesirable hybridization.[111]
2. Bonds become weaker as we move down the Periodic Table. Compare C—O and C—S, or the carbon–halogen bonds C—F, C—Cl, C—Br, C—I. This is a consequence of the first generalization, since bond distances must increase as we go down the periodic table because the number of inner electrons increases. However, it is noted that "high-level *ab initio* molecular-orbital calculations confirm that the effect of alkyl substituents on R—X bond dissociation energies varies according to the nature of X (the stabilizing

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[99] Cox, J.D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, NY, ***1970***, pp. 531–597; Cox, J.D. *Tetrahedron* **1962**, *18*, 1337.

[100] Bach, R.D.; Ayala, P.Y.; Schlegel, H.B. *J. Am. Chem. Soc.* ***1996***, *118*, 12758.

[101] Wayner, D.D.M.; Clark, K.B.; Rauk, A.; Yu, D.; Armstrong, D.A. *J. Am. Chem. Soc.* ***1997***, *119,* 8925. For the α C—H bond of tertiary amines, see Dombrowski, G.W.; Dinnocenzo, J.P.; Farid, S.; Goodman, J.L. Gould, I.R. *J. Org. Chem.* ***1999***, *64*, 427.

[102] Bordwell, F.G.; Zhang, X.-M.; Cheng, J.-P. *J. Org. Chem.* ***1993***, *58*, 6410. See also, Li, Z.; Cheng, J.-P. *J. Org. Chem.* ***2003***, *68*, 7350.

[103] Liu, W.-Z.; Bordwell, F.G. *J. Org. Chem.* ***1996***, *61*, 4778.

[104] Lucarini, M.; Pedrielli, P.; Pedulli, G.F.; Cabiddu, S.; Fattuoni, C. *J. Org. Chem.* ***1996***, *61*, 9259. For the O—H E of polymethylphenols, see de Heer, M.I.; Korth, H.-G.; Mulder, P. *J. Org. Chem.* ***1999***, *64*, 6969.

[105] Zhang, X.-M. *J. Org. Chem.* ***1998***, *63*, 1872.

[106] Bordwell, F.G.; Zhang, X.-M.; Filler, R. *J. Org. Chem.* ***1993***, *58*, 6067.

[107] Brocks, J.J.; Beckhaus, H.-D.; Beckwith, A.L.J.; Rüchardt, C. *J. Org. Chem.* ***1998***, *63*, 1935.

[108] Hadad, C.M.; Rablen, P.R.; Wiberg, K.B. *J. Org. Chem.* ***1998***, *63*, 8668.

[109] Cheng, Y.-H.; Zhao, X.; Song, K.-S.; Liu, L.; Guo, Q.-X. *J. Org. Chem.* ***2002***, *67*, 6638.

[110] Guerra, M.; Amorati, R.; Pedulli, G.F. *J. Org. Chem.* ***2004***, *69*, 5460.

[111] Feng, Y.; Liu, L.; Wang, J.-T.; Zhao, S.-W.; Guo, Q.X. *J. Org. Chem.* ***2004***, *69*, 3129; Song, K.-S.; Liu, L.; Guo, Q.X. *Tetrahedron* ***2004***, *60*, 9909.

influence of the ionic configurations to increase in the order Me < Et < *i*-Pr < *t*-Bu, accounting for the *increase* (rather than expected decrease) in the R—X bond dissociation energies with increasing alkylation in the R—OCH_3, R—OH, and R—F molecules. This effect of X can be understood in terms of the increasing contribution of the ionic R^+X^- configuration for electronegative X substituents."[112]

3. Double bonds are both shorter and stronger than the corresponding single bonds, but not twice as strong, because π overlap is less than σ overlap. This means that a σ bond is stronger than a π bond. The difference in energy between a single bond, say C—C, and the corresponding double bond is the amount of energy necessary to cause rotation around the double bond.[113]

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[112] Coote, M.L.; Pross, A.; Radom, L. *Org. Lett.* ***2003***, *5*, 4689.

[113] For a discussion of the different magnitdues of the bond energies of the two bonds of the double bond, see Miller, S.I. *J. Chem. Educ.* ***1978***, *55*, 778.

CHAPTER 2

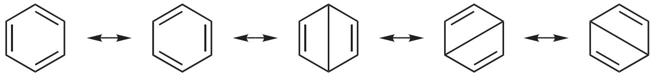
Delocalized Chemical Bonding

Although the bonding of many compounds can be adequately described by a single Lewis structure (p. 14), this is not sufficient for many other compounds. These compounds contain one or more bonding orbitals that are not restricted to two atoms, but that are spread out over three or more. Such bonding is said to be *delocalized*.[1] In this chapter, we will see which types of compounds must be represented in this way.

The two chief general methods of approximately solving the wave equation, discussed in Chapter 1, are also used for compounds containing delocalized bonds.[2] In the valence-bond method, several possible Lewis structures (called *canonical forms*) are drawn and the molecule is taken to be a weighted average of them. Each Ψ in Eq. (1.3), Chapter 1,

$$\Psi = c_1\psi_1 + c_1\psi_1 + \cdots$$

represents one of these structures. This representation of a real structure as a weighted average of two or more canonical forms is called *resonance*. For benzene the canonical forms are **1** and **2**. Double-headed arrows (↔) are used to indicate resonance. When the wave equation is solved, it is found that the energy value obtained by considering that **1** and **2** participate equally is lower than that for **1** or **2** alone. If **3**, **4**, and **5** (called *Dewar structures*) are also considered, the value



1 **2** **3** **4** **5**

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[1] The classic work on delocalized bonding is Wheland, G.W. *Resonance in Organic Chemistry*; Wiley, NY, ***1955***.

[2] There are other methods. For a discussion of the free-electron method, see Streitwieser Jr., A. *Molecular Orbital Theory for Organic Chemists*; Wiley, NY, ***1961***, pp. 27–29. For the nonpairing method, in which benzene is represented as having three electrons between adjacent carbons, see Hirst, D.M.; Linnett, J.W. *J. Chem. Soc.* ***1962***, 1035; Firestone, R.A. *J. Org. Chem.* ***1969***, *34*, 2621.

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Michael B. Smith and Jerry March

is lower still. According to this method, **1** and **2** each contribute 39% to the actual molecule and the others 7.3% each.[3] The carbon–carbon bond order is 1.463 (not 1.5, which would be the case if only **1** and **2** contributed). In the valence-bond method, the *bond order* of a particular bond is the sum of the weights of those canonical forms in which the bonds is double plus 1 for the single bond that is present in all of them.[4] Thus, according to this picture, each C—C bond is not halfway between a single and a double bond but somewhat less. The energy of the actual molecule is obviously less than that of any one Lewis structure, since otherwise it would have one of those structures. The difference in energy between the actual molecule and the Lewis structure of lowest energy is call the *resonance energy*. Of course, the Lewis structures are not real, and their energies can only be estimated.

Qualitatively, the resonance picture is often used to describe the structure of molecules, but quantitative valence-bond calculations become much more difficult as the structures become more complicated (e.g., naphthalene, and pyridine). Therefore, the molecular-orbital method is used much more often for the solution of wave equations.[5] If we look at benzene by this method (qualitatively), we see that each carbon atom, being connected to three other atoms, uses sp^2 orbitals to form σ bonds, so that all 12 atoms are in one plane. Each carbon has a p orbital (containing one electron) remaining and each of these can overlap equally with the two adjacent p orbitals. This overlap of six orbitals (see Fig. 2.1) produces six new orbitals, three of which (shown) are bonding. These three (called π orbitals) all occupy approximately the same space.[6] One of the three is of lower energy than the other two, which are degenerate. They each have the plane of the ring as a node and so are in two parts, one above and one below the plane. The two orbitals of higher energy (Fig. 2.1*b* and *c*) also have another node. The six electrons that occupy this torus-shaped cloud are called the *aromatic sextet*. The carbon–carbon bond order for benzene, calculated by the molecular-orbital method, is 1.667.[7]

For planar unsaturated and aromatic molecules, many molecular-orbital calculations (*MO calculations*) have been made by treating the σ and π electrons separately. It is assumed that the σ orbitals can be treated as localized bonds and the

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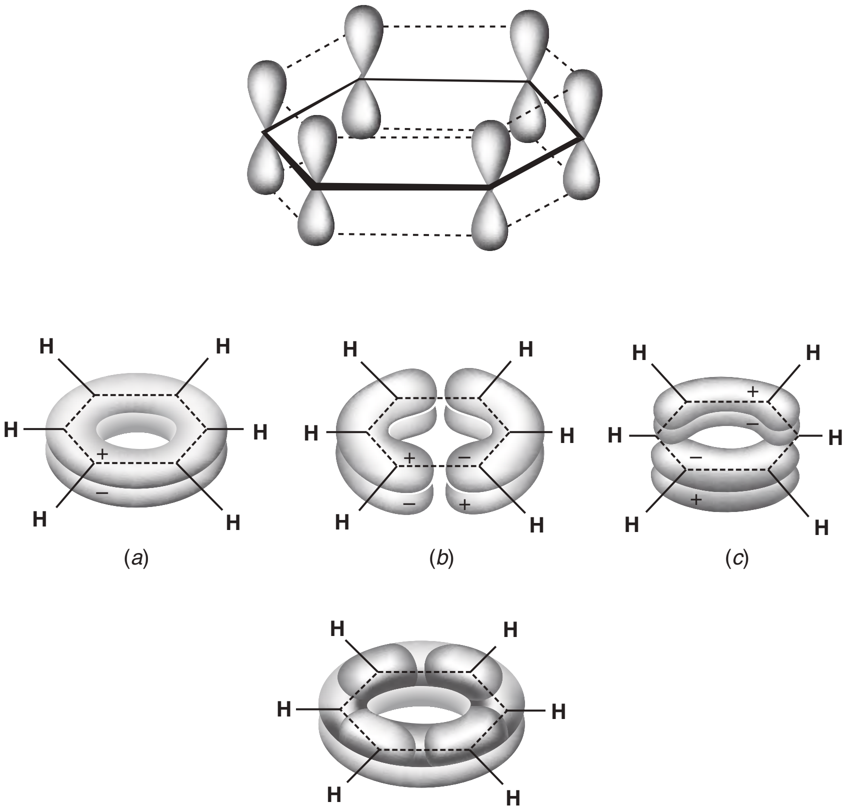
[3] Pullman, A. *Prog. Org. Chem.* ***1958***, *4*, 31, p. 33.

[4] For a more precise method of calculating valence-bond orders, see Clarkson, D.; Coulson, C.A.; Goodwin, T.H. *Tetrahedron* ***1963***, *19*, 2153. See also Herndon, W.C.; Párkányi, C. *J. Chem. Educ.* ***1976***, *53*, 689.

[5] For a review of how MO theory explains localized and delocalized bonding, see Dewar, M.J.S. *Mol. Struct. Energ.*, ***1988***, *5*, 1.

[6] According to the explanation given here, the symmetrical hexagonal structure of benzene is caused by both the σ bonds and the π orbitals. It has been contended, based on MO calculations, that this symmetry is caused by the σ framework alone, and that the π system would favor three localized double bonds: Shaik, S.S.; Hiberty, P.C.; Lefour, J.; Ohanessian, G. *J. Am. Chem. Soc.* ***1987***, *109*, 363; Stanger, A.; Vollhardt, K.P.C. *J. Org. Chem.* ***1988***, *53*, 4889. See also Cooper, D.L.; Wright, S.C.; Gerratt, J.; Raimondi, M. *J. Chem. Soc. Perkin Trans. 2* ***1989***, 255, 263; Jug, K.; Köster, A.M. *J. Am. Chem. Soc.* ***1990***, *112*, 6772; Aihara, J. *Bull. Chem. Soc. Jpn.* ***1990***, *63*, 1956.

[7] The molecular-orbital method of calculating bond order is more complicated than the valence-bond method. See Pullman, A. *Prog. Org. Chem.* ***1958***, *4*, 31, p. 36; Clarkson, D.; Coulson, C.A.; Goodwin, T.H. *Tetrahedron* ***1963***, *19*, 2153.



Superposition of (*a*), (*b*), **and** (*c*).

(*d*)

Fig. 2.1. The six *p* orbitals of benzene overlap to form three bonding orbitals, (*a*), (*b*), and (*c*). The three orbitals superimposed are shown in (*d*).

calculations involve only the π electrons. The first such calculations were made by Hückel; such calculations are often called *Hückel molecular-orbital* (HMO) *calculations*.[8] Because electron–electron repulsions are either neglected or averaged out in the HMO method, another approach, the *self-consistent field* (SCF), or *Hartree–Fock*, method, was devised.[9] Although these methods give many useful results for

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[8] See Yates, K. *Hückel Molecular Orbital Theory*, Academic Press, NY, ***1978***; Coulson, C.A.; O'Leary, B.; Mallion, R.B. *Hückel Theory for Organic Chemists*, Academic Press, NY, ***1978***; Lowry, T.H.; Richardson, K.S. *Mechanism and Theory in Organic Chemistry*, 3rd ed., Harper and Row, NY, ***1987***, pp. 100–121.

[9] Roothaan, C.C.J. *Rev. Mod. Phys.* ***1951***, *23*, 69; Pariser, R.; Parr, R.G. *J. Chem. Phys.* ***1952***, *21*, 466, 767; Pople, J.A. *Trans. Faraday Soc,.* ***1953***, *49*, 1375, *J. Phys. Chem.* ***1975***, *61*, 6; Dewar, M.J.S. *The Molecular Orbital Theory of Organic Chemistry*; McGraw-Hill, NY, ***1969***; Dewar, M.J.S., in *Aromaticity, Chem. Soc. Spec. Pub.* no. 21, ***1967***, pp. 177–215.

planar unsaturated and aromatic molecules, they are often unsuccessful for other molecules; it would obviously be better if all electrons, both σ and π, could be included in the calculations. The development of modern computers has now made this possible.[10] Many such calculations have been made[11] using a number of methods, among them an extension of the Hückel method (EHMO)[12] and the application of the SCF method to all valence electrons.[13]

One type of MO calculation that includes all electrons is called *ab initio*.[14] Despite the name (which means "from first principles") this type does involve assumptions, though not very many. It requires a large amount of computer time, especially for molecules that contain more than about five or six atoms other than hydrogen. Treatments that use certain simplifying assumptions (but still include all electrons) are called *semiempirical* methods.[15] One of the first of these was called CNDO (Complete Neglect of Differential Overlap),[16] but as computers have become more powerful, this has been superseded by more modern methods, including MINDO/3 (Modified Intermediate Neglect of Differential Overlap),[17] MNDO (Modified Neglect of Diatomic Overlap),[17] and AM1 (Austin Model 1), all of which were introduced by M.J. Dewar and co-workers.[18] Semiempirical calculations are generally regarded as less accurate than *ab initio* methods,[19] but are much faster and cheaper. Indeed, calculations for some very large molecules are possible only with the semiempirical methods.[20]

Molecular-orbital calculations, whether by *ab initio* or semiempirical methods, can be used to obtain structures (bond distances and angles), energies (e.g., heats of formation), dipole moments, ionization energies, and other properties of molecules,

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[10] For discussions of the progress made in quantum chemistry calculations, see Ramsden, C.A. *Chem. Ber.* ***1978***, *14*, 396; Hall, G.G. *Chem. Soc. Rev.* ***1973***, *2*, 21.

[11] For a review of molecular-orbital calculatons on saturated organic compounds, see Herndon, W.C. *Prog. Phys. Org. Chem.* ***1972***, *9*, 99.

[12] Hoffmann, R. *J. Chem. Phys.* ***1963***, *39*, 1397. See Yates, K. *Hückel Molecular Orbital Theory*, Academic Press, NY, ***1978***, pp. 190–201.

[13] Dewar, M.J.S. *The Molecular Orbital Theory of Chemistry*, McGraw-Hill, NY, ***1969***; Jaffé, H.H. *Acc. Chem. Res.* ***1969***, *2*, 136; Kutzelnigg, W.; Del Re, G.; Berthier, G. *Fortschr. Chem. Forsch.* ***1971***, *22*, 1.

[14] Hehre, W.J.; Radom, L.; Schleyer, P.v.R.; Pople, J.A. *Ab Initio Molecular Orbital Theory*, Wiley, NY, ***1986***; Clark, T. *A Handbook of Computational Chemistry*, Wiley, NY, ***1985***, pp. 233–317; Richards, W.G.; Cooper, D.L. *Ab Initio Molecular Orbital Calculations for Chemists*, 2nd ed., Oxford University Press: Oxford, ***1983***.

[15] For a review, see Thiel, W. *Tetrahedron* ***1988***, *44*, 7393.

[16] Pople, J.A.; Santry, D.P.; Segal, G.A. *J. Chem. Phys.* ***1965***, *43*, S129; Pople, J.A.; Segal, G.A. *J. Chem. Phys.* ***1965***, *43*, S136; ***1966***, *44*, 3289; Pople, J.A.; Beveridge, D.L. *Approximate Molecular Orbital Theory*; McGraw-Hill, NY, ***1970***.

[17] For a discussion of MNDO and MINDO/3, and a list of systems for which these methods have been used, with references, see Clark, T. *A Handbook of Computational Chemistry*, Wiley, NY, ***1985***, pp. 93–232. For a review of MINDO/3, see Lewis, D.F.V. *Chem. Rev.* ***1986***, *86*, 1111.

[18] First publications are, MINDO/3: Bingham, R.C.; Dewar, M.J.S.; Lo, D.H. *J. Am. Chem. Soc.* ***1975***, *97*, 1285; MNDO: Dewar, M.J.S.; Thiel, W. *J. Am. Chem. Soc.* ***1977***, *99*, 4899; AM1: Dewar, M.J.S.; Zoebisch, E.G.; Healy, E.F.; Stewart, J.J.P. *J. Am. Chem. Soc.* ***1985***, *107*, 3902.

[19] See, however, Dewar, M.J.S.; Storch, D.M. *J. Am. Chem. Soc.* ***1985***, *107*, 3898.

[20] Clark, T. *A Handbook of Computational Chemistry*, Wiley, NY, ***1985***, p. 141.

ions, and radicals: not only of stable ones, but also of those so unstable that these properties cannot be obtained from experimental measurements.[21] Many of these calculations have been performed on transition states (p. 302); this is the only way to get this information, since transition states are not, in general, directly observable. Of course, it is not possible to check data obtained for unstable molecules and transition states against any experimental values, so that the reliability of the various MO methods for these cases is always a question. However, our confidence in them does increase when (*1*) different MO methods give similar results, and (*2*) a particular MO method works well for cases that can be checked against experimental methods.[22]

Both the valence-bond and molecular-orbital methods show that there is delocalization in benzene. For example, each predicts that the six carbon–carbon bonds should have equal lengths, which is true. Since each method is useful for certain purposes, we will use one or the other as appropriate. Recent *ab initio, SCF* calculations confirms that the delocalization effect acts to strongly stabilize symmetric benzene, consistent with the concepts of classical resonance theory.[23]

Bond Energies and Distances in Compounds Containing Delocalized Bonds

If we add the energies of all the bonds in benzene, taking the values from a source like Table 1.7, the value for the heat of atomization turns out to be less than that actually found in benzene (Fig. 2.2). The actual value is 1323 kcal mol^{-1} (5535 kJ mol^{-1}). If we use E values for a C=C double bond obtained from cyclohexene (148.8 kcal mol^{-1}; 622.6 kJ mol^{-1}), a C—C single bond from cyclohexane (81.8 kcal mol^{-1}, 342 kJ mol^{-1}), and C–H bonds from methane (99.5 kcal mol^{-1}, 416 kJ mol^{-1}), we get a total of 1289 kcal mol^{-1} (5390 kJ mol^{-1}) for structure **1** or **2**. By this calculation the resonance energy is 34 kcal mol^{-1} (145 kJ mol^{-1}). Of course, this is an arbitrary calculation since, in addition to the fact that we are calculating a heat of atomization for a nonexistent structure (**1**), we are forced to use E values that themselves do not have a firm basis in reality. The actual C—H bond energy for benzene has been measured to be 113.5 ± 0.5 kcal mol^{-1} at 300 K and estimated to be 112.0 ± 0.6 kcal mol^{-1} (469 kJ mol^{-1}) at 0 K.[24] The resonance energy can never be measured, only estimated, since we can measure the heat of atomization of the real molecule but can only make an intelligent guess at that of the Lewis structure of lowest energy.

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[21] Another method of calculating such properies is molecular mechanics (p. $$$).

[22] Dias, J.R. *Molecular Orbital Calculations Using Chemical Graph Theory*, Spring-Verlag, Berlin, ***1993***.

[23] Glendening, E.D.; Faust, R.; Streitwieser, A.; Vollhardt, K.P.C.; Weinhold, F. *J. Am. Chem.Soc.* ***1993***, *115*, 10952.

[24] Davico, G.E.; Bierbaum, V.M.; DePuy, C.H.; Ellison, G.B.; Squires, R.R. *J. Am. Chem. Soc.* ***1995***, *117*, 2590. See also Barckholtz, C.; Barckholtz, T.A.; Hadad, C.M. *J. Am. Chem. Soc.* ***1999***, *121*, 491; Pratt, D.A.; DiLabio, G.A.; Mulder, P.; Ingold, K.U. *Acc. Chem. Res.* ***2004***, *37*, 334.

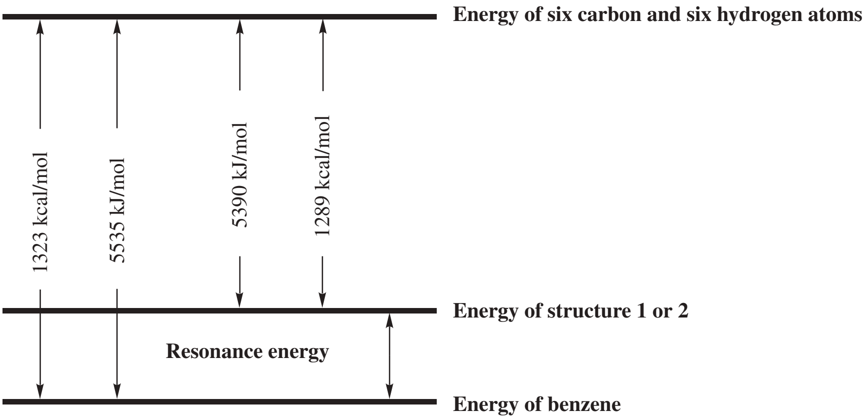

Fig. 2.2. Resonance energy in benzene.

Another method frequently used for estimation of resonance energy involves measurements of heats of hydrogenation.[25] Thus, the heat of hydrogenation of cyclohexene is 28.6 kcal mol^{-1} (120 kJ mol^{-1}), so we might expect a hypothetical **1** or **2** with three double bonds to have a heat of hydrogenation of about 85.8 kcal mol^{-1} (360 kJ mol^{-1}). The real benzene has a heat of hydrogenation of 49.8 kcal mol^{-1} (208 kJ mol^{-1}), which gives a resonance energy of 36 kcal mol^{-1} (152 kJ mol^{-1}). By any calculation the real molecule is more stable than a hypothetical **1** or **2**.

The energies of the six benzene orbitals can be calculated from HMO theory in terms of two quantities, α and β. The parameter α is the amount of energy possessed by an isolated 2*p* orbital before overlap, while β (called the *resonance integral*) is an energy unit expressing the degree of stabilization resulting from π-orbital overlap. A negative value of β corresponds to stabilization, and the energies of the six orbitals are (lowest to highest): $\alpha + 2\beta$, $\alpha + \beta$, $\alpha + \beta$, $\alpha - \beta$, $\alpha - \beta$, and $\alpha - 2\beta$.[26] The total energy of the three occupied orbitals is $6\alpha + 8\beta$, since there are two electrons in each orbital. The energy of an ordinary double bond is $\alpha + \beta$, so that structure **1** or **2** has an energy of $6\alpha + 6\beta$. The resonance energy of benzene is therefore 2β. Unfortunately, there is no convenient way to calculate the value of β from molecular-orbital theory. It is often given for benzene as about 18 kcal mol^{-1} (76 kJ mol^{-1}); this number being one-half of the resonance energy calculated from heats of combustion or hydrogenation. Using modern *ab initio* calculations, bond resonance energies for many aromatic hydrocarbons other than benzene have been reported.[27]

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[25] For a review of heats of hydrogenation, with tables of values, see Jensen, J.L. *Prog. Phys. Org. Chem.* ***1976***, *12*, 189.

[26] For the method for calculating these and similar results given in this chapter, see Higasi, K.; Baba, H.; Rembaum, A. *Quantum Organic Chemistry*, Interscience, NY, ***1965***. For values of calculated orbital energies and bond orders for many conjugated molecules, see Coulson, C.A.; Streitwieser, Jr., A. *Dictionary of π Electron Calculations*, W.H. Freeman, San Francisco, ***1965***.

[27] Aihara, J-i. *J. Chem. Soc. Perkin Trans 2* ***1996***, 2185.

Isodesmic and homodesmotic reactions are frequently used for the study of aromaticity from the energetic point of view.[28] However, the energy of the reactions used experimentally or in calculations may reflects only the relative aromaticity of benzene and not its absolute aromaticity. A new homodesmotic reactions based on radical systems predict an absolute aromaticity of 29.13 kcal mol^{-1} (121.9 kJ mol^{-1}) for benzene and an absolute antiaromaticity of 40.28 kcal mol^{-1} (168.5 kJ mol^{-1}) for cyclobutadiene at the MP4(SDQ)/6-31G-(*d*,*p*) level.[29]

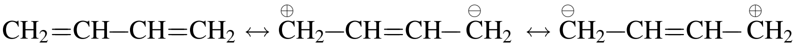
We might expect that in compounds exhibiting delocalization the bond distances would lie between the values gives in Table 1.5. This is certainly the case for benzene, since the carbon–carbon bond distance is 1.40 Å,[30] which is between the 1.48 Å for an sp^2–sp^2 C—C single bond and the 1.32 Å of the sp^2–sp^2 C=C double bond.[31]

Kinds of Molecules That Have Delocalized Bonds

There are four main types of structure that exhibit delocalization:

1. *Double (or Triple) Bonds in Conjugation.*[32] The double bonds in benzene are conjugated, of course, but the conjugation exists in acyclic molecules such as butadiene. In the molecular orbital picture (Fig. 2.3), the overlap of four orbitals gives two bonding orbitals that contain the four electrons and two vacant antibonding orbitals. It can be seen that each orbital has one more node than the one of next lower energy. The energies of the four orbitals are (lowest to highest): $\alpha + 1.618\beta$, $\alpha + 0.618\beta$, $\alpha - 0.618\beta$, and $\alpha - 1.618\beta$; hence the total energy of the two occupied orbitals is $4\alpha + 4.472\beta$. Since the energy of two isolated double bonds is $4\alpha + 4\beta$, the resonance energy by this calculation is 0.472β.

   In the resonance picture, these structures are considered to contribute:



$$CH_2{=}CH{-}CH{=}CH_2 \leftrightarrow \overset{\oplus}{C}H_2{-}CH{=}CH{-}\overset{\ominus}{C}H_2 \leftrightarrow \overset{\ominus}{C}H_2{-}CH{=}CH{-}\overset{\oplus}{C}H_2$$

6 **7** **8**

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[28] Hehre, W.J.; Ditchfield, R.; Radom, L.; Pople, J.A. *J. Am. Chem.Soc.* ***1970***, *92*, 4796; Hehre, W.J.; Radom, L.; Pople, J.A. *J. Am. Chem. Soc.* ***1971***, *93*, 289; George, P.; Trachtman, M.; Bock, C.W.; Brett, A.M. *Theor. Chim. Acta*, ***1975***, *38*, 121; George, P.; Trachtman, M.; Bock, C.W.; Brett, A.M. *J. Chem. Soc. Perkin Trans. 2* ***1976***, 1222; George, P.; Trachtman, M.; Brett, A.M. Bock, C.W.; *Tetrahedron* ***1976***, *32*, 317; George, P.; Trachtman, M.; Brett, A.M.; Bock, C.W. *J. Chem. Soc. Perkin Trans. 2* ***1977***, 1036.

[29] Suresh, C.H.; Koga, N. *J. Org. Chem.* ***2002***, *67*, 1965.

[30] Bastiansen, O.; Fernholt, L.; Seip, H.M.; Kambara, H.; Kuchitsu, K. *J. Mol. Struct.* ***1973***, *18*, 163; Tamagawa, K.; Iijima, T.; Kimura, M. *J. Mol. Struct.* ***1976***, *30*, 243.

[31] The average C—C bond distance in aromatic rings is 1.38 Å: Allen, F.H.; Kennard, O.; Watson, D.G.; Brammer, L.; Orpen, A.G.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* ***1987***, p. S8.

[32] For reviews of conjugation in open-chain hydrocarbons, see Simmons, H.E. *Prog. Phys. Org. Chem.* ***1970***, *7*, 1; Popov, E.M.; Kogan, G.A. *Russ. Chem. Rev.* ***1968***, *37*, 119.

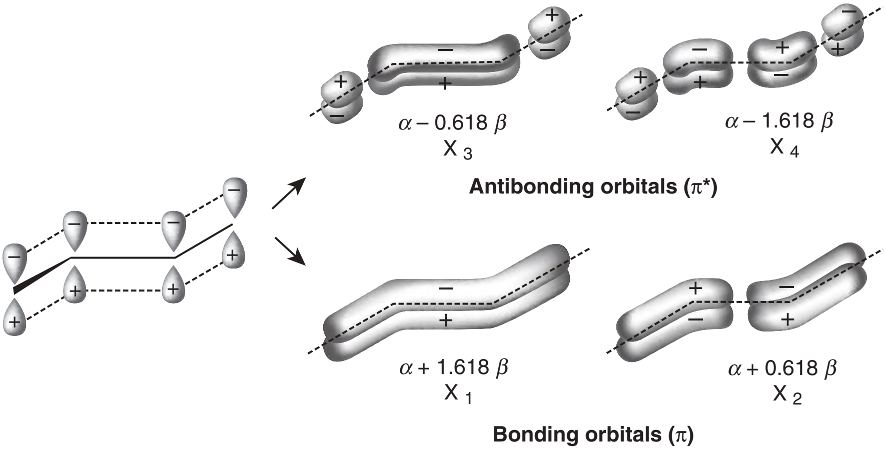

Fig. 2.3. The four π-orbitals of butadiene, formed by overlap of four *p* orbitals.

In either picture, the bond order of the central bond should be >1 and that of the other carbon–carbon bonds <2, although neither predicts that the three bonds have equal electron density. Molecular-orbital bond orders of 1.894 and 1.447 have been calculated.[33]

The existence of delocalization in butadiene and similar molecules has been questoned. The bond lengths in butadiene are 1.34 Å for the double bonds and 1.48 Å for the single bond.[34] Since the typical single-bond distance of a bond that is not adjacent to an unsaturated group is 1.53 Å (p. 26), it has been argued that the shorter single bond in butadiene provides evidence for resonance. However, this shortening can also be explained by hybridization changes (see p. 26); and other explanations have also been offered.[35] Resonance energies for butadienes, calculated from heats of combustion or hydrogenation, are only about 4 kcal mol^{-1} (17 kJ mol^{-1}), and these values may not be entirely attributable to resonance. Thus, a calculation from heat of atomization data gives a resonance energy of 4.6 kcal mol^{-1} (19 kJ mol^{-1}) for *cis*-1,3-pentadiene, and −0.2 kcal mol^{-1} (−0.8 kJ mol^{-1}), for 1,4-pentadiene. These two compounds, each of which possesses two double bonds, two C—C single bonds, and eight C—H bonds, would seem to offer as similar a comparison as we could make of a conjugated with a nonconjugated compound, but they are nevertheless not strictly comparable. The former has three sp^3 C—H and five sp^2 C—H bonds, while the latter has two and six, respectively. Also, the two single C—C bonds

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[33] Coulson, C.A. *Proc. R. Soc. London, Ser. A* ***1939***, *169*, 413.

[34] Marais, D.J.; Sheppard, N.; Stoicheff, B.P. *Tetrahedron* ***1962***, *17*, 163.

[35] Bartell, L.S. *Tetrahedron* ***1978***, *34*, 2891, *J. Chem. Educ.* ***1968***, *45*, 754; Wilson, E.B. *Tetrahedron* ***1962***, *17*, 191; Hughes, D.O. *Tetrahedron* ***1968***, *24*, 6423; Politzer, P.; Harris, D.O. *Tetrahedron* ***1971***, *27*, 1567.

of the 1,4-diene are both sp^2–sp^3 bonds, while in the 1,3-diene, one is sp^2–sp^3 and the other sp^2–sp^2. Therefore, it may be that some of the already small value of 4 kcal mol^{-1} (17 kJ mol^{-1}) is not resonance energy but arises from differing energies of bonds of different hybridization.[36]

Although bond distances fail to show it and the resonance energy is low, the fact that butadiene is planar[37] shows that there is some delocalization, even if not as much as previously thought. Similar delocalization is found in other conjugated systems (e.g., C=C–C=O[38] and C=C–C=N), in longer systems with three or more multiple bonds in conjugation, and where double or triple bonds are conjugated with aromatic rings. Diynes such as 1,3-butadiyne (**9**) are another example of conjugated molecules. Based on calculations, Rogers et al. reported that the conjugation stabilization of 1,3-butadiyne is zero.[39] Later calculations concluded that consideration of hyperconjugative interactions provides a more refined measure of conjugative stabilization.[40] When this measure is used, the conjugation energies of the isomerization and hydrogenation reactions considered agree with a conjugative stabilization of 9.3 (0.5 kcal mol^{-1} for diynes and 8.2 (0.1 kcal mol^{-1} for dienes.

$$\mathrm{H{-}C{\equiv}C{-}C{\equiv}C{-}H}$$

9

2. *Double (or Triple) Bonds in Conjugation with a p Orbital on an Adjacent Atom.* Where a *p* orbital is on an atom adjacent to a double bond, there are three parallel *p* orbitals that overlap. As previously noted, it is a general rule that the overlap of *n* atomic orbitals creates *n* molecular orbitals, so overlap of a *p* orbital with an adjacent double bond gives rise to three new orbitals, as

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[36] For negative views on delocalization in butadiene and similar molecules, see Dewar, M.J.S.; Gleicher, G.J. *J. Am. Chem. Soc.* ***1965***, *87*, 692; Brown, M.G. *Trans. Faraday Soc.* ***1959***, *55*, 694; Somayajulu, G.R. *J. Chem. Phys.* ***1959***, *31*, 919; Mikhailov, B.M. *J. Gen. Chem. USSR* ***1966***, *36*, 379. For positive views, see Miyazaki, T.; Shigetani, T.; Shinoda, H. *Bull. Chem. Soc. Jpn.* ***1971***, *44*, 1491; Berry, R.S. *J. Chem. Phys.* ***1962***, *30*, 936; Kogan, G.A.; Popov, E.M. *Bull. Acad. Sci. USSR Div. Chem. Sci.* ***1964***, 1306; Altmann, J.A.; Reynolds, W.F. *J. Mol. Struct.*, ***1977***, *36*, 149. In general, the negative argument is that resonance involving excited structures, such as **7** and **8**, is unimportant. See rule 6 on p. $$$. An excellent discussion of the controversy is found in Popov, E.M.; Kogan, G.A. *Russ. Chem. Rev.* ***1968***, *37*, 119, pp. 119–124.

[37] Marais, D.J.; Sheppard, N.; Stoicheff, B.P. *Tetrahedron* ***1962***, *17*, 163; Fisher, J.J.; Michl, J. *J. Am. Chem. Soc.* ***1987***, *109*, 1056; Wiberg, K.B.; Rosenberg, R.E.; Rablen, P.R. *J. Am. Chem. Soc.* ***1991***, *113*, 2890.

[38] For a treatise on C=C–C=O systems, see Patai, S.; Rappoport, Z. *The Chemistry of Enones*, two parts; Wiley, NY, ***1989***.

[39] Rogers, D.W.; Matsunaga, N.; Zavitsas, A.A.; McLafferty, F.J.; Liebman, J.F. *Org. Lett.* ***2003***, *5*, 2373; Rogers, D.W.; Matsunaga, N.; McLafferty, F.J.; Zavitsas, A.A.; Liebman, J.F. *J. Org. Chem.* ***2004***, *69*, 7143.

[40] Jarowski, P.D.; Wodrich, M.D.; Wannere, C.S.; Schleyer, P.v.R.; Houk, K.N. *J. Am. Chem. Soc.* ***2004***, *126*, 15036.

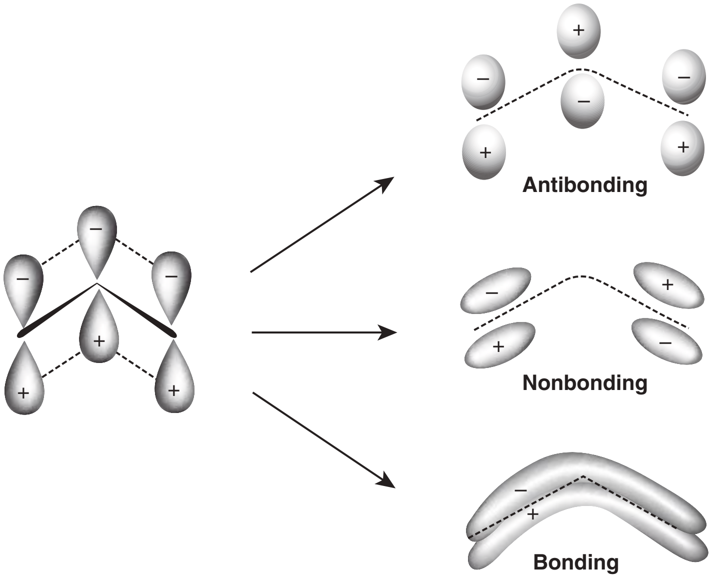
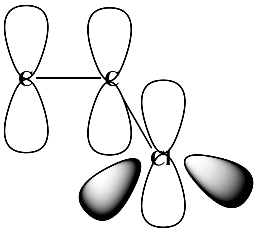


Fig. 2.4. The three orbitals of an allylic carbon, formed by overlap of three *p* orbitals.

shown in Fig. 2.4. The middle orbital is a *nonbonding orbital* of zero bonding energy. The central carbon atom does not participate in the nonbonding orbital.

There are three cases: the original *p* orbital may have contained two, one, or no electrons. Since the original double bond contributes two electrons, the total number of electrons accommodated by the new orbitals is four, three, or two. A typical example of the first situation is vinyl chloride $CH_2{=}CH{-}Cl$. Although the *p* orbital of the chlorine atom is filled, it still overlaps with the double bond (see **10**). The four electrons occupy the two molecular orbitals of lowest energies. This is our first example of resonance involving overlap between unfilled orbitals and a *filled* orbital. Canonical forms for vinyl chloride are shown in **11**.



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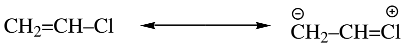
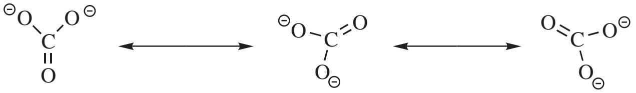


$$CH_2{=}CH{-}Cl \longleftrightarrow \overset{\ominus}{C}H_2{-}CH{=}\overset{\oplus}{Cl}$$

11

Any system containing an atom that has an unshared pair and that is directly attached to a multiple-bond atom can show this type of delocalization.

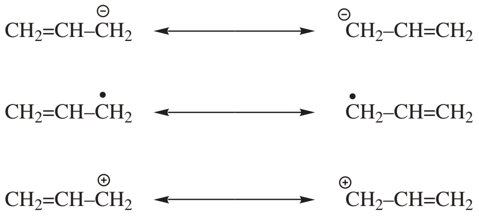
Another example is the carbonate ion:



The bonding in allylic carbanions, for example, $CH_2{=}CH{-}CH_2^-$, is similar.

The other two cases, where the original *p* orbital contains only one or no electron, are generally found only in free radicals and cations, respectively. Allylic free radicals have one electron in the nonbonding orbital. In allylic cations this orbital is vacant and only the bonding orbital is occupied. The orbital structures of the allylic carbanion, free radical, and cation differ from each other, therefore, only in that the nonbonding orbital is filled, half-filled, or empty. Since this is an orbital of zero bonding energy, it follows that the bonding π energies of the three species relative to electrons in the 2*p* orbitals of free atoms are the same. The electrons in the nonbonding orbital do not contribute to the bonding energy, positively or negatively.[41]

By the resonance picture, the three species may be described as having double bonds in conjugation with, respectively, an unshared pair, an unpaired electron, and an empty orbital as in the allyl cation **12** (see Chapter 5).



$$CH_2{=}CH{-}\overset{\ominus}{C}H_2 \longleftrightarrow \overset{\ominus}{C}H_2{-}CH{=}CH_2$$

$$CH_2{=}CH{-}\overset{\bullet}{C}H_2 \longleftrightarrow \overset{\bullet}{C}H_2{-}CH{=}CH_2$$

$$CH_2{=}CH{-}\overset{\oplus}{C}H_2 \longleftrightarrow \overset{\oplus}{C}H_2{-}CH{=}CH_2$$

12

3. *π-Allyl and Other η-Complexes.* In the presence of transition metals, delocalized cations are stabilized by donating electrons to the metal.[42] In a C—Metal bond, such as H_3C—Fe, the carbon donates (shares) one electron with them metal, and is considered to be a one-electron donor. With a π-bond, such as that found in ethylene, both electrons can be donated to the metal to

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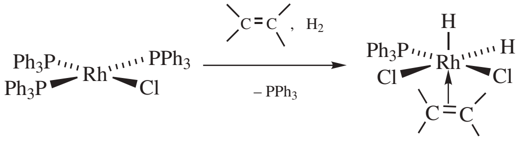
[41] It has been contended that here too, as with the benzene ring (Ref. 6), the geometry is forced upon allylic systems by the σ framework, and not the π system: Shaik, S.S.; Hiberty, P.C.; Ohanessian, G.; Lefour, J. *Nouv. J. Chim.*, ***1985***, *9*, 385. It has also been suggested, on the basis of ab initio calculations, that while the allyl cation has significant resonance stabilization, the allyl anion has little stabilization: Wiberg, K.B.; Breneman, C.M.; LePage, T.J. *J. Am. Chem. Soc.* ***1990***, *112*, 61.

[42] Crabtree, R.H. *The Organometallic Chemistry of the Transition Metals*, Wiley-Interscience, NY, ***2005***; Hill, A.F. *Organotransition Metal Chemistry*, Wiley Interscience, Canberra, ***2002***.

form a complex such as **14** by reaction of Wilkinson's catalyst (**13**) with an alkene and hydrogen gas,[43] and the π-bond is considered to be a two-electron donor. In these two cases, the electron donating ability of the group coordinated to the metal (the ligand) is indicated by terminology η^1, η^2, η^3, and so on, for a one-, two-, and three-electron donor, respectively.



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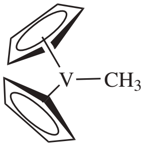
Wilkinson's catalyst

14



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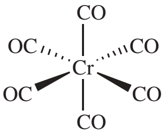

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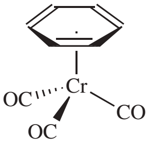

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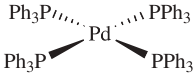

18

Ligands can therefore be categorized as η-ligands according to their electron donation to the metal. A hydrogen atom (as in **14**) or a halogen ligand (as in **13**) are η^1 ligands and an amine (NR_3), a phosphine (PR_3, as in **13**, **14**, and **18**), CO (as in **16** or **17**), an ether (OR_2) or a thioether (SR_2) are η^2 ligands. Hydrocarbon ligands include alkyl (as the methyl in **15**) or aryl with a C—metal bond (η^1), alkenes or carbenes (η^2, see p. 116), π-allyl (η^3), conjugated dienes such as 1,3-butadiene (η^4), cyclopentadienyl (η^5, as in **15** and see p 63), and arenes or benzene (η^6).[44] Note that in the formation of **14** from **13**, the two electron donor alkene displaces a two-electron donor phosphine. Other typical complexes include chromium hexacarbonyl $Cr(CO)_6$ (**16**), with six η^2-CO ligands; η^6-$C_6H_6Cr(CO)_3$ (**18**), and *tetrakis*-triphenylphosphinopalladium (0), **17**, with four η^2-phosphine ligands.

In the context of this section, the electron-delocalized ligand π-allyl (**12**) is an η^3 donor and it is well known that allylic halides react with $PdCl_2$ to form a *bis*-η^3-complex **19** (see the 3D model **20**).[45] Complexes, such as **19**, react with nucleophiles to give the corresponding coupling product (**10–60**).[46] The

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[43] Jardine, F.H., Osborn, J.A.; Wilkinson, G.; Young, G.F. *Chem. Ind. (London)* ***1965***, 560; Imperial Chem. Ind. Ltd., *Neth. Appl. 6,602,062* [*Chem. Abstr., 66*: 10556y ***1967***]; Bennett, M.A.; Longstaff, P.A. *Chem. Ind.* ***1965***, 846.

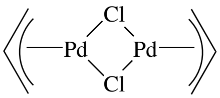
[44] Davies, S.G. *Organotransition Metal Chemistry*, Pergamon, Oxford, ***1982***, p. 4.

[45] Trost, B.M.; Strege, P.E.; Weber, L.; Fullerton, T.J.; Dietsche, T.J. *J. Am. Chem. Soc.* ***1978***, *100*, 3407.

[46] Trost, B.M.; Weber, L.; Strege, P.E.; Fullerton, T.J.; Dietsche, T.J. *J. Am. Chem. Soc.*, ***1978*** *100*, 3416.

reaction of allylic acetates or carbons and a catalytic amount of palladium (0) compounds also lead to an η^3-complex that can react with nucleophiles.[47]

$[\ \mathrm{PdCl}(\pi\text{-allyl})\ ]_2 = [\ \mathrm{PdCl}(\eta^3\mathrm{C_3H_5})\ ]_2 =$



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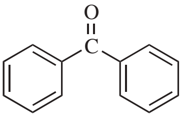
20

4. *Hyperconjugation*. The type of delocalization called *hyperconjugation*, is discussed on p. 95.

We will find examples of delocalization that cannot be strictly classified as belonging to any of these types.

Cross Conjugation[48]

In a cross-conjugated compound, three groups are present, two of which are not conjugated with each other, although each is conjugated with the third. Some examples[49] are benzophenone (**21**), triene **22** and divinyl ether **23**. Using the



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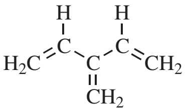

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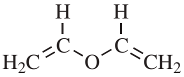

23

molecular-orbital method, we find that the overlap of six *p* orbitals in **22** gives six molecular orbitals, of which the three bonding orbitals are shown in Fig. 2.5, along with their energies. Note that two of the carbon atoms do not participate in the $\alpha + \beta$ orbital. The total energy of the three occupied orbitals is $6\alpha + 6.900\beta$, so the resonance energy is 0.900β. Molecular-orbital bond orders are 1.930 for the C-1,C-2 bond, 1.859 for the C-3,C-6 bond and 1.363 for the C-2,C-3 bond.[49] Comparing these values with those for butadiene (p. 39), we see that the C-1,C-2 bond contains more and the C-3,C-6 bond less double-bond character than the double bonds in butadiene. The resonance picture supports this conclusion, since each C-1,C-2 bond is double in three of the five canonical forms, while the C-3,C-6 bond is double in only one. In most cases, it is easier to treat cross-conjugated

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[47] Melpolder, J.B.; Heck, R.F. *J. Org. Chem.* ***1976***, *41*, 265; Trost, B.M.; Verhoeven, T.R. *J. Am. Chem. Soc.*, ***1976***, *98*, 630; ***1978***, *100*, 3435; Takahashi, K.; Miyake, A.; Hata, G. *Bull Chem. Soc. Jpn.* ***1970***, *45*, 230,1183; Trost, B.M.; Verhoeven, T.R. *J. Org. Chem.* ***1976***, *41*, 3215; Trost, B.M.; Verhoeven, T.R. *J. Am. Chem. Soc.* ***1980***, *102*, 4730.

[48] For a discussion, see Phelan, N.F.; Orchin, M. *J. Chem. Educ.* ***1968***, *45*, 633.

[49] Compound **22** is the simplest of a family of cross-conjugated alkenes, called dendralenes. For a review of these compounds, see Hopf, H. *Angew. Chem. Int. Ed.* ***1984***, *23*, 948.

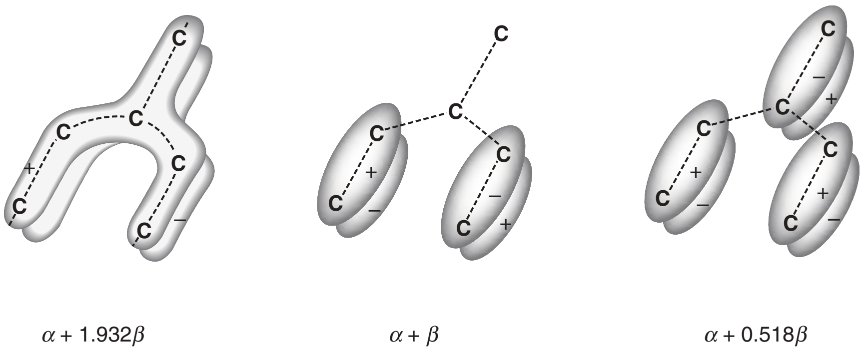
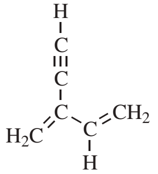


Fig. 2.5. The three bonding orbitals of 3-methylelene-1,4-pentadiene (**22**).

molecules by the molecular-orbital method than by the valence-bond method.



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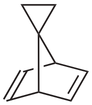

26

One consequence of this phenomenon is that the cross-conjugated C=C unit has a slightly longer bond length that the noncross conjugated bond. In **24**, for example, the cross-conjugated bond is ~0.01 Å longer.[50] The conjugative effect of a C=C or C≡C unit can be measured. An ethenyl substituent on a conjugated enone contributes 4.2 kcal mol^{-1} and an ethynyl substituent has a more variable effect but contributes ~2.3 kcal mol^{-1}.[51]

The phenomenon of homoconjugation is related to cross-conjugation in that there are C=C units in close proximity, but not conjugated one to the other. Homoconjugation arises when the termini of two orthogonal π-systems are held in close proximity by being linked by a spiro-tetrahedral carbon atom.[52] Spiro[4.4]nonatetraene (**25**)[53] is an example and it known that the HOMO (p. 1208) of **25** is raised relative to cyclopentadiene, whereas the LUMO is unaffected[54] Another example

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[50] Trætteberg, M.; Hopf, H. *Acta Chem. Scand. B* ***1994***, *48*, 989.

[51] Trætteberg, M.; Liebman, J.F.; Hulce, M.; Bohn, A.A.; Rogers, D.W. *J. Chem. Soc. Perkin Trans. 2* ***1997***, 1925.

[52] Simons, H.E.; Fukunaga, R. *J. Am. Chem. Soc.* ***1967***, *89*, 5208; Hoffmann, R.; Imamura, A.; Zeiss, G.D. *J. Am. Chem. Soc.* ***1967***, *89*, 5215; Durr, H.; Gleiter, R. *Angew. Chem. Int. Ed.* ***1978***, *17*, 559.

[53] For the synthesis of this molecule, see Semmelhack, M.F.; Foos, J.S.; Katz, S. *J. Am. Chem. Soc.* ***1973***, *95*, 7325.

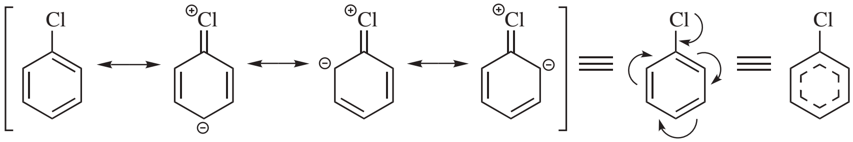
[54] Raman, J.V.; Nielsen, K.E.; Randall, L.H.; Burke, L.A.; Dmitrienko, G.I. *Tetrahedron Lett.* ***1994***, *35*, 5973.

is **26**, where there are bond length distortions caused by electronic interactions between the unsaturated bicyclic moiety and the cyclopropyl moiety.[55] It is assumed that cyclopropyl homoconjugation is responsible for this effect.

The Rules of Resonance

We have seen that one way of expressing the actual structure of a molecule containing delocalized bonds is to draw several possible structures and to assume that the actual molecule is a hybrid of them. These canonical forms have no existence except in our imaginations. The molecule does *not* rapidly shift between them. It is *not* the case that some molecules have one canonical form and some another. All the molecules of the substance have the same structure. That structure is always the same all the time and is a weighted average of all the canonical forms. In drawing canonical forms and deriving the true structures from them, we are guided by certain rules, among them the following:

1. All the canonical forms must be bona fide Lewis structures (see p. 14). For example, none of them may have a carbon with five bonds.
2. The positions of the nuclei must be the same in all the structures. This means that when we draw the various canonical forms, all we are doing is putting in the *electrons* in different ways. For this reason, shorthand ways of representing resonance are easy to devise:



27 **28**

The resonance interaction of chlorine with the benzene ring can be represented as shown in **27** or **28** and both of these representations have been used in the literature to save space. However, we will not use the curved-arrow method of **27** since arrows will be used in this book to express the actual movement of electrons in reactions. We will use representations like **28** or else write out the canonical forms. The convention used in dashed-line formulas like **28** is that bonds that are present in all canonical forms are drawn as solid lines while bonds that are not present in all forms are drawn as dashed lines. In most resonance, σ bonds are not involved, and only the π or unshared electrons are put in, in different ways. This means that if we write one canonical form for a molecule, we can then write the others by merely moving π and unshared electrons.

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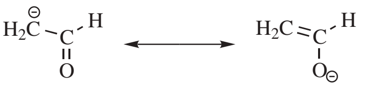
[55] Haumann, T.; Benet-Buchholz, J.; Klärner, F.-G.; Boese, R. *Liebigs Ann. Chem.* ***1997***, 1429.

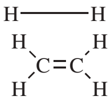
3. All atoms taking part in the resonance, that is, covered by delocalized electrons, must lie in a plane or nearly so (see p. 48). This, of course, does not apply to atoms that have the same bonding in all the canonical forms. The reason for planarity is maximum overlap of the *p* orbitals.
4. All canonical forms must have the same number of unpaired electrons. Thus $^{\bullet}CH_2{-}CH{=}CH{-}CH_2{\bullet}$ is not a valid canonical form for butadiene.
5. The energy of the actual molecule is lower than that of any form, obviously. Therefore, delocalization is a stabilizing phenomenon.[56]
6. All canonical forms do not contribute equally to the true molecule. Each form contributes in proportion to its stability, the most stable form contributing most. Thus, for ethylene, the form $^{+}CH_2{-}CH_2^{-}$ has such a high energy compared to $CH_2{=}CH_2$ that it essentially does not contribute at all. We have seen the argument that such structures do not contribute even in such cases as butadiene.[36] Equivalent canonical forms, such as **1** and **2**, contribute equally. The greater the number of significant structures that can be written and the more nearly equal they are, the greater the resonance energy, other things being equal.

It is not always easy to decide relative stabilities of imaginary structures; the chemist is often guided by intuition.[57] However, the following rules may be helpful:

a. Structures with more covalent bonds are ordinarily more stable than those with fewer (cf. **6** and **7**).
b. Stability is decreased by an increase in charge separation. Structures with formal charges are less stable than uncharged structures. Structures with more than two formal charges usually contribute very little. An especially unfavorable type of structure is one with two like charges on adjacent atoms.
c. Structures that carry a negative charge on a more electronegative atom are more stable than those in which the charge is on a less electronegative atom. Thus, **30** is more stable than **29**. Similarly, positive charges are best carried on atoms of low electronegativity.



29 **30**



31

d. Structures with distorted bond angles or lengths are unstable, for example, the structure **31** for ethane.

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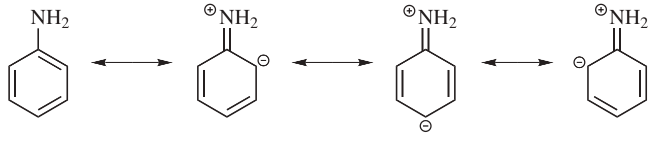
[56] It has been argued that resonance is not a stabilizing phenomenon in all systems, especially in acyclic ions: Wiberg, K.B. *Chemtracts: Org. Chem.* ***1989***, *2*, 85. See also, Siggel, M.R.; Streitwieser Jr., A.; Thomas, T.D. *J. Am. Chem. Soc.* ***1988***, *110*, 8022; Thomas, T.D.; Carroll, T.X.; Siggel, M.R. *J. Org. Chem.* ***1988***, *53*, 1812.

[57] A quantitative method for weighting canonical forms has been proposed by Gasteiger, J.; Saller, H. *Angew. Chem. Int. Ed.* ***1985***, *24*, 687.

The Resonance Effect

Resonance always results in a different distribution of electron density than would be the case if there were no resonance. For example, if **32** were the actual structure of aniline, the two unshared electrons of the nitrogen would reside entirely on that atom. The structure of **32** can be represented as a hybrid that includes contributions from the canonical forms shown, indicating that the electron density of the unshared pair does not reside entirely on the nitrogen, but is spread over the ring. This decrease in electron density at one position (and corresponding increase elsewhere) is called the *resonance* or *mesomeric effect*. We loosely say that the NH_2 contributes or donates electrons to the ring by a resonance effect, although no actual contribution takes place. The "effect" is caused by the fact that the electrons are in a different place from that we would expect if there were no resonance. In ammonia, where resonance is absent, the unshared pair *is* located on the nitrogen atom. As with the field effect (p. 20), we think of a certain molecule (in this case ammonia) as a substrate and then see what happens to the electron density when we make a substitution. When one of the hydrogen atoms of the ammonia molecule is replaced by a benzene ring, the electrons are "withdrawn" by the resonance effect, just as when a methyl group replaces a hydrogen of benzene, electrons are "donated" by the the field effect of the methyl. The idea of donation or withdrawal merely arises from the comparison of a compound with a closely related one or a real compound with a canonical form.



32

Steric Inhibition of Resonance and the Influences of Strain

Rule 3 states that all the atoms covered by delocalized electrons must lie in a plane or nearly so. Many examples are known where resonance is reduced or prevented because the atoms are sterically forced out of planarity.

Bond lengths for the *o*- and *p*-nitro groups in picryl iodide are quite different.[58] Distance *a* in **33** is 1.45 Å, whereas *b* is 1.35 Å. This phenomenon can be explained if the oxygens of the *p*-nitro group are in the plane of the ring and thus in resonance with it, so that *b* has partial double-bond character, while the oxygens of the *o*-nitro

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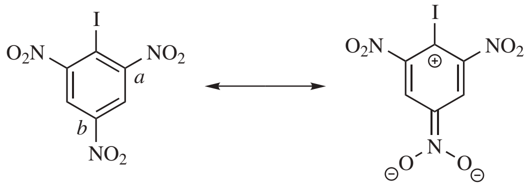
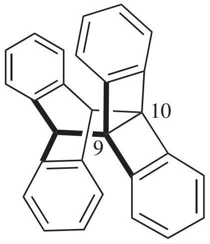
[58] Wepster, B.M. *Prog. Stereochem.* ***1958***, *2*, 99, p. 125. For another example of this type of steric inhibition of resonance, see Exner, O.; Folli, U.; Marcaccioli, S.; Vivarelli, P. *J. Chem. Soc. Perkin Trans. 2* ***1983***, 757.

groups are forced out of the plane by the large iodine atom.



33

The Dewar-type structure for the central ring of the anthracene system in **34** is possible only because the 9,10 substituents prevent the system from being planar.[59] **34** is the actual structure of the molecule and is not in resonance with forms like **35**, although in anthracene itself, Dewar structures and structures like **35** both contribute. This is a consequence of rule 2 (p. 46). In order for a **35**-like structure to contribute to resonance in **34**, the nuclei would have to be in the same positions in both forms.



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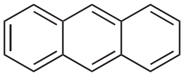

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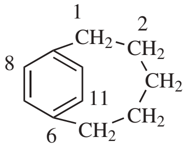

36

Even the benzene ring can be forced out of planarity.[60] In [5]paracyclophane (**36**),[61] the presence of a short bridge (this is the shortest para bridge known for a benzene ring) forces the benzene ring to become boat-shaped. The parent **36** has so far not proven stable enough for isolation, but a UV spectrum was obtained and showed that the benzene ring was still aromatic, despite the distorted ring.[62] The 8,11-dichloro analog of **36** is a stable solid, and X-ray diffraction showed

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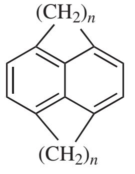
[59] Applequist, D.E.; Searle, R. *J. Am. Chem. Soc.* ***1964***, *86*, 1389.

[60] For a review of planarity in aromatic systems, see Ferguson, G.; Robertson, J.M. *Adv. Phys. Org. Chem.* ***1963***, *1*, 203.

[61] For a monograph, see Keehn, P.M.; Rosenfeld, S.M. *Cyclophanes*, 2 vols., Academic Press, NY, ***1983***. For reviews, see Bickelhaupt, F. *Pure Appl. Chem.* ***1990***, *62*, 373; Vögtle, F.; Hohner, G. *Top. Curr. Chem.* ***1978***, *74*, 1; Cram, D.J.; Cram, J.M. *Acc. Chem. Res.* ***1971***, *4*, 204; Vögtle, F.; Neumann, P. reviews in *Top. Curr. Chem.* ***1983***, *113*, 1; ***1985***, *115*, 1.

[62] Jenneskens, L.W.; de Kanter, F.J.J.; Kraakman, P.A.; Turkenburg, L.A.M.; Koolhaas, W.E.; de Wolf, W.H.; Bickelhaupt, F.; Tobe, Y.; Kakiuchi, K.; Odaira, Y. *J. Am. Chem. Soc.* ***1985***, *107*, 3716. See also Tobe, Y.; Kaneda, T.; Kakiuchi, K.; Odaira, Y. *Chem. Lett.* ***1985***, 1301; Kostermans, G.B.M.; de Wolf, W.E.; Bickelhaupt, F. *Tetrahedron Lett.* ***1986***, *27*, 1095; van Zijl, P.C.M.; Jenneskens, L.W.; Bastiaan, E.W.; MacLean, C.; de Wolf, W.E.; Bickelhaupt, F. *J. Am. Chem. Soc.* ***1986***, *108*, 1415; Rice, J.E.; Lee, T.J.; Remington, R.B.; Allen, W.D.; Clabo Jr., D.A.; Schaefer III, H.F. *J. Am. Chem. Soc.* ***1987***, *109*, 2902.

that the benzene ring is boat-shaped, with one end of the boat bending ∼27° out of the plane, and the other ∼12°.[63] This compound too is aromatic, as shown by UV and NMR spectra. [6]Paracyclophanes are also bent,[64] but in [7]paracyclophanes the bridge is long enough so that the ring is only moderately distorted. Similarly, [*n,m*]paracyclophanes (**37**), where *n* and *m* are both 3 or less (the smallest yet prepared is [2.2]paracyclophane), have bent (boat-shaped) benzene rings. All these compounds have properties that depart significantly from those of ordinary benzene compounds. Strained paracyclophanes exhibit both π- and σ-strain, and the effect of the two types of strain on the geometry is approximately additive.[65] In "belt" cyclophane **38**,[66] the molecule has a pyramidal structure with C_3 symmetry rather than the planar structure found in [18]-annulene. 1,8-Dioxa[8](2,70-pyrenophane (**39**)[67] is another severely distorted aromatic hydrocarbon, in which the bridge undergoes rapid pseudo-rotation (p. 212). A recent study showed that despite substantial changes in the hybridization of carbon atoms involving changes in the σ-electron structure of pyrenephane, such as **39**, the aromaticity of the system decreases slightly and regularly upon increasing the bend angle θ from 0 to 109.2°.[68] Heterocyclic paracyclophane analogs have been prepared, such as the report of [2.*n*](2,5)pyridinophanes.[69]



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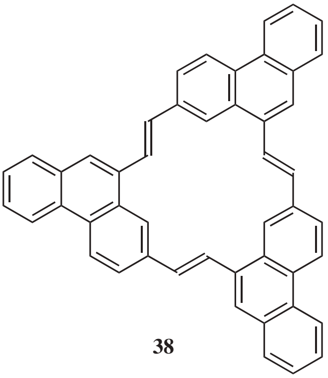

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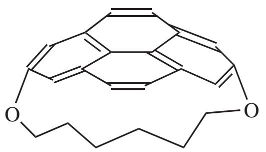

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[63] Jenneskens, L.W.; Klamer, J.C.; de Boer, H.J.R.; de Wolf, W.H.; Bickelhaupt, F.; Stam, C.H. *Angew. Chem. Int. Ed.* ***1984***, *23*, 238.

[64] See, for example, Liebe, J.; Wolff, C.; Krieger, C.; Weiss, J.; Tochtermann, W. *Chem. Ber.* ***1985***, *118*, 4144; Tobe, Y.; Ueda, K.; Kakiuchi, K.; Odaira, Y.; Kai, Y.; Kasai, N. *Tetrahedron* ***1986***, *42*, 1851.

[65] Stanger, A.; Ben-Mergui, N.; Perl, S. *Eur. J. Org. Chem.* ***2003***, 2709.

[66] Meier, H.; Müller, K. *Angew. Chem. Int. Ed.*, ***1995***, *34*, 1437.

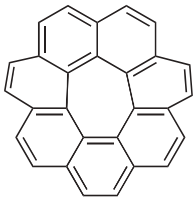
[67] Bodwell, G.J.; Bridson, J.N.; Houghton, T.J.; Kennedy, J.W.J.; Mannion, M.R. *Angew. Chem. Int. Ed.*, ***1996***, *35*, 1320.

[68] Bodwell, G.J.; Bridson, J.N.; Cyranski, M.K.; Kennedy, J.W.J.; Krygowski, T.M.; Mannion, M.R.; Miller, D.O. *J. Org. Chem.* ***2003***, *68*, 2089; Bodwell, G.J.; Miller, D.O.; Vermeij, R.J. *Org. Lett.* ***2001***, *3*, 2093

[69] Funaki, T.; Inokuma, S.; Ida, H.; Yonekura, T.; Nakamura, Y.; Nishimura, J. *Tetrahedron Lett.* ***2004***, *45*, 2393.

There are many examples of molecules in which benzene rings are forced out of planarity, including 7-circulene (**40**),[70] 9,8-diphenyltetrabenz[*a,c,h,j*]anthracene (**41**),[71] and **42**[72] (see also p. 230). These have been called tormented aromatic systems.[73] The "record" for twisting an aromatic π-electron system appears to be 9,10,11,12,13,14,15,16-octaphenyldibenzo[*a,c*]naphthacene (**43**),[74] which has an end-to-end twist of 105°. This is >1.5 times as great as that observed in any previous polyaromatic hydrocarbon.

Perchlorotriphenylene has been reported in the literature and said to show severe molecular twisting, however, recent work suggests this molecule has not actually been isolated with perchlorofluorene-9-spirocyclohexa-2′,5′-diene being formed instead.[75] The X-ray structure of the linear [3]phenylene (benzo[3,4]cyclobuta-[1,2-b]biphenylene, **44**) has been obtained, and it shows a relatively large degree of bond alternation while the center distorts to a cyclic bis-allyl frame.[76]



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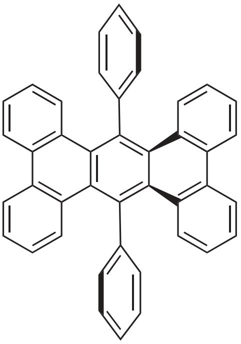

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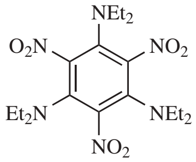

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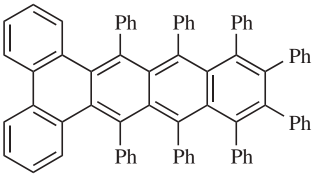

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[70] Yamamoto, K.; Harada, T.; Okamoto, Y.; Chikamatsu, H.; Nakazaki, M.; Kai, Y.; Nakao, T.; Tanaka, M.; Harada, S.; Kasai, N. *J. Am. Chem. Soc.* ***1988***, *110*, 3578.

[71] Pascal, Jr., R.A.; McMillan, W.D.; Van Engen, D.; Eason, R.G. *J. Am. Chem. Soc.* ***1987***, *109*, 4660.

[72] Chance, J.M.; Kahr, B.; Buda, A.B.; Siegel, J.S. *J. Am. Chem. Soc.* ***1989***, *111*, 5940.

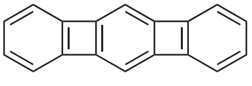
[73] Pascal, Jr., R.A. *Pure Appl. Chem.* ***1993***, *65*, 105.

[74] Qiao, X.; Ho, D.M.; Pascal Jr., R.A. *Angew. Chem. Int. Ed.*, ***1997***, *36*, 1531.

[75] Campbell, M.S.; Humphries, R.E.; Munn, N.M. *J. Org. Chem.* ***1992***, *57*, 641.

[76] Schleifenbaum, A.; Feeder, N.; Vollhardt, K.P.C. *Tetrahedron Lett.* ***2001***, *42*, 7329.

It is also possible to fuse strained rings on benzene, which induces great strain on the benzene ring. In **45**, the benzene ring is compressed by the saturated environment of the tetrahydropyran units. In this case, the strain leads to distortion of the benzene ring in **45** into a *boat* conformation.[77] Benzocyclopropene (**46**) and benzocyclobutene (**47**) are also molecules where the small annellated ring induces great strain on the benzene ring. In these cases, bonds of annellation and those adjacent to it are strained.



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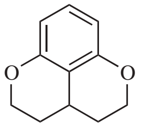

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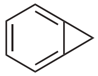

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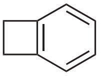

47

Strain-induced bond localization was introduced in 1930 by Mills and Nixon[78] and is commonly referred to as the *Mills–Nixon effect* (see Chapter 11, p. 677). Ortho-fused aromatic compounds, such as **46**, are known as cycloproparenes[79] and are highly strained. Cyclopropabenzene (**46**) is a stable molecule with a strain energy of 68 kcal mol^{-1} (284.5 kJ mol^{-1}).[80] and the annellated bond is always the shortest, although in **47** the adjacent bond is the shortest.[81] In cycloproparenes, there is the expectation of partial aromatic bond localization, with bond length alternation in the aromatic ring.[82] When the bridging units are saturated, the benzene ring current is essentially unchanged, but annelation with one or more cyclobutadieno units disrupts the benzene ring current.[83] The chemistry of the cycloproparenes is dominated by the influence of the high strain energy. When fused to a benzene ring, the bicyclo[1.1.0]butane unit also leads to strain-induced localization of aromatic π-bonds.[84]

*p*π–*d*π Bonding: Ylids

We have mentioned (p. 10) that, in general, atoms of the second row of the Periodic table do not form stable double bonds of the type discussed in Chapter 1

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[77] Hall, G.G *J. Chem. Soc. Perkin Trans. 2* ***1993***, 1491.

[78] Mills, W. H.; Nixon, I.G. *J. Chem. Soc.* ***1930***, 2510.

[79] Halton, B. *Chem. Rev.* ***2003***, *103*, 1327; Halton, B. *Chem. Rev.* ***1989***, *89*, 1161, and reviews cited therein.

[80] Billups, W.E.; Chow, W.Y.; Leavell, K.H.; Lewis, E.S.; Margrave, J.L.; Sass, R.L.; Shieh, J.J.; Werness, P.G.; Wood, J.L. *J. Am. Chem. Soc.* ***1973***, *95*, 7878.; Apeloig, Y.; Arad, D. *J. Am. Chem. Soc.* ***1986***, *108*, 3241.

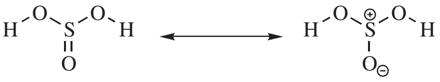
[81] Boese, R.; Bläser, D.; Billups, W.E.; Haley, M.M.; Maulitz, A.H.; Mohler, D.L.; Vollhardt, K.P.C. *Angew. Chem. Int. Ed.*, ***1994***, *33*, 313.

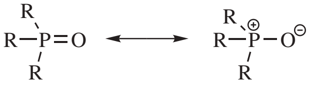
[82] Halton, B. *Pure Appl. Chem.* ***1990***, *62*, 541; Stanger, A. *J. Am. Chem. Soc.* ***1998***, *120*, 12034; Maksić, Z.B.; Eckert-Maksić, M.; Pfeifer, K.-H. *J. Mol. Struct.* ***1993***, *300*, 445; Mó, M.; Yáñez, M.; Eckert-Maksić, M.; Maksić, Z.B. *J. Org. Chem.* ***1995***, *60*, 1638; Eckert-Maksić, M.; Glasovac, Z.; Maksić, Z.B.; Zrinski, I. *J. Mol. Struct. (THEOCHEM)* ***1996***, *366*, 173; Baldridge, K.K.; Siegel, J.S. *J. Am. Chem. Soc.* ***1992***, *114*, 9583.

[83] Soncini, A.; Havenith, R.W.A.; Fowler, P.W.; Jenneskens, L.W.; Steiner, E. *J. Org. Chem.* ***2002***, *67*, 4753

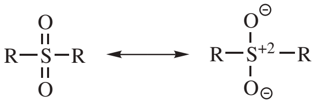
[84] Cohrs, C.; Reuchlein, H.; Musch, P.W.; Selinka, C.; Walfort, B.; Stalke, D.; Christl, M. *Eur. J. Org. Chem.* ***2003***, 901.

(π bonds formed by overlap of parallel *p* orbitals). However, there is another type of double bond that is particularly common for the second-row atoms, sulfur and phosphorus. For example, such a double bond is found in the compound H_2SO_3, as written on the left. Like an ordinary double bond, this double bond contains one *s* orbital, but the second orbital is not a π orbital formed by overlap of half-filled *p* orbitals; instead it is formed by overlap of a filled *p* orbital from the oxygen with an empty *d* orbital from the sulfur. It is called a *pπ–dπ orbital.*[85] Note that we can represent this molecule by two canonical forms, but the bond is nevertheless localized, despite the resonance. Some other examples of *pπ–dπ* bonding are Nitrogen analogs are known for some of these phosphorus compounds, but they are less stable because the resonance is lacking. For example, amine oxides, analogs of phosphine oxides, can only be written R_3N^+—O^-. The *pπ–dπ* canonical form is impossible since nitrogen is limited to eight outer-shell electrons.

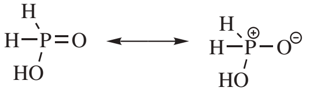




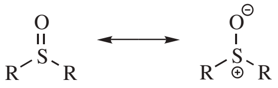
Phosphine oxides



Sulfones



Hypophorphoros acid



Sulfoxides

In all the examples given above, the atom that donates the electron pair is oxygen and, indeed, oxygen is the most common such atom. But in another important class of compounds, called *ylids*, this atom is carbon.[86] There are three main types of ylids phosphorus,[87] nitrogen,[88] and sulfur ylids,[89] although

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[85] For a monograph, see Kwart, H.; King, K. *d-Orbitals in the Chemistry of Silicon, Phosphorus, and Sulfur*; Springer, NY, ***1977***.

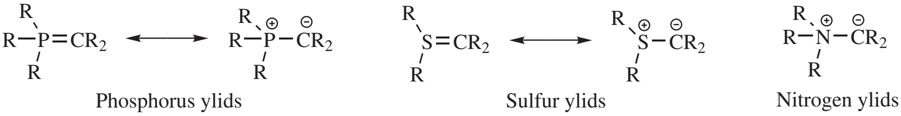
[86] For a monograph, see Johnson, A.W. *Ylid Chemistry*; Academic Press, NY, ***1966***. For reviews, see Morris, D.G., *Surv. Prog. Chem.* ***1983***, *10*, 189; Hudson, R.F. *Chem. Br.*, ***1971***, *7*, 287; Lowe, P.A. *Chem. Ind. (London)* ***1970***, 1070. For a review on the formation of ylids from the reaction of carbenes and carbenoids with heteroatom lone pairs, see Padwa, A.; Hornbuckle, S.F. *Chem. Rev.* ***1991***, *91*, 263.

[87] Although the phosphorus ylid shown has three R groups on the phosphorus atom, other phosphorus ylids are known where other atoms, for example, oxygen, replace one or more of these R groups. When the three groups are all alkyl or aryl, the phosphorus ylid is also called a phosphorane.

[88] For a review of nitrogen ylids, see Musker, W.K. *Fortschr. Chem. Forsch.* ***1970***, *14*, 295.

[89] For a monograph on sulfur ylids, see Trost, B.M.; Melvin Jr., L.S. *Sulfur Ylids*; Academic Press, NY, ***1975***. For reviews, see Fava, A, in Bernardi, F.; Csizmadia, I.G.; Mangini, A. *Organic Sulfur Chemistry*; Elsevier, NY, ***1985***, pp. 299–354; Belkin, Yu.V.; Polezhaeva, N.A. *Russ. Chem. Rev.* ***1981***, *50*, 481; Block, E. in Stirling, C.J.M. *The Chemistry of the Sulphonium Group*, part 2, Wiley, NY, ***1981***, pp. 680–702; Block, E. *Reactions of Organosulfur Compounds*; Academic Press, NY, ***1978***, pp. 91–127.

arsenic,[90] selenium, and so on, ylids are also known. Ylids may be defined as compounds in which a positively charged atom from group 15 or 16 of the Periodic table is connected to a carbon atom carrying an unshared pair of electrons. Because of $p\pi$–$d\pi$ bonding, two canonical forms can be written for phosphorus and sulfur, but there is only one for nitrogen ylids. Phosphorus ylids are much more stable than nitrogen ylids (see also p. 810). Sulfur ylids also have a low stability.



In almost all compounds that have $p\pi$–$d\pi$ bonds, the central atom is connected to four atoms or three atoms and an unshared pair and the bonding is approximately tetrahedral. The $p\pi$–$d\pi$ bond, therefore, does not greatly change the geometry of the molecule in contrast to the normal π bond, which changes an atom from tetrahedral to trigonal. Calculations show that nonstabilized phosphonium ylids have nonplanar ylidic carbon geometries whereas stabilized ylids have planar ylidic carbons.[91]

AROMATICITY[92]

In the nineteenth century, it was recognized that aromatic compounds[93] differ greatly from unsaturated aliphatic compounds,[94] but for many years chemists

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[90] For reviews of arsenic ylids, see Lloyd, D.; Gosney, I.; Ormiston, R.A. *Chem. Soc. Rev.* ***1987***, *16*, 45; Yaozeng, H.; Yanchang, S. *Adv. Organomet. Chem.* ***1982***, *20*, 115.

[91] Bachrach, S.M. *J. Org. Chem.* ***1992***, *57*, 4367.

[92] Krygowski, T.M.; Cyrañski, M.K.; Czarnocki, Z.; Häfelinger, G.; Katritzky, A.R. *Tetrahedron* ***2000***, *56*, 1783; Simkin, B.Ya.; Minkin, V.I.; Glukhovtsev, M.N., in *Advances in Heterocyclic Chemistry*, Vol. 56, Katritzky, A.R., Ed., Academic Press, San Diego, ***1993***, pp 303–428; Krygowski, T.M.; Cyranski, M.K. *Chem. Rev.* ***2001***, *101*, 1385; Katritzky, A.R.; Jug, K.; Oniciu, D.C. *Chem. Rev.* ***2001***, *101*, 1421; Katritzky, A.R.; Karelson, M.; Wells, A.P. *J. Org. Chem.* ***1996***, *61*, 1619. See also Cyranski, M.K.; Krygowski, T.M.; Katritzky, A.R.; Schleyer, P.v.R. *J. Org. Chem.* ***2002***, *67*, 1333.

[93] For books on Aromaticity, see Lloyd, D. *The Chemistry of Conjugated Cyclic Compounds*, Wiley, NY, ***1989***; *Non-Benzenoid Conjugated Carbocyclic Compounds*, Elsevier, NY, ***1984***; Garratt, P.J. *Aromaticity*, Wiley, NY, ***1986***; Balaban, A.T.; Banciu, M.; Ciorba, V. *Annulenes, Benzo-, Hetero-, Homo-Derivatives and their Valence Isomers*, 3 vols., CRC Press, Boca Raton, FL ***1987***; Badger, G.M. *Aromatic Character and Aromaticity*, Cambridge University Press, Cambridge, ***1969***; Snyder, J.P. *Nonbenzenoid Aromatics*, 2 vols., Academic Press, NY, ***1969–1971***; Bergmann, E.D.; Pullman, B. *Aromaticity, Pseudo-Aromaticity, and Anti-Aromaticity*, Israel Academy of Sciences and Humanities, Jerusalem, ***1971***; *Aromaticity*; *Chem. Soc. Spec. Pub.* No. 21, ***1967***. For reviews, see Gorelik, M.V. *Russ. Chem. Rev.* ***1990***, *59*, 116; Stevenson, G.R. *Mol. Struct. Energ.*, ***1986***, *3*, 57; Sondheimer, F. *Chimia*, ***1974***, *28*, 163; Cresp, T.M.; Sargent, M.V. *Essays Chem.* ***1972***, *4*, 91; Figeys, H.P. *Top. Carbocyclic Chem.* ***1969***, *1*, 269; Garratt, P.J.; Sargent, M.V. papers in, *Top. Curr. Chem.* ***1990***, 153 and *Pure Appl. Chem.* ***1980***, *52*, 1397.

[94] For an account of the early history of Aromaticity, see Snyder, J.P., in Snyder, J.P. *Nonbenzenoid Aromatics*, Vol. 1, Academic Press, NY, ***1971***, pp. 1–31. See also Balaban, A.T. *Pure Appl. Chem.* ***1980***, *52*, 1409.

were hard pressed to arrive at a mutually satisfactory definition of aromatic character.[95] Qualitatively, there has never been real disagreement. Definitions have taken the form that aromatic compounds are characterized by a special stability and that they undergo substitution reactions more easily than addition reactions. The difficulty arises because these definitions are vague and not easy to apply in borderline cases. Definitions of aromaticity must encompass molecules ranging form polycyclic conjugated hydrocarbons,[96] to heterocyclic compounds[97] of various ring sizes, to reactive intermediates. In 1925 Armit and Robinson,[98] recognized that the aromatic properties of the benzene ring are related to the presence of a closed loop of electrons, the *aromatic sextet* (aromatic compounds are thus the arch examples of delocalized bonding), but it still was not easy to determine whether rings other than the benzene ring possessed such a loop. With the advent of magnetic techniques, most notably NMR, it is possible to determine experimentally whether or not a compound has a closed ring of electrons; aromaticity can now be defined as the *ability to sustain an induced ring current*. A compound with this ability is called ***diatropic***. Although this definition also has its flaws,[99] it is the one most commonly accepted today. There are several methods of determining whether a compound can sustain a ring current, but the most important one is based on NMR chemical shifts.[100] In order to understand this, it is necessary to remember that, as a general rule, the value of the chemical shift of a proton in an NMR spectrum depends on the electron density of its bond; the greater the density of the electron cloud surrounding or partially surrounding a proton, the more upfield is its chemical shift (a lower value of δ). However, this rule has several exceptions; one is for protons in the vicinity of an aromatic ring. When an external magnetic field is imposed upon an aromatic ring (as in an NMR instrument), the closed loop of aromatic electrons circulates in a diamagnetic ring current, which sends out a field of its own. As can be seen in Fig. 2.6, this induced field curves around and in the area of the proton is parallel to the external field, so the field "seen" by the aromatic protons is greater than it would have been in the absence of the diamagnetic ring current. The protons are moved downfield (to higher δ) compared to where they would be if electron

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[95] For a review of the criteria used to define aromatic character, see Jones, A.J. *Pure Appl. Chem.* ***1968***, *18*, 253. For methods of assigning Aromaticity, see Jug, K.; Köster, A.M. *J. Phys. Org. Chem.* ***1991***, *4*, 163; Zhou, Z.; Parr, R.G. *J. Am. Chem. Soc.* ***1989***, *111*, 7371; Katritzky, A.R.; Barczynski, P.; Musumarra, G.; Pisano, D.; Szafran, M. *J. Am. Chem. Soc.* ***1989***, *111*, 7; Schaad, L.J.; Hess, Jr., B.A. *J. Am. Chem. Soc.* ***1972***, *94*, 3068, *J. Chem. Educ.* ***1974***, *51*, 640. See also, Bird, C.W. *Tetrahedron* ***1985***, *41*, 1409; ***1986***, *42*, 89; ***1987***, *43*, 4725.

[96] Randic, M. *Chem. Rev.* ***2003***, *103*, 3449.

[97] Balaban, A.T.; Oniciu, D.C.; Katritzky, A.R. *Chem. Rev.* ***2004***, *104*, 2777.

[98] Armit, J.W.; Robinson; R. *J. Chem. Soc.* ***1925***, *127*, 1604.

[99] Jones, A.J. *Pure Appl. Chem.* ***1968***, *18*, 253, pp. 266–274; Mallion, R.B. *Pure Appl. Chem.* **1980**, 52, 1541. Also see, Schleyer, P.v.R.; Jiao, H. *Pure Appl. Chem.* ***1996***, *68*, 209.

[100] For a review of NMR and other magnetic properties with respect to aromaticity, see Haddon, R.C.; Haddon, V.R.; Jackman, L.M. *Fortschr. Chem. Forsch.* ***1971***, *16*, 103. For an example of a magentic method other than NMR, see Dauben Jr., H.J.; Wilson, J.D.; Laity, J.L., in Snyder, J.P. *Nonbenzenoid Aromatics*, Vol. 2, Academic Press, NY, ***1971***, pp. 167–206.

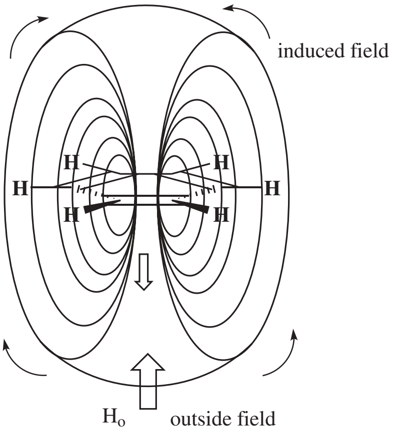
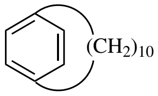


Fig. 2.6. Ring current in benzene.

density were the only factor. Thus ordinary alkene hydrogens are found at ~5–6 δ, while the hydrogens of benzene rings are located at ~7–8 δ. However, if there were protons located above or within the ring, they would be subjected to a *decreased* field and should appear at lower δ values than normal CH_2 groups (normal δ for CH_2 is ~1–2). The nmr spectrum of [10]paracyclophane (**48A**) showed that this was indeed the case[101] and that the CH_2 peaks were shifted to lower δ the closer they were to the middle of the chain. Examination of **48B** shows that a portion of the methylene chain is positioned directly over the benzene ring, making it subject to the anisotropy shift mentioned above.



48A

48B

It follows that aromaticity can be determined from an NMR spectrum. If the protons attached to the ring are shifted downfield from the normal alkene region, we can conclude that the molecule is diatropic, and hence aromatic. In addition, if the compound has protons above or within the ring (we shall see an example of the latter on p. 90), then if the compound is diatropic, these will be shifted upfield.

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[101] Waugh, J.S.; Fessenden, R.W. *J. Am. Chem. Soc.* ***1957***, *79*, 846. See also, Shapiro, B.L.; Gattuso, M.J.; Sullivan, G.R. *Tetrahedron Lett.* ***1971***, 223; Pascal, Jr., R.A.; Winans, C.G.; Van Engen, D. *J. Am. Chem. Soc.* ***1989***, *111*, 3007.

One drawback to this method is that it cannot be applied to compounds that have no protons in either category, for example, the dianion of squaric acid (p. 92). Unfortunately, ^{13}C NMR is of no help here, since these spectra do not show ring currents.[102]

Antiaromatic systems exhibit a *paramagnetic* ring current,[103] which causes protons on the outside of the ring to be shifted *upfield* while any inner protons are shifted *downfield*, in sharp contrast to a diamagnetic ring current, which causes shifts in the opposite directions. Compounds that sustain a paramagnetic ring current are called *paratropic*; and are prevalent in four- and eight-electron systems. As with aromaticity, we expect that antiaromaticity will be at a maximum when the molecule is planar and when bond distances are equal. The diamagnetic and paramagnetic effects of the ring currents associated with aromatic and antiaromatic compounds (i.e., shielding and deshielding of nuclei) can be measured by a simple and efficient criterion known as nucleus independent chemical shift (NICS).[104] The aromatic–antiaromatic ring currents reflect the extra π-effects that the molecules experience. The unique near zero value of NICS at the cyclobutadiene ring center is due to cancelation by large and opposite anistropic components.[105]

There are at least four theoretical models for aromaticity, which have recently been compared and evaluated for predictive ability.[106] The *Hess–Schaad model*[107] is good for predicting aromatic stability of benzenoid hydrocarbons, but does not predict reactivity. The *Herndon model*[108] is also good for predicting aromatic stability, but is unreliable for benzenoidicity and does not predict reactivity. The *conjugated-circuit model*[109] is very good for predicting aromatic stability, but not reactivity, and the *hardness model*[110] is best for predicting kinetic stability. Delocalization energy of π-electrons has also been used as an index for aromaticity in polycyclic aromatic hydrocarbons.[111] The claims for linear relationships between aromaticity and energetics, geometries, and magnetic criteria were said to be *invalid* for any representative set of heteroaromatics in which the number of heteroatoms varies.[112]

It should be emphasized that the old and new definitions of aromaticity are not necessarily parallel. If a compound is diatropic and therefore aromatic under the

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[102] For a review of ^{13}C NMR spectra of aromatic compounds, see Günther, H.; Schmickler, H. *Pure Appl. Chem.* ***1975***, *44*, 807.

[103] Pople, J.A.; Untch, K.G. *J. Am. Chem. Soc.* ***1966***, *88*, 4811; Longuet-Higgins, H.C. in Garratt, P.J. *Aromaticity*, Wiley, NY, ***1986***, pp. 109–111.

[104] Schleyer, P.v.R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N.J.R.v.E. *J. Am. Chem. Soc.* ***1996***, *118*, 6317.

[105] Schleyer, P.v.R.; Manoharan, M.; Wang, Z.-X.; Kiran, B.; Jiao, H.; Puchta, R.; Hommes, N.J.R.v.E. *Org. Lett.* ***2001***, *3*, 2465

[106] Plavić, D.; Babić, D.; Nikolić, S.; Trinajstić, N. *Gazz. Chim. Ital.*, ***1993***, *123*, 243.

[107] Hess, Jr., B.A.; Schaad, L.J. *J. Am. Chem. Soc.* ***1971***, *93*, 305.

[108] Herndon, W.C. *Isr. J. Chem.* ***1980***, *20*, 270.

[109] Randić,M. *Chem.Phys.Lett.* ***1976***, *38*, 68.

[110] Zhou, Z.; Parr, R.G. *J. Am. Chem. Soc.* ***1989***, *111*, 7371; Zhou, Z.; Navangul, H.V. *J. Phys. Org. Chem.* ***1990***, *3*, 784.

[111] Behrens, S.; Köster, A.M.; Jug, K. *J. Org. Chem.* ***1994***, *59*, 2546.

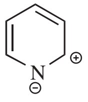
[112] Katritzky, A.R.; Karelson, M.; Sild, S.; Krygowski, T.M.; Jug, K. *J. Org. Chem.* ***1998***, *63*, 5228.

new definition, it is more stable than the canonical form of lowest energy, but this does not mean that it will be stable to air, light, or common reagents, since *this* stability is determined not by the resonance energy, but by the difference in free energy between the molecule and the transition states for the reactions involved; and these differences may be quite small, even if the resonance energy is large. A unified theory has been developed that relates ring currents, resonance energies, and aromatic character.[113] Note that aromaticity varies in magnitude relatively and sometimes absolutely with the molecular environment, which includes the polarity of the medium.[114]

The vast majority of aromatic compounds have a closed loop of six electrons in a ring (the aromatic sextet), and we consider these compounds first.[115] Note that a "formula Periodic table" for the benzenoid polyaromatic hydrocarbons has been developed.[116]

Six-Membered Rings

Not only is the benzene ring aromatic, but so are many heterocyclic analogs in which one or more heteroatoms replace carbon in the ring.[117] When nitrogen is the heteroatom, little difference is made in the sextet and the unshared pair of the nitrogen does not participate in the aromaticity. Therefore, derivatives such as *N*-oxides or pyridinium ions are still aromatic. However, for nitrogen heterocycles there are more significant canonical forms (e.g., **49**) than for benzene. Where oxygen or sulfur is the heteroatom, it must be present in its ionic form (**50**) in order to possess the valence of 3 that participation in such a system demands. Thus, pyran (**51**) is not aromatic, but the pyrylium ion (**49**) is.[118]



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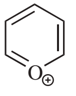

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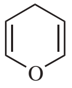

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[113] Haddon, R.C. *J. Am. Chem. Soc.* ***1979***, *101*, 1722; Haddon, R.C.; Fukunaga, T. *Tetrahedron Lett.* ***1980***, *21*, 1191.

[114] Katritzky, A.R.; Karelson, M.; Wells, A.P. *J. Org. Chem.* ***1996***, *61*, 1619.

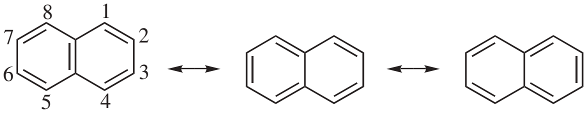
[115] Values of molecular-orbital energies for many aromatic systems, calculated by the HMO method, are given in Coulson, C.A.; Streitwieser, Jr., A. *A Dictonary of* π *Electron Calculations*, W.H. Freeman, San Francisco, ***1965***. Values calculated by a variation of the SCF method are given by Dewar, M.J.S.; Trinajstic, N. *Collect. Czech. Chem. Commun.* ***1970***, *35*, 3136, 3484.

[116] Dias, J.R. *Chem. Br.* ***1994***, 384.

[117] For reviews of Aromaticity of heterocycles, see Katritzky, A.R.; Karelson, M.; Malhotra, N. *Heterocycles* ***1991***, *32*, 127.

[118] For a review of pyrylium salts, see Balaban, A.T.; Schroth, W.; Fischer, G. *Adv. Heterocycl. Chem.* ***1969***, *10*, 241.

In systems of fused six-membered aromatic rings,[119] the principal canonical forms are usually not all equivalent. Compound **52** has a central double bond and is thus different from the other two canonical forms of naphthalene, which are equivalent to each other.[120] For naphthalene, these are the only forms that can be drawn



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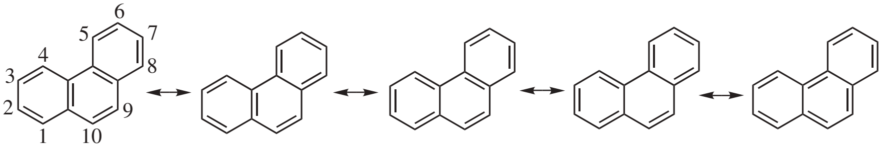
without consideration of Dewar forms or those with charge separation.[121] If we assume that the three forms contribute equally, the 1,2 bond has more double-bond character than the 2,3 bond. Molecular-orbital calculations show bond orders of 1.724 and 1.603, respectively, (cf. benzene, 1.667). In agreement with these predictions, the 1,2 and 2,3 bond distances are 1.36 and 1.415 Å, respectively,[122] and ozone preferentially attacks the 1,2 bond.[123] This nonequivalency of bonds, called *partial bond fixation*,[124] is found in nearly all fused aromatic systems. In phenanthrene, where the 9,10 bond is a single bond in only one of five forms (**53**), bond fixation becomes extreme and this bond is readily attacked by many reagents:[125] It has been observed that increased steric crowding leads to an increase in Dewar-benzene type structures.[126]



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[119] For books on this subject, see Gutman, I.; Cyvin, S.J. *Introduction to the Theory of Benzenoid Hydrocarbons*, Springer, NY, ***1989***; Dias, J.R. *Handbook of Polycyclic Hydrocarbons, Part A: Benzenoid Hydrocarbons*, Elsevier, NY, ***1987***; Clar, E. *Polycyclic Hydrocarbons*, 2 vols., Academic Press, NY, ***1964***. For a "Periodic table" that systematizes fused aromatic hydrocarbons, see Dias, J.R. *Acc. Chem. Res.* ***1985***, *18*, 241; *Top. Curr. Chem.* ***1990***, *253*, 123; *J. Phys. Org. Chem.* ***1990***, *3*, 765.

[120] As the size of a given fused ring system increases, it becomes more difficult to draw all the canonical forms. For discussions of methods for doing this, see Herndon, W.C. *J. Chem. Educ.* ***1974***, *51*, 10; Cyvin, S.J.; Cyvin, B.N.; Brunvoll, J.; Chen, R. *Monatsh. Chem.* ***1989***, *120*, 833; Fuji, Z.; Xiaofeng, G.; Rongsi, C. *Top. Curr. Chem.* ***1990***, *153*, 181; Wenchen, H.; Wenjie, H. *Top. Curr. Chem.* ***1990***, *153*, 195; Sheng, R. *Top. Curr. Chem.* ***1990***, *153*, 211; Rongsi, C.; Cyvin, S.J.; Cyvin, B.N.; Brunvoll, J.; Klein, D.J. *Top. Curr. Chem.* ***1990***, *153*, 227, and references cited in these papers. For a monograph, see Cyvin, S.J.; Gutman, I. *Kekulé Structures in Benzenoid Hydrocarbons*; Springer, NY, ***1988***.

[121] For a modern valence bond description of naphthalene, see Sironi, M.; Cooper, D.L.; Gerratt, J.; Raimondi, M. *J. Chem. Soc. Chem. Commun.* ***1989***, 675.

[122] Cruickshank, D.W.J. *Tetrahedron* ***1962***, *17*, 155.

[123] Kooyman, E.C. *Recl. Trav. Chim. Pays-Bas*, ***1947***, *66*, 201.

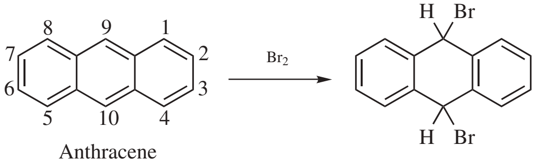
[124] For a review, see Efros, L.S. *Russ. Chem. Rev.* ***1960***, *29*, 66.

[125] See also Lai, Y. *J. Am. Chem. Soc.* ***1985***, *107*, 6678.

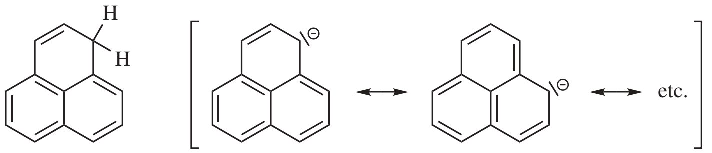
[126] Zhang, J.; Ho, D.M.; Pascal Jr., R.A. *J. Am. Chem. Soc.* ***2001***, *123*, 10919.

In general, there is a good correlation between bond distances in fused aromatic compounds and bond orders. Another experimental quantity that correlates well with the bond order of a given bond in an aromatic system is the NMR coupling constant for coupling between the hydrogens on the two carbons of the bond.[127]

The resonance energies of fused systems increase as the number of principal canonical forms increases, as predicted by rule 6 (p. 47).[128] Thus, for benzene, naphthalene, anthracene, and phenanthrene, for which we can draw, respectively, two, three, four, and five principal canonical forms, the resonance energies are, respectively, 36, 61, 84, and 92 kcal mol^{-1} (152, 255, 351, and 385 kJ mol^{-1}), calculated from heat-of-combustion data.[129] Note that when phenanthrene, which has a total resonance energy of 92 kcal mol^{-1} (385 kJ mol^{-1}), loses the 9,10 bond by attack of a reagent, such as ozone or bromine, two complete benzene rings remain, each with 36 kcal mol^{-1} (152 kJ mol^{-1}) that would be lost if benzene was similarly attacked. The fact that anthracene undergoes many reactions across the 9,10 positions can be explained in a similar manner. Resonance energies for fused systems can be estimated by counting canonical forms.[130]



Not all fused systems can be fully aromatic. Thus for phenalene (**54**) there is no way double bonds can be distributed so that each carbon has one single and one double bond.[131] However, phenalene is acidic and reacts with potassium methoxide to give the corresponding anion (**55**), which is completely aromatic. So are the corresponding radical and cation, in which the resonance energies are the same (see p. 68).[132]



54 **55**

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[127] Jonathan, N.; Gordon, S.; Dailey, B.P. *J. Chem. Phys.* ***1962***, *36*, 2443; Cooper, M.A.; Manatt, S.L. *J. Am. Chem. Soc.* ***1969***, *91*, 6325.

[128] See Herndon, W.C.; Ellzey Jr., M.L. *J. Am. Chem. Soc.* ***1974***, *96*, 6631.

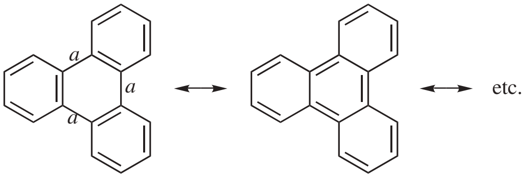
[129] Wheland, G.W. *Resonance in Organic Chemistry*, Wiley, NY, ***1955***, p. 98.

[130] Swinborne-Sheldrake, R.; Herndon, W.C. *Tetrahedron Lett.* ***1975***, 755.

[131] For reviews of phenalenes, see Murata, I. *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 159; Reid, D.H. *Q. Rev. Chem. Soc.* ***1965***, *19*, 274.

[132] Pettit, R. *J. Am. Chem. Soc.* ***1960***, *82*, 1972.

Molecules that contain fused rings, such as phenanthrene or anthracene, are generally referred to as linear or angular polyacenes. In a fused system, there are not six electrons for each ring.[133] In naphthalene, if one ring is to have six, the other must have only four. One way to explain the greater reactivity of the ring system of naphthalene compared with benzene is to regard one of the naphthalene rings as aromatic and the other as a butadiene system.[134] This effect can become extreme, as in the case of triphenylene.[135] For this compound, there are eight canonical forms like **56**, in which none of the three bonds marked *a* is a double bond and only one form (**57**) in which at least one of them is double. Thus the molecule behaves as if the 18 electrons were distributed so as to give each of the outer rings a sextet, while the middle ring is "empty." Since none of the outer rings need share any electrons with an adjacent ring, they are as stable as benzene; triphenylene, unlike most fused aromatic hydrocarbons, does not dissolve in concentrated sulfuric acid and has a low reactivity.[136] This phenomenon, whereby some rings in fused systems give up part of their aromaticity to adjacent rings, is called *annellation* and can be demonstrated by UV spectra[119] as well as reactivities. In general, an increase of size of both linear and angular polyacenes is associated with a substantial edecrease in their aromaticity, with a greater decrease for the linear polyacenes.[137]



56 **57**

A six-membered ring with a circle is often used to indicate an aromatic system, and this will be used from time to time. Kekulé structures, those having the C=C units rather than a circle, are used most often in this book. Note that one circle can be used for benzene, but it would be misleading to use two circles for naphthalene, for example, because that would imply 12 aromatic electrons, although naphthalene has only 10.[138]

Five-, Seven-, and Eight-Membered Rings

Aromatic sextets can also be present in five- and seven-membered rings. If a five-membered ring has two double bonds, and the fifth atom possesses an unshared pair

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[133] For discussions of how the electrons in fused aromatic systems interact to form $4n + 2$ systems, see Glidewell, C.; Lloyd, D. *Tetrahedron* ***1984***, *40*, 4455, *J. Chem. Educ.* ***1986***, *63*, 306; Hosoya, H. *Top. Curr. Chem.* ***1990***, *153*, 255.

[134] Meredith, C.C.; Wright, G.F. *Can. J. Chem.* ***1960***, *38*, 1177.

[135] For a review of triphenylenes, see Buess, C.M.; Lawson, D.D. *Chem. Rev.* ***1960***, *60*, 313.

[136] Clar, E.; Zander, M. *J. Chem. Soc.* ***1958***, 1861.

[137] Cyrań ski, M.K.; Stępień, B.T.; Krygowski, T.M. *Tetrahedron* ***2000***, *56*, 9663.

[138] See Belloli, R. *J. Chem. Educ.* ***1983***, *60*, 190.

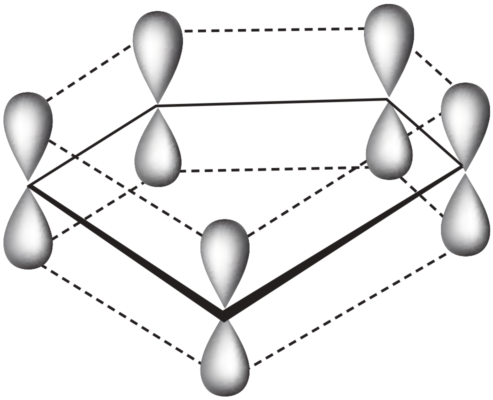
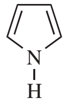
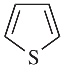


Fig. 2.7. Overlap of five *p* orbitals in molecules such as pyrrole, thiophene, and the cyclopentadienide ion

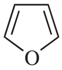
of electrons, the ring has five *p* orbitals that can overlap to create five new orbitals: three bonding and two antibonding (Fig. 2.7). There are six electrons for these orbitals: the four *p* orbitals of the double bonds each contribute one and the filled orbital contributes the other two. The six electrons occupy the bonding orbitals and constitute an aromatic sextet. The heterocyclic compounds pyrrole, thiophene, and furan are the most important examples of this kind of aromaticity, although furan has a lower degree of aromaticity than the other two.[139] Resonance energies for these three compounds are, respectively, 21, 29, and 16 kcal mol^{-1} (88, 121, and 67 kJ mol^{-1}).[140] The aromaticity can also be shown by canonical forms, for example, for pyrrole:



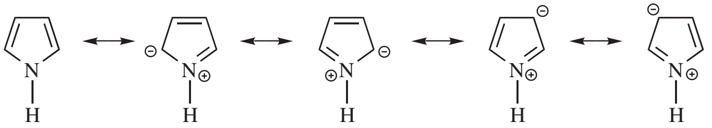
Pyrrole



Thiophene



Furan



A

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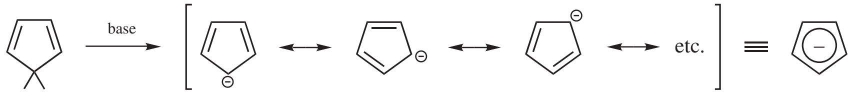
[139] The order of aromaticity of these compounds is benzene > thiophene > pyrrole > furan, as calculated by an Aromaticity index based on bond distance measurements. This index has been calculated for five- and six-membered monocyclic and bicyclic heterocycles: Bird, C.W. *Tetrahedron* ***1985***, *41*, 1409; ***1986***, *42*, 89; ***1987***, *43*, 4725.

[140] Wheland, G.W. *Resonance in Organic Chemistry*, Wiley, NY, ***1955***, p 99. See also, Calderbank, K.E.; Calvert, R.L.; Lukins, P.B.; Ritchie, G.L.D. *Aust. J. Chem.* ***1981***, *34*, 1835.

In contrast to pyridine, the unshared pair in canonical structure **A** in pyrrole is needed for the aromatic sextet. This is why pyrrole is a much weaker base than pyridine.

The fifth atom may be carbon if it has an unshared pair. Cyclopentadiene has unexpected acidic properties (p$K_a \approx 16$) since on loss of a proton, the resulting carbanion is greatly stabilized by resonance although it is quite reactive. The cyclopentadienide ion is usually represented as in **58**. Resonance in this ion is greater than in pyrrole, thiophene, and furan, since all five forms are equivalent. The resonance energy for **58** has been estimated to be 24–27 kcal mol^{-1} (100–113 kJ mol^{-1}).[141]



58

That all five carbons are equivalent has been demonstrated by labeling the starting compound with ^{14}C and finding all positions equally labeled when cyclopentadiene was regenerated[142] As expected for an aromatic system, the cyclopentadienide ion is diatropic[143] and aromatic substitutions on it have been successfully carried out.[144] Average bond order has been proposed as a parameter to evaluate the aromaticity of these rings, but there is poor correlation with non-aromatic and antiaromatic systems.[145] A model that relies on calculating relative aromaticity from appropriate molecular fragments has also been developed.[146] Bird devised the aromatic index (I_A, or aromaticity index),[147] which is a statistical evaluation of the extent of ring bond order, and this has been used as a criterion of aromaticity. Another bond-order index was proposed by Pozharskii,[148] which goes back to the work of Fringuelli and co-workers.[149] Absolute hardness (see p. 377), calculated from molecular refractions for a range of aromatic and heteroaromatic compounds, shows good linear correlation with aromaticity.[150] Indene and fluorene are also acidic (p$K_a \approx$ 20 and 23, respectively), but less so than cyclopentadiene, since annellation causes the electrons to be less available to the five-membered ring. On the other hand, the acidity of 1,2,3,4,5-pentakis(trifluoromethyl)cyclopentadiene (**59**) is greater than that of nitric acid,[151] because of the electron-

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[141] Bordwell, F.G.; Drucker, G.E.; Fried, H.E. *J. Org. Chem.* ***1981***, *46*, 632.

[142] Tkachuk, R.; Lee, C.C. *Can. J. Chem.* ***1959***, *37*, 1644.

[143] Bradamante, S.; Marchesini, A.; Pagani, G. *Tetrahedron Lett.* ***1971***, 4621.

[144] Webster, O.W. *J. Org. Chem.* ***1967***, *32*, 39; Rybinskaya, M.I.; Korneva, L.M. *Russ. Chem. Rev.* ***1971***, *40*, 247.

[145] Jursic, B.S. *J. Heterocycl. Chem.* ***1997***, *34*, 1387.

[146] Hosmane, R.S.; Liebman, J.F. *Tetrahedron Lett.* ***1992***, *33*, 2303.

[147] Bird, C.W. *Tetrahedron* ***1985***, *41*, 1409; *Tetrahedron* ***1992***, *48*, 335; *Tetrahedron* ***1996***, *52*, 9945.

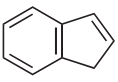
[148] Pozharskii, A.F. *Khimiya Geterotsikl Soedin* ***1985***, 867.

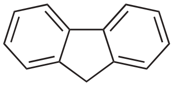
[149] Fringuelli, F. Marino, G.; Taticchi, A.; Grandolini, G. J. *Chem. Soc. Perkin Trans. 2* ***1974***, 332.

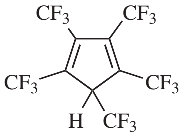
[150] Bird, C.W. *Tetrahedron* ***1997***, *53*, 3319; *Tetrahedron* ***1998***, *54*, 4641.

[151] Laganis, E.D.; Lemal, D.M. *J. Am. Chem. Soc.* ***1980***, *102*, 6633.

withdrawing effects of the trifluoromethyl groups (see p. 381). Modifications of the Bird and Pozharskii systems have been introduced that are particularly useful for five-membered ring heterocycles.[152] Recent work introduced a new local aromaticity measure, defined as the mean of Bader's electron delocalization index (DI)[153] of para-related carbon atoms in six-membered rings.[154]

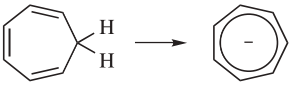

Indene


Fluorene

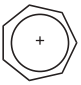


59

As seen above, acidity of compounds can be used to study the aromatic character of the resulting conjugate base. In sharp contrast to cyclopentadiene (see p. 63) is cycloheptatriene (**60**), which has no unusual acidity. This would be hard to explain without the aromatic sextet theory, since, on the basis of resonance forms or a simple consideration of orbital overlaps, **61** should be as stable as the cyclopentadienyl anion (**58**). While **61** has been prepared in solution,[155] it is less stable than **58** and far less stable than **62**, in which **60** has lost not a proton, but a hydride ion. The six double-bond electrons of **62** overlap with the empty orbital on the seventh carbon and there is a sextet of electrons covering seven carbon atoms. The cycloheptatrienyl cations (known as the *tropylium ion*, **62**) is quite stable.[156] Tropylium bromide (**63**), which could be completely covalent if the electrons of the bromine were sufficiently attracted to the ring, is actually an ionic compound:[157] Many substituted tropylium ions have been prepared to probe the aromaticity, structure, and reactivity of such systems.[158] Just as with **58**, the equivalence of the carbons



60 **61**



62

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[152] Kotelevskii, S.I.; Prezhdo, O.V. *Tetahedron* ***2001***, *57*, 5715.

[153] See Bader, R.F.W. *Atoms in Molecules: A Quantum Theory*, Clarendon, Oxford, ***1990***; Bader, R.F.W. *Acc. Chem. Res.* ***1985***, *18*, 9; Bader, R.F.W. *Chem. Rev.* ***1991***, *91*, 893.

[154] Poater, J.; Fradera, X.; Duran, M.; Solà, M. *Chem. Eur. J.* ***2003***, *9*, 400; 1113.

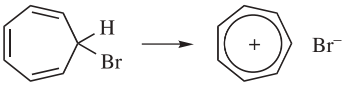
[155] Dauben Jr., H.J.; Rifi, M.R. *J. Am. Chem. Soc.* ***1963***, *85*, 3041; also see Breslow, R.; Chang, H.W. *J. Am Chem. Soc.* ***1965***, *87*, 2200.

[156] For reviews, see Pietra, F. *Chem. Rev.* ***1973***, *73*, 293; Bertelli, D.J. *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 29; Kolomnikova, G.D.; Parnes, Z.N. *Russ. Chem. Rev.* ***1967***, *36*, 735; Harmon, K.H., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 4, Wiley, NY, 1973, pp. 1579–1641.

[157] Doering, W. von E.; Knox, L.H. *J. Am. Chem. Soc.* ***1954***, *76*, 3203.

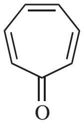
[158] Pischel, U.; Abraham, W.; Schnabel, W.; Müller, U. *Chem. Commun.* ***1997***, 1383. See Komatsu, K.; Nishinaga, T.; Maekawa, N.; Kagayama, A.; Takeuchi, K. *J. Org. Chem.* ***1994***, *59*, 7316 for a tropylium dication.

in **62** has been demonstrated by isotopic labeling.[159] The aromatic cycloheptatrienyl cations $C_7Me_7^+$ and $C_7Ph_7^+$ are known,[160] although their coordination complexes with transition metals have been problematic, possibly because they assume a boat-like rather than a planar conformation[161]



63

Another seven-membered ring that shows some aromatic character is tropone (**64**). This molecule would have an aromatic sextet if the two C=O electrons stayed away from the ring and resided near the electronegative oxygen atom. In fact, tropones are stable compounds, and tropolones (**65**) are found in nature.[162] However, analyses of dipole moments, NMR spectra, and X-ray diffraction measurements show that tropones and tropolones display appreciable bond alternations.[163]



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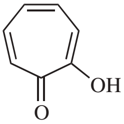

65

These molecules must be regarded as essentially non-aromatic, although with some aromatic character. Tropolones readily undergo aromatic substitution, emphasizing that the old and the new definitions of aromaticity are not always parallel. In sharp contrast to **64**, cyclopentadienone (**66**) has been isolated only in an argon matrix <38 K.[164] Above this temperature it dimerizes. Many earlier attempts to prepare it were unsuccessful.[165] As in **64**, the electronegative oxygen atom draws electron to itself, but in this case it leaves only four electrons and the molecule is

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[159] Vol'pin, M.E.; Kursanov, D.N.; Shemyakin, M.M.; Maimind, V.I.; Neiman, L.A. *J. Gen. Chem. USSR* ***1959***, *29*, 3667.

[160] Takeuchi, K.; Yokomichi, Y.; Okamoto, K. *Chem. Lett.* ***1977***,1177; Battiste, M.A. *J. Am. Chem. Soc.* ***1961***, *83*, 4101.

[161] Tamm, M.; Dreßel, B.; Fröhlich, R. *J. Org. Chem.* ***2000***, *65*, 6795.

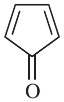
[162] For reviews of tropones and tropolones, see Pietra, F. *Acc. Chem. Res.* ***1979***, *12*, 132; Nozoe, T. *Pure Appl. Chem.* ***1971***, *28*, 239.

[163] Bertelli, D.J.; Andrews, Jr., T.G. *J. Am. Chem. Soc.* ***1969***, *91*, 5280; Bertelli, D.J.; Andrews Jr., T.G.; Crews, P.O. *J. Am. Chem. Soc.* ***1969***, *91*, 5286; Schaefer, J.P.; Reed, L.L. *J. Am. Chem. Soc.* ***1971***, *93*, 3902; Watkin, D.J.; Hamor, T.A. *J. Chem. SOc. B* ***1971***, 2167; Barrow, M.J.; Mills, O.S.; Filippini, G. *J. Chem. Soc. Chem. Commun.* ***1973***, 66.

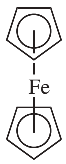
[164] Maier, G.; Franz, L.H.; Lanz, K.; Reisenauer, H.P. *Chem. Ber.* ***1985***, *118*, 3196.

[165] For a review of cyclopentadienone derivatives and of attempts to prepare the parent compound, see Ogliaruso, M.A.; Romanelli, M.G.; Becker, E.I. *Chem. Rev.* ***1965***, *65*, 261.

unstable. Some derivatives of **66** have been prepared.[130]



66



Ferrocene

67

Another type of five-membered aromatic compound is the *metallocenes* (also called *sandwich compounds*), in which two cyclopentadienide rings form a sandwich around a metallic ion. The best known of these is ferrocene, where the η^5-coordination of the two cyclopentadienyl rings to iron is apparent in the 3D model **67**. Other sandwich compounds have been prepared with Co, Ni, Cr, Ti, V, and many other metals.[166] As a reminder (see p. 43), the η terminology refers to π-donation of electrons to the metal (η^3 for π-allyl systems, η^6 for coordination to a benzene ring, etc.), and η^5 refers to donation of five π-electrons to the iron. Ferrocene is quite stable, subliming >100°C and unchanged at 400°C. The two rings rotate freely.[167] Many aromatic substitutions have been carried out on metallocenes.[168] Metallocenes containing two metal atoms and three cyclopentadienyl rings have also been prepared and are known as *triple-decker sandwiches*.[169] Even tetradecker, pentadecker, and hexadecker sandwiches have been reported.[170]

The bonding in ferrocene may be looked upon in simplified molecular-orbital terms as follows.[171] Each of the cyclopentadienide rings has five molecular orbitals: three filled bonding and two empty antibonding orbitals (p. 62). The outer

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[166] For a monograph on metallocenes, see Rosenblum, M. *Chemistry of the Iron Group Metallocenes*, Wiley, NY, ***1965***. For reviews, see Lukehart, C.M. *Fundamental Transition Metal Organometallic Chemistry*, Brooks/Cole, Monterey, CA, ***1985***, pp. 85–118; Lemenovskii, D.A.; Fedin, V.P. *Russ. Chem. Rev.* ***1986***, *55*, 127; Sikora, D.J.; Macomber, D.W.; Rausch, M.D. *Adv. Organomet. Chem.* ***1986***, *25*, 317; Pauson, P.L. *Pure Appl. Chem.* ***1977***, *49*, 839; Nesmeyanov, A.N.; Kochetkova, N.S. *Russ. Chem. Rev.* ***1974***, *43*, 710; Shul'pin, G.B.; Rybinskaya, M.I. *Russ. Chem. Rev.* ***1974***, *43*, 716; Perevalova, E.G.; Nikitina, T.V. *Organomet. React.*, ***1972***, *4*, 163; Bublitz, D.E.; Rinehart Jr., K.L. *Org. React.*, ***1969***, *17*, 1; Leonova, E.V.; Kochetkova, N.S. *Russ. Chem. Rev.* ***1973***, *42*, 278; Rausch, M.D. *Pure Appl. Chem.* ***1972***, *30*, 523. For a bibliography of reviews on metallocenes, see Bruce, M.I. *Adv. Organomet. Chem.* ***1972***, *10*, 273, pp. 322–325.

[167] For a discussion of the molecular structure, see Haaland, A. *Acc. Chem. Res.* ***1979***, *12*, 415.

[168] For a review on aromatic substitution on ferrocenes, see Plesske, K. *Angew. Chem. Int. Ed.* ***1962***, *1*, 312, 394.

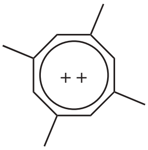
[169] For a review, see Werner, H. *Angew. Chem. Int. Ed.* ***1977***, *16*, 1.

[170] See, for example, Siebert, W. *Angew. Chem. Int. Ed.* ***1985***, *24*, 943.

[171] Rosenblum, M. *Chemistry of the Iron Group Metallocnes*, Wiley, NY, ***1965***, pp. 13–28; Coates, G.E.; Green, M.L.H.; Wade, K. *Organometallic Compounds*, 3rd ed., Vol. 2, Methuene, London, ***1968***, pp. 97–104; Grebenik, P.; Grinter, R.; Perutz, R.N. *Chem. Soc. Rev.* ***1988***, *17*, 453; 460.

shell of the Fe atom possesses nine atomic orbitals, that is, one 4*s*, three 4*p*, and five 3*d* orbitals. The six filled orbitals of the two cyclopentadienide rings overlap with the *s*, three *p*, and two of the *d* orbitals of the Fe to form twelve new orbitals, six of which are bonding. These six orbitals make up two ring-to-metal triple bonds. In addition, further bonding results from the overlap of the empty antibonding orbitals of the rings with additional filled *d* orbitals of the iron. All told, there are 18 electrons (10 of which may be considered to come from the rings and 8 from iron in the zero oxidation state) in nine orbitals; six of these are strongly bonding and three weakly bonding or nonbonding.

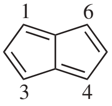
The tropylium ion has an aromatic sextet spread over seven carbon atoms. An analogous ion, with the sextet spread over eight carbon atoms, is 1,3,5,7-tetramethylcyclooctatetraene dictation (**68**). This ion, which is stable in solution at −50°C, is diatropic and approximately planar. The dication **68** is not stable above about −30°C.[172]



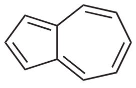
68

Other Systems Containing Aromatic Sextets

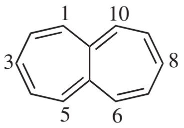
Simple resonance theory predicts that pentalene (**69**), azulene (**70**), and heptalene (**71**) should be aromatic, although no nonionic canonical form can have a double bond at the ring junction. Molecular-orbital calculations show that azulene should be stable but not the other two, and this is borne out by experiment. Heptalene has been prepared,[173] but reacts readily with oxygen, acids, and bromine, is easily hydrogenated, and polymerizes on standing. Analysis of its NMR spectrum shows



69



70



71

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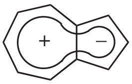
[172] This and related ions were prepared by Olah, G.A.; Staral, J.S.; Liang, G.; Paquette, L.A.; Melega, W.P.; Carmody, M.J. *J. Am. Chem. Soc.* ***1977***, *99*, 3349. See also Radom, L.; Schaefer III, H.F. *J. Am. Chem. Soc.* ***1977***, *99*, 7522; Olah, G.A.; Liang, G. *J. Am. Chem. Soc.* ***1976***, *98*, 3033; Willner, I.; Rabinovitz, M. *Nouv. J. Chim.*, ***1982***, *6*, 129.

[173] Dauben, Jr., H.J.; Bertelli, D.J. *J. Am. Chem. Soc.* ***1961***, *83*, 4659; Vogel, E.; Königshofen, H.; Wassen, J.; Müllen, K.; Oth, J.F.M. *Angew. Chem. Int. Ed.* ***1974***, *13*, 732; Paquette, L.A.; Browne, A.R.; Chamot, E. *Angew. Chem. Int. Ed.* ***1979***, *18*, 546. For a review of heptalenes, see Paquette, L.A. *Isr. J. Chem.* ***1980***, *20*, 233.

that it is not planar.[174] The 3,8-dibromo and 3,8-dicarbomethoxy derivatives of **71** are stable in air at room temperature but are not diatropic.[175] A number of methylated heptalenes and dimethyl 1,2-heptalenedicarboxylates have also been prepared and are stable nonaromatic compounds.[176] Pentalene has not been prepared,[177] but the hexaphenyl[178] and 1,3,5-tri-*tert*-butyl derivatives[179] are known. The former is air sensitive in solution. The latter is stable, but X-ray diffraction and photoelectron spectral data show bond alternation.[180] Pentalene and its methyl and dimethyl derivatives have been formed in solution, but they dimerize before they can be isolated.[181] Many other attempts to prepare these two systems have failed.



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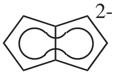

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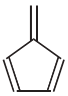

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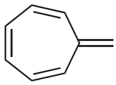

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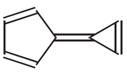

76

In sharp contrast to **69** and **71**, azulene, a blue solid, is quite stable and many of its derivatives are known.[182] Azulene readily undergoes aromatic substitution. Azulene may be regarded as a combination of **58** and **62** and, indeed, possesses a dipole moment of 0.8 *D* (see **72**).[183] Interestingly, if two electrons are added to pentalene, a stable dianion (**73**) results.[184] It can be concluded that an aromatic system of electrons will be spread over two rings only if 10 electrons (not 8 or 12) are available for aromaticity. $[n, m]$-Fluvalenes ($n \neq m$, where fulvalene is **74**) as well as azulene are known to shift their π-electrons due to the influence of dipolar aromatic resonance structures.[185] However, calculations showed that

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[174] Bertelli, D.J., in Bergmann, E.D.; Pullman, B. *Aromaticity, Pseudo-Aromaticity, and Anti-Aromaticity*, Israel Academy of Sciences and Humanities, Jerusalem, ***1971***, p. 326. See also Stegemann, J.; Lindner, H.J. *Tetrahedron Lett.* ***1977***, 2515.

[175] Vogel, E.; Ippen, J. *Angew. Chem. Int. Ed.* ***1974***, *13*, 734; Vogel, E.; Hogrefe, F. *Angew. Chem. Int. Ed.* ***1974***, *13*, 735.

[176] Hafner, K.; Knaup, G.L.; Lindner, H.J. *Bull. Soc. Chem. Jpn.* ***1988***, *61*, 155.

[177] Metal complexes of pentalene have been prepared: Knox, S.A.R.; Stone, F.G.A. *Acc. Chem. Res.* ***1974***, *7*, 321.

[178] LeGoff, E. *J. Am. Chem. Soc.* ***1962***, *84*, 3975. See also Hafner, K.; Bangert, K.F.; Orfanos, V. *Angew. Chem. Int. Ed.* ***1967***, *6*, 451; Hartke, K.; Matusch, R. *Angew. Chem. Int. Ed.* ***1972***, *11*, 50.

[179] Hafner, K.; Süss, H.U. *Angew. Chem. Int. Ed.* ***1973***, *12*, 575. See also Hafner, K.; Suda, M. *Angew. Chem. Int. Ed.* ***1976***, *15*, 314.

[180] Kitschke, B.; Lindner, H.J. *Tetrahedron Lett.* ***1977***, 2511; Bischof, P.; Gleiter, R.; Hafner, K.; Knauer, K.H.; Spanget-Larsen, J.; Süss, H.U. *Chem. Ber.* ***1978***, *111*, 932.

[181] Bloch, R.; Marty, R.A.; de Mayo, P. *J. Am. Chem. Soc.* ***1971***, *93*, 3071; *Bull. Soc. Chim. Fr.*, ***1972***, 2031; Hafner, K.; Dönges, R.; Goedecke, E.; Kaiser, R. *Angew. Chem. Int. Ed.* ***1973***, *12*, 337.

[182] For a review on azulene, see Mochalin, V.B.; Porshnev, Yu.N. *Russ. Chem. Rev.* ***1977***, *46*, 530.

[183] Tobler, H.J.; Bauder, A.; Günthard, H.H. *J. Mol. Spectrosc.*, ***1965***, *18*, 239.

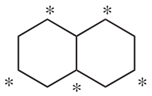
[184] Katz, T.J.; Rosenberger, M.; O'Hara, R.K. *J. Am. Chem. Soc.* ***1964***, *86*, 249. See also, Willner, I.; Becker, J.Y.; Rabinovitz, M. *J. Am. Chem. Soc.* ***1979***, *101*, 395.

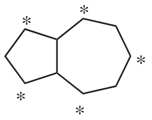
[185] Möllerstedt, H.; Piqueras, M.C.; Crespo, R.; Ottosson, H. *J. Am. Chem. Soc.* ***2004***, *126*, 13938.

dipolar resonance structures contribute only 5% to the electronic structure of heptafulvalene (**75**), although 22–31% to calicene (**76**).[186] Based on Baird's theory,[187] these molecules are influenced by aromaticity in both the ground and excited states, therefore acting as aromatic "chameleons." This premise was confirmed in work by Ottosson and co-workers.[185] Aromaticity indexes for various substituted fulvalene compounds has been reported.[188]

Alternant and Nonalternant Hydrocarbons[189]

Aromatic hydrocarbons can be divided into alternant and nonalternant hydrocarbons. In alternant hydrocarbons, the conjugated carbon atoms can be divided into two sets such that no two atoms of the same set are directly linked. For convenience, one set may be starred. Naphthalene is an alternant and azulene a nonalternant hydrocarbon:





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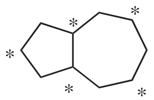
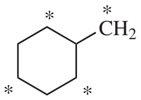


In alternant hydrocarbons, the bonding and antibonding orbitals occur in pairs; that is, for every bonding orbital with an energy $-E$ there is an antibonding one with energy $+E$ (Fig. 2.8[190]). Even-alternant hydrocarbons are those with an even number of conjugated atoms, that is, an equal number of starred and unstarred atoms. For these hydrocarbons, all the bonding orbitals are filled and the π electrons are uniformly spread over the unsaturated atoms.



As with the allylic system, odd-alternant hydrocarbons (which must be carbocations, carbanions, or radicals) in addition to equal and opposite bonding and antibonding orbitals also have a nonbonding orbital of zero energy. When an odd number of orbitals overlap, an odd number is created. Since orbitals of alternant hydrocarbons occur in $-E$ and $+E$ pairs, one orbital can have no partner and must therefore have zero bonding energy. For example, in the benzylic system the cation has an unoccupied nonbonding orbital, the free radical has one electron there and the carbanion two (Fig. 2.9). As with the allylic system, all three species have the same bonding energy. The charge distribution (or unpaired-electron distribution)

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[186] Scott, A.P.; Agranat, A.; Biedermann, P.U.; Riggs, N.V.; Radom, L. *J. Org. Chem.* ***1997***, *62*, 2026.

[187] Baird, N.C. *J. Am. Chem. Soc.* ***1972***, *94*, 4941.

[188] Stepien, B.T.; Krygowski, T.M.; Cyranski, M.K. *J. Org. Chem.* ***2002***, *67*, 5987.

[189] For discussions, see Jones, R.A.Y. *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press, Cambridge, ***1984***, pp. 122–129; Dewar, M.J.S. *Prog. Org. Chem.* ***1953***, *2*, 1.

[190] Taken from Dewar, M.J.S *Prog. Org. Chem.* ***1953***, *2*, 1, p. 8.

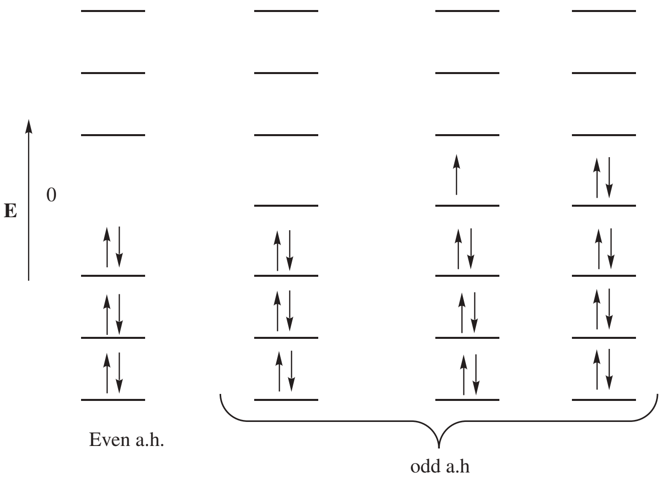


Fig. 2.8. Energy levels in odd- and even-alternant hydrocarbons.[190] The arrows represent electrons. The orbitals are shown as having different energies, but some may be degenerate.

over the entire molecule is also the same for the three species and can be calculated by a relatively simple process.[189]

For nonalternant hydrocarbons the energies of the bonding and antibonding orbitals are not equal and opposite and charge distributions are not the same in cations, anions, and radicals. Calculations are much more difficult but have been carried

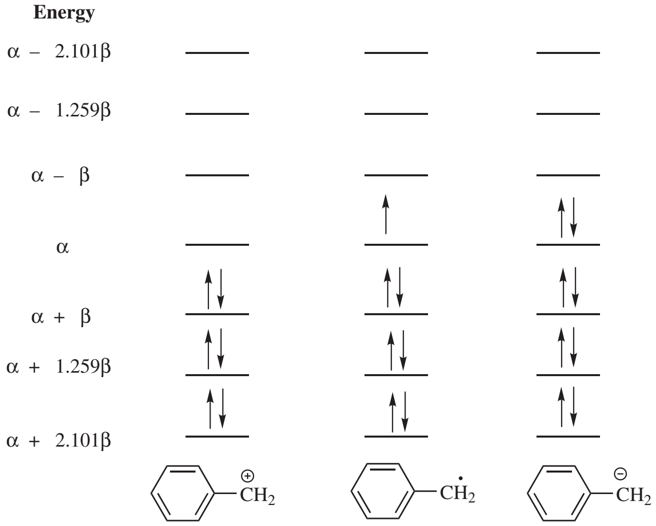


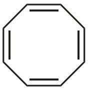
Fig. 2.9. Energy levels for the benzyl cation, free radical, and carbanion. Since α is the energy of a *p*-orbital (p. 36), the nonbonding orbital has no bonding energy.

out.[191] Theoretical approaches to calculate topological polarization and reactivity of these hydrocarbons have been reported.[192]

Aromatic Systems with Electron Numbers Other Than Six

Ever since the special stability of benzene was recognized, chemists have been thinking about homologous molecules and wondering whether this stability is also associated with rings that are similar but of different sizes, such as cyclobutadiene (**77**), cyclooctatetraene (**78**), cyclodecapentaene (**79**)[193], and so on. The general

77



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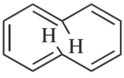
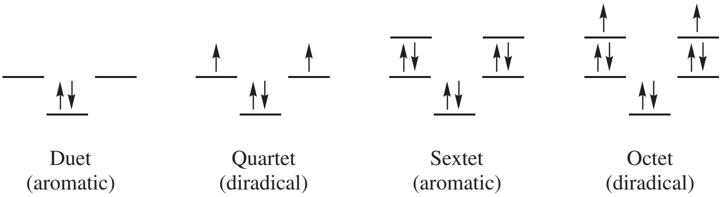


79

name *annulene* is given to these compounds, benzene being [6]annulene, and **77**–**79** being called, respectively, [4], [8], and [10]annulene. By a naïve consideration of resonance forms, these annulenes and higher ones should be as aromatic as benzene. Yet they proved remarkably elusive. The ubiquitous benzene ring is found in thousands of natural products, in coal and petroleum, and is formed by strong treatment of many noncyclic compounds. None of the other annulene ring systems has ever been found in nature and, except for cyclooctatetraene, their synthesis is not simple. Obviously, there is something special about the number six in a cyclic system of electrons.



Hückel's rule, based on molecular-orbital calculations,[194] predicts that electron rings will constitute an aromatic system only if the number of electrons in the ring is of the form $4n + 2$, where n is zero or any position integer. Systems that contain $4n$ electrons are predicted to be nonaromatic. The rule predicts that

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[191] Peters, D. *J. Chem. Soc.* ***1958***, 1023, 1028, 1039; Brown, R.D.; Burden, F.R.; Williams, G.R. *Aust. J. Chem.* ***1968***, *21*, 1939. For reviews, see Zahradnik, R., in Snyder, J.P. *Nonbenzenoid Aromatics* vol. 2, Academic Press, NY, ***1971***, pp. 1–80; Zahradnik, R. *Angew. Chem. Int. Ed.* ***1965***, *4*, 1039.

[192] Langler, R.F. *Aust. J. Chem.* ***2000***, *53*, 471; Fredereiksen, M.U.; Langler, R.F.; Staples, M.A.; Verma, S.D. *Aust. J. Chem.* ***2000***, *53*, 481.

[193] The cyclodecapentaene shown here is the cis–trans–cis–cis–trans form. For other stereoisomers, see p. 79.

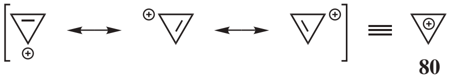
[194] For reviews of molecular-orbital calculations of nonbenzenoid cyclic conjugated hydrocarbons, see Nakajima, T. *Pure Appl. Chem.* ***1971***, *28*, 219; *Fortschr. Chem. Forsch.* ***1972***, *32*, 1.

rings of 2, 6, 10, 14, and so on, electrons will be aromatic, while rings of 4, 8, 12, and so on, will not be. This is actually a consequence of Hund's rule. The first pair of electrons in an annulene goes into the π orbital of lowest energy. After that the bonding orbitals are degenerate and occur in pairs of equal energy. When there is a total of four electrons, Hund's rule predicts that two will be in the lowest orbital but the other two will be unpaired, so that the system will exist as a diradical rather than as two pairs. The degeneracy can be removed if the molecule is distorted from maximum molecular symmetry to a structure of lesser symmetry. For example, if **77** assumes a rectangular rather than a square shape, one of the previously degenerate orbitals has a lower energy than the other and will be occupied by two electrons. In this case, of course, the double bonds are essentially separate and the molecule is still not aromatic. Distortions of symmetry can also occur when one or more carbons are replaced by heteroatoms or in other ways.[195]

In the following sections systems with various numbers of electrons are discussed. When we look for aromaticity we look for (*1*) the presence of a diamagnetic ring current; (*2*) equal or approximately equal bond distances, except when the symmetry of the system is disturbed by a heteroatom or in some other way; (*3*) planarity; (*4*) chemical stability; (*5*) the ability to undergo aromatic substitution.

Systems of Two Electrons[196]

Obviously, there can be no ring of two carbon atoms though a double bond may be regarded as a degenerate case. However, in analogy to the tropylium ion, a three-membered ring with a double bond and a positive charge on the third atom (the *cyclopropenyl cation*) is a $4n + 2$ system and hence is expected to show aromaticity. The unsubstituted **80** has been prepared,[197] as well as several derivatives, e.g.,



80

the trichloro, diphenyl, and dipropyl derivatives, and these are stable despite the angles of only 60°. In fact, the tripropylcyclopropenyl,[198] tricyclopropylcyclopropenyl,[199] chlorodipropylcyclopropenyl,[200] and chloro-bisdialkylaminocyclopropenyl[201] cations are among the most stable carbocations known, being stable

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[195] For a discussion, see Hoffmann, R. *Chem. Commun.* ***1969***, 240.

[196] For reviews, see Billups, W.E.; Moorehead, A.W., in Rappoport *The Chemistry of the Cyclopropyl Group*, pt. 2, Wiley, NY, ***1987***, pp. 1533–1574; Potts, K.T.; Baum, J.S. *Chem. Rev.* ***1974***, *74*, 189; Yoshida, Z. *Top. Curr. Chem.* ***1973***, *40*, 47; D'yakonov, I.A.; Kostikov, R.R. *Russ. Chem. Rev.* ***1967***, *36*, 557; Closs, G.L. *Adv. Alicyclic Chem.* ***1966***, *1*, 53, pp. 102–126; Krebs, A.W. *Angew. Chem. Int. Ed.* ***1965***, *4*, 10.

[197] Farnum, D.G.; Mehta, G.; Silberman, R.G. *J. Am. Chem. Soc.* ***1967***, *89*, 5048; Breslow, R.; Groves, J.T. *J. Am. Chem. Soc.* ***1970***, *92*, 984.

[198] Breslow, R.; Höver, H.; Chang, H.W. *J. Am. Chem. Soc.* ***1962***, *84*, 3168.

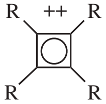
[199] Komatsu, K.; Tomioka, K.; Okamoto, K. *Tetrahedron Lett.* ***1980***, *21*, 947; Moss, R.A.; Shen, S.; Krogh-Jespersen, K.; Potenza, J.A.; Schugar, H.J.; Munjal, R.C. *J. Am. Chem. Soc.* ***1986***, *108*, 134.

[200] Ito, S.; Morita, N.; Asao, T. *Tetrahedron Lett.* ***1992***, *33*, 3773.

[201] Taylor, M.J.; Surman, P.W.J.; Clark, G.R. *J. Chem. Soc. Chem. Commun.* ***1994***, 2517.

even in water solution. The tri-*tert*-butylcyclopropenyl cation is also very stable.[202] In addition, cyclopropenone and several of its derivatives are stable

Cyclopropenone



81

compounds,[203] in accord with the corresponding stability of the tropones.[204] The ring system **80** is nonalternant and the corresponding radical and anion (which do not have an aromatic duet) have electrons in antibonding orbitals, so that their energies are much higher. As with **58** and **62**, the equivalence of the three carbon atoms in the triphenylcyclopropenyl cation has been demonstrated by ^{14}C labeling experiments.[205] The interesting dications **81** ($R = Me$ or Ph) have been prepared,[206] and they too should represent aromatic systems of two electrons.[207]

Systems of Four Electrons: Antiaromaticity

The most obvious compound in which to look for a closed loop of four electrons is cyclobutadiene (**77**).[208] Hückel's rule predicts no aromatic character here, since 4 is not a number of the form $4n + 2$. There is a long history of attempts to prepare this compound and its simple derivatives, and those experiments fully bear out Hückel's prediction. Cyclobutadienes display none of the characteristics that would lead us to call them aromatic, and there is evidence that a closed loop of four electrons is actually *antiaromatic*.[209] If such compounds simply lacked aromaticity, we would expect

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[202] Ciabattoni, J.; Nathan III, E.C. *J. Am. Chem. Soc.* ***1968***, *90*, 4495.

[203] See, for example, Kursanov, D.N.; Vol'pin, M.E.; Koreshkov, Yu.D. *J. Gen. Chem. USSR* ***1960***, *30*, 2855; Breslow, R.; Oda, M. *J. Am. Chem. Soc.* ***1972***, *94*, 4787; Yoshida, Z.; Konishi, H.; Tawara, Y.; Ogoshi, H. *J. Am. Chem. Soc.* ***1973***, *95*, 3043; Ciabattoni, J.; Nathan III, E.C. *J. Am. Chem. Soc.* ***1968***, *90*, 4495.

[204] For a reveiw of cyclopropenones, see Eicher, T.; Weber, J.L. *Top. Curr. Chem. Soc.* ***1975***, *57*, 1. For discussions of cyclopropenone structure, see Shäfer, W.; Schweig, A.; Maier, G.; Sayrac, T.; Crandall, J.K. *Tetrahedron Lett.* ***1974***, 1213; Tobey, S.W., in Bergmann, E.D.; Pullman, B. *Aromaticity, Pseudo-Aromaticity, and Anti-Aromaticity*, Israel Academy of Sciences and Humanities, Jerusalem, ***1971***, pp. 351–362; Greenberg, A.; Tomkins, R.P.T.; Dobrovolny, M.; Liebman, J.F. *J. Am. Chem. Soc.* ***1983***, *105*, 6855.

[205] D'yakonov, I.A.; Kostikov, R.R.; Molchanov, A.P. *J. Org. Chem. USSR* ***1969***, *5*, 171; ***1970***, *6*, 304.

[206] Freedman, H.H.; Young, A.E. *J. Am. Chem. Soc.* ***1964***, *86*, 734; Olah, G.A.; Staral, J.S. *J. Am. Chem. Soc.* ***1976***, *98*, 6290. See also Lambert, J.B.; Holcomb, A.G. *J. Am. Chem. Soc.* ***1971***, *93*, 2994; Seitz, G.; Schmiedel, R.; Mann, K. *Synthesis*, ***1974***, 578.

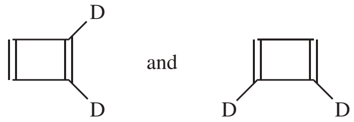
[207] See Pittman Jr., C.U.; Kress, A.; Kispert, L.D. *J. Org. Chem.* ***1974***, *39*, 378. See, however, Krogh-Jespersen, K.; Schleyer, P.v.R.; Pople, J.A.; Cremer, D. *J. Am. Chem. Soc.* ***1978***, *100*, 4301.

[208] For a monograph, see Cava, M.P.; Mitchell, M.J. *Cyclobutadiene and Related Compounds*; Academic Press, NY, ***1967***. For reviews, see Maier, G. *Angew. Chem. Int. Ed.* ***1988***, *27*, 309; ***1974***, *13*, 425–438; Bally, T.; Masamune, S. *Tetrahedron* ***1980***, *36*, 343; Vollhardt, K.P.C. *Top. Curr. Chem.* ***1975***, *59*, 113.

[209] For reviews of antiaromaticity, see Glukhovtsev, M.N.; Simkin, B.Ya.; Minkin, V.I. *Russ. Chem. Rev.* ***1985***, *54*, 54; Breslow, R. *Pure Appl. Chem.* ***1971***, *28*, 111; *Acc. Chem. Res.* ***1973***, *6*, 393.

them to be about as stable as similar nonaromatic compounds, but both theory and experiment show that they are *much less stable*.[210] An antiaromatic compound may be defined as a compound that is destabilized by a closed loop of electrons.

After years of attempts to prepare cyclobutadiene, the goal was finally reached by Pettit and co-workers.[211] It is now clear that **77** and its simple derivatives are extremely unstable compounds with very short lifetimes (they dimerize by a Diels–Alder reaction; see **15–60**) unless they are stabilized in some fashion, either at ordinary temperatures embedded in the cavity of a hemicarcerand[212] (see the structure of a carcerand on p. 128), or in matrices at very low temperatures (generally under 35 K). In either of these cases, the cyclobutadiene molecules are forced to remain apart from each other, and other molecules cannot get in. The structures of **77** and some of its derivatives have been studied a number of times using the low-temperature matrix technique.[213] The ground-state structure of **77** is a rectangular diene (not a diradical) as shown by the ir spectra of **77** and deuterated **77** trapped in matrices,[214] as well as by a photoelectron spectrum.[215] Molecular-orbital calculations agree.[216] The same conclusion was also reached in an elegant experiment in which 1,2-dideuterocyclobutadiene was generated. If **77** is a rectangular diene, the dideutero compound should exist as two isomers:



The compound was generated (as an intermediate that was not isolated) and two isomers were indeed found.[217] The cyclobutadiene molecule is not static, even in the matrices. There are two forms (**77a** and **77b**), which rapidly interconvert.[218]

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[210] For a discussion, see Bauld, N.L.; Welsher, T.L.; Cessac, J.; Holloway, R.L. *J. Am. Chem. Soc.* ***1978***, *100*, 6920.

[211] Watts, L.; Fitzpatrick, J.D.; Pettit, R. *J. Am. Chem. Soc.* ***1965***, *87*, 3253, ***1966***, *88*, 623. See also, Cookson, R.C.; Jones, D.W. *J. Chem. Soc.* ***1965***, 1881.

[212] Cram, D.J.; Tanner, M.E.; Thomas, R. *Angew. Chem. Int. Ed.* ***1991***, *30*, 1024.

[213] See, for example, Lin, C.Y.; Krantz, A. *J. Chem. Soc. Chem. Commun.* ***1972***, 1111; Chapman, O.L.; McIntosh, C.L.; Pacansky, J. *J. Am. Chem. Soc.* ***1973***, *95*, 614; Maier, G.; Mende, U. *Tetrahedron Lett.* ***1969***, 3155. For a review, see Sheridan, R.S. *Org. Photochem.* ***1987***, *8*, 159; pp. 167–181.

[214] Masamune, S.; Souto-Bachiller, F.A.; Machiguchi, T.; Bertie, J.E. *J. Am. Chem. Soc.* ***1978***, *100*, 4889.

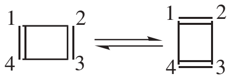
[215] Kreile, J.; Münzel, N.; Schweig, A.; Specht, H. *Chem. Phys. Lett.* ***1986***, *124*, 140.

[216] See, for example, Borden, W.T.; Davidson, E.R.; Hart, P. *J. Am. Chem. Soc.* ***1978***, *100*, 388; Kollmar, H.; Staemmler, V. *J. Am. Chem. Soc.* ***1978***, *100*, 4304; Jafri, J.A.; Newton, M.D. *J. Am. Chem. Soc.* ***1978***, *100*, 5012; Ermer, O.; Heilbronner, E. *Angew. Chem. Int. Ed.* ***1983***, *22*, 402; Voter, A.F.; Goddard III, W.A. *J. Am. Chem. Soc.* ***1986***, *108*, 2830.

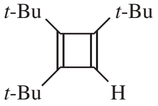
[217] Whitman, D.W.; Carpenter, B.K. *J. Am. Chem. Soc.* ***1980***, *102*, 4272. See also Whitman, D.W.; Carpenter, B.K. *J. Am. Chem. Soc.* ***1982***, *104*, 6473.

[218] Carpenter, B.K. *J. Am. Chem. Soc.* ***1983***, *105*, 1700; Huang, M.; Wolfsberg, M. *J. Am. Chem. Soc.* ***1984***, *106*, 4039; Dewar, M.J.S.; Merz, Jr., K.M.; Stewart, J.J.P. *J. Am. Chem. Soc.* ***1984***, *106*, 4040; Orendt, A.M.; Arnold, B.R.; Radziszewski, J.G.; Facelli, J.C.; Malsch, K.D.; Strub, H.; Grant, D.M.; Michl, J. *J. Am. Chem. Soc.* ***1988***, *110*, 2648. See, however, Arnold, B.R.; Radziszewski, J.G.; Campion, A.; Perry, S.S.; Michl, J. *J. Am. Chem. Soc.* ***1991***, *113*, 692.

Note that there is experimental evidence that the aromatic and antiaromatic characters of neutral and dianionic systems are measurably increased via deuteration.[219]

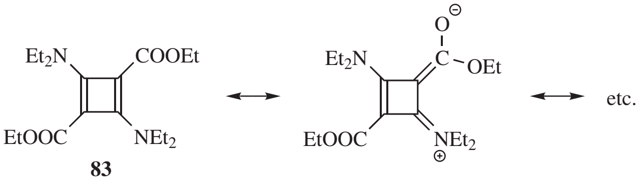


77a **77b**



82

There are some simple cyclobutadienes that are stable at room temperature for varying periods of time. These either have bulky substituents or carry certain other stabilizing substituents such as seen in tri-*tert*-butylcyclobutadiene (**83**).[220] Such compounds are relatively stable because dimerization is sterically hindered. Examination of the NMR spectrum of **83** showed that the ring proton ($\delta = 5.38$) was shifted *upfield*, compared with the position expected for a nonaromatic proton, for example, cyclopentadiene. As we will see (pp. 89–90), this indicates that the compound is antiaromatic.



83

The other type of stable cyclobutadiene has two electron-donating and two electron-withdrawing groups,[221] and is stable in the absence of water.[222] An example is **58**. The stability of these compounds is generally attributed to the resonance shown, a type of resonance stabilization called the *push–pull or captodative effect*,[223] although it has been concluded from a photoelectron spectroscopy study that second-order bond fixation is more important.[224] An X-ray crystallographic study of **83** has shown[225] the ring to be a distorted square with bond lengths of 1.46 Å and angles of 87° and 93°.

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[219] For experiments with [16]-annulene (see p 82), see Stevenson, C.D.; Kurth, T.L. *J. Am. Chem. Soc.* ***1999***, *121*, 1623

[220] Masamune, S.; Nakamura, N.; Suda, M.; Ona, H. *J. Am. Chem. Soc.* ***1973***, *95*, 8481; Maier, G.; Alzérreca, A. *Angew. Chem. Int. Ed.* ***1973***, *12*, 1015. For a discussion, see Masamune, S. *Pure Appl. Chem.* ***1975***, *44*, 861.

[221] The presence of electron-donating and -withdrawing groups on the same ring stabilizes $4n$ systems and destabilizes $4n + 2$ systems. For a review of this concept, see Gompper, R.; Wagner, H. *Angew. Chem. Int. Ed.* ***1988***, *27*, 1437.

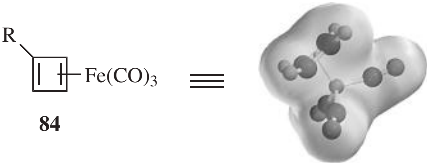
[222] Neuenschwander, M.; Niederhauser, A. *Chimia*, ***1968***, *22*, 491, *Helv. Chim. Acta*, ***1970***, *53*, 519; Gompper, R.; Kroner, J.; Seybold, G.; Wagner, H. *Tetrahedron* ***1976***, *32*, 629.

[223] Manatt, S.L.; Roberts, J.D. *J. Org. Chem.* ***1959***, *24*, 1336; Breslow, R.; Kivelevich, D.; Mitchell, M.J.; Fabian, W.; Wendel, K. *J. Am. Chem. Soc.* ***1965***, *87*, 5132; Hess Jr., B.A.; Schaad, L.J. *J. Org. Chem.* ***1976***, *41*, 3058.

[224] Gompper, R.; Holsboer, F.; Schmidt, W.; Seybold, G. *J. Am. Chem. Soc.* ***1973***, *95*, 8479.

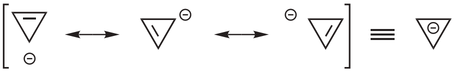
[225] Lindner, H.J.; von Ross, B. *Chem. Ber.* ***1974***, *107*, 598.

It is clear that simple cyclobutadienes, which could easily adopt a square planar shape if that would result in aromatic stabilization, do not in fact do so and are not aromatic. The high reactivity of these compounds is not caused merely by steric strain, since the strain should be no greater than that of simple cyclopropenes, which are known compounds. It is probably caused by antiaromaticity.[226]

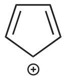


84

The cyclobutadiene system can be stabilized as a η^4-complex with metals,[227] as with the iron complex **84** (see Chapter 3), but in these cases electron density is withdrawn from the ring by the metal and there is no aromatic quartet. In fact, these cyclobutadiene–metal complexes can be looked upon as systems containing an aromatic duet. The ring is square planar,[228] the compounds undergo aromatic substitution,[229] and nmr spectra of monosubstituted derivatives show that the C-2 and C-4 protons are equivalent.[229]



85 **86**



87

Other systems that have been studied as possible aromatic or antiaromatic four-electron systems include the cyclopropenyl anion (**86**), the cyclopentadienyl cation (**87**).[230] With respect to **86**, HMO theory predicts that an unconjugated **85** (i.e., a single canonical form) is more stable than a conjugated **86**,[231] so that **85** would actually lose stability by forming a closed loop of four electrons. The HMO theory

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[226] For evidence, see Breslow, R.; Murayama, D.R.; Murahashi, S.; Grubbs, R. *J. Am. Chem. Soc.* ***1973***, *95*, 6688; Herr, M.L. *Tetrahedron* ***1976***, *32*, 2835.

[227] For reviews, see Efraty, A. *Chem. Rev.* ***1977***, *77*, 691; Pettit, R. *Pure Appl. Chem.* ***1968***, *17*, 253; Maitlis, P.M. *Adv. Organomet. Chem.* ***1966***, *4*, 95; Maitlis, P.M.; Eberius, K.W., in Snyder, J.P. *Nonbenzenoid Aromatics*, vol. 2, Academic Press, NY, ***1971***, pp. 359–409.

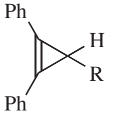
[228] Dodge, R.P.; Schomaker, V. *Acta Crystallogr.* ***1965***, *18*, 614; *Nature* (*London*) ***1960***, *186*, 798; Dunitz, J.D.; Mez, H.C.; Mills, O.S.; Shearer, H.M.M. *Helv. Chim. Acta*, ***1962***, *45*, 647; Yannoni, C.S.; Ceasar, G.P.; Dailey, B.P. *J. Am. Chem. Soc.* ***1967***, *89*, 2833.

[229] Fitzpatrick, J.D.; Watts, L.; Emerson, G.F.; Pettit, R. *J. Am. Chem. Soc.* ***1965***, *87*, 3255. For a discussion, see Pettit, R. *J. Organomet. Chem.* ***1975***, *100*, 205.

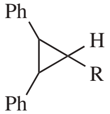
[230] For a review of cyclopentadienyl cations, see Breslow, R. *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 81.

[231] Clark, D.T. *Chem. Commun.* ***1969***, 637; Glukhovtsev, M.N.; Simkin, B.Ya.; Minkin, V.I. *Russ. Chem. Rev.* ***1985***, *54*, 54; Breslow, R. *Pure Appl. Chem.* ***1971***, *28*, 111; *Acc. Chem. Res.* ***1973***, *6*, 393.

is supported by experiment. Among other evidence,



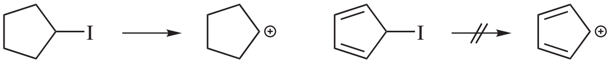
88



89

it has been shown that **88** (R = COPh) loses its proton in hydrogen-exchange reactions ~6000 times more slowly than **89** (R = COPh).[232] Where R = CN, the ratio is ~10,000.[233] This indicates that **88** are much more reluctant to form carbanions (which would have to be cyclopropenyl carbanions) than **89**, which form ordinary carbanions. Thus the carbanions of **88** are less stable than corresponding ordinary carbanions. Although derivatives of cyclopropenyl anion have been prepared as fleeting intermediates (as in the exchange reactions mentioned above), all attempts to prepare the ion or any of its derivatives as relatively stable species have so far met with failure.[234]

In the case of **87**, the ion has been prepared and has been shown to be a diradical in the ground state,[235] as predicted by the discussion on p. 73.[236] Evidence that **87** is not only nonaromatic, but also antiaromatic comes from studies on **90** and **92**.[237] When **90** is treated with silver perchlorate in propionic acid, the molecule is rapidly solvolyzed (a reaction in which the intermediate **91** is formed; see Chapter 5). Under the same conditions, **92** undergoes no solvolysis at all; that is, **87** does not form. If **87** were merely nonaromatic, it should be about as stable as **91** (which of course has no resonance stabilization at all). The fact that it is so much more reluctant to form indicates that **87** is much less stable than **91**. It is noted that under certain conditions, **91** can be generated solvolytically.[238]



90 **91** **92** **87**

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[232] Breslow, R.; Brown, J.; Gajewski, J.J. *J. Am. Chem. Soc.* ***1967***, *89*, 4383.

[233] Breslow, R.; Douek, M. *J. Am. Chem. Soc.* ***1968***, *90*, 2698.

[234] See, for example, Breslow, R.; Cortés, D.A.; Juan, B.; Mitchell, R.D. *Tetrahedron Lett.* ***1982***, *23*, 795. A triphenylcyclopropyl anion has been prepared in the gas phase, with a lifetime of 1–2 s: Bartmess, J.E.; Kester, J.; Borden, W.T.; Köser, H.G. *Tetrahedron Lett.* ***1986***, *27*, 5931.

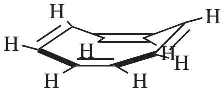
[235] Saunders, M.; Berger, R.; Jaffe, A.; McBride, J.M.; O'Neill, J.; Breslow, R.; Hoffman Jr., J.M.; Perchonock, C.; Wasserman, E.; Hutton, R.S.; Kuck, V.J. *J. Am. Chem. Soc.* ***1973***, *95*, 3017.

[236] Derivatives of **87** show similar behavior. Volz, H. *Tetrahedron Lett.* ***1964***, 1899; Breslow, R.; Chang, H.W.; Hill, R.; Wasserman, E. *J. Am. Chem. Soc.* ***1967***, *89*, 1112; Gompper, R.; Glöckner, H. *Angew. Chem. Int. Ed.* ***1984***, *23*, 53.

[237] Breslow, R.; Mazur, S. *J. Am. Chem. Soc.* ***1973***, *95*, 584. For further evidence, see Lossing, F.P.; Treager, J.C. *J. Am. Chem. Soc.* ***1975***, *97*, 1579. See also, Breslow, R.; Canary, J.W. *J. Am. Chem. Soc.* ***1991***, *113*, 3950.

[238] Allen, A.D.; Sumonja, M.; Tidwell, T.T. *J. Am. Chem. Soc.* ***1997***, *119*, 2371.

It is strong evidence for Hückel's rule that **86** and **87** are not aromatic while the cyclopropenyl cation (**80**) and the cyclopentadienyl anion (**58**) are, since simple resonance theory predicts no difference between **86** and **80** or **87** and **58** (the same number of equivalent canonical forms can be drawn for **86** as for **80** and for **87** as for **58**).



78a

Systems of Eight Electrons

Cyclooctatetraene[239] ([8]annulene, **78a**) is not planar, but tub-shaped.[240] Therefore we would expect that it is neither aromatic nor antiaromatic, since both these conditions require overlap of parallel *p* orbitals. The reason for the lack of planarity is that a regular octagon has angles of 135°, while sp^2 angles are most stable at 120°. To avoid the strain, the molecule assumes a nonplanar shape, in which orbital overlap is greatly diminished.[241] Single- and double-bond distances in **78** are, respectively, 1.46 and 1.33 Å, which is expected for a compound made up of four individual double bonds.[240] The reactivity is also what would be expected for a linear polyene. Reactive intermediates can be formed in solution. Dehydrohalogenation of bromocyclooctatetraene at −100°C has been reported, for example, and trapping by immediate electron transfer gave a stable solution of the [8]annulyne anion radical.[242]

The cyclooctadiendiynes **93** and **94** are planar conjugated eight-electron systems (the four extra triple-bond electrons do not participate), which nmr evidence show to be antiaromatic.[243] There is evidence that part of the reason for the lack of planarity in **78** itself is that a planar molecular would have to be antiaromatic.[244] The cycloheptatrienyl anion (**61**) also has eight electrons, but does not behave like an aromatic system.[151] The bond lengths for a series of molecules containing the cycloheptatrienide anion have recently been published.[245] The NMR spectrum

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[239] For a monograph, see Fray, G.I.; Saxton, R.G. *The Chemistry of Cyclooctatetraene and its Derivatives*; Cambridge University Press: Cambridge, ***1978***. For a review, see Paquette, L.A. *Tetrahedron* ***1975***, *31*, 2855. For reviews of heterocyclic 8π systems, see Kaim, W. *Rev. Chem. Intermed.* ***1987***, *8*, 247; Schmidt, R.R. *Angew. Chem. Int. Ed.* ***1975***, *14*, 581.

[240] Bastiansen, O.; Hedberg, K.; Hedberg, L. *J. Chem. Phys.* ***1957***, *27*, 1311.

[241] The compound perfluorotetracyclobutacyclooctatetraene has been found to have a planar cyclooctatetraene ring, although the corresponding tetracyclopenta analog is nonplanar: Einstein, F.W.B.; Willis, A.C.; Cullen, W.R.; Soulen, R.L. *J. Chem. Soc. Chem. Commun.* ***1981***, 526. See also, Paquette, L.A.; Wang, T.; Cottrell, C.E. *J. Am. Chem. Soc.* ***1987***, *109*, 3730.

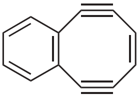
[242] Peters, S.J.; Turk, M.R.; Kiesewetter, M.K.; Stevenson, C.D. *J. Am. Chem. Soc.* ***2003***, *125*, 11264.

[243] For a review, see Huang, N.Z.; Sondheimer, F. *Acc. Chem. Res.* ***1982***, *15*, 96. See also, Dürr, H.; Klauck, G.; Peters, K.; von Schnering, H.G. *Angew. Chem. Int. Ed.* ***1983***, *22*, 332; Chan, T.; Mak, T.C.W.; Poon, C.; Wong, H.N.C.; Jia, J.H.; Wang, L.L. *Tetrahedron* ***1986***, *42*, 655.

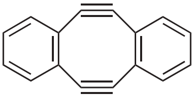
[244] Figeys, H.P.; Dralants, A. *Tetrahedron Lett.* ***1971***, 3901; Buchanan, G.W. *Tetrahedron Lett.* ***1972***, 665.

[245] Dietz, F.; Rabinowitz, M.; Tadjer, A.; Tyutyulkov, N. *J. Chem. Soc. Perkin Trans. 2* ***1995***, 735.

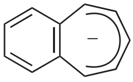
of the benzocycloheptatrienyl anion (**95**) shows that, like **82**, **93**, and **94**, this compound is antiaromatic.[246] A new antiaromatic compound 1,4-biphenylene quinone (**96**) was prepared, but it rapidly dimerizes due to instability.[247]



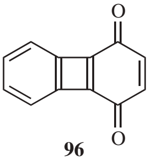
93



94



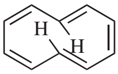
95



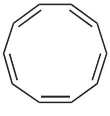
96

Systems of Ten Electrons[248]

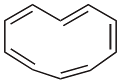
There are three geometrically possible isomers of [10]annulene: the all-*cis* (**97**), the mono-*trans* (**98**), and the *cis–trans–cis–cis–trans* (**79**). If Hückel's rule applies, they should be planar. But it is far from obvious that the molecules would adopt a planar shape, since they must overcome considerable strain to do so. For a regular decagon (**97**) the angles would have to be 144°, considerably larger than the 120° required for sp^2 angles. Some of this strain would also be present in **98**, but this kind of strain is eliminated in **79** since all the angles are 120°. However, it was pointed out by Mislow[249] that the hydrogens in the 1 and 6 positions should interfere with each other and force the molecule out of planarity.



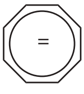
79



97



98



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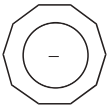
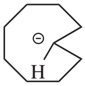
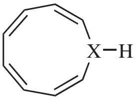


100



101



102

Compounds **97** and **98** have been prepared[250] as crystalline solids at −80°C. The NMR spectra show that all the hydrogens lie in the alkene region and it was concluded that neither compound is aromatic. Calculations on **98** suggest that

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[246] Staley, S.W.; Orvedal, A.W. *J. Am. Chem. Soc.* ***1973***, *95*, 3382.

[247] Kiliç, H.; Balci, M. *J. Org. Chem.* ***1997***, *62*, 3434.

[248] For reviews, see Kemp-Jones, A.V.; Masamune, S. *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 121; Masamune, S.; Darby, N. *Acc. Chem. Res.* ***1972***, *5*, 272; Burkoth, T.L.; van Tamelen, E.E., in Snyder,J.P. *Nonbenzenoid Aromaticity*, Vol. 1, Academic Press, NY, ***1969***, pp. 63–116; Vogel, E., in Garratt, P.J. Aromaticity, Wiley, NY, ***1986***, pp. 113–147.

[249] Mislow, K. *J. Chem. Phys.* ***1952***, *20*, 1489.

[250] Masamune,S.; Hojo, K.; Bigam, G.; Rabenstein, D.L. *J. Am. Chem. Soc.* ***1971***, *93*, 4966. [10]Annulenes had previously been prepared, but it was not known which ones: van Tamelen, E.E.; Greeley, R.H. *Chem. Commun.* ***1971***, 601; van Tamelen, E.E.; Burkoth, T.L.; Greeley, R.H. *J. Am. Chem. Soc.* ***1971***, *93*, 6120.

it may indeed be aromatic, although the other isomers are not.[251] It is known that the Hartree–Fock (HF) method incorrectly favors bond-length-alternating structures for [10]annulene, and aromatic structures are incorrectly favored by density functional theory. Improved calculations predict that the twist conformation is lowest in energy, and the naphthalene-like and heart-shaped conformations lie higher than the twist by 1.40 and 4.24 kcal mol^{-1}, respectively.[252] From ^{13}C and proton (H^1) nmr spectra it has been deduced that neither is planar. However, that the angle strain is not insurmountable has been demonstrated by the preparation of several compounds that have large angles, but that are definitely planar 10-electron aromatic systems. Among these are the dianion **99**, the anions **100** and **101**, and the azonine **102**.[253] Compound **99**[254] has angles of ~135°, while **100**[255] and **101**[256] have angles of ~140°, which are not very far from 144°. The inner proton in **101**[257] (which is the mono-trans isomer of the all-cis **100**) is found far upfield in the NMR (−3.5 δ). For **97** and **98**, the cost in strain energy to achieve planarity apparently outweighs the extra stability that would come from an aromatic ring. To emphasize the delicate balance between these factors, we may mention that the oxygen analog of **102** (X = O, oxonin) and the *N*-carbethoxy derivative of **102** (X = CH) are nonaromatic and nonplanar, while **102** (X = N) is aromatic and planar.[258] Other azaannulenes are known, including Vogel's 2,7-methanoazaannulene,[259] as well

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[251] Sulzbach, H.M.; Schleyer, P.v.R.; Jiao, H.; Xie, Y.; Schaefer III, H.F. *J. Am. Chem. Soc.* ***1995***, *117*, 1369. Also see, Sulzbach, H.M.; Schaefer III, H.F.; Klopper, W.; Lüthi, H.P. *J. Am. Chem. Soc.* ***1996***, *118*, 3519 for a discussion of Aromaticity calculations for [10]annulene.

[252] King, R.A.; Crawford, T.D.; Stanton, J.F.; Schaefer, III, H.F. *J. Am. Chem. Soc.* ***1999***, *121*, 10788.

[253] For reviews of **102** (X = N) and other nine-membered rings containing four double bonds and a hetero atom (heteronins), see Anastassiou, A.G. *Acc. Chem. Res.* ***1972***, *5*, 281, *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 1, *Pure Appl. Chem.* ***1975***, *44*, 691. For a review of heteroannulenes in general, see Anastassiou; Kasmai, H.S. *Adv. Heterocycl. Chem.* ***1978***, *23*, 55.

[254] Katz, T.J. *J. Am. Chem. Soc.* ***1960***, *82*, 3784, 3785; Goldstein, M.J.; Wenzel, T.T. *J. Chem. Soc. Chem. Commun.* ***1984***, 1654; Garkusha, O.G.; Garbuzova, I.A.; Lokshin, B.V.; Todres, Z.V. *J. Organomet. Chem.* ***1989***, *371*, 279. See also, Noordik, J.H.; van den Hark, T.E.M.; Mooij, J.J.; Klaassen, A.A.K. *Acta Crystallogr. Sect. B.* ***1974***, *30*, 833; Goldberg, S.Z.; Raymond, K.N.; Harmon, C.A.; Templeton, D.H. *J. Am. Chem. Soc.* ***1974***, *96*, 1348; Evans, W.J.; Wink, D.J.; Wayda, A.L.; Little, D.A. *J. Org. Chem.* ***1981***, *46*, 3925; Heinz, W.; Langensee, P.; Müllen, K. *J. Chem. Soc. Chem. Commun.* ***1986***, 947.

[255] Katz, T.J.; Garratt, P.J. *J. Am. Chem. Soc.* ***1964***, *86*, 5194; LaLancette, E.A.; Benson, R.E. *J. Am. Chem. Soc.* ***1965***, *87*, 1941; Simmons, H.E.; Chesnut, D.B.; LaLancette, E.A. *J. Am. Chem. Soc.* ***1965***, *87*, 982; Paquette, L.A.; Ley, S.V.; Meisinger, R.H.; Russell, R.K.; Oku, M. *J. Am. Chem. Soc.* ***1974***, *96*, 5806; Radlick, P.; Rosen, W. *J. Am. Chem. Soc.* ***1966***, *88*, 3461.

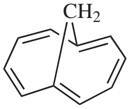
[256] Anastassiou, A.G.; Gebrian, J.H. *Tetrahedron Lett.* ***1970***, 825.

[257] Boche, G.; Weber, H.; Martens, D.; Bieberbach, A. *Chem. Ber.* ***1978***, *111*, 2480. See also, Anastassiou, A.G.; Reichmanis, E. *Angew. Chem. Int. Ed.* ***1974***, *13*, 728; Boche, G.; Bieberbach, A. *Tetrahedron Lett.* ***1976***, 1021.

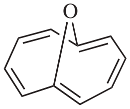
[258] Anastassiou, A.G.; Gebrian, J.H. *J. Am. Chem. Soc.* ***1969***, *91*, 4011; Chiang, C.C.; Paul, I.C.; Anastassiou, A.G.; Eachus, S.W. *J. Am. Chem. Soc.* ***1974***, *96*, 1636.

[259] Vogel, E.; Roth, H.D. *Angew. Chem. Int. Ed.* ***1964***, *3*, 228; Vogel, E.; Biskup, M.; Pretzer, W.; Böll, W.A. *Angew. Chem. Int. Ed.* ***1964***, *3*, 642.; Vogel, E.; Meckel, M.; Grimme, W. *Angew. Chem. Int. Ed.* ***1964***, *3*, 643; Vogel, E.; Pretzer, W.; Böll, W.A. *Tetrahedron Lett.* ***1965***, 3613; Sondheimer, F.; Shani, A. *J. Am. Chem. Soc.* ***1964***, *86*, 3168; Shani, A.; Sondheimer, F. *J. Am. Chem. Soc.* ***1967***, *89*, 6310; Bailey, N.A.; Mason, R. *J. Chem. Soc. Chem. Commun.* ***1967***, 1039.

as 3,8-methanoaza[10]annulene,[260] and their alkoxy derivatives.[261] Calculations for aza[10]annulene concluded that the best olefinic twist isomer is 2.1 kcal mol^{-1} (8.8 kJ mol^{-1}) more stable than the aromatic form,[262] and is probably the more stable form.



103



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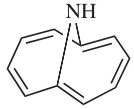

105

So far, **79** has not been prepared despite many attempts. However, there are various ways of avoiding the interference between the two inner protons. The approach that has been most successful involves bridging the 1 and 6 positions.[263] Thus, 1,6-methano[10]annulene (**103**)[264] and its oxygen and nitrogen analogs, **104**[265] and **105**,[266] have been prepared and are stable compounds that undergo aromatic substitution and are diatropic.[267] For example, the perimeter protons of **103** are found at 6.9–7.3 δ, while the bridge protons are at −0.5 δ. The crystal structure of **103** shows that the perimeter is nonplanar, but the bond distances are in the range 1.37–1.42 Å.[268] It has therefore been amply demonstrated that a closed loop of 10 electrons is an aromatic system, although some molecules that could conceivably have such a system are too distorted from planarity to be aromatic. A small distortion from planarity (as in **103**) does not prevent aromaticity, at least in part because the s orbitals so distort themselves as to maximize the favorable (parallel) overlap

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[260] Schäfer-Ridder, M.; Wagner, A.; Schwamborn, M.; Schreiner, H.; Devrout, E.; Vogel, E. *Angew. Chem. Int. Ed.* ***1978***, *17*, 853.; Destro, R.; Simonetta, M.; Vogel, E. *J. Am. Chem. Soc.* ***1981***, *103*, 2863.

[261] Vogel, E. Presented at the 3rd International Symposium on Novel Aromatic Compounds (ISNA 3), San Francisco, Aug ***1977***; Gölz, H.-J.; Muchowski, J.M.; Maddox, M.L. *Angew. Chem. Int. Ed.* ***1978***, *17*, 855; Schleyer, P.v.R.; Jiao, H.; Sulzbach, H.M.; Schaefer III H.F. *J. Am. Chem. Soc.* ***1996***, *118*, 2093.

[262] Bettinger, H.F.; Sulzbach, H.M.; Schleyer, P.v.R.; Schaefer III, H.F. *J. Org. Chem.* ***1999***, *64*, 3278.

[263] For reviews of bridged [10]-, [14]-, and [18]annulenes, see Vogel, E. *Pure Appl. Chem.* ***1982***, *54*, 1015; *Isr. J. Chem.* ***1980***, *20*, 215; *Chimia*, ***1968***, *22*, 21; Vogel, E.; Günther, H. *Angew. Chem. Int. Ed.* ***1967***, *6*, 385.

[264] Vogel, E.; Roth, H.D. *Angew. Chem. Int. Ed.* ***1964***, *3*, 228; Vogel, E.; Böll, W.A. *Angew. Chem. Int. Ed.* ***1964***, *3*, 642; Vogel, E.; Böll, W.A.; Biskup, M. *Tetrahedron Lett.* ***1966***, 1569.

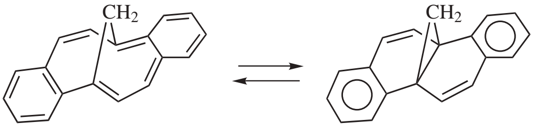
[265] Vogel, E.; Biskup, M.; Pretzer, W.; Böll, W.A. *Angew. Chem. Int. Ed.* ***1964***, *3*, 642; Shani, A.; Sondheimer, F. *J. Am. Chem. Soc.* ***1967***, *89*, 6310; Bailey, N.A.; Mason, R. *Chem. Commun.* ***1967***, 1039.

[266] Vogel, E.; Pretzer, W.; Böll, W.A. *Tetrahedron Lett.* ***1965***, 3613. See also, Vogel, E.; Biskup, M.; Pretzer, W.; Böll, W.A. *Angew. Chem. Int. Ed.* ***1964***, *3*, 642.

[267] For another type of bridged diatropic [10]annulene, see Lidert, Z.; Rees, C.W. *J. Chem. Soc. Chem. Commun.* ***1982***, 499; Gilchrist, T.L.; Rees, C.W.; Tuddenham, D. *J. Chem. Soc. Perkin Trans. 1* ***1983***, 83; McCague, R.; Moody, C.J.; Rees, C.W. *J. Chem. Soc. Perkin Trans. 1* ***1984***, 165, 175; Gibbard, H.C.; Moody, C.J.; Rees, C.W. *J. Chem. Soc. Perkin Trans. 1* ***1985***, 731, 735.

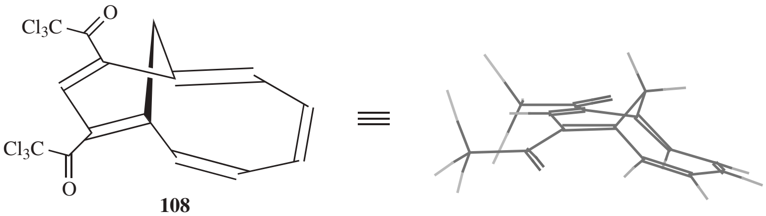
[268] Bianchi, R.; Pilati, T.; Simonetta, M. *Acta Crystallogr., Sect. B* ***1980***, *36*, 3146. See also Dobler, M.; Dunitz, J.D. *Helv. Chim Acta*, ***1965***, *48*, 1429.

of *p* orbitals to form the aromatic 10-electron loop.[269]



106 **107**

In **106**, where **103** is fused to two benzene rings in such a way that no canonical form can be written in which both benzene rings have six electrons, the aromaticity is reduced by annellation, as shown by the fact that the molecule rapidly converts to the more stable **107**, in which both benzene rings can be fully aromatic[270] (this is similar to the cycloheptatriene–norcaradiene conversions discussed on p. 1664).



108

Molecules can sustain significant distortion from planarity and retain their aromatic character. 1,3-Bis(trichloroacetyl)homoazulene (**108**) qualifies as aromatic using the geometric criterion that there is only a small average deviation from the C—C bond length in the [10]annulene perimeter.[271] X-ray crystal structure shows that the 1,5-bridge distorts the [10]-annulene π-system away from planarity (see the 3D model) with torsion angles as large as 42.2° at the bridgehead position, but **108** does not lose its aromaticity.

Systems of More than Ten Electrons: $4n + 2$ Electrons[272]

Extrapolating from the discussion of [10]annulene, we expect larger $4n + 2$ systems to be aromatic if they are planar. Mislow[249] predicted that [14]annulene (**109**)

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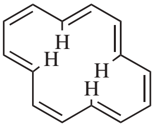
[269] For a discussion, see Haddon, R.C. *Acc. Chem. Res.* ***1988***, *21*, 243.

[270] Hill, R.K.; Giberson, C.B.; Silverton, J.V. *J. Am. Chem. Soc.* ***1988***, *110*, 497. See also, McCague, R.; Moody, C.J.; Rees, C.W.; Williams, D.J. *J. Chem. Soc. Perkin Trans. 1* ***1984***, 909.

[271] Scott, L.T.; Sumpter, C.A.; Gantzel, P.K.; Maverick, E.; Trueblood, K.N. *Tetrahedron* ***2001***, *57*, 3795.

[272] For reviews of annulenes, with particular attention to their nmr spectra, see Sondheimer, F. *Acc. Chem. Res.* ***1972***, *5*, 81–91, *Pure Appl. Chem.* ***1971***, *28*, 331, *Proc. R. Soc. London. Ser. A*, ***1967***, *297*, 173; Sondheimer, F.; Calder, I.C.; Elix, J.A.; Gaoni, Y; Garratt, P.J.; Grohmann, K.; di Maio, G.; Mayer, J.; Sargent, M.V.; Wolovsky, R. in Garratt, P.G. *Aromaticity*, Wiley, NY, ***1986***, pp. 75–107; Haddon, R.C.; Haddon, V.R.; Jackman, L.M. *Fortschr. Chem. Forsch.* ***1971***, *16*, 103. For a review of annulenoannulenes (two annulene rings fused together), see Nakagawa, M. *Angew. Chem. Int. Ed.* ***1979***, *18*, 202. For a review of reduction and oxidation of annulenes; that is, formation of radical ions, dianions, and dications, see Müllen, K. *Chem. Rev.* ***1984***, *84*, 603. For a review of annulene anions, see Rabinovitz, M. *Top. Curr. Chem.* ***1988***, *146*, 99. Also see Cyvin, S.J.; Brunvoll, J.; Chen, R.S.; Cyvin, B.N.; Zhang, F.J. *Theory of Coronoid Hydrocarbons II*, Springer-Verlag, Berlin, ***1994***.

would possess the same type of interference as **79**, although in lesser degree. This is borne out by experiment. Compound **109** is aromatic (it is diatropic; inner protons at 0.00 δ, outer protons at 7.6 δ),[273] but is completely destroyed by light and air in 1 day. X-ray analysis shows that although there are no alternating single and double bonds, the molecule is not planar.[274] A number of stable bridged [14]annulenes have been prepared,[275] for example, *trans*-15,16-dimethyldihydropyrene (**110**),[276] *syn*-1,6:8,13-diimino[14]annulene (**111**),[277] and *syn*- and *anti*-1,6:8,13-bis(methano[14]annulene) (**112** and **113**).[278] The dihydropyrene **110** (and its diethyl and dipropyl homologs) is undoubtedly aromatic: the π perimeter is approximately planar;[279] the bond distances are all 1.39–1.40 Å; and the



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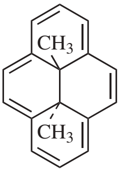

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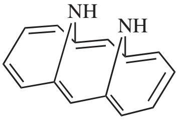

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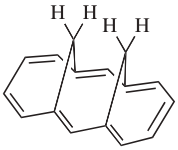

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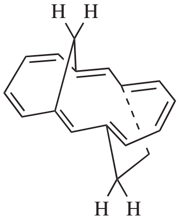

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[273] Gaoni, Y.; Melera, A.; Sondheimer, F.; Wolovsky, R. *Proc. Chem. Soc.* ***1964***, 397.

[274] Bregman, J. *Nature (London)* ***1962***, *194*, 679; Chiang, C.C.; Paul, I.C. *J. Am. Chem. Soc. 1972*, ***94***, 4741. Another 14-electron system is the dianion of [12]annulene, which is also apparently aromatic though not planar: Oth, J.F.M.; Schröder, G. *J. Chem. Soc. B*, ***1971***, 904. See also Garratt, P.J.; Rowland, N.E.; Sondheimer, F. *Tetrahedron* ***1971***, *27*, 3157; Oth, J.F.M.; Müllen, K.; Königshofen, H.; Mann, M.; Sakata, Y.; Vogel, E. *Angew. Chem. Int. Ed.* ***1974***, *13*, 284. For some other 14-electron aromatic systems, see Anastassiou, A.G.; Elliott, R.L.; Reichmanis, E. *J. Am. Chem. Soc.* ***1974***, *96*, 7823; Wife, R.L.; Sondheimer, F. *J. Am. Chem. Soc.* ***1975***, *97*, 640; Ogawa, H.; Kubo, M.; Saikachi, H.*Tetrahedron Lett.* ***1971***, 4859; Oth, J.F.M.; Müllen, K.; Königshofen, H.; Wassen, J.; Vogel, E. *Helv. Chim. Acta*, ***1974***, *57*, 2387; Willner, I.; Gutman, A.L.; Rabinovitz, M. *J. Am. Chem. Soc.* ***1977***, *99*, 4167; Röttele, H.; Schröder, G. *Chem. Ber.* ***1982***, *115*, 248.

[275] For a review, see Vogel, E. *Pure Appl. Chem.* ***1971***, *28*, 355.

[276] Boekelheide, V.; Phillips, J.B. *J. Am. Chem. Soc.* ***1967***, *89*, 1695; Boekelheide, V.; Miyasaka, T. *J. Am. Chem. Soc.* ***1967***, *89*, 1709. For reviews of dihydropyrenes, see Mitchell, R.H. *Adv. Theor. Interesting Mol.* ***1989***, *1*, 135; Boekelheide, V. *Top. Nonbenzoid Arom. Chem.* ***1973***, *1*, 47; *Pure Appl. Chem.* ***1975***, *44*, 807.

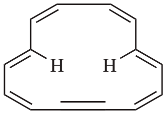
[277] Vogel, E.; Kuebart, F.; Marco, J.A.; Andree, R.; Günther, H.; Aydin, R. *J. Am. Chem. Soc.* ***1983***, *105*, 6982; Destro, R.; Pilati, T.; Simonetta, M.; Vogel, E. *J. Am. Chem. Soc.* ***1985***, *107*, 3185, 3192. For the di-*O*- analog of **102**, see Vogel, A.; Biskup, M.; Vogel, E.; Günther, H. *Angew. Chem. Int. Ed.* ***1966***, *5*, 734.

[278] Vogel, E.; Sombroek, J.; Wagemann, W. *Angew. Chem. Int. Ed.* ***1975***, *14*, 564.

[279] Hanson, A.W. *Acta Crystallogr.* ***1965***, *18*, 599, 1967, 23, 476.

molecule undergoes aromatic substitution[276] and is diatropic.[280] The outer protons are found at 8.14–8.67 δ, while the CH_3 protons are at −4.25 δ. Other nonplanar aromatic dihydropyrenes are known.[281] Annulenes **111** and **112** are also diatropic,[282] although X-ray crystallography indicates that the π periphery in at least **111** is not quite planar.[283] However, **113**, in which the geometry of the molecule greatly reduces the overlap of the *p* orbitals at the bridgehead positions with adjacent *p* orbitals, is definitely not aromatic,[284] as shown by NMR spectra[278] and X-ray crystallography, from which bond distances of 1.33–1.36 Å for the double bonds and 1.44–1.49 Å for the single bonds have been obtained.[285] In contrast, all the bond distances in **111** are ~1.38–1.40 Å.[283]

Another way of eliminating the hydrogen interferences of [14]annulene is to introduce one or more triple bonds into the system, as in dehydro[14]annulene (**114**).[286] All five known dehydro[14]annulenes are diatropic, and **87** can be nitrated or sulfonated.[287] The extra electrons of the triple bond do not form part of the aromatic system, but simply exist as a localized bond. There has been a debate concerning the extent of delocalization in dehydrobenzoannulenes,[288] but there is evidence for a weak, but discernible ring current.[289] 3,4,7,8,9,10,13,14-Octahydro[14]annulene (**116**) has been



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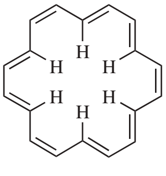

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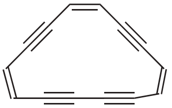

116

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[280] A number of annellated derivatives of **110** are less diatropic, as would be expected from the discussion on p. $$$: Mitchell, R.H.; Williams, R.V.; Mahadevan, R.; Lai, Y.H.; Dingle, T.W. *J. Am. Chem. Soc.* ***1982***, *104*, 2571 and other papers in this series.

[281] Bodwell, G.J.; Bridson, J.N.; Chen, S.-L.; Poirier, R.A. *J. Am. Chem. Soc.* ***2001***, *123*, 4704; Bodwell, G.J.; Fleming, J.J.; Miller, D.O. *Tetrahedron* ***2001***, *57*, 3577.

[282] As are several other similarly bridged [14]annulenes; see, for example, Flitsch, W.; Peeters, H. *Chem. Ber.* ***1973***, *106*, 1731; Huber, W.; Lex, J.; Meul, T.; Müllen, K. *Angew. Chem. Int. Ed.* ***1981***, *20*, 391; Vogel, E.; Nitsche, R.; Krieg, H. *Angew. Chem. Int. Ed.* ***1981***, *20*, 811; Mitchell, R.H.; Anker, W. *Tetrahedron Lett.* ***1981***, *22*, 5139; Vogel, E.; Wieland, H.; Schmalstieg, L.; Lex, J. *Angew. Chem. Int. Ed.* ***1984***, *23*, 717; Neumann, G.; Müllen, K. *J. Am. Chem. Soc.* ***1986***, *108*, 4105.

[283] Ganis, P.; Dunitz, J.D. *Helv. Chim. Acta*, ***1967***, *50*, 2369.

[284] For another such pair of molecules, see Vogel, E.; Nitsche, R.; Krieg, H. *Angew. Chem. Int. Ed.* ***1981***, *20*, 811. See also, Vogel, E.; Schieb, T.; Schulz, W.H.; Schmidt, K.; Schmickler, H.; Lex, J. *Angew. Chem. Int. Ed.* ***1986***, *25*, 723.

[285] Gramaccioli, C.M.; Mimun, A.; Mugnoli, A.; Simonetta, M. *Chem. Commun.* ***1971***, 796. See also, Destro, R.; Simonetta, M. *Tetrahedron* ***1982***, *38*, 1443.

[286] For a review of dehydroannulenes, see, Nakagawa, M. *Top. Nonbenzenoid Aromat. Chem.* ***1973***, *1*, 191.

[287] Gaoni, Y.; Sondheimer, F. *J. Am. Chem. Soc.* ***1964***, *86*, 521.

[288] Balaban, A.T.; Banciu, M.; Ciorba, V. *Annulenes, Benzo-, Hetero-, Homo- Derivatives and their Valence Isomers*, Vols. 1–3, CRC Press, Boca Raton, FL, ***1987***; Garratt, P.J. *Aromaticity*, Wiley, NY, ***1986***; Minkin, V.I.; Glukhovtsev, M.N.; Simkin, B.Ya. *Aromaticity and Antiaromaticity*, Wiley, NY, ***1994***.

[289] Kimball, D.B.; Wan, W.B.; Haley, M.M. *Tetrahdron Lett.* ***1998***, *39*, 6795; Bell, M.L.; Chiechi, R.C.; Johnson, C.A.; Kimball, D.B.; Matzger, A.J.; Wan, W.B.; Weakley, T.J.R.; Haley, M.M. *Tetahedron* ***2001***, *57*, 3507; Wan, W.B.; Chiechi, R.C.; Weakley, T.J.R.; Haley, M.M. *Eur. J. Org. Chem.* ***2001***, 3485.

prepared, for example, and the evidence supported its aromaticity.[290] This study suggested that increasing benzoannelation of the parent, **116**, led to a step-down in aromaticity, a result of competing ring currents in the annulenic system.

[18]Annulene (**115**) is diatropic:[291] the 12 outer protons are found at $\sim\delta = 9$ and the 6 inner protons at $\sim\delta = -3$. X-ray crystallography[292] shows that it is nearly planar, so that interference of the inner hydrogens is not important in annulenes this large. Compound **115** is reasonably stable, being distillable at reduced pressures, and undergoes aromatic substitutions.[293] The C–C bond distances are not equal, but they do not alternate. There are 12 inner bonds of ~1.38 Å and 6 outer bonds of ~1.42 Å.[292] Compound **115** has been estimated to have a resonance energy of ~37 kcal mol^{-1} (155 kJ mol^{-1}), similar to that of benzene.[294]

The known bridged [18]annulenes are also diatropic[295] as are most of the known dehydro[18]annulenes.[296] The dianions of open and bridged [16]annulenes[297] are also 18-electron aromatic systems,[298] and there are dibenzo[18]annulenes.[299]

[22]Annulene[300] and dehydro[22]annulene[301] are also diatropic. A dehydrobenzo[22]annulene has been prepared that has eight C≡C units, is planar and possesses a weak induced ring current.[302] In the latter compound there are 13 outer protons at 6.25–8.45 δ and 7 inner protons at 0.70–3.45 δ. Some aromatic bridged

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[293] Sondheimer, F. *Tetrahedron* ***1970***, *26*, 3933.

[294] Oth, J.F.M.; Bünzli, J.; de Julien de Zélicourt, Y. *Helv. Chim. Acta*, ***1974***, *57*, 2276.

[295] For some examples, see DuVernet, R.B.; Wennerström, O.; Lawson, J.; Otsubo, T.; Boekelheide, V. *J. Am. Chem. Soc.* ***1978***, *100*, 2457; Ogawa, H.; Sadakari, N.; Imoto, T.; Miyamoto, I.; Kato, H.; Taniguchi, Y. *Angew. Chem. Int. Ed.* ***1983***, *22*, 417; Vogel, E.; Sicken, M.; Röhrig, P.; Schmickler, H.; Lex, J.; Ermer, O. *Angew. Chem. Int. Ed.* ***1988***, *27*, 411.

[296] Okamura, W.H.; Sondheimer, F. *J. Am. Chem. Soc.* ***1967***, *89*, 5991; Ojima, J.; Ejiri, E.; Kato, T.; Nakamura, M.; Kuroda, S.; Hirooka, S.; Shibutani, M. *J. Chem. Soc. Perkin Trans. 1* ***1987***, 831; Sondheimer, F. *Acc. Chem. Res.* ***1972***, *5*, 81. For two that are not, see Endo, K.; Sakata, Y.; Misumi, S. *Bull. Chem. Soc. Jpn.* ***1971***, *44*, 2465.

[297] For a review of this type of polycyclic ion, see Rabinovitz, M.; Willner, I.; Minsky, A. *Acc. Chem. Res.* ***1983***, *16*, 298.

[298] Mitchell, R.H.; Boekelheide, V. *Chem. Commun.* ***1970***, 1557; Oth, J.F.M.; Baumann, H.; Gilles, J.; Schröder, G. *J. Am. Chem. Soc.* ***1972***, *94*, 3948. See also Brown, J.M.; Sondheimer, F. *Angew. Chem. Int. Ed.* ***1974***, *13*, 337; Cresp, T.M.; Sargent, M.V. *J. Chem. Soc. Chem. Commun.* ***1974***, 101; Schröder, G.; Plinke, G.; Smith, D.M.; Oth, J.F.M. *Angew. Chem. Int. Ed.* ***1973***, *12*, 325; Rabinovitz, M.; Minsky, A. *Pure Appl. Chem.* ***1982***, *54*, 1005.

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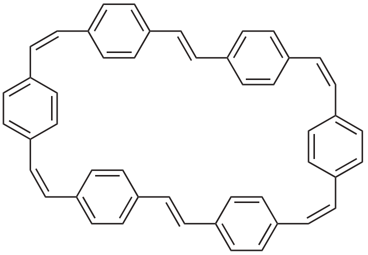
[301] McQuilkin, R.M.; Sondheimer, F. *J. Am. Chem. Soc.* ***1970***, *92*, 6341; Iyoda, M.; Nakagawa, M. *J. Chem. Soc. Chem. Commun.* ***1972***, 1003. See also, Akiyama, S.; Nomoto, T.; Iyoda, M.; Nakagawa, M. *Bull. Chem. Soc. Jpn.* ***1976***, *49*, 2579.

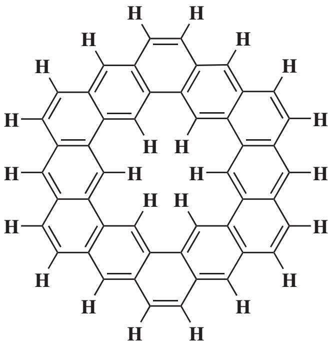
[302] Wan, W.B.; Kimball, D.B.; Haley, M.M. *Tetrahedron Lett.* ***1998***, *39*, 6795.

[22]annulenes are also known.[303] [26]Annulene has not yet been prepared, but several dehydro[26]annulenes are aromatic.[304] Furthermore, the dianion of 1,3,7,9,13,-15,19,21-octadehydro[24]annulene is another 26-electron system that is aromatic.[305] Ojima and co-workers have prepared bridged dehydro derivatives of [26], [30], and [34] annulenes.[306] All of these are diatropic. The same workers prepared a bridged tetradehydro[38]annulene,[306] which showed no ring current. On the other hand, the dianion of the cyclophane, **117**, also has 38 perimeter electrons, and this species is diatropic.[307]



117

There is now no doubt that $4n + 2$ systems are aromatic if they can be planar, although **97** and **113** among others, demonstrate that not all such systems are in fact planar enough for aromaticity. The cases of **109** and **111** prove that absolute planarity is not required for aromaticity, but that aromaticity decreases with decreasing planarity.



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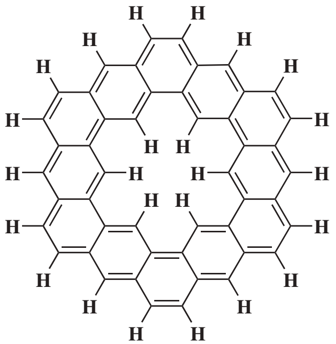

118a **118b**

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[303] For example see Broadhurst, M.J.; Grigg, R.; Johnson, A.W. *J. Chem. Soc. Perkin Trans. 1* ***1972***, 2111; Ojima, J.; Ejiri, E.; Kato, T.; Nakamura, M.; Kuroda, S.; Hirooka, S.; Shibutani, M. *J. Chem. Soc. Perkin Trans. 1* ***1987***, 831; Yamamoto, K.; Kuroda, S.; Shibutani, M.; Yoneyama, Y.; Ojima, J.; Fujita, S.; Ejiri, E.; Yanagihara, K. *J. Chem. Soc. Perkin Trans. 1* ***1988***, 395.

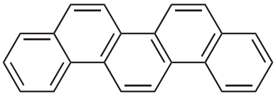
[304] Metcalf, B.W.; Sondheimer, F. *J. Am. Chem. Soc.* ***1971***, *93*, 5271; Iyoda, M.; Nakagawa, M. *Tetrahedron Lett.* ***1972***, 4253; Ojima, J.; Fujita, S.; Matsumoto, M.; Ejiri, E.; Kato, T.; Kuroda, S.; Nozawa, Y.; Hirooka, S.; Yoneyama, Y.; Tatemitsu, H. *J. Chem. Soc. Perkin Trans. 1* ***1988***, 385.

[305] McQuilkin, R.M.; Garratt, P.J.; Sondheimer, F. *J. Am. Chem. Soc.* ***1970***, *92*, 6682. See also, Huber, W.; Müllen, K.; Wennerström, O. *Angew. Chem. Int. Ed.* ***1980***, *19*, 624.

[306] Ojima, J.; Fujita, S.; Matsumoto, M.; Ejiri, E.; Kato, T.; Kuroda, S.; Nozawa, Y.; Hirooka, S.; Yoneyama, Y.; Tatemitsu, H. *J. Chem. Soc., Perkin Trans. 1* ***1988***, 385.

[307] Müllen, K.; Unterberg, H.; Huber, W.; Wennerström, O.; Norinder, U.; Tanner, D.; Thulin, B. *J. Am. Chem. Soc.* ***1984***, *106*, 7514.

The proton NMR (^{1}H NMR) spectrum of **118** (called kekulene) showed that in a case where electrons can form either aromatic sextets or larger systems, the sextets are preferred.[308] There was initial speculation that kekulene might be *superaromatic*, that is, it would show enhanced aromatic stabilization. Recent calculations suggest that there is no enhanced stabilization.[309] The 48 π electrons of **118** might, in theory, prefer structure **118a**, where each ring is a fused benzene ring, or **118b**, which has a [30]annulene on the outside and an [18]annulene on the inside. The ^{1}H NMR spectrum of this compound shows three peaks at $\delta = 7.94$, 8.37, and 10.45 in a ratio of 2:1:1. It is seen from the structure that **118** contains three groups of protons. The peak at 7.94 δ is attributed to the 12 ortho protons and the peak at 8.37 δ to the six external para protons. The remaining peak comes from the six inner protons. If the molecule preferred **118b**, we would expect to find this peak upfield, probably with a negative δ, as in the case of **115**. The fact that this peak is far downfield indicates that the electrons prefer to be in benzenoid rings. Note that in the case of the dianion of **117**, we have the opposite situation. In this ion, the 38-electron system is preferred even though 24 of these must come from the six benzene rings, which therefore cannot have aromatic sextets.



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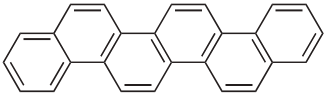
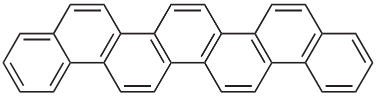


120



121

Phenacenes are a family of "graphite ribbons," where benzene rings are fused together in an alternating pattern. Phenanthrene is the simplest member of this family and other members include the 22-electron system picene (**119**); the 26-electron system fulminene (**120**); and the larger member of this family, the 30 electron [7]-phenancene, with seven rings (**121**).[310] In the series benzene to heptacene, reactivity increases although acene resonance energies per π electron are nearly constant. The inner rings of the "acenes" are more reactive, and calculations shown that those rings are more aromatic than the outer rings, and even more aromatic than benzene itself.[311]

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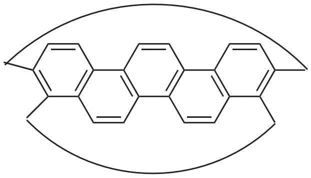
[308] Staab, H.A.; Diederich, F. *Chem. Ber.* ***1983***, *116*, 3487; Staab, H.A.; Diederich, F.; Krieger, C.; Schweitzer, D. *Chem. Ber.* ***1983***, *116*, 3504. For a similar molecule with 10 instead of 12 rings, see Funhoff, D.J.H.; Staab, H.A. *Angew. Chem. Int. Ed.* ***1986***, *25*, 742.

[309] Jiao, H.; Schleyer, P.v.R. *Angew. Chem. Int. Ed.*, ***1996***, *35*, 2383.

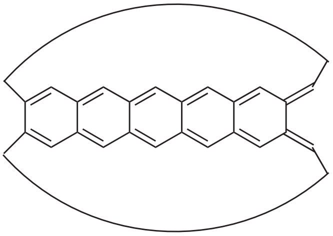
[310] Mallory, F.B.; Butler, K.E.; Evans, A.C.; Mallory, C.W. *Tetrahedron Lett.* ***1996***, *37*, 7173.

[311] Schleyer, P.v.R.; Manoharan, M.; Jiao, H.; Stahl, F. *Org. Lett.* ***2001***, *3*, 3643.

A super ring molecule is formed by rolling a polyacene molecule into one ring with one edge benzene ring folding into the other. These are called cyclopolyacenes or cyclacenes.[312] Although the *zigzag* cyclohexacenes (**122**) are highly aromatic (this example is a 22-electron system), the linear cyclohexacenes (e.g., the 24 electron **123**) are much less aromatic.[313]



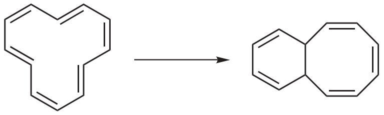
122



123

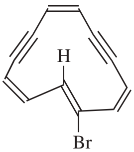
Systems of More Than Ten Electrons: 4*n* Electrons[224]

As we have seen (p. 74), these systems are expected to be not only nonaromatic, but actually antiaromatic.



124 **125**

The [12]annulene **124** has been prepared.[314] In solution, **124** undergoes rapid conformational mobility (as do many other annulenes),[315] and above −150°C in this partiuclar case, all protons are magnetically equivalent. However, at −170°C the mobility is greatly slowed and the three inner protons are found at ~8 δ while the nine outer protons are at ~6 δ. Interaction of the "internal" hydrogens in annulene **124** leads to nonplanarity. Above −50°C, **124** is unstable and rearranges to **125**. Several bridged



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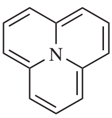

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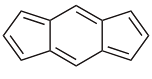

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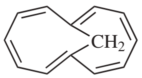

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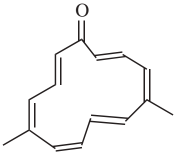

130

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[312] Ashton, P.R.; Issacs, N.S.; Kohnke, F.H.; Slawin, A.M.Z.; Spencer, C.M.; Stoddart, J.F.; Williams, D.J. *Angew. Chem. Int. Ed.* ***1988***, *27*, 966; Ashton, P.R.; Brown, G.R.; Issacs, N.S.; Giuffrida, D.; Kohnke, F.H.; Mathias, J.P.; Slawin, A.M.Z.; Smith, D.R.; Stoddart, J.F.; Williams, D.J. *J. Am. Chem. Soc.* ***1992***, *114*, 6330; Ashton, P.R.; Girreser, U.; Giuffrida, D.; Kohnke, F.H.; Mathias, J.P.; Raymo, F.M.; Slawin, A.M.Z.; Stoddart, J.F.; Williams, D.J. *J. Am. Chem. Soc.* ***1993***, *115*, 5422.

[313] Aihara, J-i. *J. Chem. Soc. Perkin Trans. 2* ***1994***, 971.

[314] Oth, J.F.M.; Röttele, H.; Schröder, G. *Tetrahedron Lett.* ***1970***, 61; Oth, J.F.M.; Gilles, J.; Schröder, G. *Tetrahedron Lett.* ***1970***, 67.

[315] For a review of conformational mobility in annulenes, see Oth, J.F.M. *Pure Appl. Chem.* ***1971***, *25*, 573.

and dehydro[12]annulenes are known, for example, 5-bromo-1,9-didehydro[12]annulene (**126**),[316] cycl[3.3.3]azine (**127**),[317] *s*-indacene (**128**),[318] and 1,7-methano[12]annulene (**129**).[319] *s*-Indacene is a planar, conjugated system perturbed by two cross-links, and studies showed that the low-energy structure has *localized* double bonds. In these compounds, both hydrogen interference and conformational mobility are prevented. In **127–129**, the bridge prevents conformational changes, while in **126** the bromine atom is too large to be found inside the ring. The NMR spectra show that all four compounds are paratropic, the inner proton of **126** being found at 16.4 δ. The dication of **112**[320] and the dianion of **103**[321] are also 12-electron paratropic species. An interesting 12-electron [13]-annulenone has recently been reported. 5,10-Dimethyl[13]annulenone (**130**) is the first monocyclic annulene larger than tropane,[322] and a linearly fused benzodehydro[12]annulene system has been reported.[323]

The results for [16]annulene are similar. The compound was synthesized in two different ways,[324] both of which gave **131**, which in solution is in equilibrium with **132**. Above −50°C there is conformational mobility, resulting in the magnetic equivalence of all protons, but at −130°C the compound is clearly paratropic: there are 4 protons at 10.56 δ and 12 at 5.35 δ. In the solid state, where the compound exists entirely as **131**, X-ray crystallography[325] shows that the molecules are nonplanar with almost complete bond alternation: the single bonds are 1.44–1.47 Å and the double bonds 1.31–1.35 Å. A number of dehydro and bridged [16]annulenes are also paratropic,[326] as are [20]annulene[327] and

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[316] Untch, K.G.; Wysocki, D.C. *J. Am. Chem. Soc.* ***1967***, *89*, 6386.

[317] Farquhar, D.; Leaver, D. *Chem. Commun.* ***1969***, 24. For a review, see Matsuda, Y.; Gotou, H. *Heterocycles* ***1987***, *26*, 2757.

[318] Hertwig, R.H.; Holthausen, M.C.; Koch, W.; Maksić, Z.B. *Angew. Chem. Int. Ed.* ***1994***, *33*, 1192.

[319] Vogel, E.; Königshofen, H.; Müllen, K.; Oth, J.F.M. *Angew. Chem. Int. Ed.* ***1974***, *13*, 281. See also, Mugnoli, A.; Simonetta, M. *J. Chem. Soc. Perkin Trans. 2* ***1976***, 822; Scott, L.T.; Kirms, M.A.; Günther, H.; von Puttkamer, H. *J. Am. Chem. Soc.* ***1983***, *105*, 1372; Destro, R.; Ortoleva, E.; Simonetta, M.; Todeschini, R. *J. Chem. Soc. Perkin Trans. 2* ***1983***, 1227.

[320] Müllen, K.; Meul, T.; Schade, P.; Schmickler, H.; Vogel, E. *J. Am. Chem. Soc.* ***1987***, *109*, 4992. This paper also reports a number of other bridged paratropic 12-, 16-, and 20-electron dianions and dications. See also Hafner, K.; Thiele, G.F. *Tetrahedron Lett.* ***1984***, *25*, 1445.

[321] Schmalz, D.; Günther, H. *Angew. Chem. Int. Ed.* ***1988***, *27*, 1692.

[322] Higuchi, H.; Hiraiwa, N.; Kondo, S.; Ojima, J.; Yamamoto, G. *Tetrahedron Lett.* ***1996***, *37*, 2601.

[323] Gallagher, M.E.; Anthony, J.E. *Tetrahedron Lett.* ***2001***, *42*, 7533.

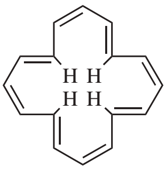
[324] Schröder, G.; Oth, J.F.M. *Tetrahedron Lett.* ***1966***, 4083; Oth, J.F.M.; Gilles, J. *Tetrahedron Lett.* ***1968***, 6259; Calder, I.C.; Gaoni, Y.; Sondheimer, F. *J. Am. Chem. Soc.* ***1968***, *90*, 4946. For monosubstituted [16]annulenes, see Schröder, G.; Kirsch, G.; Oth, J.F.M. *Chem. Ber.* ***1974***, *107*, 460.

[325] Johnson, S.M.; Paul, I.C.; King, G.S.D. *J. Chem. Soc. B* ***1970***, 643.

[326] For example, see Calder, I.C.; Garratt, P.J.; Sondheimer, F. *J. Am. Chem. Soc.* ***1968***, *90*, 4954; Murata, I.; Okazaki, M.; Nakazawa, T. *Angew. Chem. Int. Ed.* ***1971***, *10*, 576; Ogawa, H.; Kubo, M.; Tabushi, I. *Tetrahedron Lett.* ***1973***, 361; Nakatsuji, S.; Morigaki, M.; Akiyama, S.; Nakagawa, M. *Tetrahedron Lett.* ***1975***, 1233; Elix, J.A. *Aust. J. Chem.* ***1969***, *22*, 1951; Vogel, E.; Kürshner, U.; Schmickler, H.; Lex, J.; Wennerström, O.; Tanner, D.; Norinder, U.; Krüger, C. *Tetrahedron Lett.* ***1985***, *26*, 3087.

[327] Metcalf, B.W.; Sondheimer, F. *J. Am. Chem. Soc.* ***1971***, *93*, 6675. See also Oth, J.F.M.; Woo, E.P.; Sondheimer, F. *J. Am. Chem. Soc.* ***1973***, *95*, 7337; Nakatsuji, S.; Nakagawa, M. *Tetrahedron Lett.* ***1975***, 3927; Wilcox, Jr., C.F.; Farley, E.N. *J. Am. Chem. Soc.* *1984*, ***106***, 7195.

[24]annulene.[328] However, a bridged tetradehydro[32]annulene was atropic.[306]



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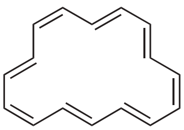

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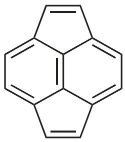

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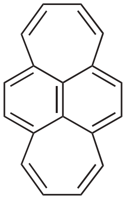

134

Both pyracyclene (**133**)[329] (which because of strain is stable only in solution) and dipleiadiene (**134**)[330] are paratropic, as shown by NMR spectra. These molecules might have been expected to behave like naphthalenes with outer bridges, but the outer π frameworks (12 and 16 electrons, respectively) constitute antiaromatic systems with an extra central double bond. With respect to **133**, the $4n + 2$ rule predicts pyracylene to be "aromatic" if it is regarded as a 10-π-electron naphthalene unit connected to two 2-π-electron etheno systems, but "antiaromatic" if it is viewed as a 12-π-electron cyclododecahexaene periphery perturbed by an internal cross-linked etheno unit.[331] Recent studies have concluded on energetic grounds that **133** is a "borderline" case, in terms of aromaticity–antiaromaticity character.[329] Dipleiadiene appears to be antiaromatic.[330]

The fact that many $4n$ systems are paratropic, even though they may be nonplanar and have unequal bond distances, indicates that if planarity were enforced, the ring currents might be even greater. That this is true is dramatically illustrated by the NMR spectrum of the dianion of **110**[332] (and its diethyl and dipropyl homologs).[333] We may recall that in **110**, the outer protons were found at 8.14–8.67 δ with the methyl protons at -4.25 δ. For the dianion, however, which is forced to have approximately the same planar geometry, but now has 16 electrons, the outer protons are shifted to about -3 δ while the methyl protons are found at ~ 21 δ, a shift of ~ 25 δ! We have already seen where the converse shift was made, when [16]annulenes that were antiaromatic were converted to 18-electron dianions that were aromatic.[254] In these cases, the changes in nmr chemical shifts were almost

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[328] Calder, I.C.; Sondheimer, F. *Chem. Commun.* ***1966***, 904. See also, Stöckel, K.; Sondheimer, F. *J. Chem. Soc. Perkin Trans. 1* ***1972***, 355; Nakatsuji, S.; Akiyama, S.; Nakagawa, M. *Tetrahedron Lett.* ***1976***, 2623; Yamamoto, K.; Kuroda, S.; Shibutani, M.; Yoneyama, Y.; Ojima, J.; Fujita, S.; Ejiri, E.; Yanagihara, K. *J. Chem. Soc., Perkin Trans. 1* ***1988***, 395.

[329] Trost, B.M.; Herdle, W.B. *J. Am. Chem. Soc.* ***1976***, *98*, 4080.

[330] Vogel, E.; Neumann, B.; Klug, W.; Schmickler, H.; Lex, J. *Angew. Chem. Int. Ed.* ***1985***, *24*, 1046.

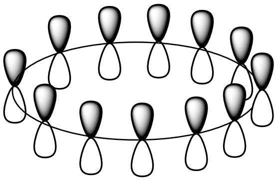
[331] Diogo, H.P.; Kiyobayashi, T.; Minas da Piedade, M.E.; Burlak, N.; Rogers, D.W.; McMasters, D.; Persy, G.; Wirz, J.; Liebman, J.F. *J. Am. Chem. Soc.* ***2002***, *124*, 2065.

[332] For a review of polycyclic dianions, see Rabinovitz, M.; Cohen, Y. *Tetrahedron* ***1988***, *44*, 6957.

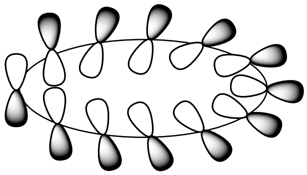
[333] Mitchell, R.H.; Klopfenstein, C.E.; Boekelheide, V. *J. Am. Chem. Soc.* ***1969***, *91*, 4931. For another example, see Deger, H.M.; Müllen, K.; Vogel, E. *Angew. Chem. Int. Ed.* ***1978***, *17*, 957.

as dramatic. Heat-of-combustion measures also show that [16]annulene is much less stable than its dianion.[334]

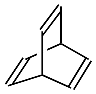
We can therefore conclude that 4*n* systems will be at a maximum where a molecule is constrained to be planar (as in **86** or the dianion of **110**) but, where possible, the molecule will distort itself from planarity and avoid equal bond distances in order to reduce. In some cases, such as cyclooctatraene, the distortion and bond alternation are great enough to be completely avoided. In other cases, for example, **124** or **131**, it is apparently not possible for the molecules to avoid at least some *p*-orbital overlap. Such molecules show evidence of paramagnetic ring currents, although the degree of is not as great as in molecules such as **86** or the dianion of **110**.



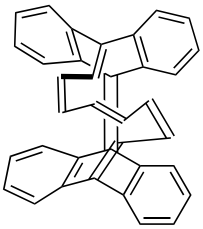
Hückel



Möbius



135



136

The concept of "Möbius aromaticity" was conceived by Helbronner in 1964[335] when he suggested that large cyclic [4*n*]annulenes might be stabilized if the π-orbitals were twisted gradually around a Möbius strip. This concept is illustrated by the diagrams labeled Hückel, which is a destabilized [4*n*] system, in contrast to the Möbius model, which is a stabilized [4*n*] system.[336] Zimmerman generalized this idea and applied the "Hückel–Möbius concept" to the analysis of ground-state systems, such as barrelene (**135**).[337] In 1998, a computational reinterpretation of existing experimental evidence for $(CH)_9^+$ as a Möbius

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[334] Stevenson, G.R.; Forch, B.E. *J. Am. Chem. Soc.* ***1980***, *102*, 5985.

[335] Heilbronner, E. *Tetrahedron Lett.* ***1964***, 1923.

[336] Kawase, T; Oda, M. *Angew. Chem. Int. Ed.*, ***2004***, *43*, 4396.

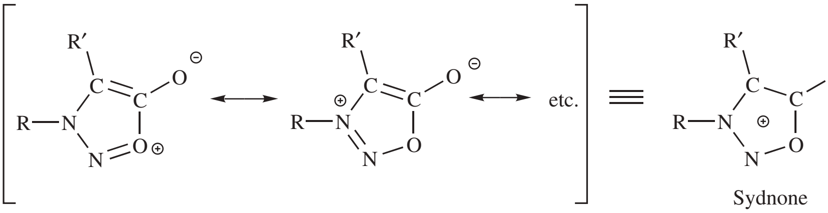
[337] Zimmerman, H.E. *J. Am. Chem. Soc.* ***1966***, *88*, 1564.; Zimmerman, H.E. *Acc. Chem. Res.* ***1972***, *4*, 272.

aromatic cyclic annulene with $4n$ π-electrons was reported.[338] A recent computational study predicted several Möbius local minima for [12]-, [16]-, and [20]annulenes.[339] A twisted [16]annulene has been prepared and calculations suggested it should show Möbius aromaticity.[340] High-performance liquid chromatography (HPLC) separation of isomers gave **136**, which the authors concluded is Möbius aromatic.

Other Aromatic Compounds

We will briefly mention three other types of aromatic compounds.

1. *Mesoionic Compounds.*[341] These compounds cannot be satisfactorily represented by Lewis structures not involving charge separation. Most of them contain five-membered rings. The most common are the *sydnones*, stable aromatic compounds that undergo aromatic substitution when R′ is hydrogen.



Sydnone

2. *The Dianion of Squaric Acid.*[342] The stability of this system is illustrated by the fact that the pK_1 of squaric acid[343] is ∼1.5 and the pK_2 is ∼3.5,[344] which means that even the second proton is given up much more readily than the proton of acetic acid, for example.[345] The analogous three-,[346]

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[338] Mauksch, M.; Gogonea, V.; Jiao, H.; Schleyer, P.v.R. *Angew. Chem. Int. Ed.*, ***1998***, *37*, 2395.

[339] Castro, C.; Isborn, C.M.; Karney, W.L.; Mauksch, M.; Schleyer, P.v.R. *Org. Lett.* ***2002***, *4*, 3431.

[340] Ajami, D.; Oeckler, O.; Simon, A.; Herges, R. *Nature (London)* ***2003***, *426*, 819.

[341] For reviews, see Newton, C.G.; Ramsden, C.A. *Tetrahedron* ***1982***, *38*, 2965; Ollis, W.D.; Ramsden, C.A. *Adv. Heterocycl. Chem.* ***1976***, *19*, 1; Ramsden, C.A. *Tetrahedron* ***1977***, *33*, 3203; Yashunskii, V.G.; Kholodov, L.E. *Russ. Chem. Rev.* ***1980***, *49*, 28; Ohta, M.; Kato, H., in Snyder, J.P. *Nonbenzenoid Aromaticity*, Vol. 1, Academic Press, NY, ***1969***, pp. 117–248.

[342] West, R.; Powell, D.L. *J. Am. Chem. Soc.* ***1963***, *85*, 2577; Ito, M.; West, R. *J. Am. Chem. Soc.* ***1963***, *85*, 2580.

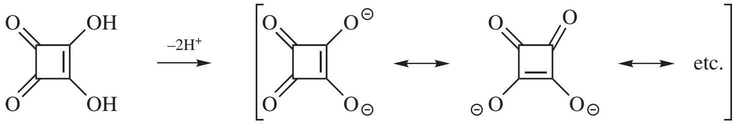
[343] For a review of squaric acid and other nonbenzenoid quinones, see Wong, H.N.C.; Chan, T.; Luh, T., in Patai, S.; Rappoport, Z. *The Chemistry of the Quinonoid Compounds*, Vol. 2, pt. 2, Wiley, NY, ***1988***, pp. 1501–1563.

[344] Ireland, D.T.; Walton, H.F. *J. Phys. Chem.* ***1967***, *71*, 751; MacDonald, D.J. *J. Org. Chem.* ***1968***, *33*, 4559.

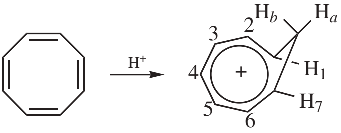
[345] There has been a controversy as to whether this dianion is in fact aromatic. See Aihara, J. *J. Am. Chem. Soc.* ***1981***, *103*, 1633.

[346] Eggerding, D.; West, R. *J. Am. Chem. Soc.* ***1976***, *98*, 3641; Pericás, M.A.; Serratosa, F. *Tetrahedron Lett.* ***1977***, 4437; Semmingsen, D.; Groth, P. *J. Am. Chem. Soc.* ***1987***, *109*, 7238.

five-, and six-membered ring compounds are also known.[347]



3. *Homoaromatic Compounds.* When cyclooctatetraene is dissolved in concentrated H_2SO_4, a proton adds to one of the double bonds to form the homotropylium ion **137**.[348] In this species, an aromatic sextet is spread over seven carbons, as in the tropylium ion. The eighth carbon is an sp^3 carbon and so cannot take part in the aromaticity. The NMR spectra show the presence of a diatropic ring current: H_b is found at $\delta = -0.3$; H_a at 5.1 δ; H_1 and H_7 at 6.4 δ; H_2–H_6 at 8.5 δ. This ion is an example of a *homoaromatic* compound, which may be defined as a compound that contains one or more[349] sp^3-hybridized carbon atoms in an otherwise conjugated cycle.[350]



137

In order for the orbitals to overlap most effectively so as to close a loop, the sp^3 atoms are forced to lie almost vertically above the plane of the

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[347] For a monograph, see West, R. *Oxocarbons*; Academic Press, NY, ***1980***. For reviews, see Serratosa, F. *Acc. Chem. Res.* ***1983***, *16*, 170; Schmidt, A.H. *Synthesis* ***1980***, 961; West, R. *Isr. J. Chem.* ***1980***, *20*, 300; West, R.; Niu, J., in Snyder, J.P. *Nonbenzenoid Aromaticity*, Vol. 1, Academic Press, NY, ***1969***, pp. 311–345, and in Zabicky, J. *The Chemistry of the Carbonyl Group*, Vol. 2, Wiley, NY, ***1970***, pp. 241–275; Maahs, G.; Hegenberg, P. *Angew. Chem. Int. Ed.* ***1966***, *5*, 888.

[348] Rosenberg, J.L.; Mahler, J.E.; Pettit, R. *J. Am. Chem. Soc.* ***1962***, *84*, 2842; Keller, C.E.; Pettit, R. *J. Am. Chem. Soc.* ***1966***, *88*, 604, 606; Winstein, S.; Kreiter, C.G.; Brauman, J.I. *J. Am. Chem. Soc.* ***1966***, *88*, 2047; Haddon, R.C. *J. Am. Chem. Soc.* ***1988***, *110*, 1108. See also, Childs, R.F.; Mulholland, D.L.; Varadarajan, A.; Yeroushalmi, S. *J. Org. Chem.* ***1983***, *48*, 1431. See also, Alkorta, I.; Elguero, J.; Eckert-Maksić, M.; Maksić, Z.B. *Tetrahedron* ***2004***, *60*, 2259.

[349] If a compound contains two such atoms it is bishomoaromatic; if three, trishomoaromatic, and so on. For examples see Paquette, L.A. *Angew. Chem. Int. Ed.* ***1978***, *17*, 106.

[350] For reviews, see Childs, R.F. *Acc. Chem. Res.* ***1984***, *17*, 347; Paquette, L.A. *Angew. Chem. Int. Ed.* ***1978***, *17*, 106; Winstein, S. *Q. Rev. Chem. Soc.* ***1969***, *23*, 141; Garratt, P.J. *Aromaticity*, Wiley, NY, ***1986***, pp. 5–45; and in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Wiley, NY, Vol. 3, ***1972***, the reviews by Story, P.R.; Clark, Jr., B.C. 1007–1098, pp. 1073–1093; Winstein, S. 965–1005. (The latter is a reprint of the *Q. Rev. Chem. Soc.* review mentioned above.)

aromatic atoms.[351] In **137**, H_b is directly above the aromatic sextet, and so is shifted far upfield in the nmr. All homoaromatic compounds so far discovered are ions, and it is questionable[352] as to whether homoaromatic character can exist in uncharged systems.[353] Homoaromatic ions of 2 and 10 electrons are also known.

New conceptual applications to 3D homoaromatic systems with cubane, dodecahedrane, and adamantane frameworks has been presented.[354] This concept includes families of spherical homoaromatics with both 2 and 8 mobile electrons. Each set has complete *spherical homoaromaticity*, that is, all the sp^2 carbon atoms in a highly symmetrical frameworks are separated by one or two sp^3-hybridized atoms.

4. *Fullerenes.* Fullerenes are a family of aromatic hydrocarbons based on the parent buckminsterfullerene (**138**; C_{60})[355] that have a variety of very interesting properties.[356] Molecular-orbital calculations showed that "fullerene aromaticity lies within 2 kcal mol^{-1} (8.4 kJ mol^{-1}) per carbon of a hypothetical ball of rolled up graphite.[357] Another class of polynuclear aromatic hydrocarbons are the *buckybowls*, which are essentially fragments of **138**. Corannulene (**139**)[358] (also called 5-circulene), for example, is the simplest curved-surface hydrocarbon possessing a carbon framework that is identified with the buckminsterfullerene

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[351] Calculations show that only ~60% of the chemical shift difference between H_a and H_b is the result of the aromatic ring current, and that even H_a is shielded; it would appear at $\delta \sim 5.5$ without the ring current: Childs, R.F.; McGlinchey, M.J.; Varadarajan, A. *J. Am. Chem. Soc.* ***1984***, *106*, 5974.

[352] Houk, K.N.; Gandour, R.W.; Strozier, R.W.; Rondan, N.G.; Paquette, L.A. *J. Am. Chem. Soc.* ***1979***, *101*, 6797; Paquette, L.A.; Snow, R.A.; Muthard, J.L.; Cynkowski, T. *J. Am. Chem. Soc.* ***1979***, *101*, 6991. See however, Liebman, J.F.; Paquette, L.A.; Peterson, J.R.; Rogers, D.W. *J. Am. Chem. Soc.* ***1986***, *108*, 8267.

[353] Examples of uncharged homoantiaromatic compounds have been claimed: Wilcox, Jr., C.F.; Blain, D.A.; Clardy, J.; Van Duyne, G.; Gleiter, R.; Eckert-Maksic, M. *J. Am. Chem. Soc.* ***1986***, *108*, 7693; Scott, L.T.; Cooney, M.J.; Rogers, D.W.; Dejroongruang, K. *J. Am. Chem. Soc.* ***1988***, *110*, 7244.

[354] Chen, Z.; Haijun Jiao, H.; Andreas Hirsch, A.; Schleyer, P.v.R. *Angew. Chem. Int. Ed.*, ***2002***, *41*, 4309

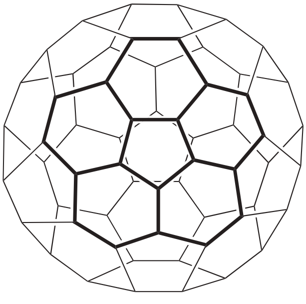
[355] Billups, W.E.; Ciufolini, M.A. *Buckminsterfullerenes*, VCH, NY, ***1993***; Taylor, R. *The Chemistry of Fullerenes*, World Scientific, River Edge, NJ, Singapore, ***1995***; Aldersey-Williams, H. *The Most Beautiful Molecule: The Discovery of the Buckyball*, Wiley, NY, ***1995***; Baggott, J.E. *Perfect Symmetry: the Accidental Discovery of Buckminsterfullerene*, Oxford University Press, Oxford, NY, ***1994***. Also see Kroto, H.W.; Heath, J.R.; O'Brien, S.C.; Curl, R.F.; Smalley, R.E. *Nature (London)* ***1985***, *318*, 162.

[356] Smalley, R.E. *Acc. Chem. Res.* ***1992***, *25*, 98; Diederich, F.; Whetten, R.L. *Acc. Chem. Res.* ***1992***, *25*, 119; Hawkins, J.M. *Acc. Chem. Res.* ***1992***, *25*, 150; Wudl, F. *Acc. Chem. Res.* ***1992***, *25*, 157; McElvany, S.W.; Ross, M.M.; Callahan, J.H. *Acc. Chem. Res.* ***1992***, *25*, 162; Johnson, R.D.; Bethune, D.S.; Yannoni, C.S. *Acc. Chem. Res.* ***1992***, *25*, 169.

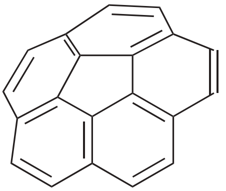
[357] Warner, P.M. *Tetrahedron Lett.* ***1994***, *35*, 7173.

[358] Barth, W.E.; Lawton, R.G. *J. Am. Chem. Soc.* ***1971***, *93*, 1730; Scott, L.T.; Hashemi, M.M.; Meyer, D.T.; Warren, H.B. *J. Am. Chem. Soc.* ***1991***, *113*, 7082.

surface. It has been synthesized by Scott,[352] and several other groups.[359] Corannulene is a flexible molecule, with a bowl-to-bowl inversion barrier of ~10–11 kcal mol^{-1} (41.8–46.0 kJ mol^{-1}).[360] Benzocorannulenes are known,[361] and other bowl-shaped hydrocarbons include acenaphtho[3,2,1,8-*ijklm*]diindeno[4,3,2,1-*cdef*-1′,2′,3′,4′*pqra*]triphenylene.[362] The inversion barrier to buckybowl inversion has been lowered by such benzannelation of the rim.[363] Other semibuckminsterfullerenes include C_{2v}-$C_{30}H_{12}$ and C_3-$C_{30}H_{12}$.[358] Larger fullerenes include C_{60},C_{80}, C_{84}, and fullerenes are known that contain an endohedral metal, such as scandium or even Sc_3N.[364] Synthetic methods often generate mixtures of fullerenes that must be separated, as in the report of new methods for separating C_{84}-fullerenes.[365] A homofullerene has been prepared.[366]



138



139

HYPERCONJUGATION

All of the delocalization discussed so far involves π electrons. Another type, called *hyperconjugation*, involves σ electrons.[367] When a carbon attached

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[359] Borchardt, A.; Fuchicello, A.; Kilway, K.V.; Baldridge, K.K.; Siegel, J.S. *J. Am. Chem. Soc.* ***1992***, *114*, 1921; Liu, C.Z.; Rabideau, P.W. *Tetrahedron Lett.* ***1996***, *37*, 3437.

[360] Biedermann, P.U.; Pogodin, S.; Agranat, I. *J. Org. Chem.* ***1999***, *64*, 3655; Rabideau, P.W.; Sygula, A. *Acc. Chem. Res.* ***1996***, *29*, 235; Mehta, G.; Panda, G. *Chem. Comm.*, ***1997***, 2081; Rabideau, P.W.; Abdourazak, A.H.; Folsom, H.E.; Marcinow, Z.; Sygula, A.; Sygula, R. *J. Am. Chem. Soc.* ***1994***, *116*, 7891; Hagan, S.; Bratcher, M.S.; Erickson, M.S.; Zimmermann, G.; Scott, L.T. *Angew. Chem. Int. Ed.*, ***1997***, *36*, 406. See also, Dinadayalane, T.C.; Sastry, G.N. *Tetrahedron* ***2003***, *59*, 8347.

[361] Dinadayalane, T.C.; Sastry, G.N. *J. Org. Chem.* ***2002***, *67*, 4605.

[362] Marcinow, Z.; Grove, D.I.; Rabideau, P.W. *J. Org. Chem.* ***2002***, *67*, 3537.

[363] Marcinow, Z.; Sygula, A.; Ellern, D.A.; Rabideau, P.W. *Org. Lett.* ***2001***, *3*, 3527.

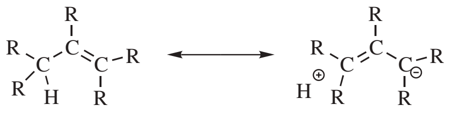
[364] Stevenson, S.; Rice, G.; Glass, T.; Harich, K.; Cromer, F.; Jordan, M.R.; Craft, J.; Hadju, E.; Bible, R.; Olmstead, M.M.; Maitra, K.; Fisher, A.J.; Balch, A.L.; Dorn, H.C. *Nature (London)* ***1999***, *401*, 55.

[365] Wang, G.-W.; Saunders, M.; Khong, A.; Cross, R.J. *J. Am. Chem. Soc.* ***2000***, *122*, 3216.

[366] Kiely, A.F.; Haddon, R.C.; Meier, M.S.; Selegue, J.P.; Brock, C.P.; Patrick, B.O.; Wang, G.-W.; Chen, Y. *J. Am. Chem. Soc.* ***1999***, *121*, 7971.

[367] For monographs, see Baker, J.W. *Hyperconjugation*, Oxford University Press, Oxford, ***1952***; Dewar, M.J.S. *Hyperconjugation*, Ronald Press, NY, ***1962***. For a review, see de la Mare, P.B.D. *Pure Appl. Chem.* ***1984***, *56*, 1755.

forms there is no bond at all between the carbon and hydrogen. The effect of **140** on the actual molecule is that the electrons in the C—H bond are closer to the carbon than they would be if **140** did not contribute at all.

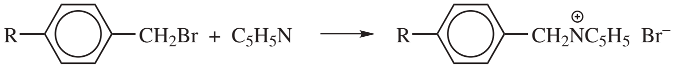


140

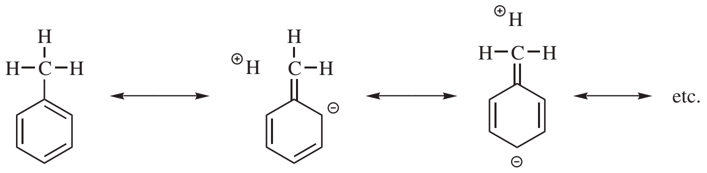
Hyperconjugation in the above case may be regarded as an overlap of the σ orbital of the C—H bond and the π orbital of the C—C bond, analogous to the π–π orbital overlap previously considered. As might be expected, those who reject the idea of resonance in butadiene (p. 39) believe it even less likely when it involves no-bond structures.

The concept of hyperconjugation arose from the discovery of apparently anomalous electron-release patterns for alkyl groups. By the field effect alone, the order of electron release for simple alkyl groups connected to an unsaturated system is *tert*-butyl > isopropyl > ethyl > methyl, and this order is observed in many phenomena. Thus, the dipole moments in the gas phase of $PhCH_3$, PhC_2H_5, $PhCH(CH_3)_2$, and $PhC(CH_3)_3$ are, respectively, 0.37, 0.58, 0.65, and 0.70 D.[368]

However, Baker and Nathan[369] observed that the rates of reaction with pyridine of *para*-substituted benzyl bromides (see reaction **10-31**) were opposite that expected from electron release by the field effect. That is, the methyl-substituted compound reacted fastest and the *tert*-butyl-substituted compounded reacted slowest.



This came to be called the *Baker–Nathan effect* and has since been found in many processes. Baker and Nathan explained it by considering that hyperconjugative forms contribute to the actual structure of toluene:



For the other alkyl groups, hyperconjugation is diminished because the number of C—H bonds is diminished and in *tert*-butyl there are none; hence, with

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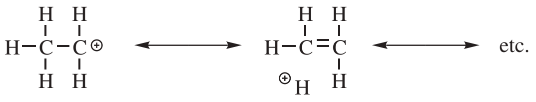
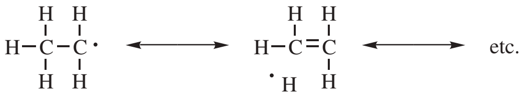
[368] Baker, J.W.; Groves, L.G. *J. Chem. Soc.* ***1939***, 1144.

[369] Baker, J.W.; Nathan, W.S. *J. Chem. Soc.* ***1935***, 1840, 1844.

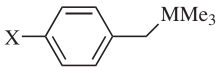
respect to this effect, methyl is the strongest electron donor and *tert*-butyl is the weakest.

However, the Baker–Nathan effect has now been shown not to be caused by hyperconjugation, but by differential solvation.[370] This was demonstrated by the finding that in certain instances where the Baker–Nathan effect was found to apply in solution, the order was completely reversed in the gas phase.[371] Since the molecular structures are unchanged in going from the gas phase into solution, it is evident that the Baker–Nathan order in these cases is not caused by a structural feature (hyperconjugation), but by the solvent. That is, each alkyl group is solvated to a different extent.[372]





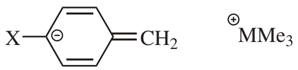
There is a large body of evidence against hyperconjugation in the ground states of neutral molecules.[373] A recent study of the one-bond coupling constants for the aromatic system **141**, however, appears to provide the first structural evidence for hyperconjugation in a neutral ground state.[374] In hyperconjugation in the ground state of neutral molecules, which Muller and Mulliken call *sacrificial hyperconjugation*,[375] the canonical forms involve not only no-bond resonance, but also a charge separation not possessed by the main form (see **141**). For carbocations and free radicals[376] and for excited states of molecules,[377] there is evidence that hyperconjugation is important. In free radicals and carbocations, the canonical



141

M = C, Si, Ge, Sn

X = NO_2, CN, H, Me, OMe



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[370] This idea was first suggested by Schubert, W.M.; Sweeney, W.A. *J. Org. Chem.* ***1956***, *21*, 119.

[371] Hehre,W.J.; McIver, Jr., R.T.; Pople, J.A.; Schleyer, P.v.R. *J. Am. Chem. Soc.* ***1974***, *96*, 7162; Arnett, E.M.; Abboud, J.M. *J. Am. Chem. Soc.* ***1975***, *97*, 3865; Glyde, E.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* ***1977***, 678. See also, Taylor, R. *J. Chem. Res. (S)*, ***1985***, 318.

[372] For an opposing view, see Cooney, B.T.; Happer, D.A.R. *Aust. J. Chem.* ***1987***, *40*, 1537.

[373] For some evidence in favor, see Laube, T.; Ha, T. *J. Am. Chem. Soc.* ***1988***, *110*, 5511.

[374] Lambert, J.B.; Singer, R.A. *J. Am. Chem. Soc.* ***1992***, *114*, 10246.

[375] Muller, N.; Mulliken, R.S. *J. Am. Chem. Soc.* ***1958***, *80*, 3489.

[376] Symons, M.C.R. *Tetrahedron* ***1962***, *18*, 333.

[377] Rao, C.N.R.; Goldman, G.K.; Balasubramanian, A. *Can. J. Chem.* ***1960***, *38*, 2508.

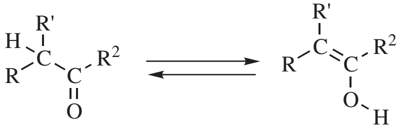
forms display no more charge separation than the main form. Muller and Mulliken call this *isovalent hyperconjugation*: Even here the main form contributes more to the hybrid than the others.

TAUTOMERISM[378]

There remains one topic to be discussed in our survey of chemical bonding in organic compounds. For most compounds, all the molecules have the same structure, whether or not this structure can be satisfactorily represented by a Lewis formula. But for many other compounds there is a mixture of two or more structurally distinct compounds that are in rapid equilibrium. When this phenomenon, called *tautomerism*,[379] exists, there is a rapid shift back and forth among the molecules. In most cases, it is a proton that shifts from one atom of a molecule to another.

Keto–Enol Tautomerism[380]

A very common form of tautomerism is that between a carbonyl compound containing an a hydrogen and its enol form:[381] Such equilibria are pH dependent, as in the case of 2-acetylcyclohexanone.[382]



Keto form **Enol form**

In simple cases ($R^2 = H$, alkyl, OR, etc.) the equilibrium lies well to the left (Table 2.1). The reason can be seen by examining the bond energies in Table 1.7.

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[378] Baker, J.W. *Tautomerism*; D. Van Nostrand Company, Inc., New York, ***1934***; Minkin, V.I.; Olekhnovich, L.P.; Zhdanov, Y.A. *Molecular Design of Tautomeric Compounds*, D. Reidel Publishing Co.: Dordrecht, Holland, ***1988***.

[379] For reviews, see Toullec, J. *Adv. Phys. Org. Chem.* ***1982***, *18*, 1; Kołsov, A.I.; Kheifets, G.M. *Russ. Chem. Rev.* ***1971***, *40*, 773; ***1972***, *41*, 452–467; Forsén, S.; Nilsson, M., in Zabicky, J. *The Chemistry of the Carbonyl Group*, Vol. 2, Wiley, NY, ***1970***, pp. 157–240.

[380] The mechanism for conversion of one tautomer to another is discussed in Chapter 12 (reaction **12-3**).

[381] Capponi, M.; Gut, I.G.; Hellrung, B.; Persy, G.; Wirz, J. *Can. J. Chem.* ***1999***, *77*, 605. For a treatise, see Rappoport, Z. *The Chemistry of Enols*, Wiley, NY, ***1990***.

[382] Iglesias, E. *J. Org. Chem*, ***2003***, *68*, 2680.

TABLE 2.1. The Enol Content of Some Carbonyl Compounds

Compound	Enol Content, %	References
Acetone	6×10^{-7}	383
$PhCOCH_3$	1.1×10^{-6}	384
Cyclopentanone	1×10^{-6}	385
CH_3CHO	6×10^{-5}	386
Cyclohexanone	4×10^{-5}	385
Butanal	5.5×10^{-4}	387
$(CH_3)_2CHCHO$	1.4×10^{-2}	388,387
Ph_2CHCHO	9.1	389
CH_3COOEt	No enol found[a]	385
CH_3COCH_2COOEt	8.4	390
$CH_3COCH_2COCH_3$	80	322
$PhCOCH_2COCH_3$	89.2	385
$EtOOCCH_2COOEt$	7.7×10^{-3}	385
$N{\equiv}C{-}CH_2COOEt$	2.5×10^{-1}	385
Indane-1-one	3.3×10^{-8}	391
Malonamide	No enol found	392

[a] Less than 1 part in 10 million.

The keto form differs from the enol form in possessing a C—H, a C—C, and a C=O bond, where the enol has a C=C, a C—O, and an O—H bond. The approximate sum of the first three is 359 kcal mol^{-1} (1500 kJ mol^{-1}) and of the second three is 347 kcal mol^{-1} (1452 kJ mol^{-1}). The keto form is therefore thermodynamically more stable by ~12 kcal mol^{-1} (48 kJ mol^{-1}) and enol forms cannot normally be isolated.[393] In certain cases, however, a larger amount of the enol form is present,

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[383] Tapuhi, E.; Jencks, W.P. *J. Am. Chem. Soc.* **1982**, *104*, 5758; Chiang, Y.; Kresge, A.J.; Tang, Y.S.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 460. See also, Hine, J.; Arata, K. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3089; Guthrie, J.P. *Can. J. Chem.* 1979, *57*, 797, 1177; Dubois, J.E.; El-Alaoui, M.; Toullec, J. *J. Am. Chem. Soc.* 1981, *103*, 5393; Toullec, J. *Tetrahedron Lett.* 1984, *25*, 4401; Chiang, Y.; Kresge, A.J.; Schepp, N.P. *J. Am. Chem. Soc.* **1989**, *111*, 3977.

[384] Keeffe, J.R.; Kresge, A.R.; Toullec, J. *Can. J. Chem.* **1986**, *64*, 1224.

[385] Gero, A. *J. Org. Chem.* **1954**, *19*, 469, 1960; Keeffe, J.R., Kresge, A.J.; Schepp, N.P. *J. Am. Chem. Soc.* **1990**, *112*, 4862; Iglesias, E. *J. Chem. Soc. Perkin Trans. 2* **1997**, 431. See these papers for values for other simple compounds.

[386] Chiang, Y.; Hojatti, M.; Keeffe, J.R.; Kresge, A.J.; Schepp, N.P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000.

[387] Bohne, C.; MacDonald, I.D.; Dunford, H.B. *J. Am. Chem. Soc.* **1986**, *108*, 7867.

[388] Chiang, Y.; Kresge, A.J.; Walsh, P.A. *J. Am. Chem. Soc.* **1986**, *108*, 6314.

[389] Chiang, Y.; Kresge, A.J.; Krogh, E.T. *J. Am. Chem. Soc.* **1988**, *110*, 2600.

[390] Moriyasu, M.; Kato, A.; Hashimoto, Y. *J. Chem. Soc. Perkin Trans. 2* 1986, 515. For enolization of β-ketoamides, see Hynes, M.J.; Clarke, E.M. *J. Chem. Soc. Perkin Trans. 2* **1994**, 901.

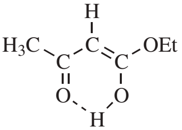
[391] Jefferson, E.A.; Keeffe, J.R.; Kresge, A.J. *J. Chem. Soc. Perkin Trans. 2* **1995**, 2041.

[392] Williams, D.L.H.; Xia, L. *J. Chem. Soc. Chem. Commun.* **1992**, 985.

[393] For reviews on the generation of unstable enols, see Kresge, A.J. *Pure Appl. Chem.* ***1991***, *63*, 213; Capon, B., in Rappoport, Z. *The Chemistry of Enols*, Wiley, NY, ***1990***, pp. 307–322.

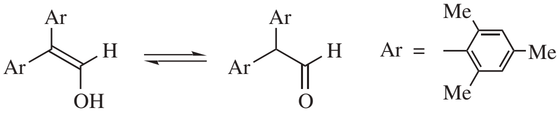
and it can even be the predominant form.[394] There are three main types of the more stable enols:[395]

1. Molecules in which the enolic double bond is in conjugation with another double bond. Some of these are shown in Table 2.1. As the table shows, carboxylic esters have a much smaller enolic content than ketones. In molecules like acetoacetic ester (**142**), the enol is also stabilized by internal hydrogen bonding, which is unavailable to the keto form:



142

2. Molecules that contain two or three bulky aryl groups.[396] An example is 2,2-dimesitylethenol (**143**). In this case the keto content at equilibrium is only 5%.[397] In cases such as this, steric hindrance (p. 230) destabilizes the keto form. In **143**, the two aryl groups are ~120° apart, but in **144** they must move closer together (~109.5°). Such compounds are often called *Fuson-type enols*.[398] There is one example of an amide with a bulky aryl group [*N*-methyl bis(2,4,6-triisopropylphenyl)acetamide] that has a measurable enol content, in sharp contrast to most amides.[399]



143 **144**

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[394] For reviews of stable enols, see Kresge, A.J. *Acc. Chem. Res.* ***1990***, *23*, 43; Hart, H.; Rappoport, Z.; Biali, S.E., in Rappoport, Z. *The Chemistry of Enols*, Wiley, NY, ***1990***, pp. 481–589; Hart, H. *Chem. Rev*, ***1979***, *79*, 515; Hart, H.; Sasaoka, M. *J. Chem. Educ.* ***1980***, *57*, 685.

[395] For some examples of other types, see Pratt, D.V.; Hopkins, P.B. *J. Am. Chem. Soc.* ***1987***, *109*, 5553; Nadler, E.B.; Rappoport, Z.; Arad, D.; Apeloig, Y. *J. Am. Chem. Soc.* ***1987***, *109*, 7873.

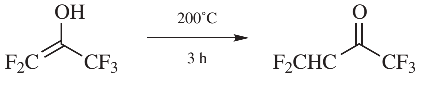
[396] For a review, see Rappoport, Z.; Biali, S.E. *Acc. Chem. Res.* ***1988***, *21*, 442. For a discussion of their structures, see Kaftory, M.; Nugiel, D.A.; Biali, D.A.; Rappoport, Z. *J. Am. Chem. Soc.* ***1989***, *111*, 8181.

[397] Biali, S.E.; Rappoport, Z. *J. Am. Chem. Soc.* ***1985***, *107*, 1007. See also, Kaftory, M.; Biali, S.E.; Rappoport, Z. *J. Am. Chem. Soc.* ***1985***, *107*, 1701; Nugiel, D.A.; Nadler, E.B.; Rappoport, Z. *J. Am. Chem. Soc.* ***1987***, *109*, 2112; O'Neill, P.; Hegarty, A.F. *J. Chem. Soc. Chem. Commun.* ***1987***, 744; Becker, H.; Andersson, K. *Tetrahedron Lett.* ***1987***, *28*, 1323.

[398] First synthesized by Fuson, R.C.; see, for example, Fuson, R.C.; Southwick, P.L.; Rowland, S.P. *J. Am. Chem. Soc.* ***1944***, *66*, 1109.

[399] Frey, J.; Rappoport, Z. *J. Am. Chem. Soc.* ***1996***, *118*, 3994.

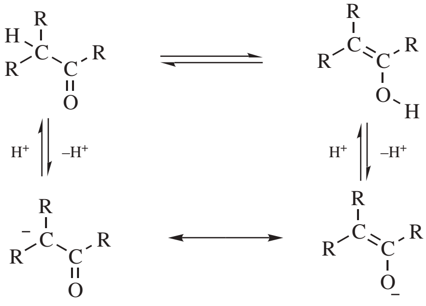
3. Highly fluorinated enols, such as **145**.[400]



145 **146**

In this case, the enol form is not more stable than the keto form (**146**). The enol form is less stable, and converts to the keto form upon prolonged heating). It can, however, be kept at room temperature for long periods of time because the tautomerization reaction (**12-3**) is very slow, owing to the electron-withdrawing power of the fluorines.

Frequently, when the enol content is high, both forms can be isolated. The pure keto form of acetoacetic ester melts at −39°C, while the enol is a liquid even at −78°C. Each can be kept at room temperature for days if catalysts, such as acids or bases, are rigorously excluded.[401] Even the simplest enol, vinyl alcohol $CH_2{=}CHOH$, has been prepared in the gas phase at room temperature, where it has a half-life of ~30 min.[402] The enol $Me_2C{=}CCHOH$ is indefinitely stable in the solid state at −78°C and has a half-life of ~24 h in the liquid state at 25°C.[403] When both forms cannot be isolated, the extent of enolization is often measured by NMR.[404]



147 **148**

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[400] For a review, see Bekker, R.A.; Knunyants, I.L. *Sov. Sci. Rev. Sect. B* ***1984***, *5*, 145.

[401] For an example of particularly stable enol and keto forms, which could be kept in the solid state for more than a year without significant interconversion, see Schulenberg, J.W. *J. Am. Chem. Soc.* ***1968***, *90*, 7008.

[402] Saito, S. *Chem. Phys. Lett.* ***1976***, *42*, 399. See also, Capon, B.; Rycroft, D.S.; Watson, T.W.; Zucco, C. *J. Am. Chem. Soc.* ***1981***, *103*, 1761; Holmes, J.L.; Lossing, F.P. *J. Am. Chem. Soc.* ***1982***, *104*, 2648; McGarrity, J.F.; Cretton, A.; Pinkerton, A.A.; Schwarzenbach, D.; Flack, H.D. *Angew. Chem. Int. Ed.* ***1983***, *22*, 405; Rodler, M.; Blom, C.E.; Bauder, A. *J. Am. Chem. Soc.* ***1984***, *106*, 4029; Capon, B.; Guo, B.; Kwok, F.C.; Siddhanta, A.K.; Zucco, C. *Acc. Chem. Res.* ***1988***, *21*, 135.

[403] Chin, C.S.; Lee, S.Y.; Park, J.; Kim, S. *J. Am. Chem. Soc.* ***1988***, *110*, 8244.

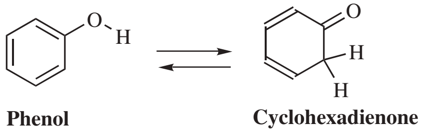
[404] Cravero, R.M.; González-Sierra, M.; Olivieri, A.C. *J. Chem. Soc. Perkin Trans. 2* ***1993***, 1067.

The extent of enolization[405] is greatly affected by solvent,[406] concentration, and temperature. Lactone enols, for example, have been shown to be stable in the gas phase, but unstable in solution.[407] Thus, acetoacetic ester has an enol content of 0.4% in water and 19.8% in toluene.[408] In this case, water reduces the enol concentration by hydrogen bonding with the carbonyl, making this group less available for internal hydrogen bonding. As an example of the effect of temperature, the enol content of pentan-2,4-dione, $CH_3COCH_2COCH_3$, was found to be 95, 68, and 44%, respectively, at 22, 180, and 275°C.[409] When a strong base is present, both the enol and the keto form can lose a proton. The resulting anion (the *enolate ion*) is the same in both cases. Since **147** and **148** differ only in placement of electrons, *they* are not tautomers, but canonical forms. The true structure of the enolate ion is a hybrid of **147** and **148** although **148** contributes more, since in this form the negative charge is on the more electronegative atom.

Other Proton-Shift Tautomerism

In all such cases, the anion resulting from removal of a proton from either tautomer is the same because of resonance. Some examples are:[410]

1. *Phenol–Keto Tautomerism.*[411]



Phenol **Cyclohexadienone**

For most simple phenols, this equilibrium lies well to the side of the phenol, since only on that side is there aromaticity. For phenol itself, there is no evidence for the existence of the keto form.[412] However, the keto form

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[405] For a review of keto–enol equilibrium constants, see Toullec, J. in Rappoport, Z. *The Chemistry of Enols*, Wiley, NY, ***1990***, pp. 323–398.

[406] For an extensive study, see Mills, S.G.; Beak, P. *J. Org. Chem.* ***1985***, *50*, 1216. For keto–enol tautomerism in aqueous alcohol solutions, see Blokzijl, W.; Engberts, J.B.F.N.; Blandamer, M.J. *J. Chem. Soc. Perkin Trans. 2* ***1994***, 455; For theoretical calculations of keto–enol tautomerism in aqueous solutions, see Karelson, M.; Maran, U.; Katritzky, A.R. *Tetrahedron* ***1996***, *52*, 11325.

[407] Tureč ek, F.; Vivekananda, S.; Sadílek, M.; Polášek, M. *J. Am. Chem. Soc,.* ***2002***, *124*, 13282.

[408] Meyer, K.H. *Leibigs Ann. Chem.* ***1911***, *380*, 212. See also, Moriyasu, M.; Kato, A.; Hashimoto, Y. *J. Chem. Soc. Perkin Trans. 2* ***1986***, 515.

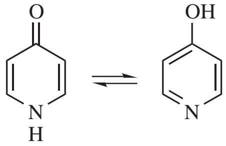
[409] Hush, N.S.; Livett, M.K.; Peel, J.B.; Willett, G.D. *Aust. J. Chem.* ***1987***, *40*, 599.

[410] For a review of the use of X-ray crystallography to determine tautomeric forms, see Furmanova, N.G. *Russ. Chem. Rev.* ***1981***, *50*, 775.

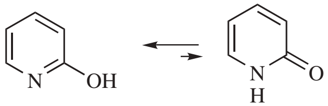
[411] For reviews, see Ershov, V.V.; Nikiforov, G.A. *Russ. Chem. Rev.* ***1966***, *35*, 817; Forsén, S.; Nilsson, M., in Zabicky, J. *The Chemistry of the Carbonyl Group*, Vol. 2, Wiley, NY, ***1970***, pp. 168–198.

[412] Keto forms of phenol and some simple derivatives have been generated as intermediates with very short lives, but long enough for spectra to be taken at 77 K. Lasne, M.; Ripoll, J.; Denis, J. *Tetrahedron Lett.* ***1980***, *21*, 463. See also, Capponi, M.; Gut, I.; Wirz, J. *Angew. Chem. Int. Ed.* ***1986***, *25*, 344.

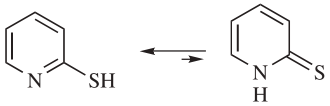
becomes important and may predominate: (*1*) where certain groups, such as a second OH group or an N=O group, are present;[413] (*2*) in systems of fused aromatic rings;[414] (*3*) in heterocyclic systems. In many heterocyclic compounds in the liquid phase or in solution, the keto form is more stable,[415] although in the vapor phase the positions of many of these equilibria are reversed.[416] For example, in the equilibrium between 4-pyridone (**149**) and 4-hydroxypyridine (**150**), **149** is the only form detectable in ethanolic solution, while **150** predominates in the vapor phase.[416] In other heterocycles, the hydroxy-form predominates. 2-Hydroxypyridone (**151**) and pyridone-2-thiol (**153**)[417] are in equilibrium with their tautomers, 2-pyridone **152** and pyridine-2-thione **154**, respectively. In both cases, the most stable form is the hydroxy tautomer, **151** and **153**.[418]



149 **150**

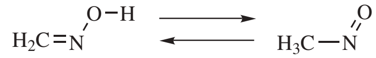


151 **152**



153 **154**

2. *Nitroso–Oxime Tautomerism.*



$$H_2C{=}N{-}O{-}H \rightleftarrows H_3C{-}N{=}O$$

The equiblirum shown for formaldhyde oxime and nitrosomethane illustrates this process.[419] In molecules where the products are stable, the equilibrium lies far to the right, and as a rule nitroso compounds are stable only when there is not a hydrogen.

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[413] Ershov, V.V.; Nikiforov, G.A. *Russ. Chem. Rev.* ***1966***, *35*, 817. See also, Highet, R.J.; Chou, F.E. *J. Am. Chem. Soc.* ***1977***, *99*, 3538.

[414] See, for example, Majerski, Z.; Trinajstić, N. *Bull. Chem. Soc. Jpn.* ***1970***, *43*, 2648.

[415] For a monograph on tautomerism in heterocyclic compounds, see Elguero, J.; Marzin, C.; Katritzky, A.R.; Linda, P. *The Tautomerism of Heterocycles*, Academic Press, NY, ***1976***. For reviews, see Katritzky, A.R.; Karelson, M.; Harris, P.A. *Heterocycles* ***1991***, *32*, 329; Beak, P. *Acc. Chem. Res.* ***1977***, *10*, 186; Katritzky, A.R. *Chimia*, ***1970***, *24*, 134.

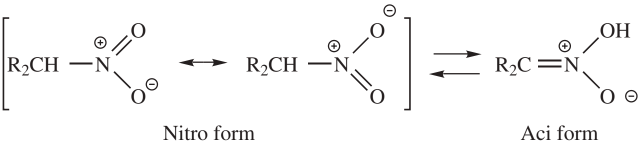
[416] Beak, P.; Fry, Jr., F.S.; Lee, J.; Steele, F. *J. Am. Chem. Soc.* ***1976***, *98*, 171.

[417] Moran, D.; Sukcharoenphon, K.; Puchta, R.; Schaefer III, H.F.; Schleyer, P.v.R.; Hoff, C.D. *J. Org. Chem.* ***2002***, *67*, 9061.

[418] Parchment, O.G.; Burton, N.A.; Hillier, I.H.; Vincent, M.A. *J. Chem. Soc. Perkin Trans. 2* ***1993***, 861.

[419] Long, J.A.; Harris, N.J.; Lammertsma, K. *J. Org. Chem.* ***2001***, *66*, 6762.

3. *Aliphatic Nitro Compounds Are in Equilibrium with Aci Forms.*



The nitro form is much more stable than the aci form in sharp contrast to the parallel case of nitroso–oxime tautomerism, undoubtedly because the nitro form has resonance not found in the nitroso case. Aci forms of nitro compounds are also called nitronic acids and azinic acids.

4. *Imine–Enamine Tautomerism.*[420]

$$R_2CH—CR{=}NR \rightleftharpoons R_2C{=}CR—NHR$$

Imine Enamine

Enamines are normally stable only when there is no hydrogen on the nitrogen ($R_2C{=}CR{-}NR_2$). Otherwise, the imine form predominates.[421] The energy of various imine–enamine tautomers has been calculated.[422] In the case of 6-aminofulvene-1-aldimines, tautomerism was observed in the solid state, as well as in solution.[423]

5. *Ring-Chain Tautomerism.* Ring-chain tautomerism[424] occurs in sugars (aldehyde vs. the pyranose or furanose structures), and in γ-oxocarboxylic acids.[425] In benzamide carboxaldehyde, **156**, whose ring-chain tautomer is **155**, the equilibrium favors the cyclic form (**156**).[426] Similarly, benzoic acid 2-carboxyaldehyde (**157**) exists largely as the cyclic form (**158**).[427] In these latter cases, and in many others, this tautomerism influences chemical reactivity. Conversion of **157** to an ester, for example, is difficult since most standard methods lead to the OR derivative of **158** rather than the ester of **157**. Ring-chain tautomerism also occurs in sprioоxathianes,[428] and in

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[420] For reviews, see Shainyan, B.A.; Mirskova, A.N. *Russ. Chem. Rev.* ***1979***, *48*, 107; Mamaev, V.P.; Lapachev, V.V. *Sov. Sci. Rev. Sect. B.* ***1985***, *7*, 1. The second review also includes other closely related types of tautomerization.

[421] For examples of the isolation of primary and secondary enamines, see Shin, C.; Masaki, M.; Ohta, M. *Bull. Chem. Soc. Jpn.* ***1971***, *44*, 1657; de Jeso, B.; Pommier, J. *J. Chem. Soc. Chem. Commun.* ***1977***, 565.

[422] Lammertsma, K.; Prasad, B.V. *J. Am. Chem. Soc.* ***1994***, *116*, 642.

[423] Sanz, D.; Perez-Torralba, M.; Alarcon, S.H.; Claramunt, R.M.; Foces-Foces, C.; Elguero, J. *J. Org. Chem.* ***2002***, *67*, 1462.

[424] For a monograph, see Valters, R.E.; Flitsch, W. *Ring-Chain Tautomerism*, Plenum, NY, ***1985***. For reviews, see Valters, R.E. *Russ. Chem. Rev.* ***1973***, *42*, 464; ***1974***, *43*, 665; Escale, R.; Verducci, J. *Bull. Soc. Chim. Fr.*, ***1974***, 1203.

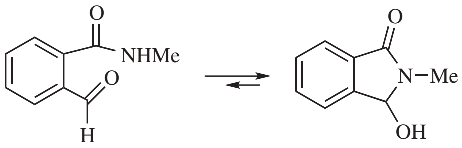
[425] Fabian, W.M.F.; Bowden, K. *Eur. J. Org. Chem.* ***2001***, 303.

[426] Bowden, K.; Hiscocks, S.P.; Perjéssy, A. *J. Chem. Soc. Perkin Trans. 2* ***1998***, 291.

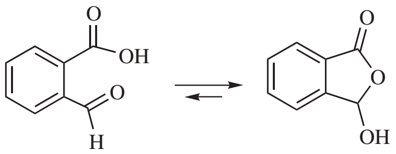
[427] Ring chain tautomer of benzoic acid 2-carboxaldehdye.

[428] Terec, A.; Grosu, I.; Muntean, L.; Toupet, L.; Plé, G.; Socaci, C.; Mager, S. *Tetrahedron* ***2001***, *57*, 8751; Muntean, L.; Grosu, I.; Mager, S.; Plé, G.; Balog, M. *Tetrahedron Lett.* ***2000***, *41*, 1967.

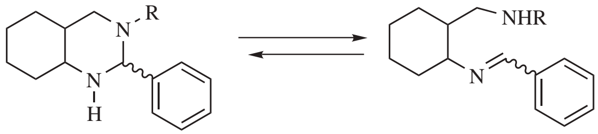
decahydroquinazolines, such as **159** and **160**,[429] as well as other 1,3-heterocycles.[430]



155 **156**

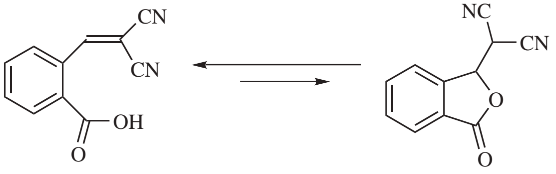


157 **158**



159 **160**

There are many other highly specialized cases of proton-shift tautomerism, including an internal Michael reaction (see **15-24**) in which 2-(2,2-dicyano-1-methylethenyl)benzoic acid (**161**) exists largely in the open chain form rather an its tautomer (**162**) in the solid state, but in solution there is an increasing amount of **162** as the solvent becomes more polar.[431]



161 **162**

Valence Tautomerism

This type of tautomerism is discussed on p. 105.

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[429] Lazar, L.; Goblyos, A.; Martinek, T.A.; Fulop, F. *J. Org. Chem.* ***2002***, *67*, 4734.

[430] Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* ***2003***, 3025.

[431] Kolsaker, P.; Arukwe, J.; Barcóczy, J.; Wiberg, A.; Fagerli, A.K. *Acta Chem. Scand. B* ***1998***, *52*, 490.

CHAPTER 3

Bonding Weaker than Covalent

In the first two chapters, we discussed the structure of molecules each of which is an aggregate of atoms in a distinct three-dimensional (3D) arrangement held together by bonds with energies on the order of 50–100 kcal mol^{-1} (200–400 kJ mol^{-1}). There are also very weak attractive forces *between* molecules, on the order of a few tenths of a kilocalorie per mole. These forces, called van der Waals forces, are caused by electrostatic attractions, such as those between dipole and dipole, induced dipole, and induced dipole, and are responsible for liquefaction of gases at sufficiently low temperatures. The bonding discussed in this chapter has energies of the order of 2–10 kcal mol^{-1} (9–40 kJ mol^{-1}), intermediate between the two extremes, and produces clusters of molecules. We will also discuss compounds in which portions of molecules are held together without any attractive forces at all.

HYDROGEN BONDING

A *hydrogen bond* is a bond between a functional group A—H and an atom or group of atoms B in the same or a different molecule.[1] With exceptions to be noted later, hydrogen bonds are *assumed to form only when A is oxygen, nitrogen, or fluorine and when B is oxygen, nitrogen, or fluorine*.[2] The oxygen may be singly or doubly

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[1] For a treatise, see Schuster, P.; Zundel, G.; Sandorfy, C. *The Hydrogen Bond*, 3 vols., North-Holland Publishing Co.: Amsterdam, The Netherlands, ***1976***. For a monograph, see Joesten, M.D.; Schaad, L.J. *Hydrogen Bonding*; Marcel Dekker, NY, ***1974***. For reviews, see Meot-Ner, M. *Mol. Struct. Energ.* ***1987***, *4*, 71; Deakyne, C.A. *Mol. Struct. Energ.* ***1987***, *4*, 105; Joesten, M.D. *J. Chem. Educ.* ***1982***, *59*, 362; Gur'yanova, E.N.; Gol'dshtein, I.P.; Perepelkova, T.I. *Russ. Chem. Rev.* ***1976***, *45*, 792; Pimentel, G.C.; McClellan, A.L. *Annu. Rev. Phys. Chem.* ***1971***, *22*, 347; Kollman, P.A.; Allen, L.C. *Chem. Rev.* ***1972***, *72*, 283; Huggins, M.L. *Angew. Chem. Int. Ed.* ***1971***, *10*, 147; Rochester, C.H., in Patai, S. The Chemistry of the Hydroxyl Group, pt. 1; Wiley, NY, ***1971***, pp. 327–392, 328–369. See also Hamilton, W.C.; Ibers, J.A. *Hydrogen Bonding in Solids*, W.A. Benjamin, NY, ***1968***. Also see, Chen, J.; McAllister, M.A.; Lee, J.K.; Houk, K.N. *J. Org. Chem.* ***1998***, *63*, 4611 for a discussion of short, strong hydrogen bonds.

[2] The ability of functional groups to act as hydrogen bond acids and bases can be obtained from either equilibrium constants for 1:1 hydrogen bonding or overall hydrogen bond constants. See Abraham, M.H.; Platts, J.A. *J. Org. Chem.* ***2001***, *66*, 3484.

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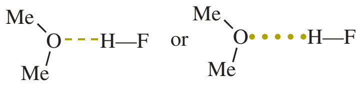
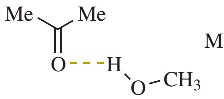
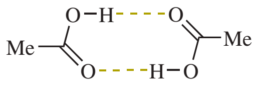
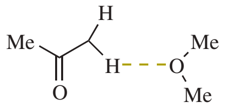
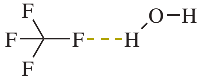
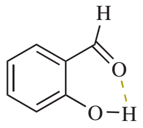
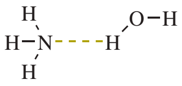
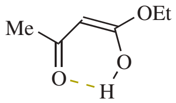
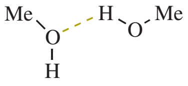
Michael B. Smith and Jerry March

bonded and the nitrogen singly, doubly, or triply bonded. The bonds are usually represented by dotted or dashed lines, as shown in the following examples:

Hydrogen bonds can exist in the solid[3] and liquid phases and in solution.[4] Many organic reactions that will be discussed in later chapters can be done in aqueous media,[5] and their efficacy is due, in part, to the hydrogen bonding nature of aqueous media.[6] Even in the gas phase, compounds that form particularly strong hydrogen bonds may remain associated.[7] Acetic acid, for example, exists in the gas phase as a dimer, as shown above, except at very low pressures.[8] In solution and in the liquid phase, hydrogen bonds rapidly form and break. The mean lifetime of the $NH_3 \cdots H_2O$ bond is 2×10^{-12} s.[9] Except for a few very strong hydrogen bonds,[10] such as the $FH \cdots F^-$ bond (which has an energy of $\sim 50\ \text{kcal mol}^{-1}$ or $210\ \text{kJ mol}^{-1}$), the strongest hydrogen bonds are the $FH \cdots F$ bond and the bonds connecting one carboxylic acid with another. The energies of these bonds are in the range of $6\text{–}8\ \text{kcal mol}^{-1}$ or $25\text{–}30\ \text{kJ mol}^{-1}$ (for carboxylic acids, this refers to the energy of each bond). In general, short contact hydrogen bonds between fluorine and HO or NH are rare.[11] Other $OH \cdots O$ and $NH \cdots N$ bonds[12] have energies of $3\text{–}6\ \text{kcal mol}^{-1}$ ($12\text{–}25\ \text{kJ mol}^{-1}$).

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[3] Steiner, T. *Angew. Chem. Int. Ed.* ***2002***, *41*, 48. See also Damodharan, L.; Pattabhi, V. *Tetrahedron Lett.* ***2004***, *45*, 9427.

[4] See Nakahara, M.; Wakai, C. *Chem. Lett.* ***1992***, 809 for a discussion of monomeric and cluster states of water molecules in organic solvents due to hydrogen bonding.

[5] Li, C.-J.; Chen, T.-H. *Organic Reactions in Aqueous Media*, Wiley, NY, ***1997***.

[6] Li, C.-J. *Chem. Rev.* ***1993***, *93*, 2023.

[7] For a review of energies of hydrogen bonds in the gas phase, see Curtiss, L.A.; Blander, M. *Chem. Rev.* ***1988***, *88*, 827.

[8] For a review of hydrogen bonding in carboxylic acids and acid derivatives, see Hadži, D.; Detoni, S., in Patai, S. *The Chemistry of Acid Derivatives*, pt. 1, Wiley, NY, ***1979***, pp. 213–266.

[9] Emerson, M.T.; Grunwald, E.; Kaplan, M.L.; Kromhout, R.A. *J. Am. Chem. Soc.* ***1960***, *82*, 6307.

[10] For a review of very strong hydrogen bonding, see Emsley, J. *Chem. Soc. Rev.* ***1980***, *9*, 91.

[11] Howard, J.A.K.; Hoy, V.J.; O'Hagan, D.; Smith, G.T. *Tetrahedron* ***1996***, *52*, 12613.

[12] For an *ab initio* study of diamine hydrogen bonds see Sorensen, J.B.; Lewin, A.H.; Bowen, J.P. *J. Org. Chem.* ***2001***, *66*, 4105.

The intramolecular O–H•••N hydrogen bond in hydroxy amines is also rather strong.[13]

To a first approximation, the strength of hydrogen bonds increases with increasing acidity of A—H and basicity of B, but the parallel is far from exact.[14] A quantitative measure of the strengths of hydrogen bonds has been established, involving the use of an α scale to represent hydrogen-bond donor acidities and a β scale for hydrogen-bond acceptor basicities.[15] The use of the β scale, along with another parameter, ξ, allows hydrogen-bond basicities to be related to proton-transfer basicities (pK values).[16] A database has been developed to locate all possible occurrences of bimolecular cyclic hydrogen-bond motifs in the Cambridge Structural Database,[17] and donor–acceptor as well as polarity parameters have been calculated for hydrogen-bonding solvents.[18]

When two compounds whose molecules form hydrogen bonds with each other are both dissolved in water, the hydrogen bond between the two molecules is usually greatly weakened or completely removed,[19] because the molecules generally form hydrogen bonds with the water molecules rather than with each other, especially since the water molecules are present in such great numbers. In amides, the oxygen atom is the preferred site of protonation or complexation with water.[20] In the case of dicarboxylic acids, arguments have been presented that there is little or no evidence for strong hydrogen bonding in aqueous solution,[21] although recent studies concluded that strong, intramolecular hydrogen bonding can exist in aqueous acetone solutions (0.31 mole-fraction water) of hydrogen maleate and hydrogen *cis*-cyclohexane-1,2-dicarboxylate.[22]

Many studies have been made of the geometry of hydrogen bonds,[23] and the evidence shows that in most (though not all) cases, the hydrogen is on or near the

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[13] Grech, E.; Nowicka-Scheibe, J.; Olejnik, Z.; Lis, T.; Pawêka, Z.; Malarski, Z.; Sobczyk, L. *J. Chem. Soc., Perkin Trans. 2* ***1996***, 343. See Steiner, T. *J. Chem. Soc., Perkin Trans. 2* ***1995***, 1315 for a discussion of hydrogen bonding in the crystal structure of α-amino acids.

[14] For reviews of the relationship between hydrogen-bond strength and acid-base properties, see Pogorelyi, V.K.; Vishnyakova, T.B. *Russ. Chem. Rev.* ***1984***, *53*, 1154; Epshtein, L.M. *Russ. Chem. Rev.* ***1979***, *48*, 854.

[15] For reviews, see Abraham, M.H.; Doherty, R.M.; Kamlet, M.J.; Taft, R.W. *Chem. Br.* ***1986***, 551; Kamlet, M.J.; Abboud, J.M.; Taft, R.W. *Prog. Phys. Org. Chem.* ***1981***, *13*, 485. For a comprehensive table and α and β values, see Kamlet, M.J.; Abboud, J.M.; Abraham, M.H.; Taft, R.W. *J. Org. Chem.* ***1983***, *48*, 2877. For a criticism of the β scale, see Laurence, C.; Nicolet, P.; Helbert, M. *J. Chem. Soc., Perkin Trans. 2* ***1986***, 1081. See also Nicolet, P.; Laurence, C.; Luçon, M. *J. Chem. Soc., Perkin Trans. 2* ***1987***, 483; Abboud, J.M.; Roussel, C.; Gentric, E.; Sraidi, K.; Lauransan, J.; Guihéneuf, G.; Kamlet, M.J.; Taft, R.W. *J. Org. Chem.* ***1988***, *53*, 1545; Abraham, M.H.; Grellier, P.L.; Prior, D.V.; Morris, J.J.; Taylor, P.J. *J. Chem. Soc., Perkin Trans. 2* ***1990***, 521.

[16] Kamlet, M.J.; Gal, J.; Maria, P.; Taft, R.W. *J. Chem. Soc., Perkin Trans. 2* ***1985***, 1583.

[17] Allen, F.H.; Raithby, P.R.; Shields, G.P.; Taylor, R. *Chem. Commun.* ***1998***, 1043.

[18] Joerg, S.; Drago, R.S.; Adams, J. *J. Chem. Soc., Perkin Trans. 2* ***1997***, 2431.

[19] Stahl, N.; Jencks, W.P. *J. Am. Chem. Soc.* ***1986***, *108*, 4196.

[20] Scheiner, S.; Wang, L. *J. Am. Chem. Soc.* ***1993***, *115*, 1958.

[21] Perrin, C.L. *Annu. Rev. Phys. Org. Chem.* ***1997***, *48*, 511.

[22] Lin, J.; Frey, P.A. *J. Am. Chem. Soc.* ***2000***, *122*, 11258.

[23] For reviews, see Etter, M.C. *Acc. Chem. Res.* ***1990***, *23*, 120; Taylor, R.; Kennard, O. *Acc. Chem. Res.* ***1984***, *17*, 320.

straight line formed by A and B.[24] This is true both in the solid state (where X-ray crystallography and neutron diffraction have been used to determine structures),[25] and in solution.[26] It is significant that the vast majority of intramolecular hydrogen bonding occurs where *six-membered rings* (counting the hydrogen as one of the six) can be formed, in which linearity of the hydrogen bond is geometrically favorable, while five-membered rings, where linearity is usually not favored (though it is known), are much rarer. A novel nine-membered intramolecular hydrogen bond has been reported.[27]

In certain cases, X-ray crystallography has shown that a single H–A can form simultaneous hydrogen bonds with two B atoms (*bifurcated* or *three-center hydrogen bonds*). An example is an adduct (**1**) formed from pentane-2,4-dione (in its enol form; see p. 98) and diethylamine, in which the O–H hydrogen simultaneously bonds[28] to an O and an N (the N–H hydrogen forms a hydrogen bond with the O of another pentane-2,4-dione molecule).[29] On the other hand, in the adduct (**2**) formed from 1,8-biphenylenediol and hexamethylphosphoramide (HMPA), the B atom (in this case oxygen) forms simultaneous hydrogen bonds with two A•••H hydrogens.[30] Another such case is found in methyl hydrazine carboxylate **3**.[31] Except for the special case of $FH\cdots F^-$ bonds (see p. 107), the hydrogen is not equidistant between A and B. For example, in ice the O–H distance is 0.97 Å, while the H•••O distance is 1.79 Å.[32] A theoretical study of the vinyl alcohol–vinyl alcoholate system concluded the hydrogen bonding is strong, but asymmetric.[33] The hydrogen bond in the enol of malonaldehyde, in organic solvents, is asymmetric with the hydrogen atom closer to the basic oxygen atom.[34] There is recent evidence, however, that symmetrical hydrogen bonds to carboxylates should be regarded as two-center rather than three-center hydrogen bonds, since the criteria traditionally used to infer three-center hydrogen bonding are inadequate for carboxylates.[35] There is

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[24] See Stewart, R. *The Proton: Applications to Organic Chemistry*; Academic Press, NY, ***1985***, pp. 148–153.

[25] A statisical analysis of X-ray crystallographic data has shown that most hydrogen bonds in crystals are nonlinear by ~10–15°: Kroon, J.; Kanters, J.A.; van Duijneveldt-van de Rijdt, J.G.C.M.; van Duijneveldt, F.B.; Vliegenthart, J.A. *J. Mol. Struct.* ***1975***, *24*, 109. See also, Ceccarelli, C.; Jeffrey, G.A.; Taylor, R. *J. Mol. Struct.* ***1981***, *70*, 255; Taylor, R.; Kennard, O.; Versichel, W. *J. Am. Chem. Soc.* ***1983***, *105*, 5761; ***1984***, *106*, 244.

[26] For reviews of a different aspect of hydrogen-bond geometry: the angle between A•••H•••B and the rest of the molecule, see Legon, A.C.; Millen, D.J. *Chem. Soc. Rev.* ***1987***, *16*, 467, *Acc. Chem. Res.* ***1987***, *20*, 39.

[27] Yoshimi, Y.; Maeda, H.; Sugimoto, A.; Mizuno, K. *Tetrahedron Lett.* ***2001***, *42*, 2341.

[28] Emsley, J.; Freeman, N.J.; Parker, R.J.; Dawes, H.M.; Hursthouse, M.B. *J. Chem. Soc., Perkin Trans. 1* ***1986***, 471.

[29] For some other three-center hydrogen bonds, see Taylor, R.; Kennard, O.; Versichel, W. *J. Am. Chem. Soc.* ***1984***, *106*, 244; Jeffrey, G.A.; Mitra, J. *J. Am. Chem. Soc.* ***1984***, *106*, 5546; Staab, H.A.; Elbl, K.; Krieger, C. *Tetrahedron Lett.* ***1986***, *27*, 5719.

[30] Hine, J.; Hahn, S.; Miles, D.E. *J. Org. Chem.* ***1986***, *51*, 577.

[31] Caminati, W.; Fantoni, A.C.; Schäfer, L.; Siam, K.; Van Alsenoy, C. *J. Am. Chem. Soc.* ***1986***, *108*, 4364.

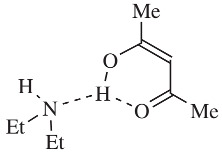
[32] Pimentel, G.C.; McClellan, A.L. *The Hydrogen Bond*; W.H. Freeman: San Francisco, ***1960***, p. 260.

[33] Chandra, A.K.; Zeegers-Huyskens, T., *J. Org. Chem.* ***2003***, *68*, 3618.

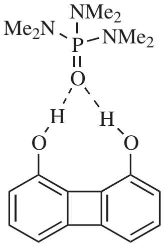
[34] Perrin, C.L.; Kim, Y.-J. *J. Am. Chem. Soc.* ***1998***, *120*, 12641.

[35] Görbitz, C.H.; Etter, M.C. *J. Chem. Soc., Perkin Trans. 2* ***1992***, 131.

also an example of cooperative hydrogen bonding (O–H•••C≡C–H•••Ph) in crystalline 2-ethynyl-6,8-diphenyl-7*H*-benzocyclohepten-7-ol (**4**).[36]



1



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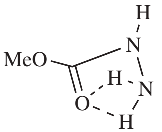

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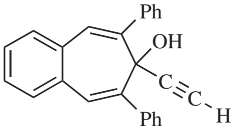

4

Hydrogen bonding has been detected in many ways, including measurements of dipole moments, solubility behavior, freezing-point lowering, and heats of mixing, but one important way is by the effect of the hydrogen bond on IR.[37] The IR frequencies of groups, such as O–H or C=O, are shifted when the group is hydrogen bonded. Hydrogen bonding always moves the peak toward lower frequencies, for both the A—H and the B groups, though the shift is greater for the former. For example, a free OH group of an alcohol or phenol absorbs at ~3590–3650 cm^{-1}, while a hydrogen-bonded OH group is found ~50–100 cm^{-1} lower.[38] In many cases, in dilute solution, there is partial hydrogen bonding, that is, some OH groups are free and some are hydrogen bonded. In such cases, two peaks appear. Infrared spectroscopy can also distinguish between inter- and intramolecular hydrogen bonding, since intermolecular peaks are intensified by an increase in concentration while intramolecular peaks are unaffected. Other types of spectra that have been used for the detection of hydrogen bonding include Raman, electronic,[39] and NMR.[40] Since hydrogen bonding involves a rapid movement of protons from one atom to another, nmr records an average value. Hydrogen bonding can be detected because it usually produces a chemical shift to a lower field. For example, carboxylic acid–carboxylate systems arising from either mono- or diacids generally exhibit a downfield resonance (16–22 ppm), which indicates "strong" hydrogen bonding

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[36] Steiner, T.; Tamm, M.; Lutz, B.; van der Maas, J. *Chem. Commun.* ***1996***, 1127.

[37] For reviews of the use of ir spectra to detect hydrogen bonding, see Symons, M.C.R. *Chem. Soc. Rev.* ***1983***, *12*, 1; Egorochkin, A.N.; Skobeleva, S.E. *Russ. Chem. Rev.* ***1979***, *48*, 1198; Tichy, M. *Adv. Org. Chem.* ***1965***, *5*, 115; Ratajczak, H.; Orville-Thomas, W.J. *J. Mol. Struct.* ***1968***, *1*, 449. For a review of studies by ir of the shapes of intramolecular hydrogen-bonded compounds, see Aaron, H.S. *Top. Stereochem.* ***1979***, *11*, 1. For a review of the use of rotational spectra to study hydrogen bonding, see Legon, A.C. *Chem. Soc. Rev.* ***1990***, *19*, 197.

[38] Tichy, M. *Adv. Org. Chem.* ***1965***, *5*, 115 contains a lengthy table of free and intramolecularly hydrogen-bonding peaks.

[39] For a discussion of the effect of hydrogen bonding on electronic spectra, see Lees, W.A.; Burawoy, A. *Tetrahedron* ***1963***, *19*, 419.

[40] For a review of the use of nmr to detect hydrogen bonding, see Davis, Jr., J.C.; Deb, K.K. *Adv. Magn. Reson.* ***1970***, *4*, 201. Also see, Kumar, G.A.; McAllister, M.A. *J. Org. Chem.* ***1998***, *63*, 6968, which shows the relationship between ^{1}H NMR chemical shift and hydrogen bond strength.

in anhydrous, aprotic solvents.[41] Hydrogen bonding changes with temperature and concentration, and comparison of spectra taken under different conditions also serves to detect and measure it. As with IR spectra, intramolecular hydrogen bonding can be distinguished from intermolecular by its constancy when the concentration is varied. The spin–spin coupling constant across a hydrogen bond, obtained by NMR studies, has been shown to provide a “fingerprint” for hydrogen-bond type.[42]

Hydrogen bonds are important because of the effects they have on the properties of compounds, among them:

1. Intermolecular hydrogen bonding raises boiling points and frequently melting points.
2. If hydrogen bonding is possible between solute and solvent, this greatly increases solubility and often results in large or even infinite solubility where none would otherwise be expected.
3. Hydrogen bonding causes lack of ideality in gas and solution laws.
4. As previously mentioned, hydrogen bonding changes spectral absorption positions.
5. Hydrogen bonding, especially the intramolecular variety, changes many chemical properties. For example, it is responsible for the large amount of enol present in certain tautomeric equilibria (see p. 98). Also, by influencing the conformation of molecules (see Chapter 4), it often plays a significant role in determining reaction rates.[43] Hydrogen bonding is also important in maintaining the 3D structures of protein and nucleic acid molecules.

Besides oxygen, nitrogen, and fluorine, there is evidence that weaker hydrogen bonding exists in other systems.[44] Although many searches have been made for hydrogen bonding where A is carbon,[45] only three types of C–H bonds have been found that are acidic enough to form weak hydrogen bonds.[46] These are found in terminal alkynes, $RC{\equiv}CH$,[47] chloroform and some other halogenated alkanes, and HCN. Sterically unhindered C–H groups ($CHCl_3$, CH_2Cl_2, $RC{\equiv}CH$) form short contact hydrogen bonds with carbonyl acceptors, where there is a significant preference for coordination with the conventional carbonyl lone-pair direction.[48]

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[41] Bruck, A.; McCoy, L.L.; Kilway, K.V. *Org. Lett.* ***2000***, *2*, 2007.

[42] Del Bene, J.E.; Perera, S.A.; Bartlett, R.J. *J. Am. Chem. Soc.* ***2000***, *122*, 3560.

[43] For reviews of the effect of hydrogen bonding on reactivity, see Hibbert, F.; Emsley, J. *Adv. Phys. Org. Chem.* ***1990***, *26*, 255; Sadekov, I.D.; Minkin, V.I.; Lutskii, A.E. *Russ. Chem. Rev.* ***1970***, *39*, 179.

[44] For a review, see Pogorelyi, V.K. *Russ. Chem. Rev.* ***1977***, *46*, 316.

[45] For a monograph on this subject, see Green, R.D. *Hydrogen Bonding by C–H Groups*; Wiley, NY, ***1974***. See also Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* ***1982***, *104*, 5063; Harlow, R.L.; Li, C.; Sammes, M.P. *J. Chem. Soc., Perkin Trans. 1* ***1984***, 547; Nakai, Y.; Inoue, K.; Yamamoto, G.; Ō ki, M. *Bull. Chem. Soc. Jpn.* ***1989***, *62*, 2923; Seiler, P.; Dunitz, J.D. *Helv. Chim. Acta* ***1989***, *72*, 1125.

[46] For a theoretical study of weak hydrogen-bonds, see Calhorda, M.J. *Chem. Commun.* ***2000***, 801.

[47] For a review, see Hopkinson, A.C., in Patai, S. *The Chemistry of the Carbon–Carbon Triple Bond*, pt. 1, Wiley, NY, ***1978***, pp. 75–136. See also DeLaat, A.M.; Ault, B.S. *J. Am. Chem. Soc.* ***1987***, *109*, 4232.

[48] Streiner, T.; Kanters, J.A.; Kroon, J. *Chem. Commun.* ***1996***, 1277.

Weak hydrogen bonds are formed by compounds containing S–H bonds.[49] There has been much speculation regarding other possibilities for B. There is evidence that Cl can form weak hydrogen bonds,[50] but Br and I form very weak bonds if at all.[51] However, the *ions* Cl^-, Br^-, and I^- form hydrogen bonds that are much stronger than those of the covalently bonded atoms.[52] As we have already seen, the $FH\cdots F^-$ bond is especially strong. In this case, the hydrogen is equidistant from the fluorines.[53] Similarly, a sulfur atom[49] can be the B component in weak hydrogen bonds,[54] but the ^-SH ion forms much stronger bonds.[55] There are theoretical studies of weak hydrogen bonding.[56] Hydrogen bonding has been directly observed (by NMR and IR) between a negatively charged carbon (see Carbanions, Chapter 5) and an OH group in the same molecule.[57] Another type of molecule in which carbon is the B component are isocyanides, $R{-}^{+}N{\equiv}C^{-}$ which form rather strong hydrogen bonds.[58] There is evidence that double and triple bonds, aromatic rings,[59] and even cyclopropane rings[60] may be the B component of hydrogen bonds, but these bonds are very weak. An interesting case is that of the *in*-bicyclo[4.4.4]-1-tetradecyl cation **5** (see in–out isomerism, p. 189). The NMR and IR spectra show that the actual structure of this ion is **6**, in which both the A and the B component of the hydrogen bond is a carbon.[61] These are sometimes

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[49] For reviews of hydrogen bonding in sulfur-containing compounds, see Zuika, I.V.; Bankovskii, Yu.A. *Russ. Chem. Rev.* ***1973***, *42*, 22; Crampton, M.R., in Patai, S. *The Chemistry of the Thiol Group*, pt. 1; Wiley, NY, ***1974***, pp. 379–396; Pogorelyi, V.K. *Russ. Chem. Rev.* ***1977***, *46*, 316.

[50] For a review of hydrogen bonding to halogens, see Smith, J.W., in Patai, S. *The Chemistry of the Carbon-Halogen Bond*, pt. 1; Wiley, NY, ***1973***, pp. 265–300. See also, Bastiansen, O.; Fernholt, L.; Hedberg, K.; Seip, R. *J. Am. Chem. Soc.* ***1985***, *107*, 7836.

[51] West, R.; Powell, D.L.; Whatley, L.S.; Lee, M.K.T.; Schleyer, P.v.R. *J. Am. Chem. Soc.* ***1962***, *84*, 3221; Fujimoto, E.; Takeoka, Y.; Kozima, K. *Bull. Chem. Soc. Jpn.* ***1970***, *43*, 991; Azrak, R.G.; Wilson, E.B. *J. Chem. Phys.* ***1970***, *52*, 5299.

[52] Allerhand, A.; Schleyer, P.v.R. *J. Am. Chem. Soc.* ***1963***, *85*, 1233; McDaniel, D.H.; Valleé, R.E. *Inorg. Chem.* ***1963***, *2*, 996; Fujiwara, F.Y.; Martin, J.S. *J. Am. Chem. Soc.* ***1974***, *96*, 7625; French, M.A.; Ikuta, S.; Kebarle, P. *Can. J. Chem.* ***1982***, *60*, 1907.

[53] A few exceptions have been found, where the presence of an unsymmetrical cation causes the hydrogen to be closer to one fluorine than to the other: Williams, J.M.; Schneemeyer, L.F. *J. Am. Chem. Soc.* ***1973***, *95*, 5780.

[54] Vogel, G.C.; Drago, R.S. *J. Am. Chem. Soc.* ***1970***, *92*, 5347; Mukherjee, S.; Palit, S.R.; De, S.K. *J. Phys. Chem.* ***1970***, *74*, 1389; Schaefer, T.; McKinnon, D.M.; Sebastian, R.; Peeling, J.; Penner, G.H.; Veregin, R.P. *Can. J. Chem.* ***1987***, *65*, 908; Marstokk, K.; Møllendal, H.; Uggerrud, E. *Acta Chem. Scand.* ***1989***, *43*, 26.

[55] McDaniel, D.H.; Evans, W.G. *Inorg. Chem.* ***1966***, *5*, 2180; Sabin, J.R. *J. Chem. Phys.* ***1971***, *54*, 4675.

[56] Calhorda, M.J. *Chem. Commun.* ***2000***, 801.

[57] Ahlberg, P.; Davidsson, O.; Johnsson, B.; McEwen, I.; Rönnqvist, M. *Bull. Soc. Chim. Fr.* ***1988***, 177.

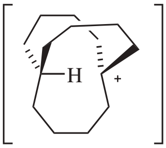
[58] Ferstandig, L.L. *J. Am. Chem. Soc.* ***1962***, *84*, 3553; Allerhand, A.; Schleyer, P.v.R. *J. Am. Chem. Soc.* ***1963***, *85*, 866.

[59] For example, see Bakke, J.M.; Chadwick, D.J. *Acta Chem. Scand. Ser. B* ***1988***, *42*, 223: Atwood, J.L.; Hamada, F.; Robinson, K.D.; Orr, G.W.; Vincent, R.L. *Nature (London)* ***1991***, *349*, 683.

[60] Joris, L.; Schleyer, P.v.R.; Gleiter, R. *J. Am. Chem. Soc.* ***1968***, *90*, 327; Yoshida, Z.; Ishibe, N.; Kusumoto, H. *J. Am. Chem. Soc.* ***1969***, *91*, 2279.

[61] McMurry, J.E.; Lectka, T.; Hodge, C.N. *J. Am. Chem. Soc.* ***1989***, *111*, 8867. See also, Sorensen, T.S.; Whitworth, S.M. *J. Am. Chem. Soc.* ***1990***, *112*, 8135.

called 3-center–2-electron C–H–C bonds.[62] A technique called generalized population analysis has been developed to study this type of multicenter bonding.[63]



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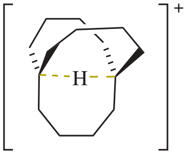
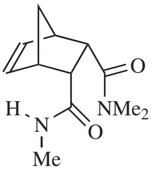


6

A weak (~1.5 kcal mol^{-1}) and rare C–H•••O=C hydrogen bond has been reported in a class of compounds known as a [6]semirubin (a dipyrrinone).[64] There is also evidence for a C–H•••N/CH•••OH bond in the crystal structures of α,β-unsaturated ketones carrying a terminal pyridine subunit,[65] and for R_3N^+–C–H•••O=C hydrogen bonding.[66]

Deuterium also forms hydrogen bonds; in some systems these seem to be stronger than the corresponding hydrogen bonds; in others, weaker.[67]



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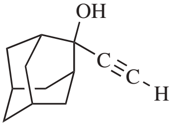

8

Weak hydrogen bonds can be formed between an appropriate hydrogen and a π bond, both with alkenes and with aromatic compounds. For example, IR data in dilute dichloromethane suggests that the predominant conformation for bis (amide) **7** contains an N–H•••π hydrogen bond involving the C=C unit.[68] The strength of an intramolecular π-facial hydrogen bond between an NH group and an aromatic ring in chloroform has been estimated to have a lower limit of -4.5 ± 0.5 kcal mol^{-1}(-18.8 kJ mol^{-1}).[69] A neutron diffraction study of crystalline 2-ethynyladamantan-2-ol (**8**) shows the presence of an unusual O–H•••π

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[62] McMurry, J.E.; Lectka, T. *Acc. Chem. Res.* ***1992***, *25*, 47.

[63] Ponec, R.; Yuzhakov, G.; Tantillo, D.J. *J. Org. Chem.* ***2004***, *69*, 2992.

[64] Huggins, M.T.; Lightner, D.A. *J. Org. Chem.* ***2001***, *66*, 8402.

[65] Mazik, M.; Bläser, D.; Boese, R. *Tetrahedron* ***2001***, *57*, 5791.

[66] Cannizzaro, C.E.; Houk, K.N. *J. Am. Chem. Soc.* ***2002***, *124*, 7163.

[67] Dahlgren Jr., G.; Long, F.A. *J. Am. Chem. Soc.* ***1960***, *82*, 1303; Creswell, C.J.; Allred, A.L. *J. Am. Chem. Soc.* ***1962***, *84*, 3966; Singh, S.; Rao, C.N.R. *Can. J. Chem.* ***1966***, *44*, 2611; Cummings, D.L.; Wood, J.L. *J. Mol. Struct.* ***1974***, *23*, 103.

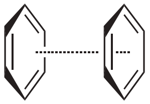
[68] Gallo, E.A.; Gelman, S.H. *Tetrahedron Lett.* ***1992***, *33*, 7485.

[69] Adams, H.; Harris, K.D.M.; Hembury, G.A.; Hunter, C.A.; Livingstone, D.; McCabe, J.F. *Chem. Commun.* ***1996***, 2531. See Steiner, T.; Starikov, E.B.; Tamm, M. *J. Chem. Soc., Perkin Trans. 2* ***1996***, 67 for a related example with 5-ethynyl-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol.

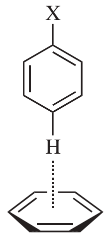
hydrogen bond, which is short and linear, as well as the more common O–H•••O and C–H•••O hydrogen bonds.[70]

π–π INTERACTIONS

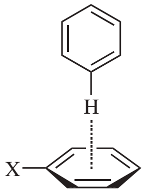
The π–π interactions are fundamental to many supramolecular organization and recognition processes.[71] There are many theoretical and experimental studies that clearly show the importance of π–π interactions.[72] Perhaps the simplest prototype of aromatic π–π interactions is the benzene dimer.[73] Within dimeric aryl systems such as this, possible π–π interactions are the sandwich and T-shaped interactions shown. It has been shown that all substituted sandwich dimers bind more strongly than benzene dimer, whereas the T-shaped configurations bind more or less favorably depending on the substituent.[74] Electrostatic, dispersion, induction, and exchange-repulsion contributions are all significant to the overall binding energies.[74]



Sandwich



T-shaped (1)



T-shaped (2)

The π-electrons of aromatic rings can interact with charged species, yielding strong cation–π interactions dominated by electrostatic and polarization effects.[75] Interactions with CH units is also possible. For CH–π interactions in both alkyl- and aryl-based model systems, dispersion effects dominate the interaction, but the electrostatics term is also relevant for aryl CH–π interactions.[76]

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[70] Allen, F.H.; Howard, J.A.K.; Hoy, V.J.; Desiraju, G.R.; Reddy, D.S.; Wilson, C.C. *J. Am. Chem. Soc.* ***1996***, *118*, 4081.

[71] Meyer, E.A.; Castellano, R.K.; Diederich, F. *Angew. Chem. Int. Ed.* **2003**, *42*, 1210.

[72] Tsuzuki, T.; Uchimaru, T.; Tanabe, K. *J. Mol. Struct.* (*THEOCHEM*) ***1994***, *307*, 107; Hobza, P.; Selzle, H.L.; Schlag, E.W. *J. Phys. Chem.* ***1996***, *100*, 18790; Tsuzuki, S.; Lüthi, H.P. *J. Chem. Phys.* ***2001***, *114*, 3949; Steed, J.M.; Dixon, T.A.; Klemperer, W. *J. Chem. Phys.* ***1979***, *70*, 4940.; Arunan, E.; Gutowsky, H.S. *J. Chem. Phys.* ***1993***, *98*, 4294; Law, K.S.; Schauer, M.; Bernstein, E.R. *J. Chem. Phys.* ***1984***, *81*, 4871; Felker, P.M.; Maxton, P.M.; Schaeffer, M.W. *Chem. Rev.* ***1994***, *94*, 1787; Venturo, V.A.; Felker, P.M. *J. Chem. Phys.* ***1993***, *99*, 748; Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Am. Chem. Soc.* ***2002***, *124*, 104; Hobza, P.; Jurečka, P. *J. Am. Chem. Soc.* ***2003***, *125*, 15608.

[73] Sinnokrot, M.O.; Valeev, E.F.; Sherrill, C.D. *J. Am. Chem. Soc.* ***2002***, *124*, 10887.

[74] Sinnokrot, M.O.; Sherrill, C.D. *J. Am. Chem. Soc.* ***2004***, *126*, 7690

[75] Lindeman, S.V.; Kosynkin, D.; Kochi, J.K. *J. Am. Chem. Soc.* ***1998***, *120*, 13268; Ma, J.C.; Dougherty, D.A. *Chem. Rev.* ***1997***, *97*, 1303; Dougherty, D.A. *Science* ***1996***, *271*, 163; Cubero, E.; Luque, F.J.; Orozco, M. *Proc. Natl. Acad. Sci. U.S.A.* ***1998***, *95*, 5976.

[76] Ribas, J.; Cubero, E.; Luque, F. J.; Orozco, M. *J. Org. Chem.* ***2002***, *67*, 7057.

Detection of π–π interactions has largely relied on NMR-based techniques, such as chemical shifts variations,[77] and Nuclear Overhauser Effect Spectroscopy (NOESY) or Rotating-Frame NOE Spectroscopy (ROESY).[78] Diffusion-ordered NMR spectroscopy (DOSY) has also been used to detect π–π stacked complexes.[79]

ADDITION COMPOUNDS

When the reaction of two compounds results in a product that contains all the mass of the two compounds, the product is called an *addition compound*. There are several kinds. In the rest of this chapter, we will discuss addition compounds in which the molecules of the starting materials remain more or less intact and weak bonds hold two or more molecules together. We can divide them into four broad classes: electron donor–acceptor complexes, complexes formed by crown ethers and similar compounds, inclusion compounds, and catenanes.

Electron Donor–Acceptor (EDA) Complexes[80]

In *EDA complexes*,[81] there is always a donor and an acceptor molecule. The donor may donate an unshared pair (an *n* donor) or a pair of electrons in a π orbital of a double bond or aromatic system (a π donor). One test for the presence of an EDA complex is the electronic spectrum. These complexes generally exhibit a spectrum (called a *charge-transfer spectrum*) that is not the same as the sum of the spectra of the two individual molecules.[82] Because the first excited state of the complex is relatively close in energy to the ground state, there is usually a peak in the visible or near-uv region and EDA complexes are often colored. Many EDA complexes are unstable and exist only in solutions in equilibrium with their components, but others are stable solids. In most EDA complexes the donor and acceptor molecules are present in an integral ratio, most often 1:1, but complexes with nonintegral ratios are also known. There are several types of acceptor molecules; we will discuss complexes formed by two of them.

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[77] Petersen, S.B.; Led, J.J.; Johnston, E.R.; Grant, D.M. *J. Am. Chem. Soc.* ***1982***, *104*, 5007.

[78] Wakita, M.; Kuroda, Y.; Fujiwara, Y.; Nakagawa, T. *Chem. Phys. Lipids* ***1992***, *62*, 45.

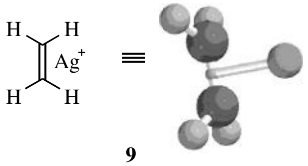
[79] Viel, S.; Mannina, L.; Segre, A. *Tetrahedron Lett.* ***2002***, *43*, 2515. See also, Ribas, J.; Cubero, E.; Luque, F.J.; Orozco, M. *J. Org. Chem.* ***2002***, *67*, 7057.

[80] For monographs, see Foster, R. *Organic Charge-Transfer Complexes*, Academic Press, NY, ***1969***; Mulliken, R.S.; Person, W.B. *Molecular Complexes*, Wiley, NY, ***1969***; Rose, J. *Molecular Complexes*, Pergamon, Elmsford, NY, ***1967***. For reviews, see Poleshchuk, O.Kh.; Maksyutin, Yu.K. *Russ. Chem. Rev.* ***1976***, *45*, 1077; Banthorpe, D.V. *Chem. Rev.* ***1970***, *70*, 295; Kosower, E.M. *Prog. Phys. Org. Chem.* ***1965***, *3*, 81; Foster, R. *Chem. Br.* ***1976***, *12*, 18.

[81] These have often been called *charge-transfer complexes*, but this term implies that the bonding involves charge transfer, which is not always the case, so that the more neutral name EDA complex is preferable. See Mulliken, R.S.; Person, W.B. *J. Am. Chem. Soc.* ***1969***, *91*, 3409.

[82] For examples of EDA complexes that do not show charge-transfer spectra, see Bentley, M.D.; Dewar, M.J.S. *Tetrahedron Lett.* ***1967***, 5043.

1. *Complexes in Which the Acceptor Is A Metal Ion and the Donor an Alkene or an Aromatic Ring* (*n* donors do not give EDA complexes with metal ions but form covalent bonds instead).[83] Many metal ions form complexes, that are often stable solids, with alkenes, dienes (usually conjugated, but not always), alkynes, and aromatic rings. The donor (or ligand) molecules in these complexes are classified by the prefix *hapto*[84] and/or the descriptor η^n (the Greek letter eta), where n indicates how many atoms the ligand uses to bond with the metal.[85] The generally accepted picture of the bonding in these complexes,[86] first proposed by Dewar,[87] can be illustrated by the ethylene complex with silver, **9**, in which the alkene unit forms an η^2-complex with the silver ion (the alkene functions as a 2-electron donating ligand to the metal). There is evidence of π-complexation of Na^+ by C=C.[88]



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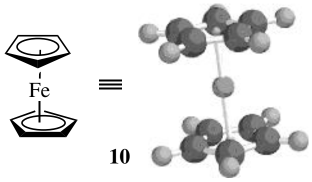

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[83] For monographs, see Collman, J.P.; Hegedus, L.S.; Norton, J.R.; Finke, R.G. *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed, University Science Books, Mill Valley, CA, ***1987***; Alper, H. *Transition Metal Organometallics in Organic Synthesis*, 2 vols., Academic Press, NY, ***1976***, ***1978***; King, R.B. *Transition-Metal Organic Chemistry*, Academic Press, NY, ***1969***; Green, M.L.H. *Organometallic Compounds*, Vol. 2, Methuen, London, ***1968***; For general reviews, see Churchill, M.R.; Mason, R. *Adv. Organomet. Chem.* **1967**, *5*, 93; Cais, M., in Patai, S. *The Chemistry of Alkenes*, Vol. 1, Wiley, NY, ***1964***, pp. 335–385. Among the many reviews limited to certain classes of complexes are transition metals–dienes, Nakamura, A. *J. Organomet. Chem.* ***1990***, *400*, 35; metals-cycloalkynes and arynes, Bennett, M.A.; Schwemlein, H.P. *Angew. Chem. Int. Ed.* ***1989***, *28*, 1296; metals-pentadienyl ions, Powell, P. *Adv. Organomet. Chem.* ***1986***, *26*, 125; complexes of main-group metals, Jutzi, P. *Adv. Organomet. Chem.* ***1986***, *26*, 217; intramolecular complexes, Omae, I. *Angew. Chem. Int. Ed.* ***1982***, *21*, 889; transition metals–olefins and acetylenes, Pettit, L.D.; Barnes, D.S. *Fortschr. Chem. Forsch.* ***1972***, *28*, 85; Quinn, H.W.; Tsai, J.H. *Adv. Inorg. Chem. Radiochem.* ***1969***, *12*, 217; Pt- and Pd-olefins and acetylenes, Hartley, F.R. *Chem. Rev.* ***1969***, *69*, 799; silver ions-olefins and aromatics, Beverwijk, C.D.M.; van der Kerk, G.J.M.; Leusink, J.; Noltes, J.G. *Organomet. Chem. Rev. Sect. A* ***1970***, *5*, 215; metals-substituted olefins, Jones, R. *Chem. Rev.* ***1968***, *68*, 785; transition metals-allylic compounds, Clarke, H.L. *J. Organomet. Chem.* ***1974***, *80*, 155; transition metals–arenes, Silverthorn, W.E. *Adv. Organomet. Chem.* ***1976***, *14*, 47; metals-organosilicon compounds, Haiduc, I.; Popa, V. *Adv. Organomet. Chem.* ***1977***, *15*, 113; metals–carbocations, Pettit, L.D.; Haynes, L.W., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 5, Wiley, NY, ***1976***, pp. 2263–2302; metals-seven-and eight-membered rings, Bennett, M.A. *Adv. Organomet. Chem.* ***1966***, *4*, 353. For a list of review articles on this subject, see Bruce, M.I. *Adv. Organomet. Chem.* ***1972***, *10*, 273, pp. 317–321.

[84] For a discussion of how this system originated, see Cotton, F.A. *J. Organomet. Chem.* ***1975***, *100*, 29.

[85] Another prefix used for complexes is μ (mu), which indicates that the ligand bridges two metal atoms.

[86] For reviews, see Pearson, A.J. *Metallo-organic Chemistry*, Wiley, NY, ***1985***; Ittel, S.D.; Ibers, J.A. *Adv. Organomet. Chem.* ***1976***, *14*, 33; Hartley, F.R. *Chem. Rev.* ***1973***, *73*, 163; *Angew. Chem. Int. Ed.* ***1972***, *11*, 596.

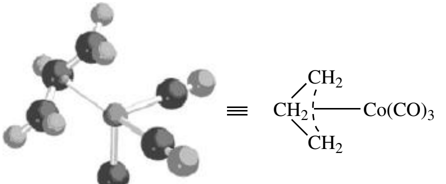
[87] Dewar, M.J.S. *Bull. Soc. Chim. Fr.* ***1951***, *18*, C79.

[88] Hu, J.; Gokel, G.W.; Barbour, L.J. *Chem. Commun.* ***2001***, 1858.

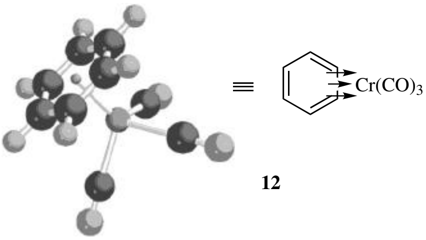
In the case of the silver complex, the bond is not from one atom of the C=C unit to the silver ion, but from the π center such that two electrons are transferred from the alkene to the metal ion.[89] Ethene has two π-electrons and is a dihapto or η^2 ligand, as are other simple alkenes. Similarly, benzene has six π-electrons and is a hexahapto or η^6 ligand. Ferrocene (**10**) has two cyclopentadienyl ligands (each is a five-electron donor or an η^5 ligand), and ferrocene is properly called bis(η^5-cyclopentadienyl)iron(II). This system can be extended to compounds in which only a single σ bond connects the organic group to the metal, for example, C_6H_5–Li (a monohapto or η^1 ligand), and to complexes in which the organic group is an ion, for example, π-allyl complexes, such as **11**, in which the allyl ligand is trihapto or η^3. Note that in a compound such as allyllithium, where a σ bond connects the carbon to the metal, the allyl group is referred to as monohapto or η^1.

$CH_2{=}CH{-}CH_2{-}Li$

Allyllithium



11



12

As mentioned, benzene is an η^6 ligand that forms complexes with silver and other metals.[90] When the metal involved has a coordination number >1, more than one donor molecule (ligand) participates. The CO group is a common ligand (a two-electron donating or η^2 ligand), and in metal complexes the CO group is classified as a metal carbonyl. Benzenechromium tricarbonyl (**12**) is a stable compound[91] that illustrates both benzene and carbonyl ligands. Three arrows are shown to represent the six-electron donation (an η^6 ligand), but the accompanying model gives a clearer picture of the bonding. Cyclooctatetraene is an eight-electron donating or η^8 ligand that also forms complexes with metals. Metallocenes (see **10**) may be considered a special case of this type of complex, although the bonding in

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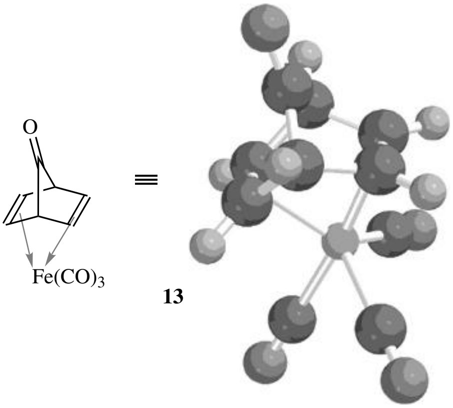
[89] For a discussion of how the nature of the metal ion affects the stability of the complex, see p. $$$.

[90] For a monograph, see Zeiss, H.; Wheatley, P.J.; Winkler, H.J.S. *BenzenoidMetal Complexes*; Ronald Press, NY, ***1966***.

[91] Nicholls, B.; Whiting, M.C. *J. Chem. Soc.* ***1959***, 551. For reviews of arene–transition-metal complexes, see Uemura, M. *Adv. Met.-Org. Chem.* ***1991***, *2*, 195; Silverthorn, W.E. *Adv. Organomet. Chem.* ***1975***, *13*, 47.

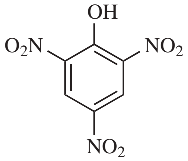
metallocenes is much stronger.



13

In a number of cases, alkenes that are too unstable for isolation have been isolated in the form of metal complexes. As example is norbornadienone, which was isolated in the form of its iron–tricarbonyl complex (**13**),[92] where the norbornadiene unit is an η^4 ligand, and each of the carbonyl units are η^2 ligands. The free dienone spontaneously decomposes to carbon monoxide and benzene (see reaction **17-28**).

2. *Complexes in Which the Acceptor Is an Organic Molecule*. Picric acid, 1,3,5-trinitrobenzene, and similar polynitro compounds are the most important of these.[93] Picric acid forms addition compounds with many aromatic hydrocarbons, aromatic amines, aliphatic amines, alkenes, and other compounds. These addition compounds are usually solids with definite melting points and are often used as derivatives of the compounds in question. They are called picrates, though they are not salts of picric acid, but addition compounds. Unfortunately, salts of picric acid are also called picrates. Similar complexes are formed between phenols and quinones (quinhydrones).[94]



Picric acid

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[92] Landesberg, J.M.; Sieczkowski, J. *J. Am. Chem. Soc.* ***1971***, *93*, 972.

[93] For a review, see Parini, V.P. *Russ. Chem. Rev.* ***1962***, *31*, 408; for a review of complexes in which the acceptor is an organic cation, see Kampar, V.E. *Russ. Chem. Rev.* ***1982***, *51*, 107; also see Ref. 80.

[94] For a review of quinone complexes, see Foster, R.; Foreman, M.I., in Patai, S. *The Chemistry of the Quinonoid Compounds*, pt. 1, Wiley, NY, ***1974***, pp. 257–333.

Alkenes that contain electron-withdrawing substituents also act as acceptor molecules, as do carbon tetrahalides[95] and certain anhydrides.[96] A particularly strong alkene acceptor is tetracyanoethylene.[97]

The bonding in these cases is more difficult to explain than in the previous case, and indeed no really satisfactory explanation is available.[98] The difficulty is that although the donor has a pair of electrons to contribute (both n and π donors are found here), the acceptor does not have a vacant orbital. Simple attraction of the dipole-induced dipole type accounts for some of the bonding,[99] but is too weak to explain the bonding in all cases;[100] for example, nitromethane, with about the same dipole moment as nitrobenzene, forms much weaker complexes. Some other type of bonding clearly must also be present in many EDA complexes. The exact nature of this bonding, called *charge-transfer bonding*, is not well understood, but it presumably involves some kind of donor–acceptor interaction.

Crown Ether Complexes and Cryptates[101]

Crown ethers are large-ring compounds containing several oxygen atoms, usually in a regular pattern. Examples are 12-crown-4 (**14**; where 12 is the size of the ring

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[95] See Blackstock, S.C.; Lorand, J.P.; Kochi, J.K. *J. Org. Chem.* ***1987***, *52*, 1451.

[96] For a review of anhydrides as acceptors, see Foster, R., in Patai, S. *The Chemistry of Acid Derivatives*, pt. 1, Wiley, NY, ***1979***, pp. 175–212.

[97] For a review of complexes formed by tetracyanoethylene and other polycyano compounds, see Melby, L.R., in Rappoport, Z. *The Chemistry of the Cyano Group*, Wiley, NY, ***1970***, pp. 639–669. See also, Fatiadi, A.J. *Synthesis* ***1987***, 959.

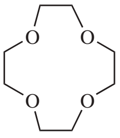
[98] For reviews, see Bender, C.J. *Chem. Soc. Rev.* ***1986***, *15*, 475; Kampar, E.; Neilands, O. *Russ. Chem. Rev.* ***1986***, *55*, 334; Bent, H.A. *Chem. Rev.* ***1968***, *68*, 587.

[99] See, for example, Le Fevre, R.J.W.; Radford, D.V.; Stiles, P.J. *J. Chem. Soc. B* ***1968***, 1297.

[100] Mulliken, R.S.; Person, W.B. *J. Am. Chem. Soc.* ***1969***, *91*, 3409.

[101] For a treatise, see Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, 3 vols.; Academic Press, NY, ***1984***. For monographs, see Weber, E. et al., *Crown Ethers and Analogs*, Wiley, NY, ***1989***; Vögtle, F. *Host Guest Complex Chemistry I, II, and III* (*Top. Curr. Chem. 98, 101, 121*); Springer, Berlin, ***1981***, ***1982***, ***1984***; Vögtle, F.; Weber, E. *Host Guest Complex Chemistry/Macrocycles*, Springer, Berlin, ***1985*** [this book contains nine articles from the *Top. Curr. Chem.* vols. just mentioned]; Hiraoka, M. *Crown Compounds*, Elsevier, NY, ***1982***; De Jong, F.; Reinhoudt, D.N. *Stability and Reactivity of Crown-Ether Complexes*, Academic Press, NY, ***1981***; Izatt, R.M.; Christensen, J.J. *Synthetic Multidentate Macrocyclic Compounds*, Academic Press, NY, ***1978***. For reviews, see McDaniel, C.W.; Bradshaw, J.S.; Izatt, R.M. *Heterocycles*, ***1990***, *30*, 665; Sutherland, I.O. *Chem. Soc. Rev.* ***1986***, *15*, 63; Sutherland, I.O., in Takeuchi, Y.; Marchand, A.P. *Applications of NMR Spectroscopy to Problems in Stereochemistry and Conformational Analysis*, VCH, NY, ***1986***; Franke, J.; Vögtle, F. *Top. Curr. Chem.* ***1986***, *132*, 135; Cram, D.J. *Angew. Chem. Int. Ed.* ***1986***, *25*, 1039; Gutsche, C.D. *Acc. Chem. Res.* ***1983***, *16*, 161; Tabushi, I.; Yamamura, K. *Top. Curr. Chem.* ***1983***, *113*, 145; Stoddart, J.F. *Prog. Macrocyclic Chem.* ***1981***, *2*, 173; De Jong, F.; Reinhoudt, D.N. *Adv. Phys. Org. Chem.* ***1980***, *17*, 279; Vögtle, E.; Weber, E., in Patai, S. *The Chemistry of Functional Groups, Supplement E*, Wiley, NY, ***1980***, pp. 59–156; Poonia, N.S. *Prog. Macrocyclic Chem.* ***1979***, *1*, 115; Reinhoudt, D.N.; De Jong, F. *Prog. Macrocyclic Chem.* ***1979***, *1*, 157; Cram, D.J.; Cram, J.M. *Acc. Chem. Res.* ***1978***, *11*, 8, *Science* ***1974***, *183*, 803; Knipe, A.C. *J. Chem. Educ.* ***1976***, *53*, 618; Gokel, G.W.; Durst, H.D. *Synthesis* ***1976***, 168; *Aldrichimica Acta* ***1976***, *9*, 3; Lehn, J.M. *Struct. Bonding* (*Berlin*) ***1973***, *16*, 1; Christensen, J.J.; Eatough, D.J.; Izatt, R.M. *Chem. Rev.* ***1974***, *74*, 351; Pedersen, C.J.; Frensdorff, H.K. *Angew. Chem. Int. Ed.* ***1972***, *11*, 16.

and 4 represents the number of coordinating atoms, here oxygen),[102] dicyclohexano-18-crown-6 (**15**), and 15-crown-5 (**16**). These compounds have the property[103] of forming complexes with positive ions, generally metallic ions (though not usually ions of transition metals) or ammonium and substituted ammonium ions.[104] The crown ether is called the *host* and the ion is the *guest*. In most cases, the ions are held tightly in the center of the cavity.[105] Each crown ether binds different ions, depending on the size of the cavity. For example, **14** binds Li^{+} [106] but not K^{+},[107] while **15** binds K^{+} but not Li^{+}.[108] Similarly, **15** binds Hg^{2+}, but not Cd^{2+} or Zn^{2+}, and Sr^{2+} but not Ca^{2+}.[109] 18-Crown-5 binds alkali and ammonium cations >1000 times weaker than 18-crown-6, presumably because the larger 18-crown-6 cavity involves more hydrogen bonds.[110] The complexes can frequently be prepared as well-defined sharp-melting solids.



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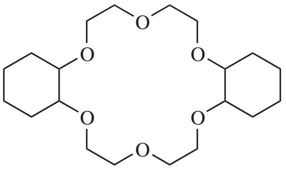

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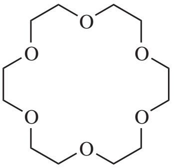


16

For a monograph on the synthesis of crown ethers, see Gokel, G.W.; Korzeniowski, S.H. *Macrocyclic Polyether Synthesis*, Springer, NY, ***1982***. For reviews, see Krakowiak, K.E.; Bradshaw, J.S.; Zamecka-Krakowiak, D.J. *Chem. Rev.* ***1989***, *89*, 929; Jurczak, J.; Pietraszkiewicz, M. *Top. Curr. Chem.* ***1986***, *130*, 183; Gokel, G.W.; Dishong, D.M.; Schultz, R.A.; Gatto, V.J. *Synthesis* ***1982***, 997; Bradshaw, J.S.; Stott, P.E. *Tetrahedron* ***1980***, *36*, 461; Laidler, D.A.; Stoddart, J.F., in Patai, S. *The Chemistry of Functional Groups, Supplement E*, Wiley, NY, ***1980***, pp. 3–42. For reviews of acyclic molecules with similar properties, see Vögtle, E. *Chimia* ***1979***, *33*, 239; Vögtle, E.; Weber, E. *Angew. Chem. Int. Ed.* ***1979***, *18*, 753. For a review of cryptands that hold two positive ions, see Lehn, J.M. *Pure Appl. Chem.* ***1980***, *52*, 2441. The 1987 Nobel Prize in Chemistry was awarded to Charles J. Pedersen, Donald J. Cram, and Jean-Marie Lehn for their work in this area. The three Nobel lectures were published in two journals (respectively, CJP, DJC, J-ML): *Angew. Chem. Int. Ed.* ***1988***, *27* pp. 1021, 1009, 89; and *Chem. Scr.* ***1988***, *28*, pp. 229, 263, 237. See also the series *Advances in Supramolecular Chemistry.*

[102] Cook, F.L.; Caruso, T.C.; Byrne, M.P.; Bowers, C.W.; Speck, D.H.; Liotta, C. *Tetrahedron Lett.* ***1974***, 4029.

[103] Discovered by Pedersen, C.J. *J. Am. Chem. Soc.* ***1967***, *89*, 2495, 7017. For an account of the discovery, see Schroeder, H.E.; Petersen, C.J. *Pure Appl. Chem.* ***1988***, *60*, 445.

[104] For a monograph, see Inoue, Y.; Gokel, G.W. *Cation Binding by Macrocycles*, Marcel Dekker, NY, ***1990***.

[105] For reviews of thermodynamic and kinetic data for this type of interaction, see Izatt, R.M.; Bradshaw, J.S.; Nielsen, S.A.; Lamb, J.D.; Christensen, J.J.; Sen, D. *Chem. Rev.* ***1985***, *85*, 271; Parsonage, N.G.; Staveley, L.A.K., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 3, Academic Press, NY, ***1984***, pp. 1–36.

[106] Anet, F.A.L.; Krane, J.; Dale, J.; Daasvatn, K.; Kristiansen, P.O. *Acta Chem. Scand.* ***1973***, *27*, 3395.

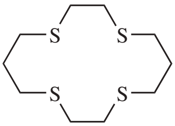
[107] Certain derivatives of 14-crown-4 and 12-crown-3 show very high selectivity for Li^{+} compared to the other alkali metal ions. See Bartsch, R.A.; Czech, B.P.; Kang, S.I.; Stewart, L.E.; Walkowiak, W.; Charewicz, W.A.; Heo, G.S.; Son, B. *J. Am. Chem. Soc.* ***1985***, *107*, 4997; Dale, J.; Eggestad, J.; Fredriksen, S.B.; Groth, P. *J. Chem. Soc., Chem. Commun.* ***1987***, 1391; Dale, J.; Fredriksen, S.B. *Pure Appl. Chem.* ***1989***, *61*, 1587.

[108] Izatt, R.M.; Nelson, D.P.; Rytting, J.H.; Haymore, B.L.; Christensen, J.J. *J. Am. Chem. Soc.* ***1971***, *93*, 1619.

[109] Kimura, Y.; Iwashima, K.; Ishimori, T.; Hamaguchi, H. *Chem. Lett.* ***1977***, 563.

[110] Raevsky, O.A.; Solov'ev, V.P.; Solotnov, A.F.; Schneider, H.-J.; Rüdiger, V. *J. Org. Chem.* ***1996***, *61*, 8113.

Apart from their obvious utility in separating mixtures of cations,[111] crown ethers have found much use in organic synthesis (see the discussion on p. 510). Chiral crown ethers have been used for the resolution of racemic mixtures (p. 138). Although crown ethers are most frequently used to complex cations, amines, phenols, and other neutral molecules have also been complexed[112] (see p. 189 for the complexing of anions).[113] Macrocycles containing nitrogen (aza-crown ethers) or sulfur atoms (thiacrown ethers),[114] such as **17** and **18**,[115] have complexing properties similar to other crown ethers, as do mixed heteroatom crown ethers such as **19**,[116] **20**,[117] or **21**.[118]



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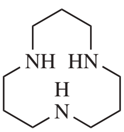

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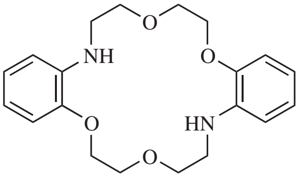

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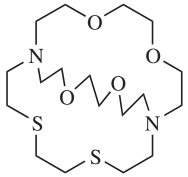

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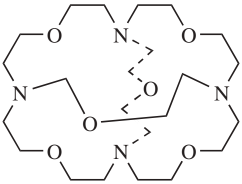

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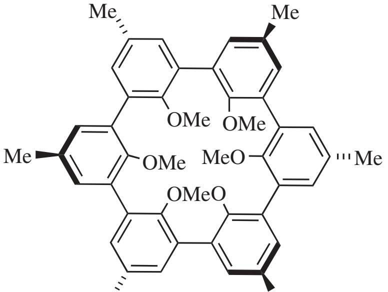

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[111] Crown ethers have been used to separate isotopes of cations, for example, ^{44}Ca from ^{40}Ca. For a review, see Heumann, K.G. *Top. Curr. Chem.* ***1985***, *127*, 77.

[112] For reviews, see Vögtle, F.; Müller, W.M.; Watson, W.H. *Top. Curr. Chem.* ***1984***, *125*, 131; Weber, E. *Prog. Macrocycl. Chem.* ***1987***, *3*, 337; Diederich, F. *Angew. Chem. Int. Ed.* ***1988***, *27*, 362.

[113] A neutral molecule (e.g., urea) and a metal ion (e.g., Li^+) were made to be joint guests in a macrocyclic host, with the metal ion acting as a bridge that induces a partial charge on the urea nitrogens: van Staveren, C.J.; van Eerden, J.; van Veggel, F.C.J.M.; Harkema, S.; Reinhoudt, D.N. *J. Am. Chem. Soc.* ***1988***, *110*, 4994. See also, Rodrigue, A.; Bovenkamp, J.W.; Murchie, M.P.; Buchanan, G.W.; Fortier, S. *Can. J. Chem.* ***1987***, *65*, 2551; Fraser, M.E.; Fortier, S.; Markiewicz, M.K.; Rodrigue, A.; Bovenkamp, J.W. *Can. J. Chem.* ***1987***, *65*, 2558.

[114] For reviews of sulfur-containing macroheterocycles, see Voronkov, M.G.; Knutov, V.I. *Sulfur Rep.* ***1986***, *6*, 137, *Russ. Chem. Rev.* ***1982***, *51*, 856. For a review of those containing S and N, see Reid, G.; Schröder, M. *Chem. Soc. Rev.* ***1990***, *19*, 239.

[115] For a review of **17** and its derivatives, see Chaudhuri, P.; Wieghardt, K. *Prog. Inorg. Chem.* ***1987***, *35*, 329. *N*-Aryl-azacrown ethers are known, see Zhang, X.-X.; Buchwald, S.L. *J. Org. Chem.* ***2000***, *65*, 8027.

[116] Gersch, B.; Lehn, J.-M.; Grell, E. *Tetrahedron Lett.* ***1996***, *37*, 2213.

[117] Newcomb, M.; Gokel, G.W.; Cram, D.J. *J. Am. Chem. Soc.* ***1974***, *96*, 6810.

[118] Graf, E.; Lehn, J.M. *J. Am. Chem. Soc.* ***1975***, *97*, 5022; Ragunathan, K.G.; Shukla, R.; Mishra, S.; Bharadwaj, P.K. *Tetrahedron Lett.* ***1993***, *34*, 5631.

Bicyclic molecules like **20** can surround the enclosed ion in three dimensions, binding it even more tightly than the monocyclic crown ethers. Bicyclics and cycles of higher order[119] are called *cryptands* and the complexes formed are called *cryptates* (monocyclic compunds are sometimes called cryptands). When the molecule contains a cavity that can accommodate a guest molecule, usually through hydrogen-bonding interactions, it is sometimes called a cavitand.[120] The tricyclic cryptand **21** has 10 binding sites and a spherical cavity.[93] Another molecule with a spherical cavity (though not a cryptand) is **22**, which complexes Li^+ and Na^+ (preferentially Na^+), but not K^+, Mg^{2+}, or Ca^{2+}.[121] Molecules such as these, whose cavities can be occupied only by spherical entities, have been called *spherands*.[77] Other types are *calixarenes*,[122] for example, **23**.[123] Spherand-type calixarenes are known.[124] There is significant hydrogen bonding involving the phenolic OH units in [4]calixarenes, but this diminishes as the size of the cavity increases in larger ring calixarenes.[125] There are also calix[6]arenes,[126] which have been shown to have conformational isomers (see p. 195) in equilibrium (cone vs. alternate) that can sometimes be isolated:[127] calix[8]arenes,[128] azacalixarenes,[129] homooxacalixarenes,[130]

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[119] For reviews, see Potvin, P.G.; Lehn, J.M. *Prog. Macrocycl. Chem.* ***1987***, *3*, 167; Kiggen, W.; Vögtle, F. *Prog. Macrocycl. Chem.* ***1987***, *3*, 309; Dietrich, B., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 2, Academic Press, NY, ***1984***, pp. 337–405; Parker, D. *Adv. Inorg. Radichem.* ***1983***, *27*, 1; Lehn, J.M. *Acc. Chem. Res.* ***1978***, *11*, 49, *Pure Appl. Chem.* ***1977***, *49*, 857.

[120] Shivanyuk, A.; Spaniol, T.P.; Rissanen, K.; Kolehmainen, E.; Böhmer, V. *Angew. Chem. Int. Ed.* ***2000***, *39*, 3497.

[121] Cram, D.J.; Doxsee, K.M. *J. Org. Chem.* ***1986***, *51*, 5068; Cram, D.J. *CHEMTECH* ***1987***, 120, *Chemtracts: Org. Chem.* ***1988***, *1*, 89; Bryany, J.A.; Ho, S.P.; Knobler, C.B.; Cram, D.J. *J. Am. Chem. Soc.* ***1990***, *112*, 5837.

[122] Shinkai, S. *Tetrahedron* ***1993***, *49*, 8933.

[123] For monographs, see Vicens, J.; Böhmer, V. *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Kluver, Dordrecht, ***1991***; Gutsche, C.D. *Calixarenes*; Royal Society of Chemistry: Cambridge, ***1989***. For reviews, see Gutsche, C.D. *Prog. Macrocycl. Chem.* ***1987***, *3*, 93, *Top. Curr. Chem.* ***1984***, *123*, 1. Also see Geraci, C.; Piatelli, M.; Neri, P. *Tetrahedron Lett.* ***1995***, *36*, 5429; Deng, G.; Sakaki, T.; Kawahara, Y.; Shinkai, S. *Tetrahedron Lett.* ***1992***, *33*, 2163; Zhong, Z.-L.; Chen, Y.-Y.; Lu, X.-R. *Tetrahedron Lett.* ***1995***, *36*, 6735; No, K.; Kim, J.E.; Kwon, K.M. *Tetrahedron Lett.* ***1995***, *36*, 8453.

[124] Agbaria, K.; Aleksiuk, O.; Biali, S.E.; Böhmer, V.; Frings, M.; Thondorf, I. *J. Org. Chem.* ***2001***, *66*, 2891. For the stereochemistry of such compounds, see Agbaria, K.; Biali, S.E.; Böhmer, V.; Brenn, J.; Cohen, S.; Frings, M., Grynszpan, F.; Harrowfield, J.Mc B.; Sobolev, A.N.; Thondorf, I. *J. Org. Chem.* ***2001***, *66*, 2900.

[125] Cerioni, G.; Biali, S.E.; Rappoport, Z. *Tetrahedron Lett.* ***1996***, *37*, 5797. For a synthesis of calix[4]arene see Molard, Y.; Bureau, C.; Parrot-Lopez, H.; Lamartine, R.; Regnourf-de-Vains, J.-B. *Tetrahedron Lett.* ***1999***, *40*, 6383.

[126] Otsuka, H.; Araki, K.; Matsumoto, H.; Harada, T.; Shinkai, S. *J. Org. Chem.* ***1995***, *60*, 4862.

[127] Neri, P.; Rocco, C.; Consoli, G.M.L.; Piatelli; M. *J. Org. Chem.* ***1993***, *58*, 6535; Kanamathareddy, S.; Gutsche, C.D. *J. Org. Chem.* ***1994***, *59*, 3871.

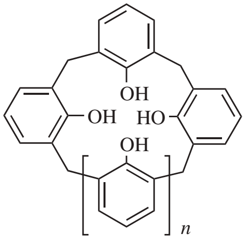
[128] Cunsolo, F.; Consoli, G.M.L.; Piatelli; M.; Neri, P. *Tetrahedron Lett.* ***1996***, *37*, 715; Geraci, C.; Piatelli, M.; Neri, P. *Tetrahedron Lett.* ***1995***, *36*, 5429.

[129] Miyazaki, Y.; Kanbara, T.; Yamamoto, T. *Tetrahedron Lett.* ***2002***, *43*, 7945; Khan, I.U.; Takemura, H.; Suenaga, M.; Shinmyozu, T.; Inazu, T. *J. Org. Chem.* ***1993***, *58*, 3158.

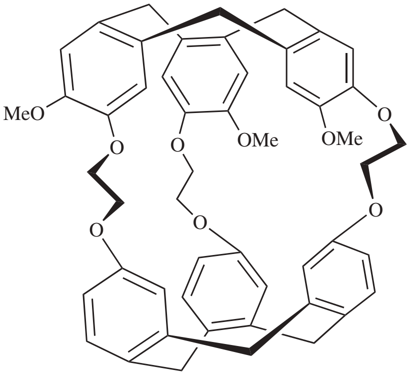
[130] Masci, B. *J. Org. Chem.* ***2001***, *66*, 1497. For dioxocalix[4]arenes, see Seri, N.; Thondorf, I.; Biali, S.E. *J. Org. Chem.* ***2004***, *69*, 4774. For tetraoxacalix[3]arenes, see Tsubaki, K.; Morimoto, T.; Otsubo, T.; Kinoshita, T.; Fuji, K. *J. Org. Chem.* ***2001***, *66*, 4083.

and calix[9–20]arenes.[131] Note that substitution of the unoccupied “meta” positions immobilizes calix[4]arenes and substantially reduces the conformational mobility (see p. 211) in calix[8]arenes.[132] Amide-bridged calix[4]arenes[133] calix[4]azulene,[134] and quinone-bridged calix[6]arenes[135] are known, and diammoniumcalix[4]arene has been prepared.[136] Enantiopure calix[4]resorcinarene derivatives are known,[137] and water soluble calix[4]arenes have been prepared.[138] There are also a variety of calix[*n*]-crown ethers,[139] some of which are cryptands.[140]

calix[4]arene, $n = 1$
calix[6]arene, $n = 3$
calix[8]arene, $n = 5$



23



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Other molecules include *cryptophanes*, for example, **24**,[141] *hemispherands* (an example is **25**[142]), and *podands*.[143] The last-named are host compounds in which two or more arms come out of a central structure. Examples are **26**[144] and **27**[145] and the latter molecule binds simple cations, such as Na^+, K^+, and Ca^{2+}. *Lariat ethers* are compounds containing a crown ether ring with one or more side chains

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[131] Stewart, D.R.; Gutsche, C.D. *J. Am. Chem. Soc.* ***1999***, *121*, 4136.

[132] Mascal, M.; Naven, R.T.; Warmuth, R. *Tetrahedron Lett.* ***1995***, *36*, 9361.

[133] Wu, Y.; Shen, X.-P.; Duan, C.-y.; Liu, Y.-i.; Xu, Z. *Tetrahedron Lett.* ***1999***, *40*, 5749.

[134] Colby, D.A.; Lash, T.D. *J. Org. Chem.* ***2002***, *67*, 1031.

[135] Akine, S.; Goto, K.; Kawashima, T. *Tetrahedron Lett.* ***2000***, *41*, 897.

[136] Aeungmaitrepirom, W.; Hagège, A.; Asfari, Z.; Bennouna, L.; Vicens, J.; Leroy, M. *Tetrahedron Lett.* ***1999***, *40*, 6389.

[137] Page, P.C.B.; Heaney, H.; Sampler, E.P. *J. Am. Chem. Soc.* ***1999***, *121*, 6751.

[138] Shimizu, S.; Shirakawa, S.; Sasaki, Y.; Hirai, C. *Angew. Chem. Int. Ed.* ***2000***, *39*, 1256.

[139] Stephan, H.; Gloe, K.; Paulus, E.F.; Saadioui, M.; Böhmer, V. *Org. Lett.* ***2000***, *2*, 839; Asfari, Z.; Thuéry, P.; Nierlich, M.; Vicens, J. *Tetrahedron Lett.* ***1999***, *40*, 499; Geraci, C.; Piattelli, M.; Neri, P. *Tetrahedron Lett.* ***1996***, *37*, 3899; Pappalardo, S.; Petringa, A.; Parisi, M.F.; Ferguson, G. *Tetrahedron Lett.* ***1996***, *37*, 3907.

[140] Pulpoka, B.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* ***1996***, *37*, 6315.

[141] For reviews, see Collet, A. *Tetrahedron* ***1987***, *43*, 5725, in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 1, Academic Press, NY, ***1984***, pp. 97–121.

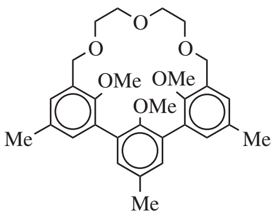
[142] Lein, G.M.; Cram, D.J. *J. Am. Chem. Soc.* ***1985***, *107*, 448.

[143] For reviews, see Kron, T.E.; Tsvetkov, E.N. *Russ. Chem. Rev.* ***1990***, *59*, 283; Menger, F.M. *Top. Curr. Chem.* ***1986***, *136*, 1.

[144] Tümmler, B.; Maass, G.; Weber, E.; Wehner, W.; Vögtle, F. *J. Am. Chem. Soc.* ***1977***, *99*, 4683.

[145] Vögtle, F.; Weber, E. *Angew. Chem. Int. Ed.* ***1974***, *13*, 814.

that can also serve as ligands, for example, **28**.[146] There is also a class of ortho cyclophanes that are crown ethers (see **29**) and have been given the name *starands*.[147]



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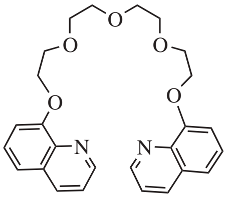

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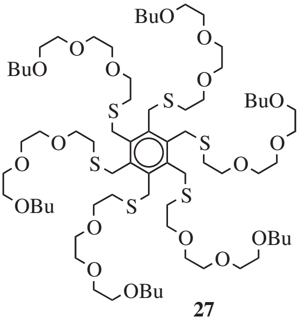

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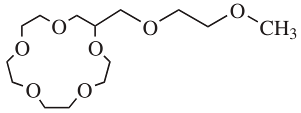

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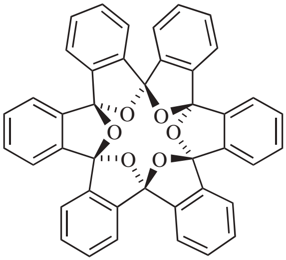

29

The bonding in these complexes is the result of ion-dipole attractions between the heteroatoms and the positive ions. The parameters of the host–guest interactions can sometimes be measured by NMR.[148]

As we have implied, the ability of these host molecules to bind guests is often very specific, often linked to the hydrogen-bonding ability of the host,[149] enabling the host to pull just one molecule or ion out of a mixture. This is called *molecular recognition*.[150] In general, cryptands, with their well-defined 3D cavities, are better for this than monocyclic crown ethers or ether derivatives. An example is the host **30**, which selectively binds the dication **31** ($n = 5$) rather than **31** ($n = 4$), and **31** ($n = 6$) rather than **31** ($n = 7$).[151] The host **32**, which is water soluble, forms 1:1 complexes with neutral aromatic hydrocarbons, such as pyrene and fluoranthene,

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[146] See Gatto, V.J.; Dishong, D.M.; Diamond, C.J. *J. Chem. Soc., Chem. Commun.* ***1980***, 1053; Gatto, V.J.; Gokel, G.W. *J. Am. Chem. Soc.* ***1984***, *106*, 8240; Nakatsuji, Y.; Nakamura, T.; Yonetani, M.; Yuya, H.; Okahara, M. *J. Am. Chem. Soc.* ***1988***, *110*, 531.

[147] Lee, W.Y.; Park, C.H. *J. Org. Chem.* ***1993***, *58*, 7149.

[148] Wang, T.; Bradshaw, J.S.; Izatt, R.M. *J. Heterocylic Chem.* ***1994***, *31*, 1097.

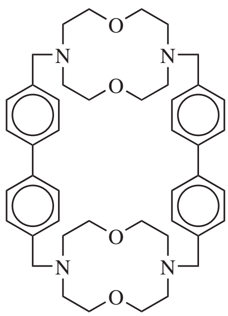
[149] Fujimoto, T.; Yanagihara, R.; Koboyashi, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* ***1995***, *68*, 2113.

[150] For reviews, see Rebek Jr., J. *Angew. Chem. Int. Ed.* ***1990***, *29*, 245; *Acc. Chem. Res.* ***1990***, *23*, 399; *Top. Curr. Chem.* ***1988***, *149*, 189; Diederich, F. *J. Chem. Educ.* ***1990***, *67*, 813; Hamilton, A.D. *J. Chem. Educ.* ***1990***, *67*, 821; Raevskii, O.A. *Russ. Chem. Rev.* ***1990***, *59*, 219.

[151] Mageswaran, R.; Mageswaran, S.; Sutherland, I.O. *J. Chem. Soc., Chem. Commun.* ***1979***, 722.

and even (though more weakly) with biphenyl and naphthalene, and is able to transport them through an aqueous phase.[152]

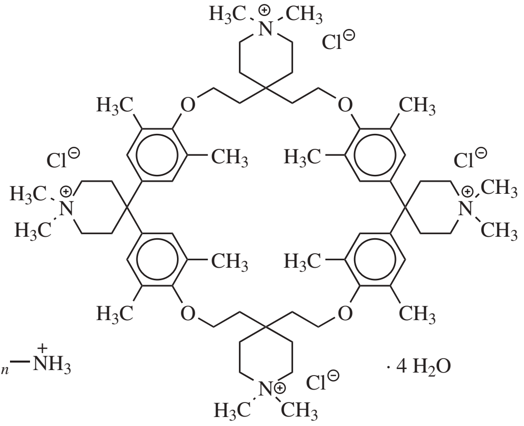
Of course, it has long been known that molecular recognition is very important in biochemistry. The action of enzymes and various other biological molecules is extremely specific because these molecules also have host cavities that are able to recognize only one or a few particular types of guest molecules. It is only in recent years that organic chemists have been able to synthesize nonnatural hosts that can also perform crude (compared to biological molecules) molecular recognition. The macrocycle **33** has been used as a catalyst, for the hydrolysis of acetyl phosphate and the synthesis of pyrophosphate.[153]



30

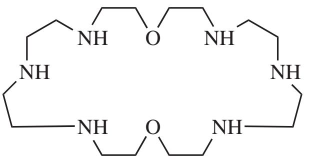
$H_3\overset{+}{N}—(CH_2)_n—\overset{+}{N}H_3$

31



32

No matter what type of host, the strongest attractions occur when combination with the guest causes the smallest amount of distortion of the host.[154] That is, a fully preorganized host will bind better than a host whose molecular shape must change in order to accommodate the guest.



33

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[152] Diederich, F.; Dick, K. *J. Am. Chem. Soc.* ***1984***, *106*, 8024; Diederich, F.; Griebe, D. *J. Am. Chem. Soc.* ***1984***, *106*, 8037. See also Vögtle, F.; Müller, W.M.; Werner, U.; Losensky, H. *Angew. Chem. Int. Ed.* ***1987***, *26*, 901.

[153] Hosseini, M.W.; Lehn, J.M. *J. Am. Chem. Soc.* ***1987***, *109*, 7047. For a discussion, see Mertes, M.P.; Mertes, K.B. *Acc. Chem. Res.* ***1990***, *23*, 413.

[154] See Cram, D.J. *Angew. Chem. Int. Ed.* ***1986***, *25*, 1039.

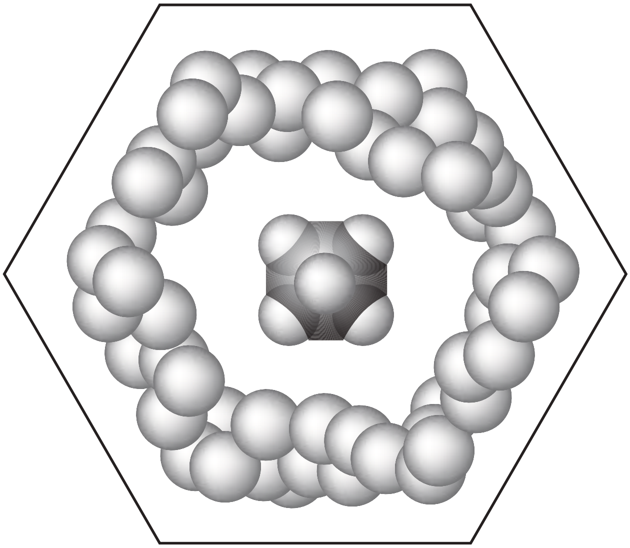

Fig. 3.1. Guest molecule in a urea lattice.[157]

Inclusion Compounds

This type of addition compound is different from either the EDA complexes or the crown ether type of complexes previously discussed. Here, the host forms a crystal lattice that has spaces large enough for the guest to fit into. There is no bonding between the host and the guest except van der Waals forces. There are two main types, depending on the shape of the space.[155] The spaces in *inclusion compounds* are in the shape of long tunnels or channels, while the other type, often called *clathrate*,[156] or *cage compounds* have spaces that are completely enclosed. In both types, the guest molecule must fit into the space and potential guests that are too large or too small will not go into the lattice, so that the addition compound will not form.[157]

One important host molecule among the inclusion compounds is urea.[158] Ordinary crystalline urea is tetragonal, but when a guest is present, urea crystallizes in a hexagonal lattice, containing the guest in long channels (Fig. 3.1).[157]

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[155] For a treatise that includes both types, see Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vols. 1–3, Academic Press, NY, ***1984***. For reviews, see Weber, E. *Top. Curr. Chem.* ***1987***, *140*, 1; Gerdil, R. *Top. Curr. Chem.* ***1987***, *140*, 71; Mak, T.C.W.; Wong, H.N.C. *Top. Curr. Chem.* ***1987***, *140*, 141. For a review of channels with helical shapes, see Bishop, R.; Dance, I.G. *Top. Curr. Chem.* ***1988***, *149*, 137.

[156] For reviews, see Goldberg, I. *Top. Curr. Chem.* ***1988***, *149*, 1; Weber, E.; Czugler, M. *Top. Curr. Chem.* ***1988***, *149*, 45; MacNicol, D.D.; McKendrick, J.J.; Wilson, D.R. *Chem. Soc. Rev.* ***1978***, *7*, 65.

[157] This picture is taken from a paper by Montel, G. *Bull. Soc. Chim. Fr.* ***1955***, 1013.

[158] For a review of urea and thiourea inclusion compounds, see Takemoto, K.; Sonoda, N., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 2, Academic Press, NY, ***1984***, pp. 47–67.

The hexagonal type of lattice can form only when a guest molecule is present, showing that van der Waals forces between the host and the guest, while small, are essential to the stability of the structure. The diameter of the channel is ∼5 Å, and which molecules can be guests is dependent only on their shapes and sizes and not on any electronic or chemical effects. For example, octane and 1-bromooctane are suitable guests for urea, but 2-bromooctane, 2-methylheptane, and 2-methyloctane are not. Also both dibutyl maleate and dibutyl fumarate are guests; neither diethyl maleate or diethyl fumarate is a guest, but dipropyl fumarate is a guest and dipropyl maleate is not.[159] In these complexes, there is usually no integral molar ratio (though by chance there may be). For example, the octane/urea ratio is 1:6.73.[160] A deuterium quadrupole echo spectroscopy study of a urea complex showed that the urea molecules do not remain rigid, but undergo 180° flips about the C=O axis at the rate of $>10^6$ sec^{-1} at 30°C.[161]

The complexes are solids, but are not useful as derivatives, since they melt with decomposition of the complex at the melting point of urea. They are useful, however, in separating isomers that would be quite difficult to separate otherwise. Thiourea also forms inclusion compounds though with channels of larger diameter, so that *n*-alkanes cannot be guests but, for example, 2-bromooctane, cyclohexane, and chloroform readily fit.

The most important host for clathrates is hydroquinone.[162] Three molecules, held together by hydrogen bonding, make a cage in which fits one molecule of guest. Typical guests are methanol (but not ethanol), SO_2, CO_2, and argon (but not neon). One important use is the isolation of anhydrous hydrazine as complex.[163] Its highly explosive nature makes the preparation of anhydrous hydrazine by distillation of aqueous hydrazine solutions difficult and dangerous. The inclusion complex can be readily isolated and reactions done in the solid state, such as the reaction with esters to give hydrazides (reaction **16-75**).[163] In contrast to the inclusion compounds, the crystal lattices here can exist partially empty. Another host is water. Usually six molecules of water form the cage and many guest molecules, among them Cl_2, propane, and methyl iodide, can fit. The water clathrates, which are solids, can normally be kept only at low temperatures; at room temperature, they decompose.[164] Another inorganic host is sodium chloride (and some other alkali halides), which can encapsulate organic molecules, such as benzene, naphthalene, and diphenylmethane.[165]

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[159] Radell, J.; Connolly, J.W.; Cosgrove Jr., W.R. *J. Org. Chem.* ***1961***, *26*, 2960.

[160] Redlich, O.; Gable, C.M.; Dunlop, A.K.; Millar, R.W. *J. Am. Chem. Soc.* ***1950***, *72*, 4153.

[161] Heatom, N.J.; Vold, R.L.; Vold, R.R. *J. Am. Chem. Soc.* ***1989***, *111*, 3211.

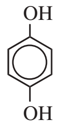
[162] For a review, see MacNicol, D.D., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 2, Academic Press, NY, ***1984***, pp. 1–45.

[163] Toda, F.; Hyoda, S.; Okada, K.; Hirotsu, K. *J. Chem. Soc., Chem. Commun.* ***1995***, 1531.

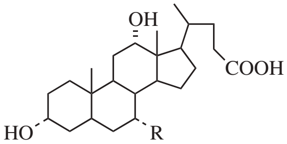
[164] For a monograph on water clathrates, see Berecz, E.; Balla-Achs, M. *Gas Hydrates*; Elsevier, NY, ***1983***. For reviews, see Jeffrey, G.A., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 1, Academic Press, NY, ***1984***, pp. 135–190; Cady, G.H. *J. Chem. Educ.* ***1983***, *60*, 915; Byk, S.Sh.; Fomina, V.I. *Russ. Chem. Rev.* ***1968***, *37*, 469.

[165] Kirkor, E.; Gebicki, J.; Phillips, D.R.; Michl, J. *J. Am. Chem. Soc.* ***1986***, *108*, 7106.

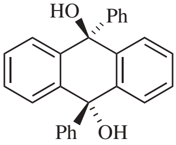
Among other hosts[166] for inclusion and/or clathrate compounds are deoxycholic acid,[167] cholic acid,[168] anthracene compounds, such as **34**,[169] dibenzo-24-crown-8,[170] and the compound **35**, which has been called a *carcerand*.[171] When carcerand-type molecules trap ions or other molecules (called guests), the resulting complex is called a carciplex.[172] It has been shown that in some cases, the motion of the guest within the carciplex is restricted.[173]



Hydroquinone



cholic acid (R = OH)
deoxycholic acid (R = H)



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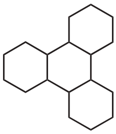
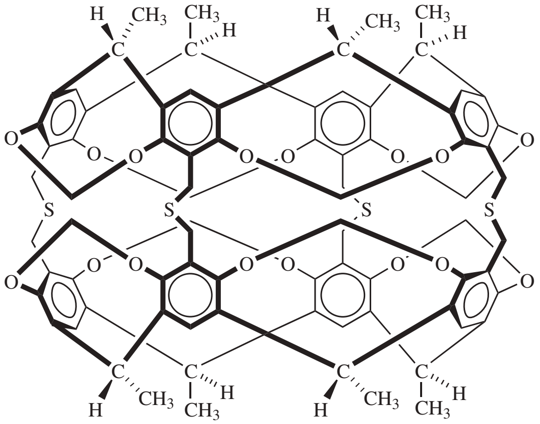


Perhydrotriphenylene



35

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[166] See also Toda, F. *Pure App. Chem.* ***1990***, *62*, 417, *Top. Curr. Chem.* ***1988***, *149*, 211; ***1987***, *140*, 43; Davies, J.E.; Finocchiaro, P.; Herbstein, F.H., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 2, Academic Press, NY, ***1984***, pp. 407–453.

[167] For a review, see Giglio, E., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 2, Academic Press, NY, ***1984***, pp. 207–229.

[168] See Miki, K.; Masui, A.; Kasei, N.; Miyata, M.; Shibakami, M.; Takemoto, K. *J. Am. Chem. Soc.* ***1988***, *110*, 6594.

[169] Barbour, L.J.; Caira, M.R.; Nassimbeni, L.R. *J. Chem. Soc., Perkin Trans. 2* ***1993***, 2321. Also see, Barbour, L.J.; Caira, M.R.; Nassimbeni, L.R. *J. Chem. Soc., Perkin Trans. 2* ***1993***, 1413 for a dihydroanthracene derivative that enclathrates diethyl ether.

[170] Lämsä, M.; Suorsa, T.; Pursiainen, J.; Huuskonen, J.; Rissanen, K. *Chem. Commun.* ***1996***, 1443.

[171] Sherman, J.C.; Knobler, C.B.; Cram, D.J. *J. Am. Chem. Soc.* ***1991***, *113*, 2194.

[172] Kurdistani, S.K.; Robbins, T.A.; Cram, D.J. *J. Chem. Soc., Chem. Commun.* ***1995***, 1259; Timmerman, P.; Verboom, W.; van Veggel, F.C.J.M.; van Duynhoven, J.P.M.; Reinhoudt, D.N. *Angew. Chem. Int. Ed.* ***1994***, *33*, 2345; van Wageningen, A.M.A.; Timmerman, P.; van Duynhoven, J.P.M.; Verboom, W.; van Veggel, F.C.J.M.; Reinhoudt, D.N. *Chem. Eur. J.* ***1997***, *3*, 639; Fraser, J.R.; Borecka, B.; Trotter, J.; Sherman, J.C. *J. Org. Chem.* ***1995***, *60*, 1207; Place, D.; Brown, J.; Deshayes, K. *Tetrahedron Lett.* ***1998***, *39*, 5915. See also: Jasat, A.; Sherman, J.C. *Chem. Rev.* ***1999***, *99*, 931.

[173] Chapman, R.G.; Sherman, J.C. *J. Org. Chem.* ***2000***, *65*, 513.

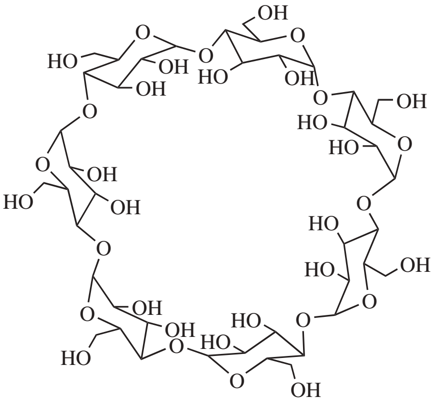

Fig. 3.2. β-Cyclodextrin.

Cyclodextrins

There is one type of host that can form both channel and cage complexes. This type is called *cyclodextrins* or *cycloamyloses*.[174] The host molecules are made up of six, seven, or eight glucose units connected in a large ring, called, respectively, α-, β-, or γ-cyclodextrin (Fig. 3.2 shows the β or seven-membered ring compound). The three molecules are in the shape of hollow truncated cones (Fig. 3.3) with primary OH groups projecting from the narrow side of the cones and secondary OH group from the wide side. As expected for carbohydrate molecules, all of them are soluble in water and the cavities normally fill with water molecules held in place by hydrogen bonds (6, 12, and 17 H_2O molecules for the α, β, and γ forms, respectively), but the insides of the cones are less polar than the outsides, so that nonpolar organic molecules readily displace the water. Thus the cyclodextrins form 1:1 cage complexes with many guests, ranging in size from the noble gases to large organic molecules. A guest molecule must not be too large or it will not fit, though many stable complexes are known in which one end of the guest molecule protrudes from the cavity (Fig. 3.4). On the other hand, if the guest is too small, it may go through the bottom hole (though some small polar molecules, e.g., methanol, do form complexes in which the cavity also contains some water molecules). Since the cavities of the three cyclodextrins are of different sizes (Fig. 3.3), a large variety of guests can be

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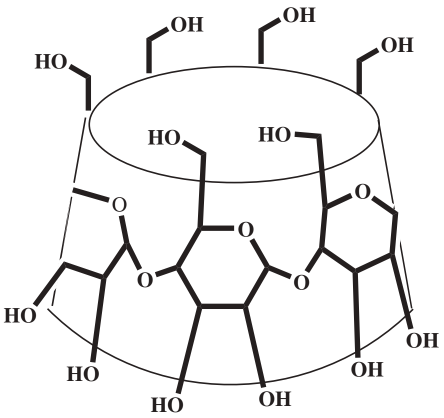
[174] For a monograph, see Bender, M.L.; Komiyama, M. *Cyclodextrin Chemistry*, Springer, NY, ***1978***. For reviews, see, in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Academic Press, NY, ***1984***, the reviews, by Saenger, W. Vol. 2, 231–259, Bergeron, R.J. Vol. 3, 391–443, Tabushi, I. Vol. 3, 445–471, Breslow, R. Vol. 3, 473–508; Croft, A.P.; Bartsch, R.A. *Tetrahedron* ***1983***, *39*, 1417; Tabushi, I.; Kuroda, Y. *Adv. Catal.*, ***1983***, *32*, 417; Tabushi, I. *Acc. Chem. Res.* ***1982***, *15*, 66; Saenger, W. *Angew. Chem. Int. Ed.* ***1980***, *19*, 344; Bergeron, R. *J. Chem. Ed.* ***1977***, *54*, 204; Griffiths, D.W.; Bender, M.L. *Adv. Catal.* ***1973***, *23*, 209.



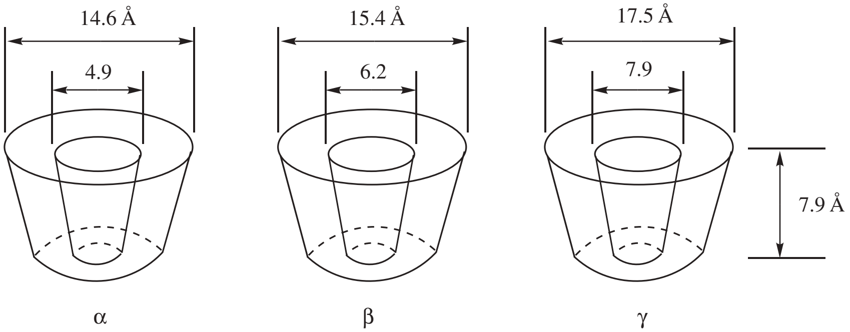


Fig. 3.3. Shape and dimensions of the α-, β-, and γ-cyclodextrin molecules.[175]

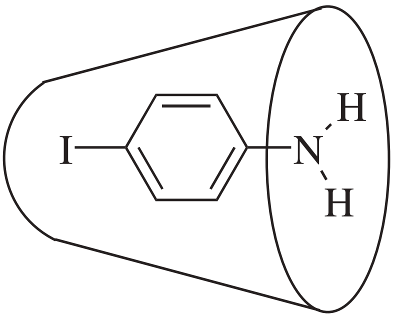


Fig. 3.4. Schematic drawing of the complex of α-cyclodextrin and *p*-iodoaniline.[176]

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[175] Szejtli, J., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 3, Academic Press, NY, ***1984***, p. 332; Nickon, A.; Silversmith, E.F. *The Name Game*, Pergamon, Elmsford, NY, p. 235.

[176] Modified from Saenger, W.; Beyer, K.; Manor, P.C. *Acta Crystallogr. Sect. B* ***1976***, *32*, 120.

accommodated. Since cyclodextrins are nontoxic (they are actually small starch molecules), they are now used industrially to encapsulate foods and drugs.[177]

The cyclodextrins also form channel-type complexes, in which the host molecules are stacked on top of each other, like coins in a row.[178] For example, α-cyclodextrin (cyclohexaamylose) forms cage complexes with acetic, propionic, and butyric acids, but channel complexes with valeric and higher acids. Capped cyclodextrins are known.[179]

Catenanes and Rotaxanes[180]

These compounds contain two or more independent portions that are not bonded to each other by any valence forces but nevertheless must remain linked. [*n*]-*Catenanes* (where *n* corresponds to the number of linked rings) are made up of two or more rings held together as links in a chain, while in *rotaxanes* a linear portion is threaded through a ring and cannot get away because of bulky end groups. Among several types of bulky molecular units, porphyrin units have been used to cap rotaxanes[181] as have C_{60} fullerenes.[182] [2]-Rotaxanes and [2]-catenanes are quite common, and [3]-catenanes are known having rather robust amide linkages.[183] More intricate variants, such as oligocatenanes,[184] molecular necklaces (a cyclic oligorotaxane in which a number of small rings are threaded onto a large ring),[185] and cyclic daisy chains (an interwoven chain in which each monomer unit acts as a donor and an acceptor for a threading

A [2]-catenane

A [3]-catenane

A rotaxane

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[177] For reviews, see Pagington, J.S. *Chem. Br.* ***1987***, *23*, 455; Szejtli, J., in Atwood, J.L.; Davies, J.E.; MacNicol, D.D. *Inclusion Compounds*, Vol. 3, Academic Press, NY, ***1984***, pp. 331–390.

[178] See Saenger, W. *Angew. Chem. Int. Ed.* ***1980***, *19*, 344.

[179] Engeldinger, E.; Armspach, D.; Matt, D. *Chem. Rev.* ***2003***, *103*, 4147.

[180] For a monograph, see Schill, *G. Catenanes, Rotaxanes, and Knots*, Academic Press, NY, ***1971***. For a review, see Schill, G., in Chiurdoglu, G. *Conformational Analysis*, Academic Press, NY, ***1971***, pp. 229–239.

[181] Solladié, N.; Chambron, J.-C.; Sauvage, J.-P. *J. Am. Chem. Soc.* ***1999***, *121*, 3684.

[182] Sasabe, H.; Kihara, N.; Furusho, Y.; Mizuno, K.; Ogawa, A.; Takata, T. *Org. Lett.* ***2004***, *6*, 3957.

[183] Safarowsky, O.; Vogel, E.; Vögtle, F. Eur. *J. Org. Chem.* ***2000***, 499.

[184] Amabilino, D.B.; Ashton, P.R.; Boyd, S.E.; Lee, J.Y.; Menzer, S.; Stoddart, J.F.; Williams, D.J. *Angew. Chem. Int. Ed.* ***1997***, *36*, 2070; Amabilino, D.B.; Ashton, P.R.; Balzani, V.; Boyd, S.E.; Credi, A.; Lee, J.Y.; Menzer, S.; Stoddart, J.F.; Venturi, M.; Williams, D.J. *J. Am. Chem. Soc.* ***1998***, *120*, 4295.

[185] Chiu, S.-H.; Rowan, S.J.; Cantrill, S.J.; Ridvan, L.; Ashton, R.P.; Garrell, R.L.; Stoddart, J.-F. *Tetrahedron* ***2002***, *58*, 807; Whang, D.; Park, K.-M.; Heo, J.; Ashton, P.R.; Kim, K. *J. Am. Chem. Soc.* ***1998***, *120*, 4899; Roh, S.-G.; Park, K.-M.; Park, G.-J.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *Angew. Chem. Int. Ed.* ***1999***, *38*, 638.

interaction)[186] are known. Ring-in-ring complexes have also been reported.[187] Molecular thread, ribbon, and belt assemblies have been synthesized.[188] Rotaxanes have been used as the basis for molecular switches,[189] and a rotaxane eciplex has been generated that may have applications to molecular-scale photonic devices.[190]

Transitional isomers are possible in [2]-rotaxanes.[191] Catenanes and rotaxanes can be prepared by statistical methods or directed syntheses.[192] Catenanes can contain heteroatoms and heterocyclic units. In some cases, the catenane exists in equilibrium with the cyclic-non-catenane structures and in some cases this exchange is thought to proceed by ligand exchange and a Möbius strip mechanism.[193] An example of a statistical synthesis of a rotaxane is a reaction where a compound **A** is bonded at two positions to another compound **B** in the presence of a large ring **C**. It is hoped that some **A** molecules would by chance be threaded through **C** before combining with the two **B** molecules, so that some rotaxane (**D**) would be formed along with the normal product **E**.[194] In a directed synthesis,[195] the separate parts of the molecule are held together by other bonds that are later cleaved.

B **A** **B** **C** **D** **E** **C**

Rotation of one unit through the other catenanes is complex, often driven by making and breaking key hydrogen bonds or π–π interactions. In the case of the

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[186] For example, see Ashton, P.R.; Baxter, I.; Cantrill, S.J.; Fyfe, M.C.T.; Glink, P.T.; Stoddart, J.F.; White, A.J.P.; Williams, D.J. *Angew. Chem. Int. Ed.* ***1998***, *37*, 1294; Hoshino, T.; Miyauchi, M.; Kawaguchi, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* ***2000***, *122*, 9876; Onagi, H.; Easton, C.J.; Lincoln, S.F. *Org. Lett.* ***2001***, *3*, 1041; Cantrill, S.J.; Youn, G.J.; Stoddart, J.F.; Williams, D.J. *J. Org. Chem.* ***2001***, *66*, 6857.

[187] Chiu, S.-H.; Pease, A.R.; Stoddart, J.F.; White, A.J.P.; Williams, D.J. *Angew. Chem. Int. Ed.* ***2002***, *41*, 270.

[188] Schwierz, H.; Vögtle, F. *Synthesis* ***1999***, 295.

[189] Jun, S.I.; Lee, J.W.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *Tetrahedron Lett.* ***2000***, *41*, 471; Elizarov, A.M.; Chiu, S.-H.; Stoddart, J.-F. *J. Org. Chem.* ***2002***, *67*, 9175.

[190] MacLachlan, M.J.; Rose, A.; Swager, T.M. *J. Am. Chem. Soc.* ***2001***, *123*, 9180.

[191] Amabilino, D.B.; Ashton, P.R.; Boyd, S.E.; Gómez-López, M.; Hayes, W.; Stoddart, J.F. *J. Org. Chem.* ***1997***, *62*, 3062.

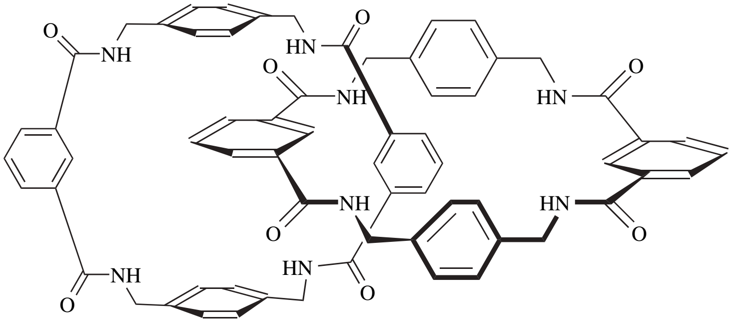
[192] For discussions, see Schill, G. *Catenanes, Rotaxanes, and Knots*, Academic Press, NY, ***1971***. For a review, see Schill, G., in Chiurdoglu, G. *Conformational Analysis*, Academic Press, NY, ***1971***, pp. 229–239; Walba, D.M. *Tetrahedron* ***1985***, *41*, 3161.

[193] Fujita, M.; Ibukuro, F.; Seki, H.; Kamo, O.; Imanari, M.; Ogura, K. *J. Am. Chem. Soc.* ***1996***, *118*, 899.

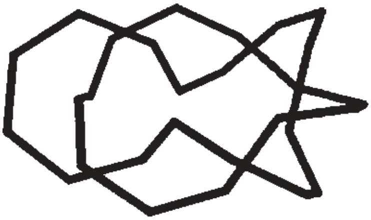
[194] Schemes of this type were carried out by Harrison, I.T.; Harrison, S. *J. Am. Chem. Soc.* ***1967***, *89*, 5723; Ogino, H. *J. Am. Chem. Soc.* ***1981***, *103*, 1303. For a different kind of statistical syntheszis of a rotaxane, see Harrison, I.T. *J. Chem. Soc., Perkin Trans. 1* ***1974***, 301; Schill, G.; Beckmann, W.; Schweikert, N.; Fritz, H. *Chem. Ber.* ***1986***, *119*, 2647. See also Agam, G.; Graiver, D.; Zilkha, A. *J. Am. Chem. Soc.* ***1976***, *98*, 5206.

[195] For a directed synthesis of a rotaxane, see Schill, G.; Zürcher, C.; Vetter, W. *Chem. Ber.* ***1973***, *106*, 228.

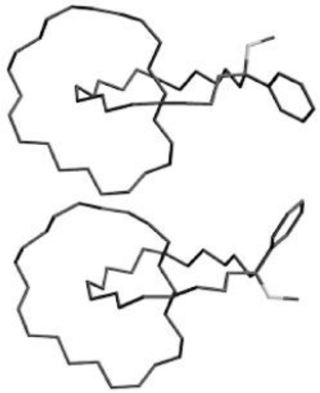
isophthaloyl [2]-catenane, **36**, the rate-determining steps do not necessarily correspond to the passage of the bulkiest groups.[196]



36



37



38

Singly and doubly interlocked [2]-catenanes[197] can exist as *topological stereoisomers*[198] (see p. 163 for a discussion of diastereomers). Catenanes **37** and **38** are such stereoisomers, and would be expected to have identical mass spectra. Analysis showed that **37** is more constrained and cannot readily accommodate an excess of energy during the mass spectrometry ionization process and, hence, breaks more easily.

Catenanes, molecular knots, and other molecules in these structural categories can exist as enantiomers. In other words, stereoisomers can be generated in some cases. This phenomenon was first predicted by Frisch and Wassermann,[199] and the

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[196] Deleuze, M.S.; Leigh, D.A; Zerbetto, F. *J. Am. Chem. Soc.* ***1999***, *121*, 2364.

[197] For the synthesis of a doubly interlocking [2]-catenane, see Ibukuro, F.; Fujita, M.; Yamaguchi, K.; Sauvage, J.-P. *J. Am. Chem. Soc.* ***1999***, *121*, 11014.

[198] See Lukin, O.; Godt, A.; Vögtle, F. *Chem. Eur. J.* ***2004***, *10*, 1879.

[199] Frisch, H.L.; Wasserman, E. *J. Am. Chem. Soc.* ***1961***, *83*, 3789.

first stereoisomeric catenanes and molecular knots were synthesized by Sauvage et al.[200] [2, 3]-Enantiomeric resolution has been achieved.[201] A chiral [3]-rotaxane containing two achiral wheels, mechanically bonded has been reported,[202] generating a cyclodiastereomeric compound,[8], and the enantiomers were separated using chiral HPLC. The terms cycloenantiomerism and cyclodiastereomerism were introduced by Prelog et al.[203] This stereoisomerism occurs in cyclic arrangements of several centrally chiral elements in combination with an orientation of the macrocycle.[202]

A rotaxane can also be an inclusion compound.[204] The molecule contains bulky end groups (or "stoppers," such as triisopropylsilyl groups, $i\mathrm{Pr_3Si}$–) and a chain that consists of a series of –O–CH_2CH_2–O– groups, but also contains two benzene rings. The ring (or bead) around the chain is a macrocycle containing two benzene rings and four pyridine rings, and is preferentially attracted to one of the benzene rings in the chain. The benzene moiety serves as a "station" for the "bead." However, symmetry of the chain can make the two "stations" equivalent, so that the "bead" is equally attracted to them, and the "bead" actually moves back and forth rapidly between the two "stations," as shown by the temperature dependence of the NMR spectrum.[205] This molecule has been called a *molecular shuttle*. A copper(I) complexed rotaxane has been prepared with two fullerene (see p. 94) stoppers.[206]

Another variation of these molecules are called molecular knots, such as **39**, where the ● represents a metal [in this case, copper(I)].[207] This is particularly interesting since knotted forms of deoxyribonuclic acid (DNA) have been reported.[208]

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[200] *Molecular Catenanes, Rotaxanes and Knots* (Eds.: Sauvage, J.-P.; Dietrich-Buchecker, C.O, Wiley-VCH, Weinheim, ***1999***; Ashton, P.R.; Bravo, J.A.; Raymo, F.M.; Stoddart, J.F.; White, A.J.P.; Williams, D. *J. Eur. J. Org. Chem.* ***1999***, 899; Mitchell, D.K.; Sauvage, J.-P. *Angew. Chem. Int. Ed.* ***1988***, *27*, 930; Nierengarten, J.-F.; Dietrich-Buchecker, C.O.; Sauvage, J.-P. *J. Am. Chem. Soc.* ***1994***, *116*, 375; Walba, D.M. *Tetrahedron* ***1985***, *41*, 3161; Chen, C.-T.; Gantzel, P.; Siegel, J.S.; Baldridge, K.K.; English, R.B.; Ho, D.M. *Angew. Chem. Int. Ed.* ***1995***, *34*, 2657.

[201] Kaida, T.; Okamoto, Y.; Chambron, J.-C.; Mitchell, D.K.; Sauvage, J.-P. *Tetrahedron Lett.* ***1993***, *34*, 1019.

[202] Schmieder, R.; Hübner, G.; Seel, C.; Vögtle, F. *Angew. Chem. Int. Ed.* ***1999***, *38*, 3528.

[203] Prelog, V.; Gerlach, H. *Helv. Chim. Acta* ***1964***, *47*, 2288; Gerlach, H.; Owtischinnkow, J.A.; Prelog, V. *Helv. Chim. Acta* ***1964***, *47*, 2294; Eliel, E.L. *Stereochemie der Kohlenstoffverbindungen*, Verlag Chemie, Weinheim, ***1966***; Eliel, E.L.; Wilen, S.H.; Mander, L.N. *Stereochemistry of Organic Compounds*, Wiley, NY, ***1994***, pp. 1176–1181; Chorev, M.; Goodman, M. *Acc. Chem. Res.* ***1993***, *26*, 266 ; Mislow, K. *Chimia*, ***1986***, *40*, 395.

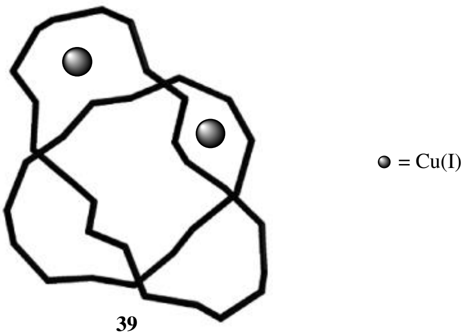
[204] For an example, see Anelli, P.L.; Spencer, N.; Stoddart, J.F. *J. Am. Chem. Soc.* ***1991***, *113*, 5131.

[205] Anelli, P.L.; Spencer, N.; Stoddart, J.F. *J. Am. Chem. Soc.* ***1991***, *113*, 5131. For a review of the synthesis and properties of molecules of this type, see Philp, D.; Stoddart, J.F. *Synlett* ***1991***, 445.

[206] Diederich, F.; Dietrich-Buchecker, C.O.; Nierengarten, S.-F.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* ***1995***, 781.

[207] Dietrich-Buchecker, C.O.; Nierengarten, J.-F.; Sauvage, J.-P. *Tetrahedron Lett.* ***1992***, *33*, 3625. See Dietrich-Buchecker, C.O.; Sauvage, J.-P. *Angew. Chem. Int. Ed.* ***1989***, *28*, 189 and Dietrich-Buchecker, C.O.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. *Angew. Chem. Int. Ed.* ***1990***, *29*, 1154 for the synthesis of other molecular knots.

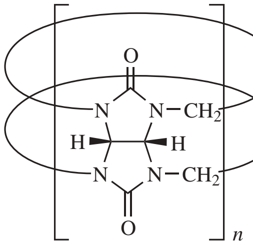
[208] Liu, L.F.; Depew, R.E.; Wang, J.C. *J. Mol. Biol.* ***1976***, *106*, 439.



39

Cucurbit[*n*]uril-Based Gyroscane

A new molecule known as gyroscane has been prepared, and proposed as a new supramolecular form.[209] The class of compounds known as cucurbit[*n*]urils, abbreviated Q_n (**40**),[210] are condensation products of glycoluril and formaldehyde. These macrocycles can act as molecular hosts. The new "supramolecular form is one in which a smaller macrocycle, Q5, is located inside a larger macrocycle, Q10, with facile rotation of one relative to the other in solution (see **41**).[210] The image of a ring rotating independently inside another ring, which resembles a gyroscope, suggests the name gyroscane for this new class of supramolecular system."[210]



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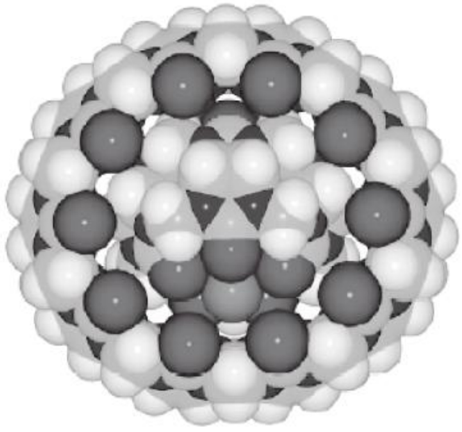

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[209] Day, A.I.; Blanch, R.J.; Arnold, A.P.; Lorenzo, S.; Lewis, G.R.; Dance, I. *Angew. Chem. Int. Ed.* ***2002***, *41*, 275.

[210] Freeman, W.A.; Mock, W.L.; Shih, N.Y. *J. Am. Chem. Soc.* ***1981***, *103*, 7367; Cintas, P. *J. Inclusion Phenom.* ***1994***, *17*, 205; Mock, W.L. *Top. Curr. Chem.* ***1995***, *175*, 1; Mock, W.L., in *Comprehensive Supramolecular Chemistry*, Vol. 2, Atwood, J.L.; Davies, J.E.D.; MacNicol, D.D.; Vogtle, F. (Eds.), Pergamon, Oxford, ***1996***, pp. 477–493; Day, A.; Arnold, A.P.; Blanch, R.J.; Snushall, B. *J. Org. Chem.* ***2001***, *66*, 8094; Kim, J.; Jung, I.-S.; Kim, S.-Y.; Lee, E.; Kang, J.-L.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *J. Am. Chem. Soc.* ***2000***, *122*, 540.