Quantum Mechanics for Organic Chemistry

Computational chemistry, as explored in this book, will be restricted to quantum mechanical descriptions of the molecules of interest. This should not be taken as a slight upon alternative approaches, principally molecular mechanics. Rather, the aim of this book is to demonstrate the power of high-level quantum computations in offering insight towards understanding the nature of organic molecules—their structures, properties, and reactions—and to show their successes and point out the potential pitfalls. Furthermore, this book will address applications of traditional ab initio and density functional theory methods to organic chemistry, with little mention of semi-empirical methods. Again, this is not to slight the very important contributions made from the application of Complete Neglect of Differential Overlap (CNDO) and its progeny. However, with the ever-improving speed of computers and algorithms, ever-larger molecules are amenable to ab initio treatment, making the semi-empirical and other approximate methods for treating the quantum mechanics of molecular systems simply less necessary. This book is therefore designed to encourage the broader use of the more exact treatments of the physics of organic molecules by demonstrating the range of molecules and reactions already successfully treated by quantum chemical computation. We will highlight some of the most important contributions that this discipline has made to the broader chemical community towards our understanding of organic chemistry.

We begin with a brief and mathematically light-handed treatment of the fundamentals of quantum mechanics necessary to describe organic molecules. This presentation is meant to acquaint those unfamiliar with the field of computational chemistry with a general understanding of the major methods, concepts, and acronyms. Sufficient depth will be provided so that one can understand why certain methods work well, but others may fail when applied to various chemical problems, allowing the casual reader to be able to understand most of any applied computational chemistry paper in the literature. Those seeking more depth and details, particularly more derivations and a fuller mathematical treatment, should consult any of three outstanding texts: *Essentials of Computational Chemistry* by

Cramer,[1] *Introduction to Computational Chemistry* by Jensen,[2] and *Modern Quantum Chemistry: Introduction to Advanced Electronic Structure Theory* by Szabo and Ostlund.[3]

Quantum chemistry requires the solution of the time-independent Schrödinger equation,

$$\hat{H}\Psi(\mathbf{R}_1, \mathbf{R}_2 \ldots \mathbf{R}_N, \mathbf{r}_1, \mathbf{r}_2 \ldots r_n) = E\Psi(\mathbf{R}_1, \mathbf{R}_2 \ldots \mathbf{R}_N, \mathbf{r}_1, \mathbf{r}_2 \ldots \mathbf{r}_n), \qquad (1.1)$$

where $\hat{H}$ is the Hamiltonian operator, $\Psi(\mathbf{R}_1, \mathbf{R}_2 \ldots \mathbf{R}_N, \mathbf{r}_1, \mathbf{r}_2 \ldots \mathbf{r}_n)$ is the wavefunction for all of the nuclei and electrons, and E is the energy associated with this wavefunction. The Hamiltonian contains all operators that describe the kinetic and potential energy of the molecule at hand. The wavefunction is a function of the nuclear positions $\mathbf{R}$ and the electron positions $\mathbf{r}$. For molecular systems of interest to organic chemists, the Schrödinger equation cannot be solved exactly and so a number of approximations are required to make the mathematics tractable.

1.1 APPROXIMATIONS TO THE SCHRÖDINGER EQUATION: THE HARTREE–FOCK METHOD

1.1.1 Nonrelativistic Mechanics

Dirac achieved the combination of quantum mechanics and relativity. Relativistic corrections are necessary when particles approach the speed of light. Electrons near heavy nuclei will achieve such velocities, and for these atoms, relativistic quantum treatments are necessary for accurate description of the electron density. However, for typical organic molecules, which contain only first- and second-row elements, a relativistic treatment is unnecessary. Solving the Dirac relativistic equation is much more difficult than for nonrelativistic computations. A common approximation is to utilize an effective field for the nuclei associated with heavy atoms, which corrects for the relativistic effect. This approximation is beyond the scope of this book, especially as it is unnecessary for the vast majority of organic chemistry.

The complete nonrelativistic Hamiltonian for a molecule consisting of n electrons and N nuclei is given by

$$\hat{H} = -\frac{h^2}{2}\sum_{I}^{N}\frac{\nabla_I^2}{m_I} - \frac{h^2}{2\,m_{\mathrm{e}}}\sum_{i}^{n}\nabla_i^2 - \sum_{i}^{n}\sum_{I}^{N}\frac{Z_I e'^2}{r_{Ii}} + \sum_{I>J}^{N}\frac{Z_I Z_J e'^2}{r_{IJ}} + \sum_{i<j}^{n}\frac{e'^2}{r_{ij}}, \quad (1.2)$$

where the lower case indexes the electrons and the upper case indexes the nuclei, h is Planck's constant, m_{e} is the electron mass, m_I the mass of nucleus I, and r is a distance between the objects specified by the subscript. For simplicity, we define

$$e'^2 = \frac{e^2}{4\pi\varepsilon_0}. \qquad (1.3)$$

1.1.2   The Born Oppenheimer Approximation

The total molecular wavefunction $\Psi(\mathbf{R}, \mathbf{r})$ depends on both the positions of all of the nuclei and the positions of all of the electrons. Because electrons are much lighter than nuclei, and therefore move much more rapidly, electrons can essentially instantaneously respond to any changes in the relative positions of the nuclei. This allows for the separation of the nuclear variables from the electron variables,

$$\Psi(\mathbf{R}_1, \mathbf{R}_2 \ldots \mathbf{R}_N, \mathbf{r}_1, \mathbf{r}_2 \ldots \mathbf{r}_n) = \Phi(\mathbf{R}_1, \mathbf{R}_2 \ldots \mathbf{R}_N)\psi(\mathbf{r}_1, \mathbf{r}_2 \ldots \mathbf{r}_n). \qquad (1.4)$$

This separation of the total wavefunction into an electronic wavefunction $\psi(\mathbf{r})$ and a nuclear wavefunction $\Phi(\mathbf{R})$ means that the positions of the nuclei can be fixed and then one only has to solve the Schrödinger equation for the electronic part. This approximation was proposed by Born and Oppenheimer[4] and is valid for the vast majority of organic molecules.

The potential energy surface (PES) is created by determining the electronic energy of a molecule while varying the positions of its nuclei. It is important to recognize that the concept of the PES relies upon the validity of the Born–Oppenheimer approximation, so that we can talk about transition states and local minima, which are critical points on the PES. Without it, we would have to resort to discussions of probability densities of the nuclear-electron wavefunction.

The Hamiltonian obtained after applying the Born–Oppenheimer approximation and neglecting relativity is

$$\hat{H} = -\frac{1}{2}\sum_i^n \nabla_i^2 - \sum_i^n \sum_I^N \frac{Z_I}{r_{Ii}} + \sum_{i<j}^n \frac{1}{r_{ij}} + V^{\mathrm{nuc}} \qquad (1.5)$$

where V^{nuc} is the nuclear–nuclear repulsion energy. Equation (1.5) is expressed in atomic units, which is why it appears so uncluttered. It is this Hamiltonian that is utilized in computational organic chemistry. The next task is to solve the Schrödinger equation (1.1) with the Hamiltonian expressed in Eq. (1.5).

1.1.3   The One-Electron Wavefunction and the Hartree–Fock Method

The wavefunction $\psi(\mathbf{r})$ depends on the coordinates of *all* of the electrons in the molecule. Hartree proposed the idea, reminiscent of the separation of variables used by Born and Oppenheimer, that the electronic wavefunction can be separated into a product of functions that depend only on one electron,

$$\psi(\mathbf{r}_1, \mathbf{r}_2 \ldots \mathbf{r}_n) = \phi_1(\mathbf{r}_1)\phi_2(\mathbf{r}_2) \ldots \phi_n(\mathbf{r}_n). \qquad (1.6)$$

This wavefunction would solve the Schrödinger equation exactly if it were not for the electron–electron repulsion term of the Hamiltonian in Eq. (1.5). Hartree next rewrote this term as an expression that describes the repulsion an electron feels

from the average position of the other electrons. In other words, the exact electron–electron repulsion is replaced with an effective field V_i^{eff} produced by the average positions of the remaining electrons. With this assumption, the separable functions ϕ_i satisfy the Hartree equations

$$\left(-\frac{1}{2}\nabla_i^2 - \sum_I^N \frac{Z_I}{r_{Ii}} + V_i^{\text{eff}}\right)\phi_i = E_i\phi_i. \qquad (1.7)$$

(Note that Eq. (1.7) defines a set of equations, one for each electron.) Solving for the set of functions ϕ_i is nontrivial because V_i^{eff} itself depends on all of the functions ϕ_i. An iterative scheme is needed to solve the Hartree equations. First, a set of functions $(\phi_1, \phi_2\ldots\phi_n)$ is assumed. These are used to produce the set of effective potential operators V_i^{eff} and the Hartree equations are solved to produce a set of improved functions ϕ_i. These new functions produce an updated effective potential, which in turn yields a new set of functions ϕ_i. This process is continued until the functions ϕ_i no longer change, resulting in a self-consistent field (SCF).

Replacing the full electron–electron repulsion term in the Hamiltonian with V^{eff} is a serious approximation. It neglects entirely the ability of the electrons to rapidly (essentially instantaneously) respond to the position of other electrons. In a later section we will address how to account for this instantaneous electron–electron repulsion.

Fock recognized that the separable wavefunction employed by Hartree (Eq. 1.6) does not satisfy the Pauli Exclusion Principle. Instead, Fock suggested using the Slater determinant

$$\psi(\mathbf{r}_1, \mathbf{r}_2\ldots\mathbf{r}_n) = \frac{1}{\sqrt{n!}}\begin{vmatrix} \phi_1(e_1) & \phi_2(e_1) & \ldots & \phi_n(e_1) \\ \phi_1(e_2) & \phi_2(e_2) & \ldots & \phi_n(e_2) \\ & & & \\ \phi_1(e_n) & \phi_2(e_n) & \ldots & \phi_n(e_n) \end{vmatrix} = |\phi_1, \phi_2\ldots\phi_n|, \qquad (1.8)$$

which is antisymmetric and satisfies the Pauli Principle. Again, an effective potential is employed, and an iterative scheme provides the solution to the Hartree–Fock (HF) equations.

1.1.4 Linear Combination of Atomic Orbitals (LCAO) Approximation

The solutions to the Hartree–Fock model, ϕ_i, are known as the molecular orbitals (MOs). These orbitals generally span the entire molecule, just as the atomic orbitals (AOs) span the space about an atom. Because organic chemists consider the atomic properties of atoms (or collection of atoms as functional groups) to still persist to some extent when embedded within a molecule, it seems reasonable to construct the MOs as an expansion of the AOs,

$$\phi_i = \sum_\mu^k c_{i\mu}\chi_\mu, \qquad (1.9)$$

where the index μ spans all of the atomic orbitals χ of every atom in the molecule (a total of k atomic orbitals), and $c_{i\mu}$ is the expansion coefficient of AO χ_μ in MO ϕ_i. Equation (1.9) thus defines the linear combination of atomic orbitals (LCAO) approximation.

1.1.5   Hartree–Fock–Roothaan Procedure

Taking the LCAO approximation for the MOs and combining it with the Hartree–Fock method led Roothaan to develop a procedure to obtain the SCF solutions.[5] We will discuss here only the simplest case where all molecular orbitals are doubly occupied, with one electron that is spin up and one that is spin down, also known as a closed-shell wavefunction. The open-shell case is a simple extension of these ideas. The procedure rests upon transforming the set of equations listed in Eq. (1.7) into the matrix form

$$\mathbf{FC} = \mathbf{SC}\boldsymbol{\varepsilon}, \tag{1.10}$$

where $\mathbf{S}$ is the overlap matrix, $\mathbf{C}$ is the $k \times k$ matrix of the coefficients $c_{i\mu}$, and $\boldsymbol{\varepsilon}$ is the $k \times k$ matrix of the orbital energies. Each column of $\mathbf{C}$ is the expansion of ϕ_i in terms of the atomic orbitals χ_μ. The Fock matrix $\mathbf{F}$ is defined for the $\mu\nu$ element as

$$\mathbf{F}_{\mu\nu} = \langle \nu | \hat{h} | \mu \rangle + \sum_j^{n/2} [2(jj|\mu\nu) - (j\nu|j\mu)], \tag{1.11}$$

where $\hat{h}$ is the core Hamiltonian, corresponding to the kinetic energy of the electron and the potential energy due to the electron–nuclear attraction, and the last two terms describe the coulomb and exchange energies, respectively. It is also useful to define the density matrix (more properly, the first-order reduced density matrix),

$$\mathbf{D}_{\mu\nu} = 2 \sum_i^{n/2} c_{i\nu}^* c_{i\mu}. \tag{1.12}$$

The expression in Eq. (1.12) is for a closed-shell wavefunction, but it can be defined for a more general wavefunction by analogy.

   The matrix approach is advantageous, because a simple algorithm can be established for solving Eq. (1.10). First, a matrix $\mathbf{X}$ is found that transforms the normalized atomic orbitals χ_μ into the orthonormal set $\chi_\mu{}'$,

$$\chi_\mu{}' = \sum_\mu^k \mathbf{X}\chi_\mu, \tag{1.13}$$

which is mathematically equivalent to

$$\mathbf{X}^{\dagger}\mathbf{S}\mathbf{X} = 1, \tag{1.14}$$

where $\mathbf{X}^{\dagger}$ is the adjoint of the matrix $\mathbf{X}$. The coefficient matrix $\mathbf{C}$ can be transformed into a new matrix $\mathbf{C}'$,

$$\mathbf{C}' = \mathbf{X}^{-1}\mathbf{C}. \tag{1.15}$$

Substituting $\mathbf{C} = \mathbf{X}\mathbf{C}'$ into Eq. (1.10) and multiplying by $\mathbf{X}^{\dagger}$ gives

$$\mathbf{X}^{\dagger}\mathbf{F}\mathbf{X}\mathbf{C}' = \mathbf{X}^{\dagger}\mathbf{S}\mathbf{X}\mathbf{C}'\boldsymbol{\varepsilon} = \mathbf{C}'\boldsymbol{\varepsilon} \tag{1.16}$$

By defining the transformed Fock matrix

$$\mathbf{F}' = \mathbf{X}^{\dagger}\mathbf{F}\mathbf{X}, \tag{1.17}$$

we obtain the simple Roothaan expression

$$\mathbf{F}'\mathbf{C}' = \mathbf{C}'\boldsymbol{\varepsilon}. \tag{1.18}$$

The Hartree–Fock–Roothaan algorithm is implemented by the following steps:

1. Specify the nuclear position, the type of nuclei, and the number of electrons.
2. Choose a basis set. The basis set is the mathematical description of the atomic orbitals. We will discuss this in more detail in a later section.
3. Calculate all of the integrals necessary to describe the core Hamiltonian, the coulomb and exchange terms, and the overlap matrix.
4. Diagonalize the overlap matrix $\mathbf{S}$ to obtain the transformation matrix $\mathbf{X}$.
5. Make a guess at the coefficient matrix $\mathbf{C}$ and obtain the density matrix $\mathbf{D}$.
6. Calculate the Fock matrix and then the transformed Fock matrix $\mathbf{F}'$.
7. Diagonalize $\mathbf{F}'$ to obtain $\mathbf{C}'$ and $\boldsymbol{\varepsilon}$.
8. Obtain the new coefficient matrix with the expression $\mathbf{C} = \mathbf{X}\mathbf{C}'$ and the corresponding new density matrix.
9. Decide if the procedure has converged. There are typically two criteria for convergence, one based on the energy and the other on the orbital coefficients. The energy convergence criterion is met when the difference in the energies of the last two iterations is less than some preset value. Convergence of the coefficients is obtained when the standard deviation of the density matrix elements in successive iterations is also below some preset value. If convergence has not been met, return to Step 6 and repeat until the convergence criteria are satisfied.

One last point concerns the nature of the molecular orbitals that are produced in this procedure. These orbitals are such that the energy matrix $\boldsymbol{\varepsilon}$ will be diagonal, with the diagonal elements being interpreted as the MO energy. These MOs are

referred to as the canonical orbitals. One must be aware that all that makes them unique is that these orbitals will produce the diagonal matrix $\boldsymbol{\varepsilon}$. Any new set of orbitals ϕ_i' produced from the canonical set by a unitary transformation

$$\phi_i' = \sum_j \mathbf{U}_{ji}\phi_j \tag{1.19}$$

will satisfy the Hartree–Fock (HF) equations and produce the exact same energy and electron distribution as that with the canonical set. No one set of orbitals is really any better or worse than another, as long as the set of MOs satisfies Eq. (1.19).

1.1.6 Restricted Versus Unrestricted Wavefunctions

The preceding development of the Hartree–Fock theory assumed a closed–shell wavefunction. The wavefunction for an individual electron describes its spatial extent along with its spin. The electron can be either spin up (α) or spin down (β). For the closed-shell wavefunction, each pair of electrons shares the same spatial orbital but each has a unique spin—one is up and the other is down. This type of wavefunction is also called a (spin) restricted wavefunction, because the paired electrons are restricted to the same spatial orbital, leading to the restricted Hartree–Fock (RHF) method. When applied to open-shell systems, this is called restricted open-shell HF (ROHF).

This restriction is *not* demanded. It is a simple way to satisfy the exclusion principle, but it is not the only means for doing so. In an unrestricted wavefunction the spin-up electron and its spin-down partner do not have the same spatial description. The Hartree–Fock–Roothaan procedure is slightly modified to handle this case by creating a set of equations for the α electrons and another set for the β electrons, and then an algorithm similar to that described above is implemented.

The downside to the (spin) unrestricted Hartree–Fock (UHF) method is that the unrestricted wavefunction usually will not be an eigenfunction of the $\hat{S}^2$ operator. As the Hamiltonian and $\hat{S}^2$ operators commute, the true wavefunction must be an eigenfunction of both of these operators. The UHF wavefunction is typically contaminated with higher spin states. A procedure called spin projection can be used to remove much of this contamination. However, geometry optimization is difficult to perform with spin projection. Therefore, great care is needed when an unrestricted wavefunction is utilized, as it must be when the molecule of interest is inherently open-shell, like in radicals.

1.1.7 The Variational Principle

The variational principle asserts that any wavefunction constructed as a linear combination of orthonormal functions will have its energy greater than or equal to the lowest energy (E_0) of the system. Thus,

$$\frac{\langle \Phi | \hat{H} | \Phi \rangle}{\langle \Phi | \Phi | \rangle} \geq E_0 \tag{1.20}$$

if

$$\Phi = \sum_i c_i \phi_i. \tag{1.21}$$

If the set of functions ϕ_i is infinite, then the wavefunction will produce the lowest energy for that particular Hamiltonian. Unfortunately, expanding a wavefunction using an infinite set of functions is impractical. The variational principle saves the day by providing a simple way to judge the quality of various truncated expansions—the lower the energy, the better the wavefunction! The variational principle is *not* an approximation to treatment of the Schrödinger equation; rather, it provides a means for judging the effect of certain types of approximate treatments.

1.1.8 Basis Sets

In order to solve for the energy and wavefunction within the Hartree–Fock–Roothaan procedure, the atomic orbitals must be specified. If the set of atomic orbitals is infinite, then the variational principle tells us that we will obtain the lowest possible energy within the HF-SCF method. This is called the Hartree–Fock limit, E_{HF}. This is *not* the actual energy of the molecule; recall that the HF method neglects instantaneous electron–electron interactions.

Because an infinite set of atomic orbitals is impractical, a choice must be made on how to truncate the expansion. This choice of atomic orbitals defines the basis set.

A natural starting point is to use functions from the exact solution of the Schrödinger equation for the hydrogen atom. These orbitals have the form

$$\chi = N x^i y^j z^k e^{-\zeta(r-\mathbf{R})}, \tag{1.22}$$

where $\mathbf{R}$ is the position vector of the nucleus upon which the function is centered and N is the normalization constant. Functions of this type are called Slater-type orbitals (STOs). The value of ζ for every STO for a given element is determined by minimizing the atomic energy with respect to ζ. These values are used for every atom of that element, regardless of the molecular environment.

At this point it is worth shifting nomenclature and discussing the expansion in terms of basis functions instead of atomic orbitals. The construction of MOs in terms of some set of functions is entirely a mathematical "trick," and we choose to place these functions at nuclei because that is the region of greatest electron density. We are not using "atomic orbitals" in the sense of a solution to the atomic Schrödinger equation, but just mathematical functions placed at nuclei for convenience. To make this more explicit, we will refer to the expansion of *basis functions* to form the MOs.

Conceptually, the STO basis is straightforward as it mimics the exact solution for the single electron atom. The exact orbitals for carbon, for example, are *not* hydrogenic orbitals, but are similar to the hydrogenic orbitals. Unfortunately, with STOs

many of the integrals that need to be evaluated to construct the Fock matrix can only be solved using an infinite series. Truncation of this infinite series results in errors, which can be significant.

Following on a suggestion of Boys,[6] Pople decided to use a combination of Gaussian functions to mimic the STO. The advantage of the Gaussian-type orbital (GTO),

$$\chi = Nx^{i}y^{j}z^{k}e^{-\alpha(r-\mathbf{R})^{2}} \tag{1.23}$$

is that with these functions, the integrals required to build the Fock matrix can be evaluated exactly. The trade-off is that GTOs do differ in shape from the STOs, particularly at the nucleus where the STO has a cusp, but the GTO is continually differentiable (Fig. 1.1). Therefore, multiple GTOs are necessary to adequately mimic each STO, increasing the computational size of the calculation. Nonetheless, basis sets comprised of GTOs are the ones most commonly used.

A number of factors define the basis set for a quantum chemical computation. First, how many basis functions should be used? The minimum basis set has one basis function for every formally occupied or partially occupied orbital in the atom. So, for example, the minimum basis set for carbon, with electron occupation $1s^{2}2s^{2}2p^{2}$, has two s-type functions and p_x, p_y, and p_z functions, for a total of five basis functions. This minimum basis set is referred to as a single-zeta (SZ) basis set. The use of the term *zeta* here reflects that each basis function mimics a single STO, which is defined by its exponent, ζ.

The minimum basis set is usually inadequate, failing to allow the core electrons to get close enough to the nucleus and the valence electrons to delocalize. An obvious solution is to double the size of the basis set, creating a double-zeta (DZ) basis. So, for carbon, the DZ basis set has four s basis functions and two p basis functions (recognizing that the term "p basis functions" refers here to the full set of p_x, p_y, and p_z functions), for a total of ten basis functions. Further improvement can be had by choosing a triple zeta (TZ) or even larger basis set.
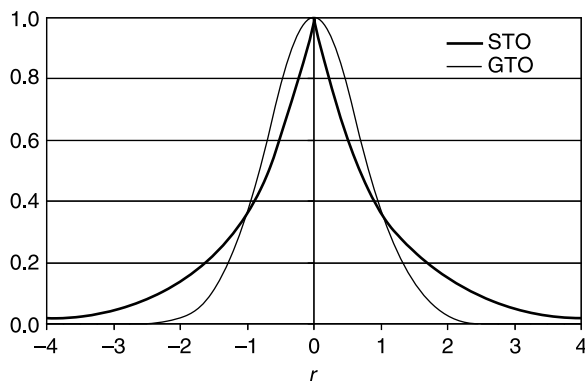

Figure 1.1. Plot of the radial component of a Slater-type orbital (STO) and a Gaussian-type orbital (GTO).

As most of chemistry focuses on the action of the valence electrons, Pople developed the split-valence basis sets,[7,8] single zeta in the core and double zeta in the valence region. A double-zeta split-valence basis set for carbon has three s basis functions and two p basis functions for a total of nine functions, a triple-zeta split valence basis set has four s basis functions and three p functions for a total of thirteen functions, and so on.

For the vast majority of basis sets, including the split-valence sets, the basis functions are not made up of a single Gaussian function. Rather, a group of Gaussian functions are contracted together to form a single basis function. This is perhaps most easily understood with an explicit example: the popular split-valence 6-31G basis. The name specifies the contraction scheme employed in creating the basis set. The dash separates the core (on the left) from the valence (on the right). In this case, each core basis function is comprised of six Gaussian functions. The valence space is split into two basis functions, frequently referred to as the "inner" and "outer" functions. The inner basis function is composed of three contracted Gaussian functions, and each outer basis function is a single Gaussian function. Thus, for carbon, the core region is a single s basis function made up of six s-GTOs. The carbon valence space has two s and two p basis functions. The inner basis functions are made up of three Gaussians, and the outer basis functions are each composed of a single Gaussian function. Therefore, the carbon 6-31G basis set has nine basis functions made up of 22 Gaussian functions (Table 1.1).

Even large, multi-zeta basis sets will not provide sufficient mathematical flexibility to adequately describe the electron distribution. An example of this deficiency is the inability to describe bent bonds of small rings. Extending the basis set by including a set of functions that mimic the atomic orbitals with angular momentum one greater than in the valence space greatly improves the basis flexibility. These added basis functions are called polarization functions. For carbon, adding polarization functions means adding a set of d GTOs, but for hydrogen, polarization functions are a set of p functions. The designation of a polarized basis set is varied. One convention indicates the addition of polarization functions with the label "+P": DZ+P indicates a double-zeta basis set with one set of polarization functions. For the split-valence sets, adding a set of polarization functions to all atoms but hydrogen is designated by an asterisk, that is, 6-31G*, and adding the set of p functions to hydrogen as well is indicated by double asterisks, that is, 6-31G**. As adding multiple sets of polarization functions has become broadly implemented, the use of asterisks has been abandoned in favor of explicit indication of the number of polarization functions within parentheses, that is, 6-311G(2df,2p) means that two sets of d functions and a set of f functions are added to nonhydrogen atoms and two sets of p functions are added to the hydrogen atoms.

For anions or molecules with many adjacent lone pairs, the basis set must be augmented with diffuse functions to allow the electron density to expand into a larger volume. For split-valence basis sets, this is designated by " + ," as in 6-31+G(d). The diffuse functions added are a full set of additional functions of the same type as are present in the valence space. So, for carbon, the diffuse functions would be

TABLE 1.1. Composition of the Carbon 6-31G and 6-31+G(d) Basis Sets.

	6-31G		6-31 + G(d)	
	Basis Functions	GTOs	Basis Functions	GTOs
Core	s	6	s	6
Valence	s (inner)	3	s (inner)	3
	s (outer)	1	s (outer)	1
	p_x (inner)	3	p_x (inner)	3
	p_x (outer)	1	p_x (outer)	1
	p_y (inner)	3	p_y (inner)	3
	p_y (outer)	1	p_y (outer)	1
	p_z (inner)	3	p_z (inner)	3
	p_z (outer)	1	p_z (outer)	1
Diffuse			s (diffuse)	1
			p_y (diffuse)	1
			p_z (diffuse)	1
			p_z (diffuse)	1
Polarization			d_{xx}	1
			d_{yy}	1
			d_{zz}	1
			d_{xy}	1
			d_{xz}	1
			d_{yz}	1
Total	9	22	19	32

an added s basis function and a set of p basis functions. The composition of the 6-31+G(d) carbon basis set is detailed in Table 1.1.

The split-valence basis sets developed by Pople are widely used. The correlation-consistent basis sets developed by Dunning are popular alternatives.[9–11] The split-valence basis sets were constructed by minimizing the energy of the atom at the HF level with respect to the contraction coefficients and exponents. The correlation-consistent basis sets were constructed to extract the maximum electron correlation energy for each atom. We will define the electron correlation energy in the next section. The correlation-consistent basis sets are designated as "cc-pVNZ," to be read as correlation-consistent polarized split-valence N-zeta, where N designates the degree to which the valence space is split. As N increases, the number of polarization functions also increases. So, for example, the cc-pVDZ basis set for carbon is double-zeta in the valence space and includes a single set of d functions, and the cc-pVTZ basis set is triple-zeta in the valence space and has two sets of d functions and a set of f functions. The addition of diffuse functions to the correlation-consistent basis sets is designated with the prefix *aug-*, as in aug-cc-pVDZ.

Basis sets are built into the common computational chemistry programs. A valuable web-enabled database for retrieval of basis sets is available from the Molecular Science Computing Facility, Environmental and Molecular Sciences Laboratory "EMSL Gaussian Basis Set Order Form" (http://www.emsl.pnl.gov/forms/basisform.html).[12]

Because, in practice, basis sets must be of some limited size far short of the HF limit, their incompleteness can lead to a spurious result known as basis set superposition error (BSSE). This is readily grasped in the context of the binding of two molecules, A and B, to form the complex AB. The binding energy is evaluated as

$$E_{\text{binding}} = E_{AB}^{ab} - \left(E_A^a + E_B^b\right), \tag{1.24}$$

where a refers to the basis set on molecule A, b refers to the basis set on molecule B, and ab indicates the union of these two basis sets. Now, in the complex AB, the basis set a will be used to (1) describe the electrons on A, (2) describe, in part, the electrons involved in the binding of the two molecules, and (3) aid in describing the electrons of B. The same is true for the basis set b. The result is that the complex AB, by having a larger basis set than available to describe either A or B individually, is treated more completely, and its energy will consequently be lowered, relative to the energy of A or B. The binding energy will therefore be larger (more negative) due to this superposition error.

The counterpoise method proposed by Boys and Bernardi attempts to remove some of the effect of BSSE. The counterpoise correction is defined as

$$E_{\text{CP}} = E_{A^*}^{ab} + E_{B^*}^{ab} - \left(E_{A^*}^a + E_{B^*}^b\right). \tag{1.25}$$

The first term on the right-hand side is the energy of molecule A in its geometry of the complex (designated with the asterisk) computed with the basis set a and the basis functions of B placed at the position of the nuclei of B, but absent the nuclei and electrons of B. These basis functions are called *ghost orbitals*. The second term is the energy of B in its geometry of the complex computed with its basis functions and the ghost orbitals of A. The last two terms correct for the geometric distortion of A and B from their isolated structure to the complex. The counterpoise corrected binding energy is then

$$E_{\text{binding}}^{\text{CP}} = E_{\text{binding}} - E_{\text{CP}}. \tag{1.26}$$

1.2   ELECTRON CORRELATION: POST-HARTREE–FOCK METHODS

The HF method ignores instantaneous electron–electron repulsion, also known as electron correlation. The electron correlation energy is defined as the difference between the *exact* energy and the energy at the HF limit:

$$E_{\text{corr}} = E_{\text{exact}} - E_{\text{HF}}. \tag{1.27}$$

How can we include electron correlation? Suppose the total electron wavefunction is composed of a linear combination of functions that depend on all n electrons

$$\Psi = \sum_i c_i \psi_i. \qquad (1.28)$$

We can then solve the Schrödinger equation with the *full* Hamiltonian (Eq. 1.5) by varying the coefficients c_i so as to minimize the energy. If the summation is over an infinite set of these N-electron functions, ψ_i, we will obtain the exact energy. If, as is more practical, some finite set of functions is used, the variational principle tells us that the energy so computed will be above the exact energy.

The HF wavefunction is an N-electron function (itself composed of 1-electron functions—the molecular orbitals). It seems reasonable to generate a set of functions from the HF wavefunction ψ_{HF}, sometimes called the reference configuration.

The HF wavefunction defines a single configuration of the N electrons. By removing electrons from the occupied MOs and placing them into the virtual (unoccupied) MOs, we can create new configurations, new N-electron functions. These new configurations can be indexed by how many electrons are relocated. Configurations produced by moving one electron from an occupied orbital to a virtual orbital are singly excited relative to the HF configuration and are called singles; those where two electrons are moved are called doubles, and so on. A simple designation for these excited configurations is to list the occupied MO(s) where the electrons are removed as a subscript and the virtual orbitals where the electrons are placed as the superscript. Thus, the generic designation of a singles configuration is ψ_i^a or ψ_S, a doubles configuration is ψ_{ij}^{ab} or ψ_D, and so on. Figure 1.2 shows a MO diagram for a representative HF configuration and examples of some singles, doubles, and triples configurations. These configurations are composed of spin-adapted Slater
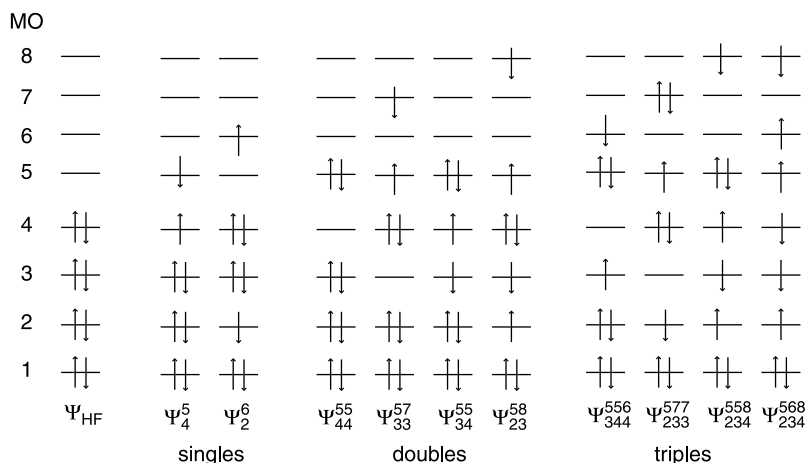

Figure 1.2. MO diagram indicating the electron occupancies of the HF configuration and representative examples of singles, doubles, and triples configurations.

determinants, each of which is constructed from the arrangements of the electrons in the various, appropriate molecular orbitals.

1.2.1   Configuration Interaction (CI)

Using the definition of configurations, we can rewrite Eq. (1.28) as

$$\Psi_{\text{CI}} = c_0\psi_{\text{HF}} + \sum_i^{\text{occ}} \sum_a^{\text{vir}} c_i^a \psi_i^a + \sum_{i,j}^{\text{occ}} \sum_{a,b}^{\text{vir}} c_{ij}^{ab} \psi_{ij}^{ab}$$

$$+ \sum_{i,j,k}^{\text{occ}} \sum_{a,b,c}^{\text{vir}} c_{ijk}^{abc} \psi_{ijk}^{abc} + \sum_{i,j,k,l}^{\text{occ}} \sum_{a,b,c,d}^{\text{vir}} c_{ijkl}^{abcd} \psi_{ijkl}^{abcd} + \cdots. \qquad (1.29)$$

In order to solve the Schrödinger equation, we need to construct the Hamiltonian matrix using the wavefunction of Eq. (1.29). Each Hamiltonian matrix element is the integral

$$\mathbf{H}_{xy} = \langle \psi_x | H | \psi_y \rangle, \qquad (1.30)$$

where H is the full Hamiltonian operator (Eq. 1.5) and ψ_x and ψ_y define some specific configuration. Diagonalization of this Hamiltonian then produces the solution: the set of coefficients that defines the configuration interaction (CI) wavefunction.[13] This is a rather daunting problem as the number of configurations is infinite in the exact solution, but still quite large for any truncated configuration set.

Fortunately, many of the matrix elements of the CI Hamiltonian are zero. Brillouin's Theorem[14] states that the matrix element between the HF configuration and *any* singly excited configuration ψ_i^a is zero. The Condon–Slater rules provide the algorithm for computing any generic Hamiltonian matrix elements. One of these rules states that configurations that differ by three or more electron occupancies will be zero. In other words, suppose we have two configurations ψ_A and ψ_B defined as the Slater determinants $\psi_A = \left| \phi_1 \phi_2 \cdots \phi_{n-3} \phi_i \phi_j \phi_k \right|$ and $\psi_B = \left| \phi_1\ \phi_2 \cdots \phi_{n-3} \phi_r \phi_s \phi_t \right|$, then

$$\langle \psi_A | H | \psi_B \rangle = 0. \qquad (1.31)$$

Therefore, the Hamiltonian matrix tends to be rather sparse, especially as the number of configurations included in the wavefunction increases.

As the Hamiltonian is both spin- and symmetry-independent, the CI expansion need only contain configurations that are of the spin and symmetry of interest. Even taking advantage of the spin, symmetry, and sparseness of the Hamiltonian matrix, we may nonetheless be left with a matrix of size well beyond our computational resources.

Two approaches towards truncating the CI expansion to some manageable length are utilized. The first is to delete some subset of virtual MOs from being

potentially occupied. Any configuration where any of the very highest energy MOs are occupied will be of very high energy and will likely contribute very little towards the description of the ground state. Similarly, we can freeze some MOs (usually those describing the core electrons) to be doubly occupied in all configurations of the CI expansion. Those configurations where the core electrons are promoted into a virtual orbital are likely to be very high in energy and unimportant.

The second approach is to truncate the expansion at some level of excitation. By Brillouin's Theorem, the single excited configurations will not mix with the HF reference. By the Condon−Slater rules, this leaves the doubles configurations as the most important for including in the CI expansion. Thus, the smallest reasonable truncated CI wavefunction includes the reference and all doubles configurations (CID):

$$\Psi_{\text{CID}} = c_0 \psi_{\text{HF}} + \sum_{i,j}^{\text{occ}} \sum_{a,b}^{\text{vir}} c_{ij}^{ab} \psi_{ij}^{ab}. \tag{1.32}$$

The most widely employed CI method includes both the singles and doubles configurations (CISD):

$$\Psi_{\text{CISD}} = c_0 \psi_{\text{HF}} + \sum_{i}^{\text{occ}} \sum_{a}^{\text{vir}} c_i^a \psi_i^a + \sum_{i,j}^{\text{occ}} \sum_{a,b}^{\text{vir}} c_{ij}^{ab} \psi_{ij}^{ab}, \tag{1.33}$$

where the singles configurations enter by their nonzero matrix elements with the doubles configurations. Higher-order configurations can be incorporated, if desired.

1.2.2 Size Consistency

Suppose one was interested in the energy of two molecules separated far from each other. (This is not as silly as it might sound—it is the description of the reactants in the reaction $A + B \rightarrow C$.) This energy could be computed by calculating the energy of the two molecules at some large separation, say 100 Å. An alternative approach is to calculate the energy of each molecule separately and then add their energies together. These two approaches should give the same energy. If the energies are identical, we call the computational method "size consistent."

Although the HF method and the complete CI method (infinite basis set and all possible configurations) are size-consistent, a truncated CI is *not* size-consistent! A simple way to understand this is to examine the CID case for the H_2 dimer, with the two molecules far apart. The CID wavefunction for the H_2 molecule includes the double excitation configuration. So, taking twice the energy of this monomer effectively includes the configuration where *all four* electrons have been excited. However, in the CID computation of the dimer, this configuration is not allowed; only doubles configurations are included, not this quadruple

configuration. The Davidson correction[15] approximates the energy of the missing quadruple configurations as

$$E_Q = (1 - c_0)(E_{CISD} - E_{HF}). \tag{1.34}$$

1.2.3 Perturbation Theory

An alternative approach towards including electron correlation is provided by perturbation theory. Suppose we have an operator $\hat{O}$ that can be decomposed into two component operators

$$\hat{O} = \hat{O}^{(0)} + \hat{O}', \tag{1.35}$$

where the eigenvectors and eigenvalues of $\hat{O}^{(0)}$ are known. The operator $\hat{O}'$ defines a perturbation upon this known system to give the true operator. If the perturbation is small, then Rayleigh–Schrödinger perturbation theory provides an algorithm for finding the eigenvectors of the full operator as an expansion of the eigenvectors of $\hat{O}^{(0)}$. The solutions derive from a Taylor series, which can be truncated to whatever order is desired.

Møller and Plesset developed the means for applying perturbation theory to a molecular system.[16] They divided the full Hamiltonian (Eq. 1.5) into essentially the HF Hamiltonian, where the solution is known and a set of eigenvectors can be created (the configurations discussed above), and a perturbation component that is essentially the instantaneous electron–electron correlation. The HF wavefunction is correct through first-order Møller–Plesset (MP1) perturbation theory. The second-order correction (MP2) involves doubles configurations, as does MP3. The fourth-order correction (MP4) involves triples and quadruples. The terms involving the triples configuration are especially time-consuming. MP4SDQ is fourth-order perturbation theory neglecting the triple contributions, an approximation that is appropriate when the HOMO–LUMO (highest occupied molecular orbital/lowest unoccupied molecular orbital) gap is large.

The major benefit of perturbation theory is that it is computationally more efficient than CI. MP theory, however, is not variational. This means that, at any particular order, the energy may be above or below the actual energy. Furthermore, because the perturbation is really not particularly small, including higher-order corrections is not guaranteed to converge the energy, and extrapolation from the energy determined at a small number of orders may be impossible. On the positive side, MP theory is size-consistent at any order.

1.2.4 Coupled-Cluster Theory

Coupled-cluster theory, developed by Cizek,[17] describes the wavefunction as

$$\Psi = e^{\hat{T}} \psi_{HF}. \tag{1.36}$$

The operator $\hat{T}$ is an expansion of operators

$$\hat{T} = \hat{T}_1 + \hat{T}_2 + \cdots + \hat{T}_n, \tag{1.37}$$

where the $\hat{T}_i$ operator generates all of the configurations with i electron excitations. Because Brillouin's Theorem states that singly-excited configurations do not mix directly with the HF configuration, the $\hat{T}_2$ operator

$$\hat{T}_2 = \sum_{i,j}^{occ} \sum_{a,b}^{vir} t_{ij}^{ab} \psi_{ij}^{ab} \tag{1.38}$$

is the most important contributor to $\hat{T}$. If we approximate $\hat{T} = \hat{T}_2$, we have the CCD (coupled-cluster doubles) method, which can be written as the Taylor expansion:

$$\Psi_{CCD} = e^{\hat{T}_2} \psi_{HF} = \left(1 + \hat{T}_2 + \frac{\hat{T}_2^2}{2!} + \frac{\hat{T}_2^3}{3!} + \cdots\right)\psi_{HF}. \tag{1.39}$$

Because of the incorporation of the third and higher terms of Eq. (1.36), the CCD method *is* size consistent. Inclusion of the $\hat{T}_1$ operator is only slightly more computationally expensive than the CCD calculation and so the CCSD (coupled-cluster singles and doubles) method is the typical coupled-cluster computation. Inclusion of the $\hat{T}_3$ operator is quite computationally demanding. An approximate treatment, where the effect of the triples contribution is incorporated in a perturbative treatment, is the CCSD(T) method,[18] which has become the "gold standard" of computational chemistry—the method of providing the most accurate evaluation of the energy. CCSD(T) requires substantial computational resources and is therefore limited to relatively small molecules. Another downside to the CC methods is that they are not variational.

There are a few minor variations on the CC methods. The quadratic configuration interaction including singles and doubles (QCISD)[19] method is nearly equivalent to CCSD. Another variation on CCSD is to use the Brueckner orbitals. Brueckner orbitals are a set of MOs produced as a linear combination of the HF MOs such that all of the amplitudes of the singles configurations (t_i^a) are zero. This method is called BD and differs from the CCSD method only in fifth order.[20] Inclusion of triples configurations in a perturbative way, BD(T), is frequently more stable (convergence of the wavefunction is often smoother) than in the CCSD(T) treatment.

1.2.5 Multiconfiguration SCF (MCSCF) Theory and Complete Active Space SCF (CASSCF) Theory

To motivate a discussion of a different sort of correlation problem, we examine how to compute the energy and properties of cyclobutadiene. A RHF calculation of rectangular D_{2h} cyclobutadiene **1** reveals four π MOs, as shown in Figure 1.3. The HF configuration for this molecule is

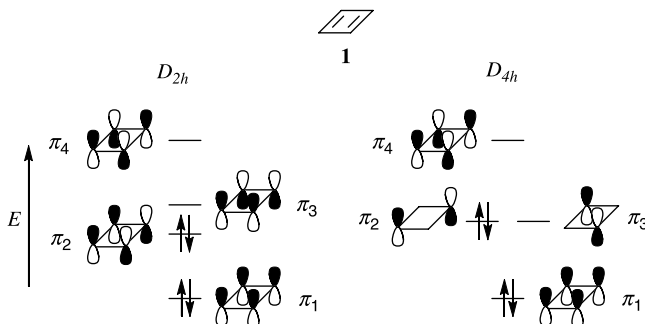$$\psi_{HF} = \left|\cdots \pi_1^2 \pi_2^2\right|. \tag{1.40}$$

Figure 1.3. π MO diagram of cyclobutadiene (**1**). Only one configuration is shown for the D_{4h} form.

As long as the HOMO–LUMO energy gap (the difference in energy of π_2 and π_3) is large, then this single configuration wavefunction is reasonable. However, as we distort cyclobutadiene more and more towards a D_{4h} geometry, the HOMO–LUMO gap grows smaller and smaller, until we reach the square planar structure where the gap is nil. Clearly, the wavefunction of Eq. (1.40) is inappropriate for D_{4h} cyclobutadiene, and also for geometries close to it, because it does not contain any contribution from the degenerate configuration $\left| \cdots \pi_1^2 \pi_3^2 \right|$. Rather, a more suitable wavefunction for cyclobutadiene might be

$$\psi = c_1 \left| \cdots \pi_1^2 \pi_2^2 \right| + c_2 \left| \cdots \pi_1^2 \pi_3^2 \right|. \tag{1.41}$$

This wavefunction appears to be a CI wavefunction with two configurations. Adding even more configurations, like spin-paired, $\left| \cdots \pi_1^2 \pi_2^1 \pi_3^1 \right|$, would capture more of the *dynamic* electron correlation. The underlying assumption to the CI expansion is that the single-configuration reference, the HF wavefunction, is a reasonable description of the molecule. For cyclobutadiene, especially as it nears the D_{4h} geometry, the HF wavefunction does not capture the inherent multiconfigurational nature of the electron distribution. The MOs used to describe the first configuration of Eq. (1.41) are *not* the best for describing the second configuration. To capture this *non-dynamic* correlation, we must determine the set of MOs that best describe *each* of the configurations of Eq. (1.41), giving us the wavefunction

$$\psi_{\text{MCSCF}} = c_1 \left| \cdots \sigma_{11}^2 \pi_1^2 \pi_2^2 \right| + c_2 \left| \cdots \sigma_{11}'^2 \pi_1'^2 \pi_3'^2 \right|, \tag{1.42}$$

where the primed orbitals are different from the unprimed set. We have explicitly indicated the highest σ-orbital in the primed and unprimed set to emphasize that all of the MOs are optimized within each configuration. In the multiconfiguration SCF (MCSCF)[21] method, the coefficient c_i of each configuration, along with the LCAO expansion of the MOs of each configuration, are solved for in an iterative, self-consistent way.

   The question arises as to how to select the configurations for the MCSCF wavefunction. In the example of cyclobutadiene, one might wonder about also

including the configurations where π_2 and π_3 are each singly occupied with net spin of zero,

$$\psi_{\text{MCSCF}} = c_1 \left| \cdots \sigma_{11}^2 \pi_1^2 \pi_2^2 \right| + c_2 \left| \cdots \sigma_{11}'^2 \pi_1'^2 \pi_3'^2 \right|$$
$$+ c_3 \left| \cdots \sigma_{11}'' \pi_1''^2 \pi_2''^1(\alpha) \pi_3''^1(\beta) \right|. \tag{1.43}$$

Perhaps a more appropriate selection might also include configurations where the electrons from π_1 are excited into the higher-lying π-orbitals. A goal of ab initio theory is to make as few approximations and as few arbitrary decisions as possible. In order to remove the possibility that an arbitrary selection of configurations might distort the result, the Complete Active Space SCF (CASSCF)[22] procedure dictates that *all* configurations involving a set of MOs (the active space) and a given number of electrons comprise the set of configurations to be used in the MCSCF procedure. This set of configurations is indicated as CASSCF(n,m), where n is the number of electrons and m is the number of MOs of the active space (both occupied and virtual). So, an appropriate calculation for cyclobutadiene is CASSCF(4,4), where all four π-electrons are distributed in all possible arrangements among the four π MOs.

As MCSCF attempts to account for the nondynamic correlation, really to correct for the inherent multiconfiguration nature of the electron distribution, how can one then also capture the dynamic correlation? The application of perturbation theory using the MCSCF wavefunction as the reference requires some choice as to the non-perturbed Hamiltonian reference. This had led to a number of variants of multireference perturbation theory. The most widely utilized is CASPT2N,[23] which is frequently referred to as CASPT2, although this designation ignores other flavors developed by the same authors. Along with CCSD(T), CASPT2N is considered to be one of the more robust methods for obtaining the highest quality treatments of molecular quantum mechanics.

1.2.6   Composite Energy Methods

Although rigorous quantum chemical methods are available, the best of them are exceptionally demanding in terms of computer performance (CPU time, memory, and hard disk needs). For all but the smallest molecules, these best methods are impractical.

How then to capture the effects of large basis sets and extensive accounting of electron correlation? The answer depends in part on what question one is seeking to answer. Are we looking for accurate energies or structures or properties? As all of these are affected by the choice of basis set and treatment of electron correlation, oftentimes to different degrees, just what methods are used depends on what information we seek. As we will demonstrate in the following chapters, prediction of geometries is usually less demanding than obtaining accurate energies. We may then get by with relatively small basis sets and low-orders of electron correlation treatment. Accurate energies are, however, quite sensitive to the computational method.

The composite methods were developed to provide an algorithm for obtaining accurate energies. They take the approach that the effect of larger basis sets, including the role of diffuse and polarization functions, and the effect of higher-order treatment of electron correlation can be approximated as additive corrections to a lower level computation. One can thereby reproduce a huge computation, say a CCSD(T) calculation with the 6-311+G(3df,2p) basis set, by summing together the results of a series of much smaller calculations.

This first model chemistry, called G1,[24] was proposed by Pople and Curtiss in the late 1980s, but was soon replaced by the more accurate G2[25] model chemistry. The baseline calculation is to compute the energy at MP4 with the 6-311G(d,p) basis set using the geometry optimized at MP2 with the 6-31G(d) basis set. Corrections are made to this baseline energy. The steps for carrying out the G2 calculation are as follows:

1. Optimize the geometry at HF/6-31G(d) and compute the zero-point vibrational energy (ZPVE).

2. Optimize the geometry at MP2/6-31G(d) and use this geometry in all subsequent calculations.

3. Compute the baseline energy: E[MP4/6-311G(d,p)].

4. Correct for diffuse functions: E[MP4/6-311+G(d,p)] − E[MP4/6-311G(d,p)].

5. Correct for addition of more polarization functions: E[MP4/6-311G(2df,p)] − E[MP4/6-311G(d,p)].

6. Correct for better treatment of electron correlation: E[QCISD(T)/6-311G(d)] − E[MP4/6-311G(d,p)].

7. Correct for third set of polarization functions alongside the diffuse functions. In order to save computational effort, compute this correction at MP2: E[MP2/6-311+G(3df,2p)] − E[MP2/6-311G(2df,p)] − E[MP2/6-311 + G(d,p)] + E[MP2/6-311G(d,p)].

8. Apply an empirical correction to minimize the difference between the computed and experimental values of the atomization energies of 55 molecules: −0.00481 ∗ (number of valence electron pairs) −0.00019 ∗ (number of unpaired valence electrons).

9. Compute the G2 energy as E[G2] = 0.8929 ∗ ZPVE(1) + (3) + (4) + (5) + (6) + (7) + (8).

Subsequently, the G2(MP2)[26] model was produced, with the major advantage of avoiding the MP4 computations in favor of MP2. The G3 model,[27] which utilizes a very large basis set in Step 7 and the MP4/6-31G(d) energy as the baseline, is somewhat more accurate than G2. There are also two other series of composite methods, the CBS-n models of Petersson[28,29] and the Wn models of Martin.[30] All of these composite methods are conceptually similar, just varying in which methods are used for the baseline and the corrections, and what sets of compounds, and what

properties will be used in the ultimate fitting procedure.[31] Because of the fitting of the calculated energy to some experimental energy (often atomization energies), these composite methods have an element of semi-empirical nature to them. The focal-point scheme developed by Allen and Schaefer[32] combines (1) the effect of basis set by extrapolating the energies from calculations with large basis sets (up to cc-pV6Z), (2) the effect of higher-order correlation by extrapolation of energies from higher-order MP (up to MP5) or CC (up to CCSDT), and (3) corrections for the assumed additivity of basis set and correlation effects. It produces extraordinary accuracy without resorting to any empirical corrections, but the size of the computations involved restricts application to molecules of less than 10 atoms.

An alternative composite method divides the system of interest into different distinct regions or layers. Each layer is then treated with an appropriate computational method. Typically, some small geometric layer is evaluated using a high-level quantum mechanical method and the larger geometric layer is evaluated using a more modest computational method, perhaps even molecular mechanics. This type of procedure is called "QM/MM." In its simplest application, the total energy is evaluated as

$$E_{\text{complete}} = E_{\text{MM}}^{\text{large}} + (E_{\text{QM}}^{\text{small}} - E_{\text{MM}}^{\text{small}}). \tag{1.44}$$

The QM/MM procedure is particularly appropriate for very large molecules such as enzymes, where the active site is evaluated with a high-level quantum computation, and the protein backbone is treated with molecular mechanics.

A number of different QM/MM algorithms have been developed.[33,34] A great deal of effort has been directed towards properly treating the interfacial regions between the layers, particularly when chemical bonds cross the boundary. A popular method is the ONIOM ("our own *n*-layered integrated molecular orbital molecular mechanics") scheme,[35] which divides the system into three layers: a small layer where the important chemistry occurs and is treated with a very accurate QM method, a medium layer usually treated with a semi-empirical MO method, and a large layer typically treated with molecular mechanics.

1.3 DENSITY FUNCTIONAL THEORY (DFT)

The electronic wavefunction is dependent on $3n$ variables: the x, y, and z coordinates of each electron. As such, it is quite complicated and difficult to readily interpret. The total electron density $\rho(\mathbf{r})$ is dependent on just three variables: the x, y, and z positions in space. Because $\rho(\mathbf{r})$ is simpler than the wavefunction and is also observable, perhaps it might offer a more direct way to obtain the molecular energy?

The Hohenberg–Kohn[36] existence theorem proves just that. There exists a unique functional such that

$$E[\rho(\mathbf{r})] = E_{\text{elec}}, \tag{1.45}$$

where E_{elec} is the exact electronic energy. Furthermore, they demonstrated that the electron density obeys the variational theorem. This means that, given a specific electron density, its energy will be greater than or equal to the exact energy. These two theorems constitute the basis of density functional theory (DFT). The hope is that evaluation of Eq. (1.45) might be easier than traditional ab initio methods because of the simpler variable dependence.

Before proceeding with an explanation of how this translates into the ability to compute properties of a molecule, we need to define the term *functional*. A mathematical *function* is one that relates a scalar quantity to another scalar quantity, that is, $y = f(x)$. A mathematical *functional* relates a function to a scalar quantity and is denoted with brackets, that is, $y = F[f(x)]$. In Eq. (1.45), the function $\rho(\mathbf{r})$ depends on the spatial coordinates, and the energy depends on the values (is a functional) of $\rho(\mathbf{r})$.

In order to solve for the energy via the DFT method, Kohn and Sham[37] proposed that the functional has the form

$$E[\rho(\mathbf{r})] = T_{e'}[\rho(\mathbf{r})] + V_{ne}[\rho(\mathbf{r})] + V_{ee}[\rho(\mathbf{r})] + E_{xc}[\rho(\mathbf{r})] \tag{1.46}$$

where V_{ne}, the nuclear–electron attraction term, is

$$V_{ne}[\rho(\mathbf{r})] = \sum_{j}^{nuclei} \int \frac{Z_j}{|\mathbf{r} - \mathbf{r}_k|} \rho(\mathbf{r}) d\mathbf{r}, \tag{1.47}$$

and V_{ee}, the classical electron–electron repulsion term, is

$$V_{ee}[\rho(\mathbf{r})] = \frac{1}{2} \int \int \frac{\rho(\mathbf{r}_1)\rho(\mathbf{r}_2)}{|\mathbf{r}_1 - \mathbf{r}_2|} d\mathbf{r}_1 d\mathbf{r}_2. \tag{1.48}$$

The real key, however, is the definition of the first term of Eq. (1.46). Kohn and Sham defined it as the kinetic energy of *noninteracting* electrons whose density is the same as the density of the real electrons, the true interacting electrons. The last term is called the exchange-correlation functional, and is a catch-all term to account for all other aspects of the true system.

The Kohn–Sham procedure is then to solve for the orbitals that minimize the energy, which reduces to the set of pseudoeigenvalue equations

$$\hat{h}_i^{KS} \chi_i = \varepsilon_i \chi_i. \tag{1.49}$$

This is closely analogous to the Hartree equations (Eq. 1.7). The Kohn–Sham orbitals are separable by definition (the electrons they describe are *noninteracting*), analogous to the HF MOs. Equation (1.49) can, therefore, be solved using a similar set of steps as was used in the Hartree–Fock–Roothaan method.

So, for a similar computational cost as the HF method, DFT produces the energy of a molecule that *includes the electron correlation*! This is the distinct advantage of

DFT over the traditional ab initio methods discussed previously—it is much more computationally efficient in providing the correlation energy.

DFT is not without its own problems, however. Although the Hohenberg–Kohn Theorem proves the existence of a functional that relates the electron density to the energy, it offers no guidance as to the form of that functional. The real problem is the exchange-correlation term of Eq. (1.44). There is no way of deriving this term, and so a series of different functionals have been proposed, leading to lots of different DFT methods. A related problem with DFT is that if the chosen functional fails, there is no way to systematically correct its performance. Unlike with CI, where one can systematically improve the result by increasing the number and type of configurations employed in the wavefunction expansion, or with MP theory, where one can move to arbitrarily higher order corrections, if a given functional does not provide a suitable result, one must go back to square one and select a new functional. Paraphrasing Cramer's[1] description of the contrast between HF and DFT, HF and the various post-HF electron correlation methods provide an *exact* solution to an *approximate* theory, but DFT provides an *exact* theory with an *approximate* solution.

1.3.1 The Exchange-Correlation Functionals

The exchange-correlation functional is generally written as a sum of two components, an exchange part and a correlation part. This is an assumption, an assumption that we have no way of knowing is true or not. These component functionals are usually written in terms of an energy density ε,

$$E_{xc}[\rho(\mathbf{r})] = E_x[\rho(\mathbf{r})] + E_c[\rho(\mathbf{r})] = \int \rho(\mathbf{r})\varepsilon_x[\rho(\mathbf{r})]d\mathbf{r} + \int \rho(\mathbf{r})\varepsilon_c[\rho(\mathbf{r})]d\mathbf{r}. \qquad (1.50)$$

The local density approximation (LDA) assumes that the value of ε_x could be determined from just the value of the density. A simple example of the LDA is Dirac's treatment of a uniform electron gas, which gives

$$\varepsilon_x^{LDA} = -C_x\rho^{1/3}. \qquad (1.51)$$

This can be extended to the local spin density approximation (LSDA) for those cases where the α and β densities are not equal. Slater's X_α method is a scaled form of Eq. (1.51), and often the terms "LSDA" and "Slater" are used interchangeably.

Local correlation functionals were developed by Vosko, Wilk, and Nusair, which involve a number of terms and empirical scaling factors.[38] The most popular versions are called VWN and VWN5. The combination of a local exchange and a local correlation energy density is the SVWN method.

In order to make improvements over the LSDA, one has to assume that the density is not uniform. The approach that has been taken is to develop functionals that are dependent on not just the electron density but also derivatives of the

density. This constitutes the generalized gradient approximation (GGA). It is at this point that the form of the functionals begins to cause the eyes to glaze over and the acronyms to appear to be random samplings from an alphabet soup. For full mathematical details, the interested reader is referred to the books by Cramer[1] or Jensen[2] or the monograph by Koch and Holhausen, *A Chemist's Guide to Density Functional Theory*.[39]

We will present here just a few of the more widely utilized functionals. The DFT method is denoted with an acronym that defines the exchange functional and the correlation functional, in that order. For the exchange component, the most widely used is one proposed by Becke.[40] It introduces a correction term to LSDA that involves the density derivative. The letter "B" signifies its use as the exchange term. Of the many correlation functionals, the two most widely used are due to Lee, Yang, and Parr[41] (referred to as "LYP") and Perdew and Wang[42] (referred to as "PW91"). Although the PW91 functional depends on the derivative of the density, the LYP functional depends on $\nabla^2\rho$. So the BPW91 designation indicates use of the Becke exchange functional with the Perdew–Wang (19)91 correlation functional.

Last are the hybrid methods that combine the exchange-correlation functionals with some admixture of the HF exchange term. The most widely used DFT method is the hybrid B3LYP functional,[43,44] which includes Becke's exchange functional along with the LYP correlation functional:

$$E_{xc}^{B3LYP} = (1 - a)E_x^{LSDA} + aE_x^{HF} + b\Delta E_x^B + (1 - c)E_c^{LSDA} + cE_c^{LYP}. \qquad (1.52)$$

The three variables (a, b, and c) are the origin of the "3" in the acronym. As these variables are fit to reproduce experimental data, B3LYP (and all other hybrid methods) contain some degree of "semi-empirical" nature. Recently, hybrid meta functionals[45–47] have been developed, which include a kinetic energy density. These new functionals have shown excellent performance[47] in situations that have been notoriously problematic for other DFT methods, such as noncovalent interactions, including π–π stacking, and transition metal–transition metal bonds.

1.4 GEOMETRY OPTIMIZATION

The first step in performing a quantum chemical calculation is to select an appropriate method from the ones discussed above. We will discuss the relative merits and demerits of the methods in the remaining chapters of the book. For now, we assume that we can choose a method that will be suitable for the task at hand. The nomenclature for designating the method is "quantum mechanical treatment/ basis set," such as MP2/6-31+G(d), which means that the energy is computed using the MP2 theory with the 6-31+G(d) basis set.

Next, we need to choose the geometry of the molecule. It is antithetical to the idea of ab initio methods to arbitrarily choose a geometry; rather, it is more consistent to

find the best geometry predicted by the quantum mechanics itself. In other words, we should optimize the geometry of the molecule such that a minimum energy structure is found.

There are many, many methods for optimizing the value of a function, and detailed discussion of these techniques is inappropriate here.[48] The general procedure is to start with a guess of the molecular geometry and then systematically change the positions of the atoms in such a way as the energy decreases, continuing to vary the positions until the minimum energy is achieved. So how does one decide how to alter the atomic positions; that is, should a particular bond be lengthened or shortened? If the derivative of the energy with respect to that bond distance is positive, that means that the energy will *increase* with an increase in the bond separation. Computation of all of the energy gradients with respect to the positions of the nuclei will offer guidance then in which directions to move the atoms. But how far should the atoms be moved; that is, how much should the bond distance be decreased? The second derivatives of the energy with respect to the atomic coordinates provides the curvature of the surface, which can be used to determine just how far each coordinate needs to be adjusted. The collection of these second derivatives is called the Hessian matrix, where each element $\mathbf{H}_{ij}$ is defined as

$$\mathbf{H}_{ij} = \frac{\partial^2 E}{\partial q_1 \partial q_2},$$
(1.53)

where q_i is an atomic coordinate (say for example the y-coordinate of the seventh atom).

Efficient geometry optimization, therefore, typically requires the first and second derivatives of the energies with respect to the atomic coordinates. Computation of these derivatives is always more time consuming than the evaluation of the energy itself. Further, analytical expression of the first and second energy derivatives is not available for some methods. The lack of these derivatives may be a deciding factor in which method might be appropriate for geometry optimization. An economical procedure is to evaluate the first derivatives and then make an educated guess at the second derivatives, which can be updated numerically as each new geometry is evaluated.

The optimization procedure followed in many computational chemistry programs is as follows:

1. Make an initial guess of the geometry of the molecule.
2. Compute the energy and gradients of this structure. Obtain the Hessian matrix as a guess or by computation.
3. Decide if the geometry meets the optimization criteria. If so, we are done.
4. If the optimization criteria are not met, use the gradients and Hessian matrix to suggest a new molecular geometry. Repeat Step 2, with the added option of obtaining the new Hessian matrix by numerical updating of the old one.

What are the criteria for determining if a structure has been optimized? A local energy minimum will have all of its gradients equal to zero. Driving a real-world quantum chemical computation all the way until every gradient vanishes will involve a huge number of iterations with very little energy change in many of the last steps. Typical practice is to set a small but nonzero value as the maximum acceptable gradient.

Testing of the gradient alone is not sufficient for defining a local energy minimum. Structures where the gradient vanishes are known as critical points, some of which may be local minima. The diagonal elements of the Hessian matrix, called its eigenvalues, identify the nature of the critical point. Six of these eigenvalues will have values near zero and correspond to the three translational and rotational degrees of freedom. If all of the remaining eigenvalues are positive, the structure is a local minimum. A transition state is characterized by having one and only one negative eigenvalue of the diagonal Hessian matrix. Computing the full and accurate Hessian matrix can therefore confirm the nature of the critical point, be it a local minimum, transition state, or some other higher-order saddle point.

At the transition state, the negative eigenvalue of the Hessian matrix corresponds with the eigenvector that is downhill in energy. This is commonly referred to as the reaction coordinate. Tracing out the steepest descent from the transition state, with the initial direction given by the eigenvector with the negative eigenvalue, gives the *minimum energy path* (MEP). If this is performed using mass-weighted coordinates, the path is called the *intrinsic reaction coordinate* (IRC).[49]

The Hessian matrix is useful in others ways, too. The square root of the element of the diagonal mass-weighted Hessian is proportional to the vibrational frequency ω_i. Within the harmonic oscillator approximation, the zero-point vibrational energy (ZPVE) is obtained as

$$ZPVE = \sum_i^{\text{vibrations}} \frac{h\omega_i}{2}. \tag{1.54}$$

The eigenvector associated with the diagonal mass-weighted Hessian defines the atomic motion associated with that particular frequency. The vibrational frequencies can also be used to compute the entropy of the molecule and ultimately the Gibbs free energy.

The molecular geometry is less sensitive to computational method than is its energy. As geometry optimization can be computationally time-consuming, often a molecular structure is optimized using a smaller, lower-level method, and then the energy is computed with a more accurate higher-level method. For example, one might optimize the geometry at the HF/6-31G(d) level and then compute the energy of *that* geometry using the CCSD(T)/6-311+G(d,p) method. This computation is designated "CCSD(T)/6-311+G(d,p)//HF/6-31G(d)" with the double slashes separating the method used for the single-point energy calculation (on the left-hand side) from the method used to optimize the geometry (on the right-hand side).

1.5 POPULATION ANALYSIS

We next take on the task of analyzing the wavefunction and electron density. All of the wavefunctions described in this chapter are represented as very long lists of coefficients. Making sense of these coefficients is nigh impossible, not just because there are so many coefficients, and not just because these coefficients multiply Gaussian functions that have distinct spatial distributions, but fundamentally because the wavefunction itself has no physical interpretation. Rather, the square of the wavefunction at a point is the probability of locating an electron at that position. It is therefore more sensible to examine the electron density $\rho(\mathbf{r})$. Plots of the electron density reveal a rather featureless distribution; molecular electron density looks very much like a sum of spherical densities corresponding to the atoms in the molecule. The classical notions of organic chemistry, like a build-up of density associated with a chemical bond, or a lone pair, or a π-cloud are not readily apparent—as seen in isoelectronic surfaces of ammonia **2** and benzene **3** in Figure 1.4.

The notion of transferable atoms and functional groups pervades organic chemistry—a methyl group has some inherent, common characteristics whether the methyl group is in hexane, toluene, or methyl acetate. One of these characteristics is, perhaps, the charge carried by an atom (or a group of atoms) within a molecule. If we can determine the number of electrons associated with an atom in a molecule, which we call the *gross atomic population N(k)*, then the charge carried by the atom (q_k) is its atomic number Z_k less its population

$$q_k = Z_k - N(k). \tag{1.55}$$

As there is no operator that produces the "atomic population," it is not an observable and so the procedure for computing $N(k)$ is arbitrary. There are two classes of methods for computing the atomic population: those based on the orbital population and those based on a spatial distribution.[50]
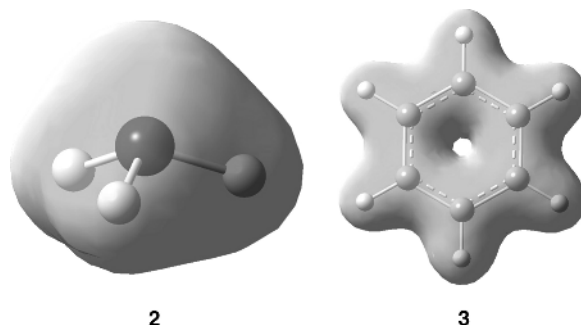

2   **3**

Figure 1.4. Isoelectronic surface of the total electron density of ammonia (**2**) and benzene (**3**). Note the lack of lone pairs or a π-cloud.

1.5.1 Orbital-Based Population Methods

Of the orbital-based methods, the earliest remains the most widely used method: that developed by Mulliken and called the Mulliken Population.[51] The total number of electrons in a molecule N must equal the integral of $\rho(\mathbf{r})$ over all space. For simplicity we will examine the case of the HF wavefunction. This integral can then be expressed as

$$N = \int \psi_{HF}\psi_{HF}d\mathbf{r} = \sum_i^{MOs} N(i) \sum_r^{AOs} c_{ir}^2 + 2\sum_i^{MOs} N(i) \sum_{r>s}^{AOs} c_{ir}c_{is}S_{rs}, \qquad (1.56)$$

where $N(i)$ is the number of electrons in MO ϕ_i, and S_{rs} is the overlap integral of atomic orbitals χ_r and χ_s. Mulliken then collected all terms of Eq. (1.56) for a given atom k, to define the *net atom population n(k)*

$$n(k) = \sum_i^{MOs} N(i) \sum_{r_k} c_{ir_k}^2 \qquad (1.57)$$

and the *overlap population N(k, l)*

$$N(k, l) = \sum_i^{MOs} N(i) \sum_{r_k, s_l} c_{ir_k} c_{is_l} S_{r_k s_l}. \qquad (1.58)$$

The net atomic population neglects the electrons associated with the overlap between two atoms. Mulliken arbitrarily divided the overlap population equally between the two atoms, producing the *gross atomic population*

$$N(k) = \sum_i^{MOs} N(i) \sum_{r_k} c_{ir_k} \left(c_{ir_k} + \sum_{s_l \neq k} c_{is_l} S_{r_k s_l} \right). \qquad (1.59)$$

The Mulliken population is easy to compute and understand. All electrons that occupy an orbital centered on atom k "belong" to that atom. However, Mulliken populations suffer from many problems. If a basis set is not balanced, the population will reflect this imbalance. Orbital populations can be negative or greater than zero. This deficiency can be removed[52] by using orthogonal basis functions (the Löwdin orbitals[53]). But perhaps most serious is that the Mulliken procedure totally neglects the spatial aspect of the atomic orbitals (basis functions). Some basis functions can be quite diffuse, and electrons in these orbitals might in fact be closer to a neighboring atom than to the nuclei upon which the function is centered. Nonetheless, the Mulliken procedure assigns these electrons back to the atom upon which the AO is centered. The Natural Population Analysis (NPA) of Weinhold[54] creates a new set of atomic orbitals that have maximal

occupancy, effectively trying to create the set of *local* atomic orbitals. NPA charges, although somewhat more expensive to compute, suffer fewer of the problems that plague the Mulliken analysis.

1.5.2   Topological Electron Density Analysis

The alternative approach is to count the number of electrons in an atom's "space." The question is how to define the volume an individual atom occupies within a molecule. The topological electron density analysis (sometimes referred to as *atoms-in-molecules* or AIM) developed by Bader[55] uses the electron density itself to partition molecular space into atomic volumes.

The molecular electron density is composed of overlapping, radially-decreasing, distorted spheres of density. One can think of each nucleus as being the location of the "mountain peak" in the electron density. Between two neighboring atoms, there will then be a "valley" separating the two "mountains." The "pass" through the valley defines the boundary between the "mountains."

To do this in a more rigorous way, the local maxima and minima of the electron density are defined as critical points, the positions where

$$\nabla\rho(\mathbf{r}) = \left(\frac{\partial}{\partial x} + \frac{\partial}{\partial y} + \frac{\partial}{\partial z}\right)\rho(\mathbf{r}) = 0. \tag{1.60}$$

The type of electron density critical point is defined by diagonalized matrix $\mathbf{L}$,

$$\mathbf{L}_{ij} = \frac{\partial^2 \rho(\mathbf{r})}{\partial r_i \partial r_j}, \tag{1.61}$$

where r_i is the x, y, or z coordinate. Each critical point is then classified by the *rank*, the number of nonzero eigenvalues of $\mathbf{L}$, and the *signature*, the number of positive eigenvalues less the number of negative eigenvalues. The nuclei are $(3, -3)$ critical points, where the density is at a local maximum in all three directions. The bond critical point $(3, -1)$ is a minimum along the path between two bonded atoms, and a maximum in the directions perpendicular to the path.

A gradient path follows the increasing electron density towards a local maximum. The collection of all such paths that terminate at the bond critical point forms a curtain, a surface that separates the two neighboring atoms from each other. If we locate all of these surfaces (known as *zero-flux surfaces*) about a given atom, it defines the atomic basin Ω_k, a unique volume that contains a single nucleus. All gradient paths that originate within this basin terminate at the atomic nucleus. We can integrate the electron density within the atomic basin to obtain the electron population of the atom

$$N(k) = \int_{\Omega_k} \rho(\mathbf{r})\mathrm{d}\mathbf{r}. \tag{1.62}$$

The bond critical point is the origin of two special gradient paths. Each one traces the ridge of maximum electron density from the bond critical point to one of the two neighboring nuclei. The union of these two gradient paths is the *bond path*, which usually connects atoms that are joined by a chemical bond.

The inherent value of the topological method is that these atomic basins are defined by the electron density distribution of the molecule. No arbitrary assumptions are required. The atomic basins are quantum mechanically well-defined spaces, individually satisfying the virial theorem. Properties of an atom defined by its atomic basin can be obtained by integration of the appropriate operator within the atomic basin. The molecular property is then simply the sum of the atomic properties.

1.6 COMPUTED SPECTRAL PROPERTIES

Once the wavefunction is in hand, all observable properties can, at least in principle, be computed. This can include spectral properties, among the most important means for identifying and characterizing compounds. The full theoretical and computational means for computing spectral properties are quite mathematically involved and beyond the scope of this chapter. The remainder of the book is a series of case studies of the applicability of computational methods towards understanding organic chemistry, particularly aiming at resolving issues of structure, energetics, and mechanism. Questions of suitability and reliability of computational methods are taken up in these later chapters. However, in this section we will discuss the question of how the various computational methods perform in terms of predicting infrared (IR), nuclear magnetic resonance (NMR), and optical rotatory dispersion (ORD) spectra.

1.6.1 IR Spectroscopy

Vibrational frequencies, used to predict IR spectra, are computed from the Hessian matrix, assuming a harmonic oscillator approximation. Errors in the predicted frequencies can be attributed then to (1) the use of an incomplete basis set, (2) incomplete treatment of electron correlation, and (3) the anharmonicity of the potential energy surface. The first two can be assessed by examining a series of computations with different basis sets and treatments of electron correlation, looking for an asymptotic trend. In terms of treating the anharmonicity, recently developed techniques demonstrate how one can directly compute the anharmonic vibrational frequencies.[56]

Due to the harmonic approximation, most methods will overestimate the vibrational frequencies. Listed in Table 1.2 are the mean absolute deviations of the vibrational frequencies for a set of 32 simple molecules with different computational methods. A clear trend is that as the method improves in accounting for

TABLE 1.2. Mean Absolute Deviation (MAD) of the Vibrational Frequencies (cm^{-1}) for 32 Molecules.[a]

Method	MAD
HF	144
MP2	99
CCSD(T)	31
BPW	69
BLYP	59
B3LYP	31
*m*PW1PW	39

[a]Computed using the 6-311G(d,p) basis set.[57]

electron correlation, the predicted vibrational frequencies are in better accord with experiment.

Another view of the dependence of the vibrational frequencies upon computational method is given in Table 1.3, where the computed vibrational frequencies of formaldehyde and ethyne are compared with experimental values. Again, as the basis set is improved and as the accounting for electron correlation becomes more complete, the computed vibrational frequencies become more in accord with experiment.

Although the computed vibrational frequencies are in error, they appear to be systematically in error. Pople[61] proposed scaling the values of the vibrational frequencies to improve their overall agreement with experiment. The problem with scaling the frequencies is that a unique *scaling factor* must be determined for every different computational level, meaning a scaling factor has to be determined for every combination of computational method and basis set. Radom[62] has established the scaling factors for a number of computational levels, including HF, MP2, and DFT with various basis sets by fitting the frequencies from 122 molecules. Scaling factors for additional methods have been suggested by Schlegel[63] and others.[64] It is also important to recognize that the vibrational frequencies enter into the calculation of the ZPVE, and a different scaling factor is required to produce the appropriately scaled ZPVEs. Careful readers may have noted a scaling factor of 0.8929 applied to the ZPVE in Step 9 of the G2 composite method (Section 1.2.6).

A common use of computed vibrational frequencies is to ascertain the identity of an unknown structure by comparison with experimental IR spectra. Two recent examples of the positive identification of transient intermediates will suffice here. In the attempt to prepare benzocyclobutenylidene (**4**), an unknown was detected. By comparing the experimental IR spectrum with the computed IR spectra of a number of different proposed intermediates **5–8**, the cycloalkyne **6** was verified as the first intermediate detected. **6** then rearranges to **7** under

TABLE 1.3. Vibrational Frequencies (cm^{-1}) and Mean Absolute Deviation (MAD) from Experiment.[a]

Method	$\omega_1(a_1)$	$\omega_2(a_1)$	$\omega_3(a_1)$	$\omega_4(b_1)$	$\omega_5(b_2)$	$\omega_6(b_2)$	MAD
			Formaldehyde				
HF/6-311G(d,p)	3081	1999	1648	1337	3147	1364	134
HF/6-311++G(d,p)	3097	1996	1650	1337	3169	1363	140
HF/cc-pVDZ	3109	2013	1637	1325	3183	1360	142
HF/cc-pVTZ	3084	1999	1652	1337	3153	1370	137
HF/aug-cc-pVTZ	3087	1992	1648	1335	3155	1367	135
MP2/6-311G(d,p)	2964	1777	1567	1211	3030	1291	19
MP2/aug-cc-pVTZ	2973	1753	1540	1198	3048	1267	22
CISD/6-311G(d,p)	3007	1879	1595	1243	3071	1316	56
CISD/aug-cc-pVTZ	3021	1875	1580	1245	3090	1305	57
QCISD/6-311G(d,p)	2945	1913	1566	1207	3003	1290	39
QCISD/aug-cc-pVTZ	2955	1803	1545	1204	3021	1275	21
CCSD/aug-cc-pVTZ	2961	1817	1549	1206	3030	1279	24
CCSD(T)/aug-cc-pVTZ	2932	1765	1530	1181	3000	1262	18
Expt[b]	2978	1778	1529	1191	2997	1299	
Method	$\omega_1(\sigma_g)$	$\omega_2(\sigma_g)$	$\omega_3(\sigma_u)$	$\omega_4(\pi_g)$	$\omega_5(\pi_u)$	MAD	
			Ethyne				
HF/6-311G(d, p)	3676	2215	3562	815	875	171	
HF/6-311++G(d,p)	3675	2206	3561	817	872	168	
HF/cc-pVDZ	3689	2224	3577	784	866	170	
HF/cc-pVTZ	3674	2213	3556	807	868	166	
HF/aug-cc-pVTZ	3674	2210	3554	810	869	166	
MP2/6-311G(d,p)	3550	1970	3460	562	770	45	
MP2/aug-cc-pVTZ	3534	1968	3432	601	754	25	
CISD/6-311G(d,p)	3587	2088	3484	642	804	63	
CISD/aug-cc-pVTZ	3583	2099	3467	682	798	68	
QCISD/6-311G(d,p)	3536	2023	3438	577	774	31	
QCISD/aug-cc-pVTZ	3527	2035	3416	630	768	17	
CCSD/aug-cc-pVTZ	3529	2044	3417	634	770	21	
CCSD(T)/aug-cc-pVTZ	3503	1995	3394	593	748	15	
Expt[c]	3495	2008	3415	624	747		

[a]Ref. 58; [b]ref. 59; [c]ref. 60.

further photolysis, and the structure of **7** was confirmed by comparison of its computed and experimental IR spectra.[65] In the second example, the carbene **9** and the strained allene **10**, which can be interconverted by irradiation at 302 nm, were identified by the comparison of their experimental and computed IR spectra.[66] The computed IR spectra were particularly helpful in identifying the stereochemistry of **9**.
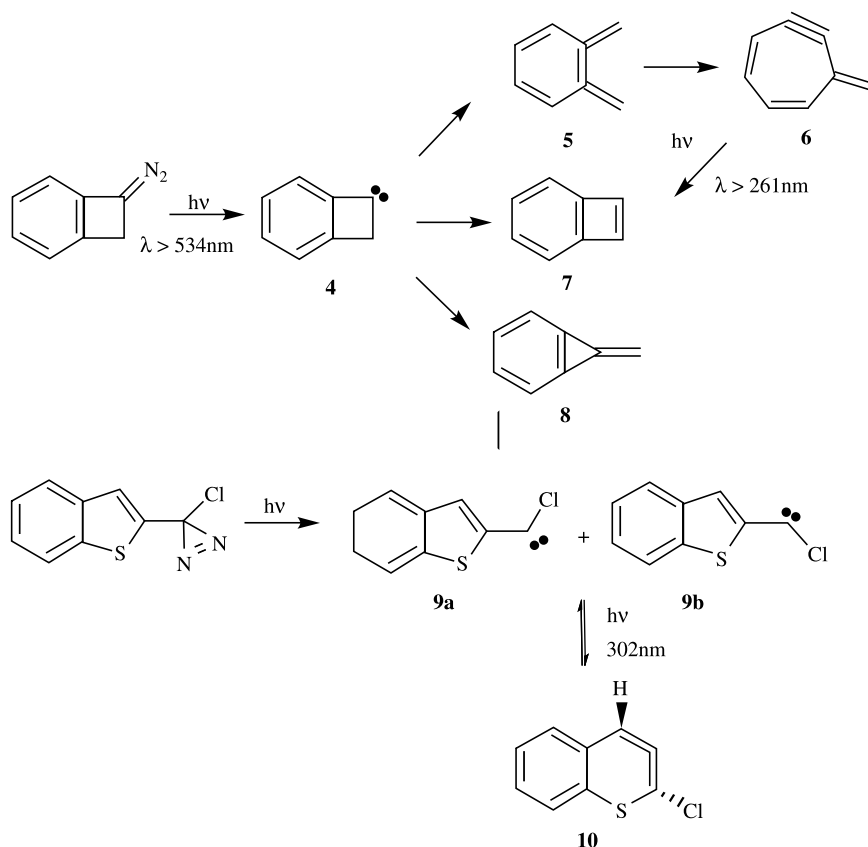
1.6.2 Nuclear Magnetic Resonance

Nuclear magnetic resonance (NMR) spectroscopy involves the energy required to flip a nuclear spin in the presence of a magnetic field. Computation of this effect requires, among other terms, derivatives of the kinetic energy of the electrons. This necessitates a definition of the origin of the coordinate system, called the "gauge origin." The magnetic properties are independent of the gauge origin, but this is only true when an exact wavefunction is utilized. Because this is not a practical option, a choice of gauge origin is necessary. The two commonly used methods are the *individual gauge for localized orbitals* (IGLO)[67] and *gauge-including atomic orbitals* (GIAO).[68,69] Although there are differences in these two methods, implementations of these methods in current computer programs are particularly robust and both methods can provide good results.

To assess the performance of computed NMR properties, particularly chemical shifts, we will focus on three recent studies. Rablen[70] examined the proton NMR shifts of 80 organic molecules using three different DFT functionals and three different basis sets. Although the correlation between the experimental and computed

chemical shifts was quite reasonable with all the methods, there were systematic differences. In analogy with the scaling of vibrational frequencies, Rablen suggested two computational models that involve linear scaling of the computed chemical shifts: a high-level model based on the computed shift at GIAO/B3LYP/ 6-311++G(2df,p)//B3LYP/6-31+G(d) and a more economical model based on the computed shift at GIAO/B3LYP/6-311++G(d,p)//B3LYP/6-31+G(d). The root mean square error (RMSE) is less than 0.15 ppm for both models.
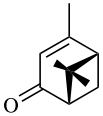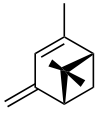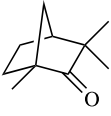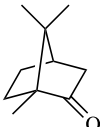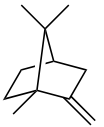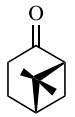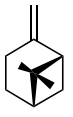
Suggesting that the relatively high error found in Rablen's study comes from the broad range of chemical structures used in the test sample, Pulay examined two separate sets of closely related molecules: a set of 14 aromatic molecules[71] and a set of eight cyclic amide[72] molecules. Again using a linear scaling procedure, the predicted B3LYP/6-311+G(d,p) proton chemical shifts have an RMSE of only 0.04 ppm for the aromatic test suite. This same computational level did well for the amides (RMSE = 0.10 ppm), but the best agreement with the experimental values in D_2O is with the HF/6-311G(d,p) values (RMSE = 0.08 ppm).

The magnetic effect of the electron distribution can be evaluated at any point, not just at nuclei, where this effect is the chemical shift. The chemical shift, evaluated at some arbitrary non-nuclear point, is called "nucleus-independent chemical shift" (NICS).[73] Its major application is in the area of aromaticity, where Schleyer has advocated its evaluation near the center of a ring as a measure of relative aromaticity. NICS will be discussed more fully in Section 2.4.

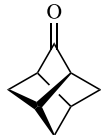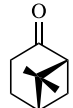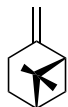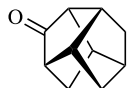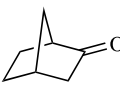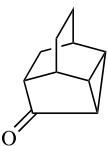### 1.6.3 Optical Rotation and Optical Rotatory Dispersion

Optical rotation and ORD provide spectral information unique to enantiomers, allowing for the determination of absolute configuration. Recent theoretical developments in DFT provide the means for computing both optical rotation and ORD.[74,75] Although HF fails to adequately predict optical rotation, a study of eight related alkenes and ketones at the B3LYP/6-31G* level demonstrated excellent agreement between the calculated and experimental optical rotation (reported as $[\alpha]_D$, with units understood throughout this discussion as $deg \cdot [dm \cdot g/cm^3]^{-1}$, see Table 1.4) and the ORD spectra.[76] A subsequent, more comprehensive study on a set of 65 molecules (including alkanes, alkenes, ketones, cyclic ethers, and amines) was carried out by Frisch.[77] Overall, the agreement between the experimental $[\alpha]_D$ values and those computed at B3LYP/aug-cc-pVDZ//B3LYP/6-31G* is reasonable; the RMS deviation for the entire set is 28.9. An RMS error this large, however, implies that molecules with small rotations might actually be computed with the wrong *sign*, the key feature needed to discriminate the absolute configuration of enantiomers. In fact, Frisch identified eight molecules in his test set where the computed $[\alpha]_D$ is of the wrong sign (Table 1.5). Frisch concludes, contrary to the authors of the earlier study, that determination of absolute configuration is not always "simple and reliable." Kongsted also warns that vibrational contributions to the optical rotation can be very important, especially for molecules that have conformational flexibility.[78] In this case, he advocates using the "effective geometry," the geometry that minimizes the electronic plus zero-point vibrational energy.

TABLE 1.4. Comparison of Experimental and Calculated Optical Rotation[a] for Ketones and Alkenes.[b]

	$[\alpha]_D$ (expt)	$[\alpha]_D$ (comp)		$[\alpha]_D$ (expt)	$[\alpha]_D$ (comp)
	−180	−251		−40	−121
	−44	−85		−68	−99
	+59	+23		−36	−50
	+7	+13		−15	+27

[a]$[\alpha]_D$ in deg · [dm · g/cm^3]$^{-1}$; [b]computed at B3LYP/6-31G* (ref. 76).

TABLE 1.5. Compounds for Which Calculated Optical Rotation[a] Disagrees in Sign with the Experimental Value.[b]

	$[\alpha]_D$ (expt)	$[\alpha]_D$ (comp)		$[\alpha]_D$ (expt)	$[\alpha]_D$ (comp)
	−15.9	3.6		−78.4	13.1
	6.6	−11.3		39.9	−11.0
	23.1	−26.1		14.4	−9.2
	29.8	−10.1		−59.9	20.0

[a]$[\alpha]_D$ in deg · [dm · g/cm^3]$^{-1}$; [b]computed at B3LYP/aug-cc-pVDZ//B3LYP/6-31G* (ref. 77).

We finish this section with a case study where computed spectra[79] enabled complete characterization of the product of the Bayer–Villiger oxidation of **11**, which can, in principle, produce four products (**12**–**15**) (Scheme 1.1). A single product was isolated and, based on proton NMR, it was initially identified as **12**. Its optical rotation is positive: $[\alpha]_{546}$(expt) = 16.5. However, the computed (B3LYP/aug-cc-pVDZ//B3LYP/6-31G*) optical rotation of **12** is negative: $[\alpha]_{546}$(comp) = −52.6. Because **13** might have been the expected product based on the migratory propensity of the tertiary carbon over a secondary carbon, a computational reinvestigation of the reaction might resolve the confusion.

The strongest IR frequencies, both experimental and computational, for the four potential products are listed in Table 1.6. The best match with the experimental spectrum is that of **12**. In particular, the most intense absorption at 1170 cm^{-1} and the two strong absorptions at 1080 and 1068 cm^{-1} are well reproduced by the computed spectrum for **12**. All of the major spectral features of the experimental vibrational circular dichroism spectrum are extremely well reproduced by the computed spectrum for **12**, with substantial disagreements with the other isomers. These results firmly establish the product of the Bayer–Villiger oxidation of **11** is **12**, and provide a warning concerning the reliability of computed optical activity.
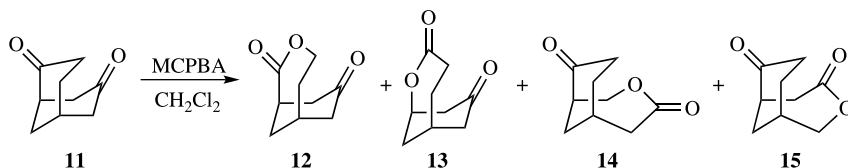
Scheme 1.1.

TABLE 1.6. Experimental and Computed Vibrational Frequencies (cm^{-1}) and Dipole Strengths of 12–15.^{a}

Expt.	12	13	14	15
1407 (79.0)	1445 (48.4)	1428 (98.8)		
1305 (153.7)	1332 (171.8)		1354 (79.2)	
1285 (91.2)	1313 (55.4)		1274 (127.1)	
		1259 (191.7)		1263 (170.7)
		1197 (216.9)		1253 (145.2)
1170 (452.6)	1189 (409.1)	1154 (446.6)	1190 (365.2)	1194 (174.5)
1090 (14.3)	1103 (181.0)	114 (153.3)	1176 (171.4)	1176 (207.7)
1080 (139.7)	1093 (21.3)		1099 (116.1)	1107 (167.2)
1068 (303.0)	1090 (122.5)	1063 (168.8)	1068 (105.7)	1067 (162.3)
984 (85.3)	999 (92.1)		852 (72.5)	

^{a}Computed at B3PW91/TZ2P, frequencies are unscaled, and dipole strengths (in parentheses) in units of 10^{-40} esu^2 cm^2 (ref. 79).

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