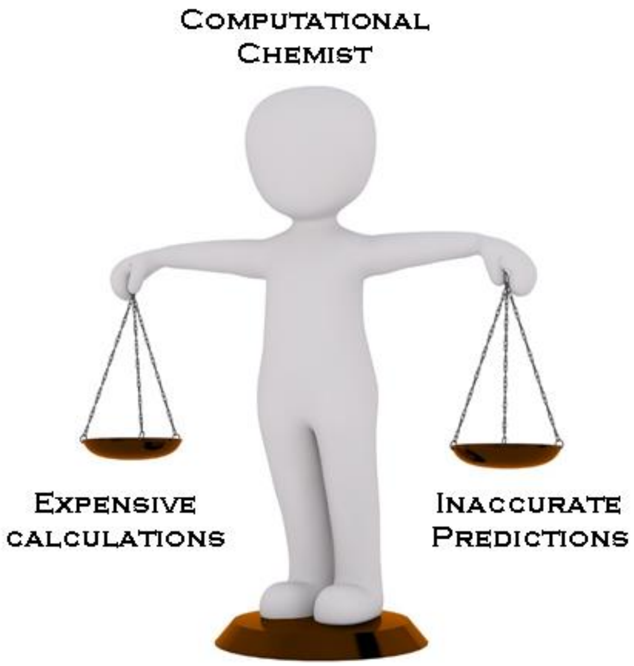
Chapter 2: Overview of the computational methods



"To err is human- to blame it on a computer is even more"

-Gaussian 09

2.1 Introduction

The motion of macro objects and planetary motion were satisfactorily explained by the development of classical mechanics in the seventeenth century. However, the classical theories were eventually refuted by the experimental evidence such as photoelectric effect, discrete spectra of atoms etc. as classical mechanics were unable to account for particles as tiny as electrons. Quantum mechanics (QM) introduced the concept of matter having both wave-like and particle-like properties. An era of computational studies began when several techniques based on the fundamental Schrödinger equation were developed in an effort to translate quantum mechanics in order to understand the properties of nanomaterials. The importance of computational theory lies in its capacity to ascertain the geometric configurations associated with stable molecules, as well as their attributes like energy, dipole moment, polarizability, thermochemical properties etc. The study of expensive systems and their properties that would normally be difficult for researchers are made easier by computational methods. Moreover, having a prior understanding of chemical reactions is beneficial to experimentalists which can be achieved through a variety of computational techniques as it aids in computing of complex reactions. Molecular dynamics, Monte Carlo, quantum mechanics, semiempirical methods, and molecular mechanics are all examples of numerical techniques that fall within the category of computational methods. These tools are used to gather data on reactivity, surface, and chemical reactions as well as qualitative and quantitative evidence on the characteristics of matter, including electronic, magnetic, optical, and structural properties [1].

The sections that follow will provide a quick overview of the computational tools and concepts used to characterize the electronic, structural and other aspects investigated in this thesis.

2.1.1 Potential Energy Surface (PES)

The potential energy surface (PES) is a key concept in computational chemistry. PES is the graphical connection between a molecule's energy and geometry [2]. It aids in locating and characterizing the structure of interest. A di-atomic molecule A-B, for example, has a single parameter that can alter its geometry: the bond length. This leads to a one-dimensional PES called 1D-PES. Likewise, if the molecule's energy depends on the bond lengths and angles, 2D-PES is generated. Another essential feature on the potential energy surface is the stationary point. It is identified as the point on the PES where the surface is parallel to the horizontal line (or plane) that corresponds to the geometrical parameter(s). For instance, the isomerization process occurs via a transition state in the isomerization of ozone to isoozone, as seen in Figure 2.1. Hence, the ozone and isoozone along with the transition state are referred to as stationary points on the potential energy surface.

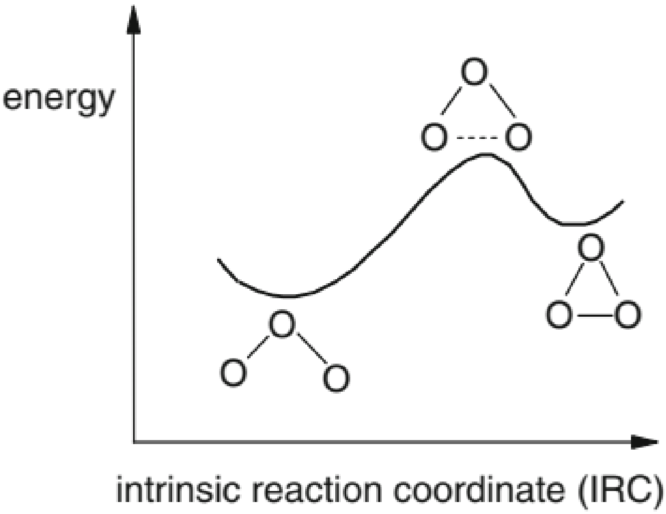


Figure 2.1: Points on potential energy surface diagram for the isomerization of ozone to isoozone.

In mathematical terms, a stationary point is represented by the first derivative of energy with respect to each geometric parameter, which is always equal to zero.

$$\frac{\partial E}{\partial q_1} = \frac{\partial E}{\partial q_2} = ... = \frac{\partial E}{\partial q_i} ... = 0$$

Minima and saddle points are two different kinds of stationary positions on the potential energy surface. A saddle point is a maximum along the reaction coordinate and a minimum along all other directions, while a minimum is a minimum along all directions. On the PES, some minima are called local minima, while the lowest energy minima are called global minima [2]. The transition state that joins two minima in the reaction coordinate is known as the first order saddle point. By using their second derivatives, they can be mathematically differentiated:

For a minimum,

$$\frac{\partial^2 E}{\partial q^2} > 0 \qquad \text{for all q.}$$

For a transition state,

$$\frac{\partial^2 E}{\partial q^2} > 0 \qquad \text{for all q, except along the reaction coordinate,}$$

$$\frac{\partial^2 E}{\partial q^2} < 0 \qquad \text{for all q, along the reaction coordinate.}$$

The fact that the second derivative of energy with respect to a single geometric coordinate is negative is a crucial feature of a first-order saddle point. Higher-order saddle points, often known as hilltops, are the places on PES where the second derivative of energy is negative with respect to several coordinates.

A PES, often referred to as a Born-Oppenheimer surface is a representation of molecular energy as a function of molecular geometry. The Born-Oppenheimer approximation is the first level of approximation in molecular quantum mechanics. It states that the position of nuclei in a molecule are stationary with respect to the electrons. This allowed the electronic part and nuclear part in a Schrodinger equation to be treated separately. Moreover, it tells us that energy (and other properties) of a molecule depends on electronic coordinates while depending parametrically on the nuclear coordinates. In essence, this approximation establishes that a molecule has a geometry adapting to its nuclear coordinates.

2.2 Computational Chemistry Tools

Molecular mechanics, ab initio methods, semiempirical methods, density functional theory, and molecular dynamics are the five categories into which computational chemistry tools fall. The following subsections provide a brief description of the tools utilized to finish the work included in this thesis.

2.2.1 Molecular Mechanics (MM)

The foundation for classical mechanics was established by Sir Isaac Newton's discovery of the laws of motion in the late seventeenth century, which also made it possible to comprehend the characteristics and actions of macroscopic objects [3]. Molecular mechanics (MM) is governed by the same theory as classical mechanics [4]. The "ball and spring" model, a mathematical representation of a molecule that views atoms and bonds as a group of balls joined by springs, is used to express MM. Bond stretching, angle bending, dihedral angles, and nonbonded interactions are some of the variables that can be used to determine a molecule's potential energy. These are referred to as force field methods because the mathematical formula and the parameters that constitute it, define a force field for the molecule's energy. Its accuracy is relied upon the kind of forcefield employed to describe the molecule and the dependability of the parameters in the application. Although MM does not specifically address electrons, it does account for their effects via parametrizing the forcefield. The potential energy of the molecule is expressed mathematically as-

$$E = E_{stretch} + E_{bend} + E_{torsion} + E_{vdw} + E_{HB} + E_{electro}$$

where, E_{stretch} = energy term for bond stretching; E_{bend}= energy term for bond angle bonding; E_{torsion} = energy term for dihedral angle rotation; E_{vdW} = energy term for van der Waals energy; E_{HB} = energy term for hydrogen bonding and E_{el} = electrostatic interactions between atoms or groups which are nonbonded.

2.2.1.1 Strength and weakness of MM theory

A typical use of MM is to generate appropriate geometry to be used as input for other computations methods. These calculations can be performed efficiently and with high accuracy provided that the forcefield has been carefully defined for each type of molecule under study. MM uses minimal processing resources and is both fast and precise. MM can provide good starting geometries for *ab initio* and density functional theory. The drug design process in the pharmaceutical business is one of the most important applications of MM. One such application of MM is the examination of putative drug candidates' that fit into biomolecule active sites.

However, this theory has some flaws, the biggest one being that it ignores electrons. Hence, it cannot throw light on the electronic properties of the molecule. One limited benefit of employing MM is the ability to calculate the energy and geometries of transition states. Care must be given with regard to the acceptance of MM parameters. Stationary points from MM might not be global minima, even if they are relative minima. Furthermore, results for polar compounds may be inaccurate if the solvent effects are ignored.

2.2.2 Molecular Dynamics (MD)

Molecular Dynamics (MD) is a computational method which analyzes the physical movements of atoms and molecules that is averaged over time and elaborates on N-body simulation [5, 6]. Proteins and nucleic acids at a specific point in time can be captured in static images by standard experimental methods such as X-ray crystallography and NMR. They can't, however, generate the dynamic information that MD can provide on motions that take place in real time [7]. MD is theoretically governed by the same classical Newton's second law of motion, F = ma, which represents the force applied independently to each atom, mass, and acceleration [3]. The atoms and molecules are allowed to interact for a predefined period of time, giving information about the dynamic evolution of the system. In essence, atomic coordinates and velocities flowing through time are used to build a trajectory, and MD is able to calculate the positions of the atoms with regard to time. The forces are calculated using the negative gradient of potential energy, which can be expressed as:

$$m_i \frac{d^2 r_i(t)}{dt^2} = F_i$$

Here, m_i is the mass, $r_i(t)$ is the position vector for the ith particle, and F_i symbolizes the force acting on it [8].

The structure, motion, thermodynamics, fluctuations, and structural modifications of proteins, nucleic acids, and their complexes can all be thoroughly examined using MD simulations. It is particularly helpful for examining the dynamic characteristics of atomic-level molecular systems.

2.2.3 *Ab-initio* Methods

Ab initio method is a significant approach which is based on the fundamental Schrödinger equation. The molecule's wavefunction and energy can be obtained by solving the fundamental equation. A number of parameters that are directly related to electron distribution can be easily calculated using this theory, including molecular geometries, energies, vibrational frequencies, spectra (IR, UV, and NMR), ionization potentials, and electron affinities [9]. It is known as *ab initio* [4], which refers to "from the beginning," since it is a quantum mechanical method that does not depend on calibration against observed chemical parameters. The *ab initio* methods are Hartree-Fock (HF) theory, Møller-Plesset Perturbation Theory (MPPT), configuration interaction (CI), couple-cluster (CC) method and density functional theory (DFT).

2.2.3.1 Hartree-Fock Method

In the *ab initio* method, the Hartree-Fock (HF) method is the most straightforward approach. In HF theory, the instantaneous mobility of other electrons is disregarded and only one electron wavefunction is taken into account to describe electronic motion. The self-consistent field (SCF) approach is another name for the HF theory which was developed by Douglas Hartree (1928) and V. A. Fock (1930) [10]. Solving the electronic Schrödinger equation yields the system's electronic energy, which is the main concept of HF theory. The entire molecular wavefunction ψ is roughly represented by the Hartree-Fock method as a Slater determinant composed up of occupied spin orbitals. A spin function is multiplied by a standard spatial orbital ψ to create each spin orbital. The time independent Schrödinger equation is expressed as:

$$\hat{H}\psi_i(\vec{\chi}_1, \vec{\chi}_2, \dots \dots, \vec{\chi}_N, \vec{R}_1, \vec{R}_2, \dots \dots .., \vec{R}_M) = E_1\psi_i(\vec{\chi}_1, \vec{\chi}_2, \dots \dots, \vec{\chi}_N, \vec{R}_1, \vec{R}_2, \dots \dots .., \vec{R}_M)$$

where, $\hat{H}$ represents the Hamiltonian operator of a molecular system having M nuclei and N electrons. E_1 is the energy Eigen value.

The Born-Oppenheimer approximation can be used to determine the wave function of electrons going through the potential field of highly charged stable nuclei. The Born-Oppenheimer approximation is based on the assumption that nuclear and electronic movement in structures can be distinguished from each other, yielding a molecular wave characterized by nuclear and electron locations.

Consequently, the electronic Hamiltonian is given as

$$\widehat{H}_{elec}=-\frac{1}{2}\sum_{i=1}^{N}\nabla_i^2-\sum_{i=1}^{N}\sum_{A=1}^{M}\frac{Z_A}{r_{iA}}+\sum_{i=1}^{N}\sum_{j>1}^{M}\frac{1}{r_{ij}}$$

The equation's first term reflects the electron's kinetic energy; the second term represents the attractive potential between electron i and nucleus A, which are separated by a distance r; and the last term indicates inter-electronic repulsion. The nuclear component is included separately to determine the total energy of the system, hence it is excluded in the above calculation.

Quantum mechanics governs the behavior of electrons and nuclei at the microscopic level, which can be used to explain the chemistry of any system. However, the challenge is to accurately define the chemistry of all systems using quantum mechanical treatment of electrons and nuclei. The main challenge is that several particles interact with one other simultaneously. The many-body issue applies to all interacting systems, not just quantum mechanics, including electrical, liquid, and planetary systems [11]. For such systems, approximate rather than exact solutions to their respective equations of motion must be pursued. The many-electron wave function in HF theory is represented by a single Slater determinant. Rather than being a straightforward combination of two orbitals, the ground state wave function is a complex function of both the variables, and the energy determined by applying the variational principle is always higher than the true energy.

The correlation energy, denoted by:

$$E_{cor} = E_0 - E_{HF}$$

is the difference between the exact ground state energy E_0 and the HF energy E_{HF}. The correlated movement of electrons under the influence of nearby electrons, which attempts to decrease inter-electronic repulsion, is the source of the term "electron correlation." The precision of the molecular orbitals increases as the number of basis functions increases. Similar outcomes to those of numerical HF approaches could be reached in the limit of an infinitely large basis set. One determinant wave function, or HF limit, yields the optimal solution to the Schrödinger equation. However, this limit could never be achieved in reality.

Electron correlation is better handled by post-HF techniques such as the Møller-Plesset (MP), configuration interaction (CI), and coupled cluster (CC) systems.

2.2.4 Semi-empirical Method

Semi-empirical approaches were developed to circumvent the enormous computing expense of employing ab-initio simulations to attain precision in relatively large molecular systems. Semi-empirical techniques use parameters taken from experimental data to make simulations easier to comprehend. The term "semi-empirical" refers to the fact that the approach is built utilizing both theory and experimental ("empirical") data [12-14]. By diagonalizing the Fock matrix, the method improves the molecular energy and wave function and is the intermediate of molecular mechanics and *ab-initio* approaches. When employed with appropriate parameters, the method's accuracy in determining the energy and structure of the chemical system produces findings that are fairly realistic. But unless the results are compared to the experimental data collection or the high-level *ab-initio* calculations, the results acquired from this method are not reliable.

Semiempirical methods employ three approximations: a) removing core electrons from the calculations; b) employing the fewest possible basis sets; and c) utilizing fewer two-electron integrals.

The semiempirical technique encompasses a number of processes, including Complete Neglect of Differential Overlap (CNDO), Pariser-Parr-Pople (PPP), Neglect of Diatomic Differential Overlap (NDDO), and Intermediate Neglect of Differential Overlap (INDO). All four of these methods, which rely on the Zero Differential Overlap (ZDO) approximation, have the differential of overlap integral set to zero.

2.2.5 Density Functional Theory (DFT)

Among the quantum chemical techniques, density functional theory has emerged as the most widely used and popular approach. Hohenberg and Kohn established this method in the middle of the 1960s, and Kohn and Sham went on to further develop it [15, 16]. The foundation for DFT's current application in computational chemistry was established in 1965 by Kohn and Sham [17]. Walter Kohn and John A. Pople both earned a share of the 1998 Nobel Prize in Chemistry for their contributions to density functional theory and the useful wavefunction-based approach, respectively.

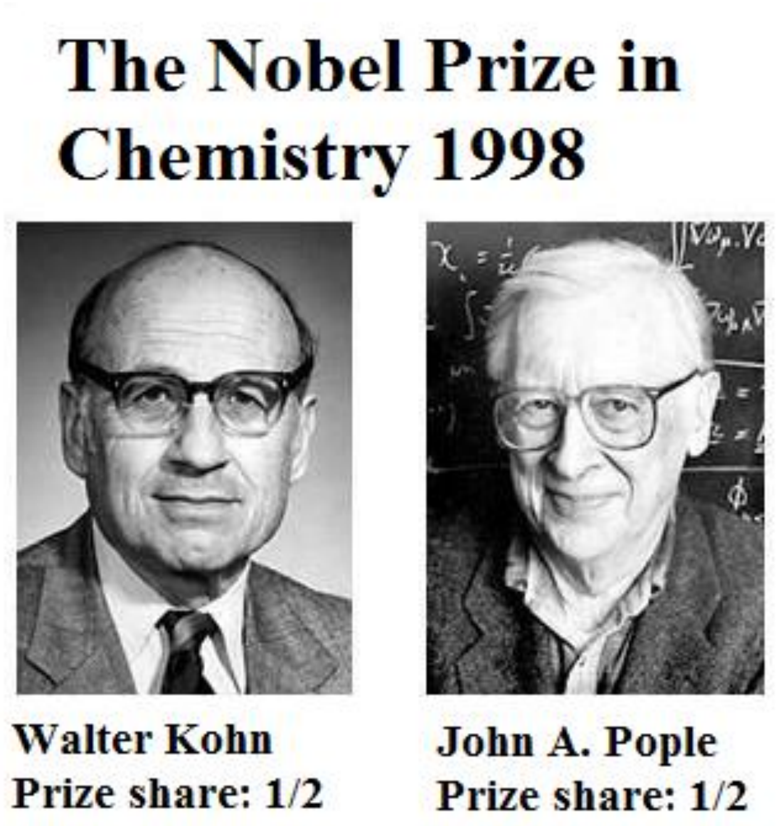


Figure 2.2: Walter Kohn and John A. Pople received Nobel Prize in chemistry in 1998.*(Picturesource:http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1998/)*

Unlike the *ab initio* method, which is based on the wavefunction, density functional theory (DFT) developed its strength in handling numerical approaches employing electron density, which is a physically observable quantity that can be determined by X-ray diffraction or electron diffraction. An *n*-electron molecule's wavefunction is determined by 4*n* variables, with 3 spatial coordinates and 1 spin coordinate for each electron. Whereas electron density is a function of the three variables (x, y, and z) that determine position [4]. In the case of the *ab initio* method, the number of electrons increases as the molecule gets bigger, which immediately raises the system's complexity. However, the unique feature of DFT's dependence just on position makes it a relatively uncomplicated method.

Hohenberg and Kohn's two theorem served as the foundation for DFT. According to the first theorem, a molecule's ground state properties is functional of its ground state electron density function [15].

Energy can be written as

$$E = [\rho_0] = E[\rho_0]$$

The first theorem is important because it assures that the electron density can be used to determine the properties of molecules.

According to the second Hohenberg and Kohn theorem, any trial electron density function will yield an energy greater than or equal to the true ground state energy. It can be expressed as

$$[\rho_t] \geq E_0\,[\rho_0]$$

where $E_0\,[\rho_0]$ is the actual ground state energy, which corresponds to the true electronic densityρ_0 and ρ_t is a trial electronic density.

Here, the trial electron density function must satisfy the following criteria

$$\int \rho_t(r)dr = n$$

where n represents the number of electrons in the molecule and $\rho_t(r) \geq 0$ for all r.

2.2.5.1 The Kohn-Sham Formalism

DFT calculations can be performed simply in terms of single particle orbitals within the Kohn-Sham formalism, which states that the ground state energy of a non-degenerate electronic system and the corresponding electronic properties are uniquely defined by the electron density, for a set of interacting electrons [18]. The fundamental idea behind the Kohn-Sham approach is that the energy functional of a system may be split into two parts: an exact portion that treats electrons as non-interacting particles and a small correction term that accounts for the electron-electron interaction. The electronic energy is given by

$$E[\rho(r)] = T_{ni}[\rho(r)] + V_{ne}[\rho(r)] + V_{ee}[\rho(r)] + \Delta T[\rho(r)] + \Delta V_{ee}[\rho(r)]$$

where, $T_{ni}[\rho(r)] =$ Kinetic energy of non-interacting electrons, $V_{ne}[\rho(r)] =$ Nuclear-electron interaction, $V_{ee}[\rho(r) =$ Electron-electron repulsion, $\Delta T[\rho(r)] =$ Correction to the kinetic energy derived from the electron-electron interaction, $\Delta V_{ee}[\rho(r)] =$ Non-classical correction to the electron-electron repulsion energy.

The equation above can be written as follows:

$$E[\rho(r)] = -\frac{1}{2}\sum_{i=1}^{n}\int \psi_i^*(r_1)\nabla_i^2\psi_i(r_1)dr_1 - \sum_{x=1}^{N}\int \frac{Z_x}{r_{X_i}}\rho(r_1)dr_1 + \frac{1}{2}\iint \frac{\rho(r_1)\rho(r_2)}{r_{12}}dr_1 dr_2 + E^{XC}[\rho]$$

where, n is the number of electrons and N is the number of nuclei. The exchange-correlation term, $E^{XC}[\rho]$ is given as:

$$E^{XC}[\rho] = \Delta T[\rho(r)] + \Delta V_{ee}[\rho(r)]$$

Additionally, the set of one electron orbitals that represent the ground state electron density is provided by

$$\rho(r) = \sum_{i=1}^{n} |\psi_i(r)|^2$$

The only variable that is not known in the DFT energy expression is the exchange-correlation functional, which is present in the comparatively tiny energy differential between the ideal and real systems. Estimating this functional is the primary challenge for DFT.

2.2.5.2 Density Functional Approximations

Calculations of the density functional are significantly affected by the approximation to the exchange-correlation functional. Over the years, many approximations have emerged as a result. Here are a few approximations in order of improvement: local density approximations (LDA), generalized gradient approximations (GGA) [19], meta-generalized gradient approximations (meta-GGA)[20] and hybrid functional.

Local density approximations (LDA): Based on a homogenous electron gas, this LDA approximation offers the most straightforward approximation currently available. The exchange-correlation functional in the context of LDA is expressed solely in terms of electron density and not in terms of density derivatives or KS orbitals. The exchange correlation function $E_{xc}\rho(\vec{r})$is given as $E_{XC}^{LDA}[\rho]=\int\rho(\vec{r})\varepsilon_{XC}[\rho(\vec{r})]d\vec{r}$ where $\varepsilon_{XC}[\rho(\vec{r})]$is the exchange-correlation energy per particle of a homogeneous electron gas of density$\rho(\vec{r})$. The exchange correlation energy has two parts: $\varepsilon_{xc}[\rho(\vec{r})]=\varepsilon_{xc}[\rho(\vec{r})]+\varepsilon_{x}[\rho(\vec{r})]$. The electron exchange energy in an electron gas is represented by the first term, while the correlation energy resulting from the instantaneous movement of electrons that causes them to approach and repel each other is described by the second term. However, the system's assumed homogenous electron gas leads to a somewhat inaccurately computed energy in the LDA functional. The use of gradient corrected ("nonlocal") functionals has essentially superseded LDA methods.

Generalized gradient approximation (GGA) and Meta-generalized gradient approximations (meta-GGA): It has been found that the ground state energy of a molecular system cannot be computed using the robust homogeneous electron gas assumption used in LDA. In order to improve the exchange-correlation energy, GGA functionals were designed which accounts for both the electro density and the gradient of the electron density. The E_{XC}^{GGA} consists of two parts exchange and correlation $E_{XC}{}^{GGA} = E_{X}{}^{GGA} + E_{C}{}^{GGA}$ In addition, numerous correlation functionals have been developed, the most well-known of which being the LYP functional created by Lee, Yang, and Parr. Perdew 1986 (P86) and Perdew-Wang correlation functional (PW91) are some of the other known functionals.

Meta-GGA approximation incorporates semi-local information in addition to the first-order density gradient utilized in GGA. Consequently, the semi-local functional of meta-GGA is explicitly dependent on either the local kinetic energy or the Laplacian of the spin density. Meta-GGA functional examples include TPSS, M06-L, B95, B98 etc.

Hybrid Functionals: The approximation has undergone additional functional improvement to improve the accuracy of the exchange-correlation energy. A percentage of Hartree-Fock exchange is added to the hybrid functional using the correlation functional, and the energy is shown as $E_{xc} = E_{x}^{HF} + E_{xc}^{DFT}$. The energy of the well-known hybrid functional B3LYP is provided by $E_{xc}^{B3LYP} = (1-a)E_{x}^{LDA} +$

$aE_x^{HF} + bE_x^{B88} + cE_c^{LYP}$ where a, b, and c are values derived from computed data for the proton affinities, ionization potentials, and atomization energies of second and third period elements as well as from fitting experimental data. B3LYP, B3P86, B3PW91 and wB97XD are some examples of popular hybrid functionals.

2.2.5.3 Basis Set

A set of mathematical functions that describe the distribution of electrons around an atom is called a basis set. The total electron distribution of a molecule is represented by the sum of these functions [21]. Therefore, the linear combination of atomic orbitals (LCAO) technique is used to approximate molecular orbitals. Slater Type Orbitals (STOs) and Gaussian Type Orbitals (GTOs) are the two categories into which the basis sets are separated [22–23]. STOs give a somewhat accurate description of atomic wave functions and are shown to be exact solutions to the hydrogen atom problem. Semi-empirical methods that negate all three- and four-centered integrals also use this orbital. Density functional techniques, which do not necessitate an exact exchange term, also employ STOs. However, due to the computing cost of STOs, Gaussian type orbitals (GTO) are an alternative. The radial-dependent linear combination of Primitive Gaussian functions forms GTOs, which are frequently used basis functions. Basis functions come in several forms, such as minimal basis sets, split valence basis sets, effective core potentials, diffuse functions, polarization functions and numerical basis sets.

In quantum chemistry, molecular wavefunctions are often described using localized basis sets where Slater or Gaussian type orbitals are centered on each individual atoms. However, when atoms interact with each other, their basis function overlap, which leads to the overestimation of interaction energies, thus stabilizing the interacting system more than the actual value. This is called basis set superposition error (BSSE). BSSE has significant impact on the accuracy of calculated parameters such as binding energies etc. BSSE can be corrected using the counterpoise method where each monomer energy is recalculated in the presence of the neighboring atom basis function (ghost orbitals) so that monomer and dimer energies can be compared on equal basis.

DFT is quite versatile and can be used in a wide range of scientific fields. When researching the electronic structure of solids, semiconductors, and insulators, it is especially helpful. This aids in the understanding and prediction of characteristics such as magnetic, electrical, and crystal band structures. DFT is helpful in the study of catalysis because it clarifies the mechanics behind the chemical reactions that occur on catalyst surfaces. This is essential for creating catalysts for industrial processes that are more effective. Due to its ability to shed light on the electrical structure and characteristics of medicinal molecules, DFT is also useful in computational drug design. All things considered, density functional theory is a potent instrument that cuts across many scientific fields, advancing our knowledge of the basic characteristics of matter and directing the creation of novel materials and technological advancements.

2.2.6 The QM/MM ONIOM method

The ONIOM (Our N- layered Integrated Molecular Orbital and Molecular Mechanics) is a multilayer computational approach which is basically used for molecules that are too big to treat only by Quantum Mechanics (QM). The method was developed by Keiji Morokuma and his coworkers in mid 1990s [24]. The system is divided into QM region and MM region. QM region consists of active sites where bond breaking/forming takes place. MM region is the rest of the system that gets treated with molecular mechanics using force field. Generally, ONIOM energy scheme consists of two options: additive scheme or subtractive scheme.

In additive scheme, the system is divided into different layers where each layer is computed separately.

$$E_{ONIOM(QM:MM)} = E_{QM} + E_{MM} + E_{QM-MM}$$

However, this method is computationally less effective. Subtractive scheme is the more popular scheme due to its efficient and accurate expression and is extensively used in Gaussian 09. In subtractive scheme, the total energy of the whole (real) system is given by QM energy of the model system plus MM energy of the real system minus MM energy of model system.

$$E_{ONIOM(QM:MM)} = E_{QM,model} + E_{MM,real} - E_{MM,model}$$

The subtractive action eliminates the "double counted" MM contributions. ONIOM has become a popular method for investigating heterogeneous catalysis as well as enzyme catalysis.

2.3. Transition state theory

Transition state theory, also known as Activated complex theory, is a theoretical model used to understand and calculate the rate of chemical reactions. It predicts that a chemical reaction proceed via high energy species called transition state (or activated complex) where bonds are broken/formed. The system has maximum energy along the reaction coordinate where transition state always results in product once the barrier is crossed. The reaction rate is determined by the concentration of transition state and its decomposition to product. According to TST, reactants and transition state are in quasi-equilibrium state which means that rate of formation of transition state and its decomposition into product is same. The rate constant is expressed via Eyring equation

$$k = \Gamma(T)\frac{k_B T}{h} e^{\left(\frac{-\Delta G^{TS}}{RT}\right)}$$

where $\Gamma(T)$ represents the transmission coefficient, which is obtained from the following expression:

$$\Gamma(T) = 1 + \frac{1}{24}\left(\frac{h\nu^{\#}}{k_B T}\right)^2$$

ΔG^{TS} is the difference of Gibbs free energy values for TS and reactants. TST provides a theoretical basis for the Arrhenius equation (which is empirical) which describes the temperature dependence of reaction rates.

Finding a transition state has always been a challenge in the computational field. Transition state search has been done using methods such as Berny algorithm [25] or the synchronous transit-guided quasi-Newton (STQN) method [26]. Berny algorithm is a geometry optimization method based on quadratic approximation which uses energies and gradients to iteratively adjust the geometry of a molecule to find a stationary point (minima or maxima). It can be used for finding a minima as well as transition state. The synchronous transit-guided quasi-Newton (STQN) method was developed by Schlegel and co-workers exclusively for finding transition state by combining guess reaction path (synchronous transit) and gradient based optimization (quasi-Newton). STQN has two variants in Gaussian, QST2 and QST3. QST2 requires structures of reactants and products, after which algorithm search for TS. QST3 requires structures of reactants, products and a guessed TS.

2.4. Software Packages utilized to perform the computational work

2.4.1 The Gaussian Package

Gaussian is a computing program that was initially released as Gaussian 70 in 1970 by research team led by John Pople [27]. The Gaussian algorithm, which is based on the fundamental ideas of quantum mechanics, makes predictions about geometries, vibrational frequencies, energies, and other characteristics of molecules that are difficult to observe in experiments, such as the kinetics of a chemical reaction, short-lived intermediates and transition structures etc. The software has been updated on a regular basis to address bugs and make it compatible with increasingly advanced computing facilities as time and research have progressed. Although Gaussian 09 is the most widely used version, Gaussian 16 is the most recent version used in quantum chemistry calculations. For the various DFT-related computations, we have utilized both Gaussian 09 and Gaussian 16 [28].

2.4.2 The Multiwfn Package

Quantum chemistry relies heavily on electronic wavefunction analysis, which can be achieved with the help of an effective tool known as Multiwfn [29]. Nearly all of the most significant wavefunction analysis techniques are supported by Multiwfn, which is free, open-source, very efficient, intuitive, and adaptable. Wavefunction studies can be carried out by Multiwfn using the output files from practically all popular quantum chemistry tools, such as Gaussian, ORCA, GAMESS-US, Molpro, NWChem etc. Tian Lu handles the Multiwfn software at the Beijing Kein Research Center for Natural Sciences. Multiwfn software is mainly used for orbital composition analysis.

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